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# PURIFICATION OF LABORATORY CHEMICALS FIFTH EDITION

Wilfred L.F. Armarego • Christina L.L. Chai



### PURIFICATION OF LABORATORY CHEMICALS

Fifth Edition

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### **Preface to the Fifth Edition**

THE DEMAND for **Purification of Laboratory Chemicals** has not abated since the publication of the fourth edition as evidenced by the number of printings and the sales. The request by the Editor for a fifth edition offered an opportunity to increase the usefulness of this book for laboratory purposes. It is with deep regret that mention should be made that Dr Douglas D. Perrin had passed away soon after the fourth edition was published. His input in the first three editions was considerable and his presence has been greatly missed. A fresh, new and young outlook was required in order to increase the utility of this book and it is with great pleasure that Dr Christina L.L. Chai, a Reader in Chemistry and leader of a research group in organic and bioorganic chemistry, has agreed to coauthor this edition. The new features of the fifth edition have been detailed below.

Chapters 1 and 2 have been reorganised and updated in line with recent developments. A new chapter on the 'Future of Purification' has been added. It outlines developments in syntheses on solid supports, combinatorial chemistry as well as the use of ionic liquids for chemical reactions and reactions in fluorous media. These technologies are becoming increasingly useful and popular so much so that many future commercially available substances will most probably be prepared using these procedures. Consequently, a knowledge of their basic principles will be helpful in many purification methods of the future.

Chapters 4, 5 and 6 (3, 4 and 5 in the 4th edn) form the bulk of the book. The number of entries has been increased to include the purification of many recent commercially available reagents that have become more and more popular in the syntheses of organic, inorganic and bio-organic compounds. Several purification procedures for commonly used liquids, e.g. solvents, had been entered with excessive thoroughness, but in many cases the laboratory worker only requires a simple, rapid but effective purification procedure for immediate use. In such cases a **Rapid purification** procedure has been inserted at the end of the respective entry, and should be satisfactory for most purposes. With the increased use of solid phase synthesis, even for small molecules, and the use of reagents on solid support (e.g. on polystyrene) for reactions in liquid media, compounds on solid support have become increasingly commercially available. These have been inserted at the end of the respective entry and have been listed in the General Index together with the above rapid purification entries.

A large number of substances are ionisable in aqueous solutions and a knowledge of their ionisation constants, stated as pK (pKa) values, can be of importance not only in their purification but also in their reactivity. Literature values of the pK's have been inserted for ionisable substances, and where values could not be found they were estimated ( $pK_{Est}$ ). The estimates are usually so close to the true values as not to affect the purification process or the reactivity seriously. The book will thus be a good compilation of pK values for ionisable substances.

Almost all the entries in Chapters 4, 5 and 6 have CAS (Chemical Abstract Service) Registry Numbers to identify them, and these have been entered for each substance. Unlike chemical names which may have more than one synonymous name, there is only one CAS Registry Number for each substance (with only a few exceptions, e.g. where a substance may have another number before purification, or before determination of absolute configuration). To simplify the method for locating the purification of a substance, a CAS Registry Number Index with the respective page numbers has been included after the General Index at the end of the book. This will also provide the reader with a rapid way to see if the purification of a particular substance has been reported in the book. The brief General Index includes page references to procedures and equipment, page references to abbreviations of compounds, e.g. TRIS, as well as the names of substances for which a Registry Number was not found.

Website references for distributors of substances or/and of equipment have been included in the text. However, since these may be changed in the future we must rely on the suppliers to inform users of their change in website references.

We wish to thank readers who have provided advice, constructive criticism and new information for inclusion in this book. We should be grateful to our readers for any further comments, suggestions, amendments and criticisms which could, perhaps, be inserted in a second printing of this edition. In particular, we thank Professor Ken-chi Sugiura (Graduate School of Science, Tokyo Metropolitan University, Japan) who has provided us with information on the purification of several organic compounds from his own experiences, and Joe Papa BS MS (EXAXOL in Clearwater, Florida, USA) who has provided us not only with his experiences in the purification of many inorganic substances in this book, but also gave us his analytical results on the amounts of other metal impurities at various stages of purification of several salts. We thank them graciously for permission to include their reports in this work. We express our gratitude to Dr William B. Cowden for his generous advice on computer hardware and software over many years and for providing an Apple LaserWriter (16/600PS) which we used to produce the master copy of this book. We also extend our sincere thanks to Dr Bart Eschler for advice on computer hardware and software and for assistance in setting up the computers (iMac and eMac) used to produce this book.

We thank Dr Pauline M. Armarego for assistance in the painstaking task of entering data into respective files, for many hours of proofreading, correcting typographical errors and checking CAS Registry Numbers against their respective entries.

One of us (W.L.F.A) owes a debt of gratitude to Dr Desmond (Des) J. Brown of the Research School of Chemistry, ANU, for unfailing support and advice over several decades and for providing data that was difficult to acquire not only for this edition but also for the previous four editions of this book.

One of us (C.L.L.C) would specially like to thank her many research students (past and present) for their unwavering support, friendship and loyalty, which enabled her to achieve what she now has. She wishes also to thank her family for their love, and would particularly like to dedicate her contribution towards this book to the memory of her brother Andrew who had said that he should have been a scientist.

We thank Mrs Joan Smith, librarian of the Research School of Chemistry, ANU, for her generous help in many library matters which have made the tedious task of checking references more enduring.

W.L.F. Armarego & C.L.L. Chai November 2002

### Preface to the First Edition

WE BELIEVE that a need exists for a book to help the chemist or biochemist who wishes to purify the reagents she or he uses. This need is emphasised by the previous lack of any satisfactory central source of references dealing with individual substances. Such a lack must undoubtedly have been a great deterrent to many busy research workers who have been left to decide whether to purify at all, to improvise possible methods, or to take a chance on finding, somewhere in the chemical literature, methods used by some previous investigators.

Although commercially available laboratory chemicals are usually satisfactory, as supplied, for most purposes in scientific and technological work, it is also true that for many applications further purification is essential.

With this thought in mind, the present volume sets out, firstly, to tabulate methods, taken from the literature, for purifying some thousands of individual commercially available chemicals. To help in applying this information, two chapters describe the more common processes currently used for purification in chemical laboratories and give fuller details of new methods which appear likely to find increasing application for the same purpose. Finally, for dealing with substances not separately listed, a chapter is included setting out the usual methods for purifying specific classes of compounds.

To keep this book to a convenient size, and bearing in mind that its most likely users will be laboratory-trained, we have omitted manipulative details with which they can be assumed to be familiar, and also detailed theoretical discussion. Both are readily available elsewhere, for example in Vogel's very useful book **Practical Organic Chemistry** (Longmans, London, 3rd ed., 1956), or Fieser's **Experiments in Organic Chemistry** (Heath, Boston, 3rd ed, 1957).

For the same reason, only limited mention is made of the kinds of impurities likely to be present, and of the tests for detecting them. In many cases, this information can be obtained readily from existing monographs.

By its nature, the present treatment is not exhaustive, nor do we claim that any of the methods taken from the literature are the best possible. Nevertheless, we feel that the information contained in this book is likely to be helpful to a wide range of laboratory workers, including physical and inorganic chemists, research students, biochemists, and biologists. We hope that it will also be of use, although perhaps to only a limited extent, to experienced organic chemists.

We are grateful to Professor A. Albert and Dr D.J. Brown for helpful comments on the manuscript.

D.D.P., W.L.F.A. & D.R.P. 1966

### **Preface to the Second Edition**

SINCE the publication of the first edition of this book there have been major advances in purification procedures. Sensitive methods have been developed for the detection and elimination of progressively lower levels of impurities. Increasingly stringent requirements for reagent purity have gone hand-in-hand with developments in semiconductor technology, in the preparation of special alloys and in the isolation of highly biologically active substances. The need to eliminate trace impurities at the micro- and nanogram levels has placed greater emphasis on ultrapurification technique. To meet these demands the range of purities of laboratory chemicals has become correspondingly extended. Purification of individual chemicals thus depends more and more critically on the answers to two questions - Purification from what, and to what permissible level of contamination. Where these questions can be specifically answered, suitable methods of purification can usually be devised.

Several periodicals devoted to ultrapurification and separations have been started. These include "Progress in Separation and Purification" Ed. (vol. 1) E.S. Perry, Wiley-Interscience, New York, vols. 1-4, 1968-1971, and **Separation and Purification Methods** Ed. E.S.Perry and C.J.van Oss, Marcel Dekker, New York, vol. 1-, 1973-. Nevertheless, there still remains a broad area in which a general improvement in the level of purity of many compounds can be achieved by applying more or less conventional procedures. The need for a convenient source of information on methods of purifying available laboratory chemicals was indicated by the continuing demand for copies of this book even though it had been out of print for several years.

We have sought to revise and update this volume, deleting sections that have become more familiar or less important, and incorporating more topical material. The number of compounds in Chapters 3 and 4 have been increased appreciably. Also, further details in purification and physical constants are given for many compounds that were listed in the first edition.

We take this opportunity to thank users of the first edition who pointed out errors and omissions, or otherwise suggested improvements or additional material that should be included. We are indebted to Mrs S.Schenk who emerged from retirement to type this manuscript.

D.D.P., W.L.F.A. & D.R.P. 1980

### **Preface to the Third Edition**

THE CONTINUING demand for this monograph and the publisher's request that we prepare a new edition, are an indication that **Purification of Laboratory Chemicals** fills a gap in many chemists' reference libraries and laboratory shelves. The present volume is an updated edition which contains significantly more detail than the previous editions, as well as an increase in the number of individual entries and a new chapter.

Additions have been made to Chapters 1 and 2 in order to include more recent developments in techniques (e.g. Schlenk-type, cf p. 10), and chromatographic methods and materials. Chapter 3 still remains the core of the book, and lists in alphabetical order relevant information on ca 4000 organic compounds. Chapter 4 gives a smaller listing of ca 750 inorganic and metal-organic substances, and makes a total increase of ca 13% of individual entries in these two chapters. Some additions have also been made to Chapter 5.

We are currently witnessing a major development in the use of physical methods for purifying large molecules and macromolecules, especially of biological origin. Considerable developments in molecular biology are apparent in techniques for the isolation and purification of key biochemicals and substances of high molecular weight. In many cases something approaching homogeneity has been achieved, as evidenced by electrophoresis, immunological and other independent criteria. We have consequently included a new section, Chapter 6, where we list upwards of 100 biological substances to illustrate their current methods of purification. In this chapter the details have been kept to a minimum, but the relevant references have been included.

The lists of individual entries in Chapters 3 and 4 range in length from single line entries to ca one page or more for solvents such as acetonitrile, benzene, ethanol and methanol. Some entries include information such as likely contaminants and storage conditions. More data referring to physical properties have been inserted for most entries [i.e. melting and boiling points, refractive indexes, densities, specific optical rotations (where applicable) and UV absorption data]. Inclusion of molecular weights should be useful when deciding on the quantities of reagents needed to carry out relevant synthetic reactions, or preparing analytical solutions. The Chemical Abstracts registry numbers have also been inserted for almost all entries, and should assist in the precise identification of the substances.

In the past ten years laboratory workers have become increasingly conscious of safety in the laboratory environment. We have therefore in three places in Chapter 1 (pp. 3 and 33, and bibliography p. 52) stressed more strongly the importance of safety in the laboratory. Also, where possible, in Chapters 3 and 4 we draw attention to the dangers involved with the manipulation of some hazardous substances.

The world wide facilities for retrieving chemical information provided by the Chemical Abstract Service (CAS on-line) have made it a relatively easy matter to obtain CAS registry numbers of substances, and most of the numbers in this monograph were obtained via CAS on-line. We should point out that two other available useful files are CSCHEM and CSCORP which provide, respectively, information on chemicals (and chemical products) and addresses and telephone numbers of the main branch offices of chemical suppliers.

The present edition has been produced on an IBM PC and a Laser Jet printer using the **Microsoft Word (4.0)** word-processing program with a set stylesheet. This has allowed the use of a variety of fonts and font sizes which has made the presentation more attractive than in the previous edition. Also, by altering the format and increasing slightly the sizes of the pages, the length of the monograph has been reduced from 568 to 391 pages. The reduction in the number of pages has been achieved in spite of the increase of ca 15% of total text.

We extend our gratitude to the readers whose suggestions have helped to improve the monograph, and to those who have told us of their experiences with some of the purifications stated in the previous editions, and in particular with the hazards that they have encountered. We are deeply indebted to Dr M.D. Fenn for the several hours that he has spent on the terminal to provide us with a large number of CAS registry numbers.

This monograph could not have been produced without the expert assistance of Mr David Clarke who has spent many hours to load the necessary fonts in the computer, and for advising one of the authors (W.L.F.A.) on how to use them together with the idiosyncrasies of Microsoft Word.

D.D.P. & W.L.F.A. 1988

### Preface to the Fourth Edition

THE AIMS of the first three editions, to provide purification procedures of commercially available chemicals and biochemicals from published literature data, are continued in this fourth edition. Since the third edition in 1988 the number of new chemicals and biochemicals which have been added to most chemical and biochemical catalogues have increased enormously. Accordingly there is a need to increase the number of entries with more recent useful reagents and chemical and biochemical intermediates. With this in mind, together with the need to reorganise and update general purification procedures, particularly in the area of biological macromolecules, as well as the time lapse since the previous publication, this fourth edition of **Purification of Laboratory Chemicals** has been produced. Chapter 1 has been reorganised with some updating, and by using a smaller font it was kept to a reasonable number of pages. Chapters 2 and 5 were similarly altered and have been combined into one chapter. Eight hundred and three hundred and fifty entries have been added to Chapter 5 (Chapter 6 in the Third Edition), making a total of 5700 entries; all resulting in an increase from 391 to 529 pages, i.e. by *ca* 35%.

Many references to the original literature have been included remembering that some of the best references happened to be in the older literature. Every effort has been made to provide the best references but this may not have been achieved in all cases. Standard abbreviations, listed on page 1, have been used throughout this edition to optimise space, except where no space advantage was achieved, in which cases the complete words have been written down to improve the flow of the sentences.

With the increasing facilities for information exchange, chemical, biochemical and equipment suppliers are making their catalogue information available on the Internet, e.g. Aldrich-Fluka-Sigma catalogue information is available on the World Wide Web by using the address http://www.sigma.sial.com, and GIBCO BRL catalogue information from http://www.lifetech.com, as well as on CD-ROMS which are regularly updated. Facility for enquiring about, ordering and paying for items is available *via* the Internet. CAS on-line can be accessed on the Internet, and CAS data is available now on CD-ROM. Also biosafety bill boards can similarly be obtained by sending SUBSCRIBE SAFETY John Doe at the address "listserv@uvmvm.uvm.edu", SUBSCRIBE BIOSAFETY at the address "listserv@mitvma.mit.edu", and SUBSCRIBE RADSAF at the address "listserv@romulus.ehs.uiuc.edu"; and the Occupational, Health and Safety information (Australia) is available at the address "http://www.worksafe.gov.au/~wsa1". Sigma-Aldrich provide Material Safety data sheets on CD-ROMs.

It is with much sadness that Dr Douglas D. Perrin was unable to participate in the preparation of the present edition due to illness. His contributions towards the previous editions have been substantial, and his drive and tenacity have been greatly missed.

The Third Edition was prepared on an IBM-PC and the previous IBM files were converted into Macintosh files. These have now been reformatted on a Macintosh LC575 computer and all further data to complete the Fourth Edition were added to these files. The text was printed with a Hewlett-Packard 4MV -600dpi Laser Jet printer which gives a clearer resolution.

I thank my wife Dr Pauline M. Armarego, also an organic chemist, for the arduous and painstaking task of entering the new data into the respective files, and for the numerous hours of proofreading as well as the corrections of typographic errors in the files. I should be grateful to my readers for any comments, suggestions, amendments and criticisms which could, perhaps, be inserted in the second printing of this edition.

W.L.F. Armarego 30 June 1996

### **CHAPTER 1**

## COMMON PHYSICAL TECHNIQUES USED IN PURIFICATION

### **INTRODUCTION**

Purity is a matter of degree. Other than adventitious contaminants such as dust, paper fibres, wax, cork, etc., that may have been incorporated into the sample during manufacture, all commercially available chemical substances are in some measure impure. Any amounts of unreacted starting material, intermediates, by-products, isomers and related compounds may be present depending on the synthetic or isolation procedures used for preparing the substances. Inorganic reagents may deteriorate because of defective packaging (glued liners affected by sulfuric acid, zinc extracted from white rubber stoppers by ammonia), corrosion or prolonged storage. Organic molecules may undergo changes on storage. In extreme cases the container may be incorrectly labelled or, where compositions are given, they may be misleading or inaccurate for the proposed use. Where any doubt exists it is usual to check for impurities by appropriate spot tests, or by recourse to tables of physical or spectral properties such as the extensive infrared and NMR libraries published by the Sigma Aldrich Chemical Co.

The important question, then, is not whether a substance is pure but whether a given sample is sufficiently pure for some intended purpose. That is, are the contaminants likely to interfere in the process or measurement that is to be studied. By suitable manipulation it is often possible to reduce levels of impurities to acceptable limits, but absolute purity is an ideal which, no matter how closely approached, can never be attained. A *negative* physical or chemical test indicates only that the amount of an impurity in a substance lies below a certain sensitivity level; no test can demonstrate that a specified impurity is entirely absent.

When setting out to purify a laboratory chemical, it is desirable that the starting material is of the best grade commercially available. Particularly among organic solvents there is a range of qualities varying from *laboratory chemical* to *spectroscopic* and *chromatographic* grades. Many of these are suitable for use as received. With many of the more common reagents it is possible to obtain from the current literature some indications of likely impurities, their probable concentrations and methods for detecting them. However, in many cases complete analyses are not given so that significant concentrations of unspecified impurities may be present.

### THE QUESTION OF PURITY

Solvents and substances that are specified as *pure* for a particular purpose may, in fact, be quite impure for other uses. Absolute ethanol may contain traces of benzene, which makes it unsuitable for ultraviolet spectroscopy, or plasticizers which make it unsuitable for use in solvent extraction.

Irrespective of the grade of material to be purified, it is essential that some criteria exist for assessing the degree of purity of the final product. The more common of these include:

- 1. Examination of physical properties such as:
  - (a) Melting point, freezing point, boiling point, and the freezing curve (i.e. the variation, with time, in the freezing point of a substance that is being slowly and continuously frozen).
  - (b) Density.
  - (c) Refractive index at a specified temperature and wavelength. The sodium D line at 589.26 nm (weighted mean of  $D_1$  and  $D_2$  lines) is the usual standard of wavelength but results from other wavelengths can often be interpolated from a plot of refractive index versus 1/(wavelength)<sup>2</sup>.

- (d) Specific conductivity. (This can be used to detect, for example, water, salts, inorganic and organic acids and bases, in non-electrolytes).
- (e) Optical rotation, optical rotatory dispersion and circular dichroism.
- 2. Empirical analysis, for C, H, N, ash, etc.
- Chemical tests for particular types of impurities, e.g. for peroxides in aliphatic ethers (with acidified KI), or for water in solvents (quantitatively by the Karl Fischer method, see Fieser and Fieser, Reagents for Organic Synthesis J. Wiley & Sons, NY, Vol 1 pp. 353, 528, 1967, Library of Congress Catalog Card No 66-27894).
- 4. Physical tests for particular types of impurities:
  - (a) Emission and atomic absorption spectroscopy for detecting organic impurities and determining metal ions.
  - (b) Chromatography, including paper, thin layer, liquid (high, medium and normal pressure) and vapour phase.
  - (c) Electron spin resonance for detecting free radicals.
  - (d) X-ray spectroscopy.
  - (e) Mass spectroscopy.
  - (f) Fluorimetry.
- 5. Examination of spectroscopic properties
  - (a) Nuclear Magnetic Resonance (<sup>1</sup>H, <sup>13</sup>C, <sup>31</sup>P, <sup>19</sup>F NMR etc)
  - (b) Infrared spectroscopy (IR)
  - (c) Ultraviolet spectroscopy (UV)
  - (d) Mass spectroscopy [electron ionisation (EI), electron ionisation (CI), electrospray ionisation (ESI), fast atom bombardment (FAB), matrix-associated laser desorption ionisation (MALDI), etc]
- 6. Electrochemical methods (see Chapter 6 for macromolecules).
- 7. Nuclear methods which include a variety of radioactive elements as in organic reagents, complexes or salts.

A substance is usually taken to be of an acceptable purity when the measured property is unchanged by further treatment (especially if it agrees with a recorded value). In general, at least two different methods, such as recrystallisation and distillation, should be used in order to ensure maximum purity. Crystallisation may be repeated (from the same solvent or better from different solvents) until the substance has a constant melting point or absorption spectrum, and until it distils repeatedly within a narrow, specified temperature range.

With liquids, the refractive index at a specified temperature and wavelength is a sensitive test of purity. Note however that this is sensitive to dissolved gases such as  $O_2$ ,  $N_2$  or  $CO_2$ . Under favourable conditions, freezing curve studies are sensitive to impurity levels of as little as 0.001 moles per cent. Analogous fusion curves or heat capacity measurements can be up to ten times as sensitive as this. With these exceptions, most of the above methods are rather insensitive, especially if the impurities and the substances in which they occur are chemically similar. In some cases, even an impurity comprising many parts per million of a sample may escape detection.

The common methods of purification, discussed below, comprise distillation (including fractional distillation, distillation under reduced pressure, sublimation and steam distillation), crystallisation, extraction, chromatographic and other methods. In some cases, volatile and other impurities can be removed simply by heating. Impurities can also sometimes be eliminated by the formation of derivatives from which the purified material is regenerated (see Chapter 2).

### SOURCES OF IMPURITIES

Some of the more obvious sources of contamination of solvents arise from storage in metal drums and plastic containers, and from contact with grease and screw caps. Many solvents contain water. Others have traces of acidic materials such as hydrochloric acid in chloroform. In both cases this leads to corrosion of the drum and contamination of the solvent by traces of metal ions, especially  $Fe^{3+}$ . Grease, for example on stopcocks of separating funnels and other apparatus, e.g. greased ground joints, is also likely to contaminate solvents during extractions and chemical manipulation.

A much more general source of contamination that has not received the consideration it merits comes from the use of plastics for tubing and containers. Plasticisers can readily be extracted by organic solvents from PVC and other plastics, so that most solvents, irrespective of their grade (including spectrograde and ultrapure) have been reported to contain 0.1 to 5ppm of plasticiser [de Zeeuw, Jonkman and van Mansvelt Anal Biochem 67 339 1975]. Where large quantities of solvent are used for extraction (particularly of small amounts of compounds), followed by evaporation, this can introduce significant amounts of impurity, even exceeding the weight of the genuine extract and giving rise to spurious peaks in gas chromatography (for example of fatty acid methyl esters [Pascaud, Anal Biochem 18 570 1967]. Likely contaminants are di(2-ethylhexyl)phthalate and dibutyl phthalate, but upwards of 20 different phthalate esters are listed as plasticisers as well as adipates, azelates, phosphates, epoxides, polyesters and various heterocyclic compounds. These plastic coatings used in cap liners for bottles. Such contamination could arise at any point in the manufacture or distribution of a solvent. The problem with cap liners is avoidable by using corks wrapped in aluminium foil, although even in this case care should be taken because aluminium foil can dissolve in some liquids e.g. benzylamine and propionic acid.

Solutions in contact with polyvinyl chloride can become contaminated with trace amounts of lead, titanium, tin, zinc, iron, magnesium or cadmium from additives used in the manufacture and moulding of PVC.

N-Phenyl-2-naphthylamine is a contaminant of solvents and biological materials that have been in contact with black rubber or neoprene (in which it is used as an antioxidant). Although it was only an artefact of the separation procedure it has been isolated as an apparent component of vitamin K preparations, extracts of plant lipids, algae, livers, butter, eye tissue and kidney tissue [Brown Chem Br 3 524 1967].

Most of the above impurities can be removed by prior distillation of the solvent, but care should be taken to avoid plastic or black rubber as much as possible.

### PRACTICES TO AVOID IMPURITIES Cleaning practices

Laboratory glassware and Teflon equipment can be cleaned satisfactorily for most purposes by careful immersion into a solution of sodium dichromate in concentrated sulfuric acid, followed by draining, and rinsing copiously with distilled water. This is an exothermic reaction and should be carried out very cautiously in an efficient fume cupboard. [To prepare the chromic acid bath, dissolve 5 g of sodium dichromate (CARE: cancer suspect agent) in 5 mL of water. The dichromate solution is then cooled and stirred while 100 mL of concentrated sulfuric acid is added slowly. Store in a glass bottle.] Where traces of chromium (adsorbed on the glass) must be avoided, a 1:1 mixture of concentrated sulfuric and nitric acid is a useful alternative. (Use in a fumehood to remove vapour and with adequate face protection.) Acid washing is also suitable for polyethylene ware but prolonged contact (some weeks) leads to severe deterioration of the plastic. Alternatively an alcoholic solution of sodium hydroxide (alkaline base bath) can be used. This strongly corrosive solution (CAUTION: Alkali causes serious burns) can be made by dissolving 120g of NaOH in 120 mL water, followed by dilution to 1 L with 95% ethanol. This solution is conveniently stored in suitable alkali resistant containers (e.g. Nalgene heavy duty rectangular tanks) with lids. Glassware can be soaked overnight in the base bath and rinsed thoroughly after soaking. For much glassware, washing with hot detergent solution, using tap water, followed by rinsing with distilled water and acetone, and heating to 200-300° overnight, is adequate. (Volumetric apparatus should not be heated: after washing it is rinsed with acetone, then hexane, and air-dried. Prior to use, equipment can be rinsed with acetone, then with petroleum ether or hexane, to remove the last traces of contaminants.) Teflon equipment should be soaked, first in acetone, then in petroleum ether or hexane for ten minutes prior to use.

For trace metal analyses, prolonged soaking of equipment in 1M nitric acid may be needed to remove adsorbed metal ions.

Soxhlet thimbles and filter papers may contain traces of lipid-like materials. For manipulations with highly pure materials, as in trace-pesticide analysis, thimbles and filter papers should be thoroughly extracted with hexane before use.

Trace impurities in silica gel for TLC can be removed by heating at 300° for 16h or by Soxhlet extraction for 3h with distilled chloroform, followed by 4h extraction with distilled hexane.

### Silylation of glassware and plasticware

Silylation of apparatus makes it repellant to water and hydrophilic materials. It minimises loss of solute by adsorption onto the walls of the container. The glassware is placed in a desiccator containing dichloromethyl silane (1mL) in a small beaker and evacuated for 5min. The vacuum is turned off and air is introduced into the desiccator which allows the silylating agent to coat the glassware uniformly. The desiccator is then evacuated, closed and set aside for 2h. The glassware is removed from the desiccator and baked at 180° for 2h before use.

Plasticware is treated similarly except that it is rinsed well with water before use instead of baking. Note that dichloromethyl silane is highly **TOXIC** and **VOLATILE**, and the whole operation should be carried out in an efficient fume cupboard.

An alternative procedure used for large apparatus is to rinse the apparatus with a 5% solution of dichloromethyl silane in chloroform, followed by several rinses with water before baking the apparatus at 180°/2h (for glass) or drying in air (for plasticware).

Plus One REPEL-SILANE ES (a solution of 2% w/v of dichloromethyl silane in octamethyl cyclooctasilane) is used to inhibit the sticking of polyacrylamide gels, agarose gels and nucleic acids to glass surfaces and is available commercially (Amersham Biosciences).

### SAFETY PRECAUTIONS ASSOCIATED WITH THE PURIFICATION OF LABORATORY CHEMICALS

Although most of the manipulations involved in purifying laboratory chemicals are inherently safe, care is necessary if hazards are to be avoided in the chemical laboratory. In particular there are dangers inherent in the inhalation of vapours and absorption of liquids and low melting solids through the skin. In addition to the toxicity of solvents there is also the risk of their flammability and the possibility of eye damage. Chemicals, particularly in admixture, may be explosive. Compounds may be carcinogenic or otherwise deleterious to health. Present day chemical catalogues specifically indicate the particular dangerous properties of the individual chemicals they list and these should be consulted whenever the use of commercially available chemicals is contemplated. Radioisotopic labelled compounds pose special problems of human exposure and of disposal of laboratory waste. Hazardous purchased chemicals are accompanied by detailed MSDS (Material Safety Data Sheets), which contain information regarding their toxicity, safety handling procedures and the necessary precautions to be taken. These should be read carefully and filed for future reference. In addition, chemical management systems such as ChemWatch which include information on hazards, handling and storage are commercially available. There are a number of websites which provide selected safety information: they include the Sigma-Aldrich website (www.sigmaaldrich.com) and other chemical websites e.g. www.ilpi.com/msds).

The most common hazards are:

- (1) Explosions due to the presence of peroxides formed by aerial oxidation of ethers and tetrahydrofuran, decahydronaphthalene, acrylonitrile, styrene and related compounds.
- (2) Compounds with low flash points (below room temperature). Examples are acetaldehyde, acetone, acetonitrile, benzene, carbon disulfide, cyclohexane, diethyl ether, ethyl acetate and *n*-hexane.
- (3) Contact of oxidising agents (KMnO<sub>4</sub>, HClO<sub>4</sub>, chromic acid) with organic liquids.
- (4) Toxic reactions with tissues.

The laboratory should at least be well ventilated and safety glasses should be worn, particularly during distillation and manipulations carried out under reduced pressure or elevated temperatures. With this in mind we have endeavoured to warn users of this book whenever greater than usual care is needed in handling chemicals. As a general rule, however, all chemicals which users are unfamiliar with should be treated with extreme care and assumed to be highly flammable and toxic. The safety of others in a laboratory should always be foremost in mind, with ample warning whenever a potentially hazardous operation is in progress. Also, unwanted solutions or solvents should never be disposed of *via* the laboratory sink. The operator should be aware of the usual means for disposal of chemicals in her/his laboratories and she/he should remove unwanted chemicals accordingly. Organic liquids for disposal should be temporarily stored, as is practically possible, in respective containers. Avoid placing all organic liquids in the same container particularly if they contain small amounts of reagents which could react with each other. Halogenated waste solvents should be kept separate from other organic liquids.

### SOME HAZARDS OF CHEMICAL MANIPULATION IN PURIFICATION AND RECOVERY OF RESIDUES

Performing chemical manipulations calls for some practical knowledge if danger is to be avoided. However, with care, hazards can be kept to an acceptable minimum. A good general approach is to consider every operation as potentially perilous and then to adjust one's attitude as the operation proceeds. A few of the most common dangers are set out below. For a larger coverage of the following sections, and of the literature, the bibliography at the end of this chapter should be consulted.

**Perchlorates and perchloric acid.** At 160° perchloric acid is an exceedingly strong oxidising acid and a strong dehydrating agent. Organic perchlorates, such as methyl and ethyl perchlorates, are unstable and are violently explosive compounds. A number of heavy-metal perchlorates are extremely prone to explode. The use of anhydrous magnesium perchlorate, *Anhydrone*, *Dehydrite*, as a drying agent for organic vapours is **not** recommended. Desiccators which contain this drying agent should be adequately shielded at all times and kept in a cool place, i.e. **never** on a window sill where sunlight can fall on it.

No attempt should be made to purify perchlorates, except for ammonium, alkali metal and alkaline earth salts which, in water or aqueous alcoholic solutions are insensitive to heat or shock. Note that perchlorates react relatively slowly in aqueous organic solvents, but as the water is removed there is an increased possibility of an explosion. Perchlorates, often used in non-aqueous solvents, are explosive in the presence of even small amounts of organic compounds when heated. Hence stringent care should be taken when purifying perchlorates, and direct flame and infrared lamps should be avoided. Tetra-alkylammonium perchlorates should be dried below 50° under vacuum (and protection). Only very small amounts of such materials should be prepared, and stored, at any one time.

**Peroxides.** These are formed by aerial oxidation or by autoxidation of a wide range of organic compounds, including diethyl ether, allyl ether, allyl phenyl ether, dibenzyl ether, benzyl butyl ether, *n*-butyl ether, *iso*-butyl ether, *t*-butyl ether, dioxane, tetrahydrofuran, olefins, and aromatic and saturated aliphatic hydrocarbons. They accumulate during distillation and can detonate violently on evaporation or distillation when their concentration becomes high. If peroxides are likely to be present materials should be tested for peroxides before distillation (for tests see entry under "Ethers", in Chapter 2). Also, distillation should be discontinued when at least one quarter of the residue is left in the distilling flask.

Heavy-metal-containing-explosives. Ammoniacal silver nitrate, on storage or treatment, will eventually deposit the highly explosive silver nitride "fulminating silver". Silver nitrate and ethanol may give silver fulminate (see Chapter 5), and in contact with azides or hydrazine and hydrazides may form silver azide. Mercury can also form such compounds. Similarly, ammonia or ammonium ions can react with gold salts to form "fulminating gold". Metal fulminates of cadmium, copper, mercury and thallium are powerfully explosive, and some are detonators [Luchs, Photog Sci Eng 10 334 1966]. Heavy metal containing solutions, particularly when organic material is present should be treated with great respect and precautions towards possible explosion should be taken.

Strong acids. In addition to perchloric acid (see above), extra care should be taken when using strong mineral acids. Although the effects of concentrated sulfuric acid are well known these cannot be stressed strongly enough. Contact with tissues will leave irreparable damage. Always dilute the concentrated acid by carefully adding the acid down the side of the flask which contains water, and the process should be carried out under cooling. This solution is not safe to handle until the acid has been thoroughly mixed with the water. Protective face, and body coverage should be used at all times. Furning sulfuric acid and chlorosulfonic acid are even more dangerous than concentrated sulfuric acid and adequate precautions should be taken. Chromic acid cleaning mixture contains strong sulfuric acid and should be treated in the same way; and in addition the mixture is potentially carcinogenic.

Concentrated and fuming nitric acids are also dangerous because of their severe deleterious effects on tissues.

**Reactive halides and anhydrides.** Substances like acid chlorides, low molecular weight anhydrides and some inorganic halides (e.g.  $PCl_3$ ) can be highly toxic and lachrymatory affecting mucous membranes and lung tissues. Utmost care should be taken when working with these materials. Work should be carried out in a very efficient fume cupboard.

**Solvents.** The flammability of low-boiling organic liquids cannot be emphasised strongly enough. These invariably have very low flash points and can ignite spontaneously. Special precautions against explosive flammability should be taken when recovering such liquids. Care should be taken with small volumes (*ca* 250mL) as well as large volumes (> 1L), and the location of all the fire extinguishers, and fire blankets, in the immediate vicinity of the apparatus should be checked. The fire extinguisher should be operational. The following flammable liquids (in alphabetical order) are common fire hazards in the laboratory: acetaldehyde, acetone, acrylonitrile, acetonitrile, benzene, carbon disulfide, cyclohexane, diethyl ether, ethyl acetate, hexane, low-boiling petroleum ether, tetrahydrofuran and toluene. Toluene should always be used in place of benzene wherever possible due to the potential *carcinogenic* effects of the liquid and vapour of the latter.

The drying of flammable solvents with sodium or potassium metal and metal hydrides poses serious potential fire hazards and adequate precautions should be stressed.

Salts. In addition to the dangers of perchlorate salts, other salts such as nitrates, azides and diazo salts can be hazardous and due care should be taken when these are dried. Large quantities should never be prepared or stored for long periods.

#### SAFETY DISCLAIMER

Experimental chemistry is a very dangerous occupation and extreme care and adequate safety precautions should be taken at all times. Although we have stated the safety measures that have to be taken under specific entries these are by no means exhaustive and some may have been unknowingly or accidentally omitted. The experimenter without prior knowledge or experience must seek further safety advice on reagents and procedures from experts in the field before undertaking the purification of any material, We take no responsibility whatsoever if any mishaps occur when using any of the procedures described in this book.

### METHODS OF PURIFICATION OF REAGENTS AND SOLVENTS

Many methods exist for the purification of reagents and solvents. A number of these methods are routinely used in synthetic as well as analytical chemistry and biochemistry. These techniques, outlined below, will be discussed in greater detail in the respective sections in this Chapter. It is important to note that more than one method of purification may need to be implemented in order to obtain compounds of highest purity.

Common methods of purification are:

- (a) Solvent Extraction and Distribution
- (b) Distillation
- (c) Recrystallisation
- (d) Sublimation
- (e) Chromatography

For substances contaminated with water or solvents, drying with appropriate absorbents and desiccants may be sufficient.

### SOLVENT EXTRACTION AND DISTRIBUTION

Extraction of a substance from suspension or solution into another solvent can sometimes be used as a purification process. Thus, organic substances can often be separated from inorganic impurities by shaking an aqueous solution or suspension with suitable immiscible solvents such as benzene, carbon tetrachloride, chloroform, diethyl ether, diisopropyl ether or petroleum ether. After several such extractions the combined organic phase is dried and the solvent is evaporated. Grease from the glass taps of conventional separating funnels is invariably soluble in the solvents used. Contamination with grease can be very troublesome particularly when the amounts of material to be extracted are very small. Instead, the glass taps should be lubricated with the extraction solvent; or better, the taps of the extraction funnels should be made of the more expensive material Teflon. Immiscible solvents suitable for extractions are given in Table 1. Addition of electrolytes (such as ammonium sulfate, calcium chloride or sodium chloride) to the aqueous phase helps to ensure that the organic layer separates cleanly and also decreases the extent of extraction into the latter. Emulsions can also be broken up by filtration (with suction) through Celite, or by adding a little octyl alcohol or some other paraffinic alcohol. The main factor in selecting a suitable immiscible solvent is to find one in which the material to be extracted is readily soluble, whereas the substance from which it is being extracted is not. The same considerations apply irrespective of whether it is the substance being purified, or one of its contaminants, that is taken into the new phase. (The second of these processes is described as washing.)

Common examples of washing with aqueous solutions include the following:

Removal of acids from water-immiscible solvents by washing with aqueous alkali, sodium carbonate or sodium bicarbonate.

Removal of phenols from similar solutions by washing with aqueous alkali.

Removal of organic bases by washing with dilute hydrochloric or sulfuric acids.

Removal of unsaturated hydrocarbons, of alcohols and of ethers from saturated hydrocarbons or alkyl halides by washing with cold concentrated sulfuric acid.

This process can also be applied to purification of the substance if it is an acid, a phenol or a base, by extracting into the appropriate aqueous solution to form the salt which, after washing with pure solvent, is again converted to

the free species and re-extracted. Paraffin hydrocarbons can be purified by extracting them with phenol (in which aromatic hydrocarbons are highly soluble) prior to fractional distillation.

For extraction of solid materials with a solvent, a *Soxhlet* extractor is commonly used. This technique is applied, for example, in the alcohol extraction of dyes to free them from insoluble contaminants such as sodium chloride or sodium sulfate.

Acids, bases and amphoteric substances can be purified by taking advantage of their ionisation constants.

#### Ionisation constants and pK.

When substances ionise their neutral species produce positive and negative species. The ionisation constants are those constant values (equilibrium constants) for the equilibria between the charged species and the neutral species, or species with a larger number of charges (e.g. between mono and dications). These ionisation constants are given as  $\mathbf{pK}$  values where  $\mathbf{pK} = -\log \mathbf{K}$  and  $\mathbf{K}$  is the dissociation constant for the equilibrium between the species [Albert and Serjeant *The Determination of Ionisation Constants*, A Laboratory Manual, 3rd Edition, Chapman & Hall, New York, London, 1984, ISBN 0412242907].

The advantage of using pK values (instead of K values) is that theory (and practice) states that the pK values of ionisable substances are numerically equal to the pH of the solution at which the concentrations of ionised and neutral species are equal. For example acetic acid has a  $pK^{25}$  value of 4.76 at 25° in H<sub>2</sub>O, then at pH 4.76 the aqueous solution contains equal amounts of acetic acid [AcOH] and acetate anion [AcO<sup>-</sup>], i.e. [AcOH]/[AcO<sup>-</sup>] of 50/50. At pH 5.76 (pK + 1) the solution contains [AcOH]/[AcO<sup>-</sup>] of 10/90, at pH 6.76 (pK + 2) the solution contains [AcOH]/[AcO<sup>-</sup>] of 10/90, at pH 2.76 (pK - 2) the solution contains [AcOH]/[AcO<sup>-</sup>] of 99/1.

One can readily appreciate the usefulness of pK value in purification procedures, e.g. as when purifying acetic acid. If acetic acid is placed in aqueous solution and the pH adjusted to  $7.76 \{[AcOH]/[AcO^-]\}$  with a ratio of 0.1/99.9, and extracted with say diethyl ether, neutral impurities will be extracted into diethyl ether leaving almost all the acetic acid in the form of AcO<sup>-</sup> in the aqueous solution. If then the pH of the solution is adjusted to 1.67 where the acid is almost all in the form AcOH, almost all of it will be extracted into diethyl ether.

Aniline will be used as a second example. It has a  $pK^{25}$  of 4.60 at 25° in H<sub>2</sub>O. If it is placed in aqueous solution at pH 1.60 it will exist almost completely (99.9%) as the anilinium cation. This solution can then be extracted with solvents e.g. diethyl ether to remove neutral impurities. The pH of the solution is then adjusted to 7.60 whereby aniline will exist as the free base (99.9%) and can be extracted into diethyl ether in order to give purer aniline.

See Table 2 for the pH values of selected buffers.

A knowledge of the pK allows the adjustment of the pH without the need of large excesses of acids or base. In the case of inorganic compounds a knowledge of the pK is useful for adjusting the ionic species for making metal complexes which could be masked or extracted into organic solvents [Perrin and Dempsey Buffers for pH and Metal ion Control, Chapman & Hall, New York, London, 1974, ISBN 0412117002], or for obtaining specific anionic species in solution e.g.  $H_2PO_4^-$ ,  $HPO_4^{2-}$  or  $PO_4^{3-}$ .

The **pK** values that have been entered in Chapters 4, 5 and 6 have been collected directly from the literature or from compilations of literature values for organic bases [Perrin Dissociation Constants of Organic Bases in Aqueous Solution, Butterworths, London, 1965, Supplement 1972, ISBN 040870408X; Albert and Serjeant The Determination of Ionisation Constants, A Laboratory Manual, 3rd Edition, Chapman & Hall, London, New York, 1984, ISBN 0412242907]; organic acids [Kortum, Vogel and Andrussow, Dissociation Constants of Organic Acids in Aqueous Solution, Butterworth, London, 1961; Serjeant and Dempsey, Dissociation Constants of Organic acids in Aqueous Solution, Pergamon Press, Oxford, New York, 1979, ISBN 0080223397; and inorganic acids and bases [Perrin, Ionisation Constants of Inorganic Acids and Bases in Aqueous Solution, Second Edition, Pergamon Press, Oxford, New York, 1979, ISBN 0080223397; and inorganic acids and bases [Perrin, Ionisation Constants of Inorganic Acids and Bases in Aqueous Solution, Second Edition, Pergamon Press, Oxford, New York, 1982, ISBN 0080292143]. Where literature values were not available, values have been predicted and assigned  $pK_{Est} \sim$ . Most predictions should be so close to true values as to make very small difference for the purposes intended in this book. The success of the predictions, i.e. how close to the true value, depends on the availability of pK values for closely related compounds because the effect of substituents or changes in structures are generally additive [Perrin, Dempsey and Serjeant, pKa Prediction for Organic Acids and Bases, Chapman & Hall, London, New York, 1981, ISBN 041222190X].

All the pK values in this book are pKa values, the acidic pK, i.e. dissociation of H<sup>+</sup> from an acid (AH) or from a conjugate base (BH<sup>+</sup>). Occasionally pKb values are reported in the literature but these can be converted using the equation pKa + pKb = 14. For strong acids e.g. sulfuric acid, and strong bases, e.g. sodium hydroxide, the pK values lie beyond the 1 to 11 scale and have to be measured in strong acidic and basic media. In these cases appropriate scales e.g. the H<sub>o</sub> (for acids) and H<sub>-</sub> (for bases) have been used [see Katritzky and Waring *J Chem Soc* 1540 1962]. These values will be less than 1 (and negative) for acids and >11 for bases. They are a rough guides to the strengths of acids and bases. Errors in the stated pK and  $pK_{Est} \sim$  values can be judged from the numerical values given. Thus pK values of 4.55, 4.5 and 4 mean that the respective errors are better than  $\pm 0.05$ ,  $\pm 0.3$  and  $\pm 0.5$ . Values taken from the literature are written as **pK**, and all the values that were estimated because they were not found in the literature are written as **pK**<sub>Est</sub>.

### pK and Temperature.

The temperatures at which the literature measurements were made are given as superscripts, e.g.  $pK^{25}$ . Where no temperature is given, it is assumed that the measurements were carried out at room temperature, e.g.  $15-25^{\circ}$ . No temperature is given for estimated values ( $pK_{Est} \sim$ ) and these have been calculated from data at room temperature. The variation of pK with temperature is given by the equation:

 $- d(pK)/dT = (pK + 0.052\Delta S^{0})/T$ 

where T is in degrees Kelvin and  $\Delta S^{\circ}$  is in Joules deg<sup>-1</sup> mol<sup>-1</sup>. The -d(pK)/dT in the range of temperatures between 5 to 70° is generally small (e.g. between ~0.0024 and ~0.04), and for chemical purification purposes is not a seriously deterring factor. It does however, vary with the compound under study because  $\Delta S^{\circ}$  varies from compound to compound. The following are examples of the effect of temperature on pK values: for imidazole the pK values are 7.57 (0°), 7.33 (10°), 7.10 (20°), 6.99 (25°), 6.89 (30°), 6.58 (40°) and 6.49 (50°), and for 3,5dinitrobenzoic acid they are 2.60 (10°), 2.73 (20°), 2.85 (30°), 2.96 (40°) and 3.07 (40°), and for *N*-acetyl- $\beta$ alanine they are 4.4788 (5°), 4.4652 (10°), 4.4564 (15°), 4.4488 (20°), 4.4452 (25°), 4.4444 (30°), 4.4434 (35°) and 4.4412 (40°).

### pK and solvent.

All stated pK values in this book are for data in dilute aqueous solutions unless otherwise stated, although the dielectric constants, ionic strengths of the solutions and the method of measurement, e.g. potentiometric, spectrophotometric etc, are not given. Estimated values are also for dilute aqueous solutions whether or not the material is soluble enough in water. Generally the more dilute the solution the closer is the pK to the real thermodynamic value. The pK in mixed aqueous solvents can vary considerably with the relative concentrations and with the nature of the solvents. For example the pK<sup>25</sup> values for *N*-benzylpenicillin are 2.76 and 4.84 in H<sub>2</sub>O and H<sub>2</sub>O/EtOH (20:80) respectively; the pK<sup>25</sup> values for (-)-ephedrine are 9.58 and 8.84 in H<sub>2</sub>O and H<sub>2</sub>O/MeOCH<sub>2</sub>CH<sub>2</sub>OH (20:80) respectively; and for cyclopentylamine the pK<sup>25</sup> values are 10.65 and 4.05 in H<sub>2</sub>O and H<sub>2</sub>O/EtOH (50:50) respectively. pK values in acetic acid or aqueous acetic acid are generally lower than in H<sub>2</sub>O.

The dielectric constant of the medium affects the equilibria where charges are generated in the dissociations e.g. AH  $A^+ + H^+$  and therefore affects the pK values. However, its effect on dissociations where there are no changes in total charge such as BH<sup>+</sup>  $B^+ + H^+$  is considerably less, with a slight decrease in pK with decreasing dielectric constant.

### DISTILLATION

One of the most widely applicable and most commonly used methods of purification of liquids or low melting solids (especially of organic chemicals) is fractional distillation at atmospheric, or some lower, pressure. Almost without exception, this method can be assumed to be suitable for all organic liquids and most of the low-melting organic solids. For this reason it has been possible in Chapter 4 to omit many procedures for purification of organic chemicals when only a simple fractional distillation is involved - the suitability of such a procedure is implied from the boiling point.

The boiling point of a liquid varies with the 'atmospheric' pressure to which it is exposed. A liquid boils when its vapour pressure is the same as the external pressure on its surface, its normal boiling point being the temperature at which its vapour pressure is equal to that of a standard atmosphere (760mm Hg). Lowering the external pressure lowers the boiling point. For most substances, boiling point and vapour pressure are related by an equation of the form,

$$\log p = \mathbf{A} + \mathbf{B}/(t + 273),$$

where p is the pressure, t is in °C, and A and B are constants. Hence, if the boiling points at two different pressures are known the boiling point at another pressure can be calculated from a simple plot of log p versus 1/(t + 273). For organic molecules that are not strongly associated, this equation can be written in the form,

$$\log p = 8.586 - 5.703 (T + 273)/(t + 273)$$

where T is the boiling point in °C at 760mm Hg. Tables 3A and 3B give computed boiling points over a range of pressures. Some examples illustrate its application. Ethyl acetoacetate, **b** 180° (with decomposition) at 760mm Hg has a predicted **b** of 79° at 16mm; the experimental value is 78°. Similarly 2,4-diaminotoluene, **b** 292° at 760mm, has a predicted **b** of 147° at 8mm; the experimental value is 148-150°. For self-associated molecules the predicted **b** are lower than the experimental values. Thus, glycerol, **b** 290° at 760mm, has a predicted **b** of 146° at 8mm; the experimental value is 182°.

Similarly an estimate of the boiling points of liquids at reduced pressure can be obtained using a nomogram (see Figure 1).

For pressures near 760mm, the change in boiling point is given approximately by,

$$\hat{\mathbf{I}}t = a(760 - p)(t + 273)$$

where a = 0.00012 for most substances, but a = 0.00010 for water, alcohols, carboxylic acids and other associated liquids, and a = 0.00014 for very low-boiling substances such as nitrogen or ammonia [Crafts *Chem Ber* 20 709 1887]. When all the impurities are non-volatile, simple distillation is adequate purification. The observed boiling point remains almost constant and approximately equal to that of the pure material. Usually, however, some of the impurities are appreciably volatile, so that the boiling point progressively rises during the distillation because of the progressive enrichment of the higher-boiling components in the distillation flask. In such cases, separation is effected by fractional distillation using an efficient column.

### Techniques.

The distillation apparatus consists basically of a distillation flask, usually fitted with a vertical fractionating column (which may be empty or packed with suitable materials such as glass helices or stainless-steel wool) to which is attached a condenser leading to a receiving flask. The bulb of a thermometer projects into the vapour phase just below the region where the condenser joins the column. The distilling flask is heated so that its contents are steadily vaporised by boiling. The vapour passes up into the column where, initially, it condenses and runs back into the flask. The resulting heat transfer gradually warms the column so that there is a progressive movement of the vapour phase-liquid boundary up the column, with increasing enrichment of the more volatile component. Because of this fractionation, the vapour finally passing into the condenser (where it condenses and flows into the receiver) is commonly that of the lowest-boiling components in the system. The conditions apply until all of the low-boiling material has been distilled, whereupon distillation ceases until the column temperature is high enough to permit the next component to distil. This usually results in a temporary fall in the temperature indicated by the thermometer.

### Distillation of liquid mixtures.

The principles involved in fractional distillation of liquid mixtures are complex but can be seen by considering a system which approximately obeys Raoult's law. (This law states that the vapour pressure of a solution at any given temperature is the sum of the vapour pressures of each component multiplied by its mole fraction in the solution.) If two substances, A and B, having vapour pressures of 600mm Hg and 360mm Hg, respectively, were mixed in a molar ratio of 2:1 (i.e. 0.666:0.333 mole ratio), the mixture would have (ideally) a vapour pressure of 520mm Hg (i.e. 600 x 0.666 + 360 x 0.333, or 399.6 + 119.88 mm Hg) and the vapour phase would contain 77% (399.6 x 100/520) of A and 23% (119.88 x 100/520) of B. If this phase was now condensed, the new liquid phase would, therefore, be richer in the volatile component A. Similarly, the vapour in equilibrium with this phase is still further enriched in A. Each such liquid-vapour equilibrium constitutes a "theoretical plate". The efficiency of a fractionating column is commonly expressed as the number of such plates to which it corresponds in operation. Alternatively, this information may be given in the form of the height equivalent to a theoretical plate, or HETP. The number of theoretical plates and equilibria between liquids and vapours are affected by the factors listed to achieve maximum separation by fractional distillation in the section below on techniques. In most cases, systems deviate to a greater or lesser extent from Raoult's law, and vapour pressures may be greater or less than the values calculated. In extreme cases (e.g. azeotropes), vapour pressure-composition curves pass through maxima or minima, so that attempts at fractional distillation lead finally to the separation of a constantboiling (azeotropic) mixture and one (but not both) of the pure species if either of the latter is present in excess.

*Elevation of the boiling point by dissolved solids.* Organic substances dissolved in organic solvents cause a rise in boiling point which is proportional to the concentration of the substance, and the extent of rise in temperature is characteristic of the solvent. The following equation applies for dilute solutions and non-associating substances:

$$\underline{MDt} = K$$

Where M is the molecular weight of the solute, Dt is the elevation of boiling point in  ${}^{\circ}C$ , c is the concentration of solute in grams for 1000gm of solvent, and K is the *Ebullioscopic Constant* (molecular elevation of the boiling point) for the solvent. K is a fixed property (constant) for the particular solvent. This has been very useful for the determination of the molecular weights of organic substances in solution.

The efficiency of a distillation apparatus used for purification of liquids depends on the difference in boiling points of the pure material and its impurities. For example, if two components of an ideal mixture have vapour pressures in the ratio 2:1, it would be necessary to have a still with an efficiency of at least seven plates (giving an enrichment of  $2^7 = 128$ ) if the concentration of the higher-boiling component in the distillate was to be reduced to less than 1% of its initial value. For a vapour pressure ratio of 5:1, three plates would achieve as much separation.

In a fractional distillation, it is usual to reject the initial and final fractions, which are likely to be richer in the lower-boiling and higher-boiling impurities respectively. The centre fraction can be further purified by repeated fractional distillation.

To achieve maximum separation by fractional distillation:

- 1. The column must be flooded initially to wet the packing. For this reason it is customary to operate a still at reflux for some time before beginning the distillation.
- 2. The reflux ratio should be high (i.e. the ratio of drops of liquid which return to the distilling flask and the drops which distil over), so that the distillation proceeds slowly and with minimum disturbance of the equilibria in the column.
- 3. The hold-up of the column should not exceed one-tenth of the volume of any one component to be separated.
- 4. Heat loss from the column should be prevented but, if the column is heated to offset this, its temperature must not exceed that of the distillate in the column.
- 5. Heat input to the still-pot should remain constant.
- 6. For distillation under reduced pressure there must be careful control of the pressure to avoid flooding or cessation of reflux.

### Types of distillation

The distilling flask. To minimise superheating of the liquid (due to the absence of minute air bubbles or other suitable nuclei for forming bubbles of vapour), and to prevent bumping, one or more of the following precautions should be taken:

(a) The flask is heated uniformly over a large part of its surface, either by using an electrical heating mantle or, by partial immersion in a bath above the boiling point of the liquid to be distilled.

(b) Before heating begins, small pieces of unglazed fireclay or porcelain (porous pot, boiling chips), pumice, diatomaceous earth, or platinum wire are added to the flask. These act as sources of air bubbles.

(c) The flask may contain glass siphons or boiling tubes. The former are inverted J-shaped tubes, the end of the shorter arm being just above the surface of the liquid. The latter comprise long capillary tubes sealed above the lower end.

(d) A steady slow stream of inert gas (e.g. N<sub>2</sub>, Ar or He) is passed through the liquid.

(e) The liquid in the flask is stirred mechanically. This is especially necessary when suspended insoluble material is present.

For simple distillations a Claisen flask is often used. This flask is, essentially, a round-bottomed flask to the neck of which is joined another neck carrying a side arm. This second neck is sometimes extended so as to form a

Vigreux column [a glass tube in which have been made a number of pairs of indentations which almost touch each other and which slope slightly downwards. The pairs of indentations are arranged to form a spiral of glass inside the tube].

For heating baths, see Table 4. For distillation apparatus on a micro or semi-micro scale see Aldrich and other glassware catalogues. Alternatively, some useful websites for suppliers of laboratory glassware are www.wheatonsci.com, www.sigmaaldrich.com and www.kimble-kontes.com.

Types of columns and packings. A slow distillation rate is necessary to ensure that equilibrium conditions operate and also that the vapour does not become superheated so that the temperature rises above the boiling point. Efficiency is improved if the column is heat insulated (either by vacuum jacketing or by lagging) and, if necessary, heated to just below the boiling point of the most volatile component. Efficiency of separation also improves with increase in the heat of vaporisation of the liquids concerned (because fractionation depends on heat equilibration at multiple liquid-gas boundaries). Water and alcohols are more easily purified by distillation for this reason.

Columns used in distillation vary in their shapes and types of packing. Packed columns are intended to give efficient separation by maintaining a large surface of contact between liquid and vapour. Efficiency of separation is further increased by operation under conditions approaching total reflux, i.e. under a high reflux ratio. However, great care must be taken to avoid flooding of the column during distillation. The minimum number of theoretical plates for satisfactory separation of two liquids differing in boiling point by  $\hat{1}t$  is approximately  $(273 + t)/3\hat{1}t$ , where t is the average boiling point in °C.

The packing of a column greatly increases the surface of liquid films in contact with the vapour phase, thereby increasing the efficiency of the column, but reducing its capacity (the quantities of vapour and liquid able to flow in opposite directions in a column without causing flooding). Material for packing should be of uniform size, symmetrical shape, and have a unit diameter less than one eighth that of the column. (Rectification efficiency increases sharply as the size of the packing is reduced but so, also, does the hold-up in the column.) It should also be capable of uniform, reproducible packing.

The usual packings are:

(a) Rings. These may be hollow glass or porcelain (Raschig rings), of stainless steel gauze (Dixon rings), or hollow rings with a central partition (Lessing rings) which may be of porcelain, aluminium, copper or nickel.

(b) Helices. These may be of metal or glass (Fenske rings), the latter being used where resistance to chemical attack is important (e.g. in distilling acids, organic halides, some sulfur compounds, and phenols). Metal single-turn helices are available in aluminium, nickel or stainless steel. Glass helices are less efficient, because they cannot be tamped to ensure uniform packing.

(c) Balls or beads. These are usually made of glass.

Condensers. Some of the more commonly used condensers are:

Air condenser. A glass tube such as the inner part of a Liebig condenser (see below). Used for liquids with boiling points above 90°. Can be of any length.

Coil condenser. An open tube, into which is sealed a glass coil or spiral through which water circulates. The tube is sometimes also surrounded by an outer cooling jacket. A double coil condenser has two inner coils with circulating water.

Double surface condenser. A tube in which the vapour is condensed between an outer and inner water-cooled jacket after impinging on the latter. Very useful for liquids boiling below 40°.

Friedrichs condenser. A "cold-finger" type of condenser sealed into a glass jacket open at the bottom and near the top. The cold finger is formed into glass screw threads.

Liebig condenser. An inner glass tube surrounded by a glass jacket through which water is circulated.

**Vacuum distillation.** This expression is commonly used to denote a distillation under reduced pressure lower than that of the normal atmosphere. Because the boiling point of a substance depends on the pressure, it is often possible by sufficiently lowering the pressure to distil materials at a temperature low enough to avoid partial or complete decomposition, even if they are unstable when boiled at atmospheric pressure.

Sensitive or high-boiling liquids should invariably be distilled or fractionally distilled under reduced pressure. The apparatus is essentially as described for distillation except that ground joints connecting the different parts of the apparatus should be air tight by using grease, or better Teflon sleaves. For low, moderately high, and very high temperatures Apiezon L, M and T greases respectively, are very satisfactory. Alternatively, it is often preferable to avoid grease and to use thin Teflon sleeves in the joints. The distilling flask, must be supplied with a capillary

bleed (which allows a fine stream of air, nitrogen or argon into the flask), and the receiver should be of the fraction collector type. When distilling under vacuum it is very important to place a loose packing of glass wool above the liquid to buffer sudden boiling of the liquid. The flask should be not more than two-thirds full of liquid. The vacuum must have attained a steady state, i.e. the liquid has been completely degassed, before the heat source is applied, and the temperature of the heat source must be raised *very slowly* until boiling is achieved.

If the pump is a filter pump off a high-pressure water supply, its performance will be limited by the temperature of the water because the vapour pressure of water at  $10^{\circ}$ ,  $15^{\circ}$ ,  $20^{\circ}$  and  $25^{\circ}$  is 9.2, 12.8, 17.5 and 23.8 mm Hg respectively. The pressure can be measured with an ordinary manometer. For vacuums in the range  $10^{-2}$  mm Hg to 10 mm Hg, rotary mechanical pumps (oil pumps) are used and the pressure can be measured with a Vacustat McLeod type gauge. If still higher vacuums are required, for example for high vacuum sublimations, a mercury diffusion pump is suitable. Such a pump can provide a vacuum up to  $10^{-6}$  mm Hg. For better efficiencies, the pump can be backed up by a mechanical pump. In all cases, the mercury pump is connected to the distillation apparatus through several traps to remove mercury vapours. These traps may operate by chemical action, for example the use of sodium hydroxide pellets to react with acids, or by condensation, in which case empty tubes cooled in solid carbon dioxide-ethanol or liquid nitrogen (contained in wide-mouthed Dewar flasks) are used.

Special oil or mercury traps are available commercially and a liquid-nitrogen (**b** -209.9°C) trap is the most satisfactory one to use between these and the apparatus. It has an advantage over liquid air or oxygen in that it is non-explosive if it becomes contaminated with organic matter. Air should not be sucked through the apparatus before starting a distillation because this will cause liquid oxygen (**b** -183°C) to condense in the liquid nitrogen trap and this is potentially explosive (especially in mixtures with organic materials). Due to the potential lethal consequences of liquid oxygen/organic material mixtures, care must be exercised when handling liquid nitrogen. Hence, it is advisable to degas the system for a short period before the trap is immersed into the liquid nitrogen (which is kept in a Dewar flask).

**Spinning-band distillation.** Factors which limit the performance of distillation columns include the tendency to flood (which occurs when the returning liquid blocks the pathway taken by the vapour through the column) and the increased hold-up (which decreases the attainable efficiency) in the column that should, theoretically, be highly efficient. To overcome these difficulties, especially for distillation under high vacuum of heat sensitive or high-boiling highly viscous fluids, spinning band columns are commercially available. In such units, the distillation columns contain a rapidly rotating, motor-driven, spiral band, which may be of polymer-coated metal, stainless steel or platinum. The rapid rotation of the band in contact with the walls of the still gives intimate mixing of descending liquid and ascending vapour while the screw-like motion of the band drives the liquid towards the still-pot, helping to reduce hold-up. There is very little pressure drop in such a system, and very high throughputs are possible, with high efficiency. For example, a 765-mm long 10-mm diameter commercial spinning-band column is reported to have an efficiency of 28 plates and a pressure drop of 0.2 mm Hg for a throughput of 330mL/h. The columns may be either vacuum jacketed or heated externally. The stills can be operated down to 10<sup>-5</sup> mm Hg. The principle, which was first used commercially in the Podbielniak Centrifugal Superfractionator, has also been embodied in descending-film molecular distillation apparatus.

Steam distillation. When two immmiscible liquids distil, the sum of their (independent) partial pressures is equal to the atmospheric pressure. Hence in steam distillation, the distillate has the composition

Moles of substance		P substance		760 — P water
Moles of water	=	Pwater	Ħ	P water
moles of water		P water		P water

where the P's are vapour pressures (in mm Hg) in the boiling mixture.

The customary technique consists of heating the substance and water in a flask (to boiling), usually with the passage of steam, followed by condensation and separation of the aqueous and non-aqueous phases in the distillate. Its advantages are those of selectivity (because only some water-insoluble substances, such as naphthalene, nitrobenzene, phenol and aniline are volatile in steam) and of ability to distil certain high-boiling substances well below their boiling point. It also facilitates the recovery of a non-steam-volatile solid at a relatively low temperature from a high-boiling solvent such as nitrobenzene. The efficiency of steam distillation is increased if superheated steam is used (because the vapour pressure of the organic component is increased relative to water). In this case the flask containing the material is heated (without water) in an oil bath and the steam passing through it is superheated by prior passage through a suitable heating device (such as a copper coil heated electrically or an oil bath).

Azeotropic distillation. In some cases two or more liquids form constant-boiling mixtures, or azeotropes. Azeotropic mixtures are most likely to be found with components which readily form hydrogen bonds or are otherwise highly associated, especially when the components are dissimilar, for example an alcohol and an aromatic hydrocarbon, but have similar boiling points.

Examples where the boiling point of the distillate is a minimum (less than either pure component) include: **Water** with ethanol, *n*-propanol and isopropanol, *tert*-butanol, propionic acid, butyric acid, pyridine,

methanol with methyl iodide, methyl acetate, chloroform,

ethanol with ethyl iodide, ethyl acetate, chloroform, benzene, toluene, methyl ethyl ketone,

benzene with cyclohexane,

acetic acid with toluene.

Although less common, azeotropic mixtures are known which have higher boiling points than their components. These include water with most of the mineral acids (hydrofluoric, hydrochloric, hydrobromic, perchloric, nitric and sulfuric) and formic acid. Other examples are acetic acid-pyridine, acetone-chloroform, aniline-phenol, and chloroform-methyl acetate.

The following azeotropes are important commercially for drying ethanol:

ethanol 95.5% (by weight) - water 4.5%	<b>b</b> 78.1°
ethanol 32.4% - benzene 67.6%	<b>b</b> 68.2°
ethanol 18.5% - benzene 74.1% - water 7.4%	<b>b</b> 64.9°

Materials are sometimes added to form an azeotropic mixture with the substance to be purified. Because the azeotrope boils at a different temperature, this facilitates separation from substances distilling in the same range as the pure material. (Conversely, the impurity might form the azeotrope and be removed in this way). This method is often convenient, especially where the impurities are isomers or are otherwise closely related to the desired substance. Formation of low-boiling azeotropes also facilitates distillation.

One or more of the following methods can generally be used for separating the components of an azeotropic mixture:

- 1. By using a chemical method to remove most of one species prior to distillation. (For example, water can be removed by suitable drying agents; aromatic and unsaturated hydrocarbons can be removed by sulfonation).
- 2. By redistillation with an additional substance which can form a ternary azeotropic mixture (as in ethanolwater-benzene example given above).
- 3. By selective adsorption of one of the components. (For example, of water on to silica gel or molecular sieves, or of unsaturated hydrocarbons onto alumina).
- 4. By fractional crystallisation of the mixture, either by direct freezing or by dissolving in a suitable solvent.

**Kügelrohr distillation.** The apparatus (Büchi, see www.buchi.com) is made up of small glass bulbs (ca 4-5cm diameter) which are joined together via Quickfit joints at each pole of the bulbs. The liquid (or low melting solid) to be purified is placed in the first bulb of a series of bulbs joined end to end, and the system can be evacuated. The first bulb is heated in a furnace at a high temperature whereby most of the material distils into the second bulb (which is outside of the furnace). The second bulb is then moved into the furnace and the furnace temperature is reduced by  $ca 5^{\circ}$  whereby the liquid in the second bulb distils into the third bulb (at this stage the first bulb is now out at the back of the furnace and the third and subsequent bulbs are outside the front of the furnace). The furnace temperature is lowered by a further  $ca 5^{\circ}$  and the third bulb is moved into the furnace. The lower boiling material will distil into the fourth bulb. The process is continued until no more material distils into the subsequent bulb. The vacuum (if applied) and the furnace are removed, the bulbs are separated and the various fractions of distillates are collected from the individual bulbs. For volatile liquids, it may be necessary to cool the receiving bulb with solid CO<sub>2</sub> held in a suitable container (Kügelrohr distillation apparatus with an integrated cooling system is available). This procedure is used for preliminary purification and the distillates are then redistilled or recrystallised.

Isopiestic or isothermal distillation. This technique can be useful for the preparation of metal-free solutions of volatile acids and bases for use in trace metal studies. The procedure involves placing two beakers, one of distilled water and the other of a solution of the material to be purified, in a desiccator. The desiccator is sealed and left to stand at room temperature for several days. The volatile components distribute themselves between the two beakers whereas the non-volatile contaminants remain in the original beaker. This technique has afforded metal-free pure solutions of ammonia, hydrochloric acid and hydrogen fluoride.

#### RECRYSTALLISATION Techniques

The most commonly used procedure for the purification of a solid material by recrystallisation from a solution involves the following steps:

- (a) The impure material is dissolved in a suitable solvent, by shaking or vigorous stirring, at or near the boiling point, to form a near-saturated solution.
- (b) The hot solution is filtered to remove any insoluble particles. To prevent crystallisation during this filtration, a heated filter funnel can be used or the solution can be diluted with more of the solvent.
- (c) The solution is then allowed to cool so that the dissolved substance crystallises out.
- (d) The crystals are separated from the mother liquor, either by centrifuging or by filtering, under suction, through a sintered glass, a Hirsch or a Büchner, funnel. Usually, centrifugation is preferred because of the greater ease and efficiency of separating crystals and mother liquor, and also because of the saving of time and effort, particularly when very small crystals are formed or when there is entrainment of solvent.
- (e) The crystals are washed free from mother liquor with a little fresh cold solvent, then dried.

If the solution contains extraneous coloured material likely to contaminate the crystals, this can often be removed by adding some activated charcoal (decolorising carbon) to the hot, but not boiling, solution which is then shaken frequently for several minutes before being filtered. (The large active surface of the carbon makes it a good adsorbent for this purpose.) In general, the cooling and crystallisation steps should be rapid so as to give small crystals which occlude less of the mother liquor. This is usually satisfactory with inorganic material, so that commonly the filtrate is cooled in an ice-water bath while being vigorously stirred. In many cases, however, organic molecules crystallise much more slowly, so that the filtrate must be set aside to cool to room temperature or left in the refrigerator. It is often desirable to subject material that is very impure to preliminary purification, such as steam distillation, Soxhlet extraction, or sublimation, before recrystallising it. A greater degree of purity is also to be expected if the crystallisation process is repeated several times, especially if different solvents are used. The advantage of several crystallisations from different solvents lies in the fact that the material sought, and its impurities, are unlikely to have similar solubilities as solvents and temperatures are varied.

For the final separation of solid material, sintered-glass discs are preferable to filter paper. Sintered glass is unaffected by strongly acid solutions or by oxidising agents. Also, with filter paper, cellulose fibres are likely to become included in the sample. The sintered-glass discs or funnels can be readily cleaned by washing in freshly prepared *chromic acid cleaning mixture*. This mixture is made by adding 100mL of concentrated sulfuric acid slowly with stirring to a solution of 5g of sodium dichromate (CARE: cancer suspect) in 5mL of water. (The mixture warms to about 70°, see p 3).

For materials with very low melting points it is sometimes convenient to use dilute solutions in acetone, methanol, pentane, diethyl ether or CHCl<sub>3</sub>-CCl<sub>4</sub>. The solutions are cooled to -78° in a dry-ice/acetone bath, to give a slurry which is filtered off through a precooled Büchner funnel. Experimental details, as applied to the purification of nitromethane, are given by Parrett and Sun [*J Chem Educ* 54 448 1977].

Where substances vary little in solubility with temperature, *isothermal crystallisation* may sometimes be employed. This usually takes the form of a partial evaporation of a saturated solution at room temperature by leaving it under reduced pressure in a desiccator.

However, in rare cases, crystallisation is not a satisfactory method of purification, especially if the impurity forms crystals that are isomorphous with the material being purified. In fact, the impurity content may even be greater in such recrystallised material. For this reason, it still remains necessary to test for impurities and to remove or adequately lower their concentrations by suitable chemical manipulation prior to recrystallisation.

*Filtration.* Filtration removes particulate impurities rapidly from liquids and is also used to collect insoluble or crystalline solids which separate or crystallise from solution. The usual technique is to pass the solution, cold or hot, through a fluted filter paper in a conical glass funnel.

If a solution is hot and needs to be filtered rapidly a Büchner funnel and flask are used and filtration is performed under a slight vacuum (water pump), the filter medium being a circular cellulose filter paper wet with solvent. If filtration is slow, even under high vacuum, a pile of about twenty filter papers, wet as before, are placed in the Büchner funnel and, as the flow of solution slows down, the upper layers of the filter paper are progressively removed. Alternatively, a filter aid, e.g. Celite, Florisil or Hyflo-supercel, is placed on top of a filter paper in the funnel. When the flow of the solution (under suction) slows down, the upper surface of the filter aid is scratched gently. Filter papers with various pore sizes are available covering a range of filtration rates. Hardened filter papers are slow filtering but they can withstand acidic and alkaline solutions without appreciable hydrolysis of the cellulose (see Table 5). When using strong acids it is preferable to use glass micro fibre filters which are commercially available (see Table 5 and 6).

Freeing a solution from extremely small particles [e.g. for optical rotatory dispersion (ORD) or circular dichroism (CD) measurements] requires filters with very small pore size. Commercially available (Millipore, Gelman, Nucleopore) filters other than cellulose or glass include nylon, Teflon, and polyvinyl chloride, and the pore diameter may be as small as 0.01micron (see Table 6). Special containers are used to hold the filters, through which the solution is pressed by applying pressure, e.g. from a syringe. Some of these filters can be used to clear strong sulfuric acid solutions.

As an alternative to the Büchner funnel for collecting crystalline solids, a funnel with a sintered glass-plate under suction may be used. Sintered-glass funnels with various porosities are commercially available and can be easily cleaned with warm chromic or nitric acid (see above).

When the solid particles are too fine to be collected on a filter funnel because filtration is extremely slow, separation by **centrifugation** should be used. Bench type centrifuges are most convenient for this purpose. The solid is placed in the centrifuge tube, the tubes containing the solutions on opposite sides of the rotor should be balanced accurately (at least within 0.05 to 0.1g), and the solutions are spun at maximum speed for as long as it takes to settle the solid (usually ca 3-5 minutes). The solid is washed with cold solvent by centrifugation, and finally twice with a pure volatile solvent in which the solid is insoluble, also by centrifugation. After decanting the supernatant, the residue is dried in a vacuum, at elevated temperatures if necessary. In order to avoid "spitting" and contamination with dust while the solid in the centrifuge tube is dried, the mouth of the tube is covered with aluminium foil and held fast with a tight rubber band near the lip. The flat surface of the aluminium foil is then perforated in several places with a pin and the tube and contents are dried in a vacuum desiccator over a desiccant.

Choice of solvents. The best solvents for recrystallisation have the following properties:

- (a) The material is much more soluble at higher temperatures than it is at room temperature or below.
- (b) Well-formed (but not large) crystals are produced.
- (c) Impurities are either very soluble or only sparingly soluble.
- (d) The solvent must be readily removed from the purified material.
- (e) There must be no reaction between the solvent and the substance being purified.
- (f) The solvent must not be inconveniently volatile or too highly flammable. (These are reasons
- why diethyl ether and carbon disulfide are not commonly used in this way.)

The following generalisations provide a rough guide to the selection of a suitable solvent:

(a) Substances usually dissolve best in solvents to which they are most closely related in chemical and physical characteristics. Thus, hydroxylic compounds are likely to be most soluble in water, methanol, ethanol, acetic acid or acetone. Similarly, petroleum ether might be used with water-insoluble substances. However, if the resemblance is too close, solubilities may become excessive.

(b) Higher members of homologous series approximate more and more closely to their parent hydrocarbon.

(c) Polar substances are more soluble in polar, than in non-polar, solvents.

Although Chapters 4, 5 and 6 provide details of the solvents used for recrystallising a large portion of commercially available laboratory chemicals, they cannot hope to be exhaustive, nor need they necessarily be the best choice. In other cases where it is desirable to use this process, it is necessary to establish whether a given solvent is suitable. This is usually done by taking only a small amount of material in a small test-tube and adding enough solvent to cover it. If it dissolves readily in the cold or on gentle warming, the solvent is unsuitable. Conversely, if it remains insoluble when the solvent is heated to boiling (adding more solvent if necessary), the solvent is again unsuitable. If the material dissolves in the hot solvent but does not crystallise readily within several minutes of cooling in an ice-salt mixture, another solvent should be tried.

**Petroleum ethers** are commercially available fractions of refined petroleum and are sold in fractions with about 20° boiling ranges. This ensures that little of the hydrocarbon ingredients boiling below the range is lost during standing or boiling when recrystallising a substance. Petroleum ethers with boiling ranges (at 760mm pressure) of  $35-60^\circ$ ,  $40-60^\circ$ ,  $60-80^\circ$ ,  $80-100^\circ$ , and  $100-120^\circ$  are generally free from unsaturated and aromatic hydrocarbons. The lowest boiling petroleum ether commercially available has b  $30-40^\circ/760$ mm and is mostly *n*-pentane. The purer spectroscopic grades are almost completely free from olefinic and aromatic hydrocarbons. Petroleum spirit (which is sometimes used synonymously with petroleum ether or light

petroleum) is usually less refined petroleum, and *ligroin* is used for fractions boiling above 100°. The lower boiling fractions consist of mixtures of *n*-pentane (**b** 36°), *n*-hexane (**b** 68.5°) and *n*-heptane (**b** 98°), and some of their isomers in varying proportions. For purification of petroleum ether b 35-60° see p. 324.

Solvents commonly used for recrystallisation, and their boiling points, are given in Table 7. For comments on the toxicity and use of **benzene** see the first pages of Chapters 4, 5 and 6.

**Mixed Solvents.** Where a substance is too soluble in one solvent and too insoluble in another, for either to be used for recrystallisation, it is often possible (provided they are miscible) to use them as a mixed solvent. (In general, however, it is preferable to use a single solvent if this is practicable.) Table 8 contains many of the common pairs of miscible solvents.

The technique of recrystallisation from mixed solvents is as follows:

The material is dissolved in the solvent in which it is the more soluble, then the other solvent (heated to near boiling) is added cautiously to the hot solution until a slight turbidity persists or crystallisation begins. This is cleared by adding several drops of the first solvent, and the solution is allowed to cool and crystallise in the usual way.

A variation of this procedure is simply to precipitate the material in a microcrystalline form from solution in one solvent at room temperature, by adding a little more of the second solvent, filtering off the crystals, adding a little more of the second solvent and repeating the process. This ensures, at least in the first or last precipitation, a material which contains as little as possible of the impurities, which may also be precipitated in this way. With salts, the first solvent is commonly water, and the second solvent is alcohol or acetone.

**Recrystallisation from the melt.** A crystalline solid melts when its temperature is raised sufficiently for the thermal agitation of its molecules or ions to overcome the restraints imposed by the crystal lattice. Usually, impurities weaken crystal structures, and hence lower the melting points of solids (or the freezing points of liquids). If an impure material is melted and cooled slowly (with the addition, if necessary, of a trace of solid material near the freezing point to avoid supercooling), the first crystals that form will usually contain less of the impurity, so that fractional solidification by partial freezing can be used as a purification process for solids with melting points lying in a convenient temperature range (or for more readily frozen liquids). Some examples of cooling baths that are useful in recrystallisation are summarised in Table 9. In some cases, impurities form higher melting eutectics with substances to be purified, so that the first material to solidify is less pure than the melt. For this reason, it is often desirable to discard the first crystals and also the final portions of the melt. Substances having similar boiling points often differ much more in melting points, so that fractional solidification can offer real advantages, especially where ultrapurity is sought. For further information on this method of recrystallisation, consult the earlier editions of this book as well as references by Schwab and Wichers (*J Res Nat Bur Stand* 25 747 1940). This method works best if the material is already nearly pure, and hence tends to be a final purification step.

Zone refining. Zone refining (or zone melting) is a particular development for fractional solidification and is applicable to all crystalline substances that show differences in the concentrations of impurities in liquid and solid states at solidification. The apparatus used in this technique consists essentially of a device in which the crystalline solid to be purified is placed in a glass tube (set vertically) which is made to move slowly upwards while it passes through a fixed coil (one or two turns) of heated wire. A narrow zone of molten crystals is formed when the tube is close to the heated coil. As the zone moves away from the coil the liquid crystallises, and a fresh molten zone is formed below it at the coil position. The machine can be set to recycle repeatedly. At its advancing side, the zone has a melting interface with the impure material whereas on the upper surface of the zone there is a constantly growing face of higher-melting, resolidified material. This leads to a progressive increase in impurity in the liquid phase which, at the end of the run, is discarded from the bottom of the tube. Also, because of the progressive increase in impurity. For this reason, it is usually necessary to make several zone-melting runs before a sample is satisfactorily purified. This is also why the method works most successfully if the material is already fairly pure. In all these operations the zone must travel slowly enough to enable impurities to diffuse or be convected away from the area where resolidification is occurring.

The technique finds commercial application in the production of metals of extremely high purity (impurities down to  $10^{-9}$  ppm), in purifying refractory oxides, and in purifying organic compounds, using commercially available equipment. Criteria for indicating that definite purification is achieved include elevation of melting point, removal of colour, fluorescence or smell, and a lowering of electrical conductivity. Difficulties likely to be found with organic compounds, especially those of low melting points and low rates of crystallisation, are supercooling and, because of surface tension and contraction, the tendency of the molten zone to seep back into the recrystallised areas. The method is likely to be useful in cases where fractional distillation is not practicable, either because of

unfavourable vapour pressures or ease of decomposition, or where super-pure materials are required. It has been used for the latter purpose for purifying anthracene, benzoic acid, chrysene, morphine, 1,8-naphthyridine and pyrene to name a few. [See E.F.G.Herington, *Zone Melting of Organic Compounds*, Wiley & Sons, NY, 1963; W.Pfann, *Zone Melting*, 2nd edn, Wiley, NY, 1966; H.Schildknecht, *Zonenschmelzen*, Verlag Chemie, Weinheim, 1964; W.R.Wilcox, R.Friedenberg et al. *Chem Rev* 64 187 1964; M.Zief and W.R.Wilcox (Eds), *Fractional Solidification*, Vol I, M Dekker Inc. NY, 1967.]

### **SUBLIMATION**

Sublimation differs from ordinary distillation because the vapour condenses to a solid instead of a liquid. Usually, the pressure in the heated system is diminished by pumping, and the vapour is condensed (after travelling a relatively short distance) onto a cold finger or some other cooled surface. This technique, which is applicable to many organic solids, can also be used with inorganic solids such as aluminium chloride, ammonium chloride, arsenious oxide and iodine. In some cases, passage of a stream of inert gas over the heated substance secures adequate vaporisation. This procedure has the added advantage of removing occluded solvent used in recrystallising the solid.

### **CHROMATOGRAPHY**

Chromatography is often used with advantage for the purification of small amounts of complex organic mixtures. Chromatography techniques all rely on the differential distribution of the various components in a mixture between the mobile phase and the stationary phase. The mobile phase can either be a gas or a liquid whereas the stationary phase can either be a solid or a liquid.

The major chromatographic techniques can also be categorised according to the nature of the mobile phase used - vapour phase chromatography for when a gas is the mobile phase and liquid chromatography for when a liquid is the mobile phase.

A very useful catalog for chromatographic products and information relating to chromatography (from gas chromatography to biochromatography) is that produced by Merck, called the ChromBook and the associated compact disk, ChromCircle.

### Vapour phase chromatography (GC or gas-liquid chromatography)

The mobile phase in vapour phase chromatography is a gas (e.g. hydrogen, helium, nitrogen or argon) and the stationary phase is a non-volatile liquid impregnated onto a porous material. The mixture to be purified is injected into a heated inlet whereby it is vaporised and taken into the column by the carrier gas. It is separated into its components by partition between the liquid on the porous support and the gas. For this reason vapour-phase chromatography is sometimes referred to as gas-liquid chromatography (g.l.c). Vapour phase chromatography is very useful in the resolution of a mixture of volatile compounds. This type of chromatography uses either packed or capillary columns. Packed columns have internal diameters of 3-5 mm with lengths of 2-6 m. These columns can be packed with a range of materials including firebrick derived materials (chromasorb P, for separation of non polar hydrocarbons) or diatomaceous earth (chromasorb W, for separation of more polar molecules such as acids, amines). Capillary columns have stationary phase bonded to the walls of long capillary tubes. The diameters in capillary columns are less than 0.5 mm and the lengths of these columns can go up to 50 m! These columns have much superior separating powers than the packed columns. Elution times for equivalent resolutions with packed columns can be up to ten times shorter. It is believed that almost any mixture of compounds can be separated using one of the four stationary phases, OV-101, SE-30, OV-17 and Carbowax-20M. The use of capillary columns in gas chromatography for analysis is now routinely carried out. An extensive range of packed and capillary columns is available from chromatographic specialists such as Supelco, Alltech, Hewlett-Packard, Phenomenex etc.

Table 10 shows some typical liquids used for stationary phases in gas chromatography.

Although vapour gas chromatography is routinely used for the analysis of mixtures, this form of chromatography can also be used for separation/purification of substances. This is known as preparative GC. In preparative GC, suitable packed columns are used and as substances emerge from the column, they are collected by condensing the vapour of these separated substances in suitable traps. The carrier gas blows the vapour through these traps hence these traps have to be very efficient. Improved collection of the effluent vaporised fractions in preparative work is attained by strong cooling, increasing the surface of the traps by packing them with glass wool, and by applying an electrical potential which neutralises the charged vapour and causes it to condense.

When the gas chromatograph is attached to a mass spectrometer, a very powerful analytical tool (gas chromatography-mass spectrometry; GC-MS) is produced. Vapour gas chromatography allows the analyses of mixtures but does not allow the definitive identification of unknown substances whereas mass spectrometry is good for the identification of a single compound but is less than ideal for the identification of mixtures of

compounds. This means that with GC-MS, both separation *and* identification of substances in mixtures can be achieved. Because of the relatively small amounts of material required for mass spectrometry, a splitting system is inserted between the column and the mass spectrometer. This enables only a small fraction of the effluent to enter the spectrometer, the rest of the effluent is usually collected or vented to the air.

#### Liquid chromatography

In contrast to vapour phase chromatography, the mobile phase in liquid chromatography is a liquid. In general, there are four main types of liquid chromatography: *adsorption*, *partition*, *ion-chromatography*, and *gel filtration*.

Adsorption chromatography is based on the difference in the extent to which substances in solution are adsorbed onto a suitable surface. The main techniques in adsorption chromatography are TLC (Thin Layer Chromatography), paper and column chromatography.

Thin layer chromatography (TLC). In thin layer chromatography, the mobile phase i.e. the solvent, creeps up the stationary phase (the absorbent) by capillary action. The adsorbent (e.g. silica, alumina, cellulose) is spread on a rectangular glass plate (or solid inert plastic sheet or aluminium foil). Some adsorbents (e.g. silica) are mixed with a setting material (e.g. CaSO<sub>4</sub>) by the manufacturers which causes the film to set hard on drying. The adsorbent can be activated by heating at 100-110° for a few hours. Other adsorbents (e.g. celluloses) adhere on glass plates without a setting agent. Thus some grades of absorbents have prefixes e.g. prefix G means that the absorbent can cling to a glass plate and is used for TLC (e.g. silica gel GF254 is for TLC plates which have a dye that fluoresces under 254nm UV light). Those lacking this binder have the letter H after any coding and is suitable for column chromatography e.g. silica gel 60H. The materials to be purified or separated are spotted in a solvent close to the lower end of the plate and allowed to dry. The spots will need to be placed at such a distance so as to ensure that when the lower end of the plate is immersed in the solvent, the spots are a few mm above the eluting solvent. The plate is placed upright in a tank containing the eluting solvent. Elution is carried out in a closed tank to ensure equilibrium. Good separations can be achieved with square plates if a second elution is performed at right angles to the first using a second solvent system. For rapid work, plates of the size of microscopic slides or even smaller are used which can decrease the elution time and cost without loss of resolution. The advantage of plastic backed and aluminium foil backed plates is that the size of the plate can be made as required by cutting the sheet with scissors or a sharp guillotine. Visualisation of substances on TLC can be carried out using UV light if they are UV absorbing or fluorescing substances or by spraying or dipping the plate with a reagent that gives coloured products with the substance (e.g. iodine solution or vapour gives brown colours with amines), or with dilute sulfuric acid (organic compounds become coloured or black when the plates are heated at 100° if the plates are of alumina or silica, but not cellulose). (see Table 11 for some methods of visualisation.) Some alumina and silica powders are available with fluorescent materials in them, in which case the whole plate fluoresces under UV light. Non-fluorescing spots are thus clearly visible, and fluorescent spots invariably fluoresce with a different colour. The colour of the spots can be different under UV light at 254nm and at 365nm. Another useful way of showing up non-UV absorbing spots is to spray the plate with a 1-2% solution of Rhodamine 6G in acetone. Under UV light the dye fluoresces and reveals the non-fluorescing spots. For preparative work, if the material in the spot or fraction is soluble in ether or petroleum ether, the desired substance can be extracted from the absorbent with these solvents which leave the water soluble dye behind.

TLC can be used as an analytical technique, or as a guide to establishing conditions for column chromatography or as a preparative technique in its own right.

The thickness of the absorbent on the TLC plates could be between 0.2mm to 2mm or more. In preparative work, the thicker plates are used and hundreds of milligrams of mixtures can be purified conveniently and quickly. The spots or areas are easily scraped off the plates and the desired substances extracted from the absorbent with the required solvent. For preparative TLC, non destructive methods for visualising spots and fractions are required. As such, the use of UV light is very useful. If substances are not UV active, then a small section of the plate (usually the right or left edge of the plate) is sprayed with a visualising agent while the remainder of the plate is kept covered.

Thin layer chromatography has been used successfully with ion-exchange celluloses as stationary phases and various aqueous buffers as mobile phases. Also, gels (e.g. Sephadex G-50 to G-200 superfine) have been adsorbed on glass plates and are good for fractionating substances of high molecular weights (1500 to 250,000). With this technique, which is called *thin layer gel filtration* (TLG), molecular weights of proteins can be determined when suitable markers of known molecular weights are run alongside (see Chapter 6).

Commercially available pre-coated plates with a variety of adsorbents are generally very good for quantitative work because they are of a standard quality. Plates of a standardised silica gel 60 (as medium porosity silica gel with a mean porosity of 6mm) released by Merck have a specific surface of 500 m<sup>2</sup>/g and a specific pore volume of 0.75 mL/g. They are so efficient that they have been called *high performance thin layer chromatography* (HPTLC) plates (Ropphahn and Halpap J Chromatogr 112 81 1975). In another variant of thin layer chromatography the

adsorbent is coated with an oil as in gas chromatography thus producing *reverse-phase thin layer chromatography*. Reversed-phase TLC plates e.g. silica gel RP-18 are available from Fluka and Merck.

A very efficient form of chromatography makes use of a circular glass plate (rotor) coated with an adsorbent (silica, alumina or cellulose). As binding to a rotor is needed, the sorbents used may be of a special quality and/or binders are added to the sorbent mixtures. For example when silica gel is required as the absorbent, silica gel 60 PF-254 with calcium sulfate (Merck catalog 7749) is used. The thickness of the absorbent (1, 2 or 4 mm) can vary depending on the amount of material to be separated. The apparatus is called a **Chromatotron** (available from Harrison Research, USA). The glass plate is rotated by a motor, and the sample followed by the eluting solvent is allowed to drip onto a central position on the plate. As the plate rotates the solvent elutes the mixture, centrifugally, while separating the components in the form of circular bands radiating from the central point. The separated bands are usually visualised conveniently by UV and as the bands approach the edge of the plate, the eluent is collected. The plate with the adsorbent can be re-used many times if care is employed in the usage, and hence this form of chromatography utilises less absorbents as well as solvents.

Recipes and instructions for coating the rotors are available from the Harrison website (http://pwl.netcom.com/~ithres/harrisonresearch.html). In addition, information on how to regenerate the sorbents and binders are also included.

Paper chromatography. This is the technique from which thin layer chromatography developed. It uses cellulose paper (filter paper) instead of the TLC adsorbent and does not require a backing like the plastic sheet in TLC. It is used in the **ascending procedure** (like in TLC) whereby a sheet of paper is hung in a jar, the materials to be separated are spotted (after dissolving in a suitable solvent and drying) near the bottom of the sheet which dips into the eluting solvent just below the spot. As the solvent rises up the paper the spots are separated according to their adsorption properties. A variety of solvents can be used, the sheet is then dried in air (fume cupboard), and can then be run again with the solvent running at right angles to the first run to give a two dimensional separation. The spots can then be visualised as in TLC or can be cut out and analysed as required. A **descending procedure** had also been developed where the material to be separated is spotted near the top of the paper and the top end is made to dip into a tray containing the eluting solvent. The whole paper is placed in a glass jar and the solvent then runs down the paper causing the materials in the spots to separate also according to their adsorption properties and to the eluting ability of the solvent. This technique is much cheaper than TLC and is still used (albeit with thicker cellulose paper) with considerable success for the separation of protein hydrolysates for sequencing analysis and/or protein identification.

Column Chromatography. The substances to be purified are usually placed on the top of the column and the solvent is run down the column. Fractions are collected and checked for compounds using TLC (UV and/or other means of visualisation). The adsorbent for chromatography can be packed dry and solvents to be used for chromatography are used to equilibrate the adsorbent by flushing the column several times until equilibration is achieved. Alternatively, the column containing the adsorbent is packed wet (slurry method) and pressure is applied at the top of the column until the column is well packed (i.e. the adsorbent is settled).

Graded Adsorbents and Solvents. Materials used in columns for adsorption chromatography are grouped in Table 12 in an approximate order of effectiveness. Other adsorbents sometimes used include barium carbonate, calcium sulfate, calcium phosphate, charcoal (usually mixed with Kieselguhr or other form of diatomaceous earth, for example, the filter aid Celite) and cellulose. The alumina can be prepared in several grades of activity (see below).

In most cases, adsorption takes place most readily from non-polar solvents, such as petroleum ether and least readily from polar solvents such as alcohols, esters, and acetic acid. Common solvents, arranged in approximate order of increasing eluting ability are also given in Table 12. Eluting power roughly parallels the dielectric constants of solvents. The series also reflects the extent to which the solvent binds to the column material, thereby displacing the substances that are already adsorbed. This preference of alumina and silica gel for polar molecules explains, for example, the use of percolation through a column of silica gel for the following purposes-drying of ethylbenzene, removal of aromatics from 2,4-dimethylpentane and of ultraviolet absorbing substances from cyclohexane.

Mixed solvents are intermediate in strength, and so provide a finely graded series. In choosing a solvent for use as an eluent it is necessary to consider the solubility of the substance in it, and the ease with which it can subsequently be removed.

**Preparation and Standardisation of Alumina.** The activity of alumina depends inversely on its water content, and a sample of poorly active material can be rendered more active by leaving for some time in a round bottomed flask heated up to about 200° in an oil bath or a heating mantle while a slow stream of a dry inert gas is passed through it. Alternatively, it is heated to red heat (380-400°) in an open vessel for 4-6h with

occasional stirring and then cooled in a vacuum desiccator: this material is then of grade I activity. Conversely, alumina can be rendered less active by adding small amounts of water and thoroughly mixing for several hours. Addition of about 3% (w/w) of water converts grade I alumina to grade II.

Used alumina can be regenerated by repeated extraction, first with boiling methanol, then with boiling water, followed by drying and heating. The degree of activity of the material can be expressed conveniently in terms of the scale due to Brockmann and Schodder (*Chem Ber B* 74 73 1941).

Alumina is normally slightly alkaline. A (less strongly adsorbing) neutral alumina can be prepared by making a slurry in water and adding 2M hydrochloric acid until the solution is acid to Congo red. The alumina is then filtered off, washed with distilled water until the wash water gives only a weak violet colour with Congo red paper, and dried.

Alumina used in TLC can be recovered by washing in ethanol for 48h with occasional stirring, to remove binder material and then washed with successive portions of ethyl acetate, acetone and finally with distilled water. Fine particles are removed by siphoning. The alumina is first suspended in 0.04M acetic acid, then in distilled water, siphoning off 30 minutes after each wash. The process is repeated 7-8 times. It is then dried and activated at 200° [Vogh and Thomson Anal Chem 53 1365 1981].

## Preparation of other adsorbents

Silica gel can be prepared from commercial water-glass by diluting it with water to a density of 1.19 and, while keeping it cooled to 5°, adding concentrated hydrochloric acid with stirring until the solution is acid to thymol blue. After standing for 3h, the precipitate is filtered off, washed on a Büchner funnel with distilled water, then suspended in 0.2M hydrochloric acid. The suspension is set aside for 2-3 days, with occasional stirring, then filtered, washed well with water and dried at 110°. It can be activated by heating up to about 200° as described for alumina.

Powdered commercial silica gel can be purified by suspending and standing overnight in concentrated hydrochloric acid (6mL/g), decanting the supernatant and repeating with fresh acid until the latter remains colourless. After filtering with suction on a sintered-glass funnel, the residue is suspended in water and washed by decantation until free of chloride ions. It is then filtered, suspended in 95% ethanol, filtered again and washed on the filter with 95% ethanol. The process is repeated with anhydrous diethyl ether before the gel is heated for 24h at 100° and stored for another 24h in a vacuum desiccator over phosphorus pentoxide.

To buffer silica gel for flash chromatography (see later), 200g of silica is stirred in 1L of  $0.2M \text{ NaH}_2\text{PO}_4$  for 30 minutes. The slurry is then filtered with suction using a sintered glass funnel. The silica gel is then activated at 110°C for 16 hours. The pH of the resulting silica gel is ~4. Similar procedures can be utilized to buffer the pH of the silica gel at various pHs (up to pH ~8: pH higher than this causes degradation of silica) using appropriate phosphate buffers.

Commercial silica gel has also been purified by suspension of 200g in 2L of 0.04M ammonia, allowed to stand for 5min before siphoning off the supernatant. The procedure was repeated 3-4 times, before rinsing with distilled water and drying, and activating the silica gel in an oven at 110° [Vogh and Thomson, Anal Chem 53 1345 1981].

Although silica gel is not routinely recycled after use (due to fear of contamination as well as the possibility of reduced activity), the costs of using new silica gel for purification may be prohibitive. In these cases, recycling may be achieved by stirring the used silica gel (1 kg) in a mixture of methanol and water (2L MeOH/4L water) for 30-40 mins. The silica gel is filtered (as described above) and reactivated at 110°C for 16 hours.

Diatomaceous earth (Celite 535 or 545, Hyflo Super-cel, Dicalite, Kieselguhr) is purified before use by washing with 3M hydrochloric acid, then water, or it is made into a slurry with hot water, filtered at the pump and washed with water at 50° until the filtrate is no longer alkaline to litmus. Organic materials can be removed by repeated extraction at 50° with methanol or chloroform, followed by washing with methanol, filtering and drying at 90-100°.

*Charcoal* is generally satisfactorily activated by heating gently to red heat in a crucible or quartz beaker in a muffle furnace, finally allowing to cool under an inert atmosphere in a desiccator. Good commercial activated charcoal is made from wood, e.g. *Norit* (from Birch wood), *Darco* and *Nuchar*. If the cost is important then the cheaper *animal charcoal* (bone charcoal) can be used. However, this charcoal contains calcium phosphate and other calcium salts and cannot be used with acidic materials. In this case the charcoal is boiled with dilute hydrochloric acid (1:1 by volume) for 2-3h, diluted with distilled water and filtered through a fine grade paper on a Büchner flask, washed with distilled water until the filtrate is almost neutral, and dried first in air then in a vacuum, and activated as above. To improve the porosity, charcoal columns are usually prepared in admixture with diatomaceous earth.

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Cellulose for chromatography is purified by sequential washing with chloroform, ethanol, water, ethanol, chloroform and acetone. More extensive purification uses aqueous ammonia, water, hydrochloric acid, water, acetone and diethyl ether, followed by drying in a vacuum. Trace metals can be removed from filter paper by washing for several hours with 0.1M oxalic or citric acid, followed by repeated washing with distilled water.

#### Flash Chromatography

A faster method of separating components of a mixture is flash chromatography (see Still et al. J Org Chem 43 2923 1978). In flash chromatography the eluent flows through the column under a pressure of  $ca \ 1$  to 4 atmospheres. The lower end of the chromatographic column has a relatively long taper closed with a tap. The upper end of the column is connected through a ball joint to a tap. Alternatively a specially designed chromatographic column with a solvent reservoir can also be used (for an example, see the Aldrich Chemical Catalog-glassware section). The tapered portion is plugged with cotton, or quartz, wool and ca 1 cm of fine washed sand (the latter is optional). The adsorbent is then placed in the column as a dry powder or as a slurry in a solvent and allowed to fill to about one third of the column. A fine grade of adsorbent is required in order to slow the flow rate at the higher pressure, e.g. Silica 60, 230 to 400 mesh with particle size 0.040-0.063mm (from Merck). The top of the adsorbent is layered with ca 1 cm of fine washed sand. The mixture in the smallest volume of solvent is applied at the top of the column and allowed to flow into the adsorbent under gravity by opening the lower tap momentarily. The top of the column is filled with eluent, the upper tap is connected by a tube to a nitrogen supply from a cylinder, or to compressed air, and turned on to the desired pressure (monitor with a gauge). The lower tap is turned on and fractions are collected rapidly until the level of eluent has reached the top of the adsorbent (do not allow the column to run dry). If further elution is desired then both taps are turned off, the column is filled with more eluting solvent and the process repeated. The top of the column can be modified so that gradient elution can be performed. Alternatively, an apparatus for producing the gradient is connected to the upper tap by a long tube and placed high above the column in order to produce the required hydrostatic pressure. Flash chromatography is more efficient and gives higher resolution than conventional chromatography at atmospheric pressure and is completed in a relatively shorter time. A successful separation of components of a mixture by TLC using the same adsorbent is a good indication that flash chromatography will give the desired separation on a larger scale.

#### Paired-ion Chromatography (PIC)

Mixtures containing ionic compounds (e.g. acids and/or bases), non-ionisable compounds, and zwitterions, can be separated successfully by paired-ion chromatography (PIC). It utilises the 'reverse-phase' technique (Eksberg and Schill Anal Chem 45 2092 1973). The stationary phase is lipophilic, such as  $\mu$ -BONDAPAK C<sub>18</sub> or any other adsorbent that is compatible with water. The mobile phase is water or aqueous methanol containing the acidic or basic counter ion. Thus the mobile phase consists of dilute solutions of strong acids (e.g. 5mM 1-heptanesulfonic acid) or strong bases (e.g. 5 mM tetrabutylammonium phosphate) that are completely ionised at the operating pH values which are usually between 2 and 8. An equilibrium is set up between the neutral species of a mixture in the stationary phase and the respective ionised (anion or cation) species which dissolve in the mobile phase containing the counter ions. The extent of the equilibrium will depend on the ionisation constants of the respective components of the mixture, and the solubility of the unionised species in the stationary phase. Since the ionisation constants and the solubility in the stationary phase will vary with the water-methanol ratio of the mobile phase, the separation may be improved by altering this ratio gradually (gradient elution) or stepwise. If the compounds are eluted too rapidly the water content of the mobile phase should be increased, e.g. by steps of 10%.

The application of pressure to the liquid phase in liquid chromatography generally increases the separation (see HPLC). Also in PIC improved efficiency of the column is observed if pressure is applied to the mobile phase (Wittmer, Nuessle and Haney Anal Chem 47 1422 1975).

## Ion-exchange Chromatography

Ion-exchange chromatography involves an electrostatic process which depends on the relative affinities of various types of ions for an immobilised assembly of ions of opposite charge. The stationary phase is an aqueous buffer with a fixed pH or an aqueous mixture of buffers in which the pH is continuously increased or decreased as the separation may require. This form of liquid chromatography can also be performed at high inlet pressures of liquid with increased column performances.

**Ion-exchange Resins.** An ion-exchange resin is made up of particles of an insoluble elastic hydrocarbon network to which is attached a large number of ionisable groups. Materials commonly used comprise synthetic ion-exchange resins made, for example, by crosslinking polystyrene to which has been attached non-

diffusible ionised or ionisable groups. Resins with relatively high crosslinkage (8-12%) are suitable for the chromatography of small ions, whereas those with low cross linkage (2-4%) are suitable for larger molecules. Applications to hydrophobic systems are possible using aqueous gels with phenyl groups bound to the rigid matrix (Phenyl-Superose/Sepharose, Pharmacia-Amersham Biosciences) or neopentyl chains (Alkyl-Superose, Pharmacia-Amersham Biosciences) or neopentyl chains (Alkyl-Superose, Pharmacia-Amersham Biosciences). (Superose is a cross-linked agarose-based medium with an almost uniform bead size.) These groups are further distinguishable as strong  $[-SO_2OH, -NR_3^+]$  or weak  $[-OH, -CO_2H, -PO(OH)_2, -NH_2]$ . Their charges are counterbalanced by diffusible ions, and the operation of a column depends on its ability and selectivity to replace these ions. The exchange that takes place is primarily an electrostatic process but adsorptive forces and hydrogen bonding can also be important. A typical sequence for the relative affinities of some common anions (and hence the inverse order in which they pass through such a column), is the following, obtained using a quaternary ammonium (strong base) anion-exchange column:

Fluoride < acetate < bicarbonate < hydroxide < formate < chloride < bromate < nitrite < cyanide < bromide < chromate < nitrate < iodide < thiocyanate < oxalate < sulfate < citrate.

For an amine (weak base) anion-exchange column in its chloride form, the following order has been observed:

Fluoride < chloride < bromide = iodide = acetate < molybdate < phosphate < arsenate < nitrate < tartrate < citrate < chromate < sulfate < hydroxide.

With strong cation-exchangers (e.g. with SO<sub>3</sub>H groups), the usual sequence is that polyvalent ions bind more firmly than mono- or di- valent ones, a typical series being as follows:

 $Th^{4+} > Fe^{3+} > Al^{3+} > Ba^{2+} > Pb^{2+} > Sr^{2+} > Ca^{2+} > Co^{2+} > Ni^{2+} = Cu^{2+} > Zn^{2+} = Mg^{2+} > UO_2^+ = Mn^{2+} > Ag^+ > Tl^+ > Cs^+ > Rb^+ > NH_4^+ = K^+ > Na^+ > H^+ > Li^+.$ 

Thus, if an aqueous solution of a sodium salt contaminated with heavy metals is passed through the sodium form of such a column, the heavy metal ions will be removed from the solution and will be replaced by sodium ions from the column. This effect is greatest in dilute solution. Passage of sufficiently strong solutions of alkali metal salts or mineral acids readily displaces all other cations from ion-exchange columns. (The regeneration of columns depends on this property.) However, when the cations lie well to the left in the above series it is often advantageous to use a complex-forming species to facilitate removal. For example, iron can be displaced from ionexchange columns by passage of sodium citrate or sodium ethylenediaminetetraacetate.

Some of the more common commercially available resins are listed in Table 13.

Ion-exchange resins swell in water to an extent which depends on the amount of crosslinking in the polymer, so that columns should be prepared from the wet material by adding it as a suspension in water to a tube already partially filled with water. (This also avoids trapping air bubbles.) The exchange capacity of a resin is commonly expressed as mg equiv./mL of wet resin. This quantity is pH-dependent for weak-acid or weak-base resins but is constant at about 0.6-2 for most strong-acid or strong-base types.

Apart from their obvious applications to inorganic species, sulfonic acid resins have been used in purifying amino acids, aminosugars, organic acids, peptides, purines, pyrimidines, nucleosides, nucleotides and polynucleotides. Thus, organic bases can be applied to the H<sup>+</sup> form of such resins by adsorbing them from neutral solution and, after washing with water, they are eluted sequentially with suitable buffer solutions or dilute acids. Alternatively, by passing alkali solution through the column, the bases will be displaced in an order that is governed by their pK values. Similarly, strong-base anion exchangers have been used for aldehydes and ketones (as bisulfite addition compounds), carbohydrates (as their borate complexes), nucleosides, nucleotides, organic acids, phosphate esters and uronic acids. Weakly acidic and weakly basic exchange resins have also found extensive applications, mainly in resolving weakly basic and acidic species. For demineralisation of solutions without large changes in pH, mixed-bed resins can be prepared by mixing a cation-exchange resin in its H<sup>+</sup> form with an anion-exchange resin in its OH<sup>-</sup> form. Commercial examples include Amberlite MB-1 (IR-120 + IRA-400) and Bio-Deminrolit (Zeo-Karb 225 and Zerolit FF). The latter is also available in a self-indicating form.

Ion-exchange Celluloses and Sephadex. A different type of ion-exchange column that finds extensive application in biochemistry for the purification of proteins, nucleic acids and acidic polysaccharides derives from cellulose by incorporating acidic and basic groups to give ion-exchangers of controlled acid and basic strengths. Commercially available cellulose-type resins are given in Tables 14 and 15. AG 501 x 8 (Bio-Rad) is a mixed-bed resin containing equivalents of AG 50W-x8 H<sup>+</sup> form and AG 1-x8 HO<sup>-</sup> form, and Bio-Rex MSZ 501 resin. A dye marker indicates when the resin is exhausted. Removal of unwanted cations, particularly of the transition metals, from amino acids and buffer can be achieved by passage of the solution through a column of Chelex 20 or Chelex 100. The metal-chelating abilities of the resin reside in the bonded iminodiacetate groups.

Chelex can be regenerated by washing in two bed volumes of 1M HCl, two bed volumes of 1M NaOH and five bed volumes of water.

Ion-exchange celluloses are available in different particle sizes. It is important that the amounts of 'fines' are kept to a minimum otherwise the flow of liquid through the column can be extremely slow to the point of no liquid flow. Celluloses with a large range of particle sizes should be freed from 'fines' before use. This is done by suspending the powder in the required buffer and allowing it to settle for one hour and then decanting the 'fines'. This separation appears to be wasteful but it is necessary for reasonable flow rates without applying high pressures at the top of the column. Good flow rates can be obtained if the cellulose column is packed dry whereby the 'fines' are evenly distributed throughout the column. Wet packing causes the 'fines' to rise to the top of the column, which thus becomes clogged.

Several ion-exchange celluloses require recycling before use, a process which must be applied for recovered celluloses. Recycling is done by stirring the cellulose with 0.1M aqueous sodium hydroxide, washing with water until neutral, then suspending in 0.1M hydrochloric acid and finally washing with water until neutral. When regenerating a column it is advisable to wash with a salt solution (containing the required counter ions) of increasing ionic strength up to 2M. The cellulose is then washed with water and recycled if necessary. Recycling can be carried out more than once if there are doubts about the purity of the cellulose and when the cellulose had been used previously for a different purification procedure than the one to be used. The basic matrix of these ion-exchangers is cellulose and it is important not to subject them to strong acid (> 1M) and strongly basic (> 1M) solutions.

When storing ion-exchange celluloses, or during prolonged usage, it is important to avoid growth of microorganisms or moulds which slowly destroy the cellulose. Good inhibitors of microorganisms are phenyl mercuric salts (0.001%, effective in weakly alkaline solutions), chlorohexidine (Hibitane at 0.002% for anion exchangers), 0.02% aqueous sodium azide or 0.005% of ethyl mercuric thiosalicylate (Merthiolate) are most effective in weakly acidic solutions for cation exchangers. Trichlorobutanol (Chloretone, at 0.05% is only effective in weakly acidic solutions) can be used for both anion and cation exchangers. Most organic solvents (e.g. methanol) are effective antimicrobial agents but only at high concentrations. These inhibitors must be removed by washing the columns thoroughly before use because they may have adverse effects on the material to be purified (e.g. inactivation of enzymes or other active preparations).

Sephadex. Other carbohydrate matrices such as Sephadex (based on dextran) have more uniform particle sizes. Their advantages over the celluloses include faster and more reproducible flow rates and they can be used directly without removal of 'fines'. Sephadex, which can also be obtained in a variety of ion-exchange forms (see Table 15) consists of beads of a cross-linked dextran gel which swells in water and aqueous salt solutions. The smaller the bead size, the higher the resolution that is possible but the slower the flow rate. Typical applications of Sephadex gels are the fractionation of mixtures of polypeptides, proteins, nucleic acids, polysaccharides and for desalting solutions.

Sephadex is a bead form of cross-linked dextran gel. Sepharose CL and Bio-Gel A are derived from agarose (see below). Sephadex ion-exchangers, unlike celluloses, are available in narrow ranges of particle sizes. These are of two medium types, the G-25 and G-50, and their dry bead diameter sizes are ca 50 to 150 microns. They are available as cation and anion exchange Sephadex. One of the disadvantages of using Sephadex ion-exchangers is that the bed volume can change considerably with alteration of pH. Ultragels also suffer from this disadvantage to a varying extent, but ion-exchangers of the bead type have been developed e.g. Fractogels, Toyopearl, which do not suffer from this disadvantage.

Sepharose (e.g. Sepharose CL and Bio-Gel A) is a bead form of agarose gel which is useful for the fractionation of high molecular weight substances, for molecular weight determinations of large molecules (molecular weight > 5000), and for the immobilisation of enzymes, antibodies, hormones and receptors usually for affinity chromatography applications.

In preparing any of the above for use in columns, the dry powder is evacuated, then mixed under reduced pressure with water or the appropriate buffer solution. Alternatively it is stirred gently with the solution until all air bubbles are removed. Because some of the wet powders change volumes reversibly with alteration of pH or ionic strength (see above), it is imperative to make allowances when packing columns (see above) in order to avoid overflowing of packing when the pH or salt concentrations are altered.

Cellex CM ion-exchange cellulose can be purified by treatment of 30-40g (dry weight) with 500mL of 1mM cysteine hydrochloride. It is then filtered through a Büchner funnel and the filter cake is suspended in 500mL of 0.05M NaCl/0.5M NaOH. This is filtered and the filter cake is resuspended in 500ml of distilled water and filtered again. The process is repeated until the washings are free from chloride ions. The filter cake is again suspended in 500mL of 0.01M buffer at the desired pH for chromatography, filtered, and the last step repeated several times.

Cellex D and other anionic celluloses are washed with 0.25M NaCl/0.25M NaOH solution, then twice with deionised water. This is followed with 0.25M NaCl and then washed with water until chloride-free. The Cellex is then equilibrated with the desired buffer as above.

*Crystalline Hydroxylapatite* is a structurally organised, highly polar material which, in aqueous solution (in buffers) strongly adsorbs macromolecules such as proteins and nucleic acids, permitting their separation by virtue of the interaction with charged phosphate groups and calcium ions, as well by physical adsorption. The procedure therefore is not entirely ion-exchange in nature. Chromatographic separations of singly and doubly stranded DNA are readily achievable whereas there is negligible adsorption of low molecular weight species.

### **Gel Filtration**

The gel-like, bead nature of wet Sephadex enables small molecules such as inorganic salts to diffuse freely into it while, at the same time, protein molecules are unable to do so. Hence, passage through a Sephadex column can be used for complete removal of salts from protein solutions. Polysaccharides can be freed from monosaccharides and other small molecules because of their differential retardation. Similarly, amino acids can be separated from proteins and large peptides.

Gel filtration using Sephadex G-types (50 to 200) is essentially useful for fractionation of large molecules with molecular weights above 1000. For Superose, the range is given as 5000 to  $5 \times 10^6$ . Fractionation of lower molecular weight solutes (e,g, ethylene glycols, benzyl alcohols) can now be achieved with Sephadex G-10 (up to Mol.Wt 700) and G-25 (up to Mol.Wt 1500). These dextrans are used only in aqueous solutions. In contrast, Sephadex LH-20 and LH-60 (prepared by hydroxypropylation of Sephadex) are used for the separation of small molecules (Mol.Wt less than 500) using most of the common organic solvents as well as water.

Sephasorb HP (ultrafine, prepared by hydroxypropylation of crossed-linked dextran) can also be used for the separation of small molecules in organic solvents and water, and in addition it can withstand pressures up to 1400 psi making it useful in HPLC. These gels are best operated at pH values between 2 and 12, because solutions with high and low pH values slowly decompose them (see further in Chapter 6).

#### High Performance Liquid Chromatography (HPLC)

When pressure is applied at the inlet of a liquid chromatographic column the performance of the column can be increased by several orders of magnitude. This is partly because of the increased speed at which the liquid flows through the column and partly because fine column packings which have larger surface areas can be used. Because of the improved efficiency of the columns, this technique has been referred to as high performance, high pressure, or high speed liquid chromatography and has found great importance in chemistry and biochemistry.

The equipment consists of a hydraulic system to provide the pressure at the inlet of the column, a column, a detector, data storage and output, usually in the form of a computer. The pressures used in HPLC vary from a few psi to 4000-5000 psi. The most convenient pressures are, however, between 500 and 1800psi. The plumbing is made of stainless steel or non-corrosive metal tubing to withstand high pressures. Plastic tubing and connectors are used for low pressures, e.g. up to ~500psi. Increase of temperature has a very small effect on the performance of a column in liquid chromatography. Small variations in temperatures, however, do upset the equilibrium of the column, hence it is advisable to place the column in an oven at ambient temperature in order to achieve reproducibility. The packing (stationary phase) is specially prepared for withstanding high pressures. It may be an adsorbent (for adsorption or solid-liquid HPLC), a material impregnated with a high boiling liquid (e.g. octadecyl sulfate, in reverse-phase or liquid-liquid or paired-ion HPLC), an ion-exchange material (in ion-exchange HPLC), or a highly porous non-ionic gel (for high performance gel filtration). The mobile phase is water, aqueous buffers, salt solutions, organic solvents or mixtures of these. The more commonly used detectors have UV, visible, diode array or fluorescence monitoring for light absorbing substances, and refractive index monitoring and evaporative light scattering for transparent compounds. UV detection is not useful when molecules do not have UV absorbing chromophores and solvents for elution should be carefully selected when UV monitoring is used so as to ensure the lack of interference in detection. The sensitivity of the refractive index monitoring is usually lower than the light absorbing monitoring by a factor of ten or more. It is also difficult to use a refractive index monitoring system with gradient elution of solvents. When substances have readily oxidised and reduced forms, e.g. phenols, nitro compounds, heterocyclic compounds etc, then electrochemical detectors are useful. These detectors oxidise and reduce these substances and make use of this process to provide a peak on the recorder.

The cells of the monitoring devices are very small ( $ca 5 \mu l$ ) and the detection is very good. The volumes of the analytical columns are quite small (ca 2mL for a 1 metre column) hence the result of an analysis is achieved very quickly. Larger columns have been used for preparative work and can be used with the same equipment. Most

machines have solvent mixing chambers for solvent gradient or ion gradient elution. The solvent gradient (for two solvents) or pH or ion gradient can be adjusted in a linear, increasing or decreasing exponential manner.

In general two different types of HPLC columns are available. Prepacked columns are those with metal casings with threads at both ends onto which capillary connections are attached. The cartridge HPLC columns are cheaper and are used with cartridge holders. As the cartridge is fitted with a groove for the holding device, no threads are necessary and the connection pieces can be reused. A large range of HPLC columns (including guard columns, i.e. small pre-columns) are available from Alltech, Supelco (see www.sigmaaldrich.com), Waters (www.waters.com), Agilent Technologies (www.chem.agilent.com), Phenomenex (www.phenomenex.com), YMC (www.ymc.co.jp/en/), Merck (www.merck.de), SGE (www.sge.com) and other leading companies. Included in this range of columns are also columns with chiral bonded phases capable of separating enantiomeric mixtures, such as Chiralpak AS and Chirex<sup>™</sup> columns (e.g. from Restek-www.restekcorp.com, Daicel-www.daicel.co.jp/ indexe.html).

HPLC systems coupled to mass spectrometers (LC-MS) are extremely important methods for the separation and identification of substances. If not for the costs involved in LC-MS, these systems would be more commonly found in research laboratories.

## Other Types of Liquid Chromatography

New stationary phases for specific purposes in chromatographic separation are being continually proposed. *Charge transfer adsorption chromatography* makes use of a stationary phase which contains immobilised aromatic compounds and permits the separation of aromatic compounds by virtue of the ability to form charge transfer complexes (sometimes coloured) with the stationary phase. The separation is caused by the differences in stability of these complexes (Porath and Dahlgren-Caldwell *J Chromatogr* 133 180 1977).

In metal chelate adsorption chromatography a metal is immobilised by partial chelation on a column which contains bi- or tri- dentate ligands. Its application is in the separation of substances which can complex with the bound metals and depends on the stability constants of the various ligands (Porath, Carlsson, Olsson and Belfrage Nature 258 598 1975; Loennerdal, Carlsson and Porath FEBS Lett 75 89 1977).

An application of chromatography which has found extensive use in biochemistry and has brought a new dimension in the purification of enzymes is *affinity chromatography*. A specific enzyme inhibitor is attached by covalent bonding to a stationary phase (e.g. AH-Sepharose 4B for acidic inhibitors and CH-Sepharose 4B for basic inhibitors), and will strongly bind only the specific enzyme which is inhibited, allowing all other proteins to flow through the column. The enzyme is then eluted with a solution of high ionic strength (e.g. 1M sodium chloride) or a solution containing a substrate or reversible inhibitor of the specific enzyme. (The ionic medium can be removed by gel filtration using a mixed-bed gel.) Similarly, an immobilised lectin may interact with the carbohydrate moiety of a glycoprotein. The most frequently used matrixes are cross-linked (4-6%) agarose and polyacrylamide gel. Many adsorbents are commercially available for nucleotides, coenzymes and vitamins, amino acids, peptides, lectins and related macromolecules and immunoglobulins. Considerable purification can be achieved by one passage through the column and the column can be reused several times.

The affinity method may be *biospecific*, for example as an antibody-antigen interaction, or chemical as in the chelation of boronate by *cis*-diols, or of unknown origin as in the binding of certain dyes to albumin and other proteins.

Hydrophobic adsorption chromatography takes advantage of the hydrophobic properties of substances to be separated and has also found use in biochemistry (Hoftsee Biochem Biophys Res Commun 50 751 1973; Jennissen and Heilmayer Jr Biochemistry 14 754 1975). Specific covalent binding with the stationary phase, a procedure that was called covalent chromatography, has been used for separation of compounds and for immobilising enzymes on a support: the column was then used to carry out specific bioorganic reactions (Mosbach Method Enzymol 44 1976; A.Rosevear, J.F.Kennedy and J.M.S.Cabral, Immobilised Enzymes and Cells: A Laboratory Manual, Adam Hilger, Bristol, 1987, ISBN 085274515X).

#### DRYING

#### **Removal of Solvents**

Where substances are sufficiently stable, removal of solvent from recrystallised materials presents no problems. The crystals, after filtering at the pump (and perhaps air-drying by suction), are heated in an oven above the boiling point of the solvent (but below this melting point of the crystals), followed by cooling in a desiccator. Where this treatment is inadvisable, it is still often possible to heat to a lower temperature under reduced pressure, for example in an Abderhalden pistol. This device consists of a small chamber which is heated externally by the vapour of a boiling solvent. Inside this chamber, which can be evacuated by a water pump or some other vacuum pump, is

placed a small boat containing the sample to be dried and also a receptacle with a suitable drying agent. Convenient liquids for use as boiling liquids in an Abderhalden pistol, and their temperatures, are given in Table 16. Alternatively an electrically heated drying pistol can also be used. In cases where heating above room temperature cannot be used, drying must be carried out in a vacuum desiccator containing suitable absorbents. For example, hydrocarbons, such as cyclohexane and petroleum ether, can be removed by using shredded paraffin wax, and acetic acid and other acids can be absorbed by pellets of sodium or potassium hydroxide. However, in general, solvent removal is less of a problem than ensuring that the water content of solids and liquids is reduced below an acceptable level.

#### **Removal of Water**

Methods for removing water from solids depends on the thermal stability of the solids or the time available. The safest way is to dry in a vacuum desiccator over concentrated sulfuric acid, phosphorus pentoxide, silica gel, calcium chloride, or some other desiccant. Where substances are stable in air and melt above 100°, drying in an air oven may be adequate. In other cases, use of an Abderhalden pistol may be satisfactory.

Often, in drying inorganic salts, the final material that is required is a hydrate. In such cases, the purified substance is left in a desiccator to equilibrate above an aqueous solution having a suitable water-vapour pressure. A convenient range of solutions used in this way is given in Table 17.

The choice of desiccants for drying liquids is more restricted because of the need to avoid all substances likely to react with the liquids themselves. In some cases, direct distillation of an organic liquid is a suitable method for drying both solids and liquids, especially if low-boiling azeotropes are formed. Examples include acetone, aniline, benzene, chloroform, carbon tetrachloride, heptane, hexane, methanol, nitrobenzene, petroleum ether, toluene and xylene. Addition of benzene can be used for drying ethanol by distillation. In carrying out distillations intended to yield anhydrous products, the apparatus should be fitted with guard-tubes containing calcium chloride or silica gel to prevent entry of moist air into the system. (Many anhydrous organic liquids are appreciably hygroscopic).

Traces of water can be removed from solvents such as benzene, 1,2-dimethoxyethane, diethyl ether, pentane, toluene and tetrahydrofuran by refluxing under nitrogen a solution containing sodium wire and benzophenone, and fractionally distilling. Drying with, and distilling from CaH<sub>2</sub> is applicable to a number of solvents including aniline, benzene, *tert*-butylamine, *tert*-butanol, 2,4,6-collidine, diisopropylamine, dimethylformamide, hexamethylphosphoramide, dichloromethane, ethyl acetate, pyridine, tertamethylethylenediamine, toluene, triethylamine.

Removal of water from gases may be by physical or chemical means, and is commonly by adsorption on to a drying agent in a low-temperature trap. The effectiveness of drying agents depends on the vapour pressure of the hydrated compound - the lower the vapour pressure the less the remaining moisture in the gas.

The most usually applicable of the specific methods for detecting and determining water in organic liquids is due to Karl Fischer. (See J.Mitchell and D.M.Smith, Aquametry, 2nd Ed, J Wiley & Sons, New York, 1977-1984, ISBN 0471022640; Fieser and Fieser Reagents for Organic Synthesis, J.Wiley & Sons, NY, Vol 1, 528 1967, ISBN 0271616X). Other techniques include electrical conductivity measurements and observation of the temperature at which the first cloudiness appears as the liquid is cooled (applicable to liquids in which water is only slightly soluble). Addition of anhydrous cobalt (II) iodide (blue) provides a convenient method (colour change to pink on hydration) for detecting water in alcohols, ketones, nitriles and some esters. Infrared absorption measurements of the broad band for water near 3500 cm<sup>-1</sup> can also sometimes be used for detecting water in non-hydroxylic substances.

For further useful information on mineral adsorbents and drying agents, go to the SigmaAldrich website, under technical library (Aldrich) for technical bulletin AL-143.

#### Intensity and Capacity of Common Desiccants

Drying agents are conveniently grouped into three classes, depending on whether they combine with water reversibly, they react chemically (irreversibly) with water, or they are molecular sieves. The first group vary in their drying intensity with the temperature at which they are used, depending on the vapour pressure of the hydrate that is formed. This is why, for example, drying agents such as anhydrous sodium sulfate, magnesium sulfate or calcium chloride should be filtered off from the liquids before the latter are heated. The intensities of drying agents belonging to this group fall in the sequence:

 $P_2O_5 >> BaO > Mg(ClO_4)_2$ , CaO, MgO, KOH (fused), conc  $H_2SO_4$ , CaSO<sub>4</sub>, Al<sub>2</sub>O<sub>3</sub> > KOH (pellets), silica gel, Mg(ClO<sub>4</sub>)<sub>2</sub>.3H<sub>2</sub>O > NaOH (fused), 95% H<sub>2</sub>SO<sub>4</sub>, CaBr<sub>2</sub>, CaCl<sub>2</sub> (fused) > NaOH (pellets), Ba(ClO<sub>4</sub>)<sub>2</sub>, ZnCl<sub>2</sub>, ZnBr<sub>2</sub> > CaCl<sub>2</sub> (technical) > CuSO<sub>4</sub> > Na<sub>2</sub>SO<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub>.

Where large amounts of water are to be removed, a preliminary drying of liquids is often possible by shaking with concentrated solutions of sodium sulfate or potassium carbonate, or by adding sodium chloride to salt out the organic phase (for example, in the drying of lower alcohols), as long as the drying agent does not react (e.g. CaCl<sub>2</sub> with alcohols and amines, see below).

Drying agents that combine irreversibly with water include the alkali metals, the metal hydrides (discussed in Chapter 2), and calcium carbide.

#### Suitability of Individual Desiccants

Alumina. (Preheated to 175° for about 7h). Mainly as a drying agent in a desiccator or as a column through which liquid is percolated.

Aluminium amalgam. Mainly used for removing traces of water from alcohols via refluxing followed by distillation.

**Barium oxide.** Suitable for drying organic bases.

Barium perchlorate. Expensive. Used in desiccators (covered with a metal guard).

Unsuitable for drying solvents or organic material where contact is necessary, because of the danger of **EXPLOSION** 

**Boric anhydride.** (Prepared by melting boric acid in an air oven at a high temperature, cooling in a desiccator, and powdering.) Mainly used for drying formic acid.

**Calcium chloride (anhydrous).** Cheap. Large capacity for absorption of water, giving the hexahydrate below 30°, but is fairly slow in action and not very efficient. Its main use is for preliminary drying of alkyl and aryl halides, most esters, saturated and aromatic hydrocarbons and ethers. Unsuitable for drying alcohols and amines (which form addition compounds), fatty acids, amides, amino acids, ketones, phenols, or some aldehydes and esters. Calcium chloride is suitable for drying the following gases: hydrogen, hydrogen chloride, carbon monoxide, carbon dioxide, sulfur dioxide, nitrogen, methane, oxygen, also paraffins, ethers, olefins and alkyl chlorides.

Calcium hydride. See Chapter 2.

**Calcium oxide.** (Preheated to 700-900° before use.) Suitable for alcohols and amines (but does not dry them completely). Need not be removed before distillation, but in that case the head of the distillation column should be packed with glass wool to trap any calcium oxide powder that might be carried over. Unsuitable for acidic compounds and esters. Suitable for drying gaseous amines and ammonia.

**Calcium sulfate (anhydrous).** (Prepared by heating the dihydrate or the hemihydrate in an oven at 235° for 2-3h; it can be regenerated.) Available commercially as Drierite. It forms the hemihydrate,  $2CaSO_4.H_2O$ , so that its capacity is fairly low (6.6% of its weight of water), and hence is best used on partially dried substances. It is very efficient (being comparable with phosphorus pentoxide and concentrated sulfuric acid). Suitable for most organic compounds. Solvents boiling below 100° can be dried by direct distillation from calcium sulfate.

**Copper (II) sulfate (anhydrous).** Suitable for esters and alcohols. Preferable to sodium sulfate in cases where solvents are sparingly soluble in water (for example, benzene or toluene).

Lithium aluminium hydride. See Chapter 2.

Magnesium amalgam. Mainly used for removing traces of water from alcohols by refluxing the alcohol in the presence of the Mg amalgam followed by distillation.

**Magnesium perchlorate (anhydrous).** (Available commercially as Dehydrite. Expensive.) Used in desiccators. Unsuitable for drying solvents or any organic material where contact is necessary, because of the danger of **EXPLOSION**.

Magnesium sulfate (anhydrous). (Prepared from the heptahydrate by drying at 300° under reduced pressure.) More rapid and effective than sodium sulfate but is slightly acidic. It has a large capacity, forming MgSO<sub>4</sub>.7H<sub>2</sub>O below 48°. Suitable for the preliminary drying of most organic compounds.

Molecular sieves. See later.

**Phosphorus pentoxide.** Very rapid and efficient, but difficult to handle and should only be used after the organic material has been partially dried, for example with magnesium sulfate. Suitable for anhydrides, alkyl and aryl halides, ethers, esters, hydrocarbons and nitriles, and for use in desiccators. Not suitable with acids, alcohols, amines or ketones, or with organic molecules from which a molecule of water can be eliminated. Suitable for drying the following gases: hydrogen, oxygen, carbon dioxide, carbon monoxide, sulfur dioxide, nitrogen, methane, ethene and paraffins. It is available on a solid support with an indicator under the name *Sicapent* (from Merck). The colour changes in Sicapent depend on the percentage of water present (e.g. in the absence of water, Sicapent is colorless but becomes green with 20% water and blue with 33% w/w water). When the quantity of water in the desiccator is high a crust of phosphoric acid forms a layer over the phosphorus pentoxide powder and decreases its efficiency. The crust can be removed with a spatula to expose the dry pwder and restore the desiccant property.

**Potassium (metal).** Properties and applications are similar to those for sodium but as the reactivity is greater than that of sodium, the hazards are greater than that of sodium. Handle with extreme care. **Potassium carbonate (anhydrous).** Has a moderate efficiency and capacity, forming the dihydrate. Suitable for an initial drying of alcohols, bases, esters, ketones and nitriles by shaking with them, then filtering off. Also suitable for salting out water-soluble alcohols, amines and ketones. Unsuitable for acids, phenols, thiols and other acidic substances.

**Potassium carbonate.** Solid potassium hydroxide is very rapid and efficient. Its use is limited almost entirely to the initial drying of organic bases. Alternatively, sometimes the base is shaken first with a concentrated solution of potassium hydroxide to remove most of the water present. Unsuitable for acids, aldehydes, ketones, phenols, thiols, amides and esters. Also used for drying gaseous amines and ammonia.

Silica gel. Granulated silica gel is a commercially available drying agent for use with gases, in desiccators, and (because of its chemical inertness) in physical instruments (pH meters, spectrometers, balances). Its drying action depends on physical adsorption, so that silica gel must be used at room temperature or below. By incorporating cobalt chloride into the material it can be made self indicating (blue when dry, pink when wet), re-drying in an oven at 110° being necessary when the colour changes from blue to pink.

**Sodium (metal).** Used as a fine wire or as chips, for more completely drying ethers, saturated hydrocarbons and aromatic hydrocarbons which have been partially dried (for example with calcium chloride or magnesium sulfate). Unsuitable for acids, alcohols, alkyl halides, aldehydes, ketones, amines and esters. Reacts violently if water is present and can cause a fire with highly flammable liquids.

Sodium hydroxide. Properties and applications are similar to those for potassium hydroxide.

Sodium-potassium alloy. Used as lumps. Lower melting than sodium, so that its surface is readily renewed by shaking. Properties and applications are similar to those for sodium.

**Sodium sulfate (anhydrous).** Has a large capacity for absorption of water, forming the decahydrate below 33°, but drying is slow and inefficient, especially for solvents that are sparingly soluble in water. It is suitable for the preliminary drying of most types of organic compounds.

**Sulfuric acid (concentrated).** Widely used in desiccators. Suitable for drying bromine, saturated hydrocarbons, alkyl and aryl halides. Also suitable for drying the following gases: hydrogen, nitrogen, carbon dioxide, carbon monoxide, chlorine, methane and paraffins. Unsuitable for alcohols, bases, ketones or phenols. Also available on a solid support with an indicator under the name *Sicacide* (from Merck) for desiccators. The colour changes in Sicacide depends on the percentage of water present (e.g. when dry Sicacide is red-violet but becomes pale violet with 27% water and pale yellow to colorless with 33% w/w water).

For convenience, many of the above drying agents are listed in Table 18 under the classes of organic compounds for which they are commonly used.

#### Molecular sieves

Molecular sieves are types of adsorbents composed of crystalline zeolites (sodium and calcium aluminosilicates). By heating them, water of hydration is removed, leaving holes of molecular dimensions in the crystal lattices. These holes are of uniform size and allow the passage into the crystals of small molecules, but not of large ones. This *sieving* action explains their use as very efficient drying agents for gases and liquids. The pore size of these sieves can be modified (within limits) by varying the cations built into the lattices. The four types of molecular sieves currently available are:

- **Type 3A sieves.** A crystalline potassium aluminosilicate with a pore size of about 3 Angstroms. This type of molecular sieves is suitable for drying liquids such as acetone, acetonitrile, methanol, ethanol and 2-propanol, and drying gases such as acetylene, carbon dioxide, ammonia, propylene and butadiene. The material is supplied as beads or pellets.
- **Type 4A sieves.** A crystalline sodium aluminosilicate with a pore size of about 4 Angstroms, so that, besides water, ethane molecules (but not butane) can be adsorbed. This type of molecular sieves is suitable for drying chloroform, dichloromethane, diethyl ether, dimethylformamide, ethyl acetate, cyclohexane, benzene, toluene, xylene, pyridine and diisopropyl ether. It is also useful for low pressure air drying. The material is supplied as beads, pellets or powder.
- **Type 5A sieves.** A crystalline calcium aluminosilicate with a pore size of about 5 Angstroms, these sieves adsorb larger molecules than type 4A. For example, as well as the substances listed above, propane, butane, hexane, butene, higher *n*-olefins, *n*-butyl alcohol and higher *n*-alcohols, and cyclopropane can be adsorbed, but not branched-chain  $C_6$  hydrocarbons, cyclic hydrocarbons such as benzene and cyclohexane, or secondary and tertiary alcohols, carbon tetrachloride or boron trifluoride. This is the type generally used for drying gases, though organic liquids such as THF and dioxane can be dried with this type of molecular sieves.

**Type 13X sieves.** A crystalline sodium aluminosilicate with a pore size of about 10 Angstroms which enables many branched-chain and cyclic compounds to be adsorbed, in addition to all the substances removed by type 5A sieves.

They are unsuitable for use with strong acids but are stable over the pH range 5-11.

Because of their selectivity, molecular sieves offer advantages over silica gel, alumina or activated charcoal, especially in their very high affinity for water, polar molecules and unsaturated organic compounds. Their relative efficiency is greatest when the impurity to be removed is present at low concentrations. Thus, at 25° and a relative humidity of 2%, type 5A molecular sieves adsorb 18% by weight of water, whereas for silica gel and alumina the figures are 3.5 and 2.5% respectively. Even at 100° and a relative humidity of 1.3% molecular sieves adsorb about 15% by weight of water.

The greater preference of molecular sieves for combining with water molecules explains why this material can be used for drying ethanol and why molecular sieves are probably the most universally useful and efficient drying agents. Percolation of ethanol with an initial water content of 0.5% through a 144 cm long column of type 4A molecular sieves reduced the water content to 10ppm. Similar results have been obtained with pyridine.

The main applications of molecular sieves to purification comprise:

- 1. Drying of gases and liquids containing traces of water.
- 2. Drying of gases at elevated temperatures.
- 3. Selective removal of impurities (including water) from gas streams.

(For example, carbon dioxide from air or ethene; nitrogen oxides from nitrogen; methanol from diethyl ether. In general, carbon dioxide, carbon monoxide, ammonia, hydrogen sulfide, mercaptans, ethane, ethene, acetylene (ethyne), propane and propylene are readily removed at 25°. In mixtures of gases, the more polar ones are preferentially adsorbed).

The following applications include the removal of straight-chain from branched-chain or cyclic molecules. For example, type 5A sieves will adsorb *n*-butyl alcohol but not its branched-chain isomers. Similarly, it separates *n*-tetradecane from benzene, or *n*-heptane from methylcyclohexane.

The following liquids have been dried with molecular sieves: acetone, acetonitrile, acrylonitrile, allyl chloride, amyl acetate, benzene, butadiene, *n*-butane, butene, butyl acetate, *n*-butylamine, *n*-butyl chloride, carbon tetrachloride, chloroethane, 1-chloro-2-ethylhexane, cyclohexane, dichloromethane, dichloroethane, 1,2dichloropropane, 1,1-dimethoxyethane, dimethyl ether, 2-ethylhexanol, 2-ethylhexylamine, *n*-heptane, *n*-hexane, isoprene, isopropyl alcohol, diisopropyl ether, methanol, methyl ethyl ketone, oxygen, *n*-pentane, phenol, propane, *n*-propyl alcohol, propylene, pyridine, styrene, tetrachloroethylene, toluene, trichloroethylene and xylene. In addition, the following gases have been dried: acetylene, air, argon, carbon dioxide, chlorine, ethene, helium, hydrogen, hydrogen chloride, hydrogen sulfide, nitrogen, oxygen and sulfur hexafluoride.

After use, molecular sieves can be regenerated by heating at between  $300^{\circ}-350^{\circ}$  for several hours, preferably in a stream of dry inert gas such as nitrogen or preferably under vacumm, then cooling in a desiccator. Special precautions must be taken before regeneration of molecular sieves used in the drying of flammable solvents.

However, care must be exercised in using molecular sieves for drying organic liquids. Appreciable amounts of impurities were *formed* when samples of acetone, 1,1,1-trichloroethane and methyl-*t*-butyl ether were dried in the liquid phase by contact with molecular sieves 4A (Connett Lab Pract 21 545 1972). Other, less reactive types of sieves may be more suitable but, in general, it seems desirable to make a preliminary test to establish that no unwanted reaction takes place. Useful comparative data for Type 4A and 5A sieves are in Table 19.

#### MISCELLANEOUS TECHNIQUES Freeze-pump-thaw and purging

Volatile contaminants, e.g. traces of low boiling solvent residue or oxygen, in liquid samples or solutions can be very deleterious to the samples on storage. These contaminants can be removed by repeated freeze-pump-thaw cycles. This involves freezing the liquid material under high vacuum in an appropriate vessel (which should be large enough to avoid contaminating the vacuum line with liquid that has bumped) connected to the vacuum line via efficient liquid nitrogen traps. The frozen sample is then thawed until it liquefies, kept in this form for some time (ca 10-15min), refreezing the sample and the cycle repeated several times without interrupting the vacuum. This procedure applies equally well to solutions, as well as purified liquids, e.g. as a means of removing oxygen from solutions for NMR and other measurements. If the presence of nitrogen, helium or argon, is not a serious contaminant then solutions can be freed from gases, e.g. oxygen, carbon dioxide, and volatile impurities by purging with N<sub>2</sub>, He or Ar at room, or slightly elevated, temperature. The gases used for purging are then removed by freeze-pump-thaw cycles or simply by keeping in a vacuum for several hours. Special NMR tubes

with a screw cap thread and a PTFE valve (Wilmad) are convenient for freeze thawing of NMR samples. Alternatively NMR tubes with "J Young" valves (Wilmad) can also be used.

#### Vacuum-lines, Schlenk and glovebox techniques

Manipulations involving materials sensitive to air or water vapour can be carried out by these procedures. Vacuum-line methods make use of quantitative transfers, and P(pressure)-V(volume)-T(temperature)measurements, of gases, and trap-to-trap separations of volatile substances.

It is usually more convenient to work under an inert-gas atmosphere using Schlenk type apparatus. The principle of Schlenk methods involve a flask/vessel which has a standard ground-glass joint and a sidearm with a tap. The system can be purged by evacuating and flushing with an inert gas (usually nitrogen, or in some cases, argon), repeating the process until the contaminants in the vapour phases have been diminished to acceptable limits. A large range of Schlenk glassware is commercially available (e.g. see Aldrich Chemical Catalog and the associated technical bulletin AL-166). With these, and tailor-made pieces of glassware, inert atmospheres can be maintained during crystallisation, filtration, sublimation and transfer.

Syringe techniques have been developed for small volumes, while for large volumes or where much manipulation is required, dryboxes (glove boxes) or dry chambers should be used.

## **ABBREVIATIONS**

Titles of periodicals are defined as in the Chemical Abstracts Service Source Index (CASSI), except that full stops have been omitted after each abbreviated word. Abbreviations of words in the texts of Chapters 4, 5 and 6 are those in common use and are self evident, e.g. distn, filtd, conc and vac are used for distillation, filtered, concentrated and vacuum.

## **TABLES**

#### TABLE 1. SOME COMMON IMMISCIBLE OR SLIGHTLY MISCIBLE PAIRS OF SOLVENTS

Carbon tetrachloride with ethanolamine, ethylene glycol, formamide or water. Dimethyl formamide with cyclohexane or petroleum ether. Dimethyl sulfoxide with cyclohexane or petroleum ether. Ethyl ether with ethanolamine, ethylene glycol or water. Methanol with carbon disulfide, cyclohexane or petroleum ether. Petroleum ether with aniline, benzyl alcohol, dimethyl formamide, dimethyl sulfoxide, formamide, furfuryl alcohol, phenol or water. Water with aniline, benzene, benzyl alcohol, carbon disulfide, carbon tetrachloride, chloroform, cyclohexane, cyclohexanol, cyclohexanone, diethyl ether, ethyl acetate, isoamyl alcohol, methyl ethyl

ketone, nitromethane, tributyl phosphate or toluene.

30

TABLE 2. Approx. pH	AQUEOUS BUFFERS Composition				
0	2N sulfuric acid or N hydrochloric acid				
1	N hydrochloric acid or 0.18N sulfuric acid				
2	Either 0.01N hydrochloric acid or 0.013N sulfuric acid Or 50 mL of 0.1M glycine (also 0.1M NaCl) + 50 mL of 0.1N hydrochloric acid				
3	Either 20 mL of the 0.2M Na <sub>2</sub> HPO <sub>4</sub> + 80 mL of 0.1M citric acid Or 50 mL of 0.1M glycine + 22.8 mL of 0.1N hydrochloric acid in 100 mL				
4	Either 38.5 mL of 0.2M Na <sub>2</sub> HPO <sub>4</sub> + 61.5 mL of 0.1M citric acid Or 18 mL of 0.2M NaOAc + 82 mL of 0.2M acetic acid				
5	Either 70 mL of 0.2M NaOAc + 30 mL of 0.2M acetic acid Or 51.5 mL of 0.2M Na <sub>2</sub> HPO <sub>4</sub> + 48.5 mL of 0.1M citric acid				
6	63 mL of 0.2M Na <sub>2</sub> HPO <sub>4</sub> + 37 mL of 0.1M citric acid				
7	82 mL of M Na <sub>2</sub> HPO <sub>4</sub> + 18 mL of 0.1M citric acid				
8	Either 50 mL of 0.1M Tris buffer + 29 mL of 0.1N hydrochloric acid, in 100 mL Or 30 mL of 0.05M borax + 70 mL of 0.2M boric acid				
9	80 mL of 0.05M borax + 20 mL of 0.2M boric acid				
10	Either 25 mL of 0.05M borax + 43 mL of 0.1N NaOH, in 100 mL Or 50 mL of 0.1M glycine + 32 mL of 0.1N NaOH, in 100 mL				
11	50 mL of 0.15M Na <sub>2</sub> HPO <sub>4</sub> + 15 mL of 0.1N NaOH				
12	50 mL of 0.15M Na <sub>2</sub> HPO <sub>4</sub> + 75 mL of 0.1N NaOH				
13	0.1N NaOH or KOH				
14	N NaOH or KOH				

These buffers are suitable for use in obtaining ultraviolet spectra. Alternatively, for a set of accurate buffers of low, but constant, ionic strength (I = 0.01) covering a pH range 2.2 to 11.6 at 20°, see Perrin Aust J Chem 16 572 1963. "In 100 mL" means that the solution is made up to 100 mL with pure water.

		Т	empera	ture in	degre	es Cen	tigrade	•			
760 mm	hHg 0	20	40	60	80	100	120	140	160	180	
0.1	-111	-99	-87	-75	-63	-51	-39	-27	-15	-4	
0.2	-105	-93	-81	-69	-56	-44	-32	-19	-7	5	
0.4	-100	-87	-74	-62	-49	-36	-24	-11	2	15	
0.6	-96	-83	-70	-57	-44	-32	-19	-6	7	20	
0.8	-94	-81	-67	-54	-41	-28	-15	-2	11	24	
1.0	-92	-78	-65	-52	-39	-25	-12	1	15	28	
2.0	-85	-71	-58	-44	-30	-16	-3	11	25	39	
4.0	-78	-64	-49	-35	-21	-7	8	22	36	51	
6.0	-74	-59	-44	-30	-15	-1	14	29	43	58	
8.0	-70	-56	-41	-26	-11	4	19	34	48	63	
10.0	-68	-53	-38	-23	-8	7	22	37	53	68	
14.0	-64	-48	-33	-23	-2	13	28	44	59	74	
16.0	-61	-45	-29	-14	2	17	33	48	64	79	
20.0	-59	-44	-28	-12	3	19	35	50	66	82	
30.0	-54	-38	-22	-6	10	26	42	58	74	90	
40.0	-50	-34	-17	-1	15	32	48	64	81	97	
50.0	-47	-30	-14	3	19	36	52	69	86	102	
60.0	-44	-28	-11	6	23	40	56	73	86	107	
80.0	-40	-23	-6	11	28	45	62	79	97	114	
100.0	-37	-19	-2	15	33	50	67	85	102	119	
150.0	-30	-12	6	23	41	59	77	95	112	130	
200.0	-25	-7	11	29	47	66	84	102	120	138	
300.0	-18	1	19	38	57	75	94	113	131	150	
400.0	-13	6	25	44	64	83	102	121	140	159	
500.0	-8	11	30	50	69	88	108	127	147	166	
600.0	-5	15	34	54	74	93	113	133	152	172	
700.0	-2	18	38	58	78	98	118	137	157	177	
750.0	0	20	40	60	80	100	120	140	160	180	
770.0	0	20	40	60	80	100	120	140	160	180	
800.0	1	21	41	61	81	101	122	142	162	182	

TABLE 3A. PREDICTED EFFECT OF PRESSURE ON BOILING POINT\*

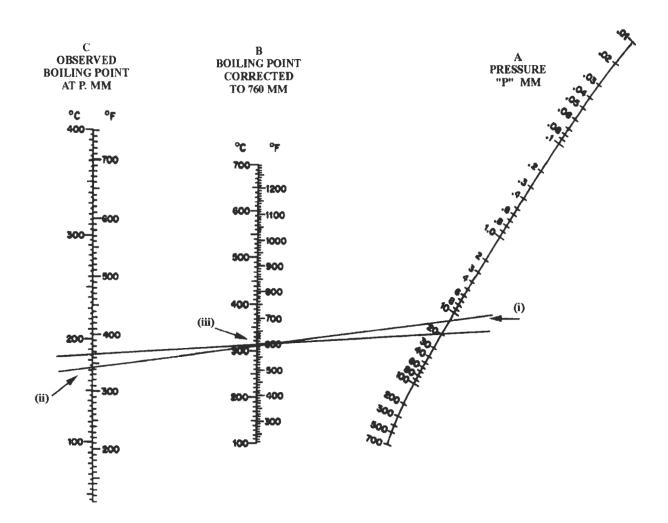
\* How to use the Table: Take as an example a liquid with a boiling point of 80°C at 760mm Hg. The Table gives values of the boiling points of this liquid at pressures from 0.1 to 800mm Hg. Thus at 50mm Hg this liquid has a boiling point of 19°C, and at 2mm Hg its boiling point would be -30°C.

760mmHg	200	220	240	260	280	300	320	340	360	380	400
0.1	8	20	32		56	68	80	92	104	115	127
0.2	17	30	42	54	67	79	91	103	116	128	140
0.4	27	40	53	65	78	91	103	116	129	141	154
0.6	33	40	59	72	85	98	111	124	137	150	163
0.8	38	51	64	77	90	103	116	130	143	156	169
1.0	41	54	68	81	94	108	121	134	147	161	174
2.0	53	66	80	94	108	121	135	149	163	176	190
4.0	65	79	93	108	122	136	151	156	179	193	208
6.0	72	87	102	116	131	146	160	175	189	204	219
8.0	78	93	108	123	137	152	167	182	197	212	227
10.0	83	98	113	128	143	158	173	188	203	218	233
14.0	90	105	120	136	151	166	182	197	212	228	243
18.0	95	111	126	142	157	173	188	204	219	235	251
20.0	97	113	129	144	160	176	191	207	223	238	254
30.0	106	123	139	155	171	187	203	219	235	251	267
40.0	113	130	146	162	179	195	211	228	244	260	277
50.0	119	135	152	168	185	202	218	235	251	268	284
60.0	123	140	157	174	190	207	224	241	257	274	291
80.0	131	148	165	182	199	216	233	250	267	284	301
100.0	137	154	171	189	206	223	241	258	275	293	310
150.0	148	166	184	201	219	237	255	273	290	308	326
200.0	156	174	193	211	229	247	265	283	302	320	338
300.0	169	187	206	225	243	262	281	299	318	337	355
400.0	178	197	216	235	254	273	292	311	330	350	369
500.0	185	205	224	244	263	282	302	321	340	360	379
600.0	192	211	231	251	270	290	310	329	349	368	388
700.0	197	217	237	257	277	296	316	336	356	376	396
750.0	200	220	239	259	279	299	319	339	359	279	399
770.0	200	220	241	261	281	301	321	341	361	381	401
800.0	202	222	242	262	282	302	322	342	262	382	403

# TABLE 3B. PREDICTED EFFECT OF PRESSURE ON BOILING POINT\*

\* How to use the Table: Taking as an example a liquid with a boiling point of 340°C at 760mm Hg, the column headed 340°C gives values of the boiling points of this liquid at each value of pressures from 0.1 to 800mm Hg. Thus, at 100mm Hg its boiling point is 258°C, and at 0.8mm Hg its boiling point will be 130°C.

#### FIGURE 1: NOMOGRAM



#### How to use Figure 1:

You can use a nomogram to estimate the boiling points of a substance at a particular pressure. For example, the boiling point of 4-methoxybenzenesulfonyl chloride is  $173^{\circ}C/14$ mm. Thus to find out what the boiling point of this compound will be at 760mm (atmospheric), draw a point on curve A (pressure) at 14mm (this is shown in (i). Then draw a point on curve C (observed boiling point) corresponding to  $173^{\circ}$  (or as close as possible). This is shown in (ii). Using a ruler, find the point of 4-methoxybenzenesulfonyl chloride (i.e. approx. 310°C) at atmospheric pressure. If you want to distil 4-methoxybenzenesulfonyl chloride at 20mm, then you will need to draw a point on curve B, i.e.  $310^{\circ}$ C) and the point of intersection on curve A corresponding to 20mm. You should have a value of  $185^{\circ}$ C, that is, the boiling point of 4-methoxybenzenesulfonyl chloride is estimated to be at  $185^{\circ}$ C at 20mm.

TABLE 4.	HEATING BATHS
Up to 100°	Water baths
-20 to 200°	Glycerol or di-n-butyl phthalate
Up to about 200°	Medicinal paraffin
Up to about 250°	Hard hydrogenated cotton-seed oil (m 40-60°) or a 1:1 mixture of cotton-seed oil and castor oil containing about 1% of hydroquinone.
-40 to 250° (to 400° under $N_2$ )	D.C. 550 silicone fluid
Up to about 260°	A mixture of 85% orthophosphoric acid (4 parts) and metaphosphoric acid (1 part)
Up to 340°	A mixture of 85% orthophosphoric acid (2 parts) and metaphosphoric acid (1 part)
60 to 500°	Fisher bath wax (highly unsaturated)
73 to 350°	Wood's Metal*
250 to 800°	Solder*
350 to 800°	Lead*

\* In using metal baths, the container (usually a metal crucible) should be removed while the metal is still molten.

TABLE 5.	۷	WHAT	MAN	FILTER	PAPE	RS		
Grade No.		1	2	3	4	5	6	113
Particle size retained (in microns)		11	8	5	12	2.4	2.8	28
Filtration speed*(sec/100mL)		40	55	155	20	<300	125	9
			1	Routine	ashless	filters		
Grade No.			40	41	42	43	44	
Particle size retained (in microns)			7.5	12	3	12	4	
Filtration speed* (sec/100mL)			68	19	200	38	125	
	]	Harden	ed			Harde	ned ash	less
Grade No.	50	52	:	54	54	0	541	542
Particle size retained(in microns)	3	8		20	9	)	20	3

Filtration speed* (sec/100mL)	250	55	10 55	12	250
		G	ass microfilters		
Grade No	GF/A	GF/B	GF/C	GF/D	GF/F
Particle size retained (in microns)	1.6	1.0	1.1	2.2	0.8
Filtration speed (sec/100mL)*	8.3	20.0	8.7	5.5	17.2

\*Filtration speeds are rough estimates of initial flow rates and should be considered on a relative basis.

TABLE 6.			MICRO	FILTER	s*				
Nucleopo	ore (poly	ycarbonate) l	Filters						
Mean Pore Size (mic	crons)	8.0	2.0	1.0	0	1	0.03	(	0.015
Av. pores/cm <sup>2</sup>		10 <sup>5</sup>	2x10 <sup>6</sup>	2x10 <sup>7</sup>	3 x I	08	6x10 <sup>8</sup>	1	-6x10 <sup>9</sup>
Water flow rate(mL/	min/cm <sup>2</sup> )	2000	2000	300		8	0.03	0	0.1-0.5
Millipore	e Filters								#
Туре		——————————————————————————————————————	se ester		7	eflon		–Micr	oweb <sup>#</sup> -
		MF/SC	MF/VF		LC	LS		WS	WH
Mean Pore Size (mic	erons)	8	0.01		10	5		3	0.45
Water flow rate (mL	/min/cm <sup>2</sup> )	850	0.2		170	70		155	55
Gelman	Membrar	nes	<u> </u>						
Туре	Celli	ulose ester——				C	opolymer		_
	GA-1	TCM-450	VM-1	DM-800		AN-200		ffryn-4	
Mean Pore Size (microns)	5	0.45	5	0.8		0.2		0.4	5
Water flow rate (mL/min/cm <sup>2</sup> )	320	50	700	200		17		5	0
Sartorius	Membra	ane Filters (S	M)						
Application		Gravi- metric	Biologica clarificatr	1 Steri satio		Partic count H <sub>2</sub> O			or ids bases
Type No.		11003	11004	1100		1101			2801

Application	Gravi- metric	Biological clarificatn	Sterili- sation	Particle count in H <sub>2</sub> O	
Type No.	11003	11004	11006	11011	
Mean PoreSize (microns)	1.2	0.6	0.45	0.01	

300

Water flow rate (mL/min/cm<sup>2</sup>)

\* Only a few representative filters are tabulated (available ranges are more extensive). # Reinforced nylon.

65

0.6

150

8

1100

#### TABLE 7. COMMON SOLVENTS USED IN RECRYSTALLISATION

Acetic acid (118 <sup>0</sup> )	*Cyclohexane (81 <sup>0</sup> )	*Methanol (64.5°)
*Acetone (56 <sup>0</sup> )	Dichloromethane (41 <sup>0</sup> )	*Methyl ethyl ketone (80 <sup>0</sup> )
Acetylacetone (139 <sup>o</sup> )	*Diethyl ether (34.5°)	Methyl isobutyl ketone (116 <sup>o</sup> )
Acetonitrile (82°C)	Dimethyl formamide (76°/39mm)	Nitrobenzene (210 <sup>o</sup> )
*Benzene (80°)	*Dioxane (101°)	Nitromethane (101 <sup>o</sup> )
Benzyl alcohol (93°/10mm)	*Ethanol (78 <sup>0</sup> )	*Petroleum ether (various)
n-Butanol (118°)	2-Ethoxyethanol (cellosolve 135 <sup>o</sup> )	Pyridine $(115.5^{\circ})$
Butyl acetate (126.5°)	*Ethyl acetate (78°)	Pyridine trihydrate (93 <sup>o</sup> )
<i>n</i> -Butyl ether (142 <sup>o</sup> )	Ethyl benzoate (98%/19mm)	*Tetrahydrofuran (64-66°)
γ-Butyrolactone (206 <sup>0</sup> )	Ethylene glycol (68°/4mm)	Toluene (110 <sup>o</sup> )
Carbon tetrachloride (77°)	Formamide (110%/10mm)	Trimethylene glycol (59°/11mm)
Chlorobenzene (132 <sup>o</sup> )	Glycerol (126°/11mm)	Water (100°)
Chloroform (61°)	Isoamyl alcohol (131°)	Xylenes (o 143-145°, m 138-139°, p 138°)
*Highly flammable, should	be heated or evaporated on ste	am or electrically heated water baths

only (preferably under nitrogen). None of these solvents should be heated over a naked flame.

#### TABLE 8.

#### PAIRS OF MISCIBLE SOLVENTS

Acetic acid: with chloroform, ethanol, ethyl acetate, acetonitrile, petroleum ether, or water. Acetone: with benzene, butyl acetate, butyl alcohol, carbon tetrachloride, chloroform, cyclohexane, ethanol, ethyl acetate, methyl acetate, acetonitrile, petroleum ether or water. Ammonia: with ethanol, methanol, pyridine. Aniline: with acetone, benzene, carbon tetrachloride, ethyl ether, n-heptane, methanol, acetonitrile or nitrobenzene. Benzene: with acetone, butyl alcohol, carbon tetrachloride, chloroform, cyclohexane, ethanol, acetonitrile, petroleum ether or pyridine. Butyl alcohol: with acetone or ethyl acetate. Carbon disulfide: with petroleum ether. Carbon tetrachloride: with cyclohexane. Chloroform: with acetic acid, acetone, benzene, ethanol, ethyl acetate, hexane, methanol or pyridine. Cyclohexane: with acetone, benzene, carbon tetrachloride, ethanol or diethyl ether. Diethyl ether: with acetone, cyclohexane, ethanol, methanol, methylal (dimethoxymethane), acetonitrile, pentane or petroleum ether. Dimethyl formamide: with benzene, ethanol or ether. Dimethyl sulfoxide: with acetone, benzene, chloroform, ethanol, diethyl ether or water. Dioxane: with benzene, carbon tetrachloride, chloroform, ethanol, diethyl ether, petroleum ether, pyridine or water. Ethanol: with acetic acid, acetone, benzene, chloroform, cyclohexane, dioxane, ethyl ether, pentane, toluene, water or xylene. Ethyl acetate: with acetic acid, acetone, butyl alcohol, chloroform, or methanol. Glycerol: with ethanol, methanol or water. Hexane: with benzene, chloroform or ethanol. Methanol: with chloroform, diethyl ether, glycerol or water. Methylal: with diethyl ether. Methyl ethyl ketone: with acetic acid, benzene, ethanol or methanol. Nitrobenzene: with aniline, methanol or acetonitrile. Pentane: with ethanol or diethyl ether. Petroleum ether: with acetic acid, acetone, benzene, carbon disulfide or diethyl ether. Phenol: with carbon tetrachloride, ethanol, diethyl ether or xylene. Pyridine: with acetone, ammonia, benzene, chloroform, dioxane, petroleum ether, toluene or water. Toluene: with ethanol, diethyl ether or pyridine. Water: with acetic acid, acetone, ethanol, methanol, or pyridine. Xylene: with ethanol or phenol.

## TABLE 9. MATERIALS FOR COOLING BATHS

Temperatur	e Composition	Tempera	ature Composition
00	Crushed ice		
-5° to -20°	Ice-salt mixtures	-77°	Solid $CO_2$ with chloroform or acetone
Up to -20°	Ice-MeOH mixtures	-78°	Solid $CO_2$ (powdered; $CO_2$ snow)
-33°	Liquid ammonia		
-40° to -50°	P Ice $(3.5-4 \text{ parts})$ - CaCl <sub>2</sub> 6H <sub>2</sub> O (5 parts)	-100°	Solid CO <sub>2</sub> with diethyl ether
-72°	Solid CO <sub>2</sub> with ethanol	-196°	liquid nitrogen (see footnote*)

Alternatively, the following liquids can be used, partially frozen, as cryostats, by adding solid  $CO_2$  from time to time to the material in a Dewar-type container and stirring to make a slush:

13º	<i>p</i> -Xylene	-55°	Diacetone
12º	Dioxane	-56°	<i>n</i> -Octane
6°	Cyclohexane	-60°	Di-isopropyl ether
5°	Benzene	-73°	Trichloroethylene or isopropyl acetate
2°	Formamide	-74°	o-Cymene or p-cymene
-8.6°	Methyl salicylate	-77°	Butyl acetate
-90	Hexane-2,5-dione	-79°	Isoamyl acetate
-10.5°	Ethylene glycol	-83°	Propylamine
-11.9°	tert-Amyl alcohol	-83.6°	Ethyl acetate
-12º	Cycloheptane or methyl benzoate	-86°	Methyl ethyl ketone
-15°	Benzyl alcohol	-89°	<i>n</i> -Butanol
-16.3°	n-Octanol	-90°	Nitroethane
-18º	1,2-Dichlorobenzene	-91°	Heptane
-22°	Tetrachloroethylene	-92°	<i>n</i> -Propyl acetate
-22.4°	Butyl benzoate	-93°	2-Nitropropane or cyclopentane
-22.8°	Carbon tetrachloride	-94°	Ethyl benzene or hexane
-24.5°	Diethyl sulfate	-94.6°	Acetone
-25°	1,3-Dichlorobenzene	-95.1°	Toluene
-29°	o-Xylene or pentachloroethane	-97º	Cumene
-30°	Bromobenzene	-98°	Methanol or methyl acetate
-32°	<i>m</i> -Toluidine	-99°	Isobutyl acetate
-32.6°	Dipropyl ketone	-104°	Cyclohexene
-38º	Thiophene	-107º	Isooctane
-41°	Acetonitrile	-108°	1-Nitropropane
-42°	Pyridine or diethyl ketone	-116º	Ethanol or diethyl ether
-44º	Cyclohexyl chloride	-117º	Isoamyl alcohol
-45°	Chlorobenzene	-126°	Methylcyclohexane
-47º	<i>m</i> -Xylene	-131°	<i>n</i> -Pentane
-50°	Ethyl malonate or <i>n</i> -butylamine	-160°	Isopentane
-52°	Benzyl acetate or diethylcarbitol		

For other organic materials used in low temperature slush-baths with liquid nitrogen see R.E.Rondeau [*J Chem Eng Data* 11 124 1966]. **\*NOTE**: Use high quality pure nitrogen, do not use liquid air or liquid nitrogen that has been in contact with air for a long period (due to the dissolution of oxygen in it) as this could EXPLODE in contact with organic matter.

Material	Temp.	Retards
Dimethylsulfolane	0-40°	Olefins and aromatic hydrocarbons
Di-n-butyl phthalate	0-40°	General purposes
Squalane	0-1 <b>50</b> °	Volatile hydrocarbons and polar molecules
Silicone oil or grease	0-250°	General purposes
Diglycerol	20-120°	Water, alcohols, amines, esters, and aromatic hydrocarbons
Dinonyl phthalate	20-130°	General purposes
Polydiethylene glycol succinate	50-200°	Aromatic hydrocarbons, alcohols, ketones, esters.
Polyethylene glycol	50-200°	Water, alcohols, amines, esters and aromatic hydrocarbons
Apiezon grease	50-200°	Volatile hydrocarbons and polar molecules
Tricresyl phosphate	50-250°	General purposes

# TABLE 10. LIQUIDS FOR STATIONARY PHASES IN GAS CHROMATOGRAPHY

# TABLE 11. METHODS OF VISUALISATION OF TLC SPOTS

Reagent	Compound	Preparation	Observations	
Iodine	General	Iodine crystals in a closed chamber or spray 1% methanol solution of Iodine	Brown spots which may disappear upon standing. Limited sensitivity.	
$H_2SO_4$	General	50% solution, followed by heating to 150°C	Black or coloured spots	
Molybdate	General	5% $(NH_4)_6Mo_7O_{24} + 0.2\%$ Ce $(SO_4)_2$ in 5% H <sub>2</sub> SO <sub>4</sub> , followed by heating to 150°C.	Deep blue spots	
Vanillin	General	0.5g vanillin, $0.5$ mL H <sub>2</sub> SO <sub>4</sub> , 9 mL ethanol	various coloured spots	
Ammonia	phenols	Ammonia vapour in a closed chamber	various coloured spots	
FeCl <sub>3</sub>	phenols, enolic compounds	1% aqueous FeCl <sub>3</sub>	various coloured spots	
2,4-DNP	aldehydes, ketones	0.5% 2,4-dinitrophenylhydrazine/2M HCl	red to yellow spots	
HCI	aromatic acids and amines	HCl vapour in a closed chamber	various coloured spots	
Ninhydrin	amino acids, and amines	0.3% ninhydrin in <i>n</i> -BuOH with 3% AcOH, followed by heating to 125°C/10 min	blue spots	
PdCl <sub>2</sub>	S and Se compds	0.5% aq. $PdCl_2$ + few drops of conc. HCl	red and yellow spots	
Anisaldehyde	carbohydrates	0.5 mL anisaldehyde in 0.5 mL conc H <sub>2</sub> SO <sub>4</sub> + 95% EtOH + a few drops of AcOH Heat at 100-110°C for 20-30 minutes	various blue spots	

## TABLE 12. GRADED ADSORBENTS AND SOLVENTS

Adsorbents (decreasing effectiveness)

Solvents (increasing eluting ability)

Fuller's earth (hydrated aluminosilicate) Magnesium oxide Charcoal Alumina Magnesium trisilicate Silica gel Calcium hydroxide Magnesium carbonate Calcium phosphate Calcium carbonate Sodium carbonate Talc Inulin Sucrose = starch Petroleum ether, b. 40-60°. Petroleum ether, b. 60-80°. Carbon tetrachloride. Cyclohexane. Benzene. Diethyl ether. Chloroform. Ethyl acetate. Acetone. Ethanol. Methanol. Pyridine. Acetic acid.

#### TABLE 13.REPRESENTATIVE ION-EXCHANGE RESINS

Sulfonated polystyrene Strong-acid cation exchanger AG 50W-x8 Amberlite IR-120 Dowex 50W-x8 Duolite 225 Permutit RS Permutite C50D

Carboxylic acid-type Weak acid cation exchangers Amberlite IRC-50 Bio-Rex 70 Chelex 100 Duolite 436 Permutit C Permutits H and H-70 Aliphatic amine-type weak base anion exchangers Amberlites IR-45 and IRA-67 Dowex 3-x4A Permutit E Permutit A 240A

Strong Base, anion exchangers AG 2x8 Amberlite IRA-400 Dowex 2-x8 Duolite 113 Permutit ESB Permutite 330D

### TABLE 14.

### 14. MODIFIED FIBROUS CELLULOSES FOR ION-EXCHANGE

Cation exchange CM cellulose (carboxymethyl) CM 22, 23 cellulose P cellulose (phosphate) SE cellulose (sulfoethyl) SM cellulose (sulfomethyl) Anion exchange DEAE cellulose (diethylaminoethyl) DE 22, 23 cellulose PAB cellulose (p-aminobenzyl) TEAE cellulose (triethylaminoethyl) ECTEOLA cellulose

SE and SM are much stronger acids than CM, whereas P has two ionisable groups (pK 2-3, 6-7), one of which is stronger, the other weaker, than for CM (3.5-4.5). For basic strengths, the sequence is: TEAE » DEAE (pK 8-95) > ECTEOLA (pK 5.5-7) > PAB. Their exchange capacities lie in the range 0.3 to 1.0 mg equiv/g.

TABLE 15.         BEAD FORM ION-EXCHANGE PACKAGINGS <sup>1</sup>						
Cation exchange	Capacity (meq/g)	Anion exchange	Capacity (meq/g)			
CM-Sephadex C-25, C-50. <sup>2</sup> (weak acid)	4.5±0.5	DEAE-Sephadex A-25, A-50.7 (weak base)	3.5±0.5			
SP-Sephadex C-25, C-50. <sup>3</sup> (strong acid)	2.3±0.3	QAE-Sephadex A-25, A-50. <sup>8</sup> (strong base)	3.0±0.4			
CM-Sepharose CL-6B. <sup>4</sup>	0.12±0.02	DEAE-Sepharose CL-6B. <sup>4</sup>	0.13±0.02			
		DEAE-Sephacel.9	1.4±0.1			
Fractogel EMD,CO <sub>2</sub> (pK -	-4.5) ,	Fractogel EMD, DMAE (pK	~9),			
$SO_3^{2-}$ (pK ~<1) .5		DEAE (pK ~10.8), TMAE (p	<b>oK</b> >13). <sup>5</sup>			
CM-32 Cellulose.		DE-32 Cellulose.				
CM-52 Cellulose. <sup>6</sup>		DE-52 Cellulose				

<sup>1</sup> May be sterilised by autoclaving at pH 7 and below 120°. <sup>2</sup> Carboxymethyl. <sup>3</sup> Sulfopropyl. <sup>4</sup> Crosslinked agarose gel, no pre-cycling required, pH range 3-10. <sup>5</sup> Hydrophilic methacrylate polymer with very little volume change on change of pH (equivalent to *Toyopearl*, Sigma), available in superfine 650S, and medium 650M particle sizes. <sup>6</sup> Microgranular, pre-swollen, no pre-cycling required. <sup>7</sup> Diethylaminoethyl. <sup>8</sup> Diethyl(2-hydroxy-propyl)aminoethyl. <sup>9</sup> Bead form cellulose, pH range 2-12, no pre-cycling required. Sephadex and Sepharose from Pharmacia-Amersham Biosciences, Fractogel from Merck, Cellulose from Whatman.

ABLE 16. Boiling points (760	LIQUIDS	FOR DRYING PISTOLS Boiling points (76	Omm)	
Ethyl chloride	12.2°	Toluene	110.5°	
Dichloromethane	39.8°	Tetrachloroethylene	121.2°	
Acetone	56.1°	Chlorobenzene	132.0°	
Chloroform	62.0°	<i>m</i> -Xylene	139.3°	
Methanol	64.5°	Isoamyl acetate	142.5°	
Carbon tetrachloride	76.5°	Tetrachloroethane	146.3°	
Ethanol	78.3°	Bromobenzene	155.0°	
Benzene	79.8°	p-Cymene	176.0°	
Trichloroethylene	86.0°	Tetralin	207.0°	
Water	100.0°			

TABLE 17.						URATED AQUEOUS SOLID SALTS
Salt	10°	15°	Temper 20°		30°	% Humidity at 20 <sup>o</sup>
LiCl.H <sub>2</sub> O			2.6			15
CaBr <sub>2</sub> .6H <sub>2</sub> O	2.1	2.7	3.3	4.0	4.8	19
KOAc			3.5			20
CaCl <sub>2</sub> .6H <sub>2</sub> O	3.5	4.5	5.6	6.9	8.3	20
CrO <sub>3</sub>			6.1			32
Zn(NO3)2.6H2O			7.4			42
K <sub>2</sub> CO <sub>3</sub> .2H <sub>2</sub> O			7.7	10.7		44
KCNS			8.2			47
Na2Cr2O7.2H2O			9.1			52
Ca(NO3)2.4H2O	6.0	7.7	9.6	11.9	14.2	55
Mg(NO3)2.6H2O			9.8			56
NaBr.2H <sub>2</sub> O	5.8	7.8	10.3	13.5	17.5	58
NaNO <sub>2</sub>			11.6			66
NaClO <sub>3</sub>			13.1			75
NaCl	6.9	9.6	13.2	17.8	21.4	75
NaOAc			13.3			76
NH4Cl			13.8			79
(NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub>			14.2			81
KBr			14.7			84
KHSO4			15.1			86
KC1			15.1	20.2	27.0	86
K <sub>2</sub> CrO <sub>4</sub>			15.4			88
ZnSO <sub>4</sub> .7H <sub>2</sub> O			15.8			90
NH4.H2PO4			16.3			93
KNO3			16.7	22.3	29.8	95
$Pb(NO_3)_2$			17.2			98
H <sub>2</sub> O	9.21	12.79	17.53	23.76	31.82	100

TABLE 18. Class	DRYING AGENTS FOR CLASSES OF COMPOUNDS Dried with
Acetals	Potassium carbonate.
Acids (organic)	Calcium sulfate, magnesium sulfate, sodium sulfate.
Acyl halides	Magnesium sulfate, sodium sulfate.
Alcohols	Calcium oxide, calcium sulfate, magnesium sulfate, potassium carbonate, followed by magnesium and iodine.
Aldehydes	Calcium sulfate, magnesium sulfate, sodium sulfate.
Alkyl halides	Calcium chloride, calcium sulfate, magnesium sulfate, phosphorus pentoxide, sodium sulfate.
Amines	Barium oxide, calcium oxide, potassium hydroxide, sodium carbonate, sodium hydroxide.
Aryl halides	Calcium chloride, calcium sulfate, magnesium sulfate, phosphorus pentoxide, sodium sulfate.
Esters	Magnesium sulfate, potassium carbonate, sodium sulfate.
Ethers	Calcium chloride, calcium sulfate, magnesium sulfate, sodium, lithium aluminium hydride.
Heterocyclic bases	Magnesium sulfate, potassium carbonate, sodium hydroxide.
Hydrocarbons	Calcium chloride, calcium sulfate, magnesium sulfate, phosphorus pentoxide, sodium (not for olefins).
Ketones	Calcium sulfate, magnesium sulfate, potassium carbonate, sodium sulfate.
Mercaptans	Magnesium sulfate, sodium sulfate.
Nitro compounds and	
Nitriles	Calcium chloride, magnesium sulfate, sodium sulfate.
Sulfides	Calcium chloride, calcium sulfate.

TABLE 19.	STATIC DRYING FOR SELECTED LIQUIDS (25°C)							
Liquid	Water	Linde Type 4 A	Linde Type 5 A	Activated Alumina	Silicic Acid Gel			
MeOH	Residual H <sub>2</sub> O % Wt % absorbed	0.54 2.50	0.55 1.50		0.60 —			
EtOH	Residual H <sub>2</sub> O % Wt % absorbed	0.25 7.00	0.25 6.80	0.45 1.50	0.68			
1-Butylamine	Residual H <sub>2</sub> O % Wt % absorbed	1.65 10.40	1.31 18.20	1.93 3.40	2.07			
2-Ethyl- hexylamine	Residual H <sub>2</sub> O % Wt % absorbed	0.25 15.10	0.08 21.10	0.43 6.10	0.53 1.70			
Diethyl ether	Residual H <sub>2</sub> O % Wt % absorbed	0.001 9.50	0.013 9.20	0.16 6.20	0.27 4.30			
Amyl acetate	Residual H <sub>2</sub> O % Wt % absorbed	0.002 9.30	_	0.33 7.40	0.38 1.80			

# TABLE 20. BOILING POINTS OF SOME USEFUL GASES AT 760 mm

Argon	-185.6°	Krypton	-152.3°
Carbon dioxide	-78.5°	Methane	-164.0°
(sublimes)		Neon	-246.0°
Carbon monoxide	-191.3°	Nitrogen	-209.9°
Ethane	-88.6°	Nitrous oxide	-88.5°
Helium	-268.6°	Nitric oxide	-195.8°
Hydrogen	-252.6°	Oxygen	-182.96°

Gas	Temperature °C	МеОН	EtOH	Et <sub>2</sub> O
Hydrogen	-10 0	54.6 51.3	45.4	37.5 (-9.2º 35.6
Chloride*	20 30	47.0 (18°) 43.0	43.4 41.0 38.1	24.9 19.47
Ammonia	15	21.6 (27.6g/100g MeOH)	13.2 (9.2g/100mL soln)	
	25	16.5 (19.8g/100g MeOH)	10.0 (6.0g/100mL soln)	

\* Saturated EtOH with HCl is ~ 5.7M at 25°C, i.e. 21.5g/100mL of solution.

TABLE 22. PREFIXES FOR QUANTITIES								
Fractional	deci (d) = 10 <sup>-1</sup>	centi (c) = 10 <sup>-2</sup>	milli (m) = 10 <sup>-3</sup>	micro (μ) = 10 <sup>-6</sup>	nano (n) = 10 <sup>-9</sup>	pico (p) = 10 <sup>-12</sup>	femto (f) = $10^{-15}$	atto (atto) = $10^{-18}$
Multiple	deca (d) = 10 <sup>1</sup>	hecto (h) = $10^2$	kilo (k) = 10 <sup>3</sup>	mega (M) = 10 <sup>6</sup>	giga (G) = 10 <sup>9</sup>	tera (T) = 10 <sup>12</sup>	penta (P) = 10 <sup>15</sup>	eka (E) = 10 <sup>18</sup>

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# **CHAPTER 2**

# **CHEMICAL METHODS**

# USED

# **IN PURIFICATION**

## **GENERAL REMARKS**

Greater selectivity in purification can often be achieved by making use of differences in chemical properties between the substance to be purified and the contaminants. Unwanted metal ions may be removed by precipitation in the presence of a *collector* (see p. 54). Sodium borohydride and other metal hydrides transform organic peroxides and carbonyl-containing impurities such as aldehydes and ketones in alcohols and ethers. Many classes of organic chemicals can be purified by conversion into suitable derivatives, followed by regeneration. This chapter describes relevant procedures.

# **REMOVAL OF TRACES OF METALS FROM REAGENTS**

#### **METAL IMPURITIES**

The presence of metal contaminants in reagents may sometimes affect the chemical or biochemical outcomes of an experiment. In these cases, it is necessary to purify the reagents used.

Metal impurities can be determined qualitatively and quantitatively by atomic absorption spectroscopy and the required purification procedures can be formulated. Metal impurities in organic compounds are usually in the form of ionic salts or complexes with organic compounds and very rarely in the form of free metal. If they are present in the latter form then they can be removed by crystallising the organic compound (whereby the insoluble metal can be removed by filtration), or by distillation in which case the metal remains behind with the residue in the distilling flask. If the impurities are in the ionic or complex forms, then extraction of the organic compound in a suitable organic solvent with aqueous acidic or alkaline solutions will reduce their concentration to acceptable levels.

When the metal impurities are present in inorganic compounds as in metals or metal salts, then advantage of the differences in chemical properties should be taken. Properties of the impurities like the solubility, the solubility product (product of the metal ion and the counter-ion concentrations), the stability constants of the metal complexes with organic complexing agents and their solubilities in organic solvents should be considered. Alternatively the impurities can be masked by the addition of complexing agents which could lower the concentration of the metal ion impurities to such low levels that they would not interfere with the main compound (see complexation below). Specific procedures and examples are provided below.

## DISTILLATION

Reagents such as water, ammonia, hydrochloric acid, nitric acid, perchloric acid, and sulfuric acid can be purified via distillation (preferably under reduced pressure and particularly with perchloric acid) using an allglass still. Isothermal distillation is convenient for ammonia: a beaker containing concentrated ammonia is placed alongside a beaker of distilled water for several days in an empty desiccator so that some of the ammonia distils over into the water. The redistilled ammonia should be kept in polyethylene or paraffin-waxed bottles. Hydrochloric acid can be purified in the same way. To ensure the absence of metal contaminants from some salts (e.g. ammonium acetate), it may be more expedient to synthesise the salts using distilled components rather than to attempt to purify the salts themselves.

# **USE OF ION EXCHANGE RESINS**

Application of ion-exchange columns has greatly facilitated the removal of heavy metal ions such as  $Cu^{2+}$ ,  $Zn^{2+}$ and Pb<sup>2+</sup> from aqueous solutions of many reagents. Thus, sodium salts and sodium hydroxide can be purified by passage through a column of a cation-exchange resin in its sodium form, prepared by washing the resin with 0.1M aqueous NaOH then washing with water until the pH of the effluent is ~7. Similarly, for acids, a resin in its H<sup>+</sup> form [prepared by washing the column with 0.1M aqueous mineral acid (HCl, H<sub>2</sub>SO<sub>4</sub>) followed by thorough washing with water until the effluent has pH ~7 is used. In some cases, where metals form anionic complexes, they can be removed by passage through an anion-exchange resin. Iron in hydrochloric acid solution can be removed in this way.

Ion exchange resins are also useful for demineralising biochemical preparations such as proteins. Removal of metal ions from protein solutions using polystyrene-based resins, however, may lead to protein denaturation. This difficulty may be avoided by using a weakly acidic cation exchanger such as Bio-Rex 70.

Heavy metal contamination of pH buffers can be removed by passage of the solutions through a Chelex X-100 column. For example when a solution of 0.02M HEPES [4-(2-HydroxyEthyl)Piperazine-1-Ethanesulfonic acid] containing 0.2M KCl (1L, pH 7.5) alone or with calmodulin, is passed through a column of Chelex X-100 (60g) in the K<sup>+</sup> form, the level of Ca<sup>2+</sup> ions falls to less than 2 x 10<sup>-7</sup> M as shown by atomic absorption spectroscopy. Such solutions should be stored in polyethylene containers that have been washed with boiling deionised water (5min) and rinsed several times with deionised water. TES [N,N,N',N'-Tetraethylsulfamide] and TRIS [Tris-(hydroxymethyl)aminomethane] have been similarly decontaminated from metal ions.

Water, with very low concentrations of ionic impurities (and approaching conductivity standards), is very readily obtained by percolation through alternate columns of cation- and anion-exchange resins, or through a mixed-bed resin, and many commercial devices are available for this purpose. For some applications, this method is unsatisfactory because the final deionised water may contain traces of organic material after passage through the columns. However, organic matter can also be removed by using yet another special column in series for this purpose (see Milli Q water preparation, Millipore Corpn., www.millipore.com).

# PRECIPITATION

In removing traces of impurities by precipitation it is necessary to include a material to act as a *collector* of the precipitated substance so as to facilitate its removal by filtration or decantation. The following are a few examples:

# **Removal of lead contaminants**

Aqueous hydrofluoric acid can be freed from lead by adding 1mL of 10% strontium chloride per 100mL of acid, lead being co-precipitated as lead fluoride with the strontium fluoride. If the hydrofluoric acid is decanted from the precipitate and the process repeated, the final lead content in the acid is less than 0.003 ppm. Similarly, lead can be precipitated from a nearly saturated sodium carbonate solution by adding 10% strontium chloride dropwise (1-2mL per 100mL) followed by filtration. (If the sodium carbonate is required as a solid, the solution can be evaporated to dryness in a platinum dish.) Removal of lead from potassium chloride uses precipitation as lead sulfide by bubbling  $H_2S$ , followed, after filtration, by evaporation and recrystallisation of the potassium chloride.

#### **Removal of iron contaminants**

Iron contaminants have been removed from potassium thiocyanate solutions by adding a slight excess of an aluminium salt, then precipitating aluminum and iron as their hydroxides by adding a few drops of ammonia. Iron is also carried down on the hydrated manganese dioxide precipitate formed in cadmium chloride or cadmium sulfate solutions by adding 0.5% aqueous potassium permanganate (0.5mL per 100mL of solution), sufficient ammonia to give a slight precipitate, and 1mL of ethanol. The solution is heated to boiling to coagulate the precipitate, then filtered. Ferrous ion can be removed from copper solutions by adding some hydrogen peroxide to the solution to oxidise the iron, followed by precipitation of ferric hydroxide by adding a small amount of sodium hydroxide.

#### **Removal of other metal contaminants**

Traces of calcium can be removed from solutions of sodium salts by precipitation at pH 9.5-10 as the 8-hydroxyquinolinate. The excess 8-hydroxyquinoline acts as a collector.

# **EXTRACTION**

In some cases, a simple solvent extraction is sufficient to remove a particular impurity. For example, traces of gallium can be removed from titanous chloride in hydrochloric acid by extraction with diisopropyl ether.

Similarly, ferric chloride can be removed from aluminium chloride solutions containing hydrochloric acid by extraction with diethyl ether. Usually, however, it is necessary to extract an undesired metal with an organic solvent in the presence of a suitable complexing agent such as dithizone (diphenylthiocarbazone) or sodium diethyl dithiocarbamate. When the former is used, weakly alkaline solutions of the substance containing the metal impurity are extracted with dithizone in chloroform (at about 25mg/L of chloroform) or carbon tetrachloride until the colour of some fresh dithizone solution remains unchanged after shaking. Dithizone complexes metals more strongly in weakly alkaline solutions. Excess dithizone in the aqueous medium is removed by extracting with the pure solvent (chloroform or carbon tetrachloride), the last traces of which, in turn, are removed by aeration. This method has been used to remove metal impurities from aqueous solutions of ammonium hydrogen citrate, potassium bromide, potassium cyanide, sodium acetate and sodium citrate. The advantage of dithizone for such a purpose lies in the wide range of metals with which it combines under these conditions. 8-Hydroxyquinoline (oxine) can also be used in this way. Sodium diethyl dithiocarbamate has been used to remove metals from aqueous hydroxylamine hydrochloride (made just alkaline to thymol blue by adding ammonia) from copper and other heavy metals by repeated extraction with chloroform until no more diethyl dithiocarbamate remained in the solution (which was then acidified to thymol blue by adding hydrochloric acid).

#### COMPLEXATION

Although not strictly a removal of an impurity, addition of a suitable complexing agent such as ethylenediaminetetraacetic acid often overcomes the undesirable effects of contaminating metal ions by reducing the concentrations of the free metal species to very low levels, i.e. sequestering metal ions by complexation. For a detailed discussion of this masking, see Masking and Demasking of Chemical Reactions, D.D.Perrin, Wiley-Interscience, New York, 1970.

# **USE OF METAL HYDRIDES**

This group of reagents is commercially available in large quantities; some of its members - notably lithium aluminium hydride (LiAlH<sub>4</sub>), calcium hydride (CaH<sub>2</sub>), sodium borohydride (NaBH<sub>4</sub>) and potassium borohydride (KBH<sub>4</sub>) - have found widespread use in the purification of chemicals.

# LITHIUM ALUMINIUM HYDRIDE

This solid is stable at room temperature, and is soluble in ether-type solvents. It reacts violently with water, liberating hydrogen, and is a powerful drying and reducing agent for organic compounds. It reduces aldehydes, ketones, esters, carboxylic acids, peroxides, acid anhydrides and acid chlorides to the corresponding alcohols. Similarly, amides, nitriles, aldimines and aliphatic nitro compounds yield amines, while aromatic nitro compounds are converted to azo compounds. For this reason it finds extensive application in purifying organic chemical substances by the removal of water and carbonyl containing impurities as well as peroxides formed by autoxidation. Reactions can generally be carried out at room temperature, or in refluxing diethyl ether, at atmospheric pressure. When drying organic liquids with this reagent it is important that the concentration of water in the liquid is below 0.1% - otherwise a violent reaction or **EXPLOSION** may occur. LiAlH<sub>4</sub> should be added cautiously to a cooled solution of organic liquid in a flask equipped with a reflux condenser.

#### CALCIUM HYDRIDE

This powerful drying agent is suitable for use with hydrogen, argon, helium, nitrogen, hydrocarbons, chlorinated hydrocarbons, esters and higher alcohols.

#### SODIUM BOROHYDRIDE

This solid which is stable in dry air up to 300°, is a less powerful reducing agent than lithium aluminium hydride, from which it differs also by being soluble in hydroxylic solvents and to a lesser extent in ether-type solvents. Sodium borohydride forms a dihydrate melting at 36-37°, and its aqueous solutions decompose slowly unless stabilised to above pH 9 by alkali. (For example, a useful sodium borohydride solution is one that is nearly saturated at 30-40° and containing 0.2% sodium hydroxide.) Its solubility in water is 25, 55 and 88g per 100mL of water at 0°, 25° and 60°, respectively. Boiling or acidification rapidly decomposes aqueous sodium borohydride solutions. The reagent, available either as a hygroscopic solid or as an aqueous sodium hydroxide solution, is useful as a water soluble reducing agent for aldehydes, ketones and organic peroxides. This explains its use for the removal of carbonyl-containing impurities and peroxides from alcohols, polyols, esters, polyesters, amino alcohols, olefins, chlorinated hydrocarbons, ethers, polyethers, amines (including aniline), polyamines and aliphatic sulfonates.

Purifications using sodium borohydride can be carried out conveniently using alkaline aqueous or methanolic solutions of sodium borohydride, allowing the reaction mixture to stand at room temperature for several hours. Other solvents that can be used with this reagent include isopropyl alcohol (without alkali), amines (including liquid ammonia, in which its solubility is 104g per 100g of ammonia at 25°, and ethylenediamine), diglyme, formamide, dimethylformamide and tetrahydrofurfuryl alcohol. Alternatively, the material to be purified can be percolated through a column of the borohydride. In the absence of water, sodium borohydride solutions in organic solvents such as dioxane or amines decompose only very slowly at room temperature. Treatment of ethers with sodium borohydride appears to inhibit peroxide formation.

# POTASSIUM BOROHYDRIDE

Potassium borohydride is similar in properties and reactions to sodium borohydride, and can similarly be used as a reducing agent for removing aldehydes, ketones and organic peroxides. It is non-hygroscopic and can be used in water, ethanol, methanol or water-alcohol mixtures, provided some alkali is added to minimise decomposition, but it is somewhat less soluble than sodium borohydride in most solvents. For example, the solubility of potassium borohydride in water at 25° is 19g per 100mL of water (as compared to sodium borohydride, 55g).

# **PURIFICATION** via DERIVATIVES

Relatively few derivatives of organic substances are suitable for use as aids to purification. This is because of the difficulty in regenerating the starting material. For this reason, we list below, the common methods of preparation of derivatives that can be used in this way.

Whether or not any of these derivatives is likely to be satisfactory for the use of any particular case will depend on the degree of difference in properties, such as solubility, volatility or melting point, between the starting material, its derivative and likely impurities, as well as on the ease with which the substance can be recovered. Purification *via* a derivative is likely to be of most use when the quantity of pure material that is required is not too large. Where large quantities (for example, more than 50g) are available, it is usually more economical to purify the material directly (for example, in distillations and recrystallisations).

The most generally useful purifications via derivatives are as follows:

# **ALCOHOLS**

Aliphatic or aromatic alcohols are converted to solid esters. *p*-Nitrobenzoates are examples of convenient esters to form because of their sharp melting points, and the ease with which they can be recrystallised as well as the ease with which the parent alcohol can be recovered. The *p*-nitrobenzoyl chloride used in the esterification is prepared by refluxing dry *p*-nitrobenzoic acid with a 3 molar excess of thionyl chloride for 30min on a steam bath (*in a fume cupboard*). The solution is cooled slightly and the excess thionyl chloride is distilled off under vacuum, keeping the temperature below  $40^{\circ}$ . Dry toluene is added to the residue in the flask, then distilled off under vacuum, the process being repeated two or three times to ensure complete removal of thionyl chloride, hydrogen chloride and sulfur dioxide. (This freshly prepared *p*-nitrobenzoyl chloride cannot be stored without decomposition; it should be used directly.) A solution of the acid chloride (1mol) in dry toluene or alcohol-free chloroform (distilled from P<sub>2</sub>O<sub>5</sub> or by passage through an activated Al<sub>2</sub>O<sub>3</sub> column) under a reflux condenser is cooled in an ice bath while the alcohol (1mol), with or without a solvent (preferably miscible with toluene or alcohol-free chloroform), is added dropwise to it. When addition is over and the reaction subsides, the mixture is refluxed for 30min and the solvent is removed under reduced pressure. The solid ester is then recrystallised to constant melting point from toluene, acetone, low boiling point petroleum ether or mixtures of these, but not from alcohols.

Hydrolysis of the ester is achieved by refluxing in aqueous N or 2N NaOH solution until the insoluble ester dissolves. The solution is then cooled, and the alcohol is extracted into a suitable solvent, e.g. ether, toluene or alcohol-free chloroform. The extract is dried (CaSO<sub>4</sub>, MgSO<sub>4</sub>) and distilled, then fractionally distilled if liquid or recrystallised if solid. (The *p*-nitrobenzoic acid can be recovered by acidification of the aqueous layer.) In most cases where the alcohol to be purified can be readily extracted from ethanol, the hydrolysis of the ester is best achieved with N or 2N ethanolic NaOH or 85% aqueous ethanolic N NaOH. The former is prepared by dissolving the necessary alkali in a minimum volume of water and diluting with absolute alcohol. The ethanolic solution is refluxed for one to two hours and hydrolysis is complete when an aliquot gives a clear solution on dilution with four or five times its volume of water. The bulk of the ethanol is distilled off and the residue is extracted as above. Alternatively, use can be made of ester formation with benzoic acid, toluic acid or 3,5dinitrobenzoic acid, by the above method.

Other derivatives can be prepared by reaction of the alcohol with an acid anhydride. For example, phthalic or 3nitrophthalic anhydride (1 mol) and the alcohol (1mol) are refluxed for half to one hour in a non-hydroxylic solvent, e.g. toluene or alcohol-free chloroform, and then cooled. The phthalate ester crystallises out, is precipitated by the addition of low boiling petroleum ether or is isolated by evaporation of the solvent. It is recrystallised from water, 50% aqueous ethanol, toluene or low boiling petroleum ether. Such an ester has a characteristic melting point and the alcohol can be recovered by acid or alkaline hydrolysis.

#### **ALDEHYDES**

The best derivative from which an aldehyde can be recovered readily is its bisulfite addition compound, the main disadvantage being the lack of a sharp melting point. The aldehyde (sometimes in ethanol) is shaken with a cold saturated solution of sodium bisulfite until no more solid adduct separates. The adduct is filtered off, washed with a little water, followed by alcohol. A better reagent to use is a freshly prepared saturated aqueous sodium bisulfite solution to which 75% ethanol is added to near-saturation. (Water may have to be added dropwise to render this solution clear.) With this reagent the aldehyde need not be dissolved separately in alcohol and the adduct is finally washed with alcohol. The aldehyde is recovered by dissolving the adduct in the least volume of water and adding an equivalent quantity of sodium carbonate (not sodium hydroxide) or concentrated hydrochloric acid to react with the bisulfite, followed by steam distillation or solvent extraction. Other derivatives that can be prepared are the Schiff bases and semicarbazones. Condensation of the aldehyde with an equivalent of primary aromatic amine yields the Schiff base, for example aniline at 100° for 10-30min. Semicarbazones are prepared by dissolving semicarbazide hydrochloride ( $ca \ lg$ ) and sodium acetate ( $ca \ l.5g$ ) in water (8-10mL) and adding the aldehyde or ketone (0.5-1g) with stirring. The semicarbazone crystallises out and is recrystallised from ethanol or aqueous ethanol. These are hydrolysed by steam distillation in the presence of oxalic acid or better by exchange with pyruvic acid (Hershberg J Org Chem 13 542 1948) [see entry under Ketones].

#### AMINES

#### Picrates

The most versatile derivative from which the free base can be readily recovered is the picrate. This is very satisfactory for primary and secondary aliphatic amines and aromatic amines and is particularly so for heterocyclic bases. The amine, dissolved in water or alcohol, is treated with excess of a saturated solution of picric acid in water or alcohol, respectively, until separation of the picrate is complete. If separation does not occur, the solution is stirred vigorously and warmed for a few minutes, or diluted with a solvent in which the picrate is insoluble. Thus, a solution of the amine and picric acid in ethanol can be treated with petroleum ether to precipitate the picrate. Alternatively, the amine can be dissolved in alcohol and aqueous picric acid added. The picrate is filtered off, washed with water or ethanol and recrystallised from boiling water, ethanol, methanol, aqueous ethanol, methanol or chloroform. The solubility of picric acid in water and ethanol is 1.4 and 6.23 % respectively at 20°.

It is not advisable to store large quantities of picrates for long periods, *particularly when they are dry due to their potential* **EXPLOSIVE** *nature*. The free base should be recovered as soon as possible. The picrate is suspended in an excess of 2N aqueous NaOH and warmed a little. Because of the limited solubility of sodium picrate, excess hot water must be added. Alternatively, because of the greater solubility of lithium picrate, aqueous 10% lithium hydroxide solution can be used. The solution is cooled, the amine is extracted with a suitable solvent such as diethyl ether or toluene, washed with 5N NaOH until the alkaline solution remains colourless, then with water, and the extract is dried with anhydrous sodium carbonate. The solvent is distilled off and the amine is fractionally distilled (under reduced pressure if necessary) or recrystallised.

If the amines are required as their hydrochlorides, picrates can often be decomposed by suspending them in acetone and adding two equivalents of 10N HCl. The hydrochloride of the base is filtered off, leaving the picric acid in the acetone. Dowex No 1 anion-exchange resin in the chloride form is useful for changing solutions of the more soluble picrates (for example, of adenosine) into solutions of their hydrochlorides, from which sodium hydroxide precipitates the free base.

#### Salts

Amines can also be purified *via* their salts, e.g. hydrochlorides. A solution of the amine in dry toluene, diethyl ether, dichloromethane or chloroform is saturated with dry hydrogen chloride (generated by addition of concentrated sulfuric acid to dry sodium chloride, or to concentrated HCl followed by drying the gas through sulfuric acid, or from a hydrogen chloride cylinder) and the insoluble hydrochloride is filtered off and dissolved in water. The solution is made alkaline and the amine is extracted, as above. Hydrochlorides can also be prepared by dissolving the amine in ethanolic HCl and adding diethyl ether or petroleum ether. Where

hydrochlorides are too hygroscopic or too soluble for satisfactory isolation, other salts, e.g. nitrate, sulfate, bisulfate or oxalate, can be used.

# Double salts

The amine (1mol) is added to a solution of anhydrous zinc chloride (1mol) in concentrated hydrochloric acid (42mL) in ethanol (200mL), or less depending on the solubility of the double salt). The solution is stirred for 1h and the precipitated salt is filtered off and recrystallised from ethanol. The free base is recovered by adding excess of 5-10N NaOH (to dissolve the zinc hydroxide that separates) and is steam distilled. Mercuric chloride in hot water can be used instead of zinc chloride and the salt is crystallised from 1% hydrochloric acid. Other double salts have been used, e.g. cuprous salts, but are not as convenient as the above salts.

#### **N-Acetyl derivatives**

Purification as their *N*-acetyl derivatives is satisfactory for primary, and to a limited extent secondary, amines. The base is refluxed with slightly more than one equivalent of acetic anhydride for half to one hour, cooled and poured into ice-cold water. The insoluble derivative is filtered off, dried, and recrystallised from water, ethanol, aqueous ethanol or benzene (CAUTION toxic!). The derivative can be hydrolysed to the parent amine by refluxing with 70% sulfuric acid for a half to one hour. The solution is cooled, poured onto ice, and made alkaline. The amine is steam distilled or extracted as above. Alkaline hydrolysis is very slow.

#### N-Tosyl derivatives

Primary and secondary amines are converted into their tosyl derivatives by mixing equimolar amounts of amine and p-toluenesulfonyl chloride in dry pyridine (ca 5-10mols) and allowing to stand at room temperature overnight. The solution is poured into ice-water and the pH adjusted to 2 with HCl. The solid derivative is filtered off, washed with water, dried (vac. desiccator) and recrystallised from an alcohol or aqueous alcohol solution to a sharp melting point. The derivative is decomposed by dissolving in liquid ammonia (*fume cupboard*) and adding sodium metal (in small pieces with stirring) until the blue colour persists for 10-15min. Ammonia is allowed to evaporate (*fume cupboard*), the residue treated with water and the solution checked that the pH is above 10. If the pH is below 10 then the solution has to be basified with 2N NaOH. The mixture is extracted with diethyl ether or toluene, the extract is dried ( $K_2CO_3$ ), evaporated and the residual amine recrystallised if solid or distilled if liquid.

# **AROMATIC HYDROCARBONS**

# Adducts

Aromatic hydrocarbons can be purified as their picrates using the procedures described for amines. Instead of picric acid, 1,3,5-trinitrobenzene or 2,4,7-trinitrofluorenone can also be used. In all these cases, following recrystallisation, the hydrocarbon can be isolated either as described for amines or by passing a solution of the adduct through an activated alumina column and eluting with toluene or petroleum ether. The picric acid and nitro compounds are more strongly adsorbed on the column.

#### Sulfonation

Naphthalene, xylenes and alkyl benzenes can be purified by sulfonation with concentrated sulfuric acid and crystallisation of the sodium sulfonates. The hydrocarbon is distilled out of the mixture with superheated steam.

#### CARBOXYLIC ACIDS

# **4-Bromophenacyl esters**

A solution of the sodium salt of the acid is prepared. If the salt is not available, the acid is dissolved in an equivalent of aqueous NaOH and the pH adjusted to 8-9 with this base. A solution of one equivalent of 4bromophenacyl bromide (for a monobasic acid, two equivalents for a dibasic acid, etc) in ten times its volume of ethanol is then added. The mixture is heated to boiling, and, if necessary, enough ethanol is added to clarify the solution which is then refluxed for half an hour to three hours depending on the number of carboxylic groups that have to be esterified. (One hour is generally sufficient for monocarboxylic acids.) On cooling, the ester should crystallise out. If it does not, then the solution is heated to boiling, and enough water is added to produce a slight turbidity. The solution is again cooled. The ester is collected, and recrystallised or fractionally distilled.

The ester is hydrolysed by refluxing for 1-2h with 1-5% of barium carbonate suspended in water or with aqueous sodium carbonate solution. The solution is cooled and extracted with diethyl ether, toluene or chloroform. It is then acidified and the acid is collected by filtration or extraction, and recrystallised or fractionally distilled.

p-Nitrobenzyl esters can be prepared in an analogous manner using the sodium salt of the acid and p-nitrobenzyl bromide. They are readily hydrolysed.

# **Alkyl esters**

Of the alkyl esters, methyl esters are the most useful because of their rapid hydrolysis. The acid is refluxed with one or two equivalents of methanol in excess alcohol-free chloroform (or dichloromethane) containing about 0.1g of *p*-toluenesulfonic acid (as catalyst), using a Dean-Stark apparatus. (The water formed by the

esterification is carried away into the trap.) When the theoretical amount of water is collected in the trap, esterification is complete. The chloroform solution in the flask is washed with 5% aqueous sodium carbonate solution, then water, and dried over anhydrous sodium sulfate or magnesium sulfate. The chloroform is distilled off and the ester is fractionally distilled through an efficient column. The ester is hydrolysed by refluxing with 5-10% aqueous NaOH solution until the insoluble ester has completely dissolved. The aqueous solution is concentrated a little by distillation to remove all of the methanol. It is then cooled and acidified. The acid is either extracted with diethyl ether, toluene or chloroform, or filtered off and isolated as above. Other methods for preparing esters are available.

#### Salts

The most useful salt derivatives for carboxylic acids are the isothiouronium salts. These are prepared by mixing almost saturated solutions containing the acid (carefully neutralised with N NaOH using phenolphthalein indicator) then adding two drops of N HCl and an equimolar amount of S-benzylisothiouronium chloride in ethanol and filtering off the salt that crystallises out. After recrystallisation from water, alcohol or aqueous alcohol the salt is decomposed by suspending or dissolving in 2N HCl and extracting the carboxylic acid from aqueous solution into diethyl ether, chloroform or toluene.

### **HYDROPEROXIDES**

These can be converted to their sodium salts by precipitation below 30° with aqueous 25% NaOH. The salt is then decomposed by addition of solid (powdered) carbon dioxide and extracted with low-boiling petroleum ether. The solvent should be removed under reduced pressure below 20°. The manipulation should be adequately shielded at all times to guard against EXPLOSIONS for the safety of the operator.

#### **KETONES**

### **Bisulfite adduct**

The adduct can be prepared and decomposed as described for aldehydes. Alternatively, because no Cannizzaro reaction is possible, it can also be decomposed with 0.5N NaOH.

#### Semicarbazones

A powdered mixture of semicarbazide hydrochloride (1mol) and anhydrous sodium acetate (1.3mol) is dissolved in water by gentle warming. A solution of the ketone (1mol) in the minimum volume of ethanol needed to dissolve it is then added. The mixture is warmed on a water bath until separation of the semicarbazone is complete. The solution is cooled, and the solid is filtered off. After washing with a little ethanol followed by water, it is recrystallised from ethanol or dilute aqueous ethanol. The derivative should have a characteristic melting point. The semicarbazone is decomposed by refluxing with excess of oxalic acid or with aqueous sodium carbonate solution. The ketone (which steam distils) is distilled off. It is extracted or separated from the distillate (after saturating with NaCl), dried with CaSO<sub>4</sub> or MgSO<sub>4</sub> and fractionally distilled using an efficient column (under vacuum if necessary). [See entry under Aldehydes.]

# PHENOLS

The most satisfactory derivatives for phenols that are of low molecular weight or monohydric are the benzoate esters. (Their acetate esters are generally liquids or low-melting solids.) Acetates are more useful for high molecular weight and polyhydric phenols.

#### **Benzoates**

The phenol (1mol) in 5% aqueous NaOH is treated (while cooling) with benzoyl chloride (1mol) and the mixture is stirred in an ice bath until separation of the solid benzoyl derivative is complete. The derivative is filtered off, washed with alkali, then water, and dried (in a vacuum desiccator over NaOH). It is recrystallised from ethanol or dilute aqueous ethanol. The benzoylation can also be carried out in dry pyridine at low temperature ( $ca 0^{\circ}$ ) instead of in NaOH solution, finally pouring the mixture into water and collecting the solid as above. The ester is hydrolysed by refluxing in an alcohol (for example, ethanol, *n*-butanol) containing two or three equivalents of the alkoxide of the corresponding alcohol (for example sodium ethoxide or sodium *n*-butoxide) and a few (ca 5-10) millilitres of water, for half an hour to three hours. When hydrolysis is complete, an aliquot will remain clear on dilution with four to five times its volume of water. Most of the solvent is distilled off. The residue is diluted with cold water and acidified, and the phenol is steam distilled. The latter is collected from the distillate, dried and either fractionally distilled or recrystallised.

#### Acetates

These can be prepared as for the benzoates using either acetic anhydride with 3N NaOH or acetyl chloride in pyridine. They are hydrolysed as described for the benzoates. This hydrolysis can also be carried out with aqueous 10% NaOH solution, completion of hydrolysis being indicated by the complete dissolution of the acetate in the aqueous alkaline solution. On steam distillation, acetic acid also distils off but in these cases the phenols (see above) are invariably solids which can be filtered off and recrystallised.

# PHOSPHATE AND PHOSPHONATE ESTERS

These can be converted to their uranyl nitrate addition compounds. The crude or partially purified ester is saturated with uranyl nitrate solution and the adduct filtered off. It is recrystallised from *n*-hexane, toluene or ethanol. For the more soluble members crystallisation from hexane using low temperatures (-40°) has been successful. The adduct is decomposed by shaking with sodium carbonate solution and water, the solvent is steam distilled (if hexane or toluene is used) and the ester is collected by filtration. Alternatively, after decomposition, the organic layer is separated, dried with CaCl<sub>2</sub> or BaO, filtered, and fractionally distilled under high vacuum.

# **MISCELLANEOUS**

Impurities can sometimes be removed by conversion to derivatives under conditions where the major component does not react or reacts much more slowly. For example, normal (straight-chain) paraffins can be freed from unsaturated and branched-chain components by taking advantage of the greater reactivity of the latter with chlorosulfonic acid or bromine. Similarly, the preferential nitration of aromatic hydrocarbons can be used to remove e.g. benzene or toluene from cyclohexane by shaking for several hours with a mixture of concentrated nitric acid (25%), sulfuric acid (58%), and water (17%).

# **GENERAL METHODS FOR THE PURIFICATION OF CLASSES OF COMPOUNDS**

Chapters 4, 5 and 6 list a large number of individual compounds, with a brief statement of how each one may be purified. For substances that are not included in these chapters the following procedures may prove helpful.

# **PROCEDURES**

If the laboratory worker does not know of a reference to the preparation of a commercially available substance, he may be able to make a reasonable guess at the synthetic method used from published laboratory syntheses. This information, in turn, can simplify the necessary purification steps by suggesting probable contaminants. However, for other than macromolecules it is important that *at least* the <sup>1</sup>H NMR spectrum and/or the mass spectrum of the substance should be measured. These measurements require no more than two to three milligrams of material and provide a considerable amount of information about the substance. From the bibliography at the end of this chapter, references to NMR, IR and mass spectral data for a large number of the compounds in the Aldrich catalogue are available and are extremely useful for identifying compounds and impurities. If the material appears to have several impurities these spectra should be followed by examination of their chromatographic properties and spot tests. Purification methods can then be devised to remove these impurities, and a monitoring method will have already been established.

Physical methods of purification depend largely on the melting and boiling points of the materials. For gases and low-boiling liquids use is commonly made of the *freeze-pump-thaw* procedure (see Chapter 1). Gas chromatography is also useful, especially for low-boiling point liquids. Liquids are usually purified by refluxing with drying agents, acids or bases, reducing agents, charcoal, etc., followed by fractional distillation under reduced pressure. For solids, general methods include fractional freezing of the melted material, taking the middle fraction. Another procedure is sublimation of the solid under reduced pressure. The other commonly used method for purifying solids is by recrystallisation from a solution in a suitable solvent, by cooling with or without the prior addition of a solvent in which the solute is not very soluble.

The nature of the procedure will depend to a large extent on the quantity of purified material that is required. For example, for small quantities (50-250mg) of a pure volatile liquid, preparative gas chromatography is probably the best method. Two passes through a suitable column may well be sufficient. Similarly, for small amounts (100-500mg) of an organic solid, column chromatography is likely to be very satisfactory, the eluate being collected as a number of separate fractions (ca 5-10mL) which are examined by FT-IR, NMR or UV spectroscopy, TLC or by some other appropriate analytical technique. (For information on suitable adsorbents and eluents the texts referred to in the bibliography at the end of Chapters 1 and 2 should be consulted.) Preparative thin layer chromatography or HPLC can also be used successfully for purifying up to 500mg of solid. HPLC is the more and more commonly used procedure for the purification of small molecules as well as large molecules such as polypeptides and DNA.

Where larger quantities (upwards of 1g) are required, most of the impurities should be removed by preliminary treatments, such as solvent extraction, liquid-liquid partition, or conversion to a derivative (*vide supra*) which can be purified by crystallisation or fractional distillation before being reconverted to the starting material. The substance is then crystallised or distilled. If the final amounts must be in excess of 25g, preparation of a derivative is sometimes omitted because of the cost involved. In all of the above cases, purification is likely to be more laborious if the impurity is an isomer or a derivative with closely similar physical properties.

# **CRITERIA OF PURITY**

Purification becomes meaningful only insofar as adequate tests of purity are applied: the higher the degree of purity that is sought, the more stringent must these tests be. If the material is an organic solid, its melting point should first be taken and compared with the recorded value. Note that the melting points of most salts, organic or inorganic, are generally decomposition points and are not reliable criteria of purity. As part of this preliminary examination, the sample might be examined by thin layer chromatography in several different solvent systems and in high enough concentrations to facilitate the detection of minor components. On the other hand, if the substance is a liquid, its boiling point should be measured. If, further, it is a high boiling liquid, its chromatographic behaviour should be examined. Liquids, especially volatile ones, can be studied very satisfactorily by gas chromatography, preferably using at least two different stationary and/or mobile phases. Atomic absorption spectroscopy is a useful and sensitive method for detecting metal impurities and the concentrations of metals and metal salts or complexes.

Application of these tests at successive steps will give a good indication of whether or not the purification is satisfactory and will also show when adequate purification has been achieved. Finally elemental analyses, e.g. of carbon, hydrogen, nitrogen, sulfur, metals etc. are very sensitive to impurities (other than with isomers), and are good criteria of purity.

# GENERAL PROCEDURES FOR THE PURIFICATION OF SOME CLASSES OF ORGANIC COMPOUNDS

In the general methods of purification described below, it is assumed that the impurities belong essentially to a class of compounds different from the one being purified. They are suggested for use in cases where substances are not listed in Chapters 4, 5 and the low molecular weight compounds in Chapter 6. In such cases, the experimenter is advised to employ them in conjunction with information given in these chapters for the purification of suitable analogues. Also, for a wider range of drying agents, solvents for extraction and solvents for recrystallisation, the reader is referred to Chapter 1. See Chapter 6 for general purification procedures used for macromolecules.

#### ACETALS

These are generally diethyl or dimethyl acetal derivatives of aldehydes. They are more stable to alkali than to acids. Their common impurities are the corresponding alcohol, aldehyde and water. Drying with sodium wire removes alcohols and water, and polymerizes aldehydes so that, after decantation, the acetal can be fractionally distilled. In cases where the use of sodium is too drastic, aldehydes can be removed by shaking with alkaline hydrogen peroxide solution and the acetal is dried with sodium carbonate or potassium carbonate. Residual water and alcohols (up to *n*-propyl) can be removed with Linde type 4A molecular sieves. The acetal is then filtered and fractionally distilled. Solid acetals (i.e. acetals of high molecular weight aldehydes) are generally low-melting and can be recrystallised from low-boiling petroleum ether, toluene or a mixture of both.

# ACIDS

### Carboxylic acids

Liquid carboxylic acids are first freed from neutral and basic impurities by dissolving them in aqueous alkali and extracting with diethyl ether. (The pH of the solution should be at least three units above the  $pK_a$  of the acid, see pK in Chapter 1). The aqueous phase is then acidified to a pH at least three units below the  $pK_a$  of the acid and again extracted with ether. The extract is dried with magnesium sulfate or sodium sulfate and the ether is distilled off. The acid is fractionally distilled through an efficient column. It can be further purified by conversion to its methyl or ethyl ester (vide supra) which is then fractionally distilled. Hydrolysis yields the original acid which is again purified as above.

Acids that are solids can be purified in this way, except that distillation is replaced by repeated crystallisation (preferable from at least two different solvents such as water, alcohol or aqueous alcohol, toluene, toluene/petroleum ether or acetic acid.) Water-insoluble acids can be partially purified by dissolution in N sodium hydroxide solution and precipitation with dilute mineral acid. If the acid is required to be free from sodium ions, then it is better to dissolve the acid in hot N ammonia, heat to *ca* 80°, adding slightly more than an equal volume of N formic acid and allowing to cool slowly for crystallisation. Any ammonia, formic acid or ammonium formate that adhere to the acid are removed when the acid is dried in a vacuum — they are volatile. The separation and purification of naturally occurring fatty acids, based on distillation, salt solubility and low temperature crystallisation, are described by K.S.Markley (Ed.), *Fatty Acids*, 2nd Edn, part 3, Chap. 20, Interscience, New York, 1964.

Aromatic carboxylic acids can be purified by conversion to their sodium salts, recrystallisation from hot water, and reconversion to the free acids.

# **Sulfonic acids**

The low solubility of sulfonic acids in organic solvents and their high solubility in water makes necessary a treatment different from that for carboxylic acids. Sulfonic acids are strong acids, they have the tendency to hydrate, and many of them contain water of crystallisation. The lower-melting and liquid acids can generally be purified with only slight decomposition by fractional distillation, preferably under reduced pressure. A common impurity is sulfuric acid, but this can be removed by recrystallisation from concentrated aqueous solutions. The wet acid can be dried by azeotropic removal of water with toluene, followed by distillation. The higher-melting acids, or acids that melt with decomposition, can be recrystallised from water or, occasionally, from ethanol. For a typical purification of aromatic sulfonic acids using their barium salts refer to benzenesulfonic acid in Chapter 4.

# **Sulfinic acids**

These acids are less stable, less soluble and less acidic than the corresponding sulfonic acids. The common impurities are the respective sulfonyl chlorides from which they have been prepared, and the thiolsulfonates (neutral) and sulfonic acids into which they decompose. The first two of these can be removed by solvent extraction from an alkaline solution of the acid. On acidification of an alkaline solution, the sulfinic acid crystallises out leaving the sulfonic acid behind. The lower molecular weight members are isolated as their metal (e.g. ferric) salts, but the higher members can be crystallised from water (made slightly acidic), or alcohol.

#### ACID CHLORIDES

The corresponding acid and hydrogen chloride are the most likely impurities. Usually these can be removed by efficient fractional distillation. Where acid chlorides are not readily hydrolysed (e.g. aryl sulfonyl chlorides) the compound can be freed from contaminants by dissolving in a suitable solvent such as alcohol-free chloroform, dry toluene or petroleum ether and shaking with dilute sodium bicarbonate solution. The organic phase is then washed with water, dried with anhydrous sodium sulfate or magnesium sulfate, and distilled or recrystallised. This procedure is *hazardous* with readily hydrolysable acid chlorides such as acetyl chloride and benzoyl chloride. Solid acid chlorides should be thoroughly dried *in vacuo* over strong drying agents and are satisfactorily recrystallised from toluene, toluene-petroleum ether, petroleum ethers, alcohol-free chloroform/toluene, and, occasionally, from dry diethyl ether. Hydroxylic or basic solvents should be strictly avoided. All operations should be carried out in a fume cupboard because of the **irritant** nature of these compounds which also attack the skin.

#### **ALCOHOLS**

# Monohydric alcohols

The common impurities in alcohols are aldehydes or ketones, and water. [*Ethanol* in Chapter 4 is typical.] Aldehydes and ketones can be removed by adding a small amount of sodium metal and refluxing for 2 hours, followed by distillation. Water can be removed in a similar way but it is preferable to use magnesium metal instead of sodium because it forms a more insoluble hydroxide, thereby shifting the equilibrium more completely from metal alkoxide to metal hydroxide. The magnesium should be activated with iodine (or a small amount of methyl iodide), and the water content should be low, otherwise the magnesium will be deactivated. If the amount of water is large it should be removed by azeotropic distillation (see below), or by drying over anhydrous MgSO<sub>4</sub> (not CaCl<sub>2</sub> which combines with alcohols). Acidic materials can be removed by treatment

with anhydrous  $Na_2CO_3$ , followed by a suitable drying agent, such as calcium hydride, and fractional distillation, using gas chromatography to establish the purity of the product [Ballinger and Long, *J Am Chem Soc* 82 795 1960]. Alternatively, the alcohol can be refluxed with freshly ignited CaO for 4 hours and then fractionally distilled [McCurdy and Laidler, *Can J Chem* 41 1867 1963].

With higher-boiling alcohols it is advantageous to add some freshly prepared magnesium ethoxide solution (only slightly more than required to remove the water), followed by fractional distillation. Alternatively, in such cases, water can be removed by azeotropic distillation with toluene. Higher-melting alcohols can be purified by crystallisation from methanol or ethanol, toluene/petroleum ether or petroleum ether. Sublimation in vacuum, molecular distillation and gas chromatography are also useful means of purification. For purification via derivatives, vide supra.

#### Polyhydric alcohols

These alcohols are more soluble in water than are monohydric alcohols. Liquids can be freed from water by shaking with type 4A Linde molecular sieves and can safely be distilled only under high vacuum. Carbohydrate alcohols can be crystallised from strong aqueous solution or, preferably, from mixed solvents such as ethanol/petroleum ether or dimethyl formamide/toluene. Crystallisation usually requires seeding and is extremely slow. Further purification can be effected by conversion to the acetyl or benzoyl derivatives which are much less soluble in water and which can readily be recrystallised, e.g. from ethanol. Hydrolysis of the acetyl derivatives, followed by removal of acetate or benzoate and metal ions by ion-exchange chromatography, gives the purified material. On no account should solutions of carbohydrates be concentrated above 40° because of darkening and formation of *caramel*. Ion exchange, charcoal or cellulose column chromatography has been used for the purification and separation of carbohydrates.

#### **ALDEHYDES**

Common impurities found in aldehydes are the corresponding alcohols, aldols and water from selfcondensation, and the corresponding acids formed by autoxidation. Acids can be removed by shaking with aqueous 10% sodium bicarbonate solution. The organic liquid is then washed with water. It is dried with anhydrous sodium sulfate or magnesium sulfate and then fractionally distilled. Water soluble aldehydes must be dissolved in a suitable solvent such as diethyl ether before being washed in this way. Further purification can be effected via the bisulfite derivative (see pp. 57 and 59) or the Schiff base formed with aniline or benzidine. Solid aldehydes can be dissolved in diethyl ether and purified as above. Alternatively, they can be steam distilled, then sublimed and crystallised from toluene or petroleum ether.

#### AMIDES

Amides are stable compounds. The lower-melting members (such as acetamide) can be readily purified by fractional distillation. Most amides are solids which have low solubilities in water. They can be recrystallised from large quantities of water, ethanol, ethanol/ether, aqueous ethanol, chloroform/toluene, chloroform or acetic acid. The likely impurities are the parent acids or the alkyl esters from which they have been made. The former can be removed by thorough washing with aqueous ammonia followed by recrystallisation, whereas elimination of the latter is by trituration or recrystallisation from an organic solvent. Amides can be freed from solvent or water by drying below their melting points. These purifications can also be used for sulfonamides and acid hydrazides.

#### AMINES

The common impurities found in amines are nitro compounds (if prepared by reduction), the corresponding halides (if prepared from them) and the corresponding carbamate salts. Amines are dissolved in aqueous acid, the pH of the solution being at least three units below the  $pK_a$  value of the base to ensure almost complete formation of the cation. They are extracted with diethyl ether to remove neutral impurities and to decompose the carbamate salts. The solution is then made strongly alkaline and the amines that separate are extracted into a suitable solvent (ether or toluene) or steam distilled. The latter process removes coloured impurities. Note that chloroform cannot be used as a solvent for primary amines because, in the presence of alkali, poisonous carbylamines (isocyanides) are formed. However, chloroform is a useful solvent for the extraction of heterocyclic bases. In this case it has the added advantage that while the extract is being freed from the chloroform most of the moisture is removed with the solvent.

Alternatively, the amine may be dissolved in a suitable solvent (e.g. toluene) and dry HCl gas is passed through the solution to precipitate the amine hydrochloride. This is purified by recrystallisation from a suitable solvent mixture (e.g. ethanol/diethyl ether). The free amine can be regenerated by adding sodium hydroxide and isolated as above. Liquid amines can be further purified via their acetyl or benzoyl derivatives (vide supra). Solid amines can be recrystallised from water, alcohol, toluene or toluene-petroleum ether. Care should be taken in handling large quantities of amines because their vapours are harmful (possibly carcinogenic) and they are readily absorbed through the skin.

# AMINO ACIDS

Because of their zwitterionic nature, amino acids are generally soluble in water. Their solubility in organic solvents rises as the fat-soluble portion of the molecule increases. The likeliest impurities are traces of salts, heavy metal ions, proteins and other amino acids. Purification of these is usually easy, by recrystallisation from water or ethanol/water mixtures. The amino acid is dissolved in the boiling solvent, decolorised if necessary by boiling with 1g of acid-washed charcoal/100g amino acid, then filtered hot, chilled, and set aside for several hours to crystallise. The crystals are filtered off, washed with ethanol, then ether, and dried.

Amino acids have high melting or decomposition points and are best examined for purity by paper or thin layer chromatography. The spots are developed with ninhydrin. Customary methods for the purification of small quantities of amino acids obtained from natural sources (i.e. 1-5g) are ion-exchange chromatography (see Chapter 1). For general treatment of amino acids see Greenstein and Winitz [*The Amino Acids*, Vols 1-3, J.Wiley & Sons, New York 1961] and individual amino acids in Chapters 4 and 6.

A useful source of details such as likely impurities, stability and tests for homogeneity of amino acids is *Specifications and Criteria for Biochemical Compounds*, 3rd edn, National Academy of Sciences, USA, 1972.

#### ANHYDRIDES

The corresponding acids, resulting from hydrolysis, are the most likely impurities. Distillation from phosphorus pentoxide, followed by fractional distillation, is usually satisfactory. With high boiling or solid anhydrides, another method involves boiling under reflux for 0.5-1h with acetic anhydride, followed by fractional distillation. Acetic acid distils first, then acetic anhydride and finally the desired anhydride. Where the anhydride is a solid, removal of acetic acid and acetic anhydride at atmospheric pressure is followed by heating under vacuum. The solid anhydride is then either crystallised as for acid chlorides or (in some cases) sublimed in a vacuum. A preliminary purification when large quantities of acid are present in a solid anhydride (such as phthalic anhydride) is by preferential solvent extraction of the (usually) more soluble anhydride from the acid (e.g. with CHCl<sub>3</sub> in the case of phthalic anhydride). All operations with liquid anhydrides should be carried out in a fume cupboard because of their LACHRYMATORY properties. Almost all anhydrides attack skin.

#### **CAROTENOIDS**

These usually are decomposed by light, air and solvents, so that degradation products are probable impurities. Chromatography and adsorption spectra permit the ready detection of coloured impurities, and separations are possible using solvent distribution, chromatography or crystallisation. Thus, in partition between immiscible solvents, xanthophyll remains in 90% methanol while carotenes pass into the petroleum ether phase. For small amounts of material, thin-layer or paper chromatography may be used, while column chromatography is suitable for larger amounts. Colorless impurities may be detected by IR, NMR or mass spectrometry. The more common separation procedures are described by P. Karrer and E. Jucker in *Carotenoids*, E.A. Braude (translator), Elsevier, NY, 1950.

Purity can be checked by chromatography (on thin-layer plates, Kieselguhr, paper or columns), by UV or NMR procedures.

#### ESTERS

The most common impurities are the corresponding acid and hydroxy compound (i.e. alcohol or phenol), and water. A liquid ester from a carboxylic acid is washed with 2N sodium carbonate or sodium hydroxide to remove acid material, then shaken with calcium chloride to remove ethyl or methyl alcohols (if it is a methyl or ethyl ester). It is dried with potassium carbonate or magnesium sulfate, and distilled. Fractional distillation then removes residual traces of hydroxy compounds. This method does not apply to esters of inorganic acids (e.g. dimethyl sulfate) which are more readily hydrolysed in aqueous solution when heat is generated in the neutralisation of the excess acid. In such cases, several fractional distillations, preferably under vacuum, are usually sufficient.

Solid esters are easily crystallisable materials. It is important to note that esters of alcohols must be recrystallised either from non-hydroxylic solvents (e.g. toluene) or from the alcohol from which the ester is derived. Thus methyl esters should be crystallised from methanol or methanol/toluene, but not from ethanol, *n*-butanol or other alcohols, in order to avoid alcohol exchange and contamination of the ester with a second ester. Useful solvents for crystallisation are the corresponding alcohols or aqueous alcohols, toluene, toluene/petroleum ether, and chloroform (ethanol-free)/toluene. Esters of carboxylic acid derived from phenols

are more difficult to hydrolyse and exchange, hence any alcoholic solvent can be used freely. Sulfonic acid esters of phenols are even more resistant to hydrolysis: they can safely be crystallised not only from the above solvents but also from acetic acid, aqueous acetic acid or boiling *n*-butanol.

Fully esterified phosphoric acid and phosphonic acids differ only in detail from the above mentioned esters. Their major contaminants are alcohols or phenols, phosphoric or phosphonic acids (from hydrolysis), and (occasionally) basic material, such as pyridine, which is used in their preparation. Water-insoluble esters are washed thoroughly and successively with dilute acid (e.g. 0.2N sulfuric acid), water, 0.2N sodium hydroxide and water. After drying with calcium chloride they are fractionally distilled. Water-soluble esters should first be dissolved in a suitable organic solvent and, in the washing process, water should be replaced by saturated aqueous sodium chloride. Some esters (e.g. phosphate and phosphonate esters) can be further purified through their uranyl adducts (*vide supra*). Traces of water or hydroxy compounds can be removed by percolation through, or shaking with, activated alumina (about 100g/L of liquid solution), followed by filtration and fractional distillation in a vacuum. For high molecular weight esters (which cannot be distilled without some decomposition) it is advisable to carry out distillation at as low a pressure as possible. Solid esters can be crystallised from toluene or petroleum ether. Alcohols can be used for recrystallising phosphoric or phosphonic esters of phenols.

#### ETHERS

The purification of diethyl ether (see Chapter 4) is typical of liquid ethers. The most common contaminants are the alcohols or hydroxy compounds from which the ethers are prepared, their oxidation products (e.g. aldehydes), peroxides and water. Peroxides, aldehydes and alcohols can be removed by shaking with alkaline potassium permanganate solution for several hours, followed by washing with water, concentrated sulfuric acid [CARE], then water. After drying with calcium chloride, the ether is distilled. It is then dried with sodium or with lithium aluminium hydride, redistilled and given a final fractional distillation. The drying process should be repeated if necessary.

Alternatively, methods for removing peroxides include leaving the ether to stand in contact with iron filings or copper powder, shaking with a solution of ferrous sulfate acidified with N sulfuric acid, shaking with a copperzinc couple, passage through a column of activated alumina, and refluxing with phenothiazine. Cerium(III) hydroxide has also been used.

A simple test for ether peroxides is to add 10mL of the ether to a stoppered cylinder containing 1mL of freshly prepared 10% solution of potassium iodide containing a drop of starch indicator. No colour should develop during one minute if free from peroxides. Alternatively, a 1% solution of ferrous ammonium sulfate, 0.1M in sulfuric acid and 0.01M in potassium thiocyanate should not increase appreciably in red colour when shaken with two volumes of the ether.

As a safety precaution against **EXPLOSION** (in case the purification has been insufficiently thorough) at least a quarter of the total volume of ether should remain in the distilling flask when the distillation is discontinued as peroxides are generally higher boiling. To minimize peroxide formation, ethers should be stored in dark bottles and, if they are liquids, they should be left in contact with type 4A Linde molecular sieves, in a cold place, over sodium amalgam. The rate of formation of peroxides depends on storage conditions and is accelerated by heat, light, air and moisture. The formation of peroxides is inhibited in the presence of diphenylamine, di-*tert*butylphenol, or other antioxidants as stabiliser.

Ethers that are solids (e.g. phenyl ethers) can be steam distilled from an alkaline solution which will hold back any phenolic impurity. After the distillate is made alkaline with sodium carbonate, the insoluble ether is collected either by extraction (e.g. with chloroform, diethyl ether or toluene) or by filtration. It is then crystallised from alcohols, alcohol/petroleum ether, petroleum ether, toluene or mixtures of these solvents, sublimed in a vacuum and recrystallised if necessary.

# HALIDES

Aliphatic halides are likely to be contaminated with halogen acids and the alcohols from which they have been prepared, whereas in aromatic halides the impurities are usually aromatic hydrocarbons, amines or phenols. In both groups the halogen is less reactive than it is in acid halides. Purification is by shaking with concentrated hydrochloric acid, followed by washing successively with water, 5% sodium carbonate or bicarbonate, and water. After drying with calcium chloride, the halide is distilled and then fractionally distilled using an efficient column. For a solid halide the above purification is carried out by dissolving it in a suitable solvent such as toluene. Solid halides can also be purified by chromatography using an alumina column and eluting with toluene or petroleum ether. They can be crystallised from toluene, petroleum ethers, toluene/petroleum ether or toluene/chloroform/petroleum ether. Care should be taken when handling organic halogen compounds because of their **TOXICITY**. It should be noted that methyl iodide is a cancer suspect.

Liquid aliphatic halides are obtained alcohol-free by distillation from phosphorus pentoxide. They are stored in dark bottles to prevent oxidation and, in some cases, the formation of phosgene.

A general method for purifying *chlorohydrocarbons* uses repeated shaking with concentrated sulfuric acid [CARE] until no further colour develops in the acid, then washing with water then a solution of sodium bicarbonate, followed by water again. After drying with calcium chloride, the chlorohydrocarbon is fractionally redistilled to constant boiling point.

#### **HYDROCARBONS**

Gaseous hydrocarbons are best freed from water and gaseous impurities by passage through suitable adsorbents and (if olefinic material is to be removed) oxidants such as alkaline potassium permanganate solution, followed by fractional cooling (see Chapter 1 for cooling baths) and fractional distillation at low temperature. To effect these purifications and also to store the gaseous sample, a vacuum line is necessary.

Impurities in hydrocarbons can be characterised and evaluated by gas chromatography and mass spectrometry. The total amount of impurities present can be estimated from the thermometric freezing curve.

Liquid aliphatic hydrocarbons are freed from aromatic impurities by shaking with concentrated sulfuric acid [CARE] whereby the aromatic compounds are sulfonated. Shaking is carried out until the sulfuric acid layer remains colourless for several hours. The hydrocarbon is then freed from the sulfuric acid and the sulfonic acids by separating the two phases and washing the organic layer successively with water, 2N sodium hydroxide, and water. It is dried with CaCl<sub>2</sub> or Na<sub>2</sub>SO<sub>4</sub>, and then distilled. The distillate is dried with sodium wire,  $P_2O_5$ , or metallic hydrides, or passage through a dry silica gel column, or preferably, and more safely, with molecular sieves (see Chapter 1) before being finally fractionally distilled through an efficient column. If the hydrocarbon is contaminated with olefinic impurities, shaking with aqueous alkaline permanganate is necessary prior to the above purification. Alicyclic and paraffinic hydrocarbons can be freed from water, non-hydrocarbon and aromatic impurities by passage through a silica gel column before the final fractional distillation. This may also remove isomers. (For the use of chromatographic methods to separate mixtures of aromatic, paraffinic and alicyclic hydrocarbons see references in the bibliography in Chapter 1 under *Chromatography, Gas Chromatography and High Performance Liquid Chromatography*). Another method of removing branched-chain and unsaturated hydrocarbons from straight-chain hydrocarbons depends on the much faster reaction of the former with chlorosulfonic acid.

Isomeric materials which have closely similar physical properties can be serious contaminants in hydrocarbons. With aromatic hydrocarbons, e.g. xylenes and alkyl benzenes, advantage is taken of differences in ease of sulfonation. If the required compound is sulfonated more readily, the sulfonic acid is isolated, crystallised (e.g. from water), and decomposed by passing superheated steam through the flask containing the acid. The sulfonic acid undergoes hydrolysis and the liberated hydrocarbon distils with the steam. It is separated from the distillate, dried, distilled and then fractionally distilled. For small quantities (10-100mg), vapour phase chromatography is the most satisfactory method for obtaining a pure sample (for column materials for packings see Chapter 1).

Azeotropic distillation with methanol or 2-ethoxyethanol (cellosolve) has been used to obtain highly purified saturated hydrocarbons and aromatic hydrocarbons such as xylenes and isopropylbenzenes.

Carbonyl-containing impurities can be removed from hydrocarbons (and other oxygen-lacking solvents such as  $CHCl_3$  and  $CCl_4$ ) by passage through a column of Celite 545 (100g) mixed with concentrated sulfuric acid (60mL). After first adding some solvent and about 10g of granular  $Na_2SO_4$ , the column is packed with the mixture and a final 7-8cm of  $Na_2SO_4$  is added at the top [Hornstein and Crowe, Anal Chem 34 1037 1962]. Alternatively, Celite impregnated with 2,4-dinitrophenylhydrazine can be used.

With solid hydrocarbons such as naphthalene and polycyclic hydrocarbons, preliminary purification by sublimation in vacuum (or high vacuum if the substance is high melting), is followed by zone refining and finally by chromatography (e.g. on alumina) using low-boiling liquid hydrocarbon eluents. These solids can be recrystallised from alcohols, alcohol/petroleum ether or from liquid hydrocarbons (e.g. toluene) and dried below their melting points. Aromatic hydrocarbons that have been purified by zone melting include anthracene, biphenyl, fluoranthrene, naphthalene, perylene, phenanthrene, pyrene and terphenyl, among others. Some polycyclic hydrocarbons, e.g. benzpyrene, are CARCINOGENIC.

Olefinic hydrocarbons have a very strong tendency to polymerise and commercially available materials are generally stabilised, e.g. with hydroquinone. When distilling compounds such as vinylpyridine or styrene, the stabiliser remains behind and the purified olefinic material is more prone to polymerisation. The most common impurities are higher-boiling dimeric or polymeric compounds. Vacuum distillation in a nitrogen atmosphere not only separates monomeric from polymeric materials but in some cases also depolymerises the impurities. The distillation flask should be charged with a polymerisation inhibitor and the purified material should be used immediately or stored in the dark and mixed with a small amount of stabiliser (e.g. 0.1% of hydroquinone or di*tert*-butylcatechol). It is also advisable to add to the flask a small amount (*ca* 5-10% by volume of liquid in the flask) of a ground mixture of Kieselguhr and NaCl which will provide nuclei for facilitating boiling and finally for cleaning the flask from insoluble polymeric residue (due to the presence of the water soluble NaCl).

#### IMIDES

Imides (e.g. phthalimide) can be purified by conversion to their potassium salts by reaction in ethanol with ethanolic potassium hydroxide. The imides are regenerated when the salts are hydrolysed with dilute acid. Like amides, imides readily crystallise from alcohols and, in some cases (e.g. quinolinic imide), from glacial acetic acid.

# **IMINO COMPOUNDS**

These substances contain the -C=NH group and, because they are strong, unstable bases, they are kept as their more stable salts, such as the hydrochlorides. (The free base usually hydrolyses to the corresponding oxo compound and ammonia.) Like amine hydrochlorides, the salts are purified by solution in alcohol containing a few drops of hydrochloric acid. After treatment with charcoal, and filtering, dry diethyl ether (or petroleum ether if ethanol is used) is added until crystallisation sets in. The salts are dried and kept in a vacuum desiccator.

#### **KETONES**

Ketones are more stable to oxidation than aldehydes and can be purified from oxidisable impurities by refluxing with potassium permanganate until the colour persists, followed by shaking with sodium carbonate (to remove acidic impurities) and distilling. Traces of water can be removed with type 4A Linde molecular sieves. Ketones which are solids can be purified by crystallisation from alcohol, toluene, or petroleum ether, and are usually sufficiently volatile for sublimation in vacuum. Ketones can be further purified via their bisulfite, semicarbazone or oxime derivatives (vide supra). The bisulfite addition compounds are formed only by aldehydes and methyl ketones but they are readily hydrolysed in dilute acid or alkali.

# MACROMOLECULES See Chapter 6.

#### NITRILES

All purifications should be carried out in an efficient fume cupboard because of the **TOXIC** nature of these compounds.

Nitriles are usually prepared either by reacting the corresponding halide or diazonium salts with a cyanide salt or by dehydrating an amide. Hence, possible contaminants are the respective halide or alcohol (from hydrolysis), phenolic compounds, amines or amides. Small quantities of phenols can be removed by chromatography on alumina. More commonly, purification of liquid nitriles or solutions of solid nitriles in a solvent such as diethyl ether is by shaking with dilute aqueous sodium hydroxide, followed by washing successively with water, dilute acid and water. After drying with sodium sulfate, the solvent is distilled off. Liquid nitriles are best distilled from a small amount of  $P_2O_5$  which, besides removing water, dehydrates any amide to the nitrile. About one fifth of the nitrile should remain in the distilling flask at the end of the distillation (*the residue may contain some inorganic cyanide*). This purification also removes alcohols and phenols. Solid nitriles can be recrystallised from ethanol, toluene or petroleum ether, or a mixture of these solvents. They can also be sublimed under vacuum. Preliminary purification by steam distillation is usually possible.

Strong alkali or heating with dilute acids may lead to hydrolysis of the nitrile, and should be avoided.

#### NITRO COMPOUNDS

Aliphatic nitro compounds are generally acidic. They are freed from alcohols or alkyl halides by standing for a day with concentrated sulfuric acid, then washed with water, dried with magnesium sulfate followed by calcium sulfate and distilled. The principal impurities are isomeric or homologous nitro compounds. In cases where the nitro compound was originally prepared by vapour phase nitration of the aliphatic hydrocarbon, fractional distillation should separate the nitro compound from the corresponding hydrocarbon. Fractional crystallisation is more effective than fractional distillation if the melting point of the compound is not too low.

The impurities present in aromatic nitro compounds depend on the aromatic portion of the molecule. Thus, benzene, phenols or anilines are probable impurities in nitrobenzene, nitrophenols and nitroanilines, respectively. Purification should be carried out accordingly. Isomeric compounds are likely to remain as impurities after the preliminary purifications to remove basic and acidic contaminants. For example, o-nitrophenol may be found in samples of p-nitrophenol. Usually, the o-nitro compounds are more steam volatile than the p-nitro isomers, and can be separated in this way. Polynitro impurities in mononitro compounds can be readily removed because of their relatively lower solubilities in solvents. With acidic or basic nitro compounds which cannot be separated in the above manner, advantage may be taken of their differences in pK values (see Chapter 1). The compounds can thus be purified by preliminary extractions with several sets of aqueous buffers

of known pH (see for example Table 19, Chapter 1) from a solution of the substance in a suitable solvent such as diethyl ether. This method is more satisfactory and less laborious the larger the difference between the pK value of the impurity and the desired compound. Heterocyclic nitro compounds require similar treatment to the nitroanilines. Neutral nitro compounds can be steam distilled.

# NUCLEIC ACIDS See Chapter 6.

# PHENOLS

Because phenols are weak acids, they can be freed from neutral impurities by dissolution in aqueous N sodium hydroxide and extraction with a solvent such as diethyl ether, or by steam distillation to remove the non-acidic material. The phenol is recovered by acidification of the aqueous phase with 2N sulfuric acid, and either extracted with ether or steam distilled. In the second case the phenol is extracted from the steam distillate after saturating it with sodium chloride (salting out). A solvent is necessary when large quantities of liquid phenols are purified. The phenol is fractionated by distillation under reduced pressure, preferably in an atmosphere of nitrogen to minimise oxidation. Solid phenols can be crystallised from toluene, petroleum ether or a mixture of these solvents, and can be sublimed under vacuum. Purification can also be effected by fractional crystallisation or zone refining. For further purification of phenols *via* their acetyl or benzoyl derivatives (*vide supra*).

# POLYPEPTIDES AND PROTEINS See Chapter 6.

#### QUINONES

These are neutral compounds which are usually coloured. They can be separated from acidic or basic impurities by extraction of their solutions in organic solvents with aqueous basic or acidic solutions, respectively. Their colour is a useful property in their purification by chromatography through an alumina column with, e.g. toluene, as eluent. They are volatile enough for vacuum sublimation, although with high-melting quinones a very high vacuum is necessary. *p*-Quinones are stable compounds and can be recrystallised from water, ethanol, aqueous ethanol, toluene, petroleum ether or glacial acetic acid. *o*-Quinones, on the other hand, are readily oxidised. They should be handled in an inert atmosphere, preferably in the absence of light.

# SALTS (ORGANIC)

#### With metal ions

Water-soluble salts are best purified by preparing a concentrated aqueous solution to which, after decolorising with charcoal and filtering, ethanol or acetone is added so that the salts crystallise. They are collected, washed with aqueous ethanol or aqueous acetone, and dried. In some cases, water-soluble salts can be recrystallised satisfactorily from alcohols. Water-insoluble salts are purified by Soxhlet extraction, first with organic solvents and then with water, to remove soluble contaminants. The purified salt is recovered from the thimble.

# With organic cations

Organic salts (e.g. trimethylammonium benzoate) are usually purified by recrystallisation from polar solvents (e.g. water, ethanol or dimethyl formamide). If the salt is too soluble in a polar solvent, its concentrated solution should be treated dropwise with a miscible nonpolar, or less polar, solvent (see Table 8, Chapter 1) until crystallisation begins.

#### With sodium alkane sulfonates

Purified from sulfites by boiling with aqueous HBr. Purified from sulfates by adding BaBr<sub>2</sub>. Sodium alkane disulfonates are finally pptd by addition of MeOH. [Pethybridge and Taba J Chem Soc Faraday Trans 1 78 1331 1982].

# SULFUR COMPOUNDS

# Disulfides

These can be purified by extracting acidic and basic impurities with aqueous base or acid, respectively. However, they are somewhat sensitive to strong alkali which slowly cleaves the disulfide bond. The lowermelting members can be fractionally distilled under vacuum. The high members can be recrystallised from alcohol, toluene or glacial acetic acid.

#### Sulfones

Sulfones are neutral and very stable compounds that can be distilled without decomposition. They are freed from acidic and basic impurities in the same way as disulfides. The low molecular weight members are quite

soluble in water but the higher members can be recrystallised from water, ethanol, aqueous ethanol or glacial acetic acid.

#### Sulfoxides

These compounds are odourless, rather unstable compounds, and should be distilled under vacuum in an inert atmosphere. They are water-soluble but can be extracted from aqueous solution with a solvent such as diethyl ether.

# Thioethers

Thioethers are neutral stable compounds that can be freed from acidic and basic impurities as described for disulfides. They can be recrystallised from organic solvents and distilled without decomposition. They have sulfurous odours.

### Thiols

Thiols, or mercaptans, are stronger acids than the corresponding aliphatic hydroxy or phenolic compounds, but can be purified in a similar manner. However, care must be exercised in handling thiols to avoid their oxidation to disulfides. For this reason, purification is best carried out in an inert atmosphere in the absence of oxidising agents. Similarly, thiols should be stored out of contact with air. They can be distilled without change, and the higher-melting thiols (which are usually more stable) can be crystallised, e.g. from water or dilute alcohol. They oxidise readily in alkaline solution but can be separated from the disulfide which is insoluble in this medium. They should be stored in the dark below 0°. All operations with thiols should be carried out in an efficient fume cupboard because of their very unpleasant odour and their TOXICITY.

# Thiolsulfonates (disulfoxides)

Thiolsulfonates are neutral and are somewhat light-sensitive compounds. Their most common impurities are sulfonyl chlorides (neutral) or the sulfinic acid or disulfide from which they are usually derived. The first can be removed by partial freezing or crystallisation, the second by shaking with dilute alkali, and the third by recrystallisation because of the higher solubility of the disulfide in solvents. Thiolsulfonates decompose slowly in dilute, or rapidly in strong, alkali to form disulfides and sulfonic acids. Thiolsulfonates also decompose on distillation but they can be steam distilled. The solid members can be recrystallised from water, alcohols or glacial acetic acid.

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# CHAPTER 3

# THE FUTURE OF PURIFICATION

# **INTRODUCTION**

The essence of research is to seek answers wherever there are questions. Regardless of what the answers are the experiments to be conducted must be carried out with utmost care. For this, one must ensure that the quality of the reactants used and the products obtained are of the highest possible purity. In general terms, one can broadly categorise experimental chemistry and biological chemistry into the following areas:

Isolation and identification of substances (natural products from nature, protein purification and characterisation, etc).

Synthesis of substances (organic, or inorganic in nature; these substances may be known substances or new compounds).

Analysis of substances (this is a key process in the identification of new or known chemical and biological substances. Methods of analysis include spectroscopic methods, derivatisation and sequencing methods).

Measurements of particular properties of a compound or substance (enzyme kinetics, reaction kinetics, FACS, fluorescence-activated cell sorting, assay).

Impressive and sophisticated strategies, in the form of new reagents, catalysts and chemical transformations, are currently available for the syntheses of molecules. In recent years there is a deviation in focus from developing new synthetic routes and reactions to improving methods for carrying out reactions. In particular, traditional reactions can be carried out in new ways such that those efficiencies of reactions are greatly improved. The efficiencies of reactions can be measured in terms of the yields of the desired product(s), or in terms of the time taken to obtain the desired product(s). Some of the 'new' lateral ways of thinking to improve efficiencies of reactions recognise the importance of purification of products in the planning of a synthetic sequence. Thus methods such as solid phase synthesis, fluorous chemistry as well as the use of ionic liquids minimise purification procedures and thus improve the ability to rapidly access pure compounds. These techniques also contribute to the efficiencies of reactions in terms of yields. In looking ahead to synthesis in the 21<sup>st</sup> century, a brief outline of the key aspects of these techniques are presented. In time many commercially available chemicals will be prepared using methods described in this chapter, and knowledge of these now should be useful to the experimenter. Some of these compounds (e.g. peptides) have already been synthesised by such methods (e.g. SPPS, see below).

# SOLID PHASE SYNTHESIS

Solid phase synthesis (SPS) has emerged as an important methodology for the rapid and efficient synthesis of molecules. The ease of work-up and purification procedures in solid phase as compared to solution phase chemistry, as well as the scope for combinatorial chemistry provides impetus for further development in this field. The earliest studies on solid phase chemistry were focused on solid phase peptide synthesis (SPPS). The concept of carrying out reactions on a polymer support as distinct to reactants in solution, was conceived by R.B. Merrifield who received the Nobel Prize in Chemistry in 1984 for his pioneering work. However since the mid 1990's, advances in solid phase chemistry have moved beyond the routine (often robotic) synthesis of small to medium peptides and oligonucleotides. SPOS (solid phase organic synthesis) has gained much prominence due to the wealth of compounds (combinatorial libraries) that can be synthesized rapidly. This is especially important for pharmaceutical companies, screening for compounds with certain biological profiles or for chemical companies, screening for new catalysts or reagents. In SPOS, it is envisaged that difficult reactions can be driven to completion by using a large excess of reagents, which are easily removed by filtration. Furthermore, expensive reagents in the form of catalysts or chiral auxiliaries may be recycled easily if supported on a polymer and hence solid phase reactions provide economy in terms of costs and labour. Another strength of SPS is the ease in purification procedures which generally involves filtration of polymer supported products (solid) from soluble

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reaction components (liquid) in what is effectively a solid-liquid extraction. In the final step of the synthetic sequence, the desired product is then cleaved from the polymer support.

Despite the relative infancy in the development of solid phase reactions, a wide range of functionalised resins are commercially available. The main uses of these functionalised resins can be roughly classified as follows:

# SOLID PHASE PEPTIDE SYNTHESIS (SPPS)

Extensive studies on the synthesis of peptides on solid phase have been carried out, so much so that the technique of SPPS can be reliably and routinely used for the synthesis of short peptides by novices in the field. A large number of resins and reagents have been developed specifically for this purpose, and much is known on problems and avoidance of racemisation, difficult couplings, compatibility of reagents and solvents. Methods for monitoring the success of coupling reactions are available. Automated synthesisers are available commercially (e.g. from Protein Technologies, Rainin Inst Inc, Tuscon AZ; protan@dakotacom.net) which can carry out as many as a dozen polypeptide syntheses simultaneously. The most satisfactory chemistry currently used is Fmoc (9-fluorenvlmethoxycarbonyl) chemistry whereby the amino group of the individual amino acid residues is protected as the Fmoc. A large number of Fmoc-amino acids are commercially available as well as polymer resins to which the specific Fmoc-amino acid (which will eventually become the carboxy terminal residue of the peptide) is attached. With automated synthesisers, the solvent used is N-methylpyrrolidone and washings are carried out with dimethylformamide. Deprotection of the polypeptide is carried out with anhydrous trifluoroacetic acid (TFA). A cycle for one residue varies with the residue but can take an hour or more. This means that 70-80 mer polypeptides could take more than a week to prepare. This is not a serious drawback because several different polypeptides can be synthesised simultaneously. The success of the synthesis is dependent on the amino acid sequence since there are some twenty or more different amino acids and the facility of forming a peptide bond varies with the pair of residues invloved. However, generally 70 to 80 mers are routinely prepared, and if the sequence is favourable, up to 120 mer polypeptides can be synthesised. After deprotection with TFA the polypeptide is usually purified by HPLC using a C18 column with reverse phase chromatography. There are many commercial firms that will supply custom made polypeptides at a price depending on the degree of purity required.

# SOLID PHASE DEOXYRIBONUCLEOTIDE SYNTHESIS

The need for oligodeoxyribonucleotides mainly as primers for the preparation of deoxyribonucleic acids (DNA) and for DNA sequencing has resulted in considerable developments in oligodeoxyribonucleotide synthesis. The solid phase procedure is the method commonly used. Automated synthesisers are commercially avalable, but with the increase in the number of firms which will provide custom made oligodeoxyribonucleotides, it is often not economical to purchase a synthesiser to make one's own oligodeoxyribonucleotides. Unlike in polypeptide synthesis where there are some twenty different residues to "string" together, in DNA synthesis there are only four deoxyribonucleotides, consequently there is usually little difficulty is synthesising 100 mers in quantities from 10  $\mu$ g to 10 milligrams of material. The deprotected deoxyribonucleic acid which is separated from the solid support is purified on an anion exchange column followed by reverse phase HPLC using C8 to C18 columns for desalting. As for the polypeptides, the cost of DNA will depend on the purification level required.

# SOLID PHASE OLIGOSACCHARIDE SYNTHESIS

Although automated solid phase peptide and oligonucleotide synthetic procedures are well established, automated solid phase oligosaccharide synthesis is considerably more difficult. The current awareness of the importance of polysaccharides as surface recognition molecules and in glycoproteins and glycolipids has prompted much interest in oligosaccharide synthesis and some progress has been made (see Kochetkov Russ Chem Rev 69 795 2000; Ito and Manabe Curr Opin Chem Biol 2 701 1998; Seeberger and Danishefsky Acc Chem Res 31 685 1998). A general method for automated oligosaccharide synthesis is not as yet available. An example of an automated synthesis of specific glycosides has been reported by Seeberger (Science 291 1523 2001; see also Houlton Chem Br 38 (4) 46 2002).

# SOLID PHASE ORGANIC SYNTHESIS (SPOS)

At the time of writing this book, SPOS is in an area of relative infancy but has considerable potential. One of the main difficulties in SPOS lies in the lack of techniques available to monitor reactions carried out on polymer supports. Unlike reactions in solution phase, reactions on solid support cannot be monitored with relative ease and this has hindered the progress as well as the efficacy of solid supported synthesis of small non-peptidic molecules. Despite these difficulties, a large body of studies is available for SPOS. Recent reviews incorporate

information on the types of reactions that can be carried out, as well as outline the difficulties and differences with SP (solid phase) reactions as compared with their solution phase counterparts (see bibliography). An interesting application of such procedures is the synthesis of polymeric esters (e.g. polycaprolactones, polyhydroxybutyrates, polylactates) and starch- and cellulose- like polymers using a plasticised starch support. These have been useful for making biodegradable trays and containers for foodstuffs (BenBrahim *Chem Br* **38(4)** 40 2002).

# POLYMER SUPPORTED REACTANTS

These have become of increasing importance in synthesis and a broad classification of polymer supported reactants are as follows: Polymer bound bases (e.g. dimethylaminopyridine, morpholine, piperidine); Polymer supported catalysts (e.g. Grubbs catalyst for metathesis reactions, palladium for hydrogenation reactions, tributylmethylammonium chloride for phase transfer reactions); Polymer supported condensation reagents {e.g. DEAD (diethyl azodicarboxylate) for Mitsonobu reactions, DEC [1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride] {or EDCI [1-ethyl-3-(3-di-methylaminopropyl) carbodiimide HCl]} for peptide synthesis; HOBt (1-hydroxybenzotriazole) for peptide synthesis; Polymer supported oxidizing agents (e.g. osmium tetroxide, perruthenate, pyridinium chlorochromate); Polymer supported reducing agents (e.g. borohydride, tributyltin fluoride); Polymer supported phosphines (for miscellaneous applications depending on the structure) and so on. Commercially available polymer supported reactants are identified in Chapters 4 and 5 of this book.

# SCAVENGER RESINS

Though not as extensively utilised as polymer supported reactants, the use of resins to clean up reactions is gaining favour. The type of commercially available scavenger resins are electrophilic scavenger resins (e.g. benzaldehyde derivatised resins to scavenge amines; isocyanate resins to scavenge amines, anilines and hydrazines; tosyl chloride resins to scavenge nucleophiles) and nucleophilic scavenger resins (e.g. diethylenetriamine resins to scavenge acids, acid chlorides, anhydrides; sulfonyl amide resins to scavenge acids, acid chlorides, aldehydes, isocyanates and chloroformates).

# **RESIN SUPPORT**

The common resin matrixes comprise of polystyrene crosslinked with divinylbenzene, graft polymers of polystyrene-polyethylene glycol (PS-PEG) and polyethyleneglycol acrylamide (PEGA) composite resins. For each type of resin matrixes, a range of functionalised polymer supports are available. In addition, a number of these resins are available with different percentage of crosslinking as well as a range of loadings of the reactive functionality. Polystyrene based resins are the most extensively used. Unfortunately these resins do not swell, i.e. do not imbibe water, in polar solvents such as water and methanol and thus cannot be used for carrying out reactions in these solvents. In contrast grafted PS-PEG resins swell in a range of solvents from toluene to water. Examples of grafted PS-PEG resins are NovaSyn® TG and NovaGel® resins. As the success of transformations to be carried out on SPOS depends in part on the swelling properties as well as the robustness of the resin, the choice of resin matrix to be used must be carefully considered. The swelling properties of a number of resin types in a variety of solvents have been documented (see NovaBiochem catalog and also Santini, Griffith and Qi *Tetrahedron Lett* 39 8951 1998). For example, the swelling of a polystyrene resin in DMF is 3 mL/g of resin as compared to that in dichloromethane which is 7 mL/g of resin. It is thought that swelling of resins in the order of greater than 4 mL/g constitutes a good solvent, between 2-4 mL/g a moderate solvent and that less than 2 mL/g a poor solvent choice for carrying out solid phase reactions.

Lightly crosslinked resins are less robust but have greater ability to swell in appropriate solvents. Typically a 1-2% crosslinked divinyl benzene polystyrene resin is employed in organic synthesis.

An extensive list of the commercially available resins is available from Sigma-Aldrich (www.sigmaaldrich.com), Novabiochem (www.novabiochem.com), Fluka and other chemical companies. Sigma-Aldrich and Novabiochem have excellent catalogs. In addition, the Novabiochem catalog and website are a rich source of useful technical information.

# **CHOICE OF RESIN FOR SPOS**

There is a large range of resins available for SPOS. These resins are derivatised polymer supports with a range of linkers. The roles of linkers are (i) to provide point(s) of attachment for the tethered molecule, akin to a solid supported protecting group(s), (ii) to provide distance from the polymeric backbone in order to minimise interactions with the backbone, (iii) to enable cleavage of product molecules under conditions compatible with the stability of the molecules and the reaction conditions employed for chemical transformations. Hence in order to

choose an appropriate resin for use in SPOS, one would need to consider the nature of the attachment of the reactant molecule onto the solid support (e.g. in order to tether the carboxy group in a reactant as an ester linkage on a solid support, one may choose to use a hydroxy functionalised linker), the stability of the resin under conditions employed in the chemical transformations (e.g. issues of orthogonality - will the conditions utilised cause premature cleavage of the linker or premature cleavage of the products?), the solvents and reactants needed in the transformations (e.g. will the solvents swell the resin?), conditions of cleavage of products (e.g. will this cause racemisation or rearrangement of the product?), the functionality of the resultant product after cleavage (e.g. will cleavage of the product result in a residual functionality in the molecule?) and so on. Linkers which leave no residual functionalities in the products upon cleavage are known as *traceless* linkers and those which need to be activated in order to be cleaved are known as *safety catch* linkers. A fascinating array of linkers (commercial or otherwise) is available and some excellent reviews are cited in the bibliography at the end of this chapter.

# **COMBINATORIAL CHEMISTRY**

The major impetus for the development of solid phase synthesis centers around applications in combinatorial chemistry. The notion that new drug leads and catalysts can be discovered in a high throughput fashion has been demonstrated many times over as is evidenced from the number of publications that have arisen (see references at the end of this chapter). A number of approaches to combinatorial chemistry exist. These include the split-mix method, serial techniques and parallel methods to generate libraries of compounds. The advances in combinatorial chemistry are also accompanied by sophisticated methods in deconvolution and identification of compounds from libraries. In a number of cases, innovative hardware and software has been developed for these purposes.

Depending on the size of the combinatorial library to be generated as well as the scale of the reactions to be carried out, a wide range of specialised glassware and equipment are commercially available. For example, in order to carry out parallel combinatorial synthesis, reaction stations equipped with temperature and stirring control are available from a number of sources (e.g. www.fisher.co.uk; www.radleys.com; www.sigmaaldrich.com). These reaction stations are readily adapted, using appropriate modules, for conditions under reflux or under inert atmosphere. For automated synthesis of large libraries of compounds, reactions can be carried out using reaction blocks on microtiter plates.

Ready to use CombiKits<sup>™</sup> which contain a variety of pre-weighed building blocks are available from Aldrich Chemical Company.

#### **MONITORING SOLID PHASE REACTIONS**

This remains the bane of solid phase reactions. Unlike solution phase reactions, where the progress of reactions can be monitored rapidly via TLC, GC or HPLC methods, procedures for the rapid monitoring of progress in solid phase reactions are limited. Although a number of spectroscopic methods have been developed for direct monitoring of reactions on solid supports, these methods usually require specialised equipment, not routinely available in chemical laboratories. These methods include on-bead IR analysis (e.g. Huber et al. Anal Chim Acta 393 213 1999; Yan and Gremlich J Chromatogr, B. 725 91 1999; Yan et al. J Org Chem 60 5736 1995) and solid state magic angle spinning NMR techniques (e.g. Warrass and Lippens J Org Chem 65 2946 2000; Rousselot-Pailley, Ede and Lippens J. Comb. Chem. 3 559 2001).

The most common methods for monitoring solid phase reactions utilized in normal research laboratories are:

# Infrared analysis of resin

This is a destructive method in which the resin is ground and pelleted as a KBr disc and analysed by FT-IR analysis. This method works best for systems where distinct functional group transformations (C=O, C-OH, C=C, etc) are expected. No special equipment is needed.

# Qualitative and quantitative analyses

There are a number of colour or UV tests which are available for monitoring the presence or absence of certain functional groups. Although some of these tests are routinely used for the quantitative analysis of functional groups in solution phase, the quantification on solid phase is less than reliable. An exception to this is the Fmoc (9-fluorenylmethoxycarbonyl) assay, which is routinely used for quantification of coupling in SPPS using Fmoc amino acids. It should also be noted that the generality of some of these colour tests on a variety of solid phase resins is not known and hence these tests serve only as a *guide* to functional group identification. Some (not an exhaustive list) of the reported methods of analyses are outlined below.

# DETECTION OF REACTIVE GROUPS ON RESINS

#### Detection of hydroxy groups on resin

A method in which the resin is treated with cyanuric chloride (trichlorotriazine, TCT) in DMF followed by a nucleophilic dye (AliR or Mordant Orange 1, beads appear red in the presence of hydroxyl groups, or with fuschin, beads appear fuschia, or with fluorescein, they become fluorescent) has been reported (Attardi and Taddei *Tetrahedron Lett* **42** 2927 2001; Attardi, Falchi and Taddei *Tetrahedron Lett* **41** 7395 2001). Another colorimetric test for the detection of polymer supported tertiary alcohols utilizes the conversion of the alcohols to the polymer supported diphenylsilylchloride ether, followed by subsequent treatment with methyl red. The beads form a readily distinguishable orange/red colour. The test is also positive for the hydroxy Wang resin and the aminomethylpolystyrene resin [Burkett, Brown and Meloni *Tetrahedron Lett* **42** 5773 2001]. Alternatively the conversion of polymer supported alcohols to the tosylate followed by displacement by *p*-nitrobenzylpyridine (PNBP) gives a strongly coloured salt upon treatment with bases such as piperidine, followed by gentle heating [Kuisle et al. *Tetrahedron* **55** 14807 1999].

# Detection of aldehyde groups on resin

The use of an acidic solution of p-anisaldehyde in ethanol to detect aldehyde functionalities on polystyrene polymer supports has been reported (beads are treated with a freshly made solution of p-anisaldehyde (2.55 mL), ethanol (88 mL), sulfuric acid (9 mL), acetic acid (1 mL) and heated at 110°C for 4 min). The colour of the beads depends on the percentage of CHO content such that at 0% of CHO groups, the beads are colourless, ~50% CHO content, the beads appear red and at 98% CHO the beads appear burgundy [Vázquez and Albericio Tetrahedron Lett 42 6691 2001]. A different approach utilises 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole (Purpald) as the visualizing agent for CHO groups. Resins containing aldehyde functionalities turn dark brown to purple after a 5 min reaction followed by a 10 minute air oxidation [Cournoyer et al. J Comb Chem 4 120 2002].

# Detection of carboxy groups on resin

The presence of a COOH functionality on a polystyrene resin can be detected using a 0.25% solution of malachite green-oxalate in ethanol in the presence of a drop of triethylamine. Beads with COOH functionalities are coloured dark green or appear as clear gel beads [Attardi, Porcu and Taddei *Tetrahedron Lett* **41** 7391 2000].

# Detection of amino groups on resin

The methods for the detection of amine functional groups are well established. For example the Kaiser test can be used to detect the presence of amine groups on resins (blue colour is observed). In the Kaiser test, two reagents are prepared. Reagent 1 comprises of a mixture of two solutions: A and B. A is a solution of phenol in absolute ethanol (40g of phenol in 10 mL of absolute ethanol, followed by treatment of this clear solution with 4g of Amberlite mixed bed resin MB-3 for 45 mins. The solution is then filtered.). Solution B is made up of 65 mg of KCN in 100 mL water; 2 mL of this solution is diluted to 100 mL of freshly distilled pyridine. The solution is then stirred with 4 g of Amberlite mixed-bed resin MB-3 and filtered. Solutions A and B are then mixed. Reagent 2 is a solution of ninhydrin (2.5g) in absolute ethanol (50 mL). For a qualitative Kaiser test, 6 drops of reagent 1 and 2 drops of reagent 2 are added to the well washed dried resin (2-5 mg) and mixed, followed by heating to 100°C for 4-6 min. A method for the quantitative determination of amino groups using this test has also been reported [Sarin et al. Anal Biochem 117 147 1981]. It is however known that the Kaiser test does not give a positive test with a secondary amino acid such as proline or some 'unnatural' amino acids. In addition some deprotected amino acids (Ser, Asn, Asp) do not show the expected intense blue colour typical of free primary amino groups.

A test for secondary amines (e.g. proline) is the Chloranil test (1 drop of a 2% acetaldehyde solution in DMF, followed by one drop of a 2% solution of p-chloranil in DMF, leave for 5 mins). A positive test gives blue stained beads.

Other tests for the detection of amino functionalities on solid supports include the TNBS (2,4,6-trinitrobenzenesulfonic acid, picrylsulfonic acid) [Hancock and Battersby Anal Biochem 71 260 1976], the DABITC [Shah et al. Anal. Commun. 34 325 1997] and the NF31 [Madder et al. Eur J Org Chem 2787 1999] tests.

# Detection of thiol groups on resin

For quantitative analysis of solid supported thiol residues on free macroporous or PEG grafts, Ellman's reagent has been used [5,5'-dithio-bis-(2-nitrobenzoic acid]. However only qualitative information can be gained using lightly crosslinked polystyrene resins [Badyal et al. *Tetrahedron Lett* **42** 8531 2001].

#### Fmoc assay

This is a very important and well tested method for the quantitative determination of loading of Fmoc protected compounds particularly that of Fmoc (fluorenylmethoxycarbonyl) amino acids on solid support. Fmoc groups can

be readily deprotected in the presence of base. Generally, in the deprotection and quantification procedures, a known amount of resin is treated with 20% piperidine in DMF at room temperature for 30 mins. The resin is washed with more DMF and the pooled filtrates are combined in a volumetric flask and made up to an accurate volume (e.g. to 10 mL) with more DMF. The UV absorbance at 301 nm of the piperidine-dibenzofulvene adduct which is formed can then be measured against a blank solution of piperidine in DMF [Meienhofer et al. Int J Pept Protein Res 13 35 1979]. The loading L is then determined using the equation :

 $L = (Absorbance value) \times (Solution volume in litres)$ 7.8 x (Weight of resin in mg)

# **IONIC LIQUIDS**

Ionic liquids are organic or inorganic salts that are liquid at room or reaction temperatures. Although ionic liquids are themselves not new discoveries (e.g. the ionic liquid [EtNH<sub>3</sub>] [NO<sub>3</sub>] was described in 1914), the use of ionic liquids in synthesis is only recent. In particular, the potential applications of ionic liquids as solvents in synthesis and in catalysis have recently been realised. The physical properties of ionic liquids make them unique solvents for synthesis. For example, ionic liquids are good solvents for both organic and inorganic substances and hence can be used to bring reagents into the same phase for reaction. Ionic liquids are also immiscible with a number of organic solvents and thus provide a non-aqueous, polar alternative for two-phase extraction systems. As ionic liquids are non-volatile, they can be used in high vacuum systems without the possibility of loss or contaminants. In addition, this also facilitates the isolation of products as the products can be distilled from the ionic liquids are frequently composed of poorly coordinating ions, they are highly polar which are important characteristics in the activation of catalysts.

Commonly used ionic liquids are N-alkylpyridinium, N, N'-dialkylimidazolium, alkylammonium and alkylphosphonium salts.

To date a number of reactions have been carried out in ionic liquids [for examples, see Dell'Anna et al. J Chem Soc, Chem Commun 434 2002; Nara, Harjani and Salunkhe Tetrahedron Lett 43 1127 2002; Semeril et al. J Chem Soc Chem Commun 146 2002; Buijsman, van Vuuren and Sterrenburg Org Lett 3 3785 2001]. These include Diels-Alder reactions, transition-metal mediated catalysis, e.g. Heck and Suzuki coupling reactions, and olefin metathesis reactions. An example of ionic liquid acceleration of reactions carried out on solid phase is given by Revell and Ganesan [Org Lett 4 3071 2002].

# **FLUOROUS CHEMISTRY**

This new approach to synthesis was introduced by Curran early in 1997 and involves the attachment of fluorous phase labels to substrates such that the subsequent fluorinated products can be extracted into the fluorous phase. For example in liquid-liquid extractions (typical work-up procedures), a three-phase extraction is now possible (organic, fluorous and aqueous phases). As organic and inorganic compounds have little or no tendency to dissolve in highly fluorinated solvents and compounds, phase labeling a compound as fluorous will enable successful extraction into the fluorous phase. However in order to carry out homogenous reactions with these fluorinated compounds, organic solvents with a good dissolving power for fluorous compounds or miscible organic and fluorous solvents can be used. Alternatively organic solvents with a few fluorine atoms e.g. trifluoroethanol, benzotrifluoride ('hybrid solvents') will dissolve both organic and fluorous compounds. A number of synthetic applications utilising fluorous chemistry have been reported in the literature. [For examples, see Schneider and Bannwarth *Helv Chim Acta* 84 735 2001; Galante, Lhoste and Sinou *Tetrahedron Lett* 42 5425 2001; Studer et al. *J Org Chem* 62 2917 1997; Crich and Neelamkavil *Tetrahedron* 58 3865 2002].

# The Future of Purification

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# **CHAPTER 4**

# PURIFICATION OF ORGANIC CHEMICALS

The general principles, techniques and methods of purification in Chapters 1 and 2 are applicable to this chapter. Most organic liquids and a number of solids can readily be purified by fractional distillation, usually at atmospheric pressure. Sometimes, particularly with high boiling or sensitive liquids, or when in doubt about stability, distillation or fractionation under reduced pressure should be carried out. To save space, the present chapter omits many substances for which the published purification methods involve simple distillation. Where boiling points are given, purification by distillation is another means of removing impurities. Literature references are omitted for methods which require simple recrystallisation from solution if the correct solvent can be guessed readily, and where no further information is given, e.g. spectra. Substances are listed alphabetically, usually with some criteria of purity, giving brief details of how they can be purified. Also noted are the molecular weights (to the first decimal place), melting points and/or boiling points together with the respective densities and refractive indexes for liquids, and optical rotations when the compounds are chiral. When the temperatures and/or the wavelengths are not given for the last three named properties then they should be assumed to be 20°C and the average of the wavelengths of the sodium D lines repectively; and densities are relative to water at 4°.

The present chapter includes commercially available organic chemicals. Most of the inorganic, metalorganic, organo- bismuth, boron, phosphorus, selenium, silicon and alkali metal compounds and metal ion salts of organic acids are in Chapter 5. Naturally occurring commercially available organic compounds for use in biochemistry, molecular biology and biology are in Chapter 6. Commercially available polymer supported reagents are indicated with § under the appropriate reagent.

**Rapid purification procedures** are noted for commonly used solvents and reagents which make them suitable for general use in synthetic chamistry.

Abbreviations of titles of periodicals are defined as in the Chemical Abstracts Service Source Index (CASSI). Other abbreviations are self evident (see Chapter 1, p. 30).

**Ionisation constants** of ionisable compounds are give as **pK** values (published from the literature) and refer to the **pKa** values at room temperature (~ 15°C to 25°C). The values at other temperatures are given as superscripts, e.g. **pK**<sup>25</sup> for 25°C. Estimated values are entered as **pK**<sub>Est</sub> (see Chapter 1, p. 7 for further information).

As a good general rule, all low boiling  $(<100^{\circ})$  organic liquids should be treated as highly flammable and toxic (because they can be inhaled in large quantities) and the necessary precautions should be taken.

**Benzene**, which has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallisation is now considered a **very dangerous substance** so it hasto be used with extreme care. We emphasise that an alternative solvent system to benzene (e.g. toluene, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if no other solvent system can be found then all operations involving benzene have to be performed in an efficient fumehood and precautions must be taken to avoid inhalation and contact with skin and eyes. Whenever benzene is mentioned in the text an asterisk e.g.  ${}^{*}C_{6}H_{6}$  or  ${}^{*}$  benzene, is inserted to remind the user that special precaution should be adopted.

**Abietic acid** [514-10-3] M 302.5, m 172-175°,  $[\alpha]_D^{25}$  -116° (-106°)(c 1, EtOH), pK 5.27. Crystd by dissolving 100g of acid in 95% EtOH (700mL), adding to H<sub>2</sub>O (600mL) and cooling. Filter, dry in a vacuum (over KOH or CaSO<sub>4</sub>) store in an O<sub>2</sub>-free atmosphere.  $\lambda$  in EtOH nm(log  $\varepsilon$ ): 2343(4.3), 241(4.4), 2505(4.2), 235(4.34) and 240(4.36). [Org Synth 23 1 1952; J Am Chem Soc 35 3736 1949; Monatsh Chem 116 1345 1985.]

S-Abscisic acid [21293-29-8] M 264.3, m 160-161°, 161-163° (sublimation),  $[\alpha]_{287}$  + 24,000°,  $[\alpha]_{245}$  -69,000° (c 1-50µg/mL in acidified MeOH or EtOH), pK<sub>Est</sub> ~3.9. Crystd from CCl<sub>4</sub>-pet.ether, EtOH + hexane and sublimes at 120°.

Acenaphthalene [208-96-8] M 152.2, m 92-93°. Dissolved in warm redistd MeOH, filtered through a sintered glass funnel and cooled to -78° to ppte the material as yellow plates [Dainton, Ivin and Walmsley Trans Faraday Soc 56 1784 1960]. Alternatively can be sublimed in vacuo.

Acenaphthaquinone [82-86-0] M 182.2, m 260-261°. Extracted with, then recrystd twice from \*C<sub>6</sub>H<sub>6</sub>. [LeFevre, Sundaram and Sundaram J Chem Soc 974 1963].

Acenaphthene [83-32-9] M 154.2, m 94.0°. Crystd from EtOH. Purified by chromatography from CCl<sub>4</sub> on alumina with \*benzene as eluent [McLaughlin and Zainal J Chem Soc 2485 1960].

**RS-Acenaphthenol** [6306-07-6] M 170.2, m 144.5-145.5°, 146°, 148°. If highly coloured (yellow), dissolve in boiling \*benzene (14g in 200mL), add charcoal (0.5g), filter through a heated funnel, concentrate to 100mL and cool to give almost colourless needles. \*Benzene vapour is TOXIC use an efficient fume cupboard. The acetate has b 166-168°/5mm (bath temp 180-185°). [Org Synth Col.Vol. III 3 1955.] It can also be recrystd from \*C<sub>6</sub>H<sub>6</sub> or EtOH [Fieser and Cason J Am Chem Soc 62 432 1940]. It forms a brick-red crystalline complex with 2,4,5,7-tetranitrofluoren-9-one which is recrystd from AcOH and dried in a vacuum over KOH and P<sub>2</sub>O<sub>5</sub> at room temp, m 170-172° [Newman and Lutz J Am Chem Soc 78 2469 1956].

Acetal (acetaldehyde diethylacetal) [105-57-7] M 118.2, b 103.7-104°, d 0.831, n 1.38054,  $n^{25}$  1.3682. Dried over Na to remove alcohols and water, and to polymerise aldehydes, then fractionally distd. Or, treat with alkaline H<sub>2</sub>O<sub>2</sub> soln at 40-45° to remove aldehydes, then the soln is saturated with NaCl, separated, dried with K<sub>2</sub>CO<sub>3</sub> and distd from Na [Vogel J Chem Soc 616 1948].

Acetaldehyde [75-07-0] M 44.1, b 20.2°, d 0.788, n 1.33113, pK<sup>25</sup> 13.57 (hydrate). Usually purified by fractional distn in a glass helices-packed column under dry N<sub>2</sub>, discarding the first portion of distillate. Or, shaken for 30min with NaHCO<sub>3</sub>, dried with CaSO<sub>4</sub> and fractionally distd at 760mm through a 70cm Vigreux column. The middle fraction was taken and further purified by standing for 2h at 0° with a small amount of hydroquinone, followed by distn [Longfield and Walters J Am Chem Soc 77 810 1955].

Acetaldehyde ammonia trimer (hexahydro-2,4,6-trimethyl-1,3,5-triazine trihydrate) [76231-37-3] M 183.3, m 94-96°, 95-97°, 97°, b 110°(partly dec). Crystd from EtOH-Et<sub>2</sub>O. When prepared it separates as the *trihydrate* which can be dried in a vacuum over CaCl<sub>2</sub> at room temp to give the anhydrous compound with the same melting point. The *dihydrate* melts at 25-28° then resolidifies and melts again at 94-95°. IRRITATES THE EYES AND MUCOUS MEMBRANES. [J Org Chem 38 3288 1973.]

Acetaldehyde dimethyl acetal [534-15-6] M 90.1, b 63-65°,  $d_4^{20}$  0.852,  $n_D^{25}$  1.36678. Distd through a fractionating column and fraction boiling at 63.8°/751mm is collected. It forms an azeotrope with MeOH. It has been purified by GLC.

Acetamide [60-35-5] M 59.1, m 81°,  $pK_1^{25}$ -1.4,  $pK_2^{25}$ +0.37. Crystd by soln in hot MeOH (0.8mL/g), diltd with Et<sub>2</sub>O and allowed to stand [Wagner *J Chem Educ* 7 1135 *1930*]. Alternate crystns are from acetone, \*benzene, chloroform, dioxane, methyl acetate or from \*benzene-ethyl acetate mixture (3:1 and 1:1). It has also been recrystd from hot water after treating with HCl-washed activated charcoal (which had been

repeatedly washed with water until free from chloride ions), then crystd again from hot 50% aq. EtOH and finally twice from hot 95% EtOH [Christoffers and Kegeles J Am Chem Soc 85 2562 1963]. Final drying is in a vacuum desiccator over  $P_2O_5$ . Acetamide is also purified by distn (b 221-223°) or by sublimation *in vacuo*. Also purified by recrystn twice from cyclohexane containing 5% (v/v) of \*benzene. Needle-like crystals separated by filtn, washed with a small volume of distd H<sub>2</sub>O and dried with a flow of dry N<sub>2</sub>. [Slebocka-Tilk et al. J Am Chem Soc 109 4620 1987.]

Acetamidine hydrochloride [124-42-5] M 94.5, m 164-166°, 165-170° (dec), 174°, pK <sup>25</sup> 12.40. It can be recrystd from small volumes of EtOH. Alternatively dissolve in EtOH, filter, add Et<sub>2</sub>O, filter the crystalline salt off under N<sub>2</sub>, dry in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub>. The salt is deliquescent and should be stored in a tightly stoppered container. Solubility in H<sub>2</sub>O is 10% at room temperature, soluble in Me<sub>2</sub>CO. The free base reacts strongly alkaline in H<sub>2</sub>O. It has  $\lambda_{max}$  224nm ( $\epsilon$  4000) in H<sub>2</sub>O. The picrate has m 252° (sintering at ~245°). [Dox Org Synth Coll Vol I 5 1941; Davies and Parsons Chem Ind (London) 628 1958; Barnes et al. J Am Chem Soc 62 1286 1940 give m 177-178°.]

N-(2-Acetamido)-2-aminoethanesulfonic acid (ACES) [7365-82-4] M 182.2, m > 220°(dec), pK<sub>Est</sub> ~1.5, pK<sub>2</sub> 6.9. Recrystd from hot aqueous EtOH.

4-Acetamidobenzaldehyde [122-85-0] M 163.2, m 156°. Recrystd from water.

*p*-Acetamidobenzenesulfonyl chloride (*N*-acetylsulfanilyl chloride) [121-60-8] M 233.7, m 149°(dec). Crystd from toluene, CHCl<sub>3</sub>, or ethylene dichloride.

 $\alpha$ -Acetamidocinnamic acid [5469-45-4] M 205.2, m 185-186° (2H<sub>2</sub>O), 190-191°(anhydr), 193-195°, pK<sub>Est</sub> ~3.2. Recrystd from H<sub>2</sub>O as the dihydrate and on drying at 100° it forms the anhydrous compound which is *hygroscopic*. Alkaline hydrolysis yields NH<sub>3</sub> and phenylpyruvic acid. [Erlenmeyer and Früstück Justus Liebigs Ann Chem 284 47 1895.]

**Z-O-(2-Acetamido-2-deoxy-D-glycopyranosylideneamino)***N***-phenylcarbamate** (PUGNAC) [132063-05-9] M 335.3, m 171-174°(dec), 174-180°(dec),  $[\alpha]_D^{20}$ +67.5° (c 0.2, MeOH). Purified by flash chromatography (silica gel and eluted with AcOEt-hexane 3:2) evaporated, and the foam recrystallised from AcOEt-MeOH. TLC on Merck SiO<sub>2</sub> gel 60 F<sub>254</sub> and detected by spraying with 0.025M I<sub>2</sub> in 10% aqueous H<sub>2</sub>SO<sub>4</sub> and heat at 200° gave R<sub>F</sub> 0.21. The acetate is hydrolysed with NH<sub>3</sub>-MeOH. [Helv Chim Acta 68 2254 1985; 73 1918 1990.]

**2-Acetamidofluorene** [53-96-3] **M 223.3, m 194°, 196-198°**. Recrystd from toluene (1.3mg in 100mL). Solubility in H<sub>2</sub>O is 1.3mg/L; UV  $\lambda_{max}$  nm(log  $\varepsilon$ ) : 288(4.43), 313(4.13). [J Org Chem 21 271 1956.] It can also be recrystd from 50% AcOH and sol in H<sub>2</sub>O is 1.3mg/100mL at 25° [Chem Ber 35 3285 1902]. 9-14C and  $\omega$ -14C 2-acetamidofluorene were recrystd from aqueous EtOH and had m 194-195° and 194° respectively. Potent CARCINOGEN. [Cancer Res 10 616 1950; Sadin et al. J Am Chem Soc 74 5073 1952.]

*N*-(2-Acetamido)iminodiacetic acid (ADA) [26239-55-4] M 190.2, m 219° (dec),  $pK_1 \sim 2.3$ ,  $pK_2$  6.6. Dissolved in water by adding one equivalent of NaOH soln (to final pH of 8-9), then acidified with HCl to ppte the free acid. Filtered and washed with water.

Acetamidomethanol [625-51-4] M 89.1, m 47-50°, 54-56°, 55°. Recryst from freshly distd Me<sub>2</sub>CO, wash the crystals with dry Et<sub>2</sub>O and dry in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. R<sub>F</sub> 0.4 on paper chromatography with CHCl<sub>3</sub>/EtOH (2:8) as solvent and developed with ammoniacal AgNO<sub>3</sub>. Also crystallises in needles from EtOAc containing a few drops of Me<sub>2</sub>CO. It is *hygroscopic* and should be stored under dry conditions. [J Am Chem Soc 73 2775 1951; Chem Ber 99 3204 1966; Justus Liebigs Ann Chem 343 265 1905.]

2-Acetamido-5-nitrothiazole [140-40-9] M 187.2, m 264-265°. Recrystd from EtOH or glacial acetic acid.

2-Acetamidophenol [614-80-2] M 151.2, m. 209°, pK<sub>Est</sub> ~9.4. Recrystd from water or aqueous EtOH.

3-Acetamidophenol [62]-42-1] M 151.2, m 148-149°, pK<sup>25</sup> ~9.59. Recrystd from water.

4-Acetamidophenol [103-90-2] M 151.2, m 169-170.5°, pK<sub>Est</sub> ~10.0. Recrystd from water or EtOH.

4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (acetamidoTEMPO) [14691-89-5] M 213.3, m 144-146°, 146-147°. Dissolve in  $CH_2Cl_2$ , wash with saturated  $K_2CO_3$ , then saturated aqueous NaCl, dry (Na<sub>2</sub>SO<sub>4</sub>), filter and evaporate. The red solid is recrystd from aqueous MeOH, m 147.5°. [J Org Chem 56 6110 1991; Bull Acad Sci USSR, Div Chem Sci 15 1422 1966.]

5-Acetamido-1,3,4-thiadiazole-2-sulfonamide [59-66-5] M 222.3, m 256-259° (dec). Recrystd from water.

Acetanilide [103-84-4] M 135.2, m 114°, pK<sup>25</sup> 0.5. Recrystd from water, aqueous EtOH, \*benzene or toluene.

Acetic acid (glacial) [64-19-7] M 60.1, m 16.6°, b 118°, d 1.049, n 1.37171, n<sup>25</sup> 1.36995, pK<sup>25</sup> 4.76. Usual impurities are traces of acetaldehyde and other oxidisable substances and water. (Glacial acetic acid is very *hygroscopic*. The presence of 0.1% water lowers its m by 0.2°.) Purified by adding some acetic anhydride to react with water present, heating for 1h to just below boiling in the presence of 2g CrO<sub>3</sub> per 100mL and then fractionally distilling [Orton and Bradfield J Chem Soc 960 1924, 983 1927]. Instead of CrO<sub>3</sub>, 2-5% (w/w) of KMnO<sub>4</sub>, with boiling under reflux for 2-6h, has been used.

Traces of water have been removed by refluxing with tetraacetyl diborate (prepared by warming 1 part of boric acid with 5 parts (w/w) of acetic anhydride at  $60^{\circ}$ , cooling, and filtering off), followed by distn [Eichelberger and La Mer J Am Chem Soc 55 3633 1933].

Refluxing with acetic anhydride in the presence of 0.2g % of 2-naphthalenesulfonic acid as catalyst has also been used [Orton and Bradfield J Chem Soc 983 1927]. Other suitable drying agents include  $CuSO_4$  and chromium triacetate:  $P_2O_5$  converts some acetic acid to the anhydride. Azeotropic removal of water by distn with thiophene-free \*benzene or with butyl acetate has been used [Birdwhistell and Griswold J Am Chem Soc 77 873 1955]. An alternative purification uses fractional freezing.

Rapid procedure: Add 5% acetic anhydride, and 2% of CrO<sub>3</sub>. Reflux and fractionally distil.

Acetic anhydride [108-24-7] M 102.1, b 138°, d 1.082, n 1.3904. Adequate purification can usually be obtained by fractional distn through an efficient column. Acetic acid can be removed by prior refluxing with CaC<sub>2</sub> or with coarse Mg filings at 80-90° for 5days, or by distn from a large excess of quinoline (1% AcOH in quinoline) at 75mm pressure. Acetic anhydride can also be dried by standing with Na wire for up to a week, removing the Na and distilling from it under vacuum. (Na reacts vigorously with acetic anhydride at 65-70°). Dippy and Evans [J Org Chem 15 451 1950] let the anhydride (500g) stand over P<sub>2</sub>O<sub>5</sub> (50g) for 3h, then decanted it and stood it with ignited K<sub>2</sub>CO<sub>3</sub> for a further 3h. The supernatant liquid was distd and the fraction b 136-138°, was further dried with P<sub>2</sub>O<sub>5</sub> for 12h, followed by shaking with ignited K<sub>2</sub>CO<sub>3</sub>, before two further distns through a five-section Young and Thomas fractionating column. The final material distd at 137.8-138.0°. Can also be purified by azeotropic distn with toluene: the azeotrope boils at 100.6°. After removal of the remaining toluene, the anhydride is distd [sample had a specific conductivity of 5 x 10<sup>-9</sup> ohm<sup>-1</sup>cm<sup>-1</sup>]. **Rapid procedure:** Shake with P<sub>2</sub>O<sub>5</sub>, separate, shake with dry K<sub>2</sub>CO<sub>3</sub> and fractionally distil.

Acetic hydrazide [1068-57-1] M 74.1, m 67°, b 127°/18mm. Cryst as needles from EtOH. Reduces NH<sub>3</sub>/AgNO<sub>3</sub>.

Acetoacetamide [5977-14-0] M 101.1, m 54-55°, 54-56°. Recrystallise from CHCl<sub>3</sub>, or Me<sub>2</sub>CO/pet ether. Crystallises from pyridine with 4mol of solvent. Slightly soluble in H<sub>2</sub>O, EtOH and AcOH but

insoluble in Et<sub>2</sub>O. Phenylhydrazone has m 128°. [Beilstein 3, 4th Suppl, p 1545; Kato Chem Pharm Bull Jpn 15 921,923 1967; Chem Ber 35 583 1902.]

Acetoacetanilide [102-01-2] M 177.2, m 86°, pK 10.68. Crystd from H<sub>2</sub>O, aqueous EtOH or pet ether (b 60-80°).

Acetoacetylpiperidide [1128-87-6] M 169.2, b 88.9°/0.1mm, n<sup>52</sup> 1.4983. Dissolved in \*benzene, extracted with 0.5M HCl to remove basic impurities, washed with water, dried, and distd at 0.1mm [Wilson J Org Chem 28 314 1963].

 $\alpha$ -Acetobromoglucose (2,3,4,6-tetraacetyl- $\alpha$ -D-glucopyranosyl bromide) [572-09-8] M 411.2, m 88-89°, [ $\alpha$ ]<sub>D</sub><sup>25</sup> +199.3° (c 3, CHCl<sub>3</sub>). Crystd from isopropyl ether or pet ether (b 40-60°) [Org Synth 65 236 1897].

Acetone [67-64-1] M 58.1, b 56.2°, d 0.791, n 1.35880,  $pK_1^{25}$  -6.1 (basic, monoprotonated),  $pK_2^{25}$  20.0 (acidic) The commercial preparation of acetone by catalytic dehydrogenation of isopropyl alcohol gives relatively pure material. Analytical reagent quality generally contains less than 1% organic impurities but may have up to about 1% H<sub>2</sub>O. Dry acetone is appreciably *hygroscopic*. The main organic impurity in acetone is mesityl oxide, formed by the aldol condensation. It can be dried with anhydrous CaSO<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub> or type 4A Linde molecular sieves, and then distd. Silica gel and alumina, or mildly acidic or basic desiccants cause acetone to undergo the aldol condensation, so that its water content is increased by passage through these reagents. This also occurs to some extent when P<sub>2</sub>O<sub>5</sub> or sodium amalgam is used. Anhydrous MgSO<sub>4</sub> is an inefficient drying agent, and CaCl<sub>2</sub> forms an addition compound. Drierite (anhydrous CaSO<sub>4</sub>) offers the minimum acid and base catalysis of aldol formation and is the recommended drying agent for this solvent [Coetzee and Siao *lnorg Chem* 14v 2 *1987*; Riddick and Bunger *Organic Solvents* Wiley-Interscience, N.Y., 3rd edn, 1970]. Acetone was shaken with Drierite (25g/L) for several hours before it was decanted and distd from fresh Drierite (10g/L) through an efficient column, maintaining atmospheric contact through a Drierite drying tube. The equilibrium water content is about 10<sup>-2</sup>M. Anhydrous Mg(ClO<sub>4</sub>)<sub>2</sub> should not be used as drying agent because of the risk of EXPLOSION with acetone vapour.

Organic impurities have been removed from acetone by adding 4g of  $AgNO_3$  in 30mL of water to 1L of acetone, followed by 10mL of M NaOH, shaking for 10min, filtering, drying with anhydrous CaSO<sub>4</sub> and distilling [Werner *Analyst (London)* **58** 335 1933]. Alternatively, successive small portions of KMnO<sub>4</sub> have been added to acetone at reflux, until the violet colour persists, followed by drying and distn. Refluxing with chromium trioxide (CrO<sub>3</sub>) has also been used. Methanol has been removed from acetone by azeotropic distn (at 35°) with methyl bromide, and treatment with acetyl chloride.

Small amounts of acetone can be purified as the NaI addition compound, by dissolving 100g of finely powdered NaI in 400g of boiling acetone, then cooling in ice and salt to  $-8^{\circ}$ . Crystals of NaI.3Me<sub>2</sub>CO are filtered off and, on warming in a flask, acetone distils off readily. [This method is more convenient than the one using the bisulfite addition compound.] Also purified by gas chromatography on a 20% free fatty acid phthalate (on Chromosorb P) column at  $100^{\circ}$ .

For efficiency of desiccants in drying acetone see Burfield and Smithers [*J Org Chem* **43** 3966 1978]. The water content of acetone can be determined by a modified Karl Fischer titration [Koupparis and Malmstadt Anal Chem **54** 1914 1982].

Rapid procedure: Dry over anhydrous CaSO<sub>4</sub> and distil.

Acetone cyanohydrin [75-86-5] M 85.1, b  $48^{\circ}/2.5$  mm,  $68-70^{\circ}/11$  mm,  $78-82^{\circ}/15$  mm,  $d_4^{20}$  0.93. Dry with Na<sub>2</sub>SO<sub>4</sub>, and distil as rapidly as possible under vacuum to avoid decomposition. Discard fractions boiling below 78-82°/15 mm. Store in the dark. USE AN EFFICIENT FUME HOOD as HCN (POISONOUS) is always present. [Org Synth Col.Vol. II 7 1940.]

Acetonedicarboxylic acid [542-05-2] M 146.1, m 138° (dec),  $pK^{25}$  3.10. Crystd from ethyl acetate and stored over P<sub>2</sub>O<sub>5</sub>. Decarboxylates in hot water.

Acetone semicarbazone [110-20-3] M 115.1, m 187°, pK<sup>25</sup> 1.33. Crystd from water or from aqueous EtOH.

Acetonitrile (methyl cyanide) [75-05-8] M 41.1, b 81.6°,  $d^{25}$  0.77683, n 1.3441,  $n^{25}$  1.34163. Commercial acetonitrile is a byproduct of the reaction of propylene and ammonia to acrylonitrile. The following procedure that significantly reduces the levels of acrylonitrile, allyl alcohol, acetone and \*benzene was used by Kiesel [Anal Chem 52 2230 1988]. Methanol (300mL) is added to 3L of acetonitrile fractionated at high reflux ratio until the boiling temperature rises from 64° to 80°, and the distillate becomes optically clear down to  $\lambda = 240$ nm. Add sodium hydride (1g) free from paraffin, to the liquid, reflux for 10min, and then distil rapidly until about 100mL of residue remains. Immediately pass the distillate through a column of acidic alumina, discarding the first 150mL of percolate. Add 5g of CaH<sub>2</sub> and distil the first 50mL at a high reflux ratio. Discard this fraction, and collect the following main fraction. The best way of detecting impurities is by gas chromatography.

Usual contaminants in commercial acetonitrile include  $H_2O$ , acetamide, NH<sub>4</sub>OAc and NH<sub>3</sub>. Anhydrous CaSO<sub>4</sub> and CaCl<sub>2</sub> are inefficient drying agents. Preliminary treatment of acetonitrile with cold, satd aq KOH is undesirable because of base-catalysed hydrolysis and the introduction of water. Drying by shaking with silica gel or Linde 4A molecular sieves removes most of the water in acetonitrile. Subsequent stirring with CaH<sub>2</sub> until no further hydrogen is evolved leaves only traces of water and removes acetic acid. The acetonitrile is then fractionally distd at high reflux, taking precaution to exclude moisture by refluxing over CaH<sub>2</sub> [Coetzee *Pure Appl Chem* 13 429 1966]. Alternatively, 0.5-1% (w/v) P<sub>2</sub>O<sub>5</sub> is often added to the distilling flask to remove most of the remaining water. Excess P<sub>2</sub>O<sub>5</sub> should be avoided because it leads to the formation of an orange polymer. Traces of P<sub>2</sub>O<sub>5</sub> can be removed by distilling from anhydrous K<sub>2</sub>CO<sub>3</sub>.

Kolthoff, Bruckenstein and Chantooni [J Am Chem Soc 83 3297 1961] removed acetic acid from 3L of acetonitrile by shaking for 24h with 200g of freshly activated alumina (which had been reactivated by heating at 250° for 4h). The decanted solvent was again shaken with activated alumina, followed by five batches of 100-150g of anhydrous CaCl<sub>2</sub>. (Water content of the solvent was then less than 0.2%). It was shaken for 1h with 10g of P<sub>2</sub>O<sub>5</sub>, twice, and distd in a 1m x 2cm column, packed with stainless steel wool and protected from atmospheric moisture by CaCl<sub>2</sub> tubes. The middle fraction had a water content of 0.7 to 2mM.

Traces of unsaturated nitriles can be removed by an initial refluxing with a small amount of aq KOH (1mL of 1% solution per L). Acetonitrile can be dried by azeotropic distn with dichloromethane, \*benzene or trichloroethylene. Isonitrile impurities can be removed by treatment with conc HCl until the odour of isonitrile has gone, followed by drying with  $K_2CO_3$  and distn.

Acetonitrile was refluxed with, and distd from alkaline KMnO<sub>4</sub> and KHSO<sub>4</sub>, followed by fractional distn from CaH<sub>2</sub>. (This was better than fractionation from molecular sieves or passage through a type H activated alumina column, or refluxing with KBH<sub>4</sub> for 24h and fractional distn)[Bell, Rodgers and Burrows J Chem Soc, Faraday Trans 1 73 315 1977; Moore et al. J Am Chem Soc 108 2257 1986].

Material suitable for polarography was obtained by refluxing over anhydrous AlCl<sub>3</sub> (15g/L) for 1h, distilling, refluxing over  $Li_2CO_3$  (10g/L) for 1h and redistg. It was then refluxed over CaH<sub>2</sub> (2g/L) for 1h and fractionally distd, retaining the middle portion. The product was not suitable for UV spectroscopy use. A better purification procedure used refluxing over anhydrous AlCl<sub>3</sub> (15g/L) for 1h, distg, refluxing over alkaline KMnO<sub>4</sub> (10g KMnO<sub>4</sub>, 10g Li<sub>2</sub>CO<sub>3</sub>/L) for 15min, and distg. A further reflux for 1h over KHSO<sub>4</sub> (15g/L), then distn, was followed by refluxing over CaH<sub>2</sub> (2g/L) for 1h, and fractional distn. The product was protected from atmospheric moisture and stored under nitrogen [Walter and Ramalay Anal Chem 45 165 1973]. Purificaton of "General Purity Reagent" for this purpose is not usually satisfactory because very large losses occur at the  $KMnO_4$ , LiCO<sub>3</sub> step. For electrochemical work involving high oxidation fluorides, further reflux over  $P_2O_5$ (1g/mL for 0.5h) and distilling (discarding 3% of first and last fractions) and repeating this step is necessary. The distillate is kept over molecular sieves in vac after degassing, for 24h and vac distd onto freshly activated 3A molecular sieves. The MeCN should have absorption at 200nm of <0.05 (H<sub>2</sub>O reference) and UV cutoff at ca175nm. Also the working potential range of purified  $Et_4N^+$  BF<sub>4</sub><sup>-</sup> (0.1mol.dcm<sup>-3</sup> in the MeCN) should be +3.0 to  $-2.7V vs Ag^+/Ag^0$ . If these criteria are not realised then further impurities can be removed by treatment with activated neutral alumina (60 mesh) in vacuo before final molecular sieves treatment [Winfield J Fluorine Chem **25** 91 1984].

Acetonitrile has been distd from AgNO<sub>3</sub>, collecting the middle fraction over freshly activated  $Al_2O_3$ . After standing for two days, the liquid was distd from the activated  $Al_2O_3$ . Specific conductivity 0.8-1.0 x 10<sup>-8</sup> mhos [Harkness and Daggett Can J Chem 43 1215 1965]. Acetonitrile <sup>14</sup>C was purified by gas chromatography and is water free and distd at 81°. [J Mol Biol 87 541 1974.]

**Rapid procedure:** Dry over anhydrous  $K_2CO_3$  for 24h, followed by further drying for 24h over 3A molecular sieves or boric anhydride, followed by distn. Alternatively, stir over  $P_2O_5$  (5% w/v) for 24h then distil. However this last method is not suitable for use in reactions with very acid sensitive compounds.

Acetonylacetone (2,5-hexanedione) [110-13-4] M 114.2, m -9°, b 76-78°/13 m m, 88°/25mm, 137°/150mm, 188°/atm,  $d_4^{20}$  0.9440,  $n_D^{20}$  1.423, pK 18.7. Purified by dissolving in Et<sub>2</sub>O, stirred with K<sub>2</sub>CO<sub>3</sub> (a quarter of the wt of dione), filtered, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> (not CaCl<sub>2</sub>), filtered, evapd and distd in a vacuum. It is then redistd through a 30cm Vigreux column (oil bath temp 150°). It is miscible with H<sub>2</sub>O and EtOH. The *dioxime* has m 137° (plates from \*C<sub>6</sub>H<sub>6</sub>), *mono-oxime* has b 130°/11mm, and the 2,4-dinitrophenylhydrazone has m 210-212° (red needles from EtOH). [Chem Ber 22 2100 1989; for enol content see J Org Chem 19 1960 1954.]

**4-Acetophenetidine** (**phenacetin**) [62-44-2] M 179.2, m 136°. Crystd from H<sub>2</sub>O or purified by soln in cold dilute alkali and reppted by addn of acid to neutralisation point. Air-dried.

Acetophenone [98-86-2] M 120.2, m 19.6°, b 54°/2.5mm, 202°/760mm,  $d^{25}$  1.0238, n <sup>25</sup> 1.5322, pK 19.2. Dried by fractional distn or by standing with anhydrous CaSO<sub>4</sub> or CaCl<sub>2</sub> for several days, followed by fractional distn under reduced pressure (from P<sub>2</sub>O<sub>5</sub>, optional), and careful, slow and repeated partial crystns from the liquid at 0° excluding light and moisture. It can also be crystd at low temperatures from isopentane. Distn can be followed by purification using gas-liquid chromatography [Earls and Jones J Chem Soc, Faraday Trans 1 71 2186 1975.]

§ A commercial polystyrene supported version is available — scavanger resin (for diol substrate).

Aceto-o-toluidide [120-66-1] M 149.2, m 110°, b  $296^{\circ}/760$  mm. Crystd from H<sub>2</sub>O, EtOH or aqueous EtOH.

Aceto-*m*-toluidide [537-92-8] M 149.2, m 65.5°, b 182-183°/14mm, 303°/760mm. Crystd from H<sub>2</sub>O, EtOH or aqueous EtOH.

Aceto-p-toluidide [103-89-9] M 149.2, m 146°, b 307°/760mm. Crystd from aqueous EtOH.

Acetoxime (acetone oxime) [127-06-0] M 73.1, m 63°, b 135°/760mm, pK<sup>40</sup> 0.99. Crystd from pet ether (b 40-60°). Can be sublimed.

Acetoxyacetone (acetol acetone) [592-20-1] M 116.1, b 65°/11mm, 73-75°/17mm, 174-176°/atm,  $d_4^{20}$  1.0757,  $n_D^{20}$  1.4141. Distil under reduced pressure, then redistil at atm pressure. It is miscible with H<sub>2</sub>O but is slowly decomposed by it. Store in dry atmosphere. The 2,4-dinitrophenylhydrazone has m 115-115.5° (from CHCl<sub>3</sub>/hexane). [J Chem Soc 59 789 1891; J Org Chem 21 68 1956; Justus Liebigs Ann Chem 335 260 1904.]

**4-Acetoxy-2-azetidinone** [28562-53-0] **M 129.1, m 38-41°.** Dissolve in CHCl<sub>3</sub>, dry (MgSO<sub>4</sub>) concentrate at 40°/70mm, or better at room temperature to avoid decomposition. Wash and stir the residual oil with hexane by decantation and discard wash. Dry the oil at high vacuum when it should solidify, **m** 34°. It can be distd at high vacuum,  $80-82^{\circ}/10^{-3}$ mm, but this results in extensive losses. The purity can be checked by TLC using Merck Silica Gel F<sub>254</sub> and eluting with EtOAc. The azetidinone has R<sub>F</sub> 0.38 (typical impurities have R<sub>F</sub> 0.67). The spots can be detected by the TDM spray. This is prepared from (A) 2.5g 4,4'-tetramethyldiaminodiphenylmethane (TDM) in 10mL AcOH and diluted with 50mL of H<sub>2</sub>O, (B) 5g KI in 100mL of H<sub>2</sub>O and (C) 0.3g ninhydrin in 10mL of AcOH and 90mL of H<sub>2</sub>O. The spray is prepared by mixing (A) and (B) with 1.5mL of (C) and stored in a brown bottle. [Justus Liebigs Ann Chem 539 1974; Org Synth 65 135 1987.]

1-Acetoxy-1,3-butadiene (1,3-butadienyl acetate) cis-trans mixture [1515-76-0] M 112.1, b 42-43°/16mm, 51-52°/20mm, 60-61°/40mm, d  $_{4}^{20}$  0.9466, n  $_{D}^{20}$  1.4622. The commercial sample is stabilised with 0.1% of *p*-tert-butylcatechol. If the material contains crotonaldehyde (by IR, used in its synthesis) it should be dissolved in Et<sub>2</sub>O, shaken with 40% aqueous sodium bisulfite, then 5% aqueous

Na<sub>2</sub>CO<sub>3</sub>, water, dried (Na<sub>2</sub>SO<sub>4</sub>) and distilled several times in a vac through a Widmer (*Helv Chim Acta* 7 59 1924) or Vigreux column [Wicterle and Hudlicky Collect Czech Chem Commun 12 564 1947; Hagemeyer and Hull Ind Eng Chem 41 2920 1949].

**1-Acetoxy-2-butoxyethane** [112-07-2] M 160.2, b 61-62°/0.2mm, 75-76°/12mm, 185.5°/740mm, 188-192°/atm,  $d_4^{20}$  0.9425,  $n_D^{20}$  1.4121. Shake with anhydrous Na<sub>2</sub>CO<sub>3</sub>, filter and distil in a vacuum. Redistn can be then be carried out at atmospheric pressure. [J Org Chem 21 1041 1956.]

3R,4R,1'R-4-Acetoxy-3-[1-(tert-butylmethylsilyloxy)ethyl]-2-azetinone see Chapter 5.

**2-Acetoxyethanol** [542-59-6] M 104.1, b 187°/761mm, 187-189°/atm,  $d_4^{20}$  1.108,  $n_D^{20}$  1.42. Dry over K<sub>2</sub>CO<sub>3</sub> (not CaCl<sub>2</sub>), and distil. [J Chem Soc 3061 1950; rate of hydrolysis: J Chem Soc 2706 1951.]

1-Acetoxy-2-ethoxyethane [111-15-9] M 132.2, b 156-159°,  $d_4^{20}$  0.97,  $n_D^{20}$  1.406. Shake with anhydr Na<sub>2</sub>CO<sub>3</sub>, filter and distil in vac. Redistn can then be carried out at atm pressure. [J Org Chem 21 1041 1956.]

1-Acetoxy-2-methoxyethane [110-49-6] M 118.1, b 141°/732mm, 140144°/atm,  $d_4^{20}$  1.009,  $n_D^{20}$  1.4011. Shake with anhydrous Na<sub>2</sub>CO<sub>3</sub>, filter and distil in a vacuum. Redistn can be then be carried out at atmospheric pressure. [J Org Chem 21 1041 1956.]

**R**-(-)- $\alpha$ -Acetoxyphenylacetic (acetyl mandelic) acid [51019-43-3] M 194.2, m 96-98°,  $[\alpha]_D^{20}$ -153.7° (c 2.06, Me<sub>2</sub>CO),  $[\alpha]_{546}^{20}$  -194° (c 2.4, Me<sub>2</sub>CO), pK<sub>Est</sub> ~2.9 Recrysts from H<sub>2</sub>O with 1mol of solvent which is removed on drying, or from solvents as for the S-isomer. [J Chem Soc 227 1943.]

S-(+)- $\alpha$ -Acetoxyphenylacetic (acetyl mandelic) acid [7322-88-5] M 194.2, m 80-81°, 95-97.5°,  $[\alpha]_D^{27}$ +158° (c 1.78, Me<sub>2</sub>CO),  $[\alpha]_{546}^{20}$ +186° (c 2, Me<sub>2</sub>CO). Recryst from \*benzene-hexane or toluene and has characteristic NMR and IR spectra. [Justus Liebigs Ann Chem 622 10 1959; J Org Chem 39 1311 1974.]

21-Acetoxypregnenolone [566-78-9] M 374.5, m 184-185°. Crystd from Me<sub>2</sub>CO.

S-(-)-2-Acetoxypropionyl chloride [36394-75-9] M 150.6, b 51-53°/11mm,  $d_4^{20}$  1.19,  $n_D^{20}$  1.423,  $[\alpha]_D^{27}$ -33°, (c 4, CHCl<sub>3</sub>),  $[\alpha]_{546}^{20}$ -38° (c 4, CHCl<sub>3</sub>). It is moisture sensitive and is hydrolysed to the corresponding acid. Check the IR spectrum. If the OH band above 3000cm<sup>-1</sup> is too large and broad then the mixture should be refluxed with pure acetyl chloride for 1h, evapd and distd under reduced pressure.

S-Acetoxysuccinic anhydride [59025-03-5] M 158.1, m 58° (RS 81.5-82.5°, 86-87°),  $[\alpha]_D^{20}$ -26.0° (c 19, Me<sub>2</sub>CO),  $[\alpha]_D^{20}$ -28.4° (c 13, Ac<sub>2</sub>O). Recryst from Ac<sub>2</sub>O and dry in a vacuum over KOH, or by washing with dry Et<sub>2</sub>O due to its deliquescent nature. [J Chem Soc 788 1933; Synth Commun 16 183 1986; J Org Chem 52 1040 1988; RS : J Am Chem Soc 88 5306 1966.]

Acetylacetone (2,4-pentanedione) [123-54-6] M 100.1, b 45°/30mm, d<sup>30.2</sup> 0.9630, n<sup>18.5</sup> 1.45178, pK<sub>1</sub><sup>25</sup>-5.0 (enol), -6.6 (keto), pK<sub>2</sub><sup>25</sup>8.95 Small amounts of acetic acid were removed by shaking with small portions of 2M NaOH until the aqueous phase remained faintly alkaline. The sample, after washing with water, was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, and distd through a modified Vigreux column [Cartledge *J Am Chem Soc* 73 4416 1951]. An additional purification step is fractional crystn from the liquid. Alternatively, there is less loss of acetylacetone if it is dissolved in four volumes of \*benzene and the soln is shaken three times with an equal volume of distd water (to extract acetic acid): the \*benzene is then removed by distn at 43-53° and 20-30mm through a helices-packed column. It is then refluxed over P<sub>2</sub>O<sub>5</sub> (10g/L) and fractionally distd under reduced pressure. The distillate (sp conductivity 4 x 10<sup>-8</sup> ohm<sup>-1</sup>cm<sup>-1</sup>) was suitable for polarography [Fujinaga and Lee *Talanta* 24 395 1977]. To recover used acetylacetone, metal ions were stripped from the soln at pH 1 (using 100mL 0.1M H<sub>2</sub>SO<sub>4</sub>/L of acetylacetone). The acetylacetone was washed with

# **Purification of Organic Chemicals**

(1:10) ammonia soln (100mL/L) and with distd water (100mL/L, twice), then treated as above. It complexes with Al, Be, Ca, Cd, Ce, Cu,  $Fe^{2+}$ ,  $Fe^{3+}$ , Mn, Mg, Ni, Pb and Zn.

N-Acetyl-L-alaninamide [15962-47-7] M 130.2, m 162°. Crystd repeatedly from EtOH-diethyl ether.

N-Acetyl-B-alanine [3025-95-4] M 127.2, m 78.3-80.3°, pK<sup>25</sup> 4.45. Crystd from acetone.

N-Acetyl-L-alanyl-L-alaninamide [30802-37-0] M 201.2, m 250-251°. Crystd repeatedly from EtOH/diethyl ether.

N-Acetyl-L-alanyl-L-alanyl-L-alaninamide [29428-34-0] M 272.3, m 295-300°. Crystd from MeOH/diethyl ether.

N-Acetyl-L-alanylglycinamide [76571-64-7] M 187.2, m 148-149°. Crystd repeatedly from EtOH/diethyl ether.

Acetyl- $\alpha$ -amino-*n*-butyric acid [34271-24-4] M 145.2, pK<sup>25</sup> 3.72. Crystd twice from water (charcoal) and air dried [King and King J Am Chem Soc 78 1089 1956].

9-Acetylanthracene [784-04-3] M 220.3, m 75-76°. Crystd from EtOH. [Masnori et al. J Am Chem Soc 108 1126 1986.]

*N*-Acetylanthranilic acid [89-52-1] M 179.1, m 182-184°, 185-186°, 190°(dec),  $pK^{20}$  3.61. Wash with distilled H<sub>2</sub>O and recrystallise from aqueous AcOH, dry and recrystallise again from EtOAc. Also recryst from water or EtOH. [J Chem Soc 2495 1931; J Am Chem Soc 77 6698 1955.]

**2-Acetylbenzoic acid** [577-56-0] **M 164.2, m 115-116°, 116-118°, pK^{25} 4.10.** Recrystallises from \*C<sub>6</sub>H<sub>6</sub> and H<sub>2</sub>O (15g/100mL). The oxime has **m** 156-157°, and the 2,4-dinitrophenylhydrazone has **m** 185-186°(needles from EtOH). [J Am Chem Soc 69 1547 1947.]

**4-Acetylbenzoic acid** [586-89-0] **M 164.2, m 207.5-209.5°, 208.6-209.4°, pK**<sup>25</sup> **3.70, 5.10** (EtOH). Dissolve in 5% aqueous NaOH, extract with Et<sub>2</sub>O, and acidify the aqueous soln. Collect the ppte, and recrystallise from boiling H<sub>2</sub>O (100 parts) using decolorising charcoal [J Org Chem 24 504 1959; J Chem Soc 265 1957; J Am Chem Soc 72 2882 1050, 74 1058 1952].

Acetylbenzonitrile [1443-80-7] M 145.2, m 57-58°. Recrystd from EtOH [Wagner et al. J Am Chem Soc 108 7727 1986].

4-Acetylbiphenyl [92-91-1] M 196.3, m 120-121°, b 325-327°/760mm. See 4'-phenyl-acetophenone on p. 327.

Acetyl-5-bromosalicylic acid [1503-53-3] M 259.1, m 168-169°, pK<sub>Est</sub> ~3.0. Crystd from EtOH.

2-Acetylbutyrolactone [517-23-7] M 128.1, b 105°/5mm, 120-123°/11mm, 142-143°/30mm, d<sup>20</sup><sub>4</sub> 1.1846, n<sup>20</sup><sub>D</sub> 1.459. Purified by distillation, which will convert any free acid to the lactone, alternatively dissolve in Et<sub>2</sub>O, wash well with 0.5N HCl, dry the organic layer and distil. The solubility in H<sub>2</sub>O is 20% v/v. The 2,4-dinitrophenylhydrazone forms orange needles from MeOH, m 146°. The lactone hydrolyses in mineral acid to 2-acetyl-4-hydroxybutyric acid which can be converted to the di-npropylamine salt with m 68-70°. The lactone is a SKIN IRRITANT. [Yakugaku Zasshi (J Pharm Soc Japan) 62 417(439) 1942; Helv Chim Acta 35 2401 1952.]

Acetyl chloride [75-36-5] M 78.5, b 52°, d 1.1051, n 1.38976. Refluxed with PCl<sub>5</sub> for several hours to remove traces of acetic acid, then distd. Redistd from one-tenth volume of dimethylaniline or quinoline to remove free HCl. A.R. quality is freed from HCl by pumping it for 1h at -78° and distg into a trap at -196°.

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Acetyl bromide [506-96-7] M 123.0, b 76-77°, d 1.65. Boiled with PBr<sub>3</sub>/Ac<sub>2</sub>O for 1h then distd off and redistd. Store dry. [Burton and Degering J Am Chem Soc 62 227 1940.] LACHRYMATORY.

Acetylcyclohexane (cyclohexyl methylketone) [823-76-7] M 126.2, b  $64^{\circ}/11$ mm, 76.2-77°/25mm, d<sup>20</sup><sub>4</sub> 0.9178, n<sup>20</sup><sub>D</sub> 1.4519. Dissolve in Et<sub>2</sub>O, shake with H<sub>2</sub>O, dry, evaporate and fractionate under reduced pressure. [UV: J Am Chem Soc 74 518 1952; enol content: J Org Chem 19 1960 1954.] The semicarbazone has m 174°; the 2,4-dinitrophenylhydrazone has m 139-140° [Helv Chim Acta 39 1290 1956].

2-Acetylcyclohexanone [874-23-7] M 140.2, m -11°, b 62-64°/2.5mm, 95-98°/10mm, 111-112°/18mm, d<sup>20</sup><sub>4</sub> 1.08, n<sup>20</sup><sub>D</sub> 1.51. Dissolve in ligroin (b 30-60°), wash with saturated aqueous NaHCO<sub>3</sub> dry over Drierite and fractionate in a vacuum. [J Am Chem Soc 75 626, 5030 1953; Chem Ber 87 108 1954.] It forms a Cu salt which crystallises in green leaflets from EtOH, m 162-163° [UV: J Chem Soc 4419 1957].

**2-Acetylcyclopentanone** [1670-46-8] M 126.2, b. 72-75°/8mm, 82-86°/12mm, 88°/18mm,  $d_4^{20}$  1.043,  $n_D^{20}$  1.490. Dissolve in pet ether (b 30-60°), wash with satd aq NaHCO<sub>3</sub>, dry over Drierite and fractionate in a vacuum. It gives a violet colour with ethanolic FeCl<sub>3</sub> and is only slowly hydrolysed by 10% aq KOH but rapidly on boiling to yield 6-oxoheptanoic acid. [J Am Chem Soc 75 5030 1953; J Chem Soc 4232 1956; UV: J Am Chem Soc 81 2342 1959.] It gives a gray green Cu salt from Et<sub>2</sub>O-pentane, m 237-238° [J Am Chem Soc 79 1488 1957].

Acetyldigitoxin- $\alpha$  [25395-32-8] M 807.0, m 217-221°,  $[\alpha]_D^{20}$ +5.0 (c 0.7, pyridine). Crystd from MeOH as plates.

Acetylene [74-86-2] M 26.0, m -80.8°, b -84°, pK ~25. If very impure it should be purified by successive passage through spiral wash bottles containing, in this order, satd aq NaHSO<sub>4</sub>, H<sub>2</sub>O, 0.2M iodine in aq KI (two bottles), sodium thiosulfate soln (two bottles), alkaline sodium hydrosulfite with sodium anthraquinone-2-sulfonate as indicator (two bottles), and 10% aqueous KOH soln (two bottles). The gas was then passed through a Dry-ice trap and two drying tubes, the first containing CaCl<sub>2</sub>, and the second, Dehydrite [Mg(ClO<sub>4</sub>)<sub>2</sub>] [Conn, Kistiakowsky and Smith J Am Chem Soc 61 1868 1939]. Acetone vapour can be removed from acetylene by passage through H<sub>2</sub>O, then concd H<sub>2</sub>SO<sub>4</sub>, or by passage through two gas traps at -65° and -80°, concd H<sub>2</sub>SO<sub>4</sub> and a soda lime tower, a tower of 1-mesh Al<sub>2</sub>O<sub>3</sub> then into H<sub>2</sub>SO<sub>4</sub> [Org Synth Coll Vol 1 229 1941, 3 853 1955; 4 793 1963].. Sometimes it contains acetone and air. These can be removed by a series of bulb-to-bulb distns, e.g. a train consisting of a conc H<sub>2</sub>SO<sub>4</sub> trap and a cold EtOH trap (-73°), or passage through H<sub>2</sub>O and H<sub>2</sub>SO<sub>4</sub>, then over KOH and CaCl<sub>2</sub>. [See Brandsma Preparative Acetylenic Chemistry, 1st Edn Elsevier 1971, for pK p15, ISBN 0444409475; 2nd Edn Elsevier 1988, ISBN 0444429603, and Chapter 5 for sodium acetylide.] It is also available commercially as 10ppm in helium, and several concentrations in N<sub>2</sub> for instrument calibration.

Sodium acetylide [1066-26-8] M 48.0, was prepd by dissolving Na (23g) in liquid NH<sub>3</sub> (1L) and bubbling acetylene until the blue color was discharged (ca 30min) and evapd to dryness [Saunders Org Synth Coll Vol III 416 1955]; and is available commercially as a suspension in xylene/light mineral oil. [See entry in Chapter 5.]

Acetylenedicarboxamide [543-21-5] M 112.1, m 294°(dec). Crystd from MeOH.

Acetylenedicarboxylic acid [142-45-0] M 114.1, m 179°(anhydrous),  $pK_1^{19}$  1.04,  $pK_2^{19}$  2.50. Crystd from aqueous ether as dipicrate. For mono K salt see entry in Chapter 5.

N-Acetylethylenediamine [1001-53-2] M 102.1, m 50-51°, 51°, b 128°/3mm, 125-130°/5mm, 133-139°/27mm, pK<sup>25</sup> 9.28. It has been fractionated under reduced pressure and fraction b 125-130°/5mm was refractionated; fraction b 132-135°/4mm was collected and solidified. It is a low melting hygroscopic solid which can be recrystd from dioxane-Et<sub>2</sub>O. It is soluble in H<sub>2</sub>O, Et<sub>2</sub>O and \*C<sub>6</sub>H<sub>6</sub>. The *p*-toluenesulfonate salt can be recrystd from EtOH-EtOAc 1:8, has m 125-126° but the free base cannot be recovered from it by basifying and extracting with CH<sub>2</sub>Cl<sub>2</sub>. The *picrate* has m 175° (from EtOH) [J Am Chem Soc 63 853 1941, 78 2570 1956].

2-Acetylfluorene [781-73-7] M 208.3, m 132°. Crystd from EtOH.

Acetyl fluoride [557-99-3] M 62.0, b 20.5%/760mm, d 1.032. Purified by fractional distn.

N-Acetyl-D-galactosamine [14215-68-0] M 221.2, m 160-161°,  $[\alpha]_{546}$  +102° (c 1, H<sub>2</sub>O). Crystd from MeOH/Et<sub>2</sub>O.

N-Acetyl-D-glucosamine [7512-17-6] M 221.2, m ca 215°,  $[\alpha]_{546}$  +49° after 2h (c 2, H<sub>2</sub>O). Crystd from MeOH/Et<sub>2</sub>O.

*N*-Acetylglutamic acid [1188-37-0] M 189.2, m 185° (*RS*); 201° (*S*),  $[\alpha]^{25}$  -16.6° (in H<sub>2</sub>O), pK<sub>Est (1)</sub> ~3.4, pK<sub>Est(2)</sub> ~4.3. Likely impurity is glutamic acid. Crystd from boiling water.

**N-Acetylglycinamide** [2620-63-5] **M 116.1, m 139-139.5°.** Repeated crystn from EtOH/Et<sub>2</sub>O. Dried in a vacuum desiccator over KOH.

*N*-Acetylglycine [543-24-8] M 117.1, m 206-208°,  $pK_1^{25}$ -1.92,  $pK_2^{25}$  3.69. Treated with acidwashed charcoal and recryst three times from water or EtOH/Et<sub>2</sub>O and dried *in vacuo* over KOH [King and King *J Am Chem Soc* 78 1089 1956].

N-Acetylglycyl-L-alaninamide [34017-20-4] M 175.2. Repeated crystn from EtOH/Et<sub>2</sub>O. Dried in a vacuum desiccator over KOH.

**N-Acetylglycylglycinamide** [27440-00-2] M 173.2, m 207-208°. Repeated crystn from EtOH/Et<sub>2</sub>O. Dried in a vacuum desiccator over KOH.

**N-Acetylglycylglycylglycinamide** [35455-24-4] **M 230.2, m 253-255°.** Repeated crystn from EtOH/Et<sub>2</sub>O. Dried in a vacuum desiccator over KOH.

*N*-Acetylhistidine (H<sub>2</sub>O) [39145-52-3] M 171.2, m 148° (RS); 169° (S)  $[\alpha]^{25}$  +46.2° (H<sub>2</sub>O). Likely impurity is histidine. Crystd from water, then 4:1 acetone:water.

*N*-Acetyl-*RS*-homocysteine thiolactone (Citiolone) [1195-16-0] [17896-21-8 for  $\pm$ ] M 159.2, m 110°, 109-111°, 111.5-112.5°. Dry in a vacuum desiccator and recrystallise from toluene as needles. It is a ninhydrin -ve substance which gives a "slow" nitroprusside test.  $\lambda_{max}$  238nm ( $\epsilon$  4,400 M<sup>-1</sup>cm<sup>-1</sup>); v (nujol) 1789s and 851ms cm<sup>-1</sup>. [J Am Chem Soc 78 1597 1956; J Chem Soc 2758 1963.]

*N*-Acetylimidazole [2466-76-4] M 110.1, m 101.5-102.5°,  $pK^{25}$  3.6. Crystd from isopropenyl acetate. Dried in a vacuum over P<sub>2</sub>O<sub>5</sub>.

**3-Acetylindole** [703-80-0] **M** 159.2, **m** 188-190°, 191-193°, 194°,  $pK^{25}$  12.99 (acidic). Recrystd from MeOH or \*C<sub>6</sub>H<sub>6</sub> containing a little EtOH. The *phenylureido* derivative has **m** 154°. [J Chem Soc 461 1946.]

Acetyl iodide [507-02-8] M 170.0, b 108%/760mm. Purified by fractional distn.

**N-Acetyl-L-leucinamide** [28529-34-2] M 177.2, m 133-134°. Recrystd from CHCl<sub>3</sub> and pet ether (b 40-60°).

**3-(S-Acetylmercapto)isobutyric acid** [RS 33325-40-5] **M 162.2, m 40-40.5°, b** c a **120°/1.25mm, pK**<sub>Est</sub> ~4.0. Distil under vacuum and recrystd from \*C<sub>6</sub>H<sub>6</sub>. [Chem Abstr 38 3616 1944.]

Acetyl methanesulfonate [5539-53-7] M 170.2, b <120°/<0.01mm. The main impurity is methanesulfonic acid. Reflux with redistd acetyl chloride for 6-10h, i.e. until no further HCl is absorbed in a trap, and exclude moisture. Dist off excess of AcCl and carefully dist below 0.001mm with the bath temp below 120° to give the anhydride as a pale yellow oil which solidifies below 0°. Below ~130° it decomp to the

disulfonic anhydride and above ~130° polymers are formed. It is used for cleaving ethers [Prep, IR, NMR: Karger and Mazur J Org Chem 36 528, 532 1971].

N-Acetyl-L-methionine [65-82-7] M 191.3, m 104°,  $[\alpha]_{546}$  -24.5° (c 1, in H<sub>2</sub>O), pK<sub>Est</sub> ~3.4. Crystd from water or ethyl acetate. Dried in a vacuum over P<sub>2</sub>O<sub>5</sub>.

Acetylmethionine nitrile [538-14-7] M 172.3, m 44-46°. Crystd from diethyl ether.

5-Acetyl-2-methoxybenzaldehyde [531-99-7] M 166.2, m 144°. Crystd from EtOH or Et<sub>2</sub>O.

N-Acetyl-N'-methyl-L-alanimide [19701-83-8] M 144.2. Crystd from EtOAc/Et<sub>2</sub>O, then from EtOH and Et<sub>2</sub>O.

4-Acetyl-1-methyl-1-cyclohexene [6090-09-1] M 138.2, b 73-75°/7.5mm, 85-86°/13 mm, 94-94.7°/20mm, 204.5-206°/747mm,  $d_4^{20}$  1.0238,  $n_D^{20}$  1.469. Purified by fractionation under reduced pressure *in vacuo*, and when almost pure it can be fractionated at atmospheric pressure, preferably in an inert atm. Forms two *semicarbazones* one of which is more soluble in \*C<sub>6</sub>H<sub>6</sub>, and both can be recryst from EtOH, more soluble has m 149°(151°), and the less soluble has m 172-175°(191°). 4-Nitrophenylhydrazone has m 166-167° and the 2,4-dinitrophenylhydrazone has m 114-115°. [Helv Chim Acta 17 129, 140 1934; Justus Liebigs Ann Chem 564 109 1949.]

N-Acetyl-6N'-methylglycinamide [7606-79-3] M 130.2. Recrystd from EtOH/Et<sub>2</sub>O mixture.

N-Acetyl-6N'-methyl-L-leucine amide [32483-15-1] M 186.3. Recrystd from EtOH/hexane mixture.

4-Acetylmorpholine [1696-20-4] M 129.2, m 13.8-14°, 14°, 14.5°, b 96-97°/6mm, 113-128°/22mm, 242-247°/760mm, d<sup>20</sup><sub>4</sub> 1.0963, n<sup>D</sup><sub>2</sub> 1.4830. Distd through an 8inch Fenske (glass helices packing) column with a manual take-off head. Purified by fractional distn. The hydrobromide has m 172-175°. [J Am Chem Soc 75 357 1953, J Org Chem 21 1072 1956.]

1-Acetylnaphthalene [941-98-0] M 170.1, m 10.5°, b 93-95°/0.1mm, 167°/12mm, 302°/atm,  $d_4^{20}$  1.12, pK -6.22 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). If the NMR spectrum indicates the presence of impurities, probably 2-acetylnaphthalene, convert the substance to its picrate by dissolving in \*benzene or EtOH and adding excess of satd-picric acid in these solvents until separation of picrates is complete. Recryst the picrate till m is 118°. Decompose the picrate with dil NaOH and extract with Et<sub>2</sub>O. Dry the extract (Na<sub>2</sub>SO<sub>4</sub>), filter, evap and dist. The 2,4-dinitrophenylhydrazone crysts from EtOH and has m 259°. [Justus Liebigs Ann Chem 380 95 1911; J Am Chem Soc 61 3438 1939.]

2-Acetylnaphthalene (2-acetonaphthenone, ß-Acetonaphthone, 2-acetonaphthalene, methyl-2-naphthylketone) [93-08-3] M 170.2, m 52-53°, 55°, 55.8°, b 164-166°/8mm, 171-173°/17mm, 301-303°/atm, pK -6.16 ( $H_0$  scale, aq  $H_2SO_4$ ). Separated from the 1-isomer by fractional crystn of the picrate in EtOH (see entry for the 1-isomer above) m 82°. Decomposition of the picrate with dil NaOH and extraction with Et<sub>2</sub>O then evaporation gives purer 2-acetylnaphthalene. If this residue solidifies it can be recrystd from pet ether, EtOH or acetic acid; otherwise it should be distild in a vac and the solid distillate is recrystd [Gorman and Rodgers J Am Chem Soc 108 5074 1986; Levanon et al. J Phys Chem 91 14 1987]. Purity should be checked by high field NMR spectroscopy. Oxime has m 145° decomp, and the semicarbazone has m 235°. [Justus Liebigs Ann Chem 380 95 1911; J Am Chem Soc 72 753 and 5626 1950, J Org Chem 5 512 1940.]

*N*-Acetyl-D-penicillamine [15537-71-0] M 191.3, m 189-190° (dec),  $[\alpha]_D$  +18° (c 1, in 50% EtOH). See *N*-acetyl penicillamine on p. 507 in Chapter 6.

N-Acetyl-L-phenylalanine [2018-61-3] M 207.2, m 170-171°,  $[\alpha]_D$  +41° (c 1, EtOH), (DL) m 152.5-153°, pK<sub>Est</sub> 3.5. Crystd from CHCl<sub>3</sub> and stored at 4°. (DL)-isomer crystd from water or acetone.

N-Acetyl-L-phenylalanine ethyl ester [2361-96-8] M 235.3, m 93-94°. Crystd from aq EtOH or H<sub>2</sub>O. [Izumiya and Fruton J Biol Chem 218 59 1956.]

1-Acetyl-2-phenylhydrazine [114-83-0] M 150.2, m 128.5°, pK<sup>25</sup> 1.3. Crystd from aq EtOH.

**1-Acetylpiperazine** [13889-98-0] **M 128.2, m 32-34°, 52°, pK^{25} 7.94.** Purified by recrystn from 40% aqueous EtOH or from EtOH-Et<sub>2</sub>O. It is an **irritant**, and is *hygroscopic*. The *hydrochloride* has **m** 191° (from EtOH), and the *tosylate* has **m** 148-149° (from EtOH-EtOAc, 1:16). The free base, however, cannot be isolated by basifying the tosylate salt and extractn with CH<sub>2</sub>Cl<sub>2</sub>. [*Chem Ber* **66** 113 1933; J Am Chem Soc 75 4949 1953, 2570 **78** 1956.]

1-Acetyl-4-piperidone [32161-06-1] M 141.2, b 124-128°/0.2mm, 218°/760mm,  $d_4^{25}$  1.1444,  $n_D^{25}$  1.5023. Purified by fractional distn through a short Vigreux column (15mm). The 2,4dinitrophenylhydrazone has m 212-213° (from EtOH). It is freely soluble in H<sub>2</sub>O but insoluble in Et<sub>2</sub>O. [J Am Chem Soc 901 71 1949.]

**3-Acetylpyridine** [350-03-8] **M** 121.1, **m** 13-14°, **b** 65-66°/1**mm**, 92-95°/8-9 **m m**, 105°(113°)/16mm, 219-221°/760mm,  $d_4^{20}$  1.1065,  $n_D^{20}$  1.1065,  $pK^{25}$  3.18. It is purified by dissolving in HCl, extracting with Et<sub>2</sub>O to remove the possible impurity of nicotinic acid, basified with NaOH and extracted with Et<sub>2</sub>O. The dried extract is filtered, evaporated and the residual oil distd. If the NMR spectrum indicates further impurities then convert to the *phenylhydrazone* (**m** 137°, yellow needles from EtOH). This is hydrolysed with HCl [*Chem Ber* 22 597 1889], the phenylhydrazine HCl is removed by filtration, NaNO<sub>2</sub> is added, the soln is basified with aq NaOH and extracted with Et<sub>2</sub>O as before and distd at atmospheric pressure to give 3-acetylpyridine as a colourless oil. Purification can be achieved by shaking with 50% aq KOH, extracting with Et<sub>2</sub>O, drying the extract and distilling at atmospheric pressure or in a vacuum. [J Am Chem Soc 79 4226 1957]. The hydrochloride has **m** 180-181° (from MeOH-EtOH), the picrate has **m** 133.8-134.8° (from H<sub>2</sub>O), and the phenylhydrazone has **m** 137° (129-130)° (from EtOH) [J Am Chem Soc 71 2285 1949]. The ketoxime has **m** 112° (from EtOH or \*C<sub>6</sub>H<sub>6</sub>. [J Am Chem Soc 55 816 1933, 63 490 1941, 67 1468 1945, 79 4226 1957.]

Acetylsalicylic acid (Aspirin) [50-78-2] M 180.2, m 133.5-135°,  $pK^{25}3.38$ ,  $(pK^{17}4.56)$ . Crystd twice from toluene, washed with cyclohexane and dried at 60° under vacuum for several hours [Davis and Hetzer J Res Nat Bur Stand 60 569 1958]. Has also been recrystd from isopropanol and from diethyl ether/pet ether (b 40-60°).

O-Acetylsalicyloyl chloride [5538-51-2] M 198.6, m 45°, 46-49°, 48-52°, b 107-110°/0.1mm, 135°/12mm, n<sub>D</sub> 1.536. Check first the IR to see if an OH frequency is present. If so then some free acid is present. Then reflux with acetyl chloride for 2-3h and fractionate at high vac. The distillate should crystallise. It can be recryst from hexane. [J Chem Soc 89 1318 1906.]

O-Acetylsalicylsalicylic acid [530-75-6] M 300.3, m 159°. Crystd from dilute acetic acid.

N-(4)-Acetylsulfanilamide [144-80-9] M 214.2, m 216°. Crystd from aqueous EtOH.

**2-Acetylthiazole** [24295-03-2] **M 127.2, b 89-91°** (90-95°)/12mm, 95-105°/15mm,  $d_4^{20}$  1.23, n<sub>D</sub> 1.55. Check NMR spectrum, if not too bad, distil through an efficient column in a vacuum. The oxime sublimes at 140-145°, m 159° (cryst from H<sub>2</sub>O) has m 163-165.5° [Helv Chim Acta 31 1142 1948; J Am Chem Soc 79 4524 1957; Helv Chim Acta 40 554 1957].

2-Acetylthiophene (methyl 2-thienyl ketone) [88-15-3] M 126.2, m 9.2-10.5°, 10.45°, 10-11°, b 77°/4mm, 89-91°/9mm, 94.5-96.5°/13mm, 213-214°/atm,  $d_4^{20}$  1.17,  $n_D^{20}$  1.5666. Fractionally distd through a 12 plate column and fraction b 77°/4mm was collected. Also wet the acetylthiophene in order to remove and free thiophene which forms an azeotrope with H<sub>2</sub>O, b 68°, Store in a brown bottle and the clear colourless liquid remains thus for extended periods. [Org Synth 28 1 1948; J Am Chem Soc 69 3093 1947.] The red 4-nitrophenylhydrazone crysts from EtOH, m 181-182°.

**3-Acetylthiophene** (methyl 3-thienyl ketone) [1468-83-3] M 126.2, m 57°, 60-63°, b 106-107°/25 mm, 208-210°/748mm. Recrystd from pet ether (b 30-60°) or EtOH. 2, 4dinitrophenylhydrazone crystallises from CHCl<sub>3</sub>, m 265°, and the semicarbazone crystallises from EtOH, m 174-175°. [J Am Chem Soc 70 1555 1948.]

**N-Acetylthiourea** [591-08-2] **M 118.2, m 164-165°, 165-168°**. Recrystd from AcOH, the solid is washed with  $Et_2O$  and dried in air then at 100°. [Collect Czech Chem Commun 24 3678 1959.]

Acetyl p-toluenesulfonate [26908-82-7] M 214.2, m 54-56°. The most likely impurity is p-toluenesulfonic acid (could be up to 10%). This can be removed by dissolving in dry  $Et_2O$  and cooling until the anhydride crystallises out. It decomp on heating; below ~130° it gives the disulfonic anhydride and above ~130° polymers are formed. It is used for cleaving ethers [Prep, IR, NMR: Karger and Mazur J Org Chem 36 528, 532 1971].

1-O-Acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose [6974-32-9] M 504.5, m 128-130°, 130-131°, 131-132°,  $[\alpha]_D^{20}$  +44.2° (c 1, CHCl<sub>3</sub>). Recrystd from EtOH or isoPrOH. [Helv Chim Acta 42 1171 1959; NMR: J Org Chem 33 1799 1968; IR: Chem Pharm Bull Jpn 11 188 1963.]

*N*-Acetyltryptophan M 246.3, [87-32-1] m 206° (RS),  $pK_{Est} \sim 3.8$ ; [1218-34-4] m 188° (S),  $[\alpha]^{25}$  +30.1° (aq NaOH). Likely impurity is tryptophan. Crystd from EtOH by adding water.

N-Acetyl-L-valine amide [37933-88-3] M 158.2, m 275°. Recrystd from CH<sub>3</sub>OH/Et<sub>2</sub>O.

cis-Aconitic acid [585-84-2] M 174.1, m 126-129°(dec). Crystd from water by cooling (sol: 1g in 2mL of water at 25°). Dried in a vacuum desiccator.

trans-Aconitic acid (1,2,3-propenetriscarboxylic acid) [4023-65-8] M 174.1, m 195°(dec), m 198-199°(dec), 204-205°(dec),  $pK_1^{25}$  2.81,  $pK_2^{25}$  4.46. Purified by dissolving in AcOH (77g/150mL), filtering and cooling. The acid separates (55g) as colourless needles. A further quantity (10g) can be obtained by reducing the vol of the filtrate. The acid is dried in air then in a vacuum desiccator over NaOH. The acid can be recrystd from Me<sub>2</sub>CO-CHCl<sub>3</sub>. The highest **m** is obtained with the very dry acid. The **m** (209°) is obtained on a Dennis bar [J Am Chem Soc 52 3128 1930, Org Synth Coll Vol II 12 1943].

cis-Aconitic anhydride [6318-55-4] M 156.1, m 75°, 76-78°, 78-78.5°. Reflux in xylene (7.5 parts) for 1h, then evaporate and recrystallise the residue from  $*C_6H_6$ . Alternatively, reflux in Ac<sub>2</sub>O, evaporate and recrystallise from  $*C_6H_6$ . It is sensitive to moisture. [IR: Acta Chem Scand 21 291 1967, Chem Ber 61 2523 1928; NMR: Biochemistry 5 2335 1966.]

Aconitine [302-27-2] M 645.8, m 204°,  $[\alpha]_{546}$  +20° (c 1, CHCl<sub>3</sub>), pK<sup>15</sup> 8.35. Crystd from EtOH, CHCl<sub>3</sub> or toluene.

Aconitine hydrobromide [6034-57-7] M 726.7, m 207°. Crystd from water or EtOH/ether.

Acridine (2,3-benzoquinoline) [260-94-6] M 179.2, m 111<sup>o</sup> (sublimes), b 346<sup>o</sup>, pK 5.58 (pK<sup>25</sup> of excited state 10.65). Crystd twice from \*benzene/cyclohexane, or from aqueous EtOH, then sublimed, removing and discarding the first 25% of the sublimate. The remainder was again crystd and sublimed, discarding the first 10-15% [Wolf and Anderson J Am Chem Soc 77 1608 1955].

Acridine can also be purified by crystn from *n*-heptane and then from ethanol/water after pre-treatment with activated charcoal, or by chromatography on alumina with pet ether in a darkened room. Alternatively, acridine can be ppted as the hydrochloride from \*benzene soln by adding HCl, after which the base is regenerated, dried at  $110^{\circ}/50$ mm, and crystd to constant melting point from pet ether [Cumper, Ginman and Vogel J Chem Soc 4518 1962]. The regenerated free base may be recrystd, chromatographed on basic alumina, then vac-sublimed and zone-refined. [Williams and Clarke, J Chem Soc, Faraday Trans 1 73 514 1977; Albert, The Acridines

Arnold Press 1966]. It can exists in five crystalline forms and is steam volatile. It is a strong IRRITANT to skin and mucous membranes and can become a chronic irritant— handle with CARE.

Acridine Orange [494-38-2] M 349.94, m 181-182° (free base). The double salt with  $ZnCl_2$  (6g) was dissolved in water (200mL) and stirred with four successive portions (12g each) of Dowex-50 ion-exchange resin (K<sup>+</sup> form) to remove the zinc. The soln was then concentrated in vacuum to 20mL, and 100mL of ethanol was added to ppte KCl which was removed. Ether (160mL) was added to the soln from which, on chilling, the dye crystallises as its chloride. It was separated by centrifuging, washed with chilled ethanol and ether, and dried under vac, before being recryst from ethanol (100mL) by adding ether (50mL), and chilling. Yield 1g. [Pal and Schubert J Am Chem Soc 84 4384 1962].

It was recrystd twice as the free base from ethanol or methanol/water by dropwise addition of NaOH (less than 0.1M). The ppte was washed with water and dried under vacuum. It was dissolved in CHCl<sub>3</sub> and chromatographed on alumina: the main sharp band was collected, concentrated and cooled to  $-20^{\circ}$ . The ppte was filtered, dried in air, then dried for 2h under vacuum at  $70^{\circ}$ . [Stone and Bradley J Am Chem Soc 83 3627 1961; Blauer and Linschitz J Phys Chem 66 453 1962.]

Acridine Yellow G [135-49-9] M 273.8, m 325°, CI 46025. Crystd from 1:1 \*benzene/methanol.

Acridone [578-95-0] M 195.2, m >300°, pK<sub>1</sub>-0.32 (basic), pK<sub>2</sub>14 (acidic). Dissolve ~1g in ca 1% NaOH (100mL), add 3M HCl to pH 4 when acridone separates as a pale yellow solid with m just above 350° (sharp). It can be recrystd from large vols of H<sub>2</sub>O to give a few mg. It is soluble in 160 parts of boiling EtOH (540 parts at 22°) [J Chem Soc 1294 1956]. A few decigms are best crystallised as the hydrochloride from 400 parts of 10N HCl (90% recovery) from which the free base is obtained by washing the salt with H<sub>2</sub>O. A small quantity can be recrystd (as the neutral species) from boiling AcOH. Larger quantities are best recrystallised from a mixture of 5 parts of freshly distd aniline and 12.5 parts of glacial acetic acid. Acridone distils unchanged at atmospheric pressure, but the boiling point was not recorded, and some sublimation occurs below 350°. It has UV:  $\lambda_{max}$  399nm. [see Albert, The Acridines Arnold Press pp. 201, 372 1966.]

*N*-(9-Acridinyl)maleimide (NAM) [49759-20-8] M 274.3, m 248°, 255-258°. Purified by chromatography on silica gel using CH<sub>2</sub>Cl<sub>2</sub> as eluant. Evaporation of pooled fractions that gave the correct NMR spectra gave a solid which was recrystd from Me<sub>2</sub>CO as pale yellow prisms. IR v (nujol): 1710 (imide); UV (MeOH):  $\lambda_{max}$  (nm), ( $\epsilon$  M<sup>-1</sup>cm<sup>-1</sup>): 251 (159 500), 343 shoulder (7 700), 360 (12 400) and 382shoulder (47 000). [*Chem Pharm Bull Jpn* 26 596 1978; *Eur J Biochem* 25 64 1972.]

Acriflavine [8048-52-0] M 196.2, pK >12. Treated twice with freshly ppted AgOH to remove proflavine, then recrystd from absolute methanol [Wen and Hsu J Phys Chem 66 1353 1962].

Acriflavin Mixture (Euflavin, 3,6-diamino-10-methylacridinium chloride) [8063-24-9] M 259.7, m 179-181°. Purified by dissolving in 50 parts of H<sub>2</sub>O, shake with a small excess of freshly ppted and washed Ag<sub>2</sub>O. The mixture is set aside overnight at 0° and filtered. The cake is not washed. The pH of the filtrate is adjusted to 7.0 with HCl and evaporated to dryness. The residue is then crystd twice from MeOH, twice from H<sub>2</sub>O and dried at  $120^{\circ}$ .  $\lambda_{max}$  at 452nm has a loge value of 4.67. It is a red powder which readily absorbs H<sub>2</sub>O. The solubility is increased in the presence of proflavin. The *dihydrochloride* is a deep red crystn powder. It is available as a mixture of 3,6-diaminoacridinium chloride (35%) and its 10-metho-chloride (65%). [see Albert, *The Acridines* Arnold Press p. 346 1966; *Chem Ber* 45 1787 1912].

Acrolein (acraldehyde) [107-02-8] M 56.1, b 52.1°, n 1.3992, d 0.839. Purified by fractional distn. under nitrogen, drying with anhydrous CaSO<sub>4</sub> and then distilling under vac. Blacet, Young and Roof [J Am Chem Soc 59 608 1937] distd under nitrogen through a 90cm column packed with glass rings. To avoid formation of diacryl, the vapour was passed through an ice-cooled condenser into a receiver cooled in an ice-salt mixture and containing 0.5g catechol. The acrolein was then distd twice from anhydrous CuSO<sub>4</sub> at low pressure, catechol being placed in the distilling flask and the receiver to avoid polymerization. [Alternatively, hydroquinone (1% of the final soln) can be used.]

Acrolein diacetyl acetal (1,1-diacetoxy-2-propene). [869-29-4] M 158.2, b 75°/10mm, 184°/atm,  $d_4^{20}$  1.08,  $n_D^{20}$  1.4203. Check the NMR spectrum. If it is not satisfactory then add Ac<sub>2</sub>O and a drop of conc H<sub>2</sub>SO<sub>4</sub> and heat at 50° for 10min. Then add anhydrous NaOAc (*ca* 3g/ 100g of liquid) and fractionate. Note that it forms an azeotrope with H<sub>2</sub>O, so do not add H<sub>2</sub>O at any time. It is a highly flammable and TOXIC liquid, keep away from the skin. [J Am Chem Soc 73 5282 1951.]

Acrolein diethyl acetal [3054-95-3] M 130.2, b 120-125°/atm,  $n_4^{20}$  1.398-1.407. Add Na<sub>2</sub>CO<sub>3</sub> (*ca* 3.5%) and distil using an efficient column, or better a spinning band column. [*Org Synth* 25 1 1945.]

Acrolein dimethyl acetal (1,1-dimethoxy-2-propene) [6044-68-4] M 102.1, b 87.5-88°/750mm, 89-90°/760mm,  $d_4^{20}$  0.86,  $n_D^{20}$  1.3962. Fractionally distil (after adding 0.5g of hydroquinone) under reduced press through an all glass column (40cm x 2.5 cm) packed with glass helices and provided with a heated jacket and a total reflux variable take-off head. Stainless steel Lessing rings (1/8 x 1/8 in) or gauze have been used as packing. It is a highly flammable and TOXIC liquid, keep away from the skin. [J Chem Soc 2657 1955.]

Acrolein semicarbazone [6055-71-6] M 113.1, m 171°. Crystd from water.

Acrylamide [79-06-1] M 71.1, m 84°, b 125°/25mm. Crystd from acetone, chloroform, ethyl acetate, methanol or \*benzene/chloroform mixture, then vac dried and kept in the dark under vac. Recryst from CHCl<sub>3</sub> (200g dissolved in 1L heated to boiling and filtered without suction in a warmed funnel through Whatman 541 filter paper. Allowed to cool to room temp and kept at -15° overnight). Crystals were collected with suction in a cooled funnel and washed with 300mL of cold MeOH. Crystals were air-dried in a warm oven. [Dawson et al. Data for Biochemical Research, Oxford Press 1986 p. 449.]

**CAUTION**: Acrylamide is extremely **TOXIC** and precautions must be taken to avoid skin contact or inhalation. Use gloves and handle in a well ventilated fume cupboard.

Acrylic acid [79-10-7] M 72.1, m 13°, b 30°/3mm, d 1.051, pK<sup>25</sup> 4.25. Can be purified by steam distn, or vacuum distn through a column packed with copper gauze to inhibit polymerisation. (This treatment also removes inhibitors such as methylene blue that may be present.) Azeotropic distn of the water with \*benzene converts aqueous acrylic acid to the anhydrous material.

Acrylonitrile [107-13-1] M 53.1, b 78°, d 0.806,  $n^{25}$  1.3886. Washed with dilute H<sub>2</sub>SO<sub>4</sub> or dilute H<sub>3</sub>PO<sub>4</sub>, then with dilute Na<sub>2</sub>CO<sub>3</sub> and water. Dried with Na<sub>2</sub>SO<sub>4</sub>, CaCl<sub>2</sub> or (better) by shaking with molecular sieves. Fractionally distd under nitrogen. Can be stabilised by adding 10ppm *tert*-butyl catechol. Immediately before use, the stabilizer can be removed by passage through a column of activated alumina (or by washing with 1% NaOH soln if traces of water are permissible in the final material), followed by distn. Alternatively, shaken with 10% (w/v) NaOH to extract inhibitor, and then washed in turn with 10% H<sub>2</sub>SO<sub>4</sub>, 20% Na<sub>2</sub>CO<sub>3</sub> and distd water. Dried for 24h over CaCl<sub>2</sub> and fractionally distd under N<sub>2</sub> taking the fraction boiling at 75.0 to 75.5°C (at 734mm Hg). Stored with 10ppm *tert*-butyl catechol. Acrylonitrile is distilled off as required. [Burton *et al*, J Chem Soc, Faraday Trans 1 75 1050 1979.]

Acryloyl chloride [814-68-6] M 90.5, b 72-74°/740mm, 74°/760mm,  $d_4^{20}$  1.1127,  $n_D^{20}$  1.4337. Distil rapidly through an efficient 25cm column after adding 0.5g of hydroquinone/200g of chloride, and then redistil carefully at atmospheric pressure preferably in a stream of dry N<sub>2</sub>. [J Am Chem Soc 72 72, 2299 1950.] The liquid is an irritant and is TOXIC.

Actarit (p-acetamidophenylacetic acid) [18699-02-0] M 193.2, m 174-175°. Crystd from MeOH + Me<sub>2</sub>CO or aq EtOH.

Adamantane [281-23-2] M 136.2, m 269.6-270.8° (sublimes). Crystd from acetone or cyclohexane, sublimed in a vacuum below its melting point. [Butler et al. J Chem Soc, Faraday Trans 1 82 535 1986.] Adamantane was also purified by dissolving in *n*-heptane (ca 10mL/g of adamantane) on a hot plate, adding activated charcoal (2g/100g of adamantane), and boiling for 30min, filtering the hot soln through a filter paper, concentrating the filtrate until crystn just starts, adding one quarter of the original volume *n*-heptane and

allowing to cool slowly over a period of hours. The supernatant was decanted off and the crystals were dried on a vacuum line at room temperature. [Walter et al. J Am Chem Soc 107 793 1985.]

1-Adamantane acetic acid [4942-47-6] M 194.3, m 136°, pK<sub>Est</sub> ~4.8. Dissolve in hot N NaOH, treat with charcoal, filter and acidify. Collect solid, wash with H<sub>2</sub>O, dry and recryst from MeOH. [Chem Ber 92 1629 1959.]

1-Adamantane carboxylic acid [828-51-3] M 180.3, m 175-176.5°, 177°, pK<sub>Est</sub> ~4.9. Possible impurities are trimethylacetic acid and C9 and C13 acids. Dissolve 15g of acid in CCl<sub>4</sub> (300mL) and shake with 110mL of 15N aqueous NH<sub>3</sub> and the ammonium salt separates and is collected. Acid impurities form soluble ammonium salts. The salt is washed with cold Me<sub>2</sub>CO (20mL) and suspended in H<sub>2</sub>O (250mL). This is treated with 12N HCl and extracted with CHCl<sub>3</sub> (100mL). The dried (Na<sub>2</sub>SO<sub>4</sub>) is evaporated and the residue recrystd from a mixture of MeOH (30mL) and H<sub>2</sub>O (*ca* 10mL) to give the pure acid (10-11g). [*Org Synth* Coll Vol.V 20 1973.] Also recrystd from absolute EtOH and dried under vacuum at 100°.

Alternatively, the acid (5g) is refluxed for 2h with 15mL of MeOH and 2mL of 98% H<sub>2</sub>SO<sub>4</sub> (cool when mixing this soln). Pour into 10 volumes of H<sub>2</sub>O and extract with the minimum volume of CHCl<sub>3</sub> to give clear separation of phases. The extract is washed with H<sub>2</sub>O and dried (CaCl<sub>2</sub>) and distd. The methyl ester is collected at 77-79°/1mm, m 38-39°. The ester is hydrolysed with the calculated amount of N KOH and refluxed until clear. Acidification with HCl provides the pure acid with 90% recovery. [Org Synth 4 1 1964.] The amide crysts from cyclohexane, m 189°. [Chem Ber 62 1629 1959.]

1,3-Adamantane diamine dihydrochloride [26562-81-2] M 239.2, m >310°,  $pK_{Est(1)} \sim 8.1$ ,  $pK_{Est(2)} \sim 10.1$ . Dissolve in boiling conc HCl (400mg in 15mL) and evaporate to dryness. Dissolve in absolute EtOH and add dry Et<sub>2</sub>O to crystallise the *dihydrochloride*. [Chem Ber 93 1366 1960.]

1,3-Adamantane dicarboxylic acid [39269-10-8] M 224.3, m 276°, 276-278°, 279°, pK<sub>Est(1)</sub> ~4.9. pK<sub>Est(2)</sub> 5.9. Dissolve in aq NaOH, treat with charcoal, filter and acidify with dilute HCl. Recryst from MeOH. [*Chem Ber* 93 1366 1960.]

**1-Adamantane methylamine** [17768-41-1] M 165.3, b 83-85°/0.3mm,  $d_4^{20}$  0.93, pK<sub>Est</sub> ~10.2. Dissolve in Et<sub>2</sub>O, dry over KOH and distil. The *N*-Tosyl derivative has m 134-135° (from EtOH). [Chem Ber 96 550 1963.]

**1-Adamantanol** (1-hydroxyadamantane) [768-95-6] M 152.4, m 288.5-290°. If 2-adamantanol is a suspected impurity then dissolve substance (10g) in acetone (100mL) and Jones's reagent { $CrO_3$  (10.3g) in H<sub>2</sub>O (30mL)} and conc H<sub>2</sub>SO<sub>4</sub> (8.7mL) is added dropwise (turns green in colour) until excess reagent is present (slight red colour). Allow to stir overnight, decant the acetone soln from the Cr salts and adamantan-2-one, and dry (Na<sub>2</sub>SO<sub>4</sub>) and evaporate to dryness. The residue (*ca* 7g) is chromatographed through Al<sub>2</sub>O<sub>3</sub> (250g) and washed with 50% \*benzene-pet ether (b 40-60°), then 100% Et<sub>2</sub>O (to remove any adamantan-2-one present) and the 1-adamantanol is then eluted with 5% MeOH in Et<sub>2</sub>O. The eluate is evaporated, and the residue is recrystd from pet ether (b 30-60°) at -70°, m 287.2-288.5°. It has characteristic IR, v 3640, 1114, 1086, 982 and 930cm<sup>-1</sup>. [J Am Chem Soc 83 182 1961.]

Alternatively, if free from the 2-isomer, dissolve in tetrahydrofuran, dilute with  $H_2O$  to ppte the alcohol. Collect, dry and sublime in a vacuum at 130°. [*Chem Ber* 92 1629 1959.]

**2-Adamantanol** (2-hydroxyadamantane) [700-57-2] M 152.4, m 296.2-297.7°. Can be purified by chromatography as for the 1-isomer. It crystallises from cyclohexane and has characteristic IR, v 3600, 1053, 1029 and 992cm<sup>-1</sup> [J Am Chem Soc 8 182 1961].

2-Adamantanone [700-58-3] M 150.2, m 256-258°(sublimes). Purified by repeated sublimation in vacuo. [Butler et al. J Chem Soc, Faraday Trans 1 82 535 1986.]

N-(1-Adamantyl)acetamide [880-52-4] M 193.3, m 149°. Wash well with H<sub>2</sub>O, dry and recrystallise from cyclohexane. It is an irritant. [Chem Ber 92 1629 1959.]

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**1-Adamantylamine** [768-94-5] **M 151.2, m 160-190°, 208-210°, pK<sup>25</sup> 10.58.** Dissolve in Et<sub>2</sub>O, dry over KOH, evaporate and sublime in a vacuum. [*Chem Ber* **93** 226 1960.]

1-Adamantylamine hydrochloride [665-66-7] M 187.7, m 360° (dec). Dissolve in dry EtOH, add a few drops of dry EtOH saturated with HCl gas, followed by dry Et<sub>2</sub>O to crystallise the hydrochloride. Dry the salt in vacuum. [Chem Ber 93 226 1960.]

**2-Adamantylamine hydrochloride** [10523-68-9] **M 187.7, m >300°, pK**<sub>Est</sub> ~10.4. The free amine in Et<sub>2</sub>O, liberated by the action of alkali in H<sub>2</sub>O, is dried over KOH, filtered, evap and sublimed at 110°/12Torr, m 230-236°. The base is dissolved in EtOH and crystd by the addition of Et<sub>2</sub>O, and dried in vac. [Justus Liebigs Ann Chem 658 151 1962].

**1-Adamantyl bromide** [768-90-1] M **215.1, m 117-119°, 118°, 119.5-120°.** If coloured, dissolve in CCl<sub>4</sub>, wash with H<sub>2</sub>O, treat with charcoal, dry (CaCl<sub>2</sub>), filter, evap to dryness. Dissolve in a small volume of MeOH and cool in a CO<sub>2</sub>/trichloroethylene bath and collect the crystals. Sublime at 90-100°/water pump vacuum. [Chem Ber **92** 1629 1959; J Am Chem Soc **83** 2700 1961.]

1-Adamantyl bromomethylketone [5122-82-7] M 257.2, m 76-79°, 78-79°. Dissolve in  $Et_2O$ , wash with  $H_2O$ , dry (MgSO<sub>4</sub>), evaporate and crystallise residue from small volumes of MeOH. LACHRYMATORY. [Chem Ber 93 2054 1960.]

**1-Adamantyl chloride** [935-56-8] **M 170.7, m 164.3-165.6°.** Crystd from aqueous MeOH and sublimed at 100°/12Torr. Also crystd from MeOH at -70°. [Chem Ber 92 1629 1959; J Am Chem Soc 83 2700 1961.]

1-Adamantyl fluoride (1-fluoroadamantane) [768-92-3] M 154.2, m 210-212° (dec), 259-260° (dec). Dissolve in Et<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, evaporate to dryness and sublime the residue at 90-100°/12mm. Recryst sublimate from MeOH, m 259-260°. [*Zh Org Khim* 30 1609 1965.] To remove 1-hydroxyadamantane impurity, dissolve in cyclohexane cool for many hours, filter off the hydroxyadamantane, and evaporate to dryness. Recrystallise the residue from pet ether at -77° and sublime in vacuum, m 210-212° dec (sealed tube). [*J Org Chem* 30 789 1965.]

**1-Adamantyl fluoroformate** [62087-82-5] M **198.2, m 31-32°.** Dissolve in *n*-hexane (*ca* 10g in 150 mL) and keep at 0° for 24h. Any 1-adamantanol present will separate. Filter and evaporate to dryness. Crystalline residue has m 31-32° (v 1242, 1824 and 2340 cm<sup>-1</sup>). There should be no OH str band above 2500 cm<sup>-1</sup>. [Z Phys Chem **357** 1647 1976; Haas et al. J Am Chem Soc **88** 1988 1966.]

**1-Adamantyl iodide (1-iodoadamantane)** [768-93-4] M 262.1, m 75.3-76.4°. Dissolve in Et<sub>2</sub>O, shake with aqueous NaHSO<sub>3</sub>, aqueous K<sub>2</sub>CO<sub>3</sub>, and H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and recrystallise from MeOH at -70° (to avoid alcoholysis) giving white crystals. [J Am Chem Soc 83 2700 1961; lit m of 151-152.5° is incorrect.] Also purified by recrystn from pet ether (40-60°C) followed by rigorous drying and repeated sublimation.

**1-Adamantyl isocyanate** [4411-25-0] M 177.3, m 144-145°. Recryst from *n*-hexane and sublime. Irritant. [Chem Ber 95 2302 1962.]

**1-Adamantyl isothiocyanate** [4411-26-1] M 193.3, m 168-169°. Dissolve in  $Et_2O$ , wash with  $H_2O$ , dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and sublime the residue in a vacuum at 140°, and recryst from MeOH. Irritant. [*Chem Ber* 95 2302 1962.]

N-(1-Adamantyl)urea [13072-69-0] M 194.2, m >250° (dec), 268-272° (dec). Wash with H<sub>2</sub>O and dioxane and recryst from EtOH. [Chem Ber 95 2302 1962.]

Adenine [73-24-5] M 135.1, m 360-365° (dec rapid heating),  $pK_1^{25}$  4.12,  $pK_2^{25}$  9.83. Crystd from distd water.

Adenosine [58-61-7] M 267.3, m 234-236°,  $[\alpha]_{546}$  -85° (c 2, 5% NaOH),  $pK_1^{25}$  3.48,  $pK_2^{25}$  12.5. Crystd from distilled water.

Adipic acid [124-04-9] M 146.1, m 154°,  $pK_1^{25}$  4.44,  $pK_2^{25}$  5.45. For use as a volumetric standard, adipic acid was crystd once from hot water with the addition of a little animal charcoal, dried at 120° for 2h, then recrystd from acetone and again dried at 120° for 2h. Other purification procedures include crystn from ethyl acetate and from acetone/petroleum ether, fusion followed by filtration and crystn from the melt, and preliminary distn under vac.

Adiponitrile (1,4-dicyanobutane) [111-69-3] M 108.14, m 2.4°, b 123°/0.5mm, 153°/6mm, 175°/26mm, 184°/30mm, 295°/atm,  $d_4^{20}$  0.9396,  $n_D^{20}$  1.4371. Reflux over P<sub>2</sub>O<sub>5</sub> and POCl<sub>3</sub>, and fractionally distil, then fractionate through an efficient column. The liquid is TOXIC and is an IRRITANT. [Chem Ber 67 1770 1934; Justus Liebigs Ann Chem 596 127 1955; Can J Chem 34 1662 1956; J Am Chem Soc 62 228 1940.]

Adonitol (Ribitol) [488-81-3] M 152.2, m 102°. Crystallise from EtOH by addition of diethyl ether.

## Adrenalin see epinephrine.

Adrenochrome [54-06-8] M 179.2, m 125-130°. Crystd from MeOH/formic acid, as hemihydrate, and stored in a vacuum desiccator.

Adrenosterone (Reichstein's G) [382-45-6] M 300.4, m 220-224°. Crystd from EtOH. Can be sublimed under high vacuum.

Agaricic acid [1-(*n*-hexadecyl)citric acid] [666-99-9] M 416.6, m 142°(dec),  $[\alpha]_D$  -9.8° (in NaOH), pK<sub>Est(1)</sub> ~2.7, pK<sub>Est(2)</sub> ~4.2, pK<sub>Est(3)</sub> ~5.5. Crystd from EtOH.

Agmatine sulfate [5-guanidinopent-1-ylamine sulfate] [2482-00-0] M 228.3, m 231°, pK<sub>Est(1)</sub> ~9.1, pK<sub>Est(2)</sub> ~13.0. Crystd from aqueous MeOH.

Agroclavin [548-42-5] M 238.3, m 198-203°(dec), 205-206°,  $[\alpha]_D^{20}$ -155° (c 1, CHCl<sub>3</sub>), pK<sub>Est</sub> ~8.0. Crystd from diethyl ether.

Ajmalicine [483-04-5] M 352.4, m 250-252°(dec), [α]<sub>546</sub> -76° (c 0.5, CHCl<sub>3</sub>), pK<sub>Est</sub> ~7.4. Crystd from MeOH.

Ajmalicine hydrochloride [4373-34-6] M 388.9, m 290°(dec),  $[\alpha]_D$  -17° (c 0.5, MeOH). Crystd from EtOH.

Ajmaline [ $\gamma$ -yohimbine] [4360-12-7] M 326.4, m 160° (MeOH), 205-206° (anhyd),  $[\alpha]_D^{20}$  +144° (c 0.8, CHCl<sub>3</sub>), pK<sub>Est</sub> ~7.5. Crystd from MeOH.

Ajmaline hydrochloride [4410-48-4] M 388.9, m 140°. Crystd from water.

Alanine (RS) [302-72-7] M 89.1, m 295-296°, (S) [56-41-7] m 297°(dec),  $[\alpha]_D^{15}$  +14.7° (in 1M HCl), pK<sub>1</sub><sup>25</sup> 2.34, pK<sub>2</sub><sup>25</sup> 9.87. Crystd from water or aqueous EtOH, e.g. crystd from 25% EtOH in water, recrystd from 62.5% EtOH, washed with EtOH and dried to constant weight in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. [Gutter and Kegeles J Am Chem Soc 75 3893 1953.] 2,2'-Iminodipropionic acid is a likely impurity.

**B-Alanine** [107-95-9] M 89.1, m 205°(dec),  $pK_1^{25}$  3.55,  $pK_2^{25}$  10.24. Crystd from filtered hot saturated aqueous soln by adding four volumes of absolute EtOH and cooling in an ice-bath. Recrystd in the same way and then finally, crystd from a warm saturated soln in 50% EtOH by adding four volumes of absolute

EtOH cooled in an ice bath. Crystals were dried in a vacuum desiccator over  $P_2O_5$ . [Donovan and Kegeles J Am Chem Soc 83 255 1961.]

S-Alaninol [S-2-Aminopropan-1-ol] [2749-11-3] M 75.1, b 167-169°/760mm,  $d_4^{20}$  0.961,  $n_D^{20}$  1.456, [ $\alpha$ ]<sub>546</sub> + 26.0° (c 2, EtOH), pK<sup>25</sup> 9.43. Purification as for S-2-amino-3-methylbutan-1-ol

Aldol (3-hydroxybutanal) [107-89-1] M 88.1, b 80-81°/20mm. An ethereal soln was washed with a saturated aqueous soln of NaHCO<sub>3</sub>, then with water. The non-aqueous layer was dried with anhydrous CaCl<sub>2</sub> and distd immediately before use. The fraction, b 80-81°/20mm, was collected, [Mason, Wade and Pouncy J Am Chem Soc 76 2255 1954].

Aldosterone [52-39-1] M 360.5, m 108-112°(hydrate), 164°(anhydr),  $[\alpha]_{D}^{25} + 161°$  (c 1, CHCl<sub>3</sub>). Crystd from aqueous acetone. Acetate, cryst from Me<sub>2</sub>CO + Et<sub>2</sub>O, has m 198-199°,  $[\alpha]_{D}^{24}$  +121.7° (c 0.7, CHCl<sub>3</sub>)

Aldrin [309-00-2] M 354.9, m 103-104.5°. Crystd from MeOH. POISONOUS

Aleuritic acid [RS-erythro-9,10,16-trihydroxyhexadecanoic acid] [533-87-9] M 304.4, m 100-101°. Crystd from aqueous EtOH. Hydrazide cryst from EtOH has m 139-140°.

Alginic acid [9005-32-7] M 48,000-186000. To 5g in 550mL water containing 2.8g KHCO<sub>3</sub>, were added 0.3mL acetic acid and 5g potassium acetate. EtOH to make the soln 25% (v/v) in EtOH was added and any insoluble material was discarded. Further addition of EtOH, to 37% (v/v), ppted alginic acid. [Pal and Schubert J Am Chem Soc 84 4384 1962.]

Aliquat 336 (methyltricaprylylammonium chloride, tri-*n*-octylmethylammonium chloride) [5137-55-3] M 404.2, d 0.884. A 30% (v/v) soln in \*benzene was washed twice with an equal volume of 1.5M HBr. [Petrow and Allen, Anal Chem 33 1303 1961.] Purified by dissolving 50g in CHCl<sub>3</sub> (100mL) and shaking with 20% NaOH soln (200mL) for 10min, and then with 20% NaCl (200mL) for 10min. Washed with small amount of H<sub>2</sub>O and filtered through a dry filter paper [Adam and Pribil Talanta 18 733 1971].

Alizarin (1,2-dihydroxyanthraquinone) [72-48-0] M 240.2, m 290°, d 0.884,  $pK_1^{25}$  7.45,  $pK_2^{25}$  11.80. Crystd from glacial acetic acid or 95% EtOH. Can also be sublimed at 110°/2mm.

Alizarin-3-methyliminodiacetic acid (Alizarin Complexone)  $(2H_2O)$  [3952-78-1] M 421.4, m 189°(dec), pK<sub>Est(1)</sub>~4.9, pK<sub>Est(2)</sub>~7.5. Purified by suspending in 0.1M NaOH (1g in 50mL), filtering the solution and extracting alizarin with 5 successive portions of CH<sub>2</sub>Cl<sub>2</sub>. Then add HCl dropwise to precipitate the reagent, stirring the solution in a bath. Filter ppte on glass filter, wash with cold water and dry in a vacuum desiccator over KOH [Ingman *Talanta* 20 135 1973].

Alizarin Yellow R [5-(4-nitrophenylazosalicylic acid), Mordant Orange I] [2243-76-7] M 287-2, m 253-254°(dec), >300°, pK<sup>25</sup> 11.17. The free acid is ppted by adding HCl to an aq soln of the Na salt. After 2 recrystns from aq AcOH, it has m 255°(dec); [m 253-254° dec was reported J Chem Soc 79 49 1901]. The free acid can be recrystd from dilute AcOH as orange brown needles. The Na salt changes colour from yellow to red when the pH is increased from 10.2 to 12.0. [J Am Chem Soc 75 5838 1953.]

**n-Alkylammonium chloride n=2,4,6**. Recrystd from EtOH or an EtOH/Et<sub>2</sub>O mixture. [Hashimoto and Thomas J Am Chem Soc 107 4655 1985; Chu and Thomas J Am Chem Soc 108 6270 1986.]

*n*-Alkyltrimethylammonium bromide n=10,12,16. Recrystd from an EtOH/Et<sub>2</sub>O mixture. [Hashimoto and Thomas J Am Chem Soc 107 4655 1985.]

Allantoin [97-59-6] M 158.1, m 238°(dec). Crystd from water or EtOH.

Allene (prodiene) [463-49-0] M 40.1, m -146°, b -32°. Frozen in liquid nitrogen, evacuated, then thawed out. This cycle was repeated several times, then the allene was frozen in a methyl cyclohexane-liquid nitrogen bath and pumped for some time. Also purified by HPLC. [Cripps and Kiefer Org Synth 42 12 1962.]

(-)-Alloaromadendrene [25246-27-9] M 204.4, b 96°/2mm, 265-267°/atm,  $[\alpha]_D^{25}$ -22° (neat),  $d_4^{20}$  0.923,  $n_D^{23}$  1.501. Fractionally distd from Na. IR has bands at 6.06 and 11.27µ due to C=CH<sub>2</sub>. [J Chem Soc 715 1953; cf J Am Chem Soc 91 6473 1969.]

*neo*-Allocimene (*tc*-2,6-dimethyl-2,4,6-octatriene) [7216-56-0] M 136.2, b 80°/13mm,196-198°/atm,  $d_4^{20}$  0.8161,  $n_D^{20}$  1.5437. Fractionally distd through an efficient column and stabilised with ca 0.1% of hydroquinone. UV:  $\lambda_{max}$  nm( $\epsilon$  M<sup>-1</sup>cm<sup>-1</sup>) 290 (32 500), 279 (41 900) and 270 (32 600). [Justus Liebigs Ann Chem 609 1 1957; Anal Chem 26 1726 1954.]

5 $\alpha$ -Allopregnane-3 $\alpha$ ,20 $\alpha$ -diol [566-58-5] M 320.5, m 248-248.5°, [ $\alpha$ ]<sub>D</sub>+17° (c 0.15, EtOH). Crystd from EtOH.

**D-Allothreonine** [2R, 3R(-)-isomer] [24830-94-2] M 119.1, m 272-273°(dec), 276°(dec),  $[\alpha]_D^{25}$ -9.1° (c 3.9, H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup> 2.11, pK<sub>2</sub><sup>25</sup> 9.10. Recrystd from aqueous EtOH or 50% EtOH. [J Chem Soc 62 1950; J Am Chem Soc 194 455 1952; IR: Greenstein & Winitz The Chemistry of the Amino Acids J. Wiley, Vol 3 1961.]

Alloxan [2,4,5,6(1H,3H]pyrimidine, tetrone] [50-71-5] M 142.0, m ~170°(dec), pK<sup>25</sup> 6.64. Crystn from water gives the tetrahydrate. Anhydrous crystals are obtained by crystn from acetone, glacial acetic acid or by sublimation *in vacuo*.

Alloxan monohydrate [2244-11-3] M 160.1, m 255°(dec), pK 6.64. Recryst from H<sub>2</sub>O as the *tetrahydrate* in large prisms or rhombs. On heating at 100°, or on exposure to air, this is converted to the *monohydrate*. Dissolve it in its own weight of boiling H<sub>2</sub>O and cool for several days below 0° [the *tetrahydrate* crystallises from soln much more slowly when free from HNO<sub>3</sub>. It is less sol in HCO<sub>3</sub> solns than in H<sub>2</sub>O]. Drying the solid over H<sub>2</sub>SO<sub>4</sub> yields the *monohydrate*. The *anhydrous* crystals can be obtained by recrystn from dry Me<sub>2</sub>CO or AcOH followed by washing with dry Et<sub>2</sub>O or by sublimation in a vacuum. On heating it turns pink at 230° and decomposes at *ca* 256°. It is acidic to litmus. [Org Synth Coll Vol III 37 1955.] It forms a compound with urea which crystallises from H<sub>2</sub>O in yellow needles that become red at 170° and dec at 185-186°.

Alloxantin [76-24-4] M 286.2, m 253-255°(dec) (yellow at 225°). Crystd from water or EtOH and kept under nitrogen. Turns red in air.

Allyl acetate [591-87-7] M 100.1, b 103°, d 0.928,  $n_4$  1.40488,  $n_D^{27}$  1.4004. Freed from peroxides by standing with crystalline ferrous ammonium sulfate, then washed with 5% NaHCO<sub>3</sub>, followed by saturated CaCl<sub>2</sub> soln. Dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd in an all-glass apparatus.

Allylacetic acid (pent-4-enoic acid) [591-80-0] M 100.1, m -22.5°, b 83-84°/12 mm, 90°/15mm,  $d_4^{20}$  0.9877,  $n_D^{20}$  1.4280, pK<sup>25</sup> 4.68. Distil through an efficient column (allyl alcohol has b 95-97°). It is characterised as the S-benzyl isothiouronium salt m 155-158° (96% EtOH, aq EtOH) [Acta Chem Scand 9 1425 1955], 4-bromophenacyl ester m 59.5-60.5° (from 90% EtOH). Solubility at 18°: in pyridine (57%), AcOH (7.3%), MeOH (5.4%), Me<sub>2</sub>CO (3.2%), MeOAc (2.8%), EtOH (5.4%), H<sub>2</sub>O (1.8%), PrOH (1.6%), isoPrOH (0.27%). [J Am Chem Soc 74 1894 1952.]

Allyl alcohol [107-18-6] M 58.1, b 98°, d<sub>4</sub> 0.857, n<sub>D</sub> 1.4134. Can be dried with  $K_2CO_3$  or CaSO<sub>4</sub>, or by azeotropic distn with \*benzene followed by distn under nitrogen. It is difficult to obtain peroxide free. Also reflux with magnesium and fractionally distd [Hands and Norman Ind Chem 21 307 1945].

Allylamine [107-11-9] M 57.1, b 52.9°, d 0.761, n 1.42051, pK<sup>25</sup> 9.49. Purified by fractional distn from calcium chloride. Causes sneezing and tears.

1-Allyl-6-amino-3-ethyluracil [642-44-4] M 195.2, m 143-144° (anhydr). Crystd from water (as monohydrate).

Allyl bromide [106-95-6] M 121, b 70°, d 1.398, n 1.46924. Washed with NaHCO<sub>3</sub>, soln then distd water, dried (CaCl<sub>2</sub> or MgSO<sub>4</sub>), and fractionally distd. Protect from strong light. LACHRYMATOR, HIGHLY TOXIC and FLAMMABLE.

Allyl butyl ether [3739-64-8] M 114.2, b 64-65°/120mm, 117.8-118°/763mm,  $d_4^{20}$  1.4057,  $n_D^{20}$  0.7829. Check the IR for the presence of OH str vibrations, if so then wash well with H<sub>2</sub>O, dry with CaCl<sub>2</sub> and distil through a good fractionating column. The liquid is an irritant. [J Org Chem 23 1666 1958; J Am Chem Soc 73 3528 1951.]

Allyl chloride [107-05-1] M 76.5, b 45.1°, d 0.939, n 1.4130. Likely impurities include 2chloropropene, propyl chloride, *i*-propyl chloride, 3,3-dichloropropane, 1,2-dichloropropane and 1,3dichloropropane. Purified by washing with conc HCl, then with Na<sub>2</sub>CO<sub>3</sub> soln, drying with CaCl<sub>2</sub>, and distn through an efficient column [Oae and Vanderwerf J Am Chem Soc 75 2724 1953]. LACHRYMATOR, TOXIC.

Allyl chloroformate [2937-50-0] M 120.5, b 56°/97mm, 109-110°/atm,  $d_4^{20}$  1.14,  $n_D^{20}$  1.4223. Wash several times with cold H<sub>2</sub>O to remove alcohol and HCl and dry over CaCl<sub>2</sub>. It is **important** to dry well before distilling *in vacuo*. Note that the receiver should be cooled in ice to avoid loss of distillate into the trap and vacuum pump. The liquid is **highly TOXIC and flammable**. [J Am Chem Soc 72 1254 1950.]

Allyl cyanide (3-butene nitrile) [109-75-1] M 67.1, b -19.6°/1.0mm, 2.9°/5 mm, 14.1°/5mm, 26.6°/20mm, 48.8°/60mm, 60.2°/100mm, 98°/400mm, 119°/760mm,  $d_4^{20}$ 0.8341, n  $_D$  1.406. It should be redistd at atmospheric pressure then distilled under a vacuum to remove final traces of HCN from the residue. Note that the residue from the first distiln may be difficult to remove from the flask and should be treated with conc HNO<sub>3</sub> then H<sub>2</sub>O and finally hot EtOH (CARE). Allyl cyanide has an onion-like odour and is stable to heat. It forms a complex with AlCl<sub>3</sub> (2:2) m 41°, and (3:2) m 120°. All operations should be done in an efficient fume hood as the liquid is flammable and HIGHLY TOXIC. [Org Synth Coll Vol I 46 1941.]

Allyl disulfide (diallyl disulfide) [2179-57-9] M 146.3, b 58-59°/5mm, 79-81°/20mm, 138-139°/atm,  $d_4^{20}$  1.01,  $n_D^{20}$  1.541. Purified by fractional distn until their molar refractivities are in uniformLy good agreement with the calculated values [*J Am Chem Soc* 69 1710 1947]. Also purified by gas chromatography [retention times: *J Org Chem* 24 175 1959; UV: *J Chem Soc* 395 1949].

 $RS-\alpha$ -Allylglycine (2-aminopent-4-enoic acid). [7685-44-1] M 115.1, m 250-255°(dec), pK<sub>Est(1)</sub> ~2.3, pK<sub>Est(2)</sub> ~9.6. Dissolve in absolute EtOH and ppte with pyridine, then recrystallise from aqueous EtOH [R<sub>F</sub> in BuOH:EtOH:NH<sub>3</sub>:H<sub>2</sub>O (4:4:1:1:) 0.37]. The hydrobromide has m 136-140° (from EtOAc) and the phenylureido derivative has m 159-161°. [Monatsh Chem 89 377 1958.]

1-N-Allyl-3-hydroxymorphinan [152-02-3] M 283.4, m 180-182°. Crystd from aqueous EtOH.

Allyl iodide (3-iodopropene) [556-56-9] M 167.7, b 103°,  $d^{12}$  1.848. Purified in a dark room by washing with aq Na<sub>2</sub>SO<sub>3</sub> to remove free iodine, then drying with MgSO<sub>4</sub> and distilling at 21mm pressure, to give a very pale yellow liquid. (This material, dissolved in hexane, was stored in a light-tight container at -5° for up to three months before free iodine could be detected, by its colour in the soln) [Sibbett and Noyes J Am Chem Soc 75 761 1953].

5-Allyl-5-isobutylbarbituric acid [77-26-9] M 224.3, m 139°, 139-140°, 140-142°, pK<sup>38</sup> 12.36. It can be recrystallised from H<sub>2</sub>O or dilute EtOH, and sublimes at 100-120°/8-12mm. It is soluble in  $*C_6H_6$ , cyclohexane, tetralin and pet ether at 20°. [J Am Chem Soc 77 1486 1955.]

Allylisocyanate [1476-23-9] M 83.1, b 84°/atm, 87-89°/atm,  $d_4^{20}$  0.94,  $n_D^{20}$  1.417. Purify as for allylisothiocyanate.

Allylisothiocyanate [57-06-7] M 99.2, m -80°, b 84-85°/80mm, 150°/760mm, 151°/atm,  $d_4^{20}$  1.017,  $n_D^{20}$  1.5268. Fractionate using an efficient column, preferably in a vacuum. It is a yellow pungent irritating and TOXIC (suspected CARCINOGEN) liquid. Store in a sealed tube under N<sub>2</sub>. The N'-benzylthiourea derivative has m 94.5° (from aq EtOH) [J Am Chem Soc 74 1104 1952].

Allyl Phenyl sulfide [5296-64-0] M 150.2, b 59-60°/1.5mm, 79-80°/3mm, 114-114.3°/23.5mm, 225-226°/740mm, 215-218°/750mm,  $d_4^{20}$  1.0275,  $n_D$  1.5760. Dissolve in Et<sub>2</sub>O, wash with alkali, H<sub>2</sub>O, dry over CaCl<sub>2</sub>, evaporate and fractionally distil, preferably under vacuum. It should not give a ppte with an alcoholic soln of Pb(OAc)<sub>2</sub>. [J Am Chem Soc 52 3356 1930, 74 48 1952.]

**N-Allylthiourea** (thiosinamine) [109-57-9] M 116.2, m 70-73°, 78°. Recrystd from H<sub>2</sub>O. Soluble in 30 parts of cold H<sub>2</sub>O, soluble in EtOH but insoluble in  $*C_6H_6$ . Also recrystd from acetone, EtOH or ethyl acetate, after decolorising with charcoal. The white crystals have a bitter taste with a slight garlic odour and are TOXIC. [Anal Chem 21 421 1949.]

N-Allylurea [557-11-9] M 100.1, m 85°. Crystd from EtOH, EtOH/ether, EtOH/chloroform or EtOH/toluene.

Aloin [10-glucopyranosyl-1,8-dihydroxy-3-(hydroxymethyl)-9(10H)anthracenone, Barbaloin] [8015-61-0] M 418.4, m 148-148.5°, 148-150°. Lemon yellow crystals from H<sub>2</sub>O (450g/1.5L) as the monohydrate which has a lower m (70-80°). [J Chem Soc 2573 1932, 3141 1956.]

D-Altrose [1990-29-0] M 180.2, m 103-105°, [a]546 +35° (c 7.6, H2O). Crystd fom aq EtOH.

Amberlite IRA-904 Anion exchange resin (Rohm and Haas) [9050-98-0]. Washed with 1M HCl, CH<sub>3</sub>OH (1:10) and then rinsed with distilled water until the washings were neutral to litmus paper. Finally extracted successively for 24h in a Soxhlet apparatus with MeOH, \*benzene and cyclohexane [Shue and Yan Anal Chem 53 2081 1981]. Strongly basic resin also used for base catalysis [Fieser & Fieser Reagents for Org Synth 1 511, Wiley 1967].

Aminoacetaldehyde dimethyl acetal (2,2-dimethoxyethylamine) [22483-09-6] M 105.1, m <-78°, b 139.5°/768mm, 137-139°/atm,  $d_4^{20}$  0.9676  $n_D^{20}$  1.4144. Dry over KOH pellets and distil through a 30cm vac jacketed Vigreux column. [J Am Chem Soc 75 3398 1953, 77 6640 1955.]

p-Aminoacetanilide [122-80-5] M 150.2, m 162-163°. Crystd from water.

Aminoacetic acid (Glycine) [56-40-6] M 75.1, m 262° (dec, goes brown at 226°, sublimes at 200°/0.1mm),  $pK_1^{25}$  2.35,  $pK_2^{25}$  9.78. Crystd from distilled water by dissolving at 90-95°, filtering, cooling to about -5°, and draining the crystals centrifugally. Alternatively, crystd from distilled water by addition of MeOH or EtOH (e.g. 50g dissolved in 100mL of warm water, and 400mL of MeOH added). The crystals can be washed with MeOH or EtOH, then with diethyl ether. Likely impurities are ammonium glycinate, iminodiacetic acid, nitrilotriacetic acid, ammonium chloride.

Aminoacetonitrile bisulfate [151-63-3] M 154.1, m 188°(dec) Crystd from aqueous EtOH.

Aminoacetonitrile hydrochloride [6011-14-9] M 92.5, m 166-167°, 172-174°, pK<sup>25</sup> 5.34. Recrystd from dil EtOH hygroscopic leaflets. Best to crystallise from absolute EtOH-Et<sub>2</sub>O (1:1) and then recryst from absolute EtOH. The m recorded range from 144° to 174°. The free base has b 58°/15mm with partial decomposition. [J Prakt Chem [2] 65 189 1902; J Am Chem Soc 56 2197 1934; J Chem Soc 1371 1947.]

**2-Aminoacetophenone hydrochloride** [5468-37-1] **M 171.6, m 188°(dec), 194°(dec), pK<sup>25</sup> 5.34.** Crystd from acetone/EtOH or 2-propanol [Castro J Am Chem Soc 108 4179 1986].

*m*-Aminoacetophenone [99-03-6] M 135.2, m 98-99°, pK<sup>25</sup> 3.56. Recrystd from EtOH.

*p*-Aminoacetophenone [99-92-3] M 135.2, m 104-106°, 105-107°, b 293°/atm, pK<sup>25</sup> 2.19 Recryst from CHCl<sub>3</sub>, \*C<sub>6</sub>H<sub>6</sub> or H<sub>2</sub>O. Soluble in hot H<sub>2</sub>O. UV (EtOH) has  $\lambda_{max}$  403nm (log  $\varepsilon$  4.42) [J Am Chem Soc 75 2720 1953]. [Anal Chem 26 726 1954.] The 2,4-dinitrophenylhydrazone has m 266-267° (from CHCl<sub>3</sub> or EtOH), and the semicarbazone has m 193-194°(dec)(from MeOH) and the hydrochloride has m 98°(dec)(from H<sub>2</sub>O).

 $\alpha$ -Amino acids see Chapter 6.

**9-Aminoacridine** [9-acridineamine] [90-45-9] M 194.2, m 241°, pK<sup>20</sup> 9.95. Crystd from EtOH or acetone and sublimes at 170-180°/0.04mm [Albert and Ritchie Org Synth Coll Vol III 53 1955; for hydrochloride see Chapter 6.]

*dl*-α-Aminoadipic acid (hydrate) [542-32-5] M 161.2, m 196-198°, pK<sub>Est(1)</sub> ~2.0, pK<sub>Est(2)</sub> ~4.5, pK<sub>Est(3)</sub> ~9.8. Crystd from water.

2-Amino-4-anilino-s-triazine [537-17-7] M 168.2, m 235-236°, pK<sub>Est</sub> ~5.5. Crystd from dioxane or 50% aqueous EtOH.

1-Aminoanthraquinone-2-carboxylic acid [82-24-6] M 276.2, m 295-296°. Crystd from nitrobenzene.

4-Aminoantipyrine [83-07-8] M 203.3, m 109°. Crystd from EtOH or EtOH/ether.

*p*-Aminoazobenzene (*p*-phenylazoaniline) [60-09-3] M 197.2, m 126°, pK<sup>25</sup> ~2.82. Crystd from EtOH, CCl<sub>4</sub>, pet ether/\*benzene, or a MeOH/water mixture.

o-Aminoazotoluene (Fast Garnet GBC base, 4'-amino-2,3'dimethylazobenzene) [97-56-3] M 225.3, m 101.4-102.6°, CI 11160, pK<sub>Est</sub> ~2.8. Crystd twice from EtOH, once from \*benzene, then dried in an Abderhalden drying apparatus [Cilento J Am Chem Soc 74 968 1952]. CARCINOGENIC.

2-Aminobenzaldehyde [529-23-7] M 121.1, m 39-40°, pK 20 1.36. Distd in steam and crystd from water or EtOH/ether.

2-Aminobenzaldehyde phenylhydrazone (Nitrin) [63363-93-9] M 211.3, m 227-229°. Crystd from acetone. [Knöpfer Monatsh Chem 31 97 1910.]

3-Aminobenzaldehyde [29159-23-7] M 121.1, m 28-30°, pKEst ~2.0. Crystd from ethyl acetate.

**4-Aminobenzamide hydrochloride** [59855-11-7] **M 199.6, m 284-285°, pK**<sub>Est</sub> ~1.7. Recrystd from EtOH.

*p*-Aminobenzeneazodimethylaniline [539-17-3] M 240.3, m 182-183°. Crystd from aqueous EtOH.

*o*-Aminobenzoic acid (anthranilic acid) [118-92-3] M 137.1, m 145°,  $pK_1^{25}$  2.94,  $pK_2^{25}$  4.72. Crystd from water (charcoal). Has also been crystd from 50% aqueous acetic acid. Can be vacuum sublimed.

*m*-Aminobenzoic acid [99-05-8] M 137.1, m 174°, pK<sub>1</sub><sup>25</sup> 3.29, pK<sub>2</sub><sup>25</sup> 5.10. Crystd from water.

*p*-Aminobenzoic acid [150-13-0] M 137.1, m 187-188°,  $pK_1^{25}$  2.45,  $pK_2^{25}$  4.85. Purified by dissolving in 4-5% aqueous HCl at 50-60°, decolorising with charcoal and carefully precipitating with 30% Na<sub>2</sub>CO<sub>3</sub> to pH 3.5-4 in the presence of ascorbic acid. It can be crystd from water, EtOH or EtOH/water mixtures.

*p*-Aminobenzonitrile [873-74-5] M 118.1, m 86-86.5°, 85-87°, pK  $^{25}$  1.74. Crystd from water, 5% aqueous EtOH or EtOH and dried over P<sub>2</sub>O<sub>5</sub> or dried *in vacuo* for 6h at 40°. [Moore et al. J Am Chem Soc 108 2257 1986; Edidin et al. J Am Chem Soc 109 3945 1987.]

4-Aminobenzophenone [1137-41-3] M 197.2, m 123-124°, pK<sup>25</sup>2.17. Dissolved in aq acetic acid, filtered and ppted with ammonia. Process repeated several times, then recrystd from aqueous EtOH.

2-Aminobenzothiazole [136-95-8] M 150.2, m 132°, pK 2° 4.48. Crystd from aqueous EtOH.

6-Aminobenzothiazole [533-30-2] M 150.2, m 87°, pK<sub>Est</sub> ~3. Crystd from aqueous EtOH.

*N*-(*p*-Aminobenzoyl)-L-glutamic acid [4271-30-1] M 266.3, m 173° (L-form),  $[\alpha]_{546}$  -17.5° (c 2, 0.1m HCl); 197° (DL), pK<sub>Est(1)</sub>~1.7, pK<sub>Est(2)</sub>~3.4, pK<sub>Est(3)</sub>~4.3. Crystd from H<sub>2</sub>O.

3-o-Aminobenzyl-4-methylthiazolium chloride hydrochloride [534-94-1] M 277.4, m 213°(dec). Crystd from aqueous EtOH.

4-Amino-1-benzylpiperidine [50541-93-0] M 190.3, b ~180°/20mm, d 0.933, n 1.543, pK<sub>Est(1)</sub>~ 8.3 pK<sub>Est(2)</sub>~ 10.4. Purified by distn *in vacuo*, and stored under N<sub>2</sub>, because it absorbs CO<sub>2</sub>. The *dihydrochloride salt* [1205-72-7] has m 270-273° (255°) after recrystn from MeOH + EtOAc or EtOH. [*J Chem Soc* 3165, 3172 1957.] The 4-methylamino-1-benzylpiperidine derivative has b 168-172°/17mm, n 1.5367 [*J Am Chem Soc* 70 4009 1948]. The 1-(1-benzyl-4-piperidinyl)-3-cyano-2-methylisothiourea derivative has m 160° from CHCl<sub>3</sub>/Et<sub>2</sub>O [Prepn, IR, NMR: Ried et al. *Chem Ber* 116 1547 1983].

o-Aminobiphenyl [90-41-5] M 169.2, m 49.0°, pK<sup>18</sup> 3.83. Crystd from aqueous EtOH (charcoal).

p-Aminobiphenyl [92-67-1] M 169.2, m 53°, b 191°/16mm, pK<sup>18</sup> 4.38. Crystd from water or EtOH. CARCINOGENIC.

2-Amino-5-bromotoluene [583-75-5] M 186.1, m 59°, pK<sup>25</sup> 3.58. Steam distd, and crystd from EtOH.

**RS-2-Aminobutyric acid** [2835-81-6] **M 103.1, m 303°(dec), pK\_1^{25} 2.29, pK\_2^{25} 9.83.** Crystd from water.

S-2-Aminobutyric acid [1492-24-6] M 103.1, m 292°(dec),  $[\alpha]_D$  + 20.4° (c 2, 2.5N HCl). Crystd from aqueous EtOH.

**3-Aminobutyric acid** [2835-82-7] **M 103.1, m 193-194°, pK\_{Est(1)} \sim 3.5, pK\_{Est(2)} \sim 10.3.** Crystd form aqueous EtOH or MeOH + Et<sub>2</sub>O.

4-Aminobutyric acid (GABA) [56-12-2] M 103.1, m 202°(dec),  $pK_1^{25}$  4.14,  $pK_2^{25}$  10.55. Crystd form aqueous EtOH or MeOH + Et<sub>2</sub>O.

**2-Amino-5-chlorobenzoic acid** [635-21-1] **M 171.6, m 100°, pK\_1^{25} 1.69, pK\_2^{25} 4.35**. Crystd from water, EtOH or chloroform.

**3-Amino-4-chlorobenzoic acid** [2840-28-0] **M 171.6, m 216-217°, pK**<sub>Est(1)</sub> ~2.7, pK<sub>Est(2)</sub> ~2.9. Crystd from water.

4-Amino-4'-chlorobiphenyl [135-68-2] M 203.5, m 134°, pKEst ~4.0. Crystd from pet ether.

**2-Amino-4-chloro-6-methylpyrimidine** [5600-21-5] **M 143.6, m 184-186°, pK**<sub>Est</sub> ~1.0. Crystd from EtOH.

2-Amino-5-chloropyridine [1072-98-6] M 128.6, m 135-136°, pK 4.38. Crystd from pet ether, sublimes at 50°/0.5mm.

1-Amino-1-cyclopentanecarboxylic acid (cycloleucine) [52-52-8] M 129.2, m 330°(dec), pK<sub>Est(1)</sub>~2.5 pK<sub>Est(2)</sub>~10.3. Crystd from aq EtOH.

2-Amino-3,5-dibromopyridine [35486-42-1] M 251.9, m 103-104°, pK<sub>Est</sub> ~2.4. Steam distd and crystd from aqueous EtOH or pet ether.

**2-Amino-4,6-dichlorophenol** [527-62-8] **M** 175.0, **m** 95-96°,  $pK_{Est(1)}$ ~3.1,  $pK_{Est(2)}$ ~6.8. Crystd from CS<sub>2</sub> or \*benzene.

3-Amino-2,6-dichloropyridine [62476-56-6] M 164.0, m 119°, b 110°/0.3mm, pK<sub>Est</sub> ~2.0. Crystd from water.

**4-Amino-***N*, *N*-**diethylaniline hydrochloride** [16713-15-8] **M 200.7, m 233.5°, pK<sup>22</sup> 6.61.** Crystd from EtOH.

4-Amino-3,5-diiodobenzoic acid [2122-61-4] M 388.9, m >350°, pK<sub>Est(1)</sub> 0.4, pK<sub>Est(2)</sub> ~1.6. Purified by soln in dilute NaOH and pptn with dilute HCl. Air dried.

2-Amino-4,6-dimethylpyridine [5407-87-4] M 122.2, m 69-70.5°, pK 7.84. Crystd from hexane, ether/pet ether or \*benzene. Residual \*benzene was removed over paraffin-wax chips in an evacuated desiccator.

2-Amino-4,6-dimethylpyrimidine [767-15-7] M 123.2, m 152-153°, pK<sup>25</sup> 4.95. Crystn from water gives m 197°, and crystn from acetone gives m 153°.

**2-Aminodiphenylamine** [534-85-0] M 184.2, m 79-80°, pK<sub>Est(1)</sub> ~3.8 (NH<sub>2</sub>), pK<sub>Est(2)</sub> <~0. Crystd from H<sub>2</sub>O.

4-Aminodiphenylamine [101-54-2] M 184.2, b 155°/0.026mm, pK<sup>25</sup> 5.20. Crystn from EtOH gives m 66°, and crystn from ligroin gives m 75°.

2-Amino-1,2-diphenylethanol [530-36-9] M 213.3, m 165°, pKEst(1) ~7.5. Crystd from EtOH.

2-Aminodiphenylmethane [28059-64-5] M 183.3, m 52°, b 172°/12mm and 190°/22mm, pK<sub>Est(1)</sub>~4.2. Crystd from ether.

2-Aminoethanethiol see cysteamine in Chapter 6.

**2-Aminoethanol** (ethanolamine) [141-43-5] M 61.1, f 10.5°, b 72-73°/12 mm, 171.1°/760mm, d 1.012, n 1.14539, pK<sup>25</sup> 9.51. Decomposes slightly when distd at atmospheric pressure, with the formation of conducting impurities. Fractional distn at about 12mm pressure is satisfactory. After distn, 2-aminoethanol was further purified by repeated washing with ether and crystn from EtOH (at low temperature). After fractional distn in the absence of CO<sub>2</sub>, it was twice crystd by cooling, followed by distn. Hygroscopic. [Reitmeier, Silvertz and Tartar J Am Chem Soc 62 1943 1940.] It can be dried by azeotropic distn with dry \*benzene.

2-Aminoethanol hydrochloride [2002-24-6] M 97.6, m 75-77°. Crystd from EtOH. It is deliquescent.

2-Aminoethyl hydrogen sulfate (sulfuric acid mono-2-aminoethyl ester) [926-39-6] M 141.1, m 285-287° (chars at 275°). Crystd from water or dissolved in water and EtOH added.

S-(2-Aminoethyl)isothiouronium bromide hydrobromide [56-10-0] M 281.0, m 194-195°. Crystd from absolute EtOH/ethyl acetate. It is hygroscopic.

(2-Aminoethyl)trimethylammonium chloride hydrochloride (chloramine chloride hydrochloride) [3399-67-5] M 175.1, m 260°(dec). Crystd from EtOH. (Material is very soluble in H<sub>2</sub>O).

**2-Aminofluorene** [153-78-6] **M 181.2, m 127.8-128.8°, 132-133°, pK^{25}4.64.** Wash well with H<sub>2</sub>O and recrystd from Et<sub>2</sub>O or 50% aqueous EtOH (25g with 400mL), and dry in a vacuum. Store in the dark. [Org Synth Coll Vol II 447 1943; Coll Vol V 30 1973].

4-Amino hippuric acid [61-78-9] M 194.2, m 198-199°, pK<sub>Est(1)</sub>~1.7(NH<sub>2</sub>), pK<sub>Est(2)</sub> ~3.4 (CO<sub>2</sub>H). Crystd from H<sub>2</sub>O.

**4-Amino-3-hydrazino-5-mercapto-1,2,4-triazole** (Purpald) [1750-12-5] M 146.2, m 228-230°(dec), 234-235°(dec),  $pK_{Est(1)}\sim 2$ ,  $pK_{Est(2)}\sim 3$  (NH<sub>2</sub>),  $pK_{Est(3)}\sim 8$  (SH). Crystd from H<sub>2</sub>O (0.6g in 300-400mL). The *benzylidene deriv* has m 245-246°(dec) from *i*-PrOH [Hoggarth J Chem Soc 4817 1952].

1-Amino-4-hydroxyanthraquinone [116-85-8] M 293.2, m 207-208°,  $pK_{Est(1)} \sim 2.6$  (NH<sub>2</sub>),  $pK_{Est(2)} \sim 9.0$  (OH). Purified by TLC on SiO<sub>2</sub> gel plates using toluene/acetone (9:1) as eluent. The main band was scraped off and extracted with MeOH. The solvent was evaporated and the dye was dried in a drying pistol [Land, McAlpine, Sinclair and Truscott *J Chem Soc*, *Faraday Trans 1* 72 2091 1976]. Crystd from aq EtOH.

*dl*-4-Amino-3-hydroxybutyric acid [924-49-2] M 119.1, m 225°(dec),  $pK_1^{25}$ ~3.80 (CO<sub>2</sub>H),  $pK_{Est(2)}$ ~9.3. Crystd from H<sub>2</sub>O or aqueous EtOH.

5-Amino-8-hydroxyquinoline hydrochloride [388]-33-2] M 196.7, pK<sub>1</sub><sup>20</sup> 5.67, pK<sub>2</sub><sup>20</sup> 11.24. Dissolved in minimum of MeOH, then Et<sub>2</sub>O was added to initiate pptn. Ppte was filtered off and dried [Lovell et al. J Phys Chem 88 1885 1984].

3-Amino-4-hydroxytoluene [95-84-1] M 123.2, m 137-138°,  $pK_{Est(1)} \sim 4.7(NH_2)$ ,  $pK_{Est(2)} \sim 9.6$  (OH). Crystd from H<sub>2</sub>O or toluene.

4-Amino-5-hydroxytoluene [2835-98-5] M 123.2, m 159°,  $pK_{Est(1)}$ ~5.4 (NH<sub>2</sub>),  $pK_{Est(2)}$ ~10.2 (OH). Crystd from H<sub>2</sub>O, 50% EtOH, or toluene.

6-Amino-3-hydroxytoluene [2835-99-6] M 123.2, m 162°(dec), pK<sub>Est(1)</sub>~5.4 (NH<sub>2</sub>), pK<sub>Est(2)</sub>~10.4 (OH). Crystd from 50% EtOH.

4-Aminoimidazole-5-carboxamide hydrochloride (AICAR HCl) [72-40-2] M 162.6, m 255-256°(dec), pK<sub>Est(1)</sub>~3.5, pK<sub>Est(2)</sub>~9.4. Recrystd from EtOH.

5-Aminoindane [24425-40-9] M 133.2, m 37-38°, b 131°/15mm, 146-147°/25mm, 247-249°/745mm, pK<sup>16</sup> 5.31. Distd and then crystd from pet ether.

**6-Aminoindazole** [6967-12-0] **M 133.2, m 210°, pK^{25} 3.99.** Crystd from H<sub>2</sub>O or EtOH and sublimed in a vacuum.

2-Amino-5-iodotoluene [13194-68-8] M 233.0, m 87°, pK<sub>Est</sub> ~3.6. Crystd from 50% EtOH.

 $\alpha$ -Aminoisobutyric acid [62-57-7] M 103.1, m sublimes at 280°, pK<sub>1</sub><sup>25</sup>2.36, pK<sub>2</sub><sup>25</sup>10.21. Crystd from aqueous EtOH and dried at 110°.

*RS*- β-Aminoisobutyric acid (α-methyl-β-alanine) [10569-72-9] M 103.1, m 176-178°, 178-180°, 181-182°, *R*-(-)- isomer [144-90-1] m 183°, [α]  $_{D}^{25}$ -21° (c 0.43, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 3.7, pK<sub>Est(2)</sub>~ 10.2. Colorless prisms from hot H<sub>2</sub>O, were powdered and dried in vacuo. The purity is checked by paper chromatography (Whatman 1) using ninhydrin spray to visualise the amino acid; R<sub>F</sub> values in 95% MeOH and *n*-PrOH/5N HCOOH (8:2) are 0.36 and 0.50 respectively. [Kupiecki and Coon Biochem Prep 7 20 1960; Pollack J Am Chem Soc 65 1335 1943.] The *R*-enantiomer, isolated from iris bulbs or human urine was crystd from H<sub>2</sub>O and sublimed in vacuo [Asen et al. J Biol Chem 234 343 1959]. The *RS*-hydrochloride was recrystd from EtOH/Et<sub>2</sub>O m 128-129°, 130° [Böhme et al. Chem Ber 92 1258, 1260, 1261 1959].

5-Aminolaevulinic acid hydrochloride [5451-09-2] M 167.6, m 156-158°(dec),  $pK_1^{22} 4.05$ ,  $pK_2^{22} 8.90$  Dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> overnight then crystd by dissolving in cold EtOH and adding dry Et<sub>2</sub>O.

Aminomalononitrile toluene-4-sulfonate [5098-14-6] M 253.4, m 168-170°, 172°(dec),  $pK_{Est} \sim 1.3$ . Colourless crysts on recrystn from MeCN (1.8g in 100mL) using activated charcoal. Wash the crystals with dry Et<sub>2</sub>O and dry at 25°/1mm. Recovery of ~80%. [Ferris et al. Org Synth Coll Vol V 32 1973.]

**3-Amino-5-mercapto-1,2,4-triazole** [16691-43-3] M **116.1, m 298°, pK**<sub>Est(1)</sub>~ **3.0, pK**<sub>Est(2)</sub>~ **9.** Recrystd from H<sub>2</sub>O and dried *in vacuo*. The *acetyl derivative* has **m** 325° (dec) after recrystn from H<sub>2</sub>O. [*Beilstein* **26, 3rd/4th Suppl** p. 1351.] Also recrystd from EtOH/H<sub>2</sub>O (3:1, 1g in 50 mL, 50% recovery), **m** 300-302° dec subject to heating rate ( $\lambda$ max 263nm, log  $\varepsilon$  4.12), and *S*-Benzyl derivative when crystd from \*C<sub>6</sub>H<sub>6</sub>/EtOH (20:1), or CHCl<sub>3</sub>/Et<sub>2</sub>O has **m** 109-111° [Godfrey and Kruzer J Chem Soc 3437 1960].

**2-Amino-4-methoxy-6-methylpyrimidine** [7749-47-5] M 139.2, m 157-159°, 158-158.5°, 158-160°,  $pK_{Est} \sim 6.0$ . Recrystd from H<sub>2</sub>O. The *picrate* has m 220-221°(dec). [Baker et al. J Am Chem Soc 69 3072, 3075 1947; Sirakawa et al. Yakugaku Zasshi 73 598 1953; Backer and Grevenstuk Recl Trav Chim, Pays-Bas 61 291 1942.]

8-Amino-6-methoxyquinoline [90-52-8] M 174.2, m 41-42°, 51°, b 137-138°/1mm, pK<sup>70.1</sup> 3.38. Distd under N<sub>2</sub> and high vac, then recrystd several times from MeOH (0.4mL/g). It remains colourless for several months when purified in this way [Elderfield and Rubin J Am Chem Soc 75 2963 1953].

1-Amino-4-methylaminoanthraquinone [1220-94-6] M 252.3,  $pK_{Est(1)} \sim 1$ ,  $pK_{Est(2)} < \sim 4$ . Purified by TLC on silica gel plates using toluene/acetone (3:1) as eluent. The main band was scraped off and extracted with MeOH. The solvent was evaporated and the residue dried in a drying pistol [Land, McAlpine, Sinclair and Truscott J Chem Soc, Faraday Trans 1 72 2091 1976].

4-Aminomethylbenzenesulfonamide hydrochloride [138-37-4] M 222.3, m 265-267°,  $pK_1^{20}$ 8.18 (NH<sub>2</sub>),  $pK_2^{20}$ 10.23 (SONH<sub>2</sub>). Crystd from dilute HCl and dried in a vacuum at 100°.

S-2-Amino-3-methyl-1-butanol (S-valinol) [2026-48-4] M 103.2, m 31-32°, b 88°/11mm, d 0.92,  $[\alpha]_{546} + 16.5°$  (c 6.32,  $l = 2 H_2O$ ),  $[\alpha]_D + 15.6°$  (EtOH), pK<sub>Est</sub> ~10.4. Purified by vacuum distn using short Vigreux column. Alternatively it is purified by steam distn. The steam distillate is acidified with HCl, the aq layer is collected and evapd. The residue is dissolved in butan-1-ol, filtered and dry Et<sub>2</sub>O added to cryst the hydrochloride salt (hygroscopic), m 113°. The free base can be obtained by suspending the salt in Et<sub>2</sub>O adding small vols of satd K<sub>2</sub>CO<sub>3</sub> until effervescence is complete and the mixture is distinctly alkaline. At this stage the aqueous layer should appear as a white sludge. The mixture is heated to boiling and refluxed for 30 min (more Et<sub>2</sub>O is added if necessary). The Et<sub>2</sub>O is decanted off from the white sludge, the

sludge is extracted twice with  $Et_2O$  (by boiling for a few minutes), the combined organic layers are dried (KOH pellets), evapd and the residue distd in a vacuum.

7-Amino-4-methylcoumarin [26093-31-2] M 175.2, m 221-442°(dec),  $pK_{Est} \sim 3.2$ . Dissolved in 5% HCl, filtered and basified with 2M ammonia. The ppte is dried in a vacuum, and crystd from dilute EtOH. It yields a blue soln and is light sensitive.

4-Amino-2-methyl-1-naphthol hydrochloride [130-24-5] M 209.6, m 283°(dec), pK<sub>Est(1)</sub>~5.6 (NH<sub>2</sub>), pK<sub>Est(2)</sub>~10.4 (OH). Crystd from dilute HCl.

**2-Amino-2-methyl-1,3-propanediol** [115-69-5] **M 105.1, m 111°, b 151-152°/10mm, pK^{25} 8.80.** Crystd three times from MeOH, dried in a stream of dry N<sub>2</sub> at room temp, then in a vacuum oven at 55°. Stored over CaCl<sub>2</sub> [Hetzer and Bates J Phys Chem 66 308 1962].

**2-Amino-2-methyl-1-propanol** ( $\beta$ -aminoisobutanol) [124-68-5] M 89.4, m 24°, 31°, b 67°/10mm, 164-166°/760mm, d 0.935, n 1.45, pK<sup>25</sup> 9.71. Purified by distn and fractional freezing. The *hydrochloride* has m 204°-206°.

**2-Amino-3-methylpyridine** [1603-40-3] M 108.1, m 33.2°, b 221-222°,  $pK^{25}$ 7.24. Crystd three times from \*benzene, most of the residual \*benzene being removed from the crystals over paraffin wax chips in an evacuated desiccator. The amine, transferred to a separating funnel under N<sub>2</sub>, was left in contact with NaOH pellets for 3h with occasional shaking. It was then placed in a vacuum distilling flask where it was refluxed gently in a stream of dry N<sub>2</sub> before being fractionally distd [Mod, Magne and Skau J Phys Chem 60 1651 1956].

2-Amino-4-methylpyridine [695-34-1] M 108.1, m 99.2°, b 230°, pK<sup>25</sup> 7.48. Crystd from EtOH or a 2:1 \*benzene/acetone mixture, and dried under vacuum.

2-Amino-5-methylpyridine [1603-41-4] M 108.1, m 76.5°, b 227°, pK<sup>25</sup> 7.22. Crystd from acetone.

**2-Amino-6-methylpyridine** [1824-81-3] M 108.1, m 44.2°, b 208-209°,  $pK^{25}$  7.41. Crystd three times from acetone, dried under vacuum at *ca* 45°. After leaving in contact with NaOH pellets for 3h, with occasional shaking, it was decanted and fractionally distd [Mod, Magne and Skau J Phys Chem 60 1651 1956]. Also recrystd from CH<sub>2</sub>Cl<sub>2</sub> by addition of pet ether. [Marzilli et al. J Am Chem Soc 108 4830 1986.]

2-Amino-5-methylpyrimidine [50840-23-8] M 109.1, m 193.5°, pK<sub>Est</sub> ~4.0. Crystd from water and \*benzene. Sublimes at 50°/0.5mm.

**4-Amino-2-methylquinoline** [6628-04-2] **M 158.2, m 168°, b 333°/760mm, pK<sup>20</sup>9.42.** Crystd from \*benzene/pet ether.

**2-Aminonaphthalene (B-naphthylamine)** [91-59-8] M 143.2, m 111-113°, pK<sup>25</sup> 4.20. See entry on p. 306.

**3-Amino-2-naphthoic** acid [5959-52-4] M 187.2, m 214°(dec),  $pK_{Est(1)}$ ~1.5  $pK_{Est(2)}$ ~4.0. Crystd from aqueous EtOH.

**4-Amino-5-naphthol-2,7-disulfonic** acid [90-20-0] M 320.3,  $pK_1^{25}$  3.63,  $pK_2^{25}$  8.83. Sufficient Na<sub>2</sub>CO<sub>3</sub> (*ca* 22g) to make the soln slightly alkaline to litmus was added to a soln of 100g of the dry acid in 750mL of hot distd water, followed by 5g of activated charcoal and 5g of Celite. The suspension was stirred for 10min and filtered by suction. The acid was ppted by adding *ca* 40mL of conc HCl (soln blue to Congo Red), then filtered by suction through sharkskin filter circular sheet (or hardened filter paper) and washed with 100mL of distd water. The purification process was repeated. The acid was dried overnight in an oven at 60° and stored in a dark bottle [Post and Moore Anal Chem 31 1872 1959].

1-Amino-2-naphthol hydrochloride [1198-27-2] M 195.7, m 250°(dec),  $pK_{Est(1)}$ ~3.7 (NH<sub>2</sub>),  $pK_{Est(2)}$ ~9.9 (OH). Crystd from the minimum volume of hot water containing a few drops of stannous chloride in an equal weight of hydrochloric acid (to reduce atmospheric oxidation).

1-Amino-2-naphthol-4-sulfonic acid [116-63-2] M 239.3, m 295°(dec),  $pK_{Est(1)}<0$ ,  $pK_{Est(2)} \sim 2.8$  (NH<sub>2</sub>),  $pK_{Est(2)} \sim 8.8$ . Purified by warming 15g of the acid, 150g of NaHSO<sub>3</sub> and 5g of Na<sub>2</sub>SO<sub>3</sub> (anhydrous) with 1L of water to *ca* 90°, shaking until most of the solid had dissolved, then filtering hot. The precipitate obtained by adding 10mL of conc HCl to the cooled filtrate was collected, washed with 95% EtOH until the washings were colourless, and dried under vacuum over CaCl<sub>2</sub>. It was stored in a dark coloured bottle, in the cold [Chanley, Gindler and Sobotka J Am Chem Soc 74 4347 1952].

6-Aminonicotinic acid [3167-49-5] M 138.1, m  $312^{\circ}(dec)$ , pK<sub>Est(1)</sub>~2.2 (CO<sub>2</sub>H), pK<sub>Est(2)</sub> ~6.5. Crystd from aq acetic acid.

**2-Amino-4-nitrobenzoic acid** [619-17-0] **M 182.1, m 269°(dec), pK\_1^{25} 0.65, pK\_2^{25} 3.70.** Crystd from water or aq EtOH.

5-Amino-2-nitrobenzoic acid [13280-60-9] M 182.1, m 235°(dec),  $pK_{Est(1)}$ ~1.1,  $pK_{Est(2)}$ ~1.2. Crystd from water.

1-Amino-4-nitronaphthalene [776-34-1] M 188.2, m 195°, pK<sup>20</sup>0.54. Crystd from EtOH or ethyl acetate.

2-Amino-4-nitrophenol [99-57-0] M 154.1, m 80-90° (hydrate), 142-143° (anhydr), pK<sub>Est(1)</sub>~3.9 (NH<sub>2</sub>), pK<sub>Est(2)</sub>~9.2. Crystd from water.

2-Amino-5-nitrophenol [121-88-0] M 154.1, m 207-208°, pK<sub>Est(1)</sub>~3.8, pK<sub>Est(2)</sub>~9.3. Crystd from water.

6-Aminopenicillanic acid [551-16-6] M 216.2, m 208-209°,  $[\alpha]_{546}$  +327° (in 0.1M HCl), pK<sub>1</sub><sup>25</sup> 2.30, pK<sub>2</sub><sup>25</sup> 4.90. Crystd from water.

**2-Aminoperimidine hydrobromide** [40835-96-9] M 264.1, m 299°,  $pK_{Est} \sim 7.9$  (free base). Purified by boiling a saturated aqueous soln with charcoal, filtering and leaving the salt to crystallise. Stored in a cool, dark place.

**2-Aminophenol** [95-55-6] **M 109.1, m 175-176°, pK\_1^{25} 4.65, pK\_2^{25} 9.75.** Purified by soln in hot water, decolorised with activated charcoal, filtered and cooled to induce crystn. Maintain an atmosphere of N<sub>2</sub> over the hot phenol soln to prevent its oxidation [Charles and Freiser J Am Chem Soc 74 1385 1952]. Can also be crystd from EtOH.

**3-Aminophenol** [591-27-5] **M 109.1, m 122-123<sup>o</sup>, pK<sub>1</sub><sup>25</sup> 4.25, pK<sub>2</sub><sup>25</sup> 9.90.** Crystd from hot water or toluene.

**4-Aminophenol** [123-30-8] **M 109.1, m 190° (under N<sub>2</sub>), pK\_1^{25}5.38, pK\_2^{25}10.4.** Crystd from EtOH, then water, excluding oxygen. Can be sublimed at 110°/0.3mm. Has been purified by chromatography on alumina with a 1:4 (v/v) mixture of absolute EtOH/\*benzene as eluent.

**4-Aminophenol hydrochloride** [51-78-5] M 145.6, m 306°(dec). Purified by treating an aqueous soln with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, filtering under an inert atmosphere, then recrystd from 50% EtOH twice and once from absolute EtOH [Livingston and Ke J Am Chem Soc 72 909 1950].

**4-Aminophenylacetic acid** [1197-55-3] **M 151.2, m 199-200°(dec),**  $pK_1^{20}$  **3.60,**  $pK_2^{20}$  **5.26.** Crystd from hot water (60-70mL/g).

**2-Amino-1-phenylbutan-1-ol**  $[\alpha-(\alpha-aminopropyl)benzyl alcohol] [(±)-threo 5897-76-7] M$ **165.1, m 79-80<sup>o</sup>, pK**<sub>Est</sub> ~**9.7.**Crystd from \*benzene/pet ether.

S-(-)-2-Amino-3-phenyl-1-propanol (L-phenylalaninol) [3182-95-4] M 151.2, m 95°. See phenylalaninol on p. 327.

**N-Aminophthalimide** [1875-48-5] M 162.2, m 200-202°,  $pK_{Est} \sim 0$ . It has been recrystd from 96% EtOH (sol ~2% at boiling temperature) to form a yellow solution. It sublimes *in vacuo* at *ca* 150°. Resolidifies after melting, and remelts at 338-341°.

4-Aminopropiophenone [70-69-9] M 163.1, m 140°, pK<sub>Est</sub> ~2.2. Crystd from water or EtOH.

4-(2-Aminopropyl)phenol [103-86-6] M 151.2, m 125-126°, pK<sub>Est(1)</sub>~9.4 (OH), pK<sub>Est(2)</sub>~9.7(NH<sub>2</sub>). Crystd from \*benzene.

1-Aminopyrene [1606-67-3] M 217.3, m 117-118°,  $pK_1^{25}$  2.91 (50% aq EtOH),  $pK_2^{25}$  2.77 (50% aq EtOH). Crystd from hexane.

**2-Aminopyridine** [504-29-0] **M 94.1, m 58°, b 204-210°, pK\_1^{25}-7.6, pK\_2^{25}6.71. Crystd from \*benzene/pet ether (b 40-60°) or CHCl<sub>3</sub>/pet ether.** 

**3-Aminopyridine** [462-08-8] **M 94.1, m 64°, b 248°, pK\_1^{25}-1.5, pK\_2^{25}6.03.** Crystd from \*benzene, CHCl<sub>3</sub>/pet ether (b 60-70°), or \*benzene/pet ether (4:1).

**4-Aminopyridine** [504-24-5] **M 94.1, m 160°, b 180°/12-13mm, pK\_1^{25}-6.55, pK\_2^{25}9.11 (9.18). Crystd from \*benzene/EtOH, then recrystd twice from water, crushed and dried for 4h at 105° [Bates and Hetzer J Res Nat Bur Stand 64A 427 1960]. Has also been crystd from EtOH, \*benzene, \*benzene/pet ether, toluene and sublimes in vacuum.** 

**2-Aminopyrimidine** [109-12-6] **M 95.1, m 126-127.5°, pK<sup>20</sup> 3.45.** Crystd from \*C<sub>6</sub>H<sub>6</sub>, EtOH or H<sub>2</sub>O.

4-Aminopyrimidine [591-54-8] M 95.1, m 149-151°, 154-156°, pK<sup>25</sup> 5.69. Recryst 10.6g from hot EtOAc (200mL), 7.4g colorless needles, first crop, evap to 25mL gave 1.7g of second crop. The *Hydroiodide* has m 180°. *Picrate* has m 225°. [Brown J Soc Chem Ind (London) 69 353 1950.]

5-Aminopyrimidine [591-55-9] M 95.1, m 171-172° (with sublimation),  $pK^{25}$  2.52. Purified by conversion to the MgCl<sub>2</sub> complex in a small vol of H<sub>2</sub>O. The complex (~ 5g) is dissolved in the minimum vol of hot H<sub>2</sub>O, passed through a column of activated Al<sub>2</sub>O<sub>3</sub> (200g) and the column washed with EtOH. Evapn of the EtOH gives a colorless residue of the aminopyrimidine which is recrystd from \*C<sub>6</sub>H<sub>6</sub> (toluene could also be used) which forms needles at first then prisms. It melts with sublimation. Acetylation yields 5acetamidopyrimidine which crysts from \*C<sub>6</sub>H<sub>6</sub>, m 148-149°. [Whittaker J Chem Soc 1565 1951.]

Aminopyrine (4-dimethylaminoantipyrene) [58-15-1] M 231.3, m 107-109°,  $pK_1^{25}$ -2.22,  $pK_2^{25}$ 4.94. Crystd from pet ether.

3-Aminoquinoline [580-17-6] M 144.2, m 93.5°, pK<sup>20</sup>4.94. Crystd from \*C<sub>6</sub>H<sub>6</sub>.

**4-Aminoquinoline** [578-68-7] **M 144.2, m 158°, pK\_1^{20}-7.11, pK\_2^{20}9.13.** Purified by zone refining.

5-Aminoquinoline [611-34-7] M 144.2, m 110°, b 184°/10mm, 310°/760mm,  $pK_1^{20}$  0.97,  $pK_2^{20}$  5.42. Crystd from pentane, then from \*benzene or EtOH.

**6-Aminoquinoline** [580-15-4] **M 144.2, m 117-119°, pK\_1^{20} 1.63, pK\_2^{20} 5.59.** Purified by column chromatography on a SiO<sub>2</sub> column using CHCl<sub>3</sub>/MeOH (4:1) as eluent. It is an **irritant**.

8-Aminoquinoline [578-66-5] M 144.2, m 70°, pK<sup>20</sup> 3.95. Crystd from EtOH or ligroin.

4-Aminosalicylic acid [65-49-6] M 153.1, m 150-151°(dec),  $pK_1^{25}1.78$  (CO<sub>2</sub>H),  $pK_2^{25}3.63$  (NH<sub>2</sub>),  $pK^{20}13.74$  (OH). Cryst from EtOH.

5-Aminosalicylic acid (5-amino-2-hydroxybenzoic acid) [89-57-6] M 153.1, m 276-280°, 283° (dec),  $pK_1^{25}$  2.74 (CO<sub>2</sub>H),  $pK_2^{25}$  5.84 (NH<sub>2</sub>). Cryst as needles from H<sub>2</sub>O containing a little NaHSO<sub>3</sub> to avoid aerial oxidation to the quinone-imine. The *Me ester* gives needles from \*C<sub>6</sub>H<sub>6</sub>, m 96°, and the *hydrazide* has m 180-182° (From H<sub>2</sub>O). [Fallab et al. *Helv Chim Acta* 34 26 1951, Shavel J Amer Pharm Assoc 42 402 1953.]

**2-Amino-5-sulfanilylthiazole** [473-30-3] **M 238.3, m 219-221°(dec), pK**<sub>Est</sub> ~4.5 (OH). Crystd from EtOH.

4-Amino-2-sulfobenzoic acid [527-76-4] M 217.1. Crystd from water.

**2-Aminothiazole** [96-50-4] **M 108.1, m 93°, b 140°/11mm, pK<sup>20</sup>5.36.** Crystd from pet ether (b 100-120°), or EtOH.

1-Amino-1,2,4-triazole [24994-60-3] M 84.1, m 91-93°, pK<sub>Est</sub> ~2. Crystd from water. [Barszez et al. J Chem Soc, Dalton Trans 2025 1986.]

**3-Amino-1,2,4-triazole** [61-82-5] **M 84.1, m 159°, pK\_1^{20} 4.04, pK\_2^{20} 11.08.** Crystd from EtOH (charcoal), then three times from dioxane [Williams, McEwan and Henry J Phys Chem 61 261 1957].

4-Amino-1,2,4-triazole [584-13-4] M 84.1, m 80-81°, pK 3.23. Crystd from water. [Barszez et al. J Chem Soc, Dalton Trans 2025 1986.]

7-Amino-4-(trifluoromethyl)coumarin, [53518-15-3] M 229.1, m 222°, pK<sub>Est</sub> ~3.1. Purified by column chromatography on a C18 column, eluted with acetonitrile/0.01M aq HCl (1:1), and crystd from isopropanol. Alternatively, it is eluted from a silica gel column with CH<sub>2</sub>Cl<sub>2</sub>, or by extracting a CH<sub>2</sub>Cl<sub>2</sub> solution (4g/L) with 1M aq NaOH (3 x 0.1L), followed by drying (MgSO<sub>4</sub>), filtration and evaporation. [Bissell J Org Chem 45 2283 1980.]

**9-Aminotriptycene** [793-41-9] **M 269.3, m 223.5-224.5°.** Recrystd from ligroin [Imashiro et al. J Am Chem Soc 109 729 1987].

5-Amino-*n*-valeric acid (5-aminopentanoic acid) [660-88-8] M 117.2, m 157-158°,  $pK_1^{25}$ 4.25,  $pK_2^{25}$ 10.66. Crystd by dissolving in H<sub>2</sub>O and adding EtOH.

5-Amino-n-valeric acid hydrochloride [627-95-2] M 153.6, m 103-104°. Crystd from CHCl<sub>3</sub>.

Amodiaquin [4-(3-dimethylaminomethyl-4-hydroxyanilino)-7-chloroquinoline] [86-42-0] M 287.5, m 208°. Crystd from 2-ethoxyethanol.

D-Amygdalin [29883-15-6] M 457.4, m 214-216°, [α]<sub>D</sub><sup>22</sup> -38° (c 1.2, H<sub>2</sub>O). Crystd from water.

*n*-Amyl acetate [628-63-7] M 130.2, b 149.2°, d 0.876, n 1.40228. Shaken with saturated NaHCO<sub>3</sub> soln until neutral, washed with water, dried with MgSO<sub>4</sub> and distd.

*n*-Amyl alcohol (1-pentanol) [71-41-0] M 88.2, b 138.1°,  $d^{15}$  0.818, n 1.4100. Dried with anhydrous K<sub>2</sub>CO<sub>3</sub> or CaSO<sub>4</sub>, filtered and fractionally distd. Has also been treated with 1-2% of sodium and

heated at reflux for 15h to remove water and chlorides. Traces of water can be removed from the near-dry alcohol by refluxing with a small amount of sodium in the presence of 2-3% *n*-amyl phthalate or succinate followed by distn (see *ethanol*).

Small amounts of amyl alcohol have been purified by esterifying with *p*-hydroxybenzoic acid, recrystallising the ester from  $CS_2$ , saponifying with ethanolic-KOH, drying with CaSO<sub>4</sub> and fractionally distilling [Olivier *Recl Trav Chim Pays-Bas* 55 1027 1936].

*tert*-Amyl alcohol [75-85-4] M 88.2, b 102.3°, d<sup>15</sup> 0.8135, n 1.4058. Refluxed with anhydrous  $K_2CO_3$ , CaH<sub>2</sub>, CaO or sodium, then fractionally distd. Near-dry alcohol can be further dried by refluxing with magnesium activated with iodine, as described for *ethanol*. Further purification is possible using fractional crystn, zone refining or preparative gas chromatography.

*n*-Amylamine [1-aminopentane] [110-58-7] M 87.2, b 105°, d 0.752, pK<sup>25</sup> 10.63. Dried by prolonged shaking with NaOH pellets, then distd.

*n*-Amyl bromide (*n*-pentylbromide) [110-53-2] M 151.1, b 129.7°, d 1.218, n 1.445. Washed with conc  $H_2SO_4$ , then water, 10% Na<sub>2</sub>CO<sub>3</sub> soln, again with water, dried with CaCl<sub>2</sub> or K<sub>2</sub>CO<sub>3</sub>, and fractionally distd just before use.

n-Amyl chloride [543-59-9] M 106.6, b 107.8°, d 0.882, n 1.41177. Same as sec-amyl chloride.

sec-Amyl chloride (1-chloro-2-methylbutane) [616-13-7] M 106.6, b 96-97°. Purified by stirring vigorously with 95% H<sub>2</sub>SO<sub>4</sub>, replacing the acid when it became coloured, until the layer remained colourless after 12h stirring. The amyl chloride was then washed with satd Na<sub>2</sub>CO<sub>3</sub> soln, then distd water, and dried with anhydrous MgSO<sub>4</sub>, followed by filtration, and distn through a 10-in Vigreux column. Alternatively a stream of oxygen containing 5% ozone was passed through the amyl chloride for three times as long as it took to cause the first coloration of starch iodide paper by the exit gas. Washing the liquid with NaHCO<sub>3</sub> soln hydrolyzed ozonides and removed organic acids prior to drying and fractional distn [Chien and Willard J Am Chem Soc 75 6160 1953].

*tert*-Amyl chloride [594-36-5] M 106.6, b 86°, d 0.866. Methods of purification commonly used for other alkyl chlorides lead to decomposition. Unsatd materials were removed by chlorination with a small amount of chlorine in bright light, followed by distn [Chien and Willard J Am Chem Soc 75 6160 1953].

Amyl ether [693-65-2] M 158.3, b 186.8°, d 0.785, n 1.41195. Repeatedly refluxed over sodium and distd.

*p-tert-Amylphenol [80-46-6]* M 146.3, m 93.5-94.2°, pK<sub>Est</sub> ~10.2. Purified via its benzoate, as for phenol. After evaporating the solvent from its soln in ether, the material was crystd (from the melt) to constant melting point [Berliner, Berliner and Nelidow J Am Chem Soc 76 507 1954].

2-n-Amylpyridine [2294-76-0] M 149.2, b 63.0<sup>o</sup>/2mm, n<sup>26</sup> 1.4861, pK<sup>25</sup> 6.00. Dried with NaOH for several days, then distd from CaO under reduced pressure, taking the middle fraction and redistilling it.

4-n-Amylpyridine [2961-50-4] M 149.2, b 78.0°/2.5mm, n 1.4908, pK<sub>Est</sub> ~6.1. Dried with NaOH for several days, then distd from CaO under reduced pressure, taking the middle fraction and redistilling it.

a-Amyrin [638-95-9] M 426.7, m 186°. Crystd from EtOH.

B-Amyrin [508-04-3] M 426.7, m 197-197.5°. Crystd from pet ether or EtOH.

Androstane [24887-75-0] M 260.5, m 50-50.5°. Crystd from acetone/MeOH.

epi-Androsterone [481-29-8] M 290.4, m 172-173<sup>o</sup>, [α]<sub>546</sub> +115<sup>o</sup> (c 1, MeOH). Crystd from aq EtOH.

cis-Androsterone [53-41-8] M 290.4. m 185-185.5°. Crystd from acetone/Et<sub>2</sub>O.

Angelic acid [565-63-9] M 100.1, m 45°, pK<sup>18</sup> 4.29. Steam distd, then crystd from H<sub>2</sub>O.

Aniline [62-53-3] M 93.1, f -6.0°, b 68.3/10mm, 184.4°/760mm, d 1.0220, n 1.585, n<sup>25</sup> 1.5832, pK<sup>25</sup> 4.60. Aniline is hygroscopic. It can be dried with KOH or CaH<sub>2</sub>, and distd at reduced pressure. Treatment with stannous chloride removes sulfur-containing impurities, reducing the tendency to become coloured by aerial oxidn. Can be crystd from Et<sub>2</sub>O at low temps. More extensive purifications involve preparation of derivatives, such as the double salt of aniline hydrochloride and cuprous chloride or zinc chloride, or *N*-acetylaniline (m 114°) which can be recrystd from water.

Recrystd aniline was dropped slowly into an aqueous soln of recrystd oxalic acid. Aniline oxalate was filtered off, washed several times with water and recrystd three times from 95% EtOH. Treatment with satd Na<sub>2</sub>CO<sub>3</sub> soln, regenerated aniline which was distd from the soln, dried and redistd under reduced pressure [Knowles Ind Eng Chem 12 881 1920].

After refluxing with 10% acetone for 10h, aniline was acidified with HCl (Congo Red as indicator) and extracted with  $Et_2O$  until colourless. The hydrochloride was purified by repeated crystn before aniline was liberated by addition of alkali, then dried with solid KOH, and distd. The product was sulfur-free and remained colourless in air [Hantzsch and Freese Chem Ber 27 2529, 2966 1894].

Non-basic materials, including nitro compounds were removed from aniline in 40% H<sub>2</sub>SO<sub>4</sub> by passing steam through the soln for 1h. Pellets of KOH were added to liberate the aniline which was steam distd, dried with KOH, distd twice from zinc dust at 20mm, dried with freshly prepared BaO, and finally distd from BaO in an allglass apparatus [Few and Smith J Chem Soc 753 1949]. Aniline is absorbed by skin and is **TOXIC** 

Aniline hydrobromide [542-11-0] M 174.0, m 286°. Crystd from water or EtOH and dried at 5mm over  $P_2O_5$ . Crystd four times from MeOH containing a few drops of conc HCl by addition of pet ether (b 60-70°), then dried to constant weight over paraffin chips, under vacuum [Gutbezahl and Grunwald J Am Chem Soc 75 559 1953]. It was ppted from EtOH soln by addition of Et<sub>2</sub>O, and the filtered solid was recrystd from EtOH and dried *in vacuo*. [Buchanan et al. J Am Chem Soc 108 1537 1986.]

Aniline hydrochloride [142-04-1] M 129.6, m 200.5-201°. Same as aniline HBr above.

Aniline hydroiodide [45497-73-2] M 220.0, m dec on heating. Same as aniline HBr, store in thedark.

*m*-Anisaldehyde [591-31-1] M 136.2, b 143°/50mm, d 1.119. Washed with saturated aq NaHCO<sub>3</sub>, then H<sub>2</sub>O, dried with anhydrous MgSO<sub>4</sub> and distd at reduced pressure under N<sub>2</sub>. Stored under N<sub>2</sub> in glass sealed ampoules.

*p*-Anisaldehyde (*p*-methoxybenzaldehyde) [123-11-5] M 136.2, m -1°, b 249°/atm, 89-90°/2mm, d 1.119, n 1.576. Washed with saturated aq NaHCO<sub>3</sub>, then H<sub>2</sub>O, steam distd, extracted distillate with Et<sub>2</sub>O, dried (MgSO<sub>4</sub>) and distd under vac and N<sub>2</sub>. Store in glass ampules under N<sub>2</sub> in the dark.

o-Anisidine [2-methoxyaniline] [90-04-0] M 123.2, m ~5°, b 109°/17mm, 119°/21mm, 225°/atm, d 1.096, n 1.575,  $pK^{25}$  4.52. It is separated from the *m*- and *p*- isomers by steam distn. It is also separated from its usual synthetic precusor *o*-nitroanisole by dissolving in dil HCl (pH <2.0) extracting the nitro impurity with Et<sub>2</sub>O, adjusting the pH to ~8.0 with NaOH extracting the amine in Et<sub>2</sub>O or steam distg. Extract the distillate with Et<sub>2</sub>O, dry extract (Na<sub>2</sub>SO<sub>4</sub>), evaporate and fractionate the residual oil. Protect the almost colorless oil from light which turns it yellow in color. [Biggs and Robinson J Chem Soc 3881961; Nodzu et al. Yakugaku Zasshi (J Pharm Soc Japan) 71 713, 715 1951.]

*m*-Anisidine [3-methoxyaniline] [536-90-3] M 123.2, m ~5°, b 79°/1mm, 128°/17mm, 251°/atm, d 1.101, n 1.583, pK<sup>25</sup> 4.20. *o*-Isomer impurity can be removed by steam distn. Possible impurity is the precursor 3-nitroanisole which can be removed as for the preceding *o*-isomer and fractionated using an efficient column. Yellow liquid. [Gilman and Kyle J Am Chem Soc 74 3027 1952; Bryson J Am Chem Soc 82 4858 1960; Kadaba and Massie J Org Chem 22 333 1957.]

*p*-Anisidine [4-methoxyaniline] [104-94-9] M 123.2, m 57°,  $pK^{25}$  5.31. Crystd from H<sub>2</sub>O or aqueous EtOH. Dried in a vacuum oven at 35° for 6h and stored in a dry box. [More et al. J Am Chem Soc 108 2257 1986.] Purified by vacuum sublimation [Guarr et al. J Am Chem Soc 107 5104 1985].

Anisole [100-66-3] M 108.1, f -37.5°, b 43°/11mm, 153.8°/760mm, d<sup>15</sup> 0.9988, n<sup>25</sup> 1.5143, pK<sup>0</sup> -6.61 (aq H<sub>2</sub>SO<sub>4</sub>). Shaken with half volume of 2M NaOH, and emulsion allowed to separate. Repeated 3 times, then washed twice with water, dried over CaCl<sub>2</sub>, filtered, dried over sodium wire and finally distd from fresh sodium under N<sub>2</sub>, using a Dean-Stark trap, samples in the trap being rejected until free from turbidity [Caldin, Parbov, Walker and Wilson J Chem Soc, Faraday Trans 1 72 1856 1976].

Dried with  $CaSO_4$  or  $CaCl_2$ , or by refluxing with sodium or BaO with crystalline FeSO<sub>4</sub> or by passage through an alumina column. Traces of phenols have been removed by prior shaking with 2M NaOH, followed by washing with water. Can be purified by zone refining.

2-p-Anisyl-1,3-indanone [117-37-3] M 252.3, m 156-157°, pK<sup>20</sup>4.09. Crystd from acetic acid or EtOH.

Anserine  $[N,\beta-alany]-1$ -methylhistidine] [584-85-0] M 240.3, m 238-239°,  $[\alpha]_D + 11.3°$  (H<sub>2</sub>O),  $pK_1^{25}$  2.64,  $pK_2^{25}$  7.04,  $pK_3^{25}$  9.49. Crystd from aqueous EtOH. It is hygroscopic.

S-Anserine nitrate [5937-77-9] M 303.3, m 225°(dec),  $[\alpha]_D^{30}$  +12.2°. Likely impurities: 1methylimidazole-5-alanine, histidine. Crystd from aqueous MeOH.

Antheraxanthin [68831-78-7] M 584.8, m 205°,  $\lambda_{max}$  460.5, 490.5nm, in CHCl<sub>3</sub>. Likely impurities: violaxanthin and mutatoxanthin. Purified by chromatography on columns of Ca(OH)<sub>2</sub> and of ZnCO<sub>3</sub>. Crystd from \*C<sub>6</sub>H<sub>6</sub>/MeOH as needles or thin plates. Stored in the dark, in an inert atmosphere, at -20°.

Anthracene [120-12-7] M 178.2, m 218°, pK -7.4 (aq  $H_2SO_4$ ). Likely impurities are anthraquinone, anthrone, carbazole, fluorene, 9,10-dihydroanthracene, tetracene and bianthryl. Carbazole is removed by continuous-adsorption chromatography [see Sangster and Irvine J Phys Chem 24 670 1956] using a neutral alumina column and passing *n*-hexane. [Sherwood in *Purification of Inorganic and Organic Materials*, Zief (ed), Marcel Dekker, New York, 1969.] The solvent is evaporated and anthracene is sublimed under vacuum, then purified by zone refining, under N<sub>2</sub> in darkness or non-actinic light.

Has been purified by co-distillation with ethylene glycol (boils at 197.5°), from which it can be recovered by additn of water, followed by crystn from 95% EtOH, \*benzene, toluene, a mixture of \*benzene/xylene (4:1), or Et<sub>2</sub>O. It has also been chromatographed on alumina with pet ether in a dark room (to avoid photo-oxidation of adsorbed anthracene to anthraquinone). Other purification methods include sublimation in a N<sub>2</sub> atmosphere (in some cases after refluxing with sodium), and recrystd from toluene [Gorman et al. J Am Chem Soc 107 4404 1985].

Anthracene has also been crystd from EtOH, chromatographed through alumina in hot \*benzene (*fume hood*) and then vac sublimed in a pyrex tube that has been cleaned and baked at 100°. (For further details see Craig and Rajikan J Chem Soc, Faraday Trans 1 74 292 1978; and Williams and Zboinski J Chem Soc, Faraday Trans 1 74 611 1978.) It has been chromatographed on alumina, recrystd from *n*-hexane and sublimed under reduced pressure. [Saltiel J Am Chem Soc 108 2674 1986; Masnori et al. J Am Chem Soc 108 1126 1986.] Alternatively, it was recrystd from cyclohexane, chromatographed on alumina with *n*-hexane as eluent, and recrystd two more times [Saltiel et al. J Am Chem Soc 109 1209 1987].

Anthracene-9-carboxylic acid [723-62-6] M 222.2, m 214°(dec), pK<sup>20</sup> 3.65. Crystd from EtOH.

**9-Anthraldehyde** [642-31-9] **M 206.2, m 104-105°.** Crystd from acetic acid or EtOH. [Masnori et al. J Am Chem Soc 108 1126 1986.]

Anthranol [529-86-2] M 196.2, m 160-170º(dec). Crystd from glacial acetic acid or aqueous EtOH.

Anthranthrone [641-13-4] M 306.3, m 300°, pK -7.9 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from chlorobenzene or nitrobenzene.

Anthraquinone [84-65-1] M 208.2, m 286°,  $pK^{25}$  -8.27 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from CHCl<sub>3</sub> (38mL/g), \*benzene, or boiling acetic acid, washing with a little EtOH and drying under vacuum over P<sub>2</sub>O<sub>5</sub>.

Anthrarufin [1,5-dihydroxy-9,10-anthraquinone] [117-12-4] M 240.1, m 280°(dec),  $pK_1^{25}$  9.90,  $pK_2^{25}$  11.05. Purified by column chromatography on silica gel with CHCl<sub>3</sub>/Et<sub>2</sub>O as eluent, followed by recrystn from acetone. Alternatively recrystd from glacial acetic acid [Flom and Barbara J Phys Chem 89 4489 1985].

1,8,9-Anthratriol [480-22-8] M 226.2, m 176-181°, pK<sub>Est</sub> ~9.5. Crystd from pet ether.

Anthrimide [1,1'-imino-bis-anthraquinone] [82-22-4] M 429.4, m >250°(dec). Crystd from chlorobenzene (red needles) or nitrobenzene (red rhombs)

Anthrone [90-44-8] M 194.2, m 155°, pK -5.5 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from a 3:1 mixture of \*benzene/pet ether (b 60-80°) (10-12mL/g), or successively from \*benzene then EtOH. Dried under vacuum.

Antipyrine [2,3-dihydro-1,5-dimethyl-3-oxo-2-phenylpyrazole] [60-80-0] M 188.2, m 114°, b 319°, pK<sup>25</sup> 1.45. Crystd from EtOH/water mixture, \*benzene, \*benzene/pet ether or hot water (charcoal), and dried under vacuum.

B-Apo-4'-carotenal, B-Apo-8'-carotenal, B-Apo-8'-carotenoic acid ethyl ester, B-Apo-8'carotenoic acid methyl ester, Apocodeine, Apomorphine see entries in Chapter 6.

**B-L-Arabinose (natural)** [87-72-9] M 150.1, m 158°,  $[\alpha]_D$  +104° (c 4, H<sub>2</sub>O after 24h). Crystd slowly twice from 80% aq EtOH, then dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

**D-Arabinose** [10323-20-3, 28697-53-2 (pyranoside)] **M 150.1, m 164°**,  $[\alpha]_{546}$  -123° (c 10, H<sub>2</sub>O after 24h), pK<sup>25</sup>12.54. Crystd three times from EtOH, vacuum dried at 60° for 24h and stored in a vacuum desiccator.

L-Arabitol [7643-75-6] M 152.2, m 102°, [α]<sub>546</sub> -16° (c 5, 8% borax soln). Crystd from 90% EtOH.

DL-Arabitol [2152-56-9] M 152.2, m 105-106°. Crystd from 90% EtOH.

Arachidic (eicosanoic C<sub>20</sub>) acid [506-30-9] M 312.5, m 77°, pK<sub>Est</sub> ~5.0. Crystd from abs EtOH.

Arachidic alcohol (1-eicosanol) [629-96-9] M 298.6, m 65.5° (71°), b 200°/3mm. Crystd from \*benzene or \*benzene/pet ether.

p-Arbutin [497-76-7] M 272.3, m 163-164°. Crystd from water.

S-Arginine [74-79-3] M 174.2, m 207°(dec),  $[\alpha]_D$  +26.5° (c 5, in 5M HCl),  $[\alpha]_{546}$  +32° (c 5, in 5M HCl),  $pK_1^{25}$  2.18,  $pK_2^{25}$  9.36,  $pK_3^{25}$  11.5. Crystd from 66% EtOH.

S-Arginine hydrochloride [1119-34-2] M 210.7, m 217°(dec),  $[\alpha]_D^{20} + 26.9°$  (c 6, M HCl). Likely impurity is ornithine. Crystd from water at pH 5-7, by adding EtOH to 80% (v/v).

S-Argininosuccinic acid [2387-71-5] M 290.3,  $[\alpha]_D^{24}$  +16.4° (H<sub>2</sub>O). Likely impurity is fumaric acid. In neutral or alkaline soln it readily undergoes ring closure to the 'anhydride'. Crystd from water by adding 1.5 vols of EtOH. Barium salt is stable at 0-5° if dry. [Westfall *Biochem J* 77 135 1960.]

S-Argininosuccinic anhydride [28643-94-9] M 272.3,  $[\alpha]_D^{23}$ -10° (H<sub>2</sub>O for anhydride formed at neutral pH). Crystd from water by adding two volumes of EtOH. An isomeric anhydride is formed if the free acid is allowed to stand at acid pH. In soln, the mixture of anhydrides and free acid is formed [see above entry].

L(+)-Ascorbic acid [50-81-7] M 176.1, m 193°(dec),  $[\alpha]_{546} + 23°$  (c 10, H<sub>2</sub>O),  $pK_1^{25}4.04$ ,  $pK_2^{25}11.34$ . Crystd from MeOH/Et<sub>2</sub>O/pet ether [Herbert et al. J Chem Soc 1270 1933].

S-Asparagine [70-47-3] M 150.1, m 234-235°, (monohydrate) [5794-13-8]  $[\alpha]_D$  +32.6° (0.1M HCl),  $pK_1^{25}$  1.98,  $pK_2^{25}$  8.84. Likely impurities are aspartic acid and tyrosine. Crystd from H<sub>2</sub>O or aqueous EtOH. Slowly effloresces in dry air.

Aspartic acid M 133.1, m 338-339° (RS, [617-45-8]); m 271° (S, requires heating in a sealed tube [56-84-8]),  $[\alpha]_D^{25} + 25.4^\circ$  (3M HCl),  $pK_1^{25}$  1.99,  $pK_2^{25}$  3.90. Likely impurities are glutamic acid, cystine and asparagine. Crystd from water by adding 4 volumes of EtOH and dried at 110°.

L-Aspartic acid ß-methyl ester hydrochloride [16856-13-6] M 183.6, m 194°, pK<sup>25</sup> 8.62. Recrystd from MeOH by using anhydrous diethyl ether [Bach et al. *Biochem Prep* 13 20 1971].

**DL-Aspartic acid dimethyl ester hydrochloride** [14358-33-9] **M 197.7, 116-117°.** Crystd from absolute MeOH. [Kovach et al. J Am Chem Soc 107 7360 1985.] Diethyl ester has pK<sup>25</sup> 6.4.

Aspergillic acid [490-02-8] M 224.3, m 97-99°, pK 5.5. Sublimed at 80°/10<sup>-3</sup>mm. Crystd from MeOH.

Astacin  $(\beta,\beta$ -carotene-3,3',4,4'-tetraone) [514-76-1] M 592.8, m 228°, 240-243°(evacuated tube),  $\varepsilon_{1cm}^{1\%}$  550,000 at 498mm (pyridine). Probable impurity is astaxanthin. Purified by chromatography on alumina/fibrous clay (1:4) or sucrose, or by partition between pet ether and MeOH (alkaline). Crystd from pyridine/water. Stored in the dark under N<sub>2</sub> at -20°. [Davis and Weedon J Chem Soc 182 1960.]

Atrolactic acid  $(0.5H_2O)$  (2-hydroxy-2-phenylpropionic acid) [515-30-0] M 166.2, m 94.5° (anhydr), 88-91° (0.5H<sub>2</sub>O), pK<sup>18</sup> 3.53. Crystd from water and dried at 55°/0.5mm.

Atropine [51-55-8] M 289.4, m 114-116°, pK<sup>18</sup> 9.85. Crystd from acetone or hot water.

Auramine O (4,4'-bis-dimethylaminobenzophenone imine hydrochloride) [2465-27-2] M 321.9,  $pK^{25}$  10.71 (free base), 9.78 (carbinolamine). Crystd from EtOH as hydrochloride, very slightly soluble in CHCl<sub>3</sub>, UV:  $\lambda_{max}$  434 (370) nm. The free base has m 136° after crystn from \*benzene. [J Chem Soc 1724 1949; Biochemistry 9 1540 1970].

Aurin tricarboxylic acid [4431-00-9] M 422.4, m 300°. The acid is dissolved in aqueous NaOH, NaHSO<sub>3</sub> solution is added until the colour is discharged and then the tricarboxylic acid is ppted with HCl [Org Synth Coll Vol I 54 1947]. Do not extract the acid with hot water because it softens forming a viscous mass. Make a solution by dissolving in aqueous NH<sub>3</sub>. See Aluminon for the ammonium salt.

8-Azaadenine [1123-54-2] M 136.1, m 345°(dec), pK<sub>1</sub><sup>20</sup> 2.65, pK<sub>2</sub><sup>20</sup> 6.29. Crystd from H<sub>2</sub>O.

**2-Azacyclotridecanone** (laurolactam) [947-04-6] M 197.3, m 152°. Crystd from  $CHCl_3$ , stored over  $P_2O_5$  in a vacuum desiccator.

8-Azaguanine [134-58-7] M 152.1, m >300°,  $pK_1^{20}$  1.04,  $pK_2^{20}$  6.29. Dissolved in hot M NH<sub>4</sub>OH, filtered, and cooled; recrystd, and washed with water.

7-Azaindole [271-63-6] M 118.1, m 105-106°,  $pK^{20}$  4.57. Repeatedly recrystd from EtOH, then vacuum sublimed [Tokumura et al. J Am Chem Soc 109 1346 1987].

1-Azaindolizine [274-76-0] M 118.1, b 72-73°/1mm, pK<sup>20</sup>1.43. Purified by distn or gas chromatography.

Azaserine [115-02-6] M 173.1, m 146-162°(dec),  $[\alpha]_D^{27.5}$ -0.5° (c 8.5, H<sub>2</sub>O, pH 5.2), pK<sub>Est(1)</sub>~4.53, pK<sub>Est(2)</sub>~5.40. Crystd from 90% EtOH.

8-Azapurine (1H-1,2,3-triazolo[4,5-d]pyrimidine, 1,2,3,4,6[3H]penta-azaindene) [273-40-5] M 121.1, m 174-175° (effervescence, m depends on heating rate),  $pK_1^{20}2.05$  (equilib with covalent hydrate),  $pK_2^{20}4.84$ . Sublimed at 120-130°/0.01mm and recryst from 3 parts of EtOH. [Albert J Chem Soc(B) 427 1966.]

Azelaic acid [123-99-9] M 188.2, m 105-106°. Crystd from H<sub>2</sub>O (charcoal) or thiophene-free \*benzene. The material cryst from H<sub>2</sub>O was dried by azeotropic distn in toluene, the residual toluene soln was cooled and filtered, the ppte being dried in a vacuum oven. Also purified by zone refining or by sublimation onto a cold finger at  $10^{-3}$  torr.

Azetidine (trimethyleneimine) [503-29-7] M 57.1, b 61-62°, d 0.846, n 1.432, pK<sup>25</sup> 11.29. It is a flammable, hygroscopic liquid smelling of ammonia, which absorbs CO<sub>2</sub> from air and should be kept under Argon. Purified by drying over solid KOH and distd through a short Vigreux column at atm pressure (under Argon) and keeping the pot temp below 210°. [Searles et al. J Am Chem Soc 78 4917 1956.]

Aziridine (ethyleneimine) [151-56-4] M 43.1, b 55-56°/756mm, 56°/760mm, d<sup>24</sup> 0.8321, pK<sup>25</sup> 8.00. Redistd in an Ar or N<sub>2</sub> atmosphere in a fume hood, and stored over KOH in sealed bottles in a refrigerator. Commercial aziridine has been dried over sodium and distd from the metal through an efficient column before use [Jackson and Edwards J Am Chem Soc 83 355 1961; Wenker J Am Chem Soc 57 2328 1935]. It is a weaker base than Me<sub>2</sub>NH (pK 10.87) but is caustic to the skin. It should not be inhaled, causes inflammation of the eyes, nose and throat and one may become sensitised. It is sol in H<sub>2</sub>O and has an ammoniacal smell and reacts with CO<sub>2</sub>. Pure aziridine is comparatively stable but polymerises in the presence of traces of H<sub>2</sub>O and is occasionally explosive in the presence of acids. CO<sub>2</sub> is sufficiently acidic to cause polymerisation (forms linear polymers) which is not free radical promoted. It is stable in the presence of bases. The violet 2:1 Cu complex crystd from EtOH containing a few drops of Aziridine and adding Et<sub>2</sub>O has m 142°(decomp). The picrate has m 142°. [O'Rourke et al. J Am Chem Soc 78 2159 1956.] It has also been dried with BaO, and distd from sodium under nitrogen. TOXIC.

Azobenzene [103-33-3] M 182.2, m 68°, pK<sup>25</sup> 2.48. Ordinary azobenzene is nearly all in the *trans*-form. It is partly converted into the *cis*-form on exposure to light [for isolation see Hartley J Chem Soc 633 1938, and for spectra of *cis*- and *trans*-azobenzenes, see Winkel and Siebert Chem Ber 74B 6701941]. trans-Azobenzene is obtained by chromatography on alumina using 1:4 \*benzene/heptane or pet ether, and crystd from EtOH (after refluxing for several hours) or hexane. All operations should be carried out in diffuse red light or in the dark.

**1,1'-Azobis(cyclohexane carbonitrile)** [2094-98-6] **M 244.3, m 114-114.5°**, ε<sub>350nm</sub> 16.0. Crystd from EtOH.

 $\alpha, \alpha'$ -Azobis(isobutyronitrile) (AIBN) [78-61-1] M 164.2, m 103°(dec). Crystd from acetone, Et<sub>2</sub>O, CHCl<sub>3</sub>, aq EtOH or MeOH. Has also been crystd from abs EtOH below 40° in subdued light. Dried under vacuum at room temp over P<sub>2</sub>O<sub>5</sub> and stored under vacuum in the dark at <-10° until used. Also crystd from CHCl<sub>3</sub> soln by addn of pet ether (b <40°). [Askham et al. J Am Chem Soc 107 7423 1985; Ennis et al. J Chem Soc, Dalton Trans 2485 1986; Inoue and Anson J Phys Chem 91 1519 1987; Tanner J Org Chem 52 2142 1987].

Azolitmin B [1395-18-2] M ~3300, m >250°(dec). Crystd from water as dark violet scales, or ppted from  $H_2O$  by addtn of EtOH as a red powder. It is an indicator which is red at pH 4.5 and blue at pH 8.3.

Azomethane [503-28-6] M 58.1, m -78°, b 1.5°. Purified by vacuum distn and stored in the dark at -80°. Can be EXPLOSIVE.

p, p'-Azoxyanisole (4,4'-dimethoxyazoxybenzene) [1562-94-3] M 258.3, transition temps: 118.1-118.8°, 135.6-136.0°,  $pK^{25}$  -5.23 (20% aq EtOH + 80% aq H<sub>2</sub>SO<sub>4</sub>). Crystd from absolute or 95% EtOH, or acetone, and dried by heating under vacuum or sublimed in a vac onto a cold finger.

Azoxybenzene [495-48-7] M 198.2, m 36°,  $pK^{25}$  -6.16 (20% aq EtOH + 80% aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH or MeOH, and dried for 4h at 25° and 10<sup>-3</sup>mm. Sublimed before use.

*p*,*p*-Azoxyphenetole [4792-83-0] M 286.3, m 137-138° (turbid liquid clarifies at 167°). Crystd from toluene or EtOH.

Azulene [275-51-4] M 128.2, m 98.5-99°, pK<sup>25</sup> -1.65 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH.

Azuleno(1,2-b)thiophene [25043-00-9] M 184.2. Crystd from cyclohexane, then sublimed in vacuo.

Azuleno(2,1-b)thiophene [248-13-5] M 184.2. Crystd from cyclohexane, then sublimed in vacuo.

Azure A (3-amino-7-dimethylaminophenazin-5-ium chloride) [531-53-3] M 291.8, CI 52005, m > 290°(dec),  $\lambda_{max}$  633nm, pK 7.2. Twice recrystd from H<sub>2</sub>O, and dried at 100°/1h in an oven.

Azure B (3-dimethylamino-7-methylaminophenazin-5-ium chloride) [531-55-5] M 305.8, CI 52010, m > 201°(dec),  $\lambda_{max}$  648nm, pK 7.4. Twice recrystd from H<sub>2</sub>O, and dried at 100°/1h in an oven.

Azure C (3-amino-7-methylaminophenazin-5-ium chloride) [531-57-7] M 277.8,  $\lambda_{max}$  616nm, pK 7.0. Twice recrystd from H<sub>2</sub>O, and dried at 100% h in an oven.

## **B.A.L.** (British Anti-Lewesite) see 1,2-dimercapto-3-propanol.

**Barbituric acid [6-hydroxypyrimidin-2,4-dione]** [67-52-7] M 128.1, m 250°(dec),  $pK_1^{25} 3.99$ ,  $pK_2^{25} 12.5$ . Crystd twice from H<sub>2</sub>O, then dried for 2 days at 100°.

Bathophenanthroline (4,7-diphenyl-1,10-phenanthroline) [1662-01-7] M 332.4, m 215-216°, 218-220°,  $pK^{25}$  4.67. Best purified by recrystn from \*C<sub>6</sub>H<sub>6</sub> or toluene. Its solubility (per L): H<sub>2</sub>O (1mg), M HCl (20mg), heptane (110mg), Et<sub>2</sub>O (530mg), Me<sub>2</sub>CO (2.3g), dioxane (3.4g), MeOH (6.0g), EtOH (10.5g), isoPrOH (10.0g), *n*-pentanol (18.7g), \*C<sub>6</sub>H<sub>6</sub> (12.2g), pyridine (33g), nitrobenzene (44.7g), CHCl<sub>3</sub> (78g) and AcOH (450.4g). [UV: Bull Soc Chim Fr 371 1972.] For di-Na salt 3H<sub>2</sub>O see entry in Chapter 5.

Batyl alcohol [544-62-7] M 344.6, m 70.5-71°. Crystd from aq Me<sub>2</sub>CO, EtOH or pet ether (b 40-60°).

**Behenoyl chloride** (docosanoyl chloride) [21132-76-3] M 359.0, m 40°. If the IR shows OH bands then it should be dissolved in oxalyl chloride in  $C_6H_6$  soln and warmed at 35° for 24h in the absence of moisture, evaporated and distd in a vacuum of  $10^{-5}$ mm. It is sol in  $C_6H_6$  and  $Et_2O$ . It is moisture sensitive and is LACHRYMATORY. [J Chem Soc 1001 1937; J Biol Chem 59 905 1924.]

Benzalacetone (*trans*-4-phenyl-3-buten-2-one) [122-57-6] M 146.2, m 42°. Crystd from pet ether (b 40-60°), or distd (b 137-142°/16mm).

Benzalacetophenone (Chalcone) [94-41-7] M 208.3, m 56-58°, b 208°/25mm,  $pK^{25}$  -5.73 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH warmed to 50° (about 5mL/g), iso-octane, or toluene/pet ether, or recrystd from MeOH, and then twice from hexane. SKIN IRRITANT.

Benzaldehyde [100-52-7] M 106.1, f -26°, b 62° (58°)/10mm, 179.0°/760mm, d 1.044, n 1.5455,  $pK^{25}$  -7.1 (aq H<sub>2</sub>SO<sub>4</sub>). To diminish its rate of oxidation, benzaldehyde usually contains additives such as hydroquinone or catechol. It can be purified *via* its bisulfite addition compound but usually distn (under nitrogen at reduced pressure) is sufficient. Prior to distn it is washed with NaOH or 10% Na<sub>2</sub>CO<sub>3</sub> (until no more CO<sub>2</sub> is evolved), then with satd Na<sub>2</sub>SO<sub>3</sub> and H<sub>2</sub>O, followed by drying with CaSO<sub>4</sub>, MgSO<sub>4</sub> or CaCl<sub>2</sub>.

anti-Benzaldoxime [932-90-1] M 121.1, m 33-34°. Crystd from diethyl ether by adding pet ether (b 60-80°). The syn-isomer [622-32-2] has b 121-124°/12mm, m 34-36°.

**Benzamide** [55-21-0] **M 121.1, m 129.5°, pK<sup>25</sup> -2.16 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from hot water (about 5mL/g), EtOH or 1,2-dichloroethane, and air dried. Crystd from dilute aqueous ammonia, water, acetone and then \*benzene (using a Soxhlet extractor). Dried in an oven at 110° for 8h and stored in a desiccator over 99% H<sub>2</sub>SO<sub>4</sub>. [Bates and Hobbs J Am Chem Soc 73 2151 1951.]

**Benzamidine** [618-39-3] **M 120.2, m 64-66°, pK<sup>20</sup> 11.6.** Liberated from chloride by treatment with 5M NaOH. Extracted into diethyl ether. Sublimed *in vacuo*.

**Benzanilide** [93-98-1] M 197.2, m 164°, pK<sup>55</sup> 1.26. Crystd from pet ether (b 70-90°) using a Soxhlet extractor, and dried overnight at 120°. Also crystd from EtOH.

**Benz[a]anthracene** [56-55-3] **M 228.3, m 159-160°.** Crystd from MeOH, EtOH or \*benzene (charcoal), then chromatographed on alumina from sodium-dried \*benzene (twice), using vacuum distn to remove \*benzene. Final purification was by vacuum sublimation.

Benz[a]anthracene-7,12-dione [2498-66-0] M 258.3, m 169.5-170.5°. Crystd from MeOH (charcoal).

Benzanthrone [82-05-3] M 230.3, m 170°, pK -3.2 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH or xylene.

\*Benzene [71-43-2] M 78.1, f 5.5°, b 80.1°, d 0.874, n 1.50110, n<sup>25</sup> 1.49790. For most purposes, \*benzene can be purified sufficiently by shaking with conc H<sub>2</sub>SO<sub>4</sub> until free from thiophene, then with H<sub>2</sub>O, dilute NaOH and water, followed by drying (with P<sub>2</sub>O<sub>5</sub>, sodium, LiAlH<sub>4</sub>, CaH<sub>2</sub>, 4X Linde molecular sieve, or CaSO<sub>4</sub>, or by passage through a column of silica gel, for a preliminary drying, CaCl<sub>2</sub> is suitable), and distn. A further purification step to remove thiophene, acetic acid and propionic acid, is crystn by partial freezing. The usual contaminants in dry thiophene-free \*benzene are non-benzenoid hydrocarbons such as cyclohexane, methylcyclohexane, and heptanes, together with naphthenic hydrocarbons and traces of toluene. Carbonyl-containing impurities can be removed by percolation through a Celite column impregnated with 2,4dinitrophenylhydrazine, phosphoric acid and H<sub>2</sub>O. (Prepared by dissolving 0.5g DNPH in 6mL of 85% H<sub>3</sub>PO<sub>4</sub> by grinding together, then adding and mixing 4mL of distd H<sub>2</sub>O and 10g Celite.) [Schwartz and Parker Anal Chem 33 1396 1961.] \*Benzene has been freed from thiophene by refluxing with 10% (w/v) of Raney nickel for 15min, after which the nickel was removed by filtration or centrifugation.

Dry \*benzene was obtained by doubly distilling high purity \*benzene from a soln containing the blue ketyl formed by the reaction of sodium-potassium alloy with a small amount of benzophenone.

Thiophene has been removed from \*benzene (absence of bluish-green coloration when 3mL of \*benzene is shaken with a soln of 10mg of isatin in 10mL of conc  $H_2SO_4$ ) by refluxing the \*benzene (1Kg) for several hours with 40g HgO (freshly pptd) dissolved in 40mL glacial acetic acid and 300mL of water. The ppte was filtered off, the aq phase was removed and the \*benzene was washed twice with  $H_2O$ , dried and distd. Alternatively, \*benzene dried with CaCl<sub>2</sub> has been shaken vigorously for half an hour with anhydrous AlCl<sub>3</sub> (12g/L) at 25-35°, then decanted, washed with 10% NaOH, and water, dried and distd. The process was repeated, giving thiophene-free \*benzene. [Holmes and Beeman *Ind Eng Chem* **26** 172 1934.]

After shaking successively for about an hour with conc  $H_2SO_4$ , distd water (twice), 6M NaOH, and distd water (twice), \*benzene was distd through a 3-ft glass column to remove most of the water. Abs EtOH was added and the \*benzene-alcohol azeotrope was distd. (This low-boiling distn leaves any non-azeotrope-forming impurities behind.) The middle fraction was shaken with distd water to remove EtOH, and again redistd. Final slow and very careful fractional distn from sodium, then LiAlH<sub>4</sub> under N<sub>2</sub>, removed traces of water and peroxides. [Peebles, Clarke and Stockmayer J Am Chem Soc 82 2780 1960.] \*Benzene liquid and vapour are very TOXIC and HIGHLY FLAMMABLE, and all operations should be carried out in an efficient fume cupboard and in the absence of naked flames in the vicinity.

**Rapid purification:** To dry benzene, alumina,  $CaH_2$  or 4A molecular sieves (3% w/v) may be used (dry for 6h). Then benzene is distd, discarding the first 5% of distillate, and stored over molecular sieves (3A, 4A) or Na wire.

 $[^{2}H_{6}]$ \*Benzene (\**benzene-d*<sub>6</sub>) [1076-43-3] M 84.2, b 80°/773.6mm, 70°/562mm, 60°/399mm, 40°/186.3mm, 20°/77.1mm, 10°/49.9mm, 0°/27.5mm, d 0.9488, d<sup>40</sup> 0.9257, n 1.4991, n<sup>40</sup> 1.4865. Hexadeuteriobenzene of 99.5% purity is refluxed over and distd from CaH<sub>2</sub> onto Linde type 5A sieves under N<sub>2</sub>.

**Benzeneazodiphenylamine** (4-phenylazodiphenylamine) [28110-26-1] M 273.3, m 82°, pK<sup>22</sup> 1.52. Purified by chromatography on neutral alumina using anhydrous  $*C_6H_6$  with 1% anhydrous MeOH. The major component, which gave a stationary band, was cut out and eluted with EtOH or MeOH. [Högfeldt and Bigeleisen J Am Chem Soc 82 15 1960.] Crystd from pet ether or EtOH. See Sudan I.

1-Benzeneazo-2-naphthol [842-07-9] M 248.3, m 134°, pK<sub>Est</sub> ~9.5 (OH). Crystd from EtOH.

1-Benzeneazo-2-naphthylamine (Yellow AB) [85-84-7] M 247.3, m 102-104°, pK<sub>Est</sub> ~4.1. Crystd from glacial acetic acid, acetic acid/water or ethanol.

**1,2-Benzenedimethanol** (1,2-bishydroxymethylbenzene) [612-14-6] M 138.2, m 61-64°, 63-64°, 64-65°, 65-66.5°, b 145°/3mm. Recrystd from  $C_6H_6$ , H<sub>2</sub>O, pet ether or pentane. It has been extracted in a Soxhlet with Et<sub>2</sub>O, evaporated and recrystd from hot pet ether. Also dissolve in Et<sub>2</sub>O, allow to evaporate till crystals are formed, filter off and wash the colourless crystals with warm pet ether or pentane. The *diacetate* has m 35°, 35-36°. [J Am Chem Soc 69 1197 1947, IR and UV: J Am Chem Soc 74 441 1952.]

*m*-Benzenedisulfonic acid [98-48-6] M 238.2,  $pK_{Est}$  <0. Freed from H<sub>2</sub>SO<sub>4</sub> by conversion to the calcium or barium salts (using Ca(OH)<sub>2</sub> or Ba(OH)<sub>2</sub>, and filtering). The calcium salt was then converted to the potassium salt, using K<sub>2</sub>CO<sub>3</sub>. Both the potassium and the barium salts were recrystd from H<sub>2</sub>O, and the acid was regenerated by passing through the H<sup>+</sup> form of a strong cation exchange resin. The acid was recrystd twice from conductivity water and dried over CaCl<sub>2</sub> at 25°. [Atkinson, Yokoi and Hallada J Am Chem Soc 83 1570 1961.] It has also been crystd from Et<sub>2</sub>O and dried in a vacuum oven.

*m*-Benzenedisulfonyl chloride [585-47-7] M 275.1, m 63°. Crystd from CHCl<sub>3</sub> (EtOH free, by passing through an alumina column) and dried at 20mm pressure.

**Benzene-1,2-dithiol** [17534-15-5] M 142.2, m 24-25°, 27-28°, b 110-112°, pKEst(1) ~6.0, pK<sub>Est(2)</sub>~9.4. Likely impurities are the oxidation products, the disulfides which could be polymeric. Dissolve in aq NaOH until the soln is alkaline. Extract with Et<sub>2</sub>O and discard the extract. Acidify with cold HCl (diluted 1:1 by vol with H<sub>2</sub>O) to Congo Red paper under N<sub>2</sub> and extract three times with Et<sub>2</sub>O. Dry the Et<sub>2</sub>O with Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil residue under reduced press in an atmosphere of N<sub>2</sub>. The distillate solidifies on cooling. [UV: J Chem Soc 3076 1958; J Am Chem Soc 81 4939 1951; Org Synth Coll Vol V 419 1973.]

**Benzenesulfinic acid** [618-41-7] **M 142.2, m 84°, pK<sup>25</sup> 2.16 (2.74).** The acid is purified by dissolving the Na salt in H<sub>2</sub>O, acidifying to Congo Red paper with HCl and adding a concentrated soln of FeCl<sub>3</sub> whereby Fe sulfinate ppts. Collect the salt, wash with a little H<sub>2</sub>O, drain, suspend in H<sub>2</sub>O and add a slight excess of 1.5M aq NaOH. The Fe(OH)<sub>3</sub> ppts, it is filtd off, the sulfinic acid in the aq soln is extracted with

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Et<sub>2</sub>O, the extract is dried (Na<sub>2</sub>SO<sub>4</sub>) and evapl to give colorless crysts of benzenesulfinic acid  $\mathbf{m}$  84° which are stored under N<sub>2</sub> in the dark, as it slowly oxidises in air to the sulfonic acid [see Org Synth 42 62 1966].

**Benzenesulfonic acid** [98-11-3] **M 158.2, m 43-44°, 50-55°** (anhydrous), 65-66°,  $pK^{25}$  -2.7, 0.70 (2.53?) Purified by dissolving in a small volume of distd H<sub>2</sub>O and stirring with slightly less than the theoretical amount of BaCO<sub>3</sub>. When effervescence is complete and the solution is still acidic, filter off the insoluble barium benzenesulfonate. The salt is collected and dried to constant weight *in vacuo*, then suspended in H<sub>2</sub>O and stirred with a little less than the equivalent (half mol.) of sulfuric acid. The insoluble BaSO<sub>4</sub> (containing a little barium benzenesulfonate) is filtd off and the filtrate containing the free acid is evapd in a high vacuum. The oily residue will eventually crystallise when completely anhydrous. A 32% commercial acid was caused to fractionally cryst at room temp over P<sub>2</sub>O<sub>5</sub> in a vac desiccator giving finally colorless deliquescent plates **m** 52.5°. The anhydrous crystn acid is deliquescent and should be stored over anhyd Na<sub>2</sub>SO<sub>4</sub> in the dark and should be used in subdued sunlight as it darkens under sunlight. The main impurify is Fe which readily separates as the Fe salt in the early fractions [Taylor and Vincent J Chem Soc 3218 1952]. It is an IRRITANT to the skin and eyes. [see Org Synth Coll Vol I 84 1948; Michael and Adair Chem Ber 10 585 1877.]

Benzenesulfonic anhydride [512-35-6] M 298.3, m 88-91°. Crystd from Et<sub>2</sub>O.

**Benzenesulfonyl chloride** [98-09-9] M 176.6, m 14.5°, b 120°/10mm, 251.2°/760mm(dec), d 1.384. Distd, then treated with 3mole % each of toluene and AlCl<sub>3</sub>, and allowed to stand overnight. The free benzenesulfonyl chloride was distd off at 1mm pressure, and then carefully fractionally distd at 10mm in an all-glass column. [Jensen and Brown J Am Chem Soc 80 4042 1958.]

Benzene-1,2,4,5-tetracarboxylic (pyromellitic) acid [89-05-4] M 254.2, m 281-284°,  $pK_1^{25}$  1.87,  $pK_2^{25}$  2.72,  $pK_3^{25}$  4.30,  $pK_4^{25}$  5.52. See entry on p. 345.

Benzene-1,2,3-tricarboxylic (hemimellitic) acid (H<sub>2</sub>O) [36362-97-7] M 210.1, m 190°(dec),  $pK_1^{25}$  2.62,  $pK_2^{25}$  3.82,  $pK_3^{25}$  5.51. Crystd from water.

Benzene-1,3,5-tricarboxylic (trimesic or trimellitic) acid [554-95-0] M 210.1, m 360°(dec),  $pK_1^{25}$  2.64,  $pK_2^{25}$  3.71,  $pK_3^{25}$  5.01. Crystd from water.

1,2,4-Benzenetriol [533-73-3] M 126.1, m 141°, pK<sub>1</sub><sup>20</sup>9.08, pK<sub>2</sub><sup>20</sup>11.82. Crystd from Et<sub>2</sub>O.

Benzethonium chloride [121-54-0] M 448.1, m 164-166°. Crystd from 1:9 MeOH/Et<sub>2</sub>O mixture.

**Benzhydrol** (diphenylmethanol) [91-01-0] M 184.2, m 69°, b 297°/748mm, 180°/20mm. Crystd from hot H<sub>2</sub>O or pet ether (b 60-70°), pet ether containing a little \*benzene, from CCl<sub>4</sub>, or EtOH (1mL/g). An additional purification step is passage of a \*benzene soln through an activated alumina column. Sublimes in a vacuum. Also crystd three times from MeOH/H<sub>2</sub>O [Naguib J Am Chem Soc 108 128 1986]. § A commercial polystyrene supported version is available.

**Benzidine** (4,4'-diaminobiphenyl) [92-87-5] M 184.2, m 128-129°,  $pK_1^{2^0}3.85$ ,  $pK_2^{2^0}4.95$ . Its soln in \*benzene was decolorized by percolation through two 2-cm columns of activated alumina, then concentrated until benzidine crystd on cooling. Recrystd alternatively from EtOH and \*benzene to constant absorption spectrum [Carlin, Nelb and Odioso J Am Chem Soc 73 1002 1951]. Has also been crystd from hot water (charcoal) and from diethyl ether. Dried under vac in an Abderhalden pistol. Stored in the dark in a stoppered container. CARCINOGENIC.

Benzidine dihydrochloride [531-85-1] M 257.2, m >250°(dec). Crystd by soln in hot  $H_2O$ , with addition of conc HCl to the slightly cooled soln. CARCINOGENIC.

Benzil [134-81-6] M 210.2, m 96-96.5°. Crystd from \*benzene after washing with alkali. (Crystn from EtOH did not free benzil from material reacting with alkali.) [Hine and Howarth J Am Chem Soc 80 2274

1958.] Has also been crystd from CCl<sub>4</sub>, diethyl ether or EtOH [Inoue et al. J Chem Soc, Faraday Trans 1 82 523 1986].

**Benzilic acid (diphenylglycollic acid)** [76-93-7] M 228.3, m 150°, pK<sup>18</sup> 3.06. Crystd from \*benzene (*ca* 6mL/g), or hot H<sub>2</sub>O.

Benzil monohydrazone [5433-88-7] M 224.3, m 151°. Crystd from EtOH.

 $\alpha$ -Benzil monoxime [14090-77-8], [E, 574-15-2], [Z, 574-16-3] M 105.1, m 140°. Crystd from \*C<sub>6</sub>H<sub>6</sub> (must not use animal charcoal).

**Benzimidazole** [51-17-2] **M 118.1, m 172-173<sup>o</sup>, pK\_1^{25}5.53, pK\_2^{25}11.70.** Crystd from water or aqueous EtOH (charcoal), and dried at 100<sup>o</sup> for 12h.

**2-Benzimidazolylacetonitrile** [4414-88-4] M 157.2, m 200-205° dec, 209.7-210.7°(corrected), 210°. Recrystd from aqueous EtOH. It has been recrystd from hot H<sub>2</sub>O using charcoal, and finally from aqueous EtOH. [J Am Chem Soc 65 1072 1943].

Benzo[b]biphenylene [259-56-3] M 202.2, m dec >250°. Purified by sublimation under reduced pressure.

Benzo-15-crown-5 [14098-44-3] M 268.3, m 78-80°. Recrystd from *n*-heptane. IRRITANT.

**Benzo-18-crown-6** [14098-24-9] M **312.2, m 42-45°, 43-43.5°.** Purified by passage through a DEAE cellulose column in cyclohexane. Recryst from *n*-hexane. Its complex with thiourea has m 127° [5-6 mol of urea to ether, J Org Chem 36 1690 1971]. The stability constants of Na<sup>+</sup>, K<sup>+</sup>, Rb<sup>+</sup>, Cs<sup>+</sup>, Tl<sup>+</sup> and Ba<sup>2+</sup> are in *Inorg Chim Acta* 28 73 1978] [NMR: J Am Chem Soc 98 3769 1976]. IRRITANT.

**Benzo[3,4]cyclobuta[1,2-b]quinoxaline** [259-57-4] **M 204.2, m dec >250°.** Purified by sublimation under reduced pressure.

**Benzofuran** (coumarone) [271-89-6] M 118.1, b 62-63°/15mm, 97.5-99.0°/80mm, 170-173°/atm, 173-175°(169)/760mm,  $d_4^{20}$  1.0945,  $n_D^{20}$  1.565. Steam distil, dissolve in Et<sub>2</sub>O, wash with 5% aqueous NaOH, saturated NaCl, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and distil. UV:  $\lambda_{max}$  245, 275, 282nm (log  $\varepsilon$  4.08, 3.45, 3.48). The *picrate* has m 102-103°. [Org Synth Coll Vol V 251 1973; NMR: Black and Heffernan Aust J Chem 18 353 1965.]

2-Benzofurancarboxylic acid [496-41-3] M 162.1, m 192-193°, pK<sub>Est</sub> ~3.2. Crystd from water.

Benzofurazan [273-09-6] M 120.1, m 55°. Purified by crystn from EtOH and sublimed.

**Benzoic acid** [65-85-0] **M 122.1, m 122.6-123.1°, pK^{25} 4.12.** For use as a volumetric standard, analytical reagent grade benzoic acid should be carefully fused to *ca* 130° (to dry it) in a platinum crucible, and then powdered in an agate mortar. Benzoic acid has been crystd from boiling water (charcoal), aq acetic acid, glacial acetic acid, \*C<sub>6</sub>H<sub>6</sub>, aq EtOH, pet ether (b 60-80°), and from EtOH soln by adding water. It is readily purified by fractional crystn from its melt and by sublimation in a vacuum at 80°.

o-Benzoic acid sulfimide (saccharin, 1,2-benzisothiazol-3(2H)-one 1,1-dioxide) [81-07-2] M 183.2, m 227-229°, 229°, 228.8-229.7°, pK<sup>25</sup> 1.31, pK<sup>25</sup> 12.8. Purified by recrystn from Me<sub>2</sub>CO [solubility 7.14% at 0°, 14.4% at 50°], or aqueous isoPrOH to give a fluorescent soln. [Am J Pharm 41 17 1952.]

**Benzoic anhydride** [93-97-0] M 226.2, m 42°. Freed from benzoic acid by washing with NaHCO<sub>3</sub>, then water, and drying. Crystd from \*benzene (0.5mL/g) by adding just enough pet ether (b 40-60°), to cause cloudiness, then cooling in ice. Can be distd at 210-220°/20mm.

(±)-Benzoin (2-hydroxy-2-phenylacetophenone) [119-53-9] M 212.3, m 137°. Crystd from CCl<sub>4</sub>, hot EtOH (8mL/g), or 50% acetic acid. Crystd from high purity \*benzene, then twice from high purity MeOH, to remove fluorescent impurities [Elliott and Radley Anal Chem 33 1623 1961]. Sublimes.

(±)-α-Benzoinoxime [441-38-3] M 227.3, m 151°. Crystd from diethyl ether.

**Benzonitrile** [100-47-0] **M 103.1, f -12.9°, b 191.1°, d 1.010, n 1.528.** Dried with CaSO<sub>4</sub>, CaCl<sub>2</sub>, MgSO<sub>4</sub> or K<sub>2</sub>CO<sub>3</sub>, and distd from P<sub>2</sub>O<sub>5</sub> in an all-glass apparatus, under reduced pressure (**b** 69°/10mm), collecting the middle fraction. Distn from CaH<sub>2</sub> causes some decomposition of solvent. Isonitriles can be removed by preliminary treatment with conc HCl until the smell of isonitrile has gone, followed by preliminary drying with K<sub>2</sub>CO<sub>3</sub>. (This treatment also removes amines).

Steam distd (to remove small quantities of carbylamine). The distillate was extracted into ether, washed with dil Na<sub>2</sub>CO<sub>3</sub>, dried overnight with CaCl<sub>2</sub>, and the ether removed by evaporation. The residue was distd at 40mm (**b** 96°) [Kice, Perham and Simons J Am Chem Soc 82 834 1960].

Conductivity grade benzonitrile (specific conductance 2 x  $10^{-8}$  mho) was obtained by treatment with anhydrous AlCl<sub>3</sub>, followed by rapid distn at 40-50° under vacuum. After washing with alkali and drying with CaCl<sub>2</sub>, the distillate was vac distd several times at 35° before being fractionally crystd several times by partial freezing. It was dried over finely divided activated alumina from which it was withdrawn as required [Van Dyke and Harrison J Am Chem Soc 73 402 1951].

**Benzo[ghi]perylene** (1,12-benzoperylene) [191-24-2] M 276.3, m 273°, 277-278.5°, 278-280°. Purified as light green crystals by recrystn from  $C_{6}H_6$  or xylene and sublimes at 320-340° and 0.05mm [UV Helv Chim Acta 42 2315 1959; Chem Ber 65 846 1932; Fluoresc. Spectrum: J Chem Soc 3875 1954]. 1,3,5-Trinitrobenzene complex m 310-313° (deep red crystals from  $C_{6}H_6$ ); picrate m 267-270° (dark red crystals from  $C_{6}H_6$ ); styphnate (2,4,6-trinitroresorcinol complex) m 234° (wine red crystals from  $C_{6}H_6$ ). It recrystallises from propan-1-ol [J Chem Soc 466 1959].

3,4-Benzophenanthrene [195-19-7] M 228.3, m 68°. Crystd from EtOH, pet ether, or EtOH/Me<sub>2</sub>CO.

**Benzophenone** [119-61-9] **M 182.2, m 48.5-49°, pK -6.0 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from MeOH, EtOH, cyclohexane, \*benzene or pet ether, then dried in a current of warm air and stored over BaO or P<sub>2</sub>O<sub>5</sub>. Also purified by zone melting and by sublimation [Itoh J Phys Chem **89** 3949 1985; Naguib et al. J Am Chem Soc **108** 128 1986; Gorman and Rodgers J Am Chem Soc **108** 5074 1986; Ohamoto and Teranishi J Am Chem Soc **108** 6378 1986; Naguib et al. J Phys Chem **91** 3033 1987].

Benzophenone oxime [574-66-3] M 197.2, m 142°, pK 11.18. Crystd from MeOH (4mL/g).

Benzopinacol [464-72-2] M 366.5, m 170-180° (depends on heating rate). Crystd from EtOH.

**Benzo[a]pyrene** (3,4 benzpyrene) [50-32-8] M 252.3, m 177.5-178°, 179.0-179.5°. A soln of 250mg in 100mL of \*benzene was diluted with an equal volume of hexane, then passed through a column of alumina, Ca(OH)<sub>2</sub> and Celite (3:1:1). The adsorbed material was developed with a 2:3 \*benzene/hexane mixture. (It showed as an intensely fluorescent zone.) The main zone was eluted with 3:1 acetone/EtOH, and was transferred into 1:1 \*benzene-hexane by adding H<sub>2</sub>O. The soln was washed, dried with Na<sub>2</sub>SO<sub>4</sub>, evaporated and crystd from \*benzene by the addition of MeOH [Lijinsky and Zechmeister J Am Chem Soc 75 5495 1953]. Alternatively it can be chromatographed on activated alumina, eluted with a cyclohexane-\*benzene mixture containing up to 8% \*benzene, and the solvent evapl under reduced pressure [Cahnmann Anal Chem 27 1235 1955], and recrystd from EtOH [Nithipatikom and McGown Anal Chem 58 3145 1986]. CARCINOGENIC.

**Benzo[e]pyrene** (1,2-benzpyrene) [192-97-2] M 252.3, m 178-179°, 178-180°. Purified by passage through an  $Al_2O_3$  column (Woelm, basic, activity I) and eluted with  $*C_6H_6$  and recrystd from 2 volumes of EtOH- $*C_6H_6$  (4:1). Forms colourless or light yellow prisms or needles. [J Chem Soc 3659 1954; Justus Liebigs Ann Chem 705 190 1967.] 1,3,5-Trinitrobenzene complex m 253-254° (orange needles from

EtOH); the *picrate* prepared by mixing 20mg in 1mL of  $C_6H_6$  with 20mg of picric acid in 2mL  $C_6H_6$ , collecting the deep red crystals, and recrystallising from  $C_6H_6$  m 228-229° [Synth J Chem Soc 398 1967; NMR: J Chem Phys 47 2020 1967]. CARCINOGEN.

**3,4-Benzoquinoline (phenanthridine)** [229-87-8] M 179.2, m 108-109°, b 350°,  $pK^{20}4.61$ . Chromatographed on activated alumina from \*benzene soln, with diethyl ether as eluent. Evapn of ether gave crystalline material which was freed from residual solvent under vacuum, then further purified by fractional crystn under N<sub>2</sub>, from its melt . Sublimes in vacuo. See also p. 324.

5,6-Benzoquinoline [85-02-9] M 179.0, m 93°, b 350°, pK<sup>20</sup> 5.11. As 3,4-benzoquinoline above.

7,8-Benzoquinoline [230-27-3] M 179.0, m 52.0-52.5°, pK<sup>20</sup>4.21. As 3,4-benzoquinoline above.

*p*-Benzoquinone [106-51-4] M 108.1, m 115.7°. Usually purified in one or more of the following ways: steam distn, followed by filtration and drying (e.g. in a desiccator over CaCl<sub>2</sub>); crystn from pet ether (b 80-100°), \*benzene (with, then without, charcoal), water or 95% EtOH; sublimation under vacuum (e.g. from room temperature to liquid N<sub>2</sub>). It slowly decomposes, and should be stored, refrigerated, in an evacuated or sealed glass vessel in the dark. It should be resublimed before use. [Wolfenden et al. J Am Chem Soc 109 463 1987.]

**1-Benzosuberone** (6,7,8,9-tetrahydrobenzocyclohepten-5-one) [826-73-3] M 160.2, b 80-85°/0.5mm, 90-93°/1mm, 138-139°/12mm, 154°/15mm, 175-175°/40mm,  $d_4^{20}$  1.086,  $n_D^{20}$  1.5638. Purified by dissolving in toluene, washing with aqueous 5% NaOH, then brine, dried (MgSO<sub>4</sub>), and distd. 2,4-Dinitrophenylhydrazone has m 210.5°, 207-208° (from CHCl<sub>3</sub> + MeOH). Z-O-Picryloxime has m 156-157° (from Me<sub>2</sub>CO+MeOH); the E-O-picryloxime has m 107°. The oxime has m 106.5-107.5°. [UV J Am Chem Soc 73 1411 1951, 75 3744 1953; Chem Ber 90 1844 1957.]

1,2,3-Benzothiadiazole [273-77-8] M 136.2, m 35°, pK<sub>Est</sub> ~<0. Crystd from pet ether.

2,1,3-Benzothiadiazole [272-13-2] M 136.2, m 44°, b 206°/760mm,  $pK_{Est} < 0$ . Crystd from pet ether.

1-Benzothiophene (benzo[b]thiophene, thianaphthene) [95-15-8] M 134.2, m 29-32°, 30°, 31-32°, 32°, b 100°/16mm, 103-105°/20mm, 221-222°/760mm,  $d_4^{32.2}$  1.1484,  $n_D^{39}$ 1.6306. It has the odour of naphthalene. If the IR spectrum is not very good then suspend in a faintly alkaline aqueous soln and steam distil. Extract the distillate with Et<sub>2</sub>O, dry the extract with CaCl<sub>2</sub>, filter, evaporate the solvent and fractionate the residue. Distillate sets solid. The *sulfoxide* has m 142°, the *picrate* has m 148-149° (yellow crystals from EtOH) and the *styphnate* has m 136-137°. [J Org Chem 10, 381 1945; Chem Ber 52B 1249 1919, 53 1551 1920; The Chemistry of Heterocyclic Compounds Hartough and Weisel eds, Interscience Publ, NY, p23, 28, 1954.]

1,2,3-Benzotriazole [95-14-7] M 119.1, m 96-97°, 98.5°, 100°, b 159°/0.2mm, 204°/15mm,  $pK_1^{20}$  1.6,  $pK_2^{20}$  8.64. Crystd from toluene, CHCl<sub>3</sub>, Me<sub>2</sub>NCHO or satd aq soln, and dried at room temperature or in a vacuum oven at 65°. Losses are less if material is distd in a vacuum. CAUTION: may EXPLODE during vac distn, necessary precautions must be taken. [Org Synth Coll Vol III 106 1955.]

**O-Benzotriazol-1-yl-N, N, N', N'-tetramethyluronium hexafluorophosphate (HBTU)** [94790-37-1] **M 379.2, m 200° (dec), 250°, 254°(dec).** Wash with  $H_2O$  (3 x),  $CH_2Cl_2$  (3 x), dry and recryst from MeCN. Dry in a vacuum and store cold in the dark [Dourtoglou et al. *Tetrahedron Lett* 1269 1978, NMR: Synthesis 572 1984].

**Benzoylacetone** (1-phenyl-1,3-butanedione) [93-91-4] M 162.2, m 58.5-59.0°. Crystd from Et<sub>2</sub>O or MeOH and dried under vacuum at 40°.

**2-Benzoylbenzoic acid** [85-52-9] **M 226.2, m 126-129°, 129.2, 130°, pK^{25} 3.54.** Recrystd from \*C<sub>6</sub>H<sub>6</sub> or cyclohexane, but is best recrystallised by dissolving in a small volume of hot toluene and then adding just enough pet ether to cause pptn and cool. Dry in a low vacuum at 80°. It can be sublimed at 230-240°/0.3mm [J Chem Soc 265 1957]. The S-benzylthiouronium salt has m 177-178° (from EtOH). [J Am Chem Soc 75 4087 1953; Chem Ber **90** 1208 1957.]

3-Benzoylbenzoic acid [579-18-0] M 226.2, m 164-166°, pK<sub>Est</sub>~3.5. Cryst from EtOH; vac subl.

**4-Benzoylbenzoic acid** [611-95-0] **M 226.2, m 196.5-198°**, **197-200°**, **pK**<sub>Est</sub> ~3.7. Dissolve in hot H<sub>2</sub>O by adding enough aqueous KOH soln till distinctly alkaline, filter and then acidify with drops of conc HCl. Filter off, wash solid with cold H<sub>2</sub>O, dry at 100°, and recrystallise from EtOH. [J Am Chem Soc 55 2540 1933.]

(S +) and (R -) 1-Benzoyl-2-tert-butyl-3-methyl-4-imidazolinone [R- 101055-57-6] [S-101055-56-5] M 260.3, m 142-143°, 145.6-146.6°, 145-147°,  $[\alpha]_{546}^{20}$  (+) and (-) 155°,  $[\alpha]_D^{20}$  (+) and (-) 133° (c 1, CHCl<sub>3</sub>). Recrystd from boiling EtOH (sol 1.43g/mL) or better by dissolving in CH<sub>2</sub>Cl<sub>2</sub> and adding pentane, filter and dry for at least 12h at 60°/0.1mm and sublimed at 135°/0.01mm. It has also been purified by flash column chromatography with Merck silica gel at 0.04-0.063mm and using Et<sub>2</sub>O/pet ether/MeOH (60:35:5) as eluent. It is then recrystd from EtOH/pet ether. [IR, NMR: Helv Chim Acta 70 237 1987; Angew Chem, Int Ed Engl 25 345 1986.] The racemate is purified in a similar manner and has m 104-105° [NMR: Helv Chim Acta 68 949 1985].

**Benzoyl chloride** [98-88-4] M 140.6, b 56°/4mm, 196.8°/745mm, d 1.2120,  $n^{10}$  1.5537. A soln of benzoyl chloride (300mL) in \*C<sub>6</sub>H<sub>6</sub> (200mL) was washed with two 100mL portions of cold 5% NaHCO<sub>3</sub> soln, separated, dried with CaCl<sub>2</sub> and distd [Oakwood and Weisgerber Org Synth III 113 1955]. Repeated fractional distn at 4mm Hg through a glass helices-packed column (avoiding porous porcelain or silicon-carbide boiling chips, and hydrocarbon or silicon greases on the ground joints) gave benzoyl chloride that did not darken on addition of AlCl<sub>3</sub>. Further purification was achieved by adding 3 mole% each of AlCl<sub>3</sub> and toluene, standing overnight, and distilling off the benzoyl chloride at 1-2mm [Brown and Jenzen J Am Chem Soc 80 2291 1958]. Refluxing for 2h with an equal weight of thionyl chloride before distn, has also been used. Strong IRRITANT. Use in a fume cupboard.

**Benzoylformic acid** (phenylglyoxylic acid) [611-73-4] M 150.14, m 62-65°, 64.5-65.5°, 67°, b 84°/0.1mm, 163-167°/15mm, pK<sup>25</sup> 1.39 (1.79). If the sample is oily then it may contain H<sub>2</sub>O. In this case dry in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> or KOH until crisp. For further purification dissolve 5.5g in hot CCl<sub>4</sub> (750mL), add charcoal (2g, this is necessary otherwise the acid may separate as an oil), filter, cool in ice-water until crystallisation is complete. Filter the acid, and the solvent on the crystals is removed by keeping the acid (4.5g) in a vacuum desiccator for 2 days. Slightly yellow crystals are obtained. It can be recrystd also from \*C<sub>6</sub>H<sub>6</sub>/pet ether, and can be distilled in vacuum. The acid is estimated by titration with standard NaOH. The phenylhydrazone is recrystallised form EtOH, m 163-164°; the semicarbazone acid has m 259°(dec) (from EtOH). The methyl ester distils at 137°/14mm, 110-111°/2mm, n<sub>D</sub><sup>20</sup> 1.5850. [J Am Chem Soc 67 1482 1945; J Org Chem 24 1825 1959.]

Benzoyl glycine (hippuric acid) [495-69-2] M 179.2, m 188°,  $pK^{40}$  3.59. Crystd from boiling H<sub>2</sub>O. Dried over P<sub>2</sub>O<sub>5</sub>.

Benzoyl isothiocyanate [532-55-8] M 163.2, m 25.5-26°, b 72.5-73°/6mm, 88-91°/20mm, 94-96°/21mm, 202.5-204°/724mm, 250-255°/atm,  $d_4^{20}$  1.213,  $n_D^{20}$  1.637. Distil over a small amount of P<sub>2</sub>O<sub>5</sub>, whereby the distillate crystallises in prisms. It is readily hydrolysed by H<sub>2</sub>O to give benzamide and benzoylurea, but with NH<sub>3</sub> it gives *benzoylurea* m 210° which can be recrystd from EtOH. [J Am Chem Soc 62 1595 1940, 76 580 1954; Org Synth Coll Vol III 735 1955.]

**Benzoyl peroxide** [94-36-0] **M 242.2, m 95°(dec).** Dissolved in CHCl<sub>3</sub> at room temperature and ppted by adding an equal volume of MeOH or pet ether. Similarly ppted from acetone by adding two volumes of distilled water. Has also been crystd from 50% MeOH, and from diethyl ether. Dried under vacuum at room

temperature for 24h. Stored in a desiccator in the dark at 0°. When purifying in the absence of water it can be **EXPLOSIVE** and it should be done on a very small scale with adequate protection. Large amounts should be kept moist with water and stored in a refrigerator. [Kim et al. J Org Chem 52 3691 1987.]

*p*-Benzoylphenol (4-hydroxybenzophenone) [1137-42-4] M 198.2, m 133.4-134.8°, pK<sup>25</sup> 7.95. Dissolved in hot EtOH (charcoal), crystd once from EtOH/H<sub>2</sub>O and twice from \*benzene [Grunwald J Am Chem Soc 73 4934 1951; Dryland and Sheppard J Chem Soc Perkin Trans 1 125 1986].

N-Benzoyl-N-phenylhydroxylamine [304-88-1] M 213.2, m 121-122°. Recrystd from hot water, \*benzene or acetic acid.

**2-Benzoylpyridine** [91-02-1] M 183.2, m 41-43°, 48-50°, 72°/0.02mm, 104-105°/0.01,  $n_D^{24}$ 1.6032, pK<sub>Est</sub> ~2.4. Dissolve in Et<sub>2</sub>O, shake with aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, dry over MgSO<sub>4</sub>, it solidifies on cooling. The solid can be recrystd from pet ether. Its hydrochloride crystallises from Me<sub>2</sub>CO, m 126-127°, and the 2,4-dinitrophenylhydrazone has m 193-195°. [J Organomet Chem 24 623 1970.]

**Benzoyl sulfide** [644-32-6] M 174.4, m 131.2-132.3°. About 300mL of solvent was blown off from a filtered soln of benzoyl disulfide (25g) in acetone (350mL). The remaining acetone was decanted from the solid which was recrysted first from 300mL of 1:1 (v/v) EtOH/ethyl acetate, then from 300mL of EtOH, and finally from 240mL of 1:1 (v/v) EtOH/ethyl acetate. Yield about 40% [Pryor and Pickering J Am Chem Soc 84 2705 1962]. Handle in a fume cupboard because of TOXICITY and obnoxious odour.

2,1-Benzoxathiol-3-one-1,1-dioxide (sulfobenzoic acid anhydride) [81-08-3] M 184.2, m 116-124°, 126-127°, 128°, b 184-186°/18mm. Purified by distn in a vacuum and readily solidifies to a crystalline mass on cooling. [J Am Chem Soc 34 1594 1912.] Alternatively purified by dissolving in the minimum vol of toluene and reflux for 2h using a Dean-Stark trap. Evaporate under reduced pressure and distil the anhydride at 18mm. It can then be recrystd three times from its own weight of dry  $*C_6H_6$ . It is sensitive to moisture and should be stored in the dark in a dry atmosphere. The O-methyloxime has m 110-112° [Tetrahedron Lett 3289 1972]. [Org Synth Coll Vol I 495 1941.] (See also p. 568 in Chapter 6.)

Benzoxazolinone [59-49-4] M 135.1, m 137-139°, 142-143°(corrected), b 121-213°/17mm, 335-337°/760mm. It can be purified by recrystn from aqueous Me<sub>2</sub>CO then by distn at atm pressure then in a vacuum. The methyl mercury salt recryst from aq EtOH has m 156-158°. [J Am Chem Soc 67 905 1945.]

N-Benzoyl-o-tolylhydroxylamine [1143-74-4] M 227.3, m 104°. Recrystd from aqueous EtOH.

Benzyl-2-acetamido-4,6-O-benzylidene-2-deoxy- $\alpha$ -D-glucopyranoside [13343-63-0] M 399.4, m 256-261°, 263-264°,  $[\alpha]_D^{26}$ +120° (c 1, pyridine). Wash with cold isoPrOH and crystallise from dioxane/isoPrOH. [J Org Chem 32 2759 1967.]

Benzyl acetate [140-11-4] M 150.2, m -51°, b 92-93°/10mm, 134°/102mm, 214.9°/760mm,  $d_4^{20}$  1.0562,  $n_D^{25}$  1.4994. Purified by fractional distn, preferably in a good vacuum. Values of  $n^{25}$  of 1.5232-1.5242 seem too high and should be 1.4994. [J Org Chem 26 5180 1961.]

Benzyl acetoacetate [5396-89-4] M 192.2, b 130°/2mm, 156-157°/10mm, 162-167°/15mm, 275-277°/atm,  $d_4^{20}$  1.114,  $n_D^{20}$  1.514. Fractionate and collect fractions of expected physical properties. Otherwise add *ca* 10% by weight of benzyl alcohol and heat in an oil bath (160-170°, open vessel) for 30min during which time excess of benzyl alcohol will have distd off, then fractionate. [*J Org Chem* 17 77 1952.]

4'-Benzylacetophenone [782-92-3] M 210.3, m 73°. Crystd from EtOH (ca 1mL/g).

**Benzyl alcohol** [100-51-6] M 107.2, f -15.3°, b 205.5°, 93°/10mm, d 0.981, n 1.54033,  $pK^{25}$  15.4. Usually purified by careful fractional distn at reduced pressure in the absence of air. Benzaldehyde, if present, can be detected by UV absorption at 283nm. Also purified by shaking with aq KOH and extracting with peroxide-free diethyl ether. After washing with water, the extract was treated with satd NaHS sol, filtered,

washed and dried with CaO and distd under reduced pressure [Mathews J Am Chem Soc 48 562 1926]. Peroxy compounds can be removed by shaking with a soln of Fe(II) followed by washing the alcohol layer with distd water and fractionally distd.

Benzylamine [100-46-9] M 107.2, b 178°/742mm, 185°/768mm, d 0.981, n 1.5392,  $pK^{25}$  9.33. Dried with NaOH or KOH, then distd under N<sub>2</sub>, through a column packed with glass helices, taking the middle fraction. Has also been distd from zinc dust under reduced pressure.

Benzylamine hydrochloride [3287-99-8] M 143.6, m 248° (rapid heating). Crystd from water.

*N*-Benzylaniline (*N*-phenylbenzylamine) [103-32-2] M 183.4, m 36°, b 306-307°, d 1.061,  $pK^{25}$  4.04. Crystd from pet ether (b 60-80°) (*ca* 0.5mL/g).

**1-Benzyl-1-aza-12-crown-4** (10-benzyl-1,4,7-trioxa-10-azacyclododecane) [84227-47-4] M 265.4, 122-125°/0.03mm, 140-143°/0.05mm,  $d_4^{20}$  1.09,  $n_D^{20}$  1.52, pK<sub>Est</sub> ~ 7.7. Dissolve in CH<sub>2</sub>Cl<sub>2</sub> or CCl<sub>4</sub> (1g in 30mL) wash with H<sub>2</sub>O (30mL), brine (30mL), H<sub>2</sub>O (30 mL) again, dry over MgSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub> and evaporate. The residue in CH<sub>2</sub>Cl<sub>2</sub> is chromatographed through Al<sub>2</sub>O<sub>3</sub> (eluting with 10% EtOAc in hexane), evaporate, collect the correct fractions and distil (Kügelrohr). Log K<sub>Na</sub> in dry MeOH at 25° for Na<sup>+</sup> complex is 2.08. [*Tetrahedron Lett* 26 151 1985; J Org Chem 53 5652 1988.]

**Benzyl bromide** [100-39-0] **M 171.0, m -4°, b 85°/12mm, 192°/760mm, d 1.438, n 1.575.** Washed with conc H<sub>2</sub>SO<sub>4</sub> (CARE), water, 10% Na<sub>2</sub>CO<sub>3</sub> or NaHCO<sub>3</sub> soln, and again with water. Dried with CaCl<sub>2</sub>, Na<sub>2</sub>CO<sub>3</sub> or MgSO<sub>4</sub> and fractionally distd in the dark, under reduced pressure. It has also been thoroughly degassed at 10<sup>-6</sup> mm and redistd in the dark. This gave material with  $\lambda_{max}$  (MeCN): 226nm ( $\varepsilon$  8200) [Mohammed and Kosower J Am Chem Soc 93 2709 1971]. Handle in a fume cupboard, extremely LACHRYMATORY.

Benzyl bromoacetate [5437-45-6] M 229.1, b 96-98°/0.1mm, 146°/12mm, 166-170°/22mm,  $d_4^{20}$  1.444,  $n_D^{25}$  1.5412. Dilute with Et<sub>2</sub>O, wash with 10% aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, dry (MgSO<sub>4</sub>) and fractionate using a Fenske (glass helices packing) column. [*J Chem Soc* 1521 1956.] LACHRYMATORY

**N-Benzyl-tert-butylamine** (*N-tert-butylbenzylamine*) [3378-72-1] M 163.3, b 91°/12 mm, 109-110°/25 mm, 218-220°/atm,  $d_4^{20}$  0.899,  $n_D^{25}$  1.4942., pK<sup>25</sup> 10.19. Dissolve in Et<sub>2</sub>O, dry over KOH pellets, filter and fractionate in a N<sub>2</sub> atmosphere to avoid reaction with CO<sub>2</sub> from the air. The hydrochloride has m 245-246°(dec) (from MeOH + Me<sub>2</sub>CO) and the perchlorate has m 200-201°. [J Am Chem Soc 80 4320 1958.]

**Benzyl carbamate** [621-84-1] **M 151.2, m 86°, 86-88°, 90-91°**. If it smells of NH<sub>3</sub> then dry in a vac desiccator and recryst from 2 vols of toluene and dry in a vac desiccator again. It forms glistening plates from toluene, and can be recrystd from H<sub>2</sub>O [J Org Chem 6 878 1941; Org Synth Coll Vol III 168 1955].

**Benzyl** chloride [100-44-7] M 126.6, m 139°, b 63°/8mm, d 1.100, n 1.538. Dried with MgSO<sub>4</sub> or CaSO<sub>4</sub>, or refluxed with fresh Ca turnings, then fractionally distd under reduced pressure, collecting the middle fraction and storing with CaH<sub>2</sub> or P<sub>2</sub>O<sub>5</sub>. Has also been purified by passage through a column of alumina. Alternatively it is dried over MgSO<sub>4</sub> and distd in a vacuum. The middle fraction is degassed by several freeze-thaw cycles and then fractionated in an 'isolated fractionating column' (which has been evacuated and sealed off at ~10<sup>-6</sup> mm) over a steam bath. The middle fraction is retained. The final samples were vacuum distd from this sample and again retaining the middle fraction. The purity is >99.9% (no other peaks are visible on GLC and the NMR spectrum is consistent with the structure. [Mohammed and Kosower J Am Chem Soc 93 1709 1971.] IRRITANT and strongly LACHRYMATORY.

N-Benzyl-ß-chloropropionamide [24752-66-7] M 197.7, m 94°. Crystd from MeOH.

Benzyl cinnamate [103-41-3] M 238.3, m 34-35°, 39°, b 154-157°/0.5mm, 228-230°/22mm. Recrystd to constant melting point from 95% EtOH and has the odour of balsam. Alternatively dissolve in Et<sub>2</sub>O, wash with 10% aqueous Na<sub>2</sub>CO<sub>3</sub>, H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and fractionate under reduced press using a short Vigreux column. It decomposes when boiled at atm press. [J Am Chem Soc **74** 547 1952; **84** 2550 1962.]

Benzyl cyanide [140-29-4] M 117.1, b 100°/8mm, 233.5°/760mm, d 1.015, n 1.523. Benzyl isocyanide can be removed by shaking vigorously with an equal volume of 50% H<sub>2</sub>SO<sub>4</sub> at 60°, washing with satd aq NaHCO<sub>3</sub>, then half-saturated NaCl soln, drying and fractionally distilling under reduced pressure. Distn from CaH<sub>2</sub> causes some decomposition of this compound: it is better to use P<sub>2</sub>O<sub>5</sub>. Other purification procedures include passage through a column of highly activated alumina, and distn from Raney nickel. *Precautions should be taken because of possible formation of free* TOXIC cyanide; use an efficient fume cupboard.

**N-Benzyl dimethylamine** [103-83-3] **M 135.2, b 66-67°/15mm, 83-84°/30mm, 98-99°/24mm,**  $d_4^{20}$  0.898,  $n_D^{20}$  1.516,  $pK^{25}$  8.91. Dry over KOH pellets and fractionate over Zn dust in a CO<sub>2</sub>—free atmosphere. It has a pKa<sup>25</sup> of 8.25 in 45% aq EtOH. Store under N<sub>2</sub> or in a vacuum. The picrate has **m** 94-95°, and the picrolonate has **m** 151° (from EtOH). [Chem Ber 63 34 1930; J Am Chem Soc 55 3001 1933; J Chem Soc 2845 1957.] The tetraphenyl borate salt has **m** 182-185°. [Anal Chem 28 1794 1956.]

Benzyldimethyloctadecylammonium chloride [122-19-0] M 442.2, m 63°. Crystd from acetone.

**2-Benzyl-1,3-dioxolane** [101-49-5] M 164.2, b 98-99°/1mm, 110°/5mm, 137-138°/34mm, 240-242°/atm,  $d_4^{20}$  1.087,  $n_D^{20}$  1.532. Dissolve in CH<sub>2</sub>Cl<sub>2</sub>, wash well with 1M NaOH, dry over K<sub>2</sub>CO<sub>3</sub>, filter, evaporate and distil through a short path still (Kügelrohr). It has also been purified by preparative gas chromatography. [Synthesis 808 1974; J Org Chem 34 3949 1969.]

Benzyl ether [103-50-4] M 198.3, b 298°, 158-160°/0.1mm, d 1.043, n 1.54057. Refluxed over sodium, then distd under reduced pressure. Also purified by fractional freezing.

**N-Benzyl-N-ethylaniline** [92-59-1] M 221.3, b 212-222°/54mm, 285-286°/710mm, 312-313°/atm (dec),  $d_4^{20}$  1.029,  $n_D^{20}$  1.595, pK<sub>Est</sub> ~4.6. Dry over KOH pellets and fractionate. The *picrate* crystallises from \*C<sub>6</sub>H<sub>6</sub> as yellow lemon crystals m 126-128° (softening at 120°). [J Chem Soc 303 1951; IR: J Chem Soc 760 1958.]

**Benzyl ethyl ether** [539-30-0] **M 136.2, b 186°, 65°/10mm, d 0.949, n 14955.** Dried with CaCl<sub>2</sub> or NaOH, then fractionally distd. [J Am Chem Soc 78 6079 1956.]

Benzyl ethyl ketone (1-phenylbutan-2-one) [1007-32-5] M 148.2, b 49-49.5°/0.01mm, 66-69°/1mm, 83-85°/5mm, 101-102°/10mm, 229-233°/atm,  $d_4^{20}$  0.989,  $n_D^{25}$  1.5015. Purified by fractionation using an efficient column. It can be converted into the oxime and distd, b 117-118°/2mm, 145-146°/15mm,  $d_{25}^{25}$  1.036,  $n_D^{25}$  1.5363, decompose oxime and the ketone is redistilled. It can also be purified via the semicarbazone which has m 154 155°. [J Am Chem Soc 77 5655 1955; J Org Chem 15 8 1950.]

S-(+)- and R-(-)- Benzyl glycidyl ether (1-benzyloxyoxirane) [S:14618-80-5] [R:16495-13-9] M 164.2, b 68°/10<sup>-4</sup> mm, 105°/0.4mm,  $d_4^{20}$  1.072,  $n_D^{20}$  1.517,  $[\alpha]_{546}^{20}$  (+) and (-) 5.5°,  $[\alpha]_D^{20}$  (+) and (-) 5.1° (c 5, toluene),  $[\alpha]_D^{20}$  (+) and (-) 1.79° (c 5.02, CHCl<sub>3</sub>),  $[\alpha]_D^{21}$  (+) and (-) 15.3° (neat). The ether in EtOAc is dried (Na<sub>2</sub>SO<sub>4</sub>) then purified by flash chromatography using pet ether/EtOAc (5:1) as eluent. The ether is then distd through a short path dist apparatus (Kugelrohr) as a colourless liquid. Alternatively, dissolve in CHCl<sub>3</sub>, wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and purify through silica gel chromatography. [J Chem Soc 1021 1967; Heterocycles 16 381 1981; Org Synth 69 82 1990; Synthesis 539 1989; Chem Pharm Bull Jpn 39 1385 1991.]

**3-Benzyl-5-(2-hydroxyethyl)-4-methylthiazolinium chloride** [4568-71-2] M 269.8, m 142-144°, 145-147°. Purified by recrystn from EtOH or H<sub>2</sub>O. If placed in a bath at 125° and heated at 2°/min the m is 140.5-141.4°. [J Biol Chem 167 699 1947, J Am Chem Soc 79 4386 1957.]

*O*-Benzylhydroxylamine hydrochloride [2687-43-6] M 159.6, m 234-238°(sublimes), pK<sub>Est</sub> ~5.9. Recrystd from H<sub>2</sub>O or EtOH.

N-Benzylideneaniline [538-51-2] M 181.2, m 48° (54°), b 300°/760mm. Steam volatile and crystd from \*benzene or 85% EtOH.

Benzyl isocyanate [3173-56-6] M 133.2, b 82-84°/10mm, 87°/14mm, 95°/17mm, 101-104°/33mm,  $d_4^{20}$  1.08,  $n_D^{20}$  1.524. Purified by fractionation through a two-plate column. It is a viscous liquid and is TOXIC. [J Chem Soc 182 1947; J Am Chem Soc 81 4838 1959; IR: Monatsh Chem 88 35 1957.]

Benzyl isothiocyanate [622-78-6] M 149.2, b 123-124°/1mm, 138-140°/20mm, 255-260°/atm,  $d_4^{20}$  1.1234,  $n_D^{20}$  1.6039. Dissolve in Et<sub>2</sub>O, filter, if there is any solid, and distil through an efficient column at 11mm with bath temperature at *ca* 150°. Characterise by reacting (0.5mL) in EtOH (1mL) with 50% NH<sub>2</sub>NH<sub>2</sub>.H<sub>2</sub>O (2 mL) to give 4-benzylthiosemicarbazide as colourless needles which are recrystallised from EtOH, m 130°. [J Chem Soc 1582 1950; Justus Liebigs Ann Chem 612 11 1958; IR and UV: Acta Chem Scand 13 442 1959.]

S-Benzyl-isothiouronium chloride [538-28-3] M 202.7, two forms, m 150° and 175°, pK<sub>Est</sub> ~9.8 (free base). Crystd from 0.2M HCl (2mL/g) or EtOH and dried in air.

Benzylmalonic acid [616-75-1] M 194.2, m 121°, pK<sub>1</sub><sup>25</sup> 2.91, pK<sub>2</sub><sup>25</sup> 5.87. Crystd from \*C<sub>6</sub>H<sub>6</sub>.

Benzylidene malononitrile [2700-22-3] M 154.2, m 83-84°. Recrystd from EtOH [Bernasconi et al. J Am Chem Soc 107 3612 1985].

**Benzyl mercaptan** [100-53-8] M 124.2, b 70.5-70.7°/9.5mm, d 1.058, n 1.5761,  $pK^{25}$  9.43. Purified via the mercury salt [see Kern J Am Chem Soc 75 1865 1953], which was crystd from \*benzene as needles (m 121°), and then dissolved in CHCl<sub>3</sub>. Passage of H<sub>2</sub>S gas regenerated the mercaptan. The HgS ppte was filtered off, and washed thoroughly with CHCl<sub>3</sub>. The filtrate and washings were evaporated to remove CHCl<sub>3</sub>, then residue was fractionally distd under reduced pressure [Mackle and McClean, *Trans Faraday Soc* 58 895 1962].

(-)-*N*-Benzyl-*N*-methylephedrinium bromide [benzyl(2-hydroxy-1-methyl-2-phenethyl) dimethylammonium bromide] [58648-09-2] M 350.3, m 209-211°, 212-214°,  $[\alpha]_D^{25}$  -3.8° (c 1.45, MeOH),  $[\alpha]_D^{20}$  -5.3° (c 1.45, MeOH). Recrystd from MeOH/Et<sub>2</sub>O. [Justus Liebigs Ann Chem 710 1978.] The chloride is recrystd from EtOAc/n-hexane, m 198-199°  $[\alpha]_D^{25}$  -8.67° (c 1.45, MeOH). [J Chem Soc, Perkin Trans 1 574 1981.]

**Benzyl 4-nitrophenyl carbonate** [13795-24-9] **M 273.2, m 78-80°**. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O (3x) and satd aq NaCl, dry (MgSO<sub>4</sub>), evap in vac and recryst residue from a small vol of MeOH, **m** 78-79°. Alternatively dissolve in Et<sub>2</sub>O, wash with N HCl (2x), 0.5N NaHCO<sub>3</sub> (4x) then H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evap Et<sub>2</sub>O and recryst residue from \*C<sub>6</sub>H<sub>6</sub>-pet ether, **m** 79-80°. [Khosła et al. *Indian J Chem* **5** 279 1967; Wolman et al. J Chem Soc (C) 596 1976.]

**Benzyloxyacetyl chloride** [19810-31-2] M 184.6, b 81°/0.2mm, 84-87°/0.4mm, 105-107°/5mm,  $d_4^{20}$  1.19,  $n_D^{20}$  1.523. Check IR to see if there are OH bands. If so then it may be contaminated with free acid formed by hydrolysis. Add oxalyl chloride (amount depends on contamination and needs to be judged, *ca* 3mols) heat at 50° in the absence of moisture for 1h and fractionate twice, b 81°/0.2mm (with bath temp at 81°). Excessive heating results in decomposition to give benzyl chloride. The *anilide* is formed by adding aniline in CHCl<sub>3</sub> soln, m 49°. [*Helv Chim Acta* 16 1130 1933.]

Benzyloxybutan-2-one [6278-91-7] M 178.2, b 90-92°/0.1mm, 88-91°/0.5mm, 121-126°/5mm,  $d_4^{20}$  1.0275,  $n_D^{20}$  1.5040. Dissolve in CHCl<sub>3</sub>, wash with H<sub>2</sub>O, aqueous saturated NaHCO<sub>3</sub>, H<sub>2</sub>O, dry (MgSO<sub>4</sub>), evaporate the CHCl<sub>3</sub>, and fractionate. [J Am Chem Soc 79 2316 1957.]

**Benzyloxycarbonyl chloride (Cbz-Cl, benzyl chloroformate)** [501-53-1] M 170.6, b 103°/20mm, d 1.195, n 1.5190. Commercial material is better than 95% pure and may contain some toluene, benzyl alcohol, benzyl chloride and HCl. After long storage (e.g. two years at 4°, Greenstein and Winitz [*The Chemistry of the Amino Acids* Vol 2 p. 890, J Wiley and Sons NY, 1961] recommended that the liquid should be flushed with a stream of dry air, filtered and stored over sodium sulfate to remove CO<sub>2</sub> and HCl which are formed by decomposition. It may further be distilled from an oil bath at a temperature below 85° because Thiel and Dent [*Annalen* 301 257 1898] stated that benzyloxycarbonyl chloride decarboxylates to benzyl chloride slowly at 100° and vigorously at 155°. Redistillation at higher vac below 85° yields material which shows no other peaks than those of benzyloxycarbonyl chloride by NMR spectroscopy. LACHRYMATORY and TOXIC.

N-Benzyloxycarbonylglycyl-L-alaninamide [17331-79-2] M 279.3, m dec >200°. Recrystd from EtOH/Et<sub>2</sub>O.

*N*-Benzyloxycarbonyl-*N*'-methyl-L-alaninamide [33628-84-1] M 236.3, m dec >200°. Recrystd from EtOAc.

**5-Benzyloxyindole** [1215-59-4] **M 223.3, m 96-97°; 100-103°, 104-106°, pK <0.** Recrystd from  $*C_6H_6$ -pet ether or pet ether. The *picrate*, red crystals from  $*C_6H_6$ , has m 142-143°. [Chem Ind (London) 1035 1953; J Am Chem Soc 76 5579 1954; fluorescence: Biochem J 107 225 1968.]

p-(Benzyloxy)phenol [103-16-2] M 200.2, m 122.5°, pK<sub>Est</sub> ~10.1. Crystd from EtOH or water, and dried over P<sub>2</sub>O<sub>5</sub> under vacuum. [Walter et al. J Am Chem Soc 108 5210 1986.]

S-(-)-3-Benzyloxypropan-1,2-diol [17325-85-8] M 182.2, m 24-26°, b 117-118°/10<sup>-4</sup>mm, 115-116°/0.02mm, 121-123°/0.2mm,  $d_4^{20}$  1.1437,  $n_D^{22}$  1.5295,  $[\alpha]_D^{25}$ -5.9° (neat). Purified by repeated fractional distn. [J Biol Chem 193 835 1951, 230 447 1958.]

**2-Benzylphenol** [28994-41-4] M 184.2, m 54.5°, b 312°/760mm, 175°/18mm,  $pK_{Est} \sim 10.0$ Crystd from EtOH, stable form has m 52° and unstable form has m 21°.

**4-Benzylphenol** (α-Phenyl-*p*-cresol) [101-53-1] M 184.2, m 84°, pK<sub>Est</sub> ~10.2. Crystd from water.

1-Benzyl-4-piperidone [3612-20-2] M 189.3, b 107-108°/0.2mm, 114-116°/0.3mm, 143-146°/5mm, 157-158°/11mm, d 1.059, n 1.538. If physical properties show contamination then dissolve in the minimum volume of H<sub>2</sub>O, made strongly alkaline with aqueous KOH, extract with toluene several times, dry the extract with K<sub>2</sub>CO<sub>3</sub>, filter, evaporate and distil the residue at high vacuum using a bath temp of 160-190°, and redistil. [*J Chem Soc* 3173 *1957*, *J Am Chem Soc* 53 1030 *1930*.] The hydrochloride has m 159-161° (from Me<sub>2</sub>CO + Et<sub>2</sub>O), and the picrate has m 174-182° (from Me<sub>2</sub>CO + Et<sub>2</sub>O). [Helv Chim Acta 41 1184 1958.]

2-Benzylpyridine [101-82-6] M 169.2, b 98.5°/4mm, d 1.054, n<sup>26</sup> 1.5771, pK<sup>25</sup> 5.13. Dried with NaOH for several days, then distd from CaO under reduced pressure, redistilling the middle fraction.

**4-Benzylpyridine** [2116-65-6] **M 169.2, b 110.0°/6mm, d 1.065, n<sup>26</sup> 1.5814, pK<sup>25</sup> 5.59.** Dried with NaOH for several days, then distd from CaO under reduced pressure, redistilling the middle fraction.

4-N-Benzylsulfanilamide [1709-54-2] M 262.3, m 175°. Crystd from dioxane/H<sub>2</sub>O.

Benzyl sulfide [538-74-9] M 214.3, m 50°. See dibenzylsulfide on p. 192.

Benzylthiocyanate [3012-37-1] M 149.2, m 43°, b 256°(dec). Crystd from EtOH or aqueous EtOH.

Benzyl toluene-p-sulfonate [1024-41-5] M 162.3, m 58°. Crystd from pet ether (b 40-60°).

Benzyltributylammonium bromide [25316-59-0] M 356.4, m 169-171°, 174-175°. Recrystd from EtOAc/EtOH and EtOH/Et<sub>2</sub>O. [J Am Chem Soc 73 4122 1951, 81 3264 1959.]

**Benzyl 2,2,2-trichloroacetimidate** [81927-55-1] **M 252.5, b 106°/0.5mm, m 3°, d 1.349, n 1.545.** Purify by distn to remove up to 1% of PhCH<sub>2</sub>OH as stabiliser. A soln in hexane can be stored for up to 2 months without decompn. It is hygroscopic and has to be stored dry. [Wessel et al. J Chem Soc, Perkin Trans 1 2247 1985.]

**Benzyltrimethylammonium chloride** [56-93-9] **M 185.7, m 238-239°(dec).** A 60% aq soln was evapd to dryness under vac on a steam bath, and then left in a vac desiccator containing a suitable dehydrating agent. The solid residue was dissolved in a small amount of boiling absolute EtOH and pptd by adding an equal volume of diethyl ether and cooling. After washing, the ppte was dried under vac [Karusch J Am Chem Soc 73 1246 1951].

**Benzyltrimethylammonium hydroxide** (Triton B) [100-85-6] M 167.3, d 0.91. A 38% soln (as supplied) was decolorized (charcoal), then evaporated under reduced pressure to a syrup, with final drying at  $75^{\circ}$  and 1mm pressure. Prepared anhydrous by prolonged drying over P<sub>2</sub>O<sub>5</sub> in a vacuum desiccator.

Berbamine [478-61-5] M 608.7, m 197-210°,  $[\alpha]_D^{20}$ +115° (CHCl<sub>3</sub>), pK<sup>20</sup>7.33. Crystd from pet ether.

Berberine [2086-83-1] M 336.4, m 145°,  $pK_1^{20}$  2.47,  $pK_2^{20}$  11.73 (pseudobase?). Crystd from pet ether or ether as yellow needles.

Berberine hydrochloride  $(2H_2O)$  [633-65-8] M 407.9, m 204-206°(dec), pK 2.47. Crystn from water gives the dihydrate. The anhydrous salt may be obtained by recrystn from EtOH/Et<sub>2</sub>O, wash with Et<sub>2</sub>O and dry in a vacuum. The *iodide* has m 250°(dec) (from EtOH). [J Chem Soc 113 503 1918; J Chem Soc 2036 1969.]

Betaine [107-43-7] M 117.1, m 301-305°(dec) (anhydrous), pK<sup>25</sup> 1.83. Crystd from aq EtOH.

Betamethasone  $(9\alpha$ -fluoro-11 $\beta$ ,17 $\alpha$ ,21-trihydroxy-16 $\beta$ -methylpregna-1,4-diene-3,20-dione) [378-44-9] M 392.5, m 231-136°(dec), 235-237°(dec),  $[\alpha]_D^{20}$ +108° (c 1, Me<sub>2</sub>CO). Crystd from ethyl acetate, and has  $\lambda_{max}$  238nm (log  $\varepsilon$  4.18) in MeOH.

**Biacetyl (butan-2,3-dione)** [431-03-8] **M 86.1, b 88°, d 0.981, n^{18.5}1.3933.** Dried with anhydrous CaSO<sub>4</sub>, CaCl<sub>2</sub> or MgSO<sub>4</sub>, then vacuum distd under nitrogen, taking the middle fraction and storing it at Dry-ice temperature in the dark (to prevent polymerization).

**Bibenzyl** [103-29-7] **M 182.3, m 52.5-53.5°.** Crystd from hexane, MeOH, or 95% EtOH. It has also been sublimed under vacuum, and further purified by percolation through columns of silica gel and activated alumina.

Bicuculline [485-49-4] M 367.4, m 215° (196°, 177°),  $[\alpha]_{546}^{20}$  +159° (c 1, CHCl<sub>3</sub>), pK 4.84. See bicuculline entry on p. 515 in Chapter 6.

**Bicyclohexyl** [92-51-3] **M** 166.3, b 238° (cis-cis), 217-219° (trans-trans). Shaken repeatedly with aqueous KMnO<sub>4</sub> and with conc H<sub>2</sub>SO<sub>4</sub>, washed with water, dried, first from CaCl<sub>2</sub> then from sodium, and distd. [Mackenzie J Am Chem Soc 77 2214 1955.]

Bicyclo[3.2.1]octane [6221-55-2] M 110.2, m 141°. Purified by zone melting.

Biguanide [56-03-1] M 101.1, m 130° pK<sub>1</sub><sup>25</sup> 3.1, pK<sub>2</sub><sup>25</sup> 12.8. Crystd from EtOH.

**Bilirubin** [635-65-4] M 584.7,  $\varepsilon_{450nm}$  55,600 in CHCl<sub>3</sub>, pK<sub>Est</sub> ~3.0. An acyclic tetrapyrrole bile pigment with impurities which can be eliminated by successive Soxhlet extraction with diethyl ether and MeOH. It crystallises from CHCl<sub>3</sub> as deep red-brown rhombs, plates or prisms, and is dried to constant weight at 80° under vacuum. [Gray et al. J Chem Soc 2264, 2276 1961.]

Biliverdine [114-25-0] M 582.6, m >300°, pK 3.0. The precursor of bilirubin (above) and forms dark green plates or prisms, with a violet reflection, from MeOH. [Gray et al. J Chem Soc 2264 1961; Sheldrick J Chem Soc, Perkin Trans 2 1457 1976.]

(±)-1,1'-Bi-(2-naphthol) [1,1'-di-(2-naphthol)] [602-09-5; 41024-90-2] M 286.3, m 215-217°, 218°,  $pK_{Est(1)}$ ~7.1,  $pK_{Est(2)}$ ~11.2. Crystd from toluene or \*benzene (10mL/g). When crystd from chlorobenzene it had m 238°. Sol in dioxane is 5%.

1,1'-Bi-(2-naphthol) [1,1'-di-(2-naphthol)] [R-(+)- 18531-94-7], [S-(-)- 18531-99-2] M 286.3, m 207.5-208.5°, 209-211°,  $[\alpha]_{D}^{20}$  (+) and (-) 37.4.0° (c 0.5, THF),  $[\alpha]_{546}^{25}$  (+) and (-) 51° (c 0.1, THF), pK as above. Dissolve in cold 2.5N NaOH, extract with CH<sub>2</sub>Cl<sub>2</sub>, and acidify with 5% HCl. Collect the white ppte and recryst from aq EtOH and dry in a vacuum [Tetrahedron 27 5999 1971]. Optically stable in dioxane-water (100°/24h). Racemisation: 72% in 1.2N HCl at 100°/24h and 68% in 0.67M KOH in BuOH at 118°/23h [J Am Chem Soc 95 2693 1973]. Cryst from \*C<sub>6</sub>H<sub>6</sub> (sol 1%) using Norite or aq EtOH after chromatography through silica gel, eluting with Me<sub>2</sub>CO-\*C<sub>6</sub>H<sub>6</sub>. [Kyba et al. J Org Chem 42 4173 1977; see also Brussee and Jansen Tetrahedron Lett 24 3261 1983; Akimoto and Yamada Tetrahedron 27 5999 1971.]

**1,1'-Binaphthyl**  $[\pm 32507-32-7 \text{ and } 604-53-5; R(-)- 24161-30-6; S(+)- 734-77-0]$  M 254.3, m 145°, **159°** (±, 2 forms), **153-154°** (+ and -),  $[\alpha]_D^{20}$  (-) and (+) ~220° (\*C<sub>6</sub>H<sub>6</sub>). Purified through a silica gel column with Me<sub>2</sub>CO-\*C<sub>6</sub>H<sub>6</sub> [or Al<sub>2</sub>O<sub>3</sub> with 10% \*C<sub>6</sub>H<sub>6</sub>/pet ether (b 30-60°)] and recrystd from EtOH, pentane, or slow evap of \*C<sub>6</sub>H<sub>6</sub>, Me<sub>2</sub>CO or Et<sub>2</sub>O solns. Half life ~10h at 25° in various solvents. [Wilson and Pincock J Am Chem Soc 97 1474 1975; Akimoto and Yamada Tetrahedron 27 5999 1971.]

2,2'-Binaphthyl (β, β'-binaphthyl) [61-78-2] M 254.3, m 188°. Crystd from \*benzene.

**Biphenyl** [92-52-4] M 154.2, m 70-71°, b 255°, d 0.992. Crystd from EtOH, MeOH, aq MeOH, pet ether (b 40-60°) or glacial acetic acid. Freed from polar impurities by passage through an alumina column in \*benzene, followed by evapn. A in CCl<sub>4</sub> has been purified by vac distn and by zone refining. Treatment with maleic anhydride removed anthracene-like impurities. Recrystd from EtOH followed by repeated vacuum sublimation and passage through a zone refiner. [Taliani and Bree J Phys Chem 88 2351 1984.]

*p*-Biphenylamine [92-67-1] M 169.2, m 53°, b 191°/15mm, pK<sup>18</sup> 4.38. See *p*-aminobiphenyl entry on p. 104.

**4-Biphenylcarbonyl chloride** [14002-51-8] **M 216.7, m 114-115°.** Dissolve in a large volume of pet ether (10 x, b 50-70°), filter through a short column of neutral alumina, evaporate to dryness *in vacuo* and recryst from pet ether (b 60-80°). LACHRYMATORY.

Biphenyl-2-carboxylic (2-phenylbenzoic) acid [947-84-2] M 198.2, m 114°, b 343-344°, pK 3.46. Crystd from  $*C_6H_6$ -pet ether or aq EtOH.

Biphenyl-4-carboxylic (4-phenylbenzoic) acid [92-92-2] M 198.2, m 228°,  $pK^{25}$  5.66 (in 50% 2-butoxyethanol). Crystd from \*C<sub>6</sub>H<sub>6</sub>-pet ether or aq EtOH.

2,4'-Biphenyldiamine [492-17-1] M 184.2, m 45°, b 363°/760mm, pK<sub>Est(1)</sub>~4.8, pK<sub>Est(2)</sub>~3.9. Crystd from aqueous EtOH.

Biphenylene [259-79-0] M 152.2, m 152°. Recrystd from cyclohexane then sublimed in vacuum.

α-(4-Biphenylyl)butyric acid [959-10-4] M 240.3, m 175-177°, pK<sub>Est</sub> ~4.5. Crystd from MeOH.

γ-(4-Biphenylyl)butyric acid [6057-60-9] M 240.3, m 118°, pK<sub>Est</sub> ~4.8. Crystd from MeOH.

**2,2'-Bipyridyl** [366-18-7] **M 156.2, m 70.5°, b 273°, pK\_1^{25}-0.52, pK\_2^{25}4.44. Crystd from hexane, or EtOH, or (after charcoal treatment of a CHCl<sub>3</sub> soln) from pet ether. Also ppted from a conc soln in EtOH by addition of H<sub>2</sub>O. Dried in a vacuum over P<sub>2</sub>O<sub>5</sub>. Further purification by chromatography on Al<sub>2</sub>O<sub>3</sub> or by sublimation. [Airoldi et al. J Chem Soc, Dalton Trans 1913 1986.]** 

4,4'-Bipyridyl [553-26-4] M 156.2, m 73°(hydrate), 114° (171-171°)(anhydrous), b  $305^{\circ}/760$ mm, 293°/743mm, pK<sub>1</sub><sup>2°</sup> 3.17, pK<sub>2</sub><sup>2°</sup> 4.82. Crystd from water, \*benzene/pet ether, ethyl acetate and sublimed *in vacuo* at 70°. Also purified by dissolving in 0.1M H<sub>2</sub>SO<sub>4</sub> and twice ppted by addition of 1M NaOH to pH 8. Recrystd from EtOH. [Man et al. J Chem Soc, Faraday Trans 1 82 869 1986; Collman et al. J Am Chem Soc 109 4606 1987.]

2,2'-Bipyridylamine [1202-34-2] M 171.2, m 95.1°, pK<sub>Est</sub> ~5.0. Crystd from Me<sub>2</sub>CO.

2,2'-Biquinolin-4,4'-dicarboxylic (2,2'-bicinchoninic) acid [1245-13-2] M 344.3, m 367°,  $pK_{Est(1)} \sim 1.5$ ,  $pK_{Est(2)} \sim 4.0$ . Dissolve in dilute NaOH and ppte with acetic acid, filter, wash well with H<sub>2</sub>O and dry at 100° in a vacuum oven. Attempts to form a picrate failed. The *methyl ester* (SOCl<sub>2</sub>-MeOH) has m 165.6-166°. [J Am Chem Soc 64 1897 1942; 68 2705 1946.] For di-K salt see entry in Chapter 5.

**2,2'-Biquinolyl**  $(\alpha, \alpha'-diquinolyl)$  [119-91-5] M 256.3, m 196°, pK<sub>Est</sub> ~4.2. Decolorised in CHCl<sub>3</sub> soln (charcoal), then crystd to constant melting point from EtOH or pet ether [Cumper, Ginman and Vogel J Chem Soc 1188 1962].

**Bis-acrylamide** (N, N'-methylene bisacrylamide) [110-26-9] M 154.2, m >300°. Recrystd from MeOH (100g dissolved in 500mL boiling MeOH) and filtered without suction in a warmed funnel. Allowed to stand at room temperature and then at -15°C overnight. Crystals collected with suction in a cooled funnel and washed with cold MeOH). Crystals air-dried in a warm oven. **TOXIC.** 

**Bis-(4-aminophenyl)methane** [101-77-9] **M 198.3, m 92-93°, b 232°/9mm, pK**<sub>Est</sub> ~4.9. See 4.4'-diaminodiphenylmethane on p. 189.

2,5-Bis-(4-aminophenyl)-1,3,4-oxadiazole (BAO) [2425-95-8] M 252.3, m 252-255°, 254-255°. Recrystd from EtOH using charcoal and under N<sub>2</sub> to avoid oxidation.

2,5-Bis(2-benzothiazolyl)hydroquinone [33450-09-8] M 440.3, m dec >200°. Purified by repeated crystn from dimethylformamide followed by sublimation in vacuum [Erusting et al. J Phys Chem 91 1404 1987].

**Bis-**(*p*-**bromophenyl**)**ether** [53563-56-7] **M 328.0, m 60.1-61.7°.** Crystd twice from EtOH, once from \*benzene and dried under vac [Purcell and Smith J Am Chem Soc 83 1063 1961].

**Bis-***N*-*tert*-**butyloxycarbonyl-L-cystine**, [10389-65-8] **M** 440.5, **m** 144.5-145°,  $[\alpha]_D^{20}$  -133.2° (c 1, MeOH), pK<sub>Est</sub> ~2.9. Crystd from in EtOAc by adding hexane [Ferraro *Biochem Prep* 13 39 1971].

2R, 3R - (+) - 1, 4-Bis-(4-chlorobenzoyl)-2,3-butanediol [85362-86-3] and 2S, 3S - (-) - 1, 4-Bis-(4-chlorobenzoyl)-2,3-butanediol [85362-85-2] M 371.3, m 76-77°,  $[\alpha]_D^{20}$  (+) and (-) 6.4° (c 3.11 CHCl<sub>3</sub>). Recrystd from toluene-hexane. [Tetrahedron 40 4617 1984.]

Bis-( $\beta$ -chloroethyl)amine hydrochloride [821-48-7] M 178.5, m 214-215°, pK<sub>Est</sub> ~5.8 (free base). Crystd from Me<sub>2</sub>CO.

Bis-( $\beta$ -chloroethyl) ether [111-44-4] M 143.0, b 94°/33mm, 178.8°, d 1.220, n 1.45750. Wash with conc H<sub>2</sub>SO<sub>4</sub>, then Na<sub>2</sub>CO<sub>3</sub> soln, dry with anhydrous Na<sub>2</sub>CO<sub>3</sub>, and finally pass through a 50cm column of activated alumina before distn. Alternatively, wash with 10% ferrous sulfate soln to remove peroxides, then H<sub>2</sub>O, dry with CaSO<sub>4</sub>, and dist in vac. Add 0.2% of catechol to stabilise it. VERY TOXIC.

N,N-Bis-(2-chloroethyl)2-naphthylamine (chlornaphthazine) [494-03-1] M 268.3, m 54-56°, b 210°/5mm, pK<sub>Est</sub> ~5.3. Crystd from pet ether. CARCINOGENIC.

Bis-(chloromethyl)durene [3022-16-0] M 231.2, m 197-198°. Crystd three times from \*benzene, then dried under vacuum in an Abderhalden pistol.

**3,3'-Bis-(chloromethyl)oxacyclobutane** [78-71-7] **M 155.0, m 18.9°.** Shaken with aqueous NaHCO<sub>3</sub> or FeSO<sub>4</sub> to remove peroxides. Separated, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, then distd under reduced pressure from a little CaH<sub>2</sub> [Dainton, Ivin and Walmsley *Trans Faraday Soc* **65** 17884 *1960*].

2,2-Bis-(p-chlorophenyl)-1,1-dichloroethane (p,p'-DDD) [72-54-8] M 320.1, m 109-111°, 111-112°. Crystd from EtOH and dried in a vac. Purity checked by TLC. TOXIC INSECTICIDE.

**2,2-Bis-(p-chlorophenyl)-1,1-dichloroethylene** (*p,p'-DDE*) [72-55-9] M **318.0, m 89-91°.** Crystd from EtOH and dried in a vac. Purity checked by TLC. **POSSIBLE CARCINOGEN.** 

2,2-Bis-(4-chlorophenyl)-1,1,1-trichloroethane (p,p'-DDT, 1,1,1-trichloro-2,2-bis(pchlorophenyl)ethane) [50-29-3] M 354.5, m 108.5-109°, 108°. Crystd from *n*-propyl alcohol (5mL/g), then dried in air or an air oven at 50-60°. Alternatively crystd from 95% EtOH, and checked by TLC.

2,2'-Bis-[di-(carboxymethyl)-amino]diethyl ether,  $(HOOCCH_2)_2NCH_2CH_2OCH_2CH_2N-(CH_2COOH)_2$  [923-73-9] M 336.3,  $pK_1^{20}1.8$ ,  $pK_2^{20}2.76$ ,  $pK_3^{20}8.84$ ,  $K_4^{20}9.47$ . Crystd from EtOH.

4,4'-Bis-(diethylamino)benzophenone [90-93-7] M 324.5, m 95-96°,  $pK_{Est(1)}$ ~1.8,  $pK_{Est(2)}$ ~3.3. Crystd from EtOH (25mL/g) and dried under vacuum.

Bis-(4-dimethylaminobenzylidene)benzidine [6001-51-0] M 454.5, m 318°, pK<sub>Est</sub> ~0. Crystd from nitrobenzene.

**1,8-Bis-(dimethylamino)naphthalene (Proton sponge)** [20734-58-1] M 214.3, m 47-48°, pK **12.34 (pK<sub>2</sub> -10.5 from half protonation in 86% H<sub>2</sub>SO<sub>4</sub>).** Crystd from EtOH and dried in a vacuum oven. Stored in the dark. Also see N, N, N', N'-Tetramethyl-1,8-naphthalenediamine on p. 364.

**Bis-(dimethylthiocarbamyl)disulfide (tetramethylthiuram disulfide, Thiram)** [137-26-8] M **240.4, m 155-156<sup>o</sup>.** See tetramethylthiuram disulfide on p. 365.

**Bis-(4-fluoro-3-nitrophenyl) sulfone** [312-30-1] **M 344.3, m 193-194°.** Recrystd from  $Me_2CO$  and  $H_2O$  (5:1). It should give a yellow colour in aqueous base. [Chem Ber 86 172 1953.]

N,N-Bis-(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES) [10191-18-1] M 213.3, m 150-155°, pK<sup>20</sup>7.17. Crystd from aqueous EtOH.

Bis-(2-hydroxyethyl)amino-tris-(hydroxymethyl)methane (BIS-TRIS) [6976-37-0] M 209.2, m 89°, pK<sup>2°</sup>6.46. Crystd from hot 1-butanol. Dried in a vacuum at 25°.

N, N-Bis-(2-hydroxyethyl)glycine [150-25-4] M 163.2, m 191-194°(dec). See N, N-di-(hdyroxyethyl)glycine (BICINE) on p. 208. **3,4-Bis-(4-hydroxyphenyl)hexane** [5635-50-7] **M 270.4, m 187°.** Freed from diethylstilboestrol by zone refining.

**1,4-Bismethylaminoanthraquinone (Disperse Blue 14)** [2475-44-7] M 266.3,  $\lambda$ max 640 (594)nm. Purified by thin-layer chromatography on silica gel plates, using toluene/acetone (3:1) as eluent. The main band was scraped off and extracted with MeOH. The solvent was evapd and the dye was dried in a drying pistol [Land, McAlpine, Sinclair and Truscott J Chem Soc, Faraday Trans 1 72 2091 1976].

Bis-(1-naphthylmethyl)amine [5798-49-2] M 329.4, m 62°, pK<sub>Est</sub> ~8.4. Crystd from pet ether.

N, N'-Bis-(nicotinic acid) hydrazide [840-78-8] M 227-228°, m dec 200°, pK<sub>Est</sub> ~3.3. Crystd from water.

**Bis-(4-nitrophenyl) carbonate** [5070-13-3] **M 304.3, m 142-143°**. Dissolve in CHCl<sub>3</sub>, wash with 2N NaOH (3 x) and once with conc HCl, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and crystallise from toluene (authors say 15 vols of \*benzene, prisms). [Helv Chim Acta 46 795 1963.]

**Bis-(2-nitrophenyl) disulfide** [1155-00-6] **M 308.3, m 192-195°, 195°, 194-197°, 198-199°.** Purified by recrystn from glacial AcOH or from  ${}^{*}C_{6}H_{6}$  and the yellow needles are dried in an oven at 100° until the odour of the solvent is absent. It is sparingly soluble in EtOH and Me<sub>2</sub>CO. [Bogert and Stull Org Synth Coll Vol I 220 1941; Bauer and Cymerman J Chem Soc 3434 1949.]

Bis-(4-nitrophenyl) ether [101-63-3] M 260.2, m 142-143°. Crystd twice from \*C<sub>6</sub>H<sub>6</sub>, and dried under vacuum.

**Bis-(4-nitrophenyl) methane** [1817-74-9] **M 258.2, m 183°.** Crystd twice from \*C<sub>6</sub>H<sub>6</sub>, and dried under vacuum.

Bisnorcholanic acid (pregnane-20-carboxylic acid) [28393-20-6] M 332.5, m 214° ( $\alpha$ -form), 242° ( $\beta$ -form), 210-211° ( $\gamma$ -form), 184° ( $\delta$ -form), 181° ( $\epsilon$ -form), pK<sub>Est</sub> ~5.0. Crystd from EtOH ( $\alpha$ -form), or acetic acid (all forms).

**3,3'-Bis-(phenoxymethyl)oxacyclobutane** [1224-69-7] **M 270.3, m 67.5-68°.** Crystd from MeOH.

**1,4-Bis-(2-pyridyl-2-vinyl)benzene** [20218-87-5] M **284.3**, pK<sub>Est</sub> ~5.4. Recrystd from xylene, then chromatography (in the dark) on basic silica gel (60-80-mesh), using  $CH_2Cl_2$  as eluent. Vacuum sublimed in the dark to a cold surface at  $10^{-3}$  torr.

**Bis-(trichloromethyl) carbonate (triphosgene)** [32315-10-9] **M 296.8, m 79-83°, 81-83°, b 203-206°(slight decomp).** A good solid substitute for phosgene (using a third mol per mol). Cryst from pet ether and wash with anhydrous cold Et<sub>2</sub>O, degas at 200mm then dry at 0.1mm (over H<sub>2</sub>SO<sub>4</sub>). It is a **lachrymator**, is **TOXIC** and should be handled with gloves and in an efficient fume hood. [Eckert and Forster Angew Chem, Int Ed Engl **26** 894 1987; Aldrichimica Acta **21** 47 1988.]

**Bistrifluoroacetamide** [407-24-9] **M 209.1, m 85°, b 135-136°/744mm, 141°/760mm.** Major impurity is trifluoroacetamide. Add trifluoroacetic anhydride, reflux for 2h and fractionate using a Vigreux column at atmospheric pressure. [J Chromatogr 78 273 1973.]

**Bis-(trifluoroacetoxy)iodobenzene** [2712-78-9] **M 430.0, m 112-114° (dec), 120-121°, 124-126°.** Cryst from warm trifluoroacetic acid and dry over NaOH pellets. Recrystd from Me<sub>2</sub>CO/pet ether. Melting point depends on heating rate. [Synthesis 445 1975.]

Biuret (allophanic acid amide, carbamoylurea) [108-19-0] M 103.1, sinters at 218° and chars at 270°,  $pK_1^{25}$ -0.88,  $pK_2^{25}$ >4. Crystd from EtOH.

Bixin (6,6'-diapo- $\psi$ , $\psi$ - carotenedioic acid monomethyl ester) [6983-79-5] M 394.5, m 198°, 217°(dec),  $\lambda$ max (CHCl<sub>3</sub>) 209, 475 and 443nm, pK<sub>Est</sub> ~4.3. Crystd from Me<sub>2</sub>CO (violet prisms) [Pattenden et al. J Chem Soc (C) 235 1970].

Blue Tetrazolium [1871-22-3] M 727.7, m 254-255°(dec). Crystd from 95% EtOH/anhydrous diethyl ether, to constant absorbance at 254nm.

*R***-2-endo-Borneol** [464-43-7] **M** 154.3, m 208°  $[\alpha]_D^{20}$  +15.8° (in EtOH). Crystd from boiling EtOH (charcoal).

(±)-Borneol [6627-72-1] M 154.3, m 130°(dec). Crystd from pet ether (b 60-80°).

Brazilin [474-07-7] M 269.3, m 130°(dec),  $pK_{Est(1)}$ ~9.3,  $pK_{Est(2)}$ ~10.0,  $pK_{Est(3)}$ ~12.5 (all phenolic). Crystd from EtOH.

Brilliant Cresyl Blue [4712-70-3] M 332.8, pK<sup>25</sup> 3.2. Crystd from pet ether.

Brilliant Green (4-dimethylaminotriphenyl carbinol) [633-03-4] M 482.7, m 209-211°(dec),  $pK^{25}$  4.75. Purified by pptn as the perchlorate from aqueous soln (0.3%) after filtering, heating to 75° and adjustment to pH 1-2. Recrystd from EtOH/water (1:4) [Kerr and Gregory Analyst (London) 94 1036 1969].

**N-Bromoacetamide** [79-15-2] **M 138.0, m 102-105°, 107-109°, 108° (anhyd).** Possible contaminant is CH<sub>3</sub>CONBr<sub>2</sub>. Recrystd from CHCl<sub>3</sub>/hexane (1:1, seed if necessary) or water and dried over CaCl<sub>2</sub>. [Oliveto and Gerold Org Synth Coll Vol IV 104 1963).

4-Bromoacetanilide [103-88-8] M 214.1, m 167°. Crystd from aq MeOH or EtOH. Purified by zone refining.

**Bromoacetic acid** [79-08-3] M 138.9, m 50°, b 118°/15mm, 208°/760mm, pK<sup>25</sup> 2.92. Crystd from pet ether (b 40-60°). Diethyl ether soln passed through an alumina column, and the ether evaporated at room temperature under vacuum. LACHRYMATORY.

Bromoacetone [598-31-2] M 137.0, b 31.5°/8mm. Stood with anhydrous CaCO<sub>3</sub>, distd under low vacuum, and stored with CaCO<sub>3</sub> in the dark at 0°. LACHRYMATORY.

**4-Bromoacetophenone** [99-90-1] **M 199.1, m 54°.** Crystd from EtOH, MeOH or from pet ether (b 80-100°). [Tanner J Org Chem 52 2142 1987.]

 $\omega$ -Bromoacetophenone (phenacyl bromide) [70-11-1] M 199.1, m 57-58°. Crystd from EtOH, MeOH or from pet ether (b 80-100°). [Tanner J Org Chem 52 2142 1987.]

4-Bromoaniline [106-40-1] M 172.0, m 66°, pK<sup>25</sup> 3.86. Crystd (with appreciable loss) from aqueous EtOH.

2-Bromoanisole [578-57-4] M 187.0, f 2.5°, b 124°/40mm, d 1.513, n<sup>25</sup> 1.5717. Crystd by partial freezing (repeatedly), then distd under reduced pressure.

**4-Bromoanisole** [104-92-7] **M 187.0, f 13.4°, b 124°/40mm, d 1.495, n<sup>25</sup> 1.5617.** Crystd by partial freezing (repeatedly), then distd under reduced pressure.

9-Bromoanthracene [1564-64-3] M 257.1, m 98-100°. Crystd from MeOH or EtOH followed by sublimation in vacuo. [Masnori et al. J Am Chem Soc 108 126 1986.]

4-Bromobenzal diacetate [55605-27-1] M 287.1, m 95°. Crystd from hot EtOH (3mL/g).

**Bromobenzene** [108-86-1] **M** 157.0, b 155.9°, d 1.495, n 1.5588,  $n^{15}$  1.56252. Washed vigorously with conc H<sub>2</sub>SO<sub>4</sub>, then 10% NaOH or NaHCO<sub>3</sub> solns, and H<sub>2</sub>O. Dried with CaCl<sub>2</sub> or Na<sub>2</sub>SO<sub>4</sub>, or passed through activated alumina, before refluxing with, and distilling from, CaH<sub>2</sub>, using a glass helix-packed column.

**4-Bromobenzene diazonium tetrafluoroborate** [673-40-5] **M 270.8, m 133° (dec), 135-140° (dec), 135° (dec).** Wash with  $Et_2O$  until the wash is colourless and allow to dry by blowing  $N_2$  over it. Store at 0-4° in the dark. [Chem Ber 64 1340 1931.]

**4-Bromobenzenesulfonyl chloride** [98-58-8] M 255.5, m 73-75°, 74.3-75.1, 75-76°, 77°, b 153°/15mm, 150.6°/13mm. Wash with cold water, dry and recryst from pet ether, or from ethyl ether cooled in powdered Dry-ice after the ether soln had been washed with 10% NaOH until colourless, then dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. Alternatively dissolve in CHCl<sub>3</sub>, wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and crystallise. [J Am Chem Soc 62 511 1940.] Test for the SO<sub>2</sub>Cl group by dissolving in EtOH and boiling with NH<sub>4</sub>CNS whereby a yellow amorphous ppte forms on cooling [J Am Chem Soc 25 198 1901].

o-Bromobenzoic acid [88-65-3] M 201.0, m 148.9°, pK<sup>20</sup> 2.88. Crystd from \*C<sub>6</sub>H<sub>6</sub> or MeOH.

*m*-Bromobenzoic acid [585-76-2] M 201.0, m 155°, pK<sup>25</sup> 3.81. Crystd from acetone/water, MeOH or acetic acid.

*p*-Bromobenzoic acid [586-76-5] M 201.0, m 251-252°, 254-256°, 257-258°,  $pK^{25}$  3.96. Crystd from MeOH, or MeOH/water mixture, 90% EtOH and Et<sub>2</sub>O. The *methyl ester* has m 81° from Et<sub>2</sub>O or dilute MeOH. [Male and Thorp J Am Chem Soc 35 269 1913; Lamneck J Am Chem Soc 76 406 1954, Vandenbelt et al. Anal Chem 26 926 1954.]

p-Bromobenzophenone [90-90-4] M 261.1, m 81°. Crystd from EtOH.

*p*-Bromobenzoyl chloride [586-75-4] M 219.5, m 36-39°, 39.8°, 41°, b 62°/0.1 mm, 104.5°/6mm, 126.4-127.2°/14mm. Check IR of a film to see if OH bands are present. If absent then recryst from pet ether and dry in a vacuum. If OH bands are weak then distil *in vacuo* and recryst if necessary. If OH bands are very strong then treat with an equal volume of redistilled SOCl<sub>2</sub> reflux for 2h then evaporate excess of SOCl<sub>2</sub> and distil residual oil or low melting solid. Store in the dark away from moisture. LACHRYMATORY. [Martin and Partington J Chem Soc 1175 1936.]

p-Bromobenzyl bromide [589-15-1] M 249.9, m 60-61°. Crystd from EtOH. LACHRYMATORY.

*p*-Bromobenzyl chloride [589-17-3] M 205.5, m 40-41°, b 105-115°/12mm. Crystd from EtOH. LACHRYMATORY.

p-Bromobiphenyl [92-66-0] M 233.1, m 88.8-89.2°. Crystd from abs EtOH and dried under vacuum.

**2-Bromobutane** [78-76-2] M 137.0, b 91.2°, d 1.255, n 1.4367,  $n^{25}$  1.4341. Washed with conc HCl, water, 10% aqueous NaHSO<sub>3</sub>, and then water. Dried with CaCl<sub>2</sub>, Na<sub>2</sub>SO<sub>4</sub> or anhydrous K<sub>2</sub>CO<sub>3</sub>, and fractionally distd through a 1m column packed with glass helices.

(+)-3-Bromocamphor-8-sulfonic acid [5344-58-1] M 311.2, m 195-196°(anhydrous),  $[\alpha]_D^{20}$  +88.3° (in H<sub>2</sub>O), pK ~0. Crystd from water.

1R(endo,anti)-3-Bromocamphor-8-sulfonic acid ammonium salt see entry in Chapter 5.

(+)-3-Bromocamphor-10-sulfonic acid hydrate [67999-30-8] M 329.2, m 119-121°,  $[\alpha]_D^{20}$  +98.3° (in H<sub>2</sub>O), pK ~0. Crystd from water.

**4-Bromo-4'-chlorobenzophenone** [27428-57-5] **M 295.6, m 150°.** Crystd from EtOH or \*C<sub>6</sub>H<sub>6</sub> and further purified by zone refining (100 passes) [Grove and Turner J Chem Soc 509 1929; Lin and Hanson J Phys Chem **91** 2279 1987].

**Bromocresol Green** (3',3",5',5"-tetrabromo-*m*-cresolsulfonephthalein) [76-60-8] M 698.0, m 218-219°(dec), 225°(dec), pK 4.51. Crystd from glacial acetic acid or dissolved in aqueous 5% NaHCO<sub>3</sub> soln and ppted from hot soln by dropwise addition of aqueous HCl. Repeated until the extinction did not increase ( $\lambda_{max}$  423nm). Indicator at pH 3.81 (yellow) and pH 5.4 (blue-green).

**Bromocresol Purple (5',5"-dibromo-***o***-cresolsulfonephthalein)** [115-40-2] **M 540.2, m 241-242°(dec), pK<sub>1</sub> -2.15, pK<sub>2</sub> 6.3.** Dissolved in aqueous 5% NaHCO<sub>3</sub> soln and ppted from hot soln by dropwise addition of aqueous HCl. Repeated until the extinction did not increase ( $\lambda_{max}$  419nm). Can also be crystd from \*benzene. Indicator at pH 5.2 (yellow) and pH 6.8 (purple).

5-Bromocytosine [2240-25-7] M 190.0, m 245-255°(dec), 250°(dec),  $pK_1^{25}$  3.04,  $pK_2^{25}$  10.33. Recryst from H<sub>2</sub>O or 50% aq EtOH. Alternatively, dissolve *ca* 3g in conc HCl (10mL) and evaporate to dryness. Dissolve the residual hydrochloride in the minimum volume of warm H<sub>2</sub>O and make faintly alkaline with aq NH<sub>3</sub>. Collect the crystals and dry in a vacuum at 100°. [*J Am Chem Soc* 56 134 1934.]

*p*-Bromo-*N*,*N*-dimethylaniline [586-77-6] M 200.1, m 55°, b 264°, pK<sup>25</sup> 4.23. Refluxed for 3h with two equivalents of acetic anhydride, then fractionally distd under reduced pressure

1-Bromo-2,4-dinitrobenzene [584-48-5] M 247.0, m 75°. Crystd from ethyl ether, isopropyl ether, 80% EtOH or absolute EtOH.

**2-(2-Bromoethyl)-1,3-dioxane** [33884-43-4] **M** 195.1, **b** 67-70°/2.8mm, 71-72°/4mm, 95°/15mm, d  $_{4}^{20}$  1.44, n  $_{D}^{20}$  1.4219. Purify by vacuum fractionation. Also dissolve in Et<sub>2</sub>O, wash with aqueous NaHCO<sub>3</sub>, dry extract with Na<sub>2</sub>SO<sub>4</sub>, filter and fractionate. NMR in CCl<sub>4</sub> has  $\delta$  1.3 (m, 1H), 2.1 (m, 3H), 3.36 (t, 2H), 3.90 (m, 4H) and 4.57 (t, H). [J Org Chem 41 560 1976; NMR, MS: Tetrahedron 35 1969 1979; J Pharm Sci 60 1250 1971.]

**2-(2-Bromoethyl)-1,3-dioxolane** [18742-02-4] M 181.1, b 68-80°/8mm, 68-73°/10mm, 78-80°/20mm,  $d_4^{20}$  1.510,  $n_D^{20}$  1.479. Dissolve in pentane, wash with 5% aqueous NaHCO<sub>3</sub>, dry (Na<sub>2</sub>SO<sub>4</sub>), and evaporate. Distil the residue. [NMR: J Org Chem 34 1122 1969; J Pharm Sci 60 1250 1971.]

N-(2-Bromoethyl)phthalimide [574-98-1] M 254.1, m 81-83°, 82.5-83.5°. The following is to be carried out in an efficient FUME HOOD. Dissolve the compound (180g) in CS<sub>2</sub> (500 mL) by refluxing for 15 min (to cause the separation of the most likely impurity, 1,2-diphthalimidoethane), filter and evaporate under reduced pressure. The product forms light tan crystals. (m 78-80°). Recryst from EtOH (charcoal) [the compound (50g) is dissolved in hot 75% EtOH (200mL), boiled for *ca* 10 min, carbon added (5g, Norite), filtered and cooled to 0°], as white crystals (40g) which can be recrystd (m 80-81°) and further recrystn gave m 82-83°. [Org Synth Coll Vol I 119 1932, Synthesis 389 1976; NMR: Bull Soc Chim Fr II-165 1979.]

**Bromoform** [75-25-2] M 252.8, f 8.1°, 55-56°/35mm, 149.6°/760mm, d<sup>15</sup> 2.9038, d<sup>30</sup> 2.86460, n<sup>15</sup> 1.60053, n 1.5988. Storage and stability of bromoform and chloroform are similar. Ethanol, added as a stabilizer, is removed by washing with  $H_2O$  or with saturated CaCl<sub>2</sub> soln, and the CHBr<sub>3</sub>, after drying with CaCl<sub>2</sub> or K<sub>2</sub>CO<sub>3</sub>, is fractionally distd. Prior to distn, CHBr<sub>3</sub> has also been washed with conc  $H_2SO_4$  until the acid layer no longer became coloured, then dilute NaOH or NaHCO<sub>3</sub>, and  $H_2O$ . A further purification step is fractional crystn by partial freezing.

**3-Bromofuran** [22037-28-1] M 147.0, b 38.5°/40mm, 50°/110mm, 102.5-103°/atm, d 1.661, n 1.4970. Purified by two steam distillations and dried over fresh CaO. It can be dried over Na metal (no obvious reaction) and fractionated. It is not very soluble in  $H_2O$  but soluble in organic solvents. Freshly distilled, it is a clear oil, but darkens on standing and eventually resinifies. It can be stored for long periods by covering the oil with an alkaline soln of hydroquinone and redistilled when required. It forms a characteristic

maleic anhydride adduct, m 131.5-132°. [J Am Chem Soc 52 2083 1930, 53 737 1931, adduct: 55 430 1933.]

(±)-2-Bromohexadecanoic acid (2-bromopalmitic acid) [18263-25-7] M 335.3, m 51-53°, 52.3-52.5°, 53°, pK<sub>Est</sub> ~3.2. Recrystd from pet ether (b 60-80°, charcoal) and finally from EtOH. The ethyl ester has b 177-178°/2mm,  $d_{28}^{28}$  1.0484,  $n_D^{20}$  1.4560. [IR: J Org Chem 21 1426 1956.]

**5-Bromoindole** [10075-50-0] **M 196.1, m 90.5-91°, 90-92°, pK 16.13 (NH).** Purified by steam distn from a faintly alkaline soln. Cool the aqueous distillate, collect the solid, dry in a vacuum desiccator over  $P_2O_5$  and recryst from aqueous EtOH (35% EtOH) or pet ether-Et<sub>2</sub>O.  $\lambda_{max}$  in MeOH: 279, 287 and 296 (loge 3.70, 3.69 and 3.53. The *picrate* has **m** 137-138°(dec) (from Et<sub>2</sub>O-pet ether). [UV: Chem Ber **95** 2205 1962; UV and NMR: Bull Soc Chim Fr 4091 1970.]

**5-Bromoisatin** [87-48-9] **M 226.0, m 245°(dec), 251-153°, 255-256°.** Forms red prisms or needles from EtOH. The *N*-acetate crystallises as yellow prisms from  $*C_6H_6$ , **m** 170-172°, and the *N*-methyl derivative form orange-red needles from MeOH, **m** 172-173°. [Chem Ber 47 360 1914, 53 1545 1920; Recl Trav Chim Pays-Bas 73 197 1954; Tetrahedron Lett 215 1978.]

6-Bromoisatin [6326-79-0] M 226.0, m 270°, pK 10.35. Recrystd from AcOH (yellow needles). It is a plant growth substance. [Sadler J Org Chem 21 169 1956.]

**2-Bromomethylanthraquinone** [7598-10-9] **M 301.1, m 200-202°.** Recryst from AcOH, the crystals are washed with a little  $Et_2O$ , dried in air and then in vac at 100°. It is prepared by bromination of 2-methylanthraquinone with  $Br_2/PhNO_2$  at 145-150°, or N-bromosuccinimide in CCl<sub>4</sub> containing a trace of (PhCOO)<sub>2</sub>.

2-(Bromomethyl)benzonitrile [22115-41-9] M 195.1, m 72-73°, 79°, b 152-155°/15mm. Purified by steam distn. Extract the distillate with Et<sub>2</sub>O, dry extract (Na<sub>2</sub>SO<sub>4</sub>), evap and distil residue. The solidified distillate can be recrystd from pet ether or cyclohexane. NMR (CDCl<sub>3</sub>)  $\delta$ : 7.8-7.2 (m 4H), 4.62 (s, 2H); IR v: 2238 cm<sup>-1</sup>. LACHRYMATORY [Chem Ber 24 2570 1891, 74 675 1934; Aust J Chem 22 577 1969.]

S-(+)-1-Bromo-2-methylbutane [534-00-9] M 151.1, b 38.2°/39mm, 49°/62mm, 60.8°(57-58°)/100mm, 65-65.6°/140mm, 116-122°/atm,  $d_4^{20}$  1.2232,  $n_D^{20}$  1.4453,  $[\alpha]_D^{20}$ +5.1° (neat, +5.8° (c 5, CHCl<sub>3</sub>). Wash with ice-cold H<sub>2</sub>O, dried by freezing, shake twice with an equal vol of H<sub>2</sub>SO<sub>4</sub> at 0°, and twice with an equal volume of H<sub>2</sub>O at 0°. Freeze dried and kept over freshly heated (and then cooled) K<sub>2</sub>CO<sub>3</sub>, and distd through a vacuum jacketed column of broken glass. Alternatively, dissolve in pet ether (b 40-60°), wash with 5% NaOH, conc H<sub>2</sub>SO<sub>4</sub> (at 0°), then H<sub>2</sub>O, dry (CaCl<sub>2</sub>), evaporate and distil. [J Am Chem Soc 74 4858 1952, 81 2779 1959; J Chem Soc 1413 1959, 2685 1950.]

**2-Bromo-3-methylindole** (2-bromoskatole) [1484-28-2] M 210.1, m 102-104°, pK<sub>Est</sub> <0. Purified by chromatography on silica gel in CHCl<sub>3</sub>/pet ether (1:2) followed by crystn from aqueous EtOH. [Phillips and Cohen J Am Chem Soc 108 2023 1986.]

4-(Bromomethyl)-7-methoxycoumarin [35231-44-8] M 269.1, m 208-209°, 213-215°, 216-218°. Cryst from boiling AcOH, crystals are washed with AcOH, EtOH and dried in a vacuum, NMR (TFA)  $\delta$  3.97s, 4.57s, 6.62s, 6.92-7.19m and 7.80d. [Biochem Biophys Res Commun 45 1262 1971.]

2-(Bromomethyl)-naphthalene [939-26-4] M 221.1, m 52-54°, 56°, 56-57°, b 133-136°/0.8mm, 214°/100mm. Dissolve in toluene, wash with saturated aqueous NaHCO<sub>3</sub>, dry (Mg SO<sub>4</sub>), evaporate and fractionally distil the residue and recrystallise the distillate from EtOH. [J Chem Soc 5044, 1952; Bull Soc Chim Fr 566 1953.] **2-Bromo-2-methylpropane** [507-19-7] M 137.0, b 71-73°, d 1.218, n 1.429. Neutralised with  $K_2CO_3$ , distd, and dehydrated using molecular sieves (5A), then vacuum distd and degassed by freeze-pump-thaw technique. Sealed under vacuum.

1-Bromonaphthalene [90-11-9] M 207.1, b 118°/6mm, d 1.489. Purified by passage through activated alumina, and three vacuum distns.

**2-Bromonaphthalene** [580-13-2] M 207.1, m 59°. Purified by fractional elution from a chromatographic column. Crystd from EtOH.

1-Bromo-2-naphthol [573-97-7] M 223.1, m 76-78°, pK<sub>Est</sub> ~8.0. Crystd from EtOH.

6-Bromo-2-naphthol [15231-91-1] M 223.1, m 122-126°, pK<sub>Est</sub> ~9.1. Crystd from EtOH.

5-Bromonicotinic acid [20826-04-4] M 202.0, m 178-182°, 189-190°,  $pK_{Est} \sim 4.4$ ,  $pK^{25}$  4.02 (50% aq EtOH). Recryst from H<sub>2</sub>O and then from EtOH using charcoal. The *amide* has m 219-219.5° (from aq EtOH) and the *methyl ester* prepared by addition of ethereal diazomethane can be purified by sublimation in a vacuum and has m 98-99°, the *acid chloride* also can be sublimed in *vacuo* and has m 74-75° and gives the methyl ester in MeOH. [J Prakt Chem 138 244 1933; J Am Chem Soc 70 2381 1948; 82 4430 1960; J Chem Soc 35 1978.]

ω-Bromo-4-nitroacetophenone [99-81-0] M 244.1, m 98°. Crystd from \*C<sub>6</sub>H<sub>6</sub>-pet ether.

o-Bromonitrobenzene [577-19-5] M 202.1, m 43°. Crystd twice from pet ether, using charcoal before the first crystn.

*m*-Bromonitrobenzene [585-79-5] M 202.1, m 55-56°. Crystd twice from pet ether, using charcoal before the first crystn.

*p*-Bromonitrobenzene [586-78-7] M 202.1, m 127°. Crystd twice from pet ether, using charcoal before the first crystn.

1-Bromooctadecane [112-89-0] M 333.4, m 26°, 27.3°, 28-30°, b 178-179°/2mm, 214-218°/15mm,  $d^{20}$  0.976,  $n_D^{20}$  1.461. Twice recrystd from the melt then distilled under vacuum three times and using the middle cut. Alternatively, wash the oil with aqueous Na<sub>2</sub>SO<sub>4</sub>, then conc H<sub>2</sub>SO<sub>4</sub> (cool) and again with aqueous Na<sub>2</sub>SO<sub>4</sub> and then fractionate. [J Am Chem Soc 55 1574 1933, 72 171 1950; IR: Aust J Chem 12 743 1959; IR: Bull Soc Chim Fr 516 1957.]

(±)-2-Bromopentane [107-81-3] M 151.1, b 117.2°/753mm, 116-117°/atm, 117.5°/740mm,  $d_4^{20}$  1.2190,  $n_D^{20}$  1.4401. Dry over K<sub>2</sub>CO<sub>3</sub> and distil through a short Vigreux column. [IR: J Am Chem Soc 74 4063 1952, 78 2199 1956.]

p-Bromophenacyl bromide [99-73-0] M 277.9, m 110-111°. Crystd from EtOH (ca 8mL/g).

o-Bromophenol [95-56-7] M 173.0, b 194°, d 1.490, pK<sup>25</sup> 8.45. Purified by at least two passes through a chromatographic column.

*p*-Bromophenol [106-41-2] M 173.0, m 64°,  $pK^{25}$  9.36. Crystd from CHCl<sub>3</sub>, CCl<sub>4</sub>, pet ether (b 40-60°), or water and dried at 70° under vacuum for 2h.

**Bromophenol Blue** (3,3',5,5'-tetrabromophenolsulfonephthalein) [115-39-9] M 670.0, m 270-271°(dec), 273°(dec),  $\lambda$ max 422max, pK 3.62. Crystd from \*benzene or acetone/glacial acetic acid, and air dried. Indicator at pH 3.0 (yellow) and pH 4.6 (purple).

(4-Bromophenoxy)acetic acid [1878-91-7] M 231.1, m 158°, pK<sup>25</sup> 3.13. Crystd from EtOH.

**3-(4-Bromophenoxy)propionic acid** [93670-18-9] **M 247.1, m 146°, pK**<sub>Est</sub> ~4.2. Crystd from EtOH.

**4-Bromophenylacetic acid** [1878-68-8] **M 215.1, m 112-113°, 113-115°, 114°, pK 4.19.** Recrystd from H<sub>2</sub>O as needles. The *acid chloride* has **b** 238°/atm, **m** 50°, and the *anilide* has **m** 174-175°. [J Chem Soc 161 1934, 1251 1948; J Org Chem 11 798 1946.]

**4-Bromophenylhydrazine** [589-21-9] M 187.1, m 108-109°, pK<sup>20</sup>-5.6 (aq H<sub>2</sub>SO<sub>4</sub>), pK<sup>25</sup> 5.05. Crystd from H<sub>2</sub>O.

4-Bromophenyl isocyanate [2492-02-9] M 189.0, m 41-42°. Crystd from pet ether (b 30-40°).

**4-Bromophenyl isothiocyanate** [1985-12-2] **M 214.1, m 56-58°.** Recryst from boiling *n*-hexane. Any insoluble material is most probably the corresponding urea. It can be purified by steam distn, cool the receiver, add NaCl and extract in Et<sub>2</sub>O, wash extract with N H<sub>2</sub>SO<sub>4</sub>; dry (MgSO<sub>4</sub>), evaporate and recrystallise the residual solid. [Org Synth Coll Vol IV 700 1963; Coll Vol I 447 1941.]

Bromopicrin (tribromonitromethane) [464-10-8] M 297.8, m 10.2-10.3°, b 85-87°/16mm, d 2.788, n 1.579. Steam distd, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and vacuum distd. TOXIC.

R-(+)-2-Bromopropionic acid [10009-70-8] M 153.0, b 78°/4mm,  $[\alpha]_D^{25} + 27.2°$  (neat), pK<sup>25</sup>4.07. Dissolve in Et<sub>2</sub>O, dry (CaCl<sub>2</sub>), evap and distil through a short column. Distillation through a Podbielniak column led to decomposition. [Podbielniak column. A plain tube containing "Heli-Grid" Nichrome or Inconel wire packing. This packing provides a number of passage-ways for the reflux liquid, while the capillary spaces ensure very even spreading of the liquid, so that there is a very large area of contact between liquid and vapour while, at the same time, channelling and flooding are minimised. A column 1m high has been stated to have an efficiency of 200-400 theoretical plates (for further details, see Podbielniak *Ind Eng Chem (Anal Ed)* 13 639 1941; Mitchell and O'Gorman Anal Chem 20 315 1948)]. Store in the dark under N<sub>2</sub>, preferably in sealed ampoules. Even at -10° it slowly decomposes. [J Am Chem Soc 76 6054 1954.]

**3-Bromopropionic acid** [590-92-1] **M 153.0, m 62.5°, 62.5-63.5°, 63-64°.** Crystallises as plates from CCl<sub>4</sub>. It is soluble in organic solvents and H<sub>2</sub>O. It has a pKa<sup>25</sup> in H<sub>2</sub>O of 4.01, and its *methyl ester* has **b** 65°/18mm and 80°/27mm. The S-benzylisothiouronium salt has **m** 136°. [Org Synth Coll Vol I 134 1948; Justus Liebigs Ann Chem **599** 140 1956.]

**N-(3-Bromopropyl)phthalimide** [5460-29-7] **M 268.1, m 72-74°, 74°.** Place in a Soxhlet and extract with Et<sub>2</sub>O, whereby the bis-phthalimido impurity is not extracted. Evaporate the Et<sub>2</sub>O and recryst from EtOH or aqueous EtOH or pet ether. [Chem Ber 21 2669 1888; Justus Liebigs Ann Chem 614 83 1958; Can J Chem 31 1060 1953.]

**2-Bromopyridine** [109-04-6] **M 158.0, b 49.0°/2.7mm, d 1.660, n 1.5713, pK<sup>25</sup> 0.90.** Dried over KOH for several days, then distd from CaO under reduced pressure, taking the middle fraction.

**Bromopyrogallol Red** (5,5'-dibromopyrogallolsulfonephthalein) [16574-43-9] M 576.2, m 300°,  $\lambda$  max 538nm ( $\epsilon$  54,500 H<sub>2</sub>O pH 5.6-7.5), pK<sub>1</sub> 2.9, pK<sub>2</sub> 4.39, pK<sub>3</sub> 9.15, pK<sub>4</sub> 11.72. Crystd from 50% EtOH, or aq alkaline soln by acid [Suk Collect Czech Chem Commun 31 3127 1966].

**Bromopyruvic acid** [1113-59-3] **M 167.0, m 79-82°, pK**<sub>Est</sub> ~1.6. Dried by azeotropic distn (toluene), and then recrystd from dry CHCl<sub>3</sub>. Dried for 48h at 20° (0.5 Torr) over P<sub>2</sub>O<sub>5</sub>. Stored at 0°. [Labandiniere et al. J Org Chem 52 157 1987].

5-Bromosalicyl hydroxamic acid [5798-94-7] M 210.1, m 232°(dec), pK<sub>Est(1)</sub>~ 1.5, pK<sub>Est(2)</sub>~ 7.0, pK<sub>Est(3)</sub>~ 8.7. Crystd from EtOH.

**4-Bromostyrene** [2039-82-9] **M 183.1, b 49.5-50°/2.5mm, 87-88°/12mm, 102-104°/20mm, d 1.3984, n 1.5925**. It polymerises above 75° in the presence of benzoyl peroxide. To purify, if it has not gone to a solid resin, dissolve in Et<sub>2</sub>O, dry (MgSO<sub>4</sub>), add *ca* 0.1g of 4-*tert* butylcatechol (polymerisation inhibitor) per 100g of bromostyrene. Filter, evap under reduced press (use as high a vac as possible) and distil. Store in dark bottles in the presence of the inhibitor (concn as above). [Org Synth Coll Vol III 204 1955.]

**N-Bromosuccinimide** [128-08-5] M 178.0, m 183-184°(dec). N-Bromosuccinimide (30g) was dissolved rapidly in 300mL of boiling water and filtered through a fluted filter paper into a flask immersed in an ice bath, and left for 2h. The crystals were filtered, washed thoroughly with ca 100mL of ice-cold water and drained on a Büchner funnel before drying under vac over  $P_2O_5$  or CaCl<sub>2</sub> [Dauben and McCoy J Am Chem Soc 81 4863 1959]. Has also been crystd from acetic acid or water (10 parts, washed in water and dried *in vacuo*, [Wilcox et al. J Am Chem Soc 108 7693 1986; Shell et al. J Am Chem Soc 108 2013 1986.]

**Bromotetronic acid** [21151-51-9] **M 179.0, m 183°(dec), pK<sup>25</sup> 2.23.** Decolorised, and free bromine was removed by charcoal treatment of an ethyl acetate soln, then recrystd from ethyl acetate [Schuler, Bhatia and Schuler J Phys Chem 78 1063 1974].

**Bromotheophylline** [10381-75-6] M 259.1, m 309°, 315-320° (with browning and dec),  $pK_{Est(1)} \sim 5.5$ ,  $pK_{Est(2)} \sim 9.2$ . It is purified by dissolving in the minimum volume of dilute NaOH (charcoal), filter and acidify to pH ca 3.5-4 and the solid that separates is collected, dried *in vacuo* at 100° and stored in a dark container. [J Prakt Chem [2] 118 158 1928; Chem Ber 28 3142 1895.]

**Bromothymol Blue** (3',3"-dibromothymolsulfonephthalein) [76-59-5] M 624.4, m 201-203°,  $pK_1$  -0.66,  $pK_2$  6.99. Dissolved in aq 5% NaHCO<sub>3</sub> soln and ppted from the hot soln by dropwise addn of aq HCl. Repeated until the extinction did not increase ( $\lambda_{max}$  420nm). Indicator at pH 6.0 (yellow) and 7.6 (blue).

p-Bromotoluene [106-38-7] M 171.0, m 28°, b 184°, d 1.390. Crystd from EtOH [Taylor and Stewart J Am Chem Soc 108 6977 1986].

α-Bromo-4-toluic acid [6232-88-8] M 215.1, m 229-230°, pK<sub>Est</sub> ~3.2. Crystd from Me<sub>2</sub>CO.

**Bromotrichloromethane** [75-62-7] M 198.5, f -5.6°, m 21°, b 104.1°, d 2.01, n 1.5061. Washed with aq NaOH soln or dilute Na<sub>2</sub>CO<sub>3</sub>, then with H<sub>2</sub>O, and dried with CaCl<sub>2</sub>, BaO, MgSO<sub>4</sub> or P<sub>2</sub>O<sub>5</sub> before distilling in diffuse light and storing in the dark. Has also been purified by treatment with charcoal and by fractional crystn by partial freezing. Purified also by vigorous stirring with portions of conc H<sub>2</sub>SO<sub>4</sub> until the acid did not discolour during several hours stirring. Washed with Na<sub>2</sub>CO<sub>3</sub> and water, dried with CaCl<sub>2</sub> and then illuminated with a 1000W projection lamp at 15cm for 10h, after making it 0.01M in bromine. Passed through a 30 x 1.5cm column of activated alumina and fractionally redistilling through a 12-in Vigreux column. [Firestone and Willard J Am Chem Soc 83 3511 1961; see also Cadogan and Duell J Chem Soc 4154 1962.]

**1-Bromo-3,3,3-trifluoroethane** [421-06-7] **M 163.0, m -94°, b 26-27°, d 1.788, n 1.332.** Washed with water, dried (CaCl<sub>2</sub>) and distd.

**Bromotrifluoromethane** (Freon 13B1) [75-63-8] M 148.9, b -59°, d 1.590. Passed through a tube containing  $P_2O_5$  on glass wool into a vac system where it was frozen out in a quartz sample tube and degassed by a series of cycles of freezing, evacuating and thawing.

**5-Bromouracil** [51-20-7] **M 191.0, m 293°, 303-305°, 312°(dec), pK\_1^{25}-7.25, pK\_2^{25}7.83.** Purified by dissolving in 2N NaOH (charcoal), filter and acidify with HCl. The ppte is dried *in vacuo* at 100° and recryst (prisms) twice from H<sub>2</sub>O. [J Am Chem Soc 56 134 1934, UV: J Am Chem Soc 81 3786 1959; J Org Chem 23 1377 1958.] **5-Bromovaleric** ( $\gamma$ -bromopentanoic) acid [2067-33-6] M 181.0, m 40°, pK<sub>Est</sub> ~4.6. Crystd from pet ether.

α-Bromo-p-xylene [104-81-4] M 185.1, m 35°, b 218-220°/740mm. Crystd from EtOH or pentane.

Bromural [N-(aminocarbonyl)-2-bromo-3-methylbutanamide, bromisovalum] [496-67-3] M 223.1, m 154-155°. Crystd from toluene, and air dried.

Bufotenine hydrogen oxalate [2963-79-3] M 294.3, m 96.5°. Crystd from Et<sub>2</sub>O.

**1,3-Butadiene** [106-99-0] **M 54.1, b -2.6°.** Dried by condensing with a soln of triethylaluminium in decahydronaphthalene; then flash distd. Also dried by passage over anhydrous CaCl<sub>2</sub> or distd from NaBH<sub>4</sub>. Also purified by passage through a column packed with molecular sieves (4A), followed by cooling in Dry-ice/MeOH bath overnight, filtering off the ice and drying over CaH<sub>2</sub> at -78° and distd in a vacuum line.

*n*-Butane [106-97-8] M 58.1, m -135°, b -0.5°. Dried by passage over anhydrous  $Mg(ClO_4)_2$  and molecular sieves type 4A. Air was removed by prolonged and frequent degassing at -107°.

1,4-Butanediol (tetramethylene glycol) [110-63-4] M 90.1, f 20.4°, b 107-108°/4 mm, 127°/20mm, d 1.02, n 1.4467. Distd and stored over Linde type 4A molecular sieves, or crystd twice from anhydrous diethyl ether/acetone, and redistd. Also purified by recrystn from the melt and doubly distd *in vacuo* in the presence of Na<sub>2</sub>SO<sub>4</sub>.

meso-2,3-Butanediol [513-85-9] M 90.1, m 25°. Crystd from isopropyl ether.

threo-2,3-butanediol [R,R(-): 24347-58-8] [S,S (+):19132-06-0] M 90.1, m 16-19°, 19.7°, b 77,5-78°/10mm, 179-180°/atm,  $[\alpha]_{D}^{20}$  (-) or (+) 13.1° (neat). Purified by fractional distn. The bis-(4-nitrobenzoate) has m 141-142° and  $[\alpha]_{D}^{25} \pm 52°$  (c 4 CHCl<sub>3</sub>). [J Am Chem Soc 79 734 1957, 74 425 1952, Can J Res 27 457 1949.]

1-Butanesulfonyl chloride [2386-60-9] M 156.6, b 75-76°/7mm, 98°/13mm,  $d_4^{20}1.2078$ ,  $n_D^{20}$ 1.4559. It has a pungent odour and is LACHRYMATORY. If IR shows OH bands then dissolve in Et<sub>2</sub>O, wash with cold saturated aq NaHCO<sub>3</sub> (care since CO<sub>2</sub> will be generated) then H<sub>2</sub>O, dry over solid Na<sub>2</sub>SO<sub>4</sub>, filter evaporate and distil the residue twice. Characterised by shaking a soln in Et<sub>2</sub>O or \*C<sub>6</sub>H<sub>6</sub> with aq NH<sub>3</sub>, collect the solid and recryst from CHCl<sub>3</sub>, CCl<sub>4</sub> or Et<sub>2</sub>O-pet ether, m 48°. [J Am Chem Soc 60 1488 1938; J Org Chem 5 83 1940.]

1-Butanethiol [109-79-5] M 90.2, b 98.4°,  $d^{25}$  0.837, n 1.443,  $n^{25}$  1.440,  $pK_{Est} \sim 11.3$ . Dried with CaSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>, then refluxed from magnesium; or dried with, and distd from CaO, under nitrogen [Roberts and Friend J Am Chem Soc 108 7204 1986.] Has been separated from hydrocarbons by extractive distn with aniline.

Dissolved in 20% NaOH, extracted with a small amount of  $*C_6H_6$ , then steam distd, until clear. The soln was then cooled and acidified slightly with 15% H<sub>2</sub>SO<sub>4</sub>. The thiol was distd out, dried with CaSO<sub>4</sub> or CaCl<sub>2</sub>, and fractionally distd under N<sub>2</sub> [Mathias and Filho J Phys Chem 62 1427 1958]. Also purified by pptn as lead mercaptide from alcoholic soln, with regeneration by adding dilute HCl to the residue after steam distn. All operations should be carried out in a fume cupboard due to the TOXICITY and obnoxious odour of the thiol.

**2-Butanethiol** [513-53-1] M 90.2, b 37.4°/134mm,  $d^{25}$  0.846,  $n^{25}$  1.4338,  $pK_{Est} \sim 11.4$ . Purified as for 1-butanethiol.

*n*-Butanol [71-36-3] M 74.1, b 117.7°,  $d^{25}$  0.80572, n 1.39922,  $n^{15}$  1.40118. Dried with MgSO<sub>4</sub>, CaO, K<sub>2</sub>CO<sub>3</sub>, Ca or solid NaOH, followed by refluxing with, and distn from, calcium, magnesium activated with iodine, aluminium amalgam or sodium. Can also dry with molecular sieves, or by refluxing with *n*-butyl phthalate or succinate. (For method, see *Ethanol.*) *n*-Butanol can also be dried by efficient fractional distn, water passing over in the first fractn as a binary azeotrope (contains about 37% water). An ultraviolet-

transparent distillate has been obtained by drying with magnesium amd distilling from sulfanilic acid. To remove bases, aldehydes and ketones, the alcohol has been washed with dil  $H_2SO_4$ , then NaHSO<sub>4</sub> soln; esters were removed by boiling for 1.5h with 10% NaOH.

Also purified by adding 2g NaBH<sub>4</sub> to 1.5L butanol, gently bubbling with argon and refluxing for 1 day at 50°. Then added 2g of freshly cut sodium (washed with butanol) and refluxed for 1 day. Distd and the middle fraction collected [Jou and Freeman J Phys Chem 81 909 1977].

**2-Butanone** (methyl ethyl ketone, MEK) [78-93-0] M 72.1, b 79.6°, d 0.853, n 1.37850, n<sup>25</sup> 1.37612, pK<sup>25</sup> -7.2 (aq H<sub>2</sub>SO<sub>4</sub>). In general, purification methods are the same as for acetone. Aldehydes can be removed by refluxing with KMnO<sub>4</sub> + CaO, until the Schiff aldehyde test is negative, prior to distn. Shaking with satd K<sub>2</sub>CO<sub>3</sub>, or passage through a small column of activated alumina, removes cyclic impurities. The ketone can be dried by careful distn (an azeotrope containing 11% water boils at 73.4°), or by CaSO<sub>4</sub>, P<sub>2</sub>O<sub>5</sub>, Na<sub>2</sub>SO<sub>4</sub>, or K<sub>2</sub>CO<sub>3</sub>, followed by fractional distn. Purification as the bisulfite addition compound is achieved by shaking with excess satd Na<sub>2</sub>SO<sub>3</sub>, cooled to 0°, filtering off the ppte, washing with a little ethyl ether and drying in air; this is followed by decomposition with a slight excess of Na<sub>2</sub>CO<sub>3</sub> soln and steam distn, the distillate being satd with K<sub>2</sub>CO<sub>3</sub> so that the ketone can be separated, dried with K<sub>2</sub>CO<sub>3</sub>, filtered, and distd. Purification as the *NaI addition compound* (m 73-74°) is more convenient. (For details, see *Acetone.*) Small quantities of 2-butanone can be purified by conversion to the semicarbazone, recrystn to constant melting point, drying under vac over CaCl<sub>2</sub> and paraffin wax, refluxing for 30min with excess oxalic acid, followed by steam distn, salting out, drying and distilling [Cowan, Jeffery and Vogel J Chem Soc 171 1940].

cis-2-Butene [590-18-1] M 56.1, b 2.95-3.05°/746mm. The gas is dried with CaH<sub>2</sub>. Purified by gas chromatography. HIGHLY FLAMMABLE.

trans-2-Butene [624-64-6] M 56.1, b 0.3-0.4%/744mm. The gas is dried with CaH<sub>2</sub>. Purified by gas chromatography. HIGHLY FLAMMABLE.

**2-Butene-1,4-dicarboxylic acid** (*trans-3*-hexenedioic acid, *trans-B*-hydromuconic acid) [4436-74-2] M 144.1, m 194-197°, 195-196°,  $pK_{Est(1)}$ ~4.2,  $pK_{Est(2)}$ ~5.00. Crystd from boiling water, then dried at 50-60° in a vacuum oven.

But-3-en-2-one (methyl vinyl ketone) [78-94-4] M 70.1, b 79-80°/760mm, d 0.842. See entry on p.302.

**2-tert-Butoxycarbonyloxyimino-2-phenylacetonitrile** (BOC-ON) [58632-95-4] M **246.3**, m **87-89°**. Triturate solid with 90% aq MeOH, filter, wash with 90% aq MeOH and dry in a vac. Recryst from MeOH (needles or plates), but use warm MeOH and cool to cryst, *do not boil as it decomposes slowly*. IR has  $v \, 1785$  (C=O) cm<sup>-1</sup> and NMR (CDCl<sub>3</sub>) usually shows two *tert*-butyl singlets for *syn* and *anti* isomers. Store in a brown bottle (fridge). It evolves CO<sub>2</sub> at room temp (stoppered bottle can explode!), but can be stored over silica gel which can extend its useful life to more than a year. [Itoh et al. Org Synth **59** 95 1980.]

**2-Butoxyethanol (butyl cellosolve)** [111-76-2] **M 118.2, b 171°/745mm, d 0.903, n 1.4191.** Peroxides can be removed by refluxing with anhydrous  $SnCl_2$  or by passage under slight pressure through a column of activated alumina. Dried with anhydrous  $K_2CO_3$  and  $CaSO_4$ , filtered and distd, or refluxed with, and distd from NaOH.

**4-Butoxyphenylacetic acid** [4547-57-3] **M 208.3, m 86-87°, 88.5°, pK**<sub>Est</sub> ~4.4. Purified by recrystn from pet ether (b 40-60°). [J Am Chem Soc 68 2592 1946.]

**n-Butyl acetate** [123-86-4] M 116.2, b 126.1°, d 0.882, n 1.394. Distd, refluxed with successive small portions of KMnO<sub>4</sub> until the colour persisted, dried with anhydrous CaSO<sub>4</sub>, filtered and redistd.

tert-Butyl acetate [540-88-5] M 116.2, b 97-98°, d 0.72. Washed with 5% Na<sub>2</sub>CO<sub>3</sub> soln, then saturated aqueous CaCl<sub>2</sub>, dried with CaSO<sub>4</sub> and distd.

tert-Butyl acetoacetate [1694-31-1] M 158.2, b 71°/10mm, 85°/20mm,  $d_4^{20}$  0.954,  $n_4^{20}$  1.42. Dist under reduced press through a short column. [Org Synth 42 28 1962.] HARMFUL VAPOUR.

tert-Butylacetylchloride [7065-46-5] M 134.6, b 68-71°/100mm, 81°/180mm, 128-132°/atm,  $d_4^{20}$  0.964,  $n_D^{20}$  1.423. Distil under vacuum. If IR shows OH group then treat with thionyl chloride or oxalyl chloride at ca 50° for 30min, evap and fractionate using a short column. Strongly LACHRYMATORY, use a good fume hood. [J Am Chem Soc 72 222 1950; J Org Chem 22 1551 1957.]

**Butyl acrylate** [141-32-2] **M 128.2, b 59°/25mm, d 0.894, n<sup>12</sup> 1.4254.** Washed repeatedly with aqueous NaOH to remove inhibitors such as hydroquinone, then with distilled water. Dried with CaCl<sub>2</sub>. Fractionally distd under reduced pressure in an all-glass apparatus. The middle fraction was sealed under nitrogen and stored at 0° in the dark until used [Mallik and Das J Am Chem Soc 82 4269 1960].

( $\pm$ )-sec-Butyl alcohol [15892-23-6] M 74.1, b 99.4°, d 0.808. Purification methods are the same as for *n*-Butanol. These include drying with K<sub>2</sub>CO<sub>3</sub> or CaSO<sub>4</sub>, followed by filtration and fractional distn, refluxing with CaO, distn, then refluxing with magnesium and redistn; and refluxing with, then distn from CaH<sub>2</sub>. Calcium carbide has also been used as a drying agent. Anhydrous alcohol is obtained by refluxing with secbutyl phthalate or succinate. (For method see *Ethanol*.) Small amounts of alcohol can be purified by conversion to the alkyl hydrogen phthalate and recrystn [Hargreaves, J Chem Soc 3679 1956]. For purification of optical isomers, see Timmermans and Martin [J Chem Phys 25 411 1928].

tert-Butyl alcohol [75-65-0] M 74.1, m 23-25°, 25.7°, b 28.3°/60mm, 43.3°/123.8 mm, 61.8°/315mm, 72.5°/507mm, 82.45°/760mm,  $d_4^{20}$  0.7858,  $n_D^{20}$  1.3878. Synthesised commercially by the hydration of 2-methylpropene in dilute H<sub>2</sub>SO<sub>4</sub>. Dried with CaO, K<sub>2</sub>CO<sub>3</sub>, CaSO<sub>4</sub> or MgSO<sub>4</sub>, filtered and fractionally distd. Dried further by refluxing with, and distilling from, either magnesium activated with iodine, or small amounts of calcium, sodium or potassium, under nitrogen. Passage through a column of type 4A molecular sieve is another effective method of drying. So, also, refluxing with *tert*-butyl phthalate or succinate. (For method see *Ethanol.*) Other methods include refluxing with excess aluminium *tert*butylate, or standing with CaH<sub>2</sub>, and distilling as needed. Further purification is achieved by fractional crystn by partial freezing, taking care to exclude moisture. *tert*-Butyl alcohol samples containing much water can be dried by adding \*benzene, so that the water distils off as a tertiary azcotrope, b 67.3°. Traces of isobutylene have been removed from dry *tert*-butyl alcohol by bubbling dry pre-purified nitrogen through for several hours at 40-50° before using. It form azeotropic mixtures with a large number of compounds. It has also been purified by distn from CaH<sub>2</sub> into Linde 4A molecular sieves which had been activated at 350° for 24h [Jaeger et al. J Am *Chem Soc* 101 717 1979].

Rapid purification: Dry tert-butanol with CaH<sub>2</sub> (5% w/v), distil and store over 3A molecular sieves.

*n*-Butylamine [109-73-9] M 73.1, b 77.8°, d 0.740, n 1.4009,  $n^{25}$  1.399,  $pK^{25}$  10.66. Dried with solid KOH,  $K_2CO_3$ , LiAlH<sub>4</sub>, CaH<sub>2</sub> or MgSO<sub>4</sub>, then refluxed with, and fractionally distd from P<sub>2</sub>O<sub>5</sub>, CaH<sub>2</sub>, CaO or BaO. Further purified by pptn as the *hydrochloride*, m 213-213.5°, from ether soln by bubbling HCl gas into it. Re-ppted three times from EtOH by adding ether, followed by liberation of the free amine using excess strong base. The amine was extracted into ether, which was separated, dried with solid KOH, the ether removed by evapn and then the amine was distd. It was stored in a desiccator over solid NaOH [Bunnett and Davis J Am Chem Soc 82 665 1960; Lycan et al. Org Synth Coll Vol II 319 1943]. SKIN IRRITANT.

**R**-(-)-sec-Butylamine [13250-12-9] M 73.1, b 61-63°/atm, 62.5°/atm,  $d_4^{20}$  0.731,  $n_D^{20}$  1.393,  $[\alpha]_D^{20}$ +7.5° (neat), pK 10.56. Dry over solid NaOH overnight and fractionate through a short helices packed column. The L-hydrogen tartrate salt has m 139-140° (from H<sub>2</sub>O), the 1H<sub>2</sub>O has m 96° [ $\alpha$ ]<sub>D</sub><sup>21</sup>+18.1° (c 11, H<sub>2</sub>O); the hydrochloride has m 152° [ $\alpha$ ]<sub>D</sub><sup>21</sup>-1.1° (c 13, H<sub>2</sub>O) and the benzoyl derivative crystallises from EtOH as needles m 97°,  $[\alpha]_D^{21}$ -34.9° (c 11, H<sub>2</sub>O). [J Chem Soc 921 1956; Acta Chem Scand 11 898 1957.]

*tert*-Butylamine [75-64-9] M 73.1, b 42°, d 0.696, pK 10.68. Dried with KOH or LiAlH<sub>4</sub>. Distd from CaH<sub>2</sub> or BaO.

n-Butyl p-aminobenzoate [94-25-7] M 193.2, m 57-59°, pKEst ~2.5. Crystd from EtOH.

tert-Butylammonium bromide [60469-70-7] M 154.1, m >250°(dec). Recrystd several times from absolute EtOH and thoroughly dried at 105°.

4-tert-Butylaniline [769-92-6] M 149.2, m 14.5-15°, 15-16°, b 98.5-99°/3mm, 122°/20mm,  $d_4^{20}$  0.945,  $n_D^{20}$  1.538, pK<sup>25</sup> 4.95. Isolate as sulfate salt then liberate the free base with 10% aqueous NaOH, separate layers, dry over solid KOH and dist twice from Zn dust in a vacuum and store in brown containers. It has pKa<sup>25</sup> (H<sub>2</sub>O) 4.95 and (50% aq EtOH) 4.62. [J Am Chem Soc 76 2349 1954.] The anilide has m 171.5-172.3°, and the hydrochloride has m 270-274°. [J Chem Soc 680 1952; J Am Chem Soc 76 6179 1954.]

2-tert-Butylanthracene [13719-97-6] M 234.3, m 148-149°. Recrystd from EtOH and finally purified by TLC.

*n*-Butylbenzene [104-51-8] M 134.2, b 183.3°, d 0.860, n 1.4897,  $n^{25}$  1.487. Distd from sodium. Washed with small portions of conc H<sub>2</sub>SO<sub>4</sub> until the acid was no longer coloured, then with water and aqueous Na<sub>2</sub>CO<sub>3</sub>. Dried with anhydrous MgSO<sub>4</sub>, and distd twice from Na, collecting the middle fraction [Vogel J Chem Soc 607 1948].

*tert*-Butylbenzene [98-06-6] M 134.2, b 169.1°, d 0.867, n 1.493,  $n^{25}$  1.490. Washed with cold conc H<sub>2</sub>SO<sub>4</sub> until a fresh portion of acid was no longer coloured, then with 10% aqueous NaOH, followed by distd water until neutral. Dried with CaSO<sub>4</sub> and distd in a glass helices-packed column, taking the middle fraction.

4-tert-Butyl benzoyl chloride [1710-98-1] M 196.7, b 135°/10mm, 149.9-150.5°/14mm, 266-268°(dec),  $d_4^{20}$  1.082,  $n_D^{20}$  1.536. Distil under vac. If IR shows OH group then treat with thionyl chloride or oxalyl chloride at ca 50° for 30min, evap and fractionate in a vac using a short column. Strongly LACHRYMATORY, use a good fume hood. [Bull Chem Soc Jpn 32 960 1959; J Am Chem Soc 72 5433 1950.]

*n*-Butyl bromide [109-65-9] M 137.0, b 101-102°,  $d^{25}$  1.2678, n 1.4399,  $n^{25}$  1.4374. Washed with conc H<sub>2</sub>SO<sub>4</sub>, water, 10% Na<sub>2</sub>CO<sub>3</sub> and again with H<sub>2</sub>O. Dried with CaCl<sub>2</sub>, CaSO<sub>4</sub> or K<sub>2</sub>CO<sub>3</sub>, and distd. Redistd after drying with P<sub>2</sub>O<sub>5</sub>, or passed through two columns containing 5:1 silica gel/Celite mixture and stored with freshly activated alumina.

*tert*-Butyl bromoacetate [5292-43-3] M 195.1, b 52°/10mm, 74-76°/25mm,  $d_4^{20}$  1.324,  $n_D^{25}$  1.4162. Dissolve in Et<sub>2</sub>O, wash well with ice cold 10% aqueous K<sub>2</sub>CO<sub>3</sub>, dry over CaCl<sub>2</sub>, filter and evaporate the Et<sub>2</sub>O then fractionate through a Vigreux column in a vacuum. LACHRYMATORY [Org Synth 34 28 1954, Coll Vol III 144 1955; J Am Chem Soc 64 2274 1942, 65 986 1943.]

4-tert-Butylcalix[4]arene [60705-62-6] M 648.9, m >300° (dec), 380° (dec), 344-346°. Recrystd from CHCl<sub>3</sub> in large solvated prisms (m 380° dec) effloresces on drying in air; tetra-acetate crysts from  $Ac_2O$  in colourless prisms m 332-333° dec. Crysts from  $CCl_4$  or chlorobenzene + EtOH (m >300°) and tetra-acetate cryst from CHCl<sub>3</sub> + EtOH m >290° dec. Crysts from toluene in white plates with toluene of crystallisation m 344-346° (330-332°); the tetra-acetate crystallises with 1AcOH of crystallisation m 383-386° (softening at 330-340°, also m 283-286°), but acetylation with  $Ac_2O$ -NaOAc gives triacetate which recrysts from AcOH with 1AcOH of crystn m 278-281°. 4-tert-Butylcalix[4]arene (100mg) is unchanged after boiling for 4h with 10N KOH (0.04mL) in xylene (4mL). [Br J Pharmacol 10 73 1955; Monatsh Chem 109 767 1978; J Am Chem Soc 103 3782 1981; see also J.Vicens and V.Böhner eds, Calixarenes, Kluawer Academic Publ., Boston, 1991.]

4-tert-Butylcalix[6]arene [78092-53-2] M 972.3, m >300°, 380-381°. Recryst from CHCl<sub>3</sub> or CHCl<sub>3</sub> - MeOH as a white solid from the mother liquors of the calix[8]arene preparation. The hexa-acetate  $(Ac_2O-H_2SO_4)$  crystallises from CHCl<sub>3</sub>-MeOH m 360-362° dec, and the  $(SiMe_3)_6$  derivative crystallises from

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CHCl<sub>3</sub>-MeOH m 410-412°. Stability in KOH-xylene is same as for the 4-*tert*-butylcalix[4]arene. [J Am Chem Soc 103 3782 1981; see also J.Vicens and V.Böhner eds, Calixarenes, Kluawer Academic Publ., Boston, 1991.]

4-tert-Butylcalix[8]arene [68971-82-4] M 1297.8, m 411-412°. Recryst from CHCl<sub>3</sub> in fine colourless glistening needles. It melts sharply between 400-401° and 411-412° depending on the sample and is sensitive to traces of metal ions. TLC on silica gel (250µm thick) and elution with CHCl<sub>3</sub>-hexane (3:4); it has  $R_F 0.75$ . The octa-acetate is prepared from 8g in Ac<sub>2</sub>O (50mL) and 2 drops of conc H<sub>2</sub>SO<sub>4</sub> refluxed for 2h. On cooling a colourless ppte separates and is recryst from Ac<sub>2</sub>O (1.2g 48%) m 353-354°. The (SiMe<sub>3</sub>)<sub>8</sub> is prepared from 4-tert-butylcalix[8]arene (0.65g) in pyridine (4mL) with excess of hexamethyldisilazane (1mL) and trimethylchlorosilane (0.5mL) and refluxed under N<sub>2</sub> for 2h. Cool, evaporate the pyridine, triturate gummy residue with MeOH. Chromatography on silica gel using hexane-CH<sub>2</sub>Cl<sub>2</sub> gave 0.5g (61%) with one spot on TLC. Crystallises from hexane-Me<sub>2</sub>CO as colourless needles m 358-360°. [J Am Chem Soc 103 3782 1981; J Org Chem 43 4905 1978; 44 3962 1979; J Chem Soc, Chem Commun 533 1981; see also J.Vicens and V.Böhner eds, Calixarenes, Kluawer Academic Publ., Boston, 1991.]

tert-Butyl carbazate [870-46-2] M 132.2, m 41-42°, b 64°/0.01mm, 55-57°/0.4mm. Dist in a Claisen flask with a water or oil bath at ca 80°. After a couple of drops have distd the carbazate is collected as an oil which solidifies to a snow white solid. It can be crystd with 90% recovery from a 1:1 mixt of pet ether (b 30-60°) and pet ether (b 60-70°). [Org Synth 44 20 1964.]

4-tert-Butylcatchol [98-29-3] M 166.22, m 47-48°, 55-56°, 75°, b 265°/atm,  $pK_{Est(1)} \sim 9.5$ ,  $pK_{Est(2)} \sim 13.0$ . Vacuum distd and recrystd from pentane or pet ether (or \*C<sub>6</sub>H<sub>6</sub>).

*n*-Butyl chloride [109-69-3] M 92.6, b 78°, d 0.886, n 1.4021. Shaken repeatedly with conc  $H_2SO_4$  (until no further colour developed in the acid), then washed with water, aq NaHCO<sub>3</sub> or Na<sub>2</sub>CO<sub>3</sub>, and more water. Dried with CaCl<sub>2</sub>, or MgSO<sub>4</sub> (then with  $P_2O_5$  if desired), decanted and fractionally distd. Alternatively, a stream of oxygen continuing *ca* three times as long as was necessary to obtain the first coloration of starch iodide paper by the exit gas. After washing with NaHCO<sub>3</sub> soln to hydrolyze ozonides and to remove the resulting organic acid, the liquid was dried and distd [Chien and Willard J Am Chem Soc 75 6160 1953].

*tert*-Butyl chloride [507-20-0] M 92.6, f -24.6°, b 50.4°, d 0.851, n 1.38564. Purification methods commonly used for other alkyl halides lead to decomposition. Some impurities can be removed by photochlorination with a small amount of chlorine prior to use. The liquid can be washed with ice water, dried with CaCl<sub>2</sub> or CaCl<sub>2</sub> + CaO and fractionally distd. It has been further purified by repeated fractional crystn by partial freezing.

tert-Butyl chloroacetate [107-59-5] M 150.6, b 48-49°/11mm, 60.2°/15mm, 155°/atm (dec),  $d_4^{25}$  1.4204,  $n_D^{20}$  1.4259. Check the NMR spectrum, if satisfactory then dist in a vac, if not then dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, 10% H<sub>2</sub>SO<sub>4</sub> until the acid extract does not become cloudy when made alkaline with NaOH. Wash the organic layer again with H<sub>2</sub>O, then satd aq NaHCO<sub>3</sub>, dry over Na<sub>2</sub>SO<sub>4</sub>, evap and fractionate through a carborundum-packed column or a 6-inch Widmer column (see tert-butyl ethyl malonate for precautions to avoid decomposition during distn). [J Chem Soc 940 1940; J Am Chem Soc 75 4995 1953; Org Synth Coll Vol 144 1944.]

6-tert-Butyl-1-chloro-2-naphthol [525-27-9] M 232.7, m 76°, b 185°/15mm, pK<sub>Est</sub> ~8.0. Crystd from pet ether.

*tert*-Butyl cyanide (trimethylacetonitrile) [630-18-2] M 83.1, m 16-18°, d 0.765, b 104-106°. Purified by a two stage vac distn and degassed by freeze-pump-thaw technique. Stored under vac at 0°. TOXIC, use efficient fume hood.

*tert*-Butyl cyanoacetate [1116-98-9] M 141.2, b 40-42°/0.1mm, 54-56°/0.3mm, 90°/10mm, 107-108°/23mm,  $d_4^{20}$  0.989,  $n_D^{20}$ 1.4198. The IR spectrum of a film should have bands at 1742 (ester

CO) and 2273 (C=N) but not OH band (ca 3500 broad) cm<sup>-1</sup>. If it does not have the last named band then fractionally dist, otherwise dissolve in Et<sub>2</sub>O, wash with satd aq NaHCO<sub>3</sub>, dry over K<sub>2</sub>CO<sub>3</sub>, evap Et<sub>2</sub>O, and dist residue under a vacuum (see tert-butyl ethyl malonate for precautions to avoid decomposition during distn). [J Chem Soc 423 1955; Helv Chim Acta **42** 1214 1959].

4-tert-Butyl-1-cyclohexanone [98-53-3] M 154.3, m 49-50°. Crystd from pentane.

*n*-Butyl disulfide [629-45-8] M 178.4, b 110-113°/15mm, d 0.938,  $n^{22}$  1.494. Shaken with lead peroxide, filtered and distd in vacuum under N<sub>2</sub>.

*n*-Butyl ether (di-*n*-butyl ether) [142-96-1] M 130.2, b 52-53°/26mm, 142.0°/760mm, d 0.764, n 1.39925, n<sup>25</sup> 1.39685, pK<sup>25</sup> -5.40 (aq H<sub>2</sub>SO<sub>4</sub>). Peroxides (detected by the liberation of iodine from weakly acid (HCl) solns of 2% KI) can be removed by shaking 1L of ether with 5-10mL of a soln comprising 6.0g of ferrous sulfate and 6mL conc H<sub>2</sub>SO<sub>4</sub> and 110mL of water, with aq Na<sub>2</sub>SO<sub>3</sub>, or with acidified NaI, water, then Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. After washing with dil NaOH, KOH, or Na<sub>2</sub>CO<sub>3</sub>, then water, the ether is dried with CaCl<sub>2</sub> and distd. It can be further dried by distn from CaH<sub>2</sub> or Na (after drying with P<sub>2</sub>O<sub>5</sub>), and stored in the dark with Na or NaH. The ether can also be purified by treating with CS<sub>2</sub> and NaOH, expelling the excess sulfide by heating. The ether is then washed with water, dried with NaOH and distd [Kusama and Koike *J Chem Soc Japan, Pure Chem Sect* 72 229 1951]. Other purification procedures include passage through an activated alumina column to remove peroxides, or through a column of silica gel, and distn after adding about 3% (v/v) of a 1M soln of MeMgI in *n*-butyl ether.

*n*-Butyl ethyl ethyl [628-81-9] M 102.2, b 92.7°, d 0.751, n 1.38175,  $n^{25}$  1.3800. Purified by drying with CaSO<sub>4</sub>, by passage through a column of activated alumina (to remove peroxides), followed by prolonged refluxing with Na and then fractional distn.

tert-Butyl ethyl ether [637-92-3] M 102.2, b 71-72°, d 0.741. Dried with CaSO<sub>4</sub>, passed through an alumina column, and fractionally distd.

tert-Butyl ethyl malonate [32864-38-3] M 188.2, b 83-85°/8mm, 93-95°/17mm, 107-109°/24mm,  $d_4^{25}$  0.994,  $n_D^{24}$  1.4150. Likely impurity is monoethyl malonate, check IR for OH bands at 3330 br. To ca 50g of ester add ice cold NaOH (50g in 200mL of H<sub>2</sub>O and 200g of ice). Swirl a few times (filter off ice if necessary), place in a separating funnel and extract with 2 x 75mL of Et<sub>2</sub>O. Dry extract (MgSO<sub>4</sub>) (since traces of acid decompose the t-Bu group of the ester, the distillation flask has to be washed with aq NaOH, rinsed with H<sub>2</sub>O and allowed to dry). Addition of some K<sub>2</sub>CO<sub>3</sub> or MgO before distilling is recommended to inhibit decomposition. Distil under reduced press through a 10 cm Vigreux column. Decomposition is evidenced by severe foaming due to autocatalytic decomposition and cannot be prevented from accelerating except by stopping the distillation and rewashing the distillation flask with alkali again. [J Am Chem Soc 66 1287 1944, 64 2714 1942; Org Synth Coll Vol IV 417 1963; Org Synth 37 35 1957.]

*n*-Butyl formate [592-84-7] M 102.1, b 106.6°, d 0.891, n 1.3890. Washed with satd NaHCO<sub>3</sub> soln in the presence of satd NaCl, until no further reaction occurred, then with saturated NaCl soln, dried (MgSO<sub>4</sub>) and fractionally distd.

Butyl glycolate [7397-62-8] M 132.2, b 191-192°/755mm, 187-190°/atm,  $d_4^{20}$  1.019,  $n_D^{20}$  1.4263. Dissolve in CHCl<sub>3</sub> (EtOH-free), wash with 5% KHCO<sub>3</sub> until effervescence ceases (if free acid is present), dry over CaCl<sub>2</sub>, filter, evaporate and distil through a short column. [Bøhme and Opfer Z Anal Chem 139 255 1953; cf J Am Chem Soc 73 5265 1951.]

*tert*-Butyl hydroperoxide (TBHP) [75-91-2] M 90.1, f 5.4°, m 0.5-2.0°, b 38°/18mm, d 0.900, n 1.4013, pK<sup>20</sup> 12.8. Care should be taken when handling this peroxide because of the possibility of EXPLOSION. It explodes when heating over an open flame. Alcoholic and volatile impurities can be removed by prolonged refluxing at 40° under reduced pressure, or by steam distn. For example, Bartlett, Benzing and Pincock [J Am Chem Soc 82 1762 1960] refluxed at 30mm pressure in an azeotropic separation apparatus until two phases no longer separated, and then distilled at 41°/23mm. Pure

material is stored under N<sub>2</sub>, in the dark at 0°. Crude commercial material has been added to 25% NaOH below 30°, and the crystals of the sodium salt have been collected, washed twice with \*benzene and dissolved in distd water. After adjusting the pH of the soln to 7.5 by adding solid CO<sub>2</sub>, the peroxide was extracted into pet ether, from which, after drying with K<sub>2</sub>CO<sub>3</sub>, it was recovered by distilling off the solvent under reduced pressure at room temperature [O'Brien, Beringer and Mesrobian *J Am Chem Soc* 79 6238 1957]. The temperatures should be kept below 75°. It has also been distilled through a helices packed column (*ca* 15 plates) and material collected had b 34-35°/20 mm. Similarly, a soln in pet ether has been extracted with cold aq NaOH, and the hydroperoxide has been regenerated by adding at 0°, KHSO<sub>4</sub> at a pH not higher than 4.5, then extracted into diethyl ether, dried with MgSO<sub>4</sub>, filtered and the ether evapd in a rotary evaporator under reduced pressure [Milac and Djokic *J Am Chem Soc* 84 3098 1962].

A 3M soln of TBHP in  $CH_2Cl_2$  is prepared by swirling 85mL (0.61mol) of commercial TBHP (70% TBHP-30% H<sub>2</sub>O, **d** 0.935 *ca* 7.2mmol/mL) with 140mL of  $CH_2Cl_2$  in a separating funnel. The milky mixture is allowed to stand until the phases separate (*ca* 30min). The organic (lower) layer (*ca* 200mL) containing 0.60mole of TBHP was separated from the aqueous layer (*ca* 21mL) and used without further drying. TBHP is assayed by iodometric titration. With 90% grade TBHP (w/w, d 0.90, *ca* 9.0mmole/mL) no separation of layers occurs; i.e. when TBHP (66.67mL, 0.60mole) is added to  $CH_2Cl_2$  (140mL) the resulting soln (*ca* 200mL) is clear. [*J Am Chem Soc* 77 60032 1955, 74 4742 1952; Akashi, Palermo and Sharpless *J Org Chem* 43 2063 1978 states quality of available grades, handling and compatibility for reactions.]

**2-tert-Butyl hydroquinone** [1948-33-0] M 166.2, m 125-127°, 127-128°, 129°,  $pK_{Est(1)} \sim 10.5$ .  $pK_{Est(2)} \sim 11.6$ . Recrysts from H<sub>2</sub>O or MeOH and dried in a vacuum at 70°. Store in a dark container. [Angew Chem 69 699 1957.]

*n*-Butyl iodide (1-iodobutane) [542-69-8] M 184.0, b 130.4°, d 1.616,  $n^{25}$  1.44967. Dried with MgSO<sub>4</sub> or P<sub>2</sub>O<sub>5</sub>, fractionally distd through a column packed with glass helices, taking the middle fraction and storing with calcium or mercury in the dark. Also purified by prior passage through activated alumina or by shaking with conc H<sub>2</sub>SO<sub>4</sub> then washing with Na<sub>2</sub>SO<sub>3</sub> soln. It has also been treated carefully with sodium to remove free HI and H<sub>2</sub>O, before distilling in a column containing copper turnings at the top. Another purification consisted of treatment with bromine, followed by extraction of free halogen with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, washing with H<sub>2</sub>O, drying and fractional distn.

*tert*-Butyl iodide [558-17-8] M 184.0, b 100°(dec), d 1.544. Vacuum distn has been used to obtain a distillate which remained colourless for several weeks at  $-5^{\circ}$ . More extensive treatment has been used by Boggs, Thompson and Crain [J Phys Chem 61 625 1957] who washed with aq NaHSO<sub>3</sub> soln to remove free iodine, dried for 1h with Na<sub>2</sub>SO<sub>3</sub> at 0°, and purified by four or five successive partial freezings of the liquid to obtain colourless material which was stored at  $-78^{\circ}$ .

*tert*-Butyl isocyanate [1609-86-5] M 99.1, m 10.5-11.5°, b 30.5-32°/10mm, 64°/52mm,  $d_{25}^{25}$  0.9079,  $n_D^{25}$  1.470. It is LACHRYMATORY and TOXIC, and should have IR with 2251 (C=N) cm<sup>-1</sup> and no OH bands. The NMR should have one band at 1.37 ppm from TMS. Purified by fractional distn under reduced pressure. [J Org Chem 36 3056 1971; J Prakt Chem. 125 152 1930.]

*tert*-Butyl isocyanide [7188-38-7] M 83.1, b 91-92°/730mm, 90°/758mm, d<sup>20</sup> 0.735. Dissolve in pet ether (b 40-60°) wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), remove pet ether under slight vacuum, dist using a vacuum-jacketed Vigreux column at atmospheric pressure, IR: v 2134 cm<sup>-1</sup>. [*Chem Ber* 93 239 1960.]

*tert*-butyl isocyanoacetate [2769-72-4] M 141.2, b 50°/0.1mm, 49-50°/10mm, 63-65°/15mm,  $d_4^{20}$  0.970,  $n_D^{20}$  1.420. If it contains some free acid (OH bands in IR) then dissolve in Et<sub>2</sub>O, shake with 20% Na<sub>2</sub>CO<sub>3</sub>, dry over anhydrous K<sub>2</sub>CO<sub>3</sub>, evaporate and distil. [*Chem Ber* 94 2814 1961.]

*n*-Butyl methacrylate [97-88-1] M 142.2, b 49-52°/0.1mm, d 0.896, n 1.424. Purified as for butyl acrylate.

*tert*-Butyl methacrylate [585-07-9] M 142.2, f -48°, b 135-136°/760mm, d 0.878, n 1.415. Purified as for butyl acrylate.

2-tert-Butyl-4-methoxyphenol (2-tert-butyl-4-hydroxyanisole) [121-00-6] M 180.3, m 64.1°, pK<sub>Est</sub> ~10.8. Fractionally distd *in vacuo*, then passed as a soln in CHCl<sub>3</sub> through alumina, and the solvent evaporated from the eluate. Recrystd from pet ether.

*n*-Butyl methyl ether [628-28-4] M 88.2, b 70°, d 0.744, pK -3.50 (aq H<sub>2</sub>SO<sub>4</sub>). Dried with CaSO<sub>4</sub>, passed through an alumina column to remove peroxides, and fractionally distd.

tert-Butyl methyl ether [1634-04-4] M 88.2, b 56°, n 1.369. Same as for n-butyl methyl ether.

*tert*-Butyl methyl ketone [75-97-8] M 100.2, b 105°/746mm, 106°/760mm, d 0.814, n 1.401. Refluxed with a little KMnO<sub>4</sub>. Dried with CaSO<sub>4</sub> and distd.

8-sec-Butylmetrazole [25717-83-3] M 194.3, m 70°. Crystd from pet ether, and dried for 2 days under vacuum over P<sub>2</sub>O<sub>5</sub>.

*tert*-Butyl nitrite [540-80-7] M 103.1, b 34°/250mm, 61-63°/atm,  $d_4^{20}$  0.8671,  $n_D^{25}$  1.3660. If it is free from OH bands (IR) then distil through a 12inch helices packed column under reduced pressure, otherwise wash with aq 5% NaHCO<sub>3</sub> (effervescence), then H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>) and fractionate through a 10 theoretical plates column at *ca* 10mm pressure. [J Chem Soc 1968 1954, J Am Chem Soc 70 1516 1948; UV: J Org Chem 21 993 1956; IR: Bull Soc Chim Belg 60 240 1951.]

*p-tert-ButyInitrobenzene [3282-56-2]* M 179.2, m 28.4°. Fractionally crystd three times by partially freezing a mixture of the mono-nitro isomers, then recryst from MeOH twice and dried under vacuum [Brown J Am Chem Soc 81 3232 1959].

N-(n-Butyl)-5-nitro-2-furamide [14121-89-2] M 212.2, m 89-90°. Recrystd twice from EtOH/water mixture.

Butyloxirane (1-hexene oxide) [1436-34-6] M 100.2, b 116-117°/atm, 116-119°/atm,  $d_4^{20}$  0.833,  $n_D^{20}$  1.44051. Purified by fractional distn through a 2ft helices packed column at atmospheric pressure in a N<sub>2</sub> atm. [J Org Chem 30 1271 1965; J Chem Soc 2433 1927; <sup>13</sup>C NMR J Chem Soc Perkin Trans 2 861 1975.]

tert-Butyl peracetate [107-71-1] M 132.2, b 23-24°/0.5mm, n<sup>25</sup> 1.4030. Washed with NaHCO<sub>3</sub> from a \*benzene soln, then redistd to remove \*benzene [Kochi J Am Chem Soc 84 774 1962]. Handle with adequate protection due to possible EXPLOSIVE nature.

*tert*-Butylperoxy isobutyrate [109-13-7] M 160.2, f -45.6°. After diluting 90mL of the material with 120mL of pet ether, the mixture was cooled to 5° and shaken twice with 90mL portions of 5% NaOH soln (also at 5°). The non-aqueous layer, after washing once with cold water, was dried at 0° with a mixture of anhydrous MgSO<sub>4</sub> and MgCO<sub>3</sub> containing *ca* 40% MgO. After filtering, this material was passed, twice, through a column of silica gel at 0° (to remove *tert*-butyl hydroperoxide). The soln was evapd at 0°/0.5-1mm to remove the solvent, and the residue was recrystd several times from pet ether at -60°, then subjected to high vac to remove traces of solvent [Milos and Golubovic J Am Chem Soc 80 5994 1958]. Handle with adequate protection due to possible EXPLOSIVE nature.

tert-Butyl perphthalic acid [15042-77-0] M 238.2, pK<sub>Est</sub> ~6.2. Crystd from Et<sub>2</sub>O and dried over H<sub>2</sub>SO<sub>4</sub>. Possibly EXPLOSIVE.

*p-tert-Butylphenol* [98-54-4] M 150.2, m 99°, pK<sup>25</sup> 10.39. Crystd to constant melting point from pet ether (b 60-80°). It sublimes. Also purified *via* its benzoate, as for phenol.

*p-tert-Butylphenoxyacetic acid* [1798-04-5] M 208.3, m 88-89°,  $pK_{Est} \sim 2.9$ . Crystd from pet ether/\*C<sub>6</sub>H<sub>6</sub> mixture.

*tert*-Butyl phenyl carbonate [6627-89-0] M 194.2, b 74-78°/0.5mm,  $83^{\circ}/0.6mm$ ,  $d_4^{20}1.05$ ,  $n_D^{20}1.480$ . If IR is free from OH then purify by redistillation, otherwise, dissolve in Et<sub>2</sub>O, wash with 5% HCl, then H<sub>2</sub>O, dry over MgSO<sub>4</sub>, evap and distil through a Claisen head under vacuum. Care should be taken in the distillation as distn of large quantities can lead to decomposition with liberation of CO<sub>2</sub> and isobutylene, use the necessary precautions. [J Am Chem Soc 79 98 1957.]

*n*-Butyl phenyl ether [1126-79-0] M 150.2, b 210.5°, d 0.935. Dissolved in diethyl ether, washed first with 10% aq NaOH to remove traces of phenol, then repeatedly with distilled water, followed by evaporation of the solvent and distn under reduced pressure [Arnett and Wu J Am Chem Soc 82 5660 1960].

N-tert-Butyl a-phenyl nitrone [3376-24-7] M 177.2, m 73-74°. Crystd from hexane.

**Butyl phthalate** [84-74-2] **M 278.4, f -35°, b 340°/760mm, d 1.043.** Freed from alcohol by washing with  $H_2O$ , or from acids and butyl hydrogen phthalate by washing with dilute NaOH. Distd at 10torr or less. (See also p. 195.)

**4-tert-Butyl pyridine** [3978-81-2] **M** 135.2, **f** -44.4°, **b** 194-197°atm, 197°/765mm,  $d_4^{20}$  **0.923**,  $n_D^{20}$  1.495, pK<sup>25</sup> 5.82. It is dried over solid KOH and is purified by fractional distn through an efficient column under dry N<sub>2</sub>. Its picrate has **m** 153.9-154°, and the hydrochloride has **m** 151.7-154.8° (from Me<sub>2</sub>CO). [J Am Chem Soc 73 3308, 3310 1951, IR: J Am Chem Soc 100 214 1978; J Chem Soc 4454 1960.]

**Butyl stearate** [123-95-5] **M 340.6, m 26.3°, d 0.861.** Acidic impurities removed by shaking with 0.05M NaOH or a 2% NaHCO<sub>3</sub> soln, followed by several water washes, then purified by fractional freezing of the melt and fractional crystn from solvents with boiling points below 100°.

S-tert-Butyl thioacetate [999-90-6] M 132.2, b 31-32°/11mm, 38°/14mm, 44-45°/28mm, 67°/54mm, 135.6-135.9°/773mm,  $d_4^{25}$ 0.9207,  $n_D^{20}$ 1.4532. Dissolve in CHCl<sub>3</sub> (EtOH-free), wash with H<sub>2</sub>O, 10% H<sub>2</sub>SO<sub>4</sub>, saturated aqueous NaHCO<sub>3</sub> (care CO<sub>2</sub> liberated), H<sub>2</sub>O again, dried over Drierite and anhydrous K<sub>2</sub>CO<sub>3</sub>, and fractionate under reduced pressure. [J Am Chem Soc 72 3021 1950.]

*p-tert*-Butyltoluene [98-51-1] M 148.3, f -53.2°, b 91°/28mm, d 0.854, n 1.4920. A sample containing 5% of the *meta*-isomer was purified by selective mercuration. Fractional distn of the solid arylmercuric acetate, after removal from the residual hydrocarbon, gave pure *p-tert*-butyltoluene [Stock and Brown J Am Chem Soc 81 5615 1959].

*tert*-Butyl 2,4,6-trichlorophenyl carbonate [16965-08-5] M 297.6, m 64-66°. Crystd from a mixture of MeOH (90mL) and water (6mL) using charcoal [Broadbent et al. J Chem Soc (C) 2632 1967].

*N-tert*-Butyl urea [1118-12-3] M 116.2, m 182°, 185°(dec). Possible impurity is N,N'-di-*tert*-butyl urea which is quite insol in H<sub>2</sub>O. Recrystd from hot H<sub>2</sub>O, filter off insol material, and cool to 0° to -5° with stirring. Dry in vac at room temp over KOH or H<sub>2</sub>SO<sub>4</sub>. If dried at higher temperatures it sublimes slowly. It can be recrystd from EtOH as long white needles or from 95% aq EtOH as plates. During melting point determination the bath temp has to be raised rapidly as the urea sublimes slowly above 100° at 760mm. [Org Synth Coll Vol III 151 1955.]

*n*-Butyl vinyl ether [111-34-2] M 100.2, b 93.3°, d 0.775. After five washings with equal volumes of water to remove alcohols (made slightly alkaline with KOH), the ether was dried with sodium and distd under vacuum, taking the middle fraction [Coombes and Eley J Chem Soc 3700 1957]. Stored over KOH.

2-Butyne [503-17-3] M 54.1, b 0<sup>o</sup>/253mm, d 0.693. Stood with sodium for 24h, then fractionally distd under reduced pressure.

2-Butyne-1,4-diol [110-65-6] M 86.1, m 54-57°, 56-58°, b 238°. Crystd from EtOAc.

*n*-Butyraldehyde [123-72-8] M 72.1, b 74.8°, d 0.810, n 1.37911,  $n^{15}$  1.38164. Dried with CaCl<sub>2</sub> or CaSO<sub>4</sub>, then fractionally distd under N<sub>2</sub>. Lin and Day [*J Am Chem Soc* 74 5133 1952] shook with batches of CaSO<sub>4</sub> for 10min intervals until a 5mL sample, on mixing with 2.5mL of CCl<sub>4</sub> containing 0.5g of aluminium isopropoxide, gave no ppte and caused the soln to boil within 2min. Water can be removed from *n*-butyraldehyde by careful distn as an azeotrope distilling at 68°. The aldehyde has also been purified through its bisulfite compound which, after decomposing with excess NaHCO<sub>3</sub> soln, was steam distd, extracted under N<sub>2</sub> into ether and, after drying, the extract was fractionally distd [Kyte, Jeffery and Vogel *J Chem Soc* 4454 1960].

Butyramide [514-35-5] M 87.1, m 115°, b 230°. Crystd from acetone, \*benzene, CCl<sub>4</sub>-pet ether, 20% EtOH or water. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>, CaCl<sub>2</sub> or 99% H<sub>2</sub>SO<sub>4</sub>.

*n*-Butyric acid [107-92-6] M 88.1, f -5.3°, b 163.3°, d 0.961,  $n^{25}$  1.396,  $pK^{25}$  2.82. Distd, mixed with KMnO<sub>4</sub> (20g/L), and fractionally redistd, discarding the first third [Vogel J Chem Soc 1814 1948].

n-Butyric anhydride [106-31-0] M 158.2, b 198°, d 0.968. Dried by shaking with P<sub>2</sub>O<sub>5</sub>, then distd.

 $\gamma$ -Butyrolactone [96-48-0] M 86.1, b 83.8°/12mm, d 1.124. Dried with anhydrous CaSO<sub>4</sub>, then fractionally distd. Handle in a fume cupboard due to TOXICITY.

**Butyronitrile** [109-74-0] **M 69.1, b 117.9°, d 0.793, n 1.3846, n<sup>30</sup> 1.37954.** Treated with conc HCl until the smell of the isonitrile had gone, then dried with  $K_2CO_3$  and fractionally distd [Turner J Chem Soc 1681 1956]. Alternatively it was twice heated at 75° and stirred for several hours with a mixture of 7.7g Na<sub>2</sub>CO<sub>3</sub> and 11.5g KMnO<sub>4</sub> per L of butyronitrile. The mixture was cooled, then distd. The middle fraction was dried over activated alumina. [Schoeller and Wiemann J Am Chem Soc 108 22 1986.]

Butyryl chloride (butanoyl chloride) [141-75-3] M 106.6, f -89°, b 101-102°/atm,  $d_4^{20}$ 1.026,  $n_D^{20}$  1.412. Check IR to see if there is a significant peak at 3000-3500 cm<sup>-1</sup> (br) for OH. If OH is present then reflux with less than one mol equiv of SOCl<sub>2</sub> for 1h and distil directly. The fraction boiling between 85-100° is then refractionated at atm pressure. Keep all apparatus free from moisture and store the product in sealed glass ampoules under N<sub>2</sub>. LACHRYMATORY - handle in a good fume hood. [Org Synth Coll Vol I 147 1941.]

**Cacotheline** (2,3-dihydro-4-nitro-2,3-dioxo-9,10-secostrychnidin-10-oic acid) [561-20-6] M 508.4,  $pK_{Est(1)}$ ~4.4 (CO<sub>2</sub>H),  $pK_{Est(2)}$ ~10.2 (N). Yellow crystals from H<sub>2</sub>O. It is then dried over H<sub>2</sub>SO<sub>4</sub> which gives the *dihydrate*, and in a vacuum over H<sub>2</sub>SO<sub>4</sub> at 105° to give the anhydrous compound. The *hydrochloride* separates as the hydrate (on heating in vacuum at 80°) in orange-yellow prisms or plates, **m** 250°(dec), and forms a *resorcinol complex* which gives brown crystals from EtOH, **m** 325°, and a *hydroquinone complex* as dark red crystals from EtOH, **m** 319°. [*Chem Ber* 43 1042 1910, 86 232, UV: 242 1953; complexes: Gatto Gazz Chim Ital 85 1441 1955.] Used in the titrimetric estimation of Sn<sup>2+</sup> ions [Szrvas and Lantos *Talanta* 10 477 1963].

Caffeic (3,4-dihydroxycinnamic) acid [331-39-5] M 180.2, m 195°, 223-225°,  $pK_1^{25}$  4.62,  $pK_2^{25}$  9.07 Crystd from water.

Caffeine [58-08-2] M 194.2, m 237°, pK<sub>1</sub><sup>40</sup> -0.10, pK<sub>2</sub><sup>55</sup> 1.22. Crystd from water or absolute EtOH.

(+)-Calarene (+  $\beta$ -gurjunen, 1,3,3,11-tetramethyltricyclo[5.4.0.0<sup>2,4</sup>]undecan-7-ane, (1a*R*)-1,1,7c,7ac-tetramethyl-1a,2,3,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[ $\alpha$ ]naphthalene, new name 1(10)aristolene) [17334-55-3] M 204.35, b 45-47°/0.008-0.01mm, 255-258°/atm, d<sub>4</sub><sup>20</sup> 0.9340, n<sub>D</sub><sup>0</sup> 1.55051, [ $\alpha$ ]<sub>D</sub><sup>20</sup> +58° (EtOH), +81.8° (neat). Purified by gas chromatography (7% propylene glycol adipate on unglazed tile particles of size 0.2-0.3mm, 400 cm column length and 0.6 cm diameter, at 184°, with N<sub>2</sub> carrier gas at a flow rate of 0.54 mL/sec using a thermal detector). Also purified by chromatography on alumina (200 times the weight of calarene) and eluted with pet ether. UV:  $\lambda_{max}$  200 and 210 nm ( $\epsilon$  9560, 5480) in EtOH. [IR: Sorm Collect Czech Chem Commun 18 512 1953, 29 795 1964; Tetrahedron Lett 827 1962, 225 1963.]

Calcon carboxylic acid [3-hydroxy-4-(2-hydroxy-4-sulfo-1-naphthylazo)naphthalene-2carboxylic acid] [3737-95-9] M 428.4, m 300°,  $\lambda$  max 560nm, pK<sub>1</sub> 1.2, pK<sub>2</sub> 3.8, pK<sub>3</sub> 9.26, pK<sub>4</sub> 13.14. Purified through its *p*-toluidinium salt. The dye was dissolved in warm 20% aq MeOH and treated with *p*-toluidine to ppte the salt after cooling. Finally recrystd from hot water. [Itoh and Ueno Analyst (London) 95 583 1970.] Patton and Reeder (Anal Chem 28 1026 1956) indicator and complexes with Ca in presence of Mg and other metal ions.

Calmagite [3147-14-6] M 358.4, m 300°, pK<sub>1</sub> 8.1, pK<sub>2</sub> 12.4. Crude sample was extracted with anhydrous diethyl ether [Lindstrom and Diehl Anal Chem 32 1123 1960]. Complexes with Ca, Mg and Th.

**Campesterol** (24*R*-24-methylcholest-5-en-3 $\beta$ -ol) [474-62-4] M 400.7, m 156-159°, 157-158°,  $[\alpha]_D^{24}$ -35.1° (c 1.2, CHCl<sub>3</sub>). Recryst twice from hexane and once from Me<sub>2</sub>CO. The *benzoyl* derivative has m 158-160° [ $\alpha$ ]\_D^{23}-8.6° (CHCl<sub>3</sub>), the acetyl derivative has m 137-138° (from EtOH) and  $[\alpha]_D^{23}$ -35.1° (c 2.9, CHCl<sub>3</sub>) [J Am Chem Soc 63 1155 1941].

1*R*,4*S*-(-)-Camphanic acid [13429-83-9] M 198.2, m 190-192°, 198-200°,  $[\alpha]_{548}^{20}$  -22.5° (c 1, dioxane), -4.4° (c 8, EtOH), pK<sub>Est</sub> ~3.8. Dissolve in CH<sub>2</sub>Cl<sub>2</sub>, dry (MgSO<sub>4</sub>), filter, evaporate and residue is sublimed at 120°/0.5mm or 140°/1mm. [*Helv Chim Acta* 61 2773 1978.]

1*R*,4*S*-(-)-Camphanic acid chloride [39637-74-6] M 216.7, m 65-66.5°, 70.5-71°,  $[\alpha]_{548}$  -23° (c 2, CCl<sub>4</sub>), -7.5° (c 0.67, \*benzene). Soluble in toluene (50g/100mL at 0°) and crysts from pet ether (b 40-60°). It sublimes at 70°/5mm, Store dry at 0°, v (CCl<sub>4</sub>) 1805s and 1780m cm<sup>-1</sup>. [*J Chem Soc, Dalton Trans* 2229 1976.]

**RS-Camphene** [565-00-4] **M 136.2, m 51-52°, b 40-70°/10mm.** Crystd twice from EtOH, then repeatedly melted and frozen at 30mm pressure. [Williams and Smyth J Am Chem Soc 84 1808 1962.] Alternatively it is dissolved in Et<sub>2</sub>O, dried over CaCl<sub>2</sub> and Na, evaporated and the residue sublimed in a vacuum [NMR: Chem Ber 111 2527 1978].

(-)-Camphene (15-2,2-dimethyl-3-methylene norbornane) [5794-04-7] M 136.2, m 49.2-49.6°, 49-50°, b 79-80°/58mm, 91.5°/100mm,  $d_4^{54}$  0.8412,  $n_D^{54}$  1.4564,  $[\alpha]_D^{25}$ -106.2° (c 40, \*C<sub>6</sub>H<sub>6</sub>), -117.5° (c 19, toluene), -113.5° (c 9.7, Et<sub>2</sub>O). Purified by fractionation through a Stedman column (see p. 441) at 100mm in a N<sub>2</sub> atmosphere, crystallised from EtOH and sublimed in a vacuum below its melting point. It is characterised by its camphenilone semicarbazone, m 217-218.5°, or camphor semicarbazone, m 236-238°. [NMR: Chem Ber 111 2527 1978; Justus Liebigs Ann Chem 623 217 1959; Bain et al. J Am Chem Soc 72 3124 1950]

Camphor (1*R*-bornan-2-one) [R-(+)-464-49-3]; S-(-)-464-48-2] M 136.2, m 178.8°, 179.97°(open capillary), b 204°/atm,  $[\alpha]_{546}^{35}$  (+) and (-) 59.6° (in EtOH),  $[\alpha]_D^{20}$  (+) and (-) 44.3° (c 10, EtOH),  $[\alpha]_{579}^{179}$  (+) and (-) 70.85° (melt). Crystd from EtOH, 50% EtOH/water, MeOH, or pet ether or from glacial acetic acid by addition of water. It can be sublimed (50°/14mm) and also fractionally crystd from its own melt. It is steam volatile. It should be stored in tight containers as it is appreciably volatile at room temperature. The solubility is 0.1% (H<sub>2</sub>O), 100% (EtOH), 173% (Et<sub>2</sub>O) and 300% (CHCl<sub>3</sub>). The *R*-oxime (from Et<sub>2</sub>O, CHCl<sub>3</sub>, or dil EtOH) m 119°  $[\alpha]_D^{20}$ -42.4° (c 3, EtOH); the  $\pm$  oxime has m 118-119°. [Chem Ber 67 1432 1934; Allan and Rodgers J Chem Soc (B) 632 1971; UV, NMR: Fairley et al. J Chem Soc, Perkin Trans 1 2109 1973; J Am Chem Soc 62 8 1940.]

Camphoric acid (1,2,2-trimethyl-cyclopentan-1*r*,3*c*-dicarboxylic acid) [1R,2S)-(+)-124-83-4; 1S,2R)-(-)-560-09-8] M 200.2, m 186-188°, 187°, 186.5-189°,  $[\alpha]_{546}^{20}$  (+) and (-) 57° (c 1,

EtOH),  $[\alpha]_D^{20}$  (+) and (-) 47.7° (c 4, EtOH) ,  $pK_1^{25}$  4.71,  $pK_2^{25}$  5.83 (for + isomer). Purified by repptn from an alkaline soln by HCl, filtered, and recrystd from water several times, rejecting the first crop. It forms leaflets from EtOH and Me<sub>2</sub>CO and H<sub>2</sub>O and is insol in CHCl<sub>3</sub>. Sol in H<sub>2</sub>O is 0.8% at 25° and 10% at 100°; 50% (EtOH) and 5% in ethylene glycol. The (±)-acid has m 202-203°. The (+)-1-methyl ester had m 86° (from pet ether)  $[\alpha]_D^{20}$  +45° (c 4, EtOH), and the (+)-3-methyl ester has m 77° (from pet ether)  $[\alpha]_D^{17.5}$  +53.9° (c 3, EtOH). [J Am Chem Soc 53 1661 1931; Helv Chim Acta 30 933 1947; Acta Chem Scand 2 597 1948; J Am Chem Soc 80 6316 1958.]

(±)-Camphoric anhydride [595-30-2] M 182.2, transitn temp 135°, m 223.5°. Crystd from EtOH.

**Camphorquinone** (borna-2,3-dione) [1R-(-)-10334-26-6; 1S-(+)-2767-84-2] M 166.2, m 198.7°, 198-199°, 197-201°,  $[\alpha]_D^{25}(-)$  and (+) 101.1° (c 2, EtOH). It can be purified by steam distillation, recrystn (yellow prisms) from EtOH, \*C<sub>6</sub>H<sub>6</sub> or Et<sub>2</sub>O-pet ether and can be sublimed in a vacuum. The  $(\pm)$ -quinone forms needles from EtOH, m 197-198°, 203°. [Helv Chim Acta 13 1026; Chem Ber 67 1432 1934.]

RS-Camphorquinone [10373-78-1] M 166.2, m 199-202°. Purification is same as for above isomers.

(IR)-(-)Camphor-10-sulfonic acid [35963-20-3] M 232.3, m 197.4-198°(dec), 197-198°,  $[\alpha]_D^{20}$ -20.7° (c 5.4, H<sub>2</sub>O), pK<sub>Est</sub> ~-1. Forms prisms from AcOH or EtOAc, and is deliquescent in moist air. Store in tightly stoppered bottles. The *NH<sub>4</sub> salt* forms needles from H<sub>2</sub>O  $[\alpha]_D^{16} \pm 20.5°$  (c 5, H<sub>2</sub>O). [J Chem Soc 127 279 1925; J Am Chem Soc 78 3063 1956.]

(1S)-(+)Camphor-10-sulfonic acid [3144-16-9] M 232.3, m 193°(dec), 197-198°,  $[\alpha]_{546}^{20}$ +27.5° (c 10, H<sub>2</sub>O),  $[\alpha]_D^{20}$ +43.5° (c 4.3, EtOH), pK<sub>Est</sub> ~-1. Crystd from ethyl acetate and dried under vacuum.

**Camphor-10-sulfonyl chloride** [1S-(+)- 21286-54-4; 1R-(-)- 39262-22-1] **M 250.7, m 67-68°, 70°,**  $[\alpha]_D^{20}$  (+) and (-) 32.2° (c 3, CHCl<sub>3</sub>). If free from OH bands in the IR then recryst from Et<sub>2</sub>O or pet ether, otherwise treat with SOCl<sub>2</sub> at 50° for 30min, evaporate, dry residue over KOH in a vacuum and recrystallise. The (±)-acid chloride has **m** 85°. Characterised as the *amide* (prisms from EtOH) **m** 132°,  $[\alpha_D^{17}$ (+) and (-) 1.5° (EtOH). [Read and Storey J Chem Soc 2761 1930; J Am Chem Soc 58 62 1936.]

**2,10-Camphorsultam** [1R-(+)- 108448-77-7; 1S-(-)- 94594-90-8] **M** 215.3, **m** 181-183°, 185-187°,  $[\alpha]_D^{20}$  (+) and (-) 32° (c 5, CHCl<sub>3</sub>). The (-)-enantiomer is recrystd from 95% EtOH. It dissolves in dil aq NaOH and can be pptd without hydrolysis by acidifying. It forms the N-Na salt in EtOH (by addition of Na to the EtOH soln) and the salt can be methylated with MeI to give the (-)-N-Me lactam with **m** 80° after recrystn from hot H<sub>2</sub>O and has  $[\alpha]_D^{25}$ -59.6° (c 5, CHCl<sub>3</sub>) [Shriner et al. J Am Chem Soc 60 2794 1938].

S-Canavanine [543-38-4] M 176.2, m 184°,  $[\alpha]_D^{17}$  +19.4° (c 2, H<sub>2</sub>O),  $pK_1^{25}2.43$ ,  $pK_2^{25}9.41$ . Crystd from aqueous EtOH.

S(L)-Canavanine sulfate [2219-31-0] M 274.3, m 172°(dec). See L-canavanine sulfate on p. 518 in Chapter 6.

Cannabinol [521-35-7] M 310.4, m 76-77°, b 185°/0.05mm. Crystd from pet ether. Sublimed.

**Canthaxanthin** (*trans*) [514-78-3] M 564.9, m 211-212°,  $A_{1cm}^{1\%}$  2200 (470nm) in cyclohexane. Purified by chromatography on a column of deactivated alumina or magnesium oxide, or on a thin layer of silica gel G (Merck), using dichloromethane/diethyl ether (9:1) to develop the chromatogram. Stored in the dark and in an inert atmosphere at -20°.

Capric acid (decanoic acid) [334-48-5] M 172.3, m 31.5°, b 148°/11mm, d 0.886,  $n^{25}$  1.424, pK<sub>Est</sub> ~4.9. Purified by conversion to its *methyl ester*, b 114.0°/15mm (using excess MeOH, in the presence of H<sub>2</sub>SO<sub>4</sub>). After removal of the H<sub>2</sub>SO<sub>4</sub> and excess MeOH, the ester was distd under vacuum through a 3ft

column packed with glass helices. The acid was then obtained from the ester by saponification. [Trachtman and Miller J Am Chem Soc 84 4828 1962].

n-Caproamide (n-hexanamide) [628-02-4] M 115.2, m 100°. Crystd from hot water.

Caproic acid (hexanoic acid) [142-62-1] M 116.2, b 205.4°, d 0.925, n 1.417,  $pK^{25}$  4.85. Dried with MgSO<sub>4</sub> and fractionally distilled from CaSO<sub>4</sub>.

ε-Caprolactam (azepan-2-one, aza-2-cycloheptanone, 2-oxohexamethyleneimine) [105-60-2] M 113.2, m 70°, 70.5-71.5°, 70-71°, 262.5°/760mm. Distd at reduced pressure, crystd from acetone or pet ether and redistd. Purified by zone melting. Very hygroscopic. Discolours in contact with air unless small amounts (0.2g/L) of NaOH, Na<sub>2</sub>CO<sub>3</sub> or NaBO<sub>2</sub> are present. Crystd from a mixture of pet ether (185mL of b 70°) and 2-methyl-2-propanol (30mL), from acetone, or pet ether. Distd under reduced pressure and stored under nitrogen. [Synthesis 614 1978.]

**Capronitrile** (hexanenitrile) [124-12-9] M 125.2, b 163.7°, n 1.4069, n<sup>25</sup> 1.4048. Washed twice with half-volumes of conc HCl, then with saturated aqueous NaHCO<sub>3</sub>, dried with MgSO<sub>4</sub>, and distilled.

Caprylolactam (azanon-2-one, azacyclononan-2-one, 8-aminooctanoic acid lactam) [935-30-8] M 141.2, m 72°, 73°, 74-76°, 75°, 76-77°, b 119-122°/0.7mm, 150-151°/7-8mm, 164°/14mm,  $d_4^{73}$  1.009,  $n_D^{73}$  1.489, pK<sup>25</sup> 0.55 (AcOH). Dissolve in CHCl<sub>3</sub>, decolorise with charcoal, evaporate to dryness and recrystallise from CHCl<sub>3</sub>-hexane. Sublime at high vacuum. The oxime has m 117° (from \*C<sub>6</sub>H<sub>6</sub> or pet ether). [J Med Chem 14 501 1971; Justus Liebigs Ann Chem 607 67 1957.]

Capsaicin (*E*-*N*-[(4-hydroxy-3-methoxyphenyl)-methyl]-8-methyl-6-nonenamide) [404-86-4] M 305.4, m 64-66°, 65°, 66.1°, b 210-220°/0.01mm. Recrystd from pet ether (b 40-60°), or pet ether-Et<sub>2</sub>O (9:1). Also purified by chromatography on neutral Al<sub>2</sub>O<sub>3</sub> (grade V) and eluted successively with  $C_{6}H_{6}$ ,  $C_{6}H_{6}$ -EtOAc (17:3) and  $C_{6}H_{6}$ -EtOAc (7:3), and distilled at 120°/10<sup>-5</sup>mm, and repeatedly recrystd from isopropanol (charcoal), needles. [*J Chem Soc* 11025 1955, *J Chem Soc*(C) 442 1968.]

Capsorubin (3,3'-dihydroxy- $\kappa$ , $\kappa$ -carotene-6,6'dione) [470-38-2] M 604.9, m 218°,  $\lambda_{max}$  443, 468, 503 nm, in hexane. Possible impurities: zeaxanthin and capsanthin. Purified by chromatography on a column of CaCO<sub>3</sub> or MgO. Crystd from \*benzene/pet ether or CS<sub>2</sub>.

Captan (N-trichloromethylmercapto-cyclohex-4-ene-1,2-dicarboxamide) [133-06-2] M 300.5, m 172-173°. Crystd from CCl<sub>4</sub>. Large quantities internally cause diarrhoea and vomiting.

Captopril (S-1-[3-mercapto-2-methyl-1-oxopropyl]-L-proline) [62571-86-2] M 217.3, m 103-104°(polymorphic unstable form m 86°, melts at 87-88° solidifies and then melts again at 104-105°),  $[\alpha]_D^{22}$  -131° (c 1.7, EtOH), pK<sub>1</sub> 3.7, pK<sub>2</sub> 9.8. Purified by recrystn from EtOAc-hexane. Also purified by dissolving in EtOAc and chromatographed on a column of Wakogel C200 using a linear gradient of MeOH in EtOAc (0-100°) and fractions which give a positive nitroprusside test (for SH) are combined, evap and recrystd from EtOAc-hexane (1:1), white crystals  $[\alpha]_D^{20}$ -128.2° (c 2.0, EtOH).[Nam J Pharm Sci 73 1843 1984]. Alternatively, dissolve in H<sub>2</sub>O, apply to a column of AG-50Wx2 (BioRad) and eluted with H<sub>2</sub>O. The free acid is converted to the dicyclohexylamine salt in MeCN by addition until the pH is 8-9 (moist filter paper). The salt is converted to the free acid by shaking with EtOAc and 10% aq KHSO4 or passage through an AG50Wx2 column. The EtOAc soln is dried (MgSO4) and recrystd as above from EtOAc-hexane [Biochem J 16 5484 1977; NMR and IR: Horii and Watanabe Yakugaku Zasshi (J Pharm Soc Japan) 81 1786 1961].

4-(Carbamoylmethoxy)acetanilide [14260-41-4] M 208.2, m 208°. Crystd from water.

3-Carbamoyl-1-methylpyridinium chloride (1-methylnicotinamide chloride, Trigonellamide) [1005-24-9] M 172.6, m 240°(dec). Crystd from MeOH. Carbanilide (sym-diphenylurea) [102-07-8] M 212.3, m 242°. Crystd from EtOH or a large volume (40mL/g) of hot water.

9-Carbazolacetic acid [524-80-1] M 225.2, m 215°, pK<sub>Est</sub> ~3.5. Crystd from ethyl acetate.

**Carbazole** [86-74-8] **M 167.2, m 240-243°, pK <0.** Dissolved (60g) in conc  $H_2SO_4$  (300mL), extracted with three 200mL portions of \*benzene, then stirred into 1600mL of an ice-water mixture. The ppte was filtered off, washed with a little water, dried, crystd from \*benzene and then from pyridine/\*benzene. [Feldman, Pantages and Orchin *J Am Chem Soc* 73 4341 1951]. Has also been crystd from EtOH or toluene, sublimed in vacuum, zone-refined, and purified by TLC.

**Carbazole-9-carbonyl chloride** [73500-82-0] **M 300.0, m 100-103°, 103.5-104.5°**. Recrystd from  $*C_6H_6$ . If it is not very pure (presence of OH or NH bands in the IR) dissolve in pyridine, shake with phosgene in toluene, evaporate and recrystallise the residue. Carry out this experiment in a good fume cupboard as COCl<sub>2</sub> is very **TOXIC**, and store the product in the dark. It is moisture sensitive. The *amide* has **m** 246.5-247°, and the *dimethylaminoethylamide hydrochloride* has **m** 197-198°. [Weston et al. *J Am Chem Soc* **75** 4006 1953.]

4-Carboethoxy-3-methyl-2-cyclohexen-1-one (Hagemann's ester) [487-51-4] M 182, b 79-80°/0.2mm, 121-123°/4mm, 142-144°/15mm, d<sup>20</sup> 1.038. Dissolve in ether, shake with solid K<sub>2</sub>CO<sub>3</sub>, aqueous saturated NaHCO<sub>3</sub>, dry (MgSO<sub>4</sub>) and distil. Semicarbazone has m 165-167° (169°). [J Am Chem Soc 65, 631, 1943.]

1-Carbethoxy-4-methylpiperazine hydrochloride [532-78-5] M 204.7, m 168.5-169°, pK 7.31. Crystd from absolute EtOH.

**N-Carboethoxyphthalimide** (*N*-ethoxycarbonylphthalimide) [22509-74-6] M 219.2, m 87-89°, 90-92°. Crystd from toluene-pet ether (or \*benzene-pet ether). Partly soluble in Et<sub>2</sub>O, \*benzene and CHCl<sub>3</sub>. [*Chem Ber* 54 1112 1921.]

γ-Carboline {9H-pyrido[3,4-b]indole} [244-69-9] M 168.2, m 225°, pK-0. Crystd from water.

**Carbon Black** Leached for 24h with 1:1 HCl to remove oil contamination, then washed repeatedly with distd water. Dried in air, and eluted for one day each with \*benzene and acetone. Again dried in air at room temp, then heated in a vacuum for 24h at 600° to remove adsorbed gases. [Tamamushi and Tamaki *Trans Faraday Soc* 55 1007 1959.]

**Carbon disulfide** [75-15-0] **M 76.1, b 46.3°, d 1.264, n 1.627.** Shaken for 3h with three portions of KMnO<sub>4</sub> soln (5g/L), twice for 6h with mercury (to remove sulfide impurities) until no further darkening of the interface occurred, and finally with a soln of HgSO<sub>4</sub> (2.5g/L) or cold, satd HgCl<sub>2</sub>. Dried with CaCl<sub>2</sub>, MgSO<sub>4</sub>, or CaH<sub>2</sub> (with further drying by refluxing with P<sub>2</sub>O<sub>5</sub>), followed by fractional distn in diffuse light. **Alkali metals cannot be used as drying agents**. Has also been purified by standing with bromine (0.5mL/L) for 3-4h, shaking with KOH soln, then copper turnings (to remove unreacted bromine), and drying with CaCl<sub>2</sub>. CS<sub>2</sub> is highly **TOXIC** and highly **FLAMMABLE**. Work in a good fumehood.

Small quantities of CS<sub>2</sub> have been purified (including removal of hydrocarbons) by mechanical agitation of a 45-50g sample with a soln of 130g of sodium sulfide in 150mL of H<sub>2</sub>O for 24h at 35-40°. The aqueous sodium thiocarbonate soln was separated from unreacted CS<sub>2</sub>, then ppted with 140g of copper sulfate in 350g of water, with cooling. After filtering off the copper thiocarbonate, it was decomposed by passing steam into it. The distillate was separated from H<sub>2</sub>O and distd from P<sub>2</sub>O<sub>5</sub>. [Ruff and Golla Z Anorg Chem 138 17 1924.]

**Carbon tetrabromide** [558-13-4] **M 331.7, m 92.5°.** Reactive bromide was removed by refluxing with dilute aqueous Na<sub>2</sub>CO<sub>3</sub>, then steam distd, crystd from EtOH, and dried in the dark under vacuum. [Sharpe and Walker J Chem Soc 157 1962.] Can be sublimed at 70° at low pressure.

Carbon tetrachloride [56-23-5] M 153.8, b 76.8°, d<sup>25</sup> 1.5842. For many purposes, careful fractional distn gives adequate purification. Carbon disulfide can be removed by shaking vigorously for several hours with saturated KOH, separating, and washing with water: this treatment is repeated. The CCl<sub>4</sub> is shaken with conc H<sub>2</sub>SO<sub>4</sub> until there is no further coloration, then washed with water, dried with CaCl<sub>2</sub> or MgSO<sub>4</sub> and distd (from P<sub>2</sub>O<sub>5</sub> if desired). It must not be dried with sodium. An initial refluxing with mercury for 2h removes sulfides. Other purification steps include passage of dry CCl<sub>4</sub> through activated alumina, and distn from KMnO<sub>4</sub>. Carbonyl containing impurities can be removed by percolation through a Celite column impregnated with 2,4-dinitrophenylhydrazine (DNPH), H<sub>3</sub>PO<sub>4</sub> and water. (Prepared by dissolving 0.5g DNPH in 6mL of 85% H<sub>3</sub>PO<sub>4</sub> by grinding together, then mixing with 4mL of distd water and 10g Celite.) [Schwartz and Parks Anal Chem 33 1396 1961]. Photochlorination of CCl4 has also been used: CCl4 to which a small amount of chlorine has been added is illuminated in a glass bottle (e.g. for 24h with a 200W tungsten lamp near it), and, after washing out the excess chlorine with 0.02M Na<sub>2</sub>SO<sub>3</sub>, the CCl<sub>4</sub> is washed with distd water and distd from  $P_2O_5$ . It can be dried by passing through 4A molecular sieves and distd. Another purification procedure is to wash CCl<sub>4</sub> with aq NaOH, then repeatedly with water and N<sub>2</sub> gas bubbled through the liquid for several hours. After drying over CaCl<sub>2</sub> it is percolated through silica gel and distd under dry N<sub>2</sub> before use [Klassen and Ross J Phys Chem 91 3664 1987].

**Rapid purification:** Distil, discarding the first 10% of distillate or until the distillate is clear. The distilled  $CCl_4$  is then stored over 5A molecular sieves.

**Carbon tetrafluoride** [75-73-0] **M 88.0, b -15°.** Purified by repeated passage over activated charcoal at solid-CO<sub>2</sub> temperatures. Traces of air were removed by evacuating while alternately freezing and melting. Alternatively, liquefied by cooling in liquid air and then fractionally distilled under vacuum. (The chief impurity originally present was probably  $CF_3Cl$ ).

Carbon tetraiodide [507-25-5] M 519.6, m 168°(dec). Sublimed in vacuo.

N, N'-Carbonyldiimidazole [530-62-1] M 162.2, m 115.5-116°. Crystd from \*benzene or tetrahydrofuran, in a dry-box.

**1,1'-Carbonyldi(1,2,4-triazole)** [41864-22-6] M **164.1, m 134-136°, 145-150°.** Dissolve in tetrahydrofuran and evaporate at 10mm until it crystallises. Wash crystals with cold tetrahydrofuran and dry in a vacuum desiccator over  $P_2O_5$  in which it can be stored for months. [Recl Trav Chim Pays-Bas **80** 1372 1961; Potts J Org Chem **27** 2631 1962; Staab Justus Liebigs Ann Chem **106** 75 1957.]

Carbonyl sulfide [463-58-1] M 60.1. See carbonyl sulfide entry on p. 409 in Chapter 5.

o-Carboxyphenylacetonitrile [6627-91-4] M 161.2, m 114-115°. Crystd (with considerable loss) from \*benzene or glacial acetic acid.

(-)-Caryophyllene oxide (1-S-5c-6t-epoxy-6c,10,10-trimethyl-2-methylene-1r,9t-bicyclo-[7.2.0]undecane) [1/39-30-6] M 220.4, m 62-63°, 63.5-64°, 64°, b 114-117°/1.8mm, 141- $142°/11mm, d<sup>20</sup><sub>4</sub> 0.9666, n<sup>20</sup><sub>D</sub> 1.49564, <math>[\alpha]^{20}_{D}-79°$  (c 2,CHCl<sub>3</sub>),  $[\alpha]^{20}_{D}-68°$  (supercooled melt). Purified by TLC on silica gel with EtOAc-pet ether (b 60-80°) (15:85), and recrystallised from MeOH or \*C<sub>6</sub>H<sub>6</sub>. [NMR: Warnhoff Can J Chem 42 1664 1964, Ramage and Whitehead J Chem Soc 4336 1954.]

(±)-Catechin [7295-85-4] M 272.3, m 177° (anhyd). Crystd from hot water. Dried at 100°.

Catechol (1,2-dihydroxybenzene, pyrocatechol) [120-80-9] M 110.1, m 105°,  $pK_1^{25}$  9.45,  $pK_2^{25}$  12.8. Crystd from \*benzene or toluene. Sublimed under vacuum. [Rozo et al. Anal Chem 58 2988 1986.]

**Cation exchange resin.** Conditioned before use by successive washing with water, EtOH and water, and taken through two H<sup>+</sup>-Na<sup>+</sup>-H<sup>+</sup> cycles by successive treatment with M NaOH, water and M HCl then washed with water until neutral.

(+)-Cedrol (octahydro-3,6,8,8-tetramethyl-1-3a,7-methanoazulen-6-ol, 8aS-6c-hydroxy-3c,6t,8,8-tetramethyl[8ar-H)-octahydro-3H,3at,7t-methanoazulene), [77-53-2] m 82-86°, 86-87°,  $[\alpha]_D^{28}$  +10.5° (c 5,CHCl<sub>3</sub>),  $[\alpha]_D^{18}$  +13.1° (c 5.5, EtOH),  $[\alpha]_D^{18}$  +14.3° (c 10, dioxane). Purified by recrystn from aqueous MeOH. It is estimated colorimetrically with H<sub>3</sub>PO<sub>4</sub> in EtOH followed by vanillin and HCl [Hayward and Seymour Anal Chem 20 572 1948]. The 3,5-dinitrobenzoyl derivative has m 92-93°. [J Am Chem Soc 83 3114 1961.]

β-Cellobiose [528-50-7] M 342.3, m 228-229°(dec),  $[α]_D^{25}$ +33.3° (c 2, water). Crystd from 75% aqueous EtOH.

Cellulose triacetate [9012-09-3] M 72,000-74,000. Extracted with cold EtOH, dried in air, washed with hot distd water, again dried in air, then dried at 50° for 30min. [Madorsky, Hart and Straus J Res Nat Bur Stand 60 343 1958.]

Cerulenin (helicocerin, 2R,3S-2,3-epoxy-4-oxo-7E,10E-dodecadienamide) [17397-89-6] M 223.3, m 93-94°, 93-95°, b 120°/10<sup>-8</sup>mm,  $[\alpha]_D^{16}$ +63° (c 2, MeOH). White needles from \*C<sub>6</sub>H<sub>6</sub>. Also purified by repeated chromatography from Florisil and silica gel. It is soluble in EtOH, MeOH, \*C<sub>6</sub>H<sub>6</sub>, slightly soluble in H<sub>2</sub>O and pet ether. The dl-form has m 40-42° (from \*C<sub>6</sub>H<sub>6</sub>-hexane), and the 2R,3S-tetrahydrocerulenin has m 86-87°,  $[\alpha]_D^{20}$  +44.4 (c 0.25, MeOH after 24h). [Tetrahedron Lett 2095 1978, 2039 1979; J Am Chem Soc 99 2805 1977; J Org Chem 47 1221 1982.]

Cetyl acetate [629-70-9] M 284.5, m 18.3°. Vacuum distd twice, then crystd several times from diethyl ether/MeOH.

Cetyl alcohol (1-hexadecanol) [36653-82-4] M 242.5, m 49.3°. Crystd from aqueous EtOH or from cyclohexane. Purified by zone refining. Purity checked by gas chromatography.

Cetylamide [629-54-9] M 255.4, m 106-107°, b 235-236°/12mm. Crystd from thiophene-free \*benzene and dried under vacuum over  $P_2O_5$ .

Cetylamine (1-hexadecylamine) [143-27-1] M 241.5, m 48°, b 162-165°/5.2mm,  $pK^{25}$  10.60. Crystd from thiophene-free \*benzene and dried under vacuum over  $P_2O_5$ .

Cetylammonium chloride [1602-97-7] M 278.0, m 178°. Crystd from MeOH.

Cetyl bromide (1-bromohexadecane) [112-82-3] M 305.4, m 15°, b 193-196°/14mm. Shaken with  $H_2SO_4$ , washed with water, dried with  $K_2CO_3$  and fractionally distd.

Cetyl ether [4113-12-6] M 466.9, m 54°. Vacuum distd then crystd several times from MeOH/\*benzene.

Cetylpyridinium chloride ( $H_2O$ ) [6004-24-6] M 358.0, m 80-83°. Crystd from MeOH or EtOH/diethyl ether and dried *in vacuo*. [Moss et al. J Am Chem Soc 108 788 1986; Lennox and McClelland J Am Chem Soc 108 3771 1986.]

**Cetyltrimethylammonium bromide (cetrimonium bromide, CTAB)** [57-09-0] M 364.5, m 227-235°(dec). Crystd from EtOH, EtOH/\*benzene or from wet acetone after extracting twice with pet ether. Shaken with anhydrous diethyl ether, filtered and dissolved in a little hot MeOH. After cooling in the refrigerator, the ppte was filtered at room temperature and redissolved in MeOH. Anhydrous ether was added and, after warming to obtain a clear soln, it was cooled and crystalline material was filtered. [Dearden and Wooley J Phys Chem 91 2404 1987; Hakemi et al. J Am Chem Soc 91 120 1987.]

Cetyltrimethylammonium chloride [112-02-7] M 320.0. Crystd from acetone/ether mixture, EtOH/ether, or from MeOH. [Moss et al. J Am Chem Soc 109 4363 1987.]

**Charcoal.** Charcoal (50g) was added to 1L of 6M HCl and boiled for 45min. The supernatant was discarded, and the charcoal was boiled with two more lots of HCl, then with distilled water until the supernatant no longer gave a test for chloride ion. The charcoal (which was now phosphate-free) was filtered on a sintered-glass funnel and air dried at 120° for 24h. [Lippin, Talbert and Cohn J Am Chem Soc 76 2871 1954.] The purification can be carried out using a Soxhlet extractor (without cartridge), allowing longer extraction times. Treatment with conc  $H_2SO_4$  instead of HCl has been used to remove reducing substances.

Chaulmoogric acid [(13-cyclopent-2-enylyl)tridecanoic acid] [29106-32-9] M 280.4, m 68.5°, b 247-248°/20mm,  $[\alpha]_D^{20}$  +60° (c 4, CHCl<sub>3</sub>), pK<sub>Est</sub> ~5.0. Crystd from pet ether or EtOH. The *Me ester* [24828-59-9] has m 22°, b 227°/20mm and  $[\alpha J_D^{15}$  +50° (c 5, CHCl<sub>3</sub>).

Chelerythrine [34316-15-9] M 389.4, m 207°. Crystd from CHCl<sub>3</sub> by addition of MeOH.

Chelex 100 [11139-85-8]. Washed successively with 2M ammonia, water, 2M nitric acid and water. Chelex 100 may develop an odour on long standing. This can be removed by heating to 80° for 2h in 3M ammonia, then washing with water. [Ashbrook J Chromatogr 105 151 1975.]

Chelidonic acid (4-oxopyran-2,6-dicarboxylic acid) [99-32-1] M 184.1, m 262°, pK<sub>2</sub><sup>25</sup>2.36. Crystd from aqueous EtOH.

Chenodesoxycholic acid [474-25-9] M 392.6, m 143°. See 3a,7a-dihydroxycholanic acid on p. 207.

Chimyl alcohol (1-O-n-hexadecylglycerol) [(±) 506-03-6; 10550-58-0 (chimyl alcohol)] M 316.5, m 64°. Crystd from hexane.

Chloral [75-87-6; 302-17-0 (hydrate)] M 147.4, b 98°, pK<sup>25</sup> 10.04. Distd, then dried by distilling through a heated column of CaSO<sub>4</sub>.

Chloralacetone chloroform [512-47-0] M 324.9, m 65°. Crystd from \*benzene.

 $\alpha$ -Chloralose (*R*-1,2-*O*-[2,2,2-trichloroethylidene]- $\alpha$ -D-glucofuranose) [15879-93-3] M 309.5, m 180-182°, 187°, 186-188°,  $[\alpha]_D^{26}$  +19.5° (c 11, pyridine). Recryst from EtOH, 38% aqueous EtOH, Et<sub>2</sub>O, H<sub>2</sub>O or CHCl<sub>3</sub> The solubility is 0.44% in H<sub>2</sub>O at 15°, 0.83% in H<sub>2</sub>O at 37°, 6.7% in EtOH at 25°. [Whiton and Hixon *J Am Chem Soc* 55 2438 1933; Helv Chim Acta 6 621 1923.] The βisomer is less soluble in H<sub>2</sub>O, EtOH or Et<sub>2</sub>O and has m 237.5-238° [*J Am Chem Soc* 59 1955 1937; Acta Chem Scand 19 359 1965].

**2-Chloroacetophenone** [532-27-4] **M 154.6, m 54-56°.** Crystd from MeOH [Tanner J Org Chem 52 2142 1987].

p-Chloranil (2,3,5,6-tetrachloro-1,4-benzoquinone) [118-75-2] M 245.9, m 290°, 294.2-294.6° (sealed tube). Crystd from acetic acid, acetone, \*benzene, EtOH or toluene, drying under vac over P<sub>2</sub>O<sub>5</sub>, or from acetic acid, drying over NaOH in a vacuum desiccator. It can be sublimed under vacuum at 290°. Sample may contain significant amounts of the *o*-chloranil isomer as impurity. Purified by triple sublimation under vacuum. Recrystd before use. It is a skin and mucous membrane irritant. [UV: Rec Trav Chim Pays Bas 276 684 1924; Brook J Chem Soc 5040 1952.]

Chloranilic acid (2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone) [87-88-7] M 209.0, m 283-284°  $pK_1^{25}$  1.22,  $pK_2^{25}$  3.01. A soln of 8g in 1L of boiling water was filtered while hot, then extracted twice at about 50° with 200mL portions of \*benzene. The aq phase was cooled in ice-water. The crystals were filtered off, washed with three 10mL portions of water, and dried at 115°. It can be sublimed in vacuum. [J Phys Chem 61 765 1957.] The diacetate has m 182-185° [J Am Chem Soc 46 1866 1924; Thamer and Voight J Phys Chem 56 225 1952].

**Chlorendic anhydride** (1,4,5,6,7,7,-hexachloro-5-norbornene-2,3-dicarboxylic anhydride) [115-27-5] M 370.9, m 234-236°. 235-237°, 238°. Steam distn or recrystn from H<sub>2</sub>O yields the diacid. The purified diacid yields the anhydride with Ac<sub>2</sub>O. [Prill J Am Chem Soc 69 62 1947.]

Chloroacetaldehyde dimethyl acetal [97-97-2] M 124.6, m -34.4°, b 64°/23mm, 71-72°/35mm,  $d_4^{20}$  1.0172,  $n_D^{20}$  1.4175. Purified by fractional distillation. [Melhotra J Indian Chem Soc 36 4405 1959; Bull Soc Chim Belg 61 393 1952.]

 $\alpha$ -Chloroacetamide [79-07-2] M 93.5, m 121°, b 224-225°/743mm. Crystd from acetone and dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

p-Chloroacetanilide [539-03-7] M 169.6, m 179°. Crystd from EtOH or aqueous EtOH.

**Chloroacetic acid** [79-11-8] **M 94.5, m 62.8°, b 189°, pK^{25} 2.87.** Crystd from CHCl<sub>3</sub>, CCl<sub>4</sub>, \*benzene or water. Dried over P<sub>2</sub>O<sub>5</sub> or conc H<sub>2</sub>SO<sub>4</sub> in a vacuum desiccator. Further purification by distn from MgSO<sub>4</sub>, and by fractional crystn from the melt. Stored under vac or under dry N<sub>2</sub>. [Bernasconi et al. J Am Chem Soc 107 3621 1985.]

Chloroacetic anhydride [541-88-8] M 171.0, m 46°, d 1.5494. Crystd from \*benzene.

**Chloroacetone** [78-95-5] **M 92.5, b 119°/763mm, d 1.15.** Dissolved in water and shaken repeatedly with small amounts of diethyl ether which extracts, preferentially, 1,1-dichloroacetone present as an impurity. The chloroacetone was then extracted from the aqueous phase using a large amount of diethyl ether, and distd at slightly reduced pressure. It was dried with CaCl<sub>2</sub> and stored at Dry-ice temperature. Alternatively, it was stood with CaSO<sub>4</sub>, distd and stored over CaSO<sub>4</sub>. **LACHRYMATORY.** 

**Chloroacetonitrile** [107-14-2] **M 75.5, b 125°.** Refluxed with  $P_2O_5$  for one day, then distd through a helices-packed column. Also purified by gas chromatography. **LACHRYMATOR, HIGHLY TOXIC.** 

o-Chloroaniline [95-51-2] M 127.6, m -1.9°, b 208.8°, d 1.213, n 1.588,  $pK^{25}$  2.66. Freed from small amounts of the *p*-isomer by dissolving in one equivalent of H<sub>2</sub>SO<sub>4</sub> and steam distilling. The *p*isomer remains behind as the sulfate. [Sidgwick and Rubie *J Chem Soc* 1013 1921.] An alternative method is to dissolve in warm 10% HCl (11mL/g of amine) and on cooling, the hydrochloride of o-chloroaniline separates out. The latter can be recrystd until the acetyl derivative has a constant melting point. (In this way, yields are better than for the recrystn of the picrate from EtOH or of the acetyl derivative from pet ether.) [King and Orton *J Chem Soc* 1377 1911].

*p*-Chloroaniline [106-47-8] M 127.6, m 70-71°,  $pK^{25}$  3.98. Crystd from MeOH, pet ether (b 30-60°), or 50% aq EtOH, then \*benzene/pet ether (b 60-70°), then dried in a vacuum desiccator. Can be distd under vacuum (b 75-77°/33mm).

*p*-Chloroanisole [623-12-1] M 142.6, b 79°/11.5mm, 196.6°/760mm, d 1.164,  $n^{25.5}$  1.5326. Washed with 10% (vol) aqueous H<sub>2</sub>SO<sub>4</sub> (three times), 10% aqueous KOH (three times), and then with water until neutral. Dried with MgSO<sub>4</sub> and fractionally distd from CaH<sub>2</sub> through a glass helices-packed column under reduced pressure.

9-Chloroanthracene [716-53-0] M 212.9, m 105-107°. Crystd from EtOH. [Masnori J Am Chem Soc 108 1126 1986.]

10-Chloro-9-anthraldehyde [10527-16-9] M 240.7, m 217-219°. Crystd from EtOH.

o-Chlorobenzaldehyde [89-98-5] M 140.6, m 11°, b 213-214°, d 1.248, n 1.566. Washed with 10% Na<sub>2</sub>CO<sub>3</sub> soln, then fractionally distd in the presence of a small amount of catechol.

**3-Chlorobenzaldehyde** [587-04-2] **M 140.6, m 18°, b 213-214°, d 1.241, n 1.564.** Purified by low temperature crystn from pet ether (b 40-60°).

4-Chlorobenzaldehyde [104-88-1] M 140.6, m 47°. Crystd from EtOH/water (3:1), then sublimed twice at 2mm pressure at a temperature slightly above the melting point.

**Chlorobenzene** [108-90-7] **M** 112.6, **b** 131.7°, **d** 1.107, **n** 1.52480. The main impurities are likely to be chlorinated impurities originally present in the \*benzene used in the synthesis of chlorobenzene, and also unchlorinated hydrocarbons. A common purification procedure is to wash several times with conc H<sub>2</sub>SO<sub>4</sub> then with aq NaHCO<sub>3</sub> or Na<sub>2</sub>CO<sub>3</sub>, and water, followed by drying with CaCl<sub>2</sub>, K<sub>2</sub>CO<sub>3</sub> or CaSO<sub>4</sub>, then with P<sub>2</sub>O<sub>5</sub>, and distn. It can also be dried with Linde 4A molecular sieve. Passage through, and storage over, activated alumina has been used to obtain low conductance material. [Flaherty and Stern J Am Chem Soc 80 1034 1958.]

4-Chlorobenzenesulfonyl chloride [98-60-2] M 211.1, m 53°, b 141°/15mm. Crystd from ether in powdered Dry-ice, after soln had been washed with 10% NaOH until colourless and dried with Na<sub>2</sub>SO<sub>4</sub>.

4-Chlorobenzhydrazide [536-40-3] M 170.6, m 164°. Crystd from water.

**2-Chlorobenzoic acid** [118-91-2] **M 156.6, m 139-140°, pK^{25} 2.91.** Crystd successively from glacial acetic acid, aq EtOH, and pet ether (b 60-80°). Other solvents include hot water or toluene (*ca* 4mL/g). Crude material can be given an initial purification by dissolving 30g in 100mL of hot water containing 10g of Na<sub>2</sub>CO<sub>3</sub>, boiling with 5g of charcoal for 15min, then filtering and adding 31mL of 1:1 aq HCl: the ppte is washed with a little water and dried at 100°.

**3-Chlorobenzoic acid** [535-80-8] M **156.6**, m **154-156°**, **158°**,  $d_4^{25}$  **1.496**, pK<sup>25</sup> **3.82** (5.25 in **50% dimethylacetamide**). Crystd successively from glacial acetic acid, aqueous EtOH and pet ether (b 60-80°). It also recrysts from \*C<sub>6</sub>H<sub>6</sub> or Et<sub>2</sub>O-hexane, and sublimes at 55° in a vacuum. [Anal Chem **26** 726 1954] The methyl ester has m 21°, b 231°/atm. The S-benzyl thiouronium salt has m 164-165° (from EtOH) [Acta Chem Scand 9 1425 1955; J Chem Soc 1318 1960].

4-Chlorobenzoic acid [74-11-3] M 156.6, m 238-239°, pK<sup>25</sup> 3.99. Same as for *m*-chlorobenzoic acid. Has also been crystd from hot water, and from EtOH.

2-Chlorobenzonitrile [873-32-5] M 137.6, m 45-46°. Crystd to constant melting point from \*benzene/pet ether (b 40-60°).

4-Chlorobenzophenone [134-85-0] M 216.7, m 75-76°. Recrystd for EtOH. [Wagner et al. J Am Chem Soc 108 7727 1986.]

**2-Chlorobenzothiazole** [615-20-3] **M 169.6, m 21°, 90-91.4°/4mm, 135-136°/28mm, d\_4^{20} 1.303, n\_D^{20} 1.6398.** It is purified by fractional distn in vacuo. The 2-chloro-3-methylbenzothiazolinium 2,4-dinitrobenzenesulfonate crystallises from Ac<sub>2</sub>O, **m** 162-163° (dec). [J Am Chem Soc **73** 4773 1951; J Org Chem **19** 1830 1954; J Chem Soc **2190** 1930.]

o-Chlorobenzotrifluoride [88-16-4] M 180.6, b 152.3°. Dried with CaSO<sub>4</sub>, and distd at high reflux ratio through a silvered vacuum-jacketed glass column packed with one-eight inch glass helices [Potter and Saylor J Am Chem Soc 73 90 1951].

m-Chlorobenzotrifluoride [98-15-7] M 180.6, b 137.6°. Same as for o-chlorobenzotrifluoride above.

p-Chlorobenzotrifluoride [98-56-6] M 180.6, b 138.6°. Same as for o-chlorobenzotrifluoride above.

**2-Chlorobenzoxazole** [615-18-9] M 153.6, b 95-96°/20mm, 198-202°/atm,  $d_4^{20}$  1.331,  $n_D^{20}$  1.570. Purified by fractional distn, preferably in a vacuum. [Siedel J Prakt Chem (2) 42 456 1890; J Am Chem Soc 75 712 1953.]

*p*-Chlorobenzyl chloride [104-83-6] M 161.0, m 28-29°, b 96°/15mm. Dried with CaSO<sub>4</sub>, then fractionally distd under reduced pressure. Crystd from heptane or dry diethyl ether. LACHRYMATORY.

*p*-Chlorobenzylisothiuronium chloride [544-47-8] M 237.1, m 197°, pK<sub>Est</sub> ~9.6 (free base). Crystd from conc HCl by addition of water.

**2-Chlorobutane** [78-86-4] M 92.6, b 68.5°, d 0.873,  $n^{25}$  1.3945. Purified in the same way as *n*-butyl chloride.

2-(4-Chlorobutyl)-1,3-dioxolane [118336-86-0] M 164.6, b 56-58°/0.1mm,  $d_4^{20}$  1.106,  $n_D^{20}$ 1.457. If the IR has a CHO band then just distil in vacuum. If it is present then dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, then saturated NaHCO<sub>3</sub>, dry over MgSO<sub>4</sub>, evaporate and distil. [J Am Chem Soc 73 1365 1951.]

*N*-Chlorocarbonyl isocyanate [27738-96-1] M 105.5, m -68°, b 63.6°/atm,  $d_4^{20}$  1.310. Fractionally distd at atmospheric pressure using a 40cm column. TOXIC vapour use a good fume hood. Store dry, v 2260 (NCO), 1818 (CO) and 1420 (NCO sym) cm<sup>-1</sup>. [Chem Ber 106 1752 1975.]

*trans*-4-Chlorocinnamic acid [1615-02-7] M 182.6, m 243°, 248-250°, 249-251°, pK<sup>25</sup> 4.41. Recrystd from EtOH or aq EtOH (charcoal). [Org Synth Coll Vol IV 731 1963, Walling and Wolfstin J Am Chem Soc 69 852 1947.]

Chlorocyclohexane [542-18-7] M 118.6, b 142.5°, d 1.00,  $n^{25}$  1.46265. Washed several times with dilute NaHCO<sub>3</sub>, then repeatedly with distilled water. Dried with CaCl<sub>2</sub> and fractionally distd.

4-Chloro-2,6-diaminopyrimidine (2,4-diamino-6-chloropyrimidine) [156-83-2] M 144.6, m 198°, 199-202°,  $pK^{25}$  3.57. Purified by recrystn from boiling H<sub>2</sub>O (charcoal) as needles; also crystallises from Me<sub>2</sub>CO. [Büttner Chem Ber 36 2232 1903; Roth J Am Chem Soc 72 1914 1950; UV: J Chem Soc 3172 1962.]

4-Chloro-3,5-dimethylphenol [88-04-0] M 156.6, m 115.5°, pK<sup>25</sup> 9.70. Crystd from \*benzene or toluene.

1-Chloro-2,4-dinitrobenzene [97-00-7] M 202.6, m 48-50°, 51°, 52-54°, 54°, b 315°/atm,  $d_4^{22}$  1.697. Usually crystd from EtOH or MeOH. Has also been crystd from Et<sub>2</sub>O, \*C<sub>6</sub>H<sub>6</sub>, \*C<sub>6</sub>H<sub>6</sub>-pet ether or isopropyl alcohol. A preliminary purification step has been to pass its soln in \*benzene through an alumina column. Also purified by zone refining. It exists in three forms: one stable and two unstable. The stable form crysts as yellow needles from Et<sub>2</sub>O, m 51°, b 315°/atm with some dec, and is sol in EtOH. The labile forms also crystallises from Et<sub>2</sub>O, m 43°, and is more soluble in organic solvents. The second labile form has m 27°. [Hoffman and Dame, J Am Chem Soc 41 1015 1919, Welsh J Am Chem Soc 63 3276 1941; J Chem Soc 2476 1957.]

4-Chloro-3,5-dinitrobenzoic acid [118-97-8] M 246.6, m 159-161°, pK<sub>Est</sub> ~2.5. Crystd from EtOH/water, EtOH or \*benzene.

**2-Chloro-3,5-dinitropyridine** [2578-45-2] M 203.5, m 62-65°, 63-65°, 64°,  $pK_{Est} < -5$ . Dissolve in CHCl<sub>3</sub>, shake with saturated NaHCO<sub>3</sub>, dry (MgSO<sub>4</sub>), evaporate and apply to an Al<sub>2</sub>O<sub>3</sub> column, elute with pet ether (b 60-80°), evaporate and recryst from \*C<sub>6</sub>H<sub>6</sub> or pet ether. [Chem Pharm Bull Jpn 8 28 1960; Recl Trav Chim Pays-Bas 72 573 1953.] 2-Chloroethanol (ethylene chlorohydrin) [107-07-3] M 80.5, b 51.0°/31 mm, 128.6°/760mm, d 1.201, n<sup>15</sup> 1.444. Dried with, then distd from, CaSO<sub>4</sub> in the presence of a little Na<sub>2</sub>CO<sub>3</sub> to remove traces of acid.

**2-Chloroethyl bromide** (1-bromo-2-chloroethane) [107-04-0] M 143.4, b 106-108°. Washed with conc H<sub>2</sub>SO<sub>4</sub>, water, 10% Na<sub>2</sub>CO<sub>3</sub> soln, and again with water, then dried with CaCl<sub>2</sub> and fractionally distd before use.

2-Chloroethyl chloroformate [627-11-2] M 143.0, b 52-54°/12mm, 153°/760mm,  $d_4^{18}$  1.3760,  $n_D^{20}$  1.446. Purified by fractional distn, preferably in a vacuum and stored in dry atmosphere. [J Chem Soc 2735 1957.]

1-(2-Chloroethyl)pyrrolidine hydrochloride [7250-67-1] M 170.1, m 167-170°, 173.5-174°,  $pK_{Est} \sim 8.5$  (free base). Purified by recrystn from isopropanol-di-isopropyl ether (charcoal) and recrystallised twice more. The *free base*, b 55-56°/11mm, 60-63°/23mm and 90°/56mm, is relatively unstable and should be converted to the hydrochloride immediately, by dissolving in isopropanol and bubbling dry HCl through the soln at 0°, and filtering off the hydrochloride and recrystallising it. The *picrate* has m 107.3-107.8° (from EtOH) [Cason J Org Chem 24 247 1959; J Am Chem Soc 70 3098 1948].

2-Chloroethyl vinyl ether [110-75-8] M 106.6, b 109°/760mm, d 1.048, n 1.437. Washed repeatedly with equal volumes of water made slightly alkaline with KOH, dried with sodium, and distd under vacuum. TOXIC.

**Chloroform** [67-66-3] **M** 119.4, b 61.2°, d<sup>15</sup> 1.49845, d<sup>10</sup> 1.47060, n<sup>15</sup> 1.44858. Reacts slowly with oxygen or oxidising agents, when exposed to air and light, giving, mainly, phosgene, Cl<sub>2</sub> and HCl. Commercial CHCl<sub>3</sub> is usually stabilized by addn of up to 1% EtOH or of dimethylaminoazobenzene. Simplest purifications involve washing with water to remove the EtOH, drying with K<sub>2</sub>CO<sub>3</sub> or CaCl<sub>2</sub>, refluxing with P<sub>2</sub>O<sub>5</sub>, CaCl<sub>2</sub>, CaSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>, and distilling. **It must not be dried with sodium.** The distd CHCl<sub>3</sub> should be stored in the dark to avoid photochemical formation of phosgene. As an alternative purification, CHCl<sub>3</sub> can be shaken with several small portions of conc H<sub>2</sub>SO<sub>4</sub>, washed thoroughly with water, and dried with CaCl<sub>2</sub> or K<sub>2</sub>CO<sub>3</sub> before filtering and distilling. EtOH can be removed from CHCl<sub>3</sub> by passage through a column of activated alumina, or through a column of silica gel 4-ft long by 1.75-in diameter at a flow rate of 3mL/min. (The column, which can hold about 8% of its weight of EtOH, is regenerated by air drying and then heating at 600° for 6h. It is pre-purified by washing with CHCl<sub>3</sub>, then EtOH, leaving in conc H<sub>2</sub>SO<sub>4</sub> for about 8hr, washing with water until the washings are neutral, then air drying, followed by activation at 600° for 6h. Just before use it is reheated for 2h to 154°.) [McLaughlin, Kaniecki and Gray Anal Chem **30** 1517 1958].

Carbonyl-containing impurities can be removed from CHCl<sub>3</sub> by percolation through a Celite column impregnated with 2,4-dinitrophenylhydrazine, phosphoric acid and water. (Prepared by dissolving 0.5g DNPH in 6mL of 85% H<sub>3</sub>PO<sub>4</sub> by grinding together, then mixing with 4mL of distilled water and 10g of Celite.) [Schwartz and Parks Anal Chem 33 1396 1961]. Chloroform can be dried by distn from powdered type 4A Linde molecular sieves. For use as a solvent in IR spectroscopy, chloroform is washed with water (to remove EtOH), then dried for several hours over anhydrous CaCl<sub>2</sub> and fractionally distd. This treatment removes material absorbing near 1600 cm<sup>-1</sup>. (Percolation through activated alumina increases this absorbing impurity). [Goodspeed and Millson Chem Ind (London) 1594 1967].

**Rapid purification:** Pass through a column of basic alumina (Grade I, 10g/mL of CHCl<sub>3</sub>), and either dry by standing over 4A molecular sieves, or alternatively, distil from P<sub>2</sub>O<sub>5</sub> (3% w/v). Use immediately.

Chlorogenic [3-(3,4-dihydroxycinnamoyl)quinic] acid [327-97-9] M 354.3, m 208°,  $[\alpha]_D^{25}$ -36° (c 1, H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup> 3.59, pK<sub>2</sub><sup>25</sup> 8.59. Crystd from water. Dried at 110°.

Chlorohydroquinone (2-chloro-1,4-dihydroxybenzene) [6/5-67-8] M 144.6, m 106°, b 263°,  $pK_1^{25}8.81$ ,  $pK_2^{25}10.78$ . Crystd from CHCl<sub>3</sub> or toluene.

5-Chloro-8-hydroxy-7-iodoquinoline (vioform) [130-26-7] M 305.5, m 178-179°, pK<sub>Est(1)</sub>~2.6, pK<sub>Est(2)</sub>~7.0. Crystd from abs EtOH.

**5-Chloroindole** [17422-32-1] **M 151.6, m 69-71°, 72-73°, b 120-130°/0.4mm, pK<sub>Est</sub> <0** It is distd at high vacuum and recrystallises from pet ether (b 40-60°) or (b 80-100°) as glistening plates. The *picrate* has m 147° (146.5-147.5°)(from  $*C_6H_6$ ). [J Chem Soc 3493 1955; J Org Chem 44 578 1979].

4-Chloroiodobenzene [637-87-6] M 238.5, m 53-54°. Crystd from EtOH.

2,3-Chloromaleic anhydride [1122-17-4] M 167.0, m 121-121.5°. See 2,3-dichloromaleic anhydride on p. 198.

5-Chloro-2-methoxyaniline (2-amino-4-chloroanisole) [95-03-4] M 157.6, m 81-83°, 82-84°, 84°,  $pK^{25}$  3.56. Purified by steam distn and recrystn from H<sub>2</sub>O or 40% aqueous EtOH. The *N*-acetate forms needles from hot H<sub>2</sub>O m 104°; the *N*-benzoyl derivative forms needles from aq EtOH m 77-78°; the picrate has m 194° dec. [J Am Chem Soc 48 2657 1926.]

**9-Chloromethyl anthracene** [24463-19-2] M **226.7, m 141-142° dec, 141-142.5°**. If it is free from OH in the IR then recryst from hexane- $*C_6H_6$  or  $*C_6H_6$  as needles. If OH is present then some solvolysis has occurred. In this case treat 8.5g with SOCl<sub>2</sub> (4.8g) in dioxane (60mL) and reflux for 5h, then evaporate to dryness and wash the residue with cold  $*C_6H_6$  and recrystallise. With KI/Me<sub>2</sub>CO it forms the *iodomethyl* derivative. [Martin et al. *Helv Chim Acta* **38** 2009 1955; J Org Chem **21** 1512 1956.]

**2-Chloro-3-methylindole** (2-chloroskatole) [51206-73-6] M 165.6, m 114.5-115.5°, pK<sub>Est</sub> <0. Purified by chromatography on silica gel in CH<sub>2</sub>Cl<sub>2</sub>/pet ether (1:2), followed by recrystn from aqueous EtOH or aqueous acetic acid. [Phillips and Cohen J Am Chem Soc 108 2023 1986.]

Chloromethyl methyl ether (MOMCl) [107-30-2] M 80.5, b 55-57°, d 1.060, n 1.396. If suspect (check IR), shake with satd aq CaCl<sub>2</sub> soln, dry over CaCl<sub>2</sub> and fractionally distil taking middle fraction. [Marvel and Porter Org Synth Coll Vol I 377 1941.] VERY TOXIC and CARCINOGENIC.

4-Chloro-2-methylphenol [1570-64-5] M 142.6, m 49°, pK<sup>25</sup> 9.71. Purified by zone melting.

4-Chloro-3-methylphenol [59-50-7] M 142.6, m 66°, pK<sup>25</sup> 9.55. Crystd from pet ether.

4-Chloro-2-methylphenoxyacetic acid (MCPA) [94-74-6] M 200.6, m 113-117°, 120°, 122-123°,  $pK^{20}$  3.62 (3.05). It is insoluble in H<sub>2</sub>O (sol 0.55g/L at 20°), and recrystallises from \*C<sub>6</sub>H<sub>6</sub> or chlorobenzene as plates [Acta Chem Scand 6 993 1952]. The S-benzylthiouronium salt has m 164-165°, and the Cu<sup>2+</sup> salt has m 247-249°dec [Armarego et al. Nature 183 1176 1959; UV: Duvaux and Grabe Acta Chem Scand 4 806 1950; IR: Jöberg Acta Chem Scand 4 798 1950].

Chloromethyl phenyl sulfide [7205-91-6] M 158.7, b 63°/0.1mm, 98°/12mm, 113-115°/20mm. Dissolve in CH<sub>2</sub>Cl<sub>2</sub> or CCl<sub>4</sub> and dry over CaCl<sub>2</sub>, or pass through a tube of CaCl<sub>2</sub> and fractionally distil using a fractionating column. *Harmful vapours*. It gives the *sulfone* (b 130°/1mm and m 53° from EtOH) on oxidation with permonophthalic acid. [Justus Liebigs Ann Chem 563 54 64 1949.]

**N-(Chloromethyl)phthalimide** [17564-64-6] **M 195.6, m 131-135°, 134-135°, 136.5°.** Purified by recrystn from EtOAc or CCl<sub>4</sub> [J Am Chem Soc 70 2822 1948; Böhme et al. Chem Ber 92 1258 1959].

4-(Chloromethyl)pyridine hydrochloride [1822-51-1] M 164.0, m 170-175°, 172-173°, pK<sub>Est</sub> ~5.6. Purified by recrystn from EtOH or EtOH-dry Et<sub>2</sub>O. It melts between 171° and 175° and the clear melt resolidifies on further heating at 190° and turns red to black at 280° but does not melt again. The picrate-hydrochloride (prepared in EtOH) has m 146-147°. The free base is an oil, [Mosher and Tessieri J Am Chem Soc 73 4925 1951.]

2-Chloro-1-methylpyridinium iodide [14338-32-0] M 255.5, m 203-205°, 205-206°(dec), 207°. Purified by dissolving in EtOH and adding dry Et<sub>2</sub>O. The solid is washed with Me<sub>2</sub>CO and dried at

20°/0.35mm. Store in the dark. Attempted recrystn from Me<sub>2</sub>CO-EtOH-pet ether (b 40-60°) caused some exchange of the Cl substituent by I. The *picrate* has **m** 106-107°, and the *perchlorate* has **m** 212-213°. [UV and solvolysis: Barlin and Benbow J Chem Soc, Perkin Trans 2 790 1974.]

1-Chloronaphthalene [90-13-1] M 162.6, f -2.3°, b 136-136.5°/20mm, 259.3°/760mm, d 1.194, n 1.6326. Washed with dilute NaHCO<sub>3</sub>, then dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd under reduced pressure. Alternatively, before distn, it was passed through a column of activated alumina, or dried with CaCl<sub>2</sub>, then distd from sodium. It can be further purified by fractional crystn by partial freezing or by crystn of its picrate to constant melting point (132-133°) from EtOH, and recovering from the picrate.

2-Chloronaphthalene [91-58-7] M 162.6, m 61°, b 264-266°. Crystd from 25% EtOH/water and dried under vacuum.

1-Chloro-2-naphthol [633-99-8] M 178.6, m 70°, pK<sub>Est</sub> ~8.3. Cryst from pet ether. Acetate has m 42-43°.

2-Chloro-1-naphthol [606-40-6] M 178.6, m 64-65°, pK<sub>Est</sub> ~7.9. Crystd from pet ether.

4-Chloro-1-naphthol [604-44-4] M 178.6, m 116-117°, 120-121°, pK<sup>25</sup> 8.86. Crystd from EtOH or chloroform.

6-Chloronicotinic acid [5326-23-8] M 157.6, m 190-193°, 198-199°(dec),  $pK^{25}$  4.22 (50% aq EtOH). Purified by recrystn from hot H<sub>2</sub>O and is sublimed in a vacuum. [Pechmann and Welsch Chem Ber 17 2384 1884; Herz and Murty J Org Chem 26 122 1961.]

4-Chloro-2-nitroaniline [89-63-4] M 172.6, m 116-116.5°, pK<sup>25</sup> -0.99. Crystd from hot water or EtOH/water and dried for 10h at 60° under vacuum.

2-Chloro-4-nitrobenzamide [3011-89-0] M 200.6, m 172°. Crystd from EtOH.

2-Chloro-1-nitrobenzene [88-73-3] M 157.6, m 32.8-33.2°. Crystd from EtOH, MeOH or pentane (charcoal).

3-Chloro-1-nitrobenzene [121-73-3] M 157.6, m 45.3-45.8°. Crystd from MeOH or 95% EtOH (charcoal), then pentane.

4-Chloro-1-nitrobenzene [100-00-5] M 157.6, m 80-83°, 83.5-84°, b 113°/8mm, 242°/atm, d 100.5 1.2914. Crystd from 95% EtOH (charcoal) and sublimes in a vacuum. [Emmons J Am Chem Soc 76 3470 1954; Newman and Forres J Am Chem Soc 69 1221 1947.]

4-Chloro-7-nitrobenzofurazane (7-chloro-4-nitrobenzoxadiazole) [10199-89-0] M 199.6, m 96.5-97°, 97°, 99-100°. Wash the solid with H<sub>2</sub>O and recrystallise from aqueous EtOH (1:1) as pale yellow needles. It sublimes in a vacuum [UV, NMR: Bolton, Gosh and Katritzky J Chem Soc 1004 1966].

**1-Chloro-2-nitroethane** [625-47-8] M **109.5**, b **37-38°/20mm**, n **1.4224**,  $n^{25}$  **1.4235**. Dissolved in alkali, extracted with ether (discarded), then the aqueous phase was acidified with hydroxylamine hydrochloride, and the nitro compound fractionally distd under reduced pressure. [Pearson and Dillon J Am Chem Soc 75 2439 1953.]

**2-Chloro-3-nitropyridine** [5470-18-8] **M** 158.5, **m** 100-103°, 101-102°, 103-104° (sublimes),  $pK^{20}$ -2.6. Forms needles from H<sub>2</sub>O. Purified by continuous sublimation over a period of 2 weeks at 50-60°/0.1mm [Barlin J Chem Soc 2150 1964]. The N-oxide has **m** 99-100°(from CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O). [Taylor and Driscoll J Org Chem 25 1716 1960; Ochiai and Kaneko Chem Pharm Bull Jpn 8 28 1960.]

2-Chloro-5-nitropyridine [4548-45-2] M 158.5, m 108°, pK<sub>Est</sub> ~-2.6. Crystd from \*benzene or \*benzene/pet ether.

**3-Chloroperbenzoic acid** [937-14-4] **M 172.6, m 92-94°(dec), pK^{25} 7.57.** Recrystd from CH<sub>2</sub>Cl<sub>2</sub> [Traylor and Mikztal J Am Chem Soc 109 2770 1987]. Peracid of 99+% purity can be obtained by washing commercial 85% material with phosphate buffer pH 7.5 and drying the residue under reduced pressure. Alternatively the peracid can be freed from m-chlorobenzoic acid by dissolving 50g/L of \*benzene and washing with an aq soln buffered at pH 7.4 (NaH<sub>2</sub>PO<sub>4</sub>/NaOH) (5 x 100mL). The organic layer was dried over MgSO<sub>4</sub> and carefully evaporated under vacuum. Necessary care should be taken in case of EXPLOSION. The solid was recrystd twice from CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O and stored at 0° in a plastic container as glass catalyses the decomposition of the peracid. The acid is assayed iodometrically. [J Org Chem 29 1976 1964; Bortolini et al. J Org Chem 52 5093 1987.]

2-Chlorophenol [95-57-8] M 128.6, m 8.8°, b 61-62°/10mm, 176°/atm, pK<sup>25</sup> 8.34. Passed at least twice through a gas chromatograph column. Also purified by fractional distn.

**3-Chlorophenol** [108-43-0] M 128.6, m 33°, b 44.2°/1mm, 214°/atm, pK<sup>25</sup> 9.13. Could not be obtained solid by crystn from pet ether. Purified by distn under reduced pressure.

**4-Chlorophenol** [106-48-9] **M 128.6, m 43°, 100-101°/10mm, pK<sup>25</sup> 9.38.** Distd, then crystd from pet ether (b 40-60°) or hexane, and dried under vacuum over  $P_2O_5$  at room temp. It has pKa 9.38 at 20° in water. [Bernasconi and Paschalis J Am Chem Soc 108 2969 1986.]

Chlorophenol Red (3,3'-dichlorophenolsulfonephthalein) [4430-20-0] M 423.3, m dec on heating,  $\lambda_{max}$  573nm, pK<sup>25</sup> 5.96. Crystd from glacial acetic acid. It is yellow at pH 4.8 and violet at pH 6.7.

4-Chlorophenoxyacetic acid [122-88-3] M 186.6, m 157°, pK<sup>20</sup> 3.00. Crystd from EtOH.

α-4-Chlorophenoxypropionic acid [3307-39-9] M 200.6, m 116°, pK<sub>Est</sub> ~3.2. Crystd from EtOH.

B-4-Chlorophenoxypropionic acid [3284-79-5] M 200.6, m 138°, pK<sub>Est</sub> ~4.2. Crystd from EtOH.

**3-Chlorophenylacetic acid** [1878-65-5] **M 170.6, m 74°, pK<sup>25</sup> 4.11.** Crystd from EtOH/water, or as needles from  $C_6H_6$  or  $H_2O$  (charcoal). The *acid chloride* (prepared by boiling with SOCl<sub>2</sub>) has **b** 127-129°/15mm. [Dippy and Williams J Chem Soc 161 1934; Misra and Shukla J Indian Chem Soc 28 480 1951.]

4-Chlorophenylacetic acid [1878-66-6] M 170.6, m 105°, 106°, pK<sup>25</sup> 4.12. Same as for 3chlorophenylacetic acid.

4-Chloro-1-phenylbutan-1-one [939-52-6] M 182.7, m 19-20°, b 134-137°/5mm,  $d_4^{20}$  1.149,  $n_D^{20}$  1.55413. Fractionate several times using a short column. It can be recrystd from anhydrous pet ether at -20° as glistening white rosettes and filtered at 0° and dried in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub>. The semicarbazone has m 136-137°. [J Am Chem Soc 46 1882 1924, 51 1174 1929, Hart and Curtis J Am Chem Soc 79 931 1957.]

1-(2-Chlorophenyl)-1-(4-chlorophenyl)-2,2-dichloroethane (Mitotane, o,p'-DDD) [53-19-0] M 320.1, m 75.8-76.8°, 76-78°. Purified by recrystallisation from pentane and from MeOH or EtOH. It is sol in isooctane and CCl<sub>4</sub>. [Haller et al. J Am Chem Soc 67 1600 1945.]

3-(4-Chlorophenyl)-1,1-dimethylurea (monuron) [150-68-5] M 198.7, m 171°. Crystd from MeOH.

4-Chloro-1,2-phenylenediamine [95-83-0] M 142.6, m 69-70°,  $pK_1^{25}$ -0.27 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$ 3.35 (3.67). Recrystd from pet. ether.

4-Chlorophenyl isocyanate [104-12-1] M 153.6, m 28-31°, 31-32°, 32°, 32.5°, b 80.6-80.9°/9.5mm, 115-117°/45mm. Purified by recrystn from pet ether (b 30-40°) or better by fractional distn. TOXIC irritant.

4-Chlorophenyl isothiocyanate [2131-55-7] M 169.6, m 44°, 43-45°, 45°, 46°, 47°, b 110-115°/4mm, 135-136°/24mm. Check the IR first. Triturate with pet ether (b 30-60°) and decant the solvent. Repeat 5 times. The combined extracts are evap under reduced press to give almost pure compound as a readily crystallisable oil with a pleasant anise odour. It can be recrystd from the minimum vol of EtOH at 50° (do not boil too long in case it reacts). It can be purified by vac distn. IRRITANT. [Org Synth Coll Vol V 223 1973.]

4-Chlorophenyl 2-nitrobenzyl ether [109669-56-9] M 263.7, m 69°. Crystd from EtOH.

4-Chlorophenyl 4-nitrobenzyl ether [5442-44-4] M 263.7, m 102°. Crystd from EtOH.

**9-Chloro-9-phenylxanthene** (Pixyl chloride) [42506-03-6] M 292.8, m 105-106°. Possible impurity is 9-hydroxy-9-phenylxanthene. If material contains a lot of the hydroxy product then boil 10g in CHCl<sub>3</sub> (50mL) with redistd acetyl chloride (1mL) until liberation of HCl is complete. Evapn leaves the chlorophenylxanthene as the hydrochloride which on heating with \*benzene loses HCl; and on adding pet ether prisms of chlorophenylxanthene separate and contain 0.5mol of \*benzene. The \*benzene-free compound is obtained on drying and melts to a colourless liquid. [Justus Liebigs Ann Chem 370 142 1909.] The 9-phenylxanthyl group is called pixyl. [J Chem Soc, Chem Commun 639 1978.]

Chlorophyll a [479-61-8] M 983.5, m 117-120°, 150-153°, 178-180° (sinters at ~150°),  $[\alpha]_{D}^{20}$  -262° (Me<sub>2</sub>CO). Forms green crystals from Me<sub>2</sub>CO, Et<sub>2</sub>O + H<sub>2</sub>O, Et<sub>2</sub>O + hexane + H<sub>2</sub>O or Et<sub>2</sub>O + pentane +  $H_2O$ . It is sparingly soluble in MeOH and insol in pet ether. In alkaline soln it gives a blue-green colour with deep red fluorescence. A very crude chlorophyll mixture has been purified by chromatography on low melting polyethylene (MI 0.044; 'Dow' melting index MI <2) and developed with 70% aq Me<sub>2</sub>CO. The order of effluent from the bottom of the column is: xanthophylls, chlorophyll b, chlorophyll a, phaeophytins and carotenes. A mixture of chlorophylls a and b is best separated by chromatography on sugar and the order is chlorophyll b elutes first followed by chlorophyll a. To an  $Me_2CO-H_2O$  soln of chlorophylls 200mL of isooctane is added and the mixt shaken in a separating funnel and the  $H_2O$  is carefully removed. The iso-octane layer is dried (Na<sub>2</sub>SO<sub>4</sub>) and applied to a glass column (5cm diameter) dry packed with 1000mL of powdered sucrose which has been washed with 250mL of iso-octane. Elution with 0.5% of isopropanol in iso-octane gives chlorophyll a. Keeping the eluate overnight at 0° yields micro crystals which are collected by filtration or centrifugation (Yield 40mg). UV<sub>EtOH</sub> has  $\lambda_{max}$  660, 613, 577, 531, 498, 429 and 409 nm. [Anderson and Calvin Nature 194 285 1962; Stoll and Weidemann Helv Chim Acta 16 739 757 1933; NMR: Katz et al. J Am Chem Soc 90 6841 1968, 85 3809 1963 for a and b; ORD: Inhoffen et al. Justus Liebigs Ann Chem 704 208 1967; Willstätter and Isler Justus Liebigs Ann Chem 390 269, 233 1912.]

Chlorophyll b [519-62-0] M 907.52, sinters at 86-92°, sinters at 170°, dec at 160-170°, m 183-185°, 190-195°,  $[\alpha]_D^{20}$  -267° (Me<sub>2</sub>CO + MeOH),  $[\alpha]_{720}^{25}$  -133° (MeOH + Pyridine 95:5). See purification of chlorophyll *a*, and is separated from "*a*" by chromatography on sucrose [UV, IR: Stoll and Weidemann *Helv Chim Acta* 42 679, 681 1959]. It forms red-black hexagonal bipyramids or four sided plates from dilute EtOH and has been recrystd from CHCl<sub>3</sub>-MeOH. It is soluble in MeOH, EtOH, EtOAc and insoluble in pet ether. [J Am Chem Soc 88 5037 1966.]

Chloropicrin (trichloronitromethane) [76-06-2] M 164.5, b 112°. Dried with MgSO<sub>4</sub> and fractionally distd. EXTREMELY NEUROTOXIC, use appropriate precautions.

**RS-2-Chloropropionic acid** [598-78-7] **M 108.5, b 98°/3mm, d 1.182, n 1.453 pK^{25} 2.89.** Dried with P<sub>2</sub>O<sub>5</sub> and fractionally distd under vacuum.

S-(-)-2-Chloropropionic acid [29617-66-1] M 108.5, b 77°/10mm, 80.7°/10mm, 185-188°/atm,  $d_4^{25}$  1.2485,  $n_D^{25}$  1.436,  $[\alpha]_D^{25}$ -14.6° (neat). Purified by twice fractionating through a 115cm Podbielniak column (calcd 50 theoretical plates at atm pressure, see p. 141) using a take-off ratio of 1:5. Ths acid chloride is prepared by dissolving the acid in SOCl<sub>2</sub> adding a few drops of PCl<sub>3</sub>, refluxing and then distilling through a 30 cm column, b 53°/100mm,  $[\alpha]_D^{25}$  - 4.6° (neat),  $d_4^{25}$  1.2689,  $n_D^{25}$  1.4368. [Fu et al. J Am Chem Soc 76 6954 1954].

3-Chloropropionic acid [107-94-8] M 108.5, m 41°, pK<sup>25</sup> 4.08. Crystd from pet ether or \*benzene.

3-Chloropropyl bromide (1-bromo-3-chloropropane) [109-70-6] M 157.5, b 142-145°,  $n^{25}$  1.4732. Washed with conc H<sub>2</sub>SO<sub>4</sub>, water, 10% Na<sub>2</sub>CO<sub>3</sub> soln, water again and then dried with CaCl<sub>2</sub> and fractionally distd just before use [Akagi, Oae and Murakami J Am Chem Soc 78 4034 1956].

6-Chloropurine [87-42-3] M 154.6, m 179°(dec), pK<sub>1</sub><sup>20</sup>0.45, pK<sub>2</sub><sup>20</sup>7.88. Crystd from water.

2-Chloropyrazine [14508-49-7] M 114.5, b 62-63°/31mm, 153-154°/atm,  $d_4^{20}$  1.302,  $n_D^{26}$  1.535, pK<sub>Est</sub> <0. Fractionally distil through a short column packed with glass helices. It has a penetrating mildly pungent odour with a high vapour pressure at room temperature. [Erickson and Spoerri J Am Chem Soc 68 400 1946; J Org Chem 28 1682 1963.]

**2-Chloropyridine** [109-09-1] M 113.6, b 49.0°/7mm, d 1.20, n 1.532,  $pK^{20}0.49$  (0.72). Dried with NaOH for several days, then distd from CaO under reduced pressure.

**3-Chloropyridine** [626-60-8] **M 113.6, b 148°, d 1.194, n 1.5304, pK<sup>25</sup> 2.84.** Distd from KOH pellets.

**4-Chloropyridine** [626-61-9] M **113.6, b 85-86°/100mm, 147-148°/760mm, pK^{20} 3.84.** Dissolved in distilled water and excess of 6M NaOH was added to give pH 12. The organic phase was separated and extracted with four volumes of diethyl ether. The combined extracts were filtered through paper to remove water and the solvent evaporated. The dark brown residual liquid was kept under high vacuum [Vaidya and Mathias J Am Chem Soc 108 5514 1986]. It can be distd but readily darkens and is best kept as the hydrochloride [7379-35-3] M 150.1, m 163-165°(dec).

**2-Chloropyrimidine** [1722-12-9] M 114.5, m 63-65°, 66°, b 91°/26mm,  $pK^{20}$ -1.90. It has been recrystd from \*C<sub>6</sub>H<sub>6</sub>, pet ether or a mixture of both. It sublimes at 50°/18mm and can be distd in a vacuum. [IR: Short and Thompson J Chem Soc 168 1952; Boarland and McOmie J Chem Soc 1218 1951.]

**2-Chloroquinoline** [612-62-4] M 163.6, m 34°, b 147-148°/15mm,  $d^{35}$  1.235,  $n^{25}$  1.629, pK<sub>Est</sub> ~0.3. Purified by crystn of its picrate to constant melting point (123-124°) from \*benzene, regenerating the base and distilling under vacuum [Cumper, Redford and Vogel J Chem Soc 1183 1962]. 2-Chloroquinoline can be crystd from EtOH. Its picrate has m 122° (from EtOH).

4-Chloroquinoline [611-35-8] M 163.6, m 29-32°, 31°, b 130°/15mm, 261°/744mm, pK 3.72. Possible impurities include the 2-isomer. Best purified by converting to the *picrate* (m 212-213° dec) in EtOH and recryst from EtOH (where the picrate of the 2-chloroquinoline stays in soln) or EtOAc. The picrate is decomposed with 5% aqueous NaOH, extracted in CHCl<sub>3</sub>, washed with H<sub>2</sub>O, dried (MgSO<sub>4</sub>), evapd and distd in a vacuum. It can be steam distd from slightly alkaline aqueous solns, the aqueous distillate is extracted with Et<sub>2</sub>O, evaporated and distd. The distillate solidifies on cooling. [Bobránski Chem Ber 71 578 1938.]

8-Chloroquinoline [611-33-6] M 163.6, b 171-171.5°/24mm, d 1.278, n 1.644, pK<sup>25</sup> 3.12. Purified by crystn of its ZnCl<sub>2</sub> complex (m 228°) from aqueous EtOH.

4-Chlororesorcinol [95-88-5] M 144.6, m 105°, pK<sub>Est(1)</sub>~9.2, pK<sub>Est(2)</sub> ~10.1. Crystd from boiling CCl<sub>4</sub> (10g/L, charcoal) and air dried.

5-Chlorosalicaldehyde [635-93-8] M 156.6, m 98.5-99°. Steam distd, then crystd from aq EtOH.

N-Chlorosuccinimide [128-09-6] M 133.5, m 149-150°. Rapidly crystd from \*benzene, or glacial acetic acid and washed well with water then dried *in vacuo*. [Phillips and Cohen J Am Chem Soc 108 2023 1986.]

**2-Chlorothiophene** (2-thienyl chloride) [96-43-5] M 118.6, b 126-128°, d 1.285, n 1.551. Purified by fractional distn at atmospheric pressure or by gas chromatography.

8-Chlorotheophylline [85-18-7] M 214.6, m 311°(dec), pK<sub>Est(1)</sub>~5.4, pK<sub>Est(2)</sub>~9.1. Crystd from H<sub>2</sub>O.

4-Chlorothiophenol [106-54-7] M 144.6, m 51-52°, pK<sup>25</sup> 6.14. Recrystd from aqueous EtOH [D'Sousa et al. J Org Chem 52 1720 1987].

2-Chlorotoluene [95-49-8] M 126.6, b 159°, d 1.083, n 1.5255. Dried for several days with CaCl<sub>2</sub>, then distd from Na using a glass helices-packed column.

**3-Chlorotoluene** [108-41-8] **M 126.6, m -48°, b 161-163°, d 1.072, n 1.522.** Purified as for 2-chlorotoluene above.

4-Chlorotoluene [106-43-4] M 126.6, f 7.2°, b 162.4°, d 1.07, n 1.521. Dried with BaO, fractionally distd, then fractionally crystd by partial freezing.

2-Chlorotriethylamine hydrochloride [869-24-9] M 172.1, m 208-210°, pK<sub>Est</sub> ~8.6 (free base). Crystd from absolute MeOH (to remove highly coloured impurities).

**Chlorotrifluoroethylene** [79-38-9] **M 116.5, b -26 to -24**°. Scrubbed with 10% KOH soln, then 10% H<sub>2</sub>SO<sub>4</sub> soln to remove inhibitors, and dried. Passed through silica gel.

**Chlorotrifluoromethane** [75-72-9] **M 104.5, m -180°, b -81.5°.** Main impurities were  $CO_2$ ,  $O_2$ , and  $N_2$ . The  $CO_2$  was removed by passage through saturated aqueous KOH, followed by conc H<sub>2</sub>SO<sub>4</sub>. The  $O_2$  was removed using a tower packed with activated copper on Kieselguhr at 200°, and the gas dried over P<sub>2</sub>O<sub>5</sub>.

Chlorotriphenylmethane see triphenylmethyl chloride (trityl chloride).

**5-Chlorouracil** (5-chloro-2,4(6)-dihydroxypyrimidine) [1820-81-1] M 146.5, m 314-418° dec, 324-325° dec,  $pK_1^{25}$ 7.95,  $pK_2^{25}$ >13. Recrystallised from hot H<sub>2</sub>O (4g/500mL) using charcoal. [McOmie et al. J Chem Soc 3478 1955; West and Barrett J Am Chem Soc 76 3146 1954.]

5β-Cholanic acid [25312-65-6] M 360.6, m 164-165°,  $[\alpha]_D^{14}$  +21.7° (CHCl<sub>3</sub>), pK<sub>Est</sub> ~4.9. Crystd from EtOH. The *Ethyl ester* has m 93-94° (from 80% EtOH), b 273°/12mm,  $[\alpha]_D^{20}$  +21° (CHCl<sub>3</sub>).

Cholanthrene (1,2,-dihydrobenz[j]aceanthrylene) [479-23-2] M 254.3, m 173°. Crystd from \*benzene/diethyl ether.

5 $\alpha$ -Cholestane [481-21-0] M 372.7, m 80°,  $[\alpha]_{546}^{20}$  +29.5° (c 2, CHCl<sub>3</sub>). Crystd from diethyl ether/EtOH.

5 $\alpha$ -Cholestan-3 $\beta$ -ol [80-97-7] M 388.7, m 142-143°(monohydrate),  $[\alpha]_{546}^{20}$  +28° (c 1, CHCl<sub>3</sub>),  $[\alpha]_D$  +27.4° (in CHCl<sub>3</sub>). Crystd from EtOH or slightly aqueous EtOH, or MeOH. [Mizutani and Whitten J Am Chem Soc 107 3621 1985.]

**Cholest-2-ene** [15910-23-3] **M 370.6, m 75-76°,**  $[\alpha]_D^{24}$  +64°. Recrystd from MeOH or diethyl ether/acetone. [Berzbrester and Chandran J Am Chem Soc 109 174 1987.]

**Cholesterol** [57-88-5] M 386.7, m 148.9-149.4°,  $[\alpha]_D^{25}$  -35° (hexane). Crystd from ethyl acetate, EtOH or isopropyl ether/MeOH. [Hiromitsu and Kevan J Am Chem Soc 109 4501 1987.] For extensive details of purification through the dibromide, see Fieser [J Am Chem Soc 75 5421 1953] and Schwenk and Werthessen [Arch Biochem Biophys 40 334 1952], and by repeated crystn from acetic acid, see Fieser [J Am Chem Soc 75 4395 1953].

**Cholesteryl acetate** [604-35-3] **M 428.7, m 112-115°**,  $[\alpha]_{546}^{20}$  -51° (c 5, CHCl<sub>3</sub>). Crystd from *n*-pentanol.

**Cholesteryl myristate** [1989-52-2] **M 597.0.** Crystd from *n*-pentanol. Purified by column chromatography with MeOH and evaporated to dryness. Recrystd and finally, dried in vacuum over  $P_2O_5$ . [Malanik and Malat Anal Chim Acta 76 464 1975].

Cholesteryl oleate [303-43-5] M 651.1, m 48.8-49.4°. Purified by chromatography on silica gel.

**Cholic acid** [81-25-4] **M 408.6, m 198-200°,**  $[\alpha]_{546}$  +41° (c 0.6, EtOH), pK<sup>20</sup> 4.98. Crystd from EtOH. Dried under vacuum at 94°.

**Choline chloride** [67-48-1] **M 139.6, m 302-305°(dec).** Extremely deliquescent. Purity checked by AgNO<sub>3</sub> titration or by titration of free base after passage through an anion-exchange column. Crystd from absolute EtOH, or EtOH-diethyl ether, dried under vacuum and stored in a vacuum desiccator over  $P_2O_5$  or Mg(ClO<sub>4</sub>)<sub>2</sub>.

4-Chromanone [491-37-2] M 148.2, m 35-37°, 39°, 41°, b 92-93°/3mm, 130-132°/15mm, 160°/50mm. It has been recryst from pet ether, or purified by dissolving in  $C_6H_6$  washing with H<sub>2</sub>O, drying (MgSO<sub>4</sub>), evaporate and dist in a vacuum, then recryst the residue. The liquid has a pleasant lemon-like odour. The semicarbazone has m 227°. [Loudon and Razdan J Chem Soc 4299 1954.] The oxime is prepared from 3g of chromanone, 3g NH<sub>2</sub>OH.HCl in EtOH (50mL), 6g K<sub>2</sub>CO<sub>3</sub> and refluxed on a water bath for 6h. The soln is poured into H<sub>2</sub>O, the solid is filtered off, dried and dissolved in hot  $C_6H_6$  which on addition of pet ether yields the oxime as glisteneing needles m 140°. Decomposition of this gives very pure chromanone. The benzal derivative is prepared from 3g of chromanone, 4g PhCHO in 50mL EtOH, heated to boiling, 10mL of conc HCl are added dropwise and set aside for several days. The derivative separates and is recryst from EtOH to give yellow needles, m 112° [J Am Chem Soc 45 2711 1923]. Reaction with Pb(OAc)<sub>4</sub> yields the 3acetoxy derivative m 74° (from pet ether + trace of EtOAc) [Cavill et al. J Chem Soc 4573 1954].

Chrysene [218-01-9] M 228.3, m 255-256°. Purified by chromatography on alumina from pet ether in a darkened room. Its soln in  $C_6H_6$  was passed through a column of decolorising charcoal, then crystd by concentration of the eluate. Also purified by crystn from  $C_6H_6$  or  $C_6H_6$ -pet ether, and by zone refining. [Gorman et al. J Am Chem Soc 107 4404 1985]. It was freed from 5H-benzo[b]carbazole by dissolving in N,N-dimethylformamide and successively adding small portions of alkali and iodomethane until the fluorescent colour of the carbazole anion no longer appeared when alkali was added. The chrysene (and alkylated 5H-benzo[b]carbazole) separated on addition of water. Final purification was by crystn from ethylcyclohexane and from 2-methoxyethanol [Bender, Sawicki and Wilson Anal Chem 36 1011 1964]. It can be sublimed in a vacuum.

Chrysoidine G (4-phenylazo-1,3-benzenediamine monohydrochloride) [532-82-1] M 248.7, m 118-118.5°,  $pK_1$  3.32,  $pK_2$  5.21. Red-brown powder which is recrystd from H<sub>2</sub>O. It gives a yellow soln in conc H<sub>2</sub>SO<sub>4</sub> which turns orange on dilution. Its solubility at 15° is 5.5% (H<sub>2</sub>O), 4.75% (EtOH), 6.0% (cellosolve), 9.5% (ethylene glycol), 0.005% (xylene) and insol in \*C<sub>6</sub>H<sub>6</sub>. The hydroiodide has m 184° (from EtOH) and the picrate forms red needles m 196°. [Bull Chem Soc Jpn 31 864 1958; Chem Ber 10 213 1877.]

**1,8-Cineole** (1,8-epoxy-p-menthane) [470-82-6] M 154.2, f 1.3°, b 176.0°, d 0.9251. See eucaliptol on p. 242.

trans-Cinnamaldehyde [14271-10-9] M 132.2, m -4°, -7.5°, -9°, b 80°/0.4 mm, 85.8°/1.1mm, 125-128°/11mm, 152.2°/40mm, 163.7°/60mm, 199.3°/200mm, 246°/760 mm dec,  $d_4^{20}$  1.0510,  $n_D^{20}$  1.623. Purified by steam distn (sol 1 in 700 parts H<sub>2</sub>O) followed by distn *in vacuo*. The cis-isomer has b 67-69°/40mm and  $d_4^{20}$  1.0436 and  $n_D^{20}$  1.5937. The trans-semicarbazone has m 210° dec from CHCl<sub>3</sub>-MeOH (cis-semicarbazone has m 196°); the trans-phenylsemicarbazone has m 177° from CHCl<sub>3</sub>-MeOH (the cis-phenylsemicarbazone has m 146°); the trans-2,4-dinitrophenylhydrazone has m 250° dec from MeOH as the cis-isomer [Gamboni et al. Helv Chim Acta 38 255 1955; Peine Chem Ber 17 2117 1884; J Org Chem 26 4814 1961; J Am Chem Soc 86 198 1964].

cis-Cinnamic acid (Z-3-phenyl-2-propenoic acid) [102-94-3] M 148.2, m 68° (for allo-form), pK<sup>25</sup> 3.93. The cis-acid is prepared by catalytic reduction of phenylpropiolic acid and after distn in high vacuum at ~95° gives the most stable allo-isomer m 68°. Recrystn from pet ether yields Liebermann's isocinnamic acid m 58°. When the allo-acid (m 68°) is heated at 20° above its melting point in a sealed capillary for 0.5h and allowed to cool slowly Erlenmyer's iso-cinnamic acid m 42° is formed. This form can also be obtained in larger amounts by heating the allo-acid at 80° for 3h and on cooling it remains liquid for several weeks but gives the 42° acid on innoculation with the crystals from the capillary tube. This form is unchanged in 6 weeks when kept in a dark cupboard. All three forms have the same pK values and the same rate of bromination. There is also a very labile form with m 32°. [Liebermann, Chem Ber 26 1572 1893; Claisen and Crismer Justus Liebigs Ann Chem 218 135 1883; Robinson and James J Chem Soc 1453 1933; Berthoud and Urech Helv Chim Acta 13 437 1930; McCoy and McCoy J Org Chem 33 2354 1968.]

trans-Cinnamic (E-3-phenyl-2-propenoic) acid [140-10-3; 621-82-9 for E-Z mixture] M 148.2, m 134.5-135°,  $pK^{25}$  4.42 (4.50). Crystd from \*benzene, CCl<sub>4</sub>, hot water, water/EtOH (3:1), or 20% aqueous EtOH. Dried at 60° in vacuo. Steam volatile.

Cinnamic anhydride [538-56-7] M 278.4, m 136°. Crystd from \*C<sub>6</sub>H<sub>6</sub> or toluene/pet ether (b 60-80°).

N-Cinnamoyl-N-phenylhydroxylamine [7369-44-0] M 239.3, m 158-163°. Recrystd from EtOH.

Cinnamyl alcohol [104-54-1] M 134.2, m 33°, b 143.5°/14mm,  $\lambda_{max}$  251nm ( $\varepsilon$  18,180M<sup>-1</sup> cm<sup>-1</sup>). Crystd from diethyl ether/pentane.

Cinnoline [253-66-7] M 130.2, m 38°,  $pK^{20}$  2.37. Crystd from pet ether. Kept under N<sub>2</sub> in sealed tubes in the dark at 0°.

Citraconic acid [498-23-7] M 130.1, m 91°,  $pK_1^{25}$  2.2,  $pK_2^{25}$  5.60 (cis). Steam distd and crystd from EtOH/ligroin.

Citraconic anhydride [616-02-4] M 112.1, m 8-9°, b 47°/0.03mm, 213°/760mm,  $d_4^{20}$  1.245,  $n_D^{20}$  1.472. Possible contamination is from the acid formed by hydrolysis. If the IR has OH bands then reflux with Ac<sub>2</sub>O for 30 min, evaporate then distil the residue in a vacuum; otherwise distil in a vacuum. Store in a dry atmosphere. [Biochem J 191 269 1980.]

Citrazinic acid (2,6-dihydroxyisonicotinic acid) [99-11-6] M 155.1,  $m > 300^\circ$ ,  $pK_1$  3.0,  $pK_2$  4.76. Yellow powder with a greenish shade, but is white when ultra pure and turns blue on long standing. It is insoluble in H<sub>2</sub>O but slightly soluble in hot HCl and soluble in alkali or carbonate solutions. Purified by precipitation from alkaline solutions with dilute HCl, and dry in a vacuum over P<sub>2</sub>O<sub>5</sub>. The *ethyl ester* has  $m 232^\circ$  (evacuated tube) and a pKa of 4.81 in MeOCH<sub>2</sub>CH<sub>2</sub>OH [IR: Pitha Coll Czech Chem Comm 28 1408 1963].

Citric acid (H<sub>2</sub>O) [5949-29-1; 77-92-9 (anhydr)] M 210.1, m 156-157°, 153° (anhyd),  $pK_1^{25} 2.96$ ,  $pK_2^{25} 4.38$ ,  $pK_3^{25} 5.68$ . Crystd from water.

Citronellal (3,7-dimethyloctan-6-al) [R(+): 2385-77-5; S(-): 5949-05-3] M 154.3, b 67°/4mm, 89°/14mm, 104-105°/21mm, 207°/760mm,  $[\alpha]_{546}^{20}$  (+) and (-) 20°,  $[\alpha]_D^{20}$  (+) and (-) 16.5° (neat). Fractionally distd. Alternatively extracted with NaHSO<sub>3</sub> solution, washed with Et<sub>2</sub>O then acidified to decompose the bisulfite adduct and extracted with Et<sub>2</sub>O, dried (Na<sub>2</sub>SO<sub>4</sub>), evaporated and distd. Check for purity by hydroxylamine titration. The ORD in MeOH (c 0.167) is:  $[\alpha]_{700}$  +9°,  $[\alpha]_{589}$  +11°,  $[\alpha]_{275}$  +12° and  $[\alpha]_{260}$ 12°. The semicarbazone has m 85°, and the 2,4-dinitrophenylhydrazone has m 79-80°. [IR: J Chem Soc 3457 1950; ORD: Djerassi and Krakower J Am Chem Soc 81 237 1959.]

β-Citronellene (2,6-dimethylocta-2,7-diene) [S-(+): 2436-90-0; R-(-): 10281-56-8] M 138.3, b 153-154°/730mm, 155°/atm,  $d_4^{22}$  0.757,  $n_D^{22}$  1.431,  $[\alpha]_{546}^{20}$  (+) and (-) 13°,  $[\alpha]_{546}^{20}$  (+) and (-) 10° (neat). Purified by distillation over Na three times and fractionation. [(-) Arigoni and Jeager Helv Chim Acta 37 881 12954; (+) Eschenmoser and Schinz Helv Chim Acta 33 171 1950.]

β-Citronellol (3,7-dimethyloctan-6-ol) [R-(+): 11171-61-9; S-(-): 106-22-9] M 156.3, b 47°/1mm, 102-104(110°)°/10mm, 112-113°/12mm, 221-224°/atm, 225-226°/atm,  $d_4^{24}$ 0.8551,  $n_D^{24}$  1.4562,  $[\alpha]_{546}^{20}$  (+) and (-) 6.3°,  $[\alpha]_D^{20}$  (+) and (-) 5.4° (neat). Purified by distn through a cannon packed (Ni) column and the main cut collected at 84°/14mm and redistd. Also purified via the benzoate. [IR: Eschenazi J Org Chem 26 3072 1961; Bull Soc Chim Fr 505 1951.]

S-Citrulline (2-amino-5-ureidopentanoic acid) [372-75-8] M 175.2, m 222°,  $[\alpha]_D^{20} + 24.2°$  (in 5M HCl), pK<sup>25</sup> 9.71. Likely impurities are arginine, and ornithine. Crystd from water by adding 5 volumes of EtOH. Also crystd from water by addn of MeOH.

Clofazimine [2-(4-chloroanilino)-3-isopropylimino-5-(4-chlorophenyl)-3,4-dihydrophenazine] [2030-63-9] M 473.5, m 210-212°. Recrystd from acetone.

Coenzyme  $Q_0$  (2,3-Dimethoxy-5-methyl-1,4-benzoquinone, 3,4-dimethoxy-2,5-toluquinone, fumigatin methyl ether), colchicine and colchicoside see entries in Chapter 6.

Conessine [546-06-5] M 356.6, m 125°, 127-128.5°,  $[\alpha]_D^{20}$  -1.9° (in CHCl<sub>3</sub>) and +25.3° (in EtOH), pK<sub>Est(1)</sub>~10.4, pK<sub>Est(2)</sub>~10.7,. Crystd from acetone. The *dihydrochloride* has m >340° and  $[\alpha]_D^{20}$  +9.3° (c 0.9, H<sub>2</sub>O).

**Coniferyl alcohol** [4-hydroxy-3-methoxy-cinnamyl alcohol, 3-(4-hydroxy-3-methoxyphenyl)-2-propen-1-ol] [458-35-5] M 180.2, m 73-75°, b 163-165°/3mm,  $pK^{25}$  9.54. It is soluble in EtOH and insoluble in H<sub>2</sub>O. It can be recrystd from EtOH and distd in a vacuum. It polymerises in dilute acid. The *benzoyl derivative* has m 95-96° (from pet ether), and the *tosylate* has m 66°. [Derivatives: Freudenberg and Achtzehn Chem Ber 88 10 1955; UV: Herzog and Hillmer Chem Ber 64 1288 1931.]

Congo Red [573-58-0] M 696.7,  $\lambda_{max}$  497nm, pK<sub>2</sub><sup>28</sup> 4.19. Crystd from aq EtOH (1:3). Dried in air.

(-)- $\alpha$ -Copaene {*IR*, 2*S*, 6*S*, 7*S*, 8*S*-8-isopropyl-1, 3-dimethyltricyclo[4.4.0.0<sup>2,7</sup>]dec-3-ene} [3856-25-5] M 204.4, b 119-120°/10mm, 246-251°, d 0.908, n 1.489,  $[\alpha]_D^{20}$ -6.3° (c 1.2, CHCl<sub>3</sub>). Purified by distn, preferably under vacuum.

4,5-Coprosten-3-ol (cholest-4-ene-3B-ol) [517-10-2] M 386.7, m 132°. Crystd from MeOH/diethyl ether.

Coprosterol (5 $\alpha$ -cholestan-3 $\beta$ -ol, dihydrocholesterol) [80-97-7] M 388.7, m 101°, 139-140°,  $[\alpha]_D^{20} + 24^{\circ}$  (c 1, CHCl<sub>3</sub>). See entry on p. 169.

**Coronene** [191-07-1] M 300.4, m 438-440°,  $\lambda_{max}$  345nm (log  $\varepsilon$  4.07). Crystd from \*benzene or toluene, then sublimed in vacuum.

Cortisol, corticosterone, cortisone and cortisone-21-acetate see entries in Chapter 6.

Coumalic acid (2-pyrone-5-carboxylic acid) [500-05-0] M 140.1, m 205-210°(dec),  $pK_{Est} \sim 0$ . Crystd from MeOH. *Methyl ester*, from pet ether, has m 74-74° and b 178-180°/60 mm.

Coumarin [91-64-5] M 146.2, m 68-69°, b 298°, pK -4.97 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from ethanol or water and sublimed *in vacuo* at 43° [Srinivasan and deLevie J Phys Chem 91 2904 1987].

Coumarin-3-carboxylic acid [531-81-7] M 190.2, m 188°(dec), pK<sub>Est</sub> ~1.5. Crystd from water.

Creatine  $(H_2O)$  and creatinine see entries in Chapter 6.

o-Cresol [95-48-7] M 108.1, m 30.9°, b 191°, n<sup>41</sup> 1.536, n<sup>46</sup> 1.534, pK<sup>25</sup> 10.22. Can be freed from *m*- and *p*-isomers by repeated fractional distn, Crystd from \*benzene by addition of pet ether. Fractional crystd by partial freezing of its melt.

*m*-Cresol [108-39-4] M 108.1, f 12.0°, b 202.7°, d 1.034, **m** 1.544, pK<sup>25</sup> 10.09. Separation of the *m*- and *p*-cresols requires chemical methods, such as conversion to their sulfonates [Brüchner Anal Chem 75 289 1928]. An equal volume of H<sub>2</sub>SO<sub>4</sub> is added to *m*-cresol, stirred with a glass rod until soln is complete. Heat for 3h at 103-105°. Dilute carefully with 1-1.5 vols of water, heat to boiling point and steam distil until all unsulfonated cresol has been removed. Cool and extract residue with ether. Evaporate the soln until the boiling point reaches 134° and steam distil off the *m*-cresol. Another purification involves distn, fractional crystn from the melt, then redistn. Freed from *p*-cresol by soln in glacial acetic acid and bromination by about half of an equivalent amount of bromine in glacial acetic acid. The acetic acid was distd off, then fractional distn of the residue under vac gave bromocresols from which 4-bromo-*m*-cresol was obtained by crystn from hexane. Addn of the bromocresol in glacial acetic acid slowly to a reaction mixture of HI and red phosphorus or (more smoothly) of HI and hypophosphorus acid, in glacial acetic acid, at reflux, removed the bromine. After an hour, the soln was distd at atmospheric pressure until layers were formed. Then it was cooled and diluted with water. The cresol was extracted with ether, washed with water, NaHCO<sub>3</sub> soln and again with water, dried with a little CaCl<sub>2</sub> and distd [Baltzly, Ide and Phillips J Am Chem Soc 77 2522 1955].

*p*-Cresol [106-44-5] M 108.1, m 34.8°, b 201.9°, n<sup>41</sup> 1.531, n<sup>46</sup> 1.529, pK<sup>25</sup> 10.27. Can be separated from *m*-cresol by fractional crystn of its melt. Purified by distn, by pptn from \*benzene soln with pet ether, and *via* its benzoate, as for phenol. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>. Has also been crystd from pet ether (b 40-60°) and by conversion to sodium *p*-cresoxyacetate which, after crystn from water was decomposed by heating with HCl in an autoclave [Savard Ann Chim (Paris) 11 287 1929].

o-Cresolphthalein complexon [2411-89-4] M 636.6, m 186°(dec),  $\lambda$ max 575nm, pK<sub>1</sub> 2.2, pK<sub>2</sub> 2.9, pK<sub>3</sub> 7.0, pK<sub>4</sub> 7.8, pK<sub>5</sub> 11.4, pK<sub>6</sub> 12.0. o-Cresolphthalein (a complexone precursor without the two bis-carboxymethylamino groups) is a contaminant and is one of the starting materials. It can be removed by dissolving the reagent in water and adding a 3-fold excess of sodium acetate and fractionally precipitating it by dropwise addition of HCl to the clear filtrate. Wash the ppte with cold H<sub>2</sub>O and dry the monohydrate at 30° in a vacuum. The pure material gives a single spot on paper chromatography (eluting solvent EtOH/water/phenol, 6:3:1; and developing with NaOH). [Anderegg et al. Helv Chim Acta 37 113 1954.] Complexes with Ba, Ca, Cd, Mg and Sr.

o-Cresol Red [1733-12-6] M 382.4, m 290°(dec), pK<sup>25</sup> 1.26. Crystd from glacial acetic acid. Air dried. Dissolved in aqueous 5% NaHCO<sub>3</sub> soln and ppted from hot soln by dropwise addition of aqueous HCl. Repeated until extinction coefficients did not increase.

o-Cresotic acid (methylsalicylic acid) [83-40-9] M 152.2, m 163-164°,  $pK_1^{25}$  3.32. Crystd from water.

m-Cresotic acid [50-85-1] M 152.2, m 177°, pK<sub>1</sub><sup>25</sup> 3.15, pK<sub>2</sub><sup>25</sup> 13.35. Crystd from water.

p-Cresotic acid [89-56-5] M 152.2, m 151°, pK<sub>1</sub><sup>25</sup> 3.40, pK<sub>2</sub><sup>25</sup> 13.45. Crystd from water.

Crocetin diethyl ester [5056-14-4] M 384.5, m 218-219°, 222.5°,  $A_{1cm}^{1\%}$  ( $\lambda$ max) 2340 (400nm), 3820 (422nm), 3850 (450nm) in pet ether. Purified by chromatography on a column of silica gel G. Crystd from \*benzene. Stored in the dark, under an inert atmosphere, at 0°.

Crotonaldehyde (2-butenal) [123-73-9] M 70.1, b 104-105°, d 0.851, n 1.437. Fractionally distd under N<sub>2</sub>, through a short Vigreux column. Stored in sealed ampoules. Stabilised with 0.01% of 2,6-ditert-butyl-*p*-cresol

*trans*-Crotonic acid [107-93-7] M 86.1, m 72-72.5°,  $pK_1^{25}$ -6.17 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{18}$  4.71. Distd under reduced pressure. Crystd from pet ether (b 60-80°) or water, or by partial freezing of the melt.

*E*- and *Z*-Crotonitrile (mixture) [4786-20-3] M 67.1, b 120-121°, d 1.091, n 1.4595. Separated by preparative GLC on a column using 5% FFAP on Chromosorb G. [Lewis et al. *J Am Chem Soc* 108 2818 1986.]

 $\gamma$ -Crotonolactone [2(5*H*)-furanone] [497-23-4] M 84.1, m 3-4°, 76-77°/3.5mm, 90.5-91°/11.5mm, 92-93°/14mm, 107-109°/24mm, 212-214°/760mm,  $d_4^{20}$  1.197,  $n_D^{20}$  1.470. Fractionally distd under reduced pressure. IR: (CCl<sub>4</sub>) 1784 and 1742 cm<sup>-1</sup>, UV no max above 205nm ( $\varepsilon$  1160 cm<sup>-1</sup> M<sup>-1</sup>) and <sup>1</sup>H NMR: (CCl<sub>3</sub>)  $\tau$ : 2.15 (pair of triplets 1H), 3.85 (pair of triplets 1H) and 5.03 (triplet 2H). [Org Synth Coll Vol V 255 1973; Smith and Jones Can J Chem 37 2007, 2092 1959].

**Crotyl bromide** [29576-14-5] **M 135.0, b 103-105°/740mm, n^{25} 1.4792.** Dried with MgSO<sub>4</sub>, CaCO<sub>3</sub> mixture. Fractionally distd through an all-glass Todd column. [Todd column. A column (which may be a Dufton type, fitted with a Monel metal rod and spiral, or a Hempel type, fitted with glass helices) which is surrounded by an open heating jacket so that the temperature can be adjusted to be close to the distillation temperature (Todd Ind Eng Chem (Anal Ed) 17 175 1945)].

15-Crown-5 [33100-27-5] M 220.3, b 93-96% (0.1mm, d 1.113, n 1.465. Dried over 3A molecular sieves.

**18-Crown-6** [17455-13-9] **M 264.3, m 37-39°.** Recryst from acetonitrile and vacuum dried. Purified by pptn of 18-crown-6/nitromethane 1:2 complex with  $Et_2O$ /nitromethane (10:1 mixture). The complex is decomposed in vacuum and distilled under reduced pressure. Also recryst from acetonitrile and vacuum dried.

Cryptopine [482-74-6] M 369.4, m 220-221°. Crystd from \*benzene.

Cryptoxanthin [472-70-8] M 552.9,  $A_{1cm}^{1\%}$  2370 (452nm), 2080 (480nm) in pet ether. Purified by chromatography on MgO, CaCO<sub>3</sub> or deactivated alumina, using EtOH or diethyl ether to develop the column. Crystd from CHCl<sub>3</sub>/EtOH. Stored in the dark, under inert atmosphere, at -20°.

Crystal Violet Chloride {Gentian violet, N-4[bis[4-(dimethylaminophenyl)methylene]-2,5 $cyclohexadien-1-ylidene]-N-methylmethaninium chloride} [548-62-9] M 408.0, pK 9.36.$ Crystd from water (20mL/g), the crystals being separated from the chilled soln by centrifugation, then washedwith chilled EtOH (sol 1g in 10 mL of hot EtOH) and diethyl ether and dried under vac. It is sol in CHCl<sub>3</sub> butinsol in Et<sub>2</sub>O. The carbinol was ppted from an aqueous soln of the HCl dye, using excess NaOH, thendissolved in HCl and recrystd from water as the chloride [UV and kinetics: Turgeon and La Mer J Am Chem Soc74 5988 1952]. The carbinol base has m 195° (needles from EtOH). The diphthalate (blue and turns red inH<sub>2</sub>O) crystallises from H<sub>2</sub>O, m 153-154° (dec 185-187°)[Chamberlain and Dull J Am Chem Soc 50 30891928].

Cumene (isopropyl benzene) [98-82-8] M 120.2, b 69-70°/41mm, 152.4°/760mm, d 0.864, n 1.49146,  $n^{25}$  1.48892. Usual purification is by washing with several small portions of conc H<sub>2</sub>SO<sub>4</sub> (until the acid layer is no longer coloured), then with water, 10% aq Na<sub>2</sub>CO<sub>3</sub>, again with water, and drying with MgSO<sub>4</sub>, MgCO<sub>3</sub> or Na<sub>2</sub>SO<sub>4</sub>, followed by fractional distn. It can then be dried with, and distd from, Na, NaH or CaH<sub>2</sub>. Passage through columns of alumina or silica gel removes oxidation products. Has also been steam

distd from 3% NaOH, and azeotropically distd with 2-ethoxyethanol (which was subsequently removed by washing out with water).

Cumene hydroperoxide [80-15-9] M 152.2, b 60°/0.2mm, d 1.028,  $n^{24}$  1.5232. Purified by adding 100mL of 70% material slowly and with agitation to 300mL of 25% NaOH in water, keeping the temperature below 30°. The resulting crystals of the sodium salt were filtered off, washed twice with 25 mL portions of \*benzene, then stirred with 100mL of \*benzene for 20min. After filtering off the crystals and repeating the washing, they were suspended in 100mL of distilled water and the pH was adjusted to 7.5 by addn of 4M HCl. The free hydroperoxide was extracted into two 20mL portions of *n*-hexane, and the solvent was evaporated under vacuum at room temperature, the last traces being removed at 40-50° and 1mm [Fordham and Williams Canad J Res 27B 943 1949]. Petroleum ether, but not diethyl ether, can be used instead of \*benzene, and powdered solid CO<sub>2</sub> can replace the 4M HCl. The material is potentially EXPLOSIVE.

Cuminaldehyde (4-isopropylbenzaldehyde) [122-03-2] M 148.2, b 82-84°/3.5 mm, 120°/23mm, 131-135°/35mm, 235-236°/760mm, d<sup>20</sup> 0.978, n<sub>D</sub><sup>20</sup> 1.5301. Likely impurity is the benzoic acid. Check the IR for the presence of OH from CO<sub>2</sub>H and the CO frequencies. If acid is present then dissolve in Et<sub>2</sub>O, wash with 10% NaHCO<sub>3</sub> until effervescence ceases, then with brine, dry over CaCl<sub>2</sub>, evap and distil the residual oil, preferably under vacuum. It is almost insoluble in H<sub>2</sub>O, but soluble in EtOH and Et<sub>2</sub>O. The *thiosemicarbazone* has m 147° after recrystn from aqueous EtOH, or MeOH or \*C<sub>6</sub>H<sub>6</sub>. [Crounse J Am Chem Soc 71 1263 1949; Bernstein et al. J Am Chem Soc 73 906 1951; Gensler and Berman J Am Chem Soc 80 4949 1958.]

Cuprein (6'-hydroxycinchonidine) [524-63-0] M 310.4, m 202°,  $[\alpha]_D^7$  -176° (in MeOH), pK<sup>15</sup> 7.63. Crystd from EtOH.

Curcumin [bis-(4-hydroxy-3-methoxycinnamoyl)methane] [458-37-7] M 368.4, m 183°. Crystd from EtOH or acetic acid.

**Cyanamide** [420-04-2] **M 42.0, m 41°, pK\_1^{25}-0.36, pK\_2^{25}10.27.** See cyanamide on p. 416 in Chapter 5.

Cyanoacetamide [107-91-5] M 84.1, m 119.4°. Crystd from MeOH/dioxane (6:4), then water. Dried over  $P_2O_5$  under vacuum.

Cyanoacetic acid [372-09-8] M 85.1, m 70.9-71.1°, pK<sup>25</sup> 2.47. Crystd to constant melting point from \*benzene/acetone (2:3), and dried over silica gel.

Cyanoacetic acid hydrazide [140-87-4] M 99.1, m 114.5-115°. Crystd from EtOH.

p-Cyanoaniline [873-74-5] M 118.1, m 85-87°. See p-aminobenzonitrile on p. 104.

9-Cyanoanthracene (anthracene-9-carbonitrile) [1210-12-4] M 203.2, m 134-137°. Purified by crystn from EtOH or toluene, and vacuum sublimed in the dark and in an inert atmosphere [Ebied et al. J Chem Soc, Faraday Trans 1 76 2170 1980; Kikuchi et al. J Phys Chem 91 574 1987].

**9-Cyanoanthracene photodimer** [33998-38-8] **M 406.4, dec to monomer above** ~147°. Purified by dissolving in the minimum amount of CHCl<sub>3</sub> followed by addition of EtOH at 5° [Ebied et al. J Chem Soc, Faraday Trans 1 75 1111 1979; 76 2170 1980].

p-Cyanobenzoic acid [619-65-8] M 147.1, m 219°, pK<sup>25</sup> 3.55. Crystd from water and dried in vacuum desiccator over Sicapent.

4-Cyanobenzoyl chloride [6068-72-0] M 165.6, m 68-70°, 69-70°, 73-74°, b 132°/8 mm, 150-151°/25 mm. If the IR shows presence of OH then treat with SOCl<sub>2</sub> boil for 1h, evaporate and distil in

vacuum. The distillate solidifies and can be recrystallised from pet ether. It is moisture sensitive and is an **IRRITANT.** [Ashley et al. J Chem Soc 103 1942; Fison et al. J Org Chem 16 648 1951.]

Cyanoguanidine (dicyanodiamide) [461-58-5] M 84.1, m 209.5°, pK -0.4. Crystd from water or EtOH.

**5-Cyanoindole** [15861-24-2] M 142.2, m 106-108°, 107-108°, pK <0. Dissolve in 95% EtOH boil in the presence of charcoal, filter, evaporate to a small volume and add enough H<sub>2</sub>O to cause crystallisation and cool. Recrystd directly from aqueous EtOH and dried in a vacuum. UV:  $\lambda_{max}$  276 nm (log  $\varepsilon$  3.6) in MeOH. [Lindwall and Mantell J Org Chem 18 345 1953, 20 1458 1955; Thesing at al. Chem Ber 95 2205 1962; NMR: Lallemend and Bernath Bull Soc Chim Fr 4091 1970.]

*p*-Cyanophenol [767-00-0] M 119.1, m 113°, pK<sup>25</sup> 7.97. Crystd from pet ether, \*benzene or water and kept under vacuum over P<sub>2</sub>O<sub>5</sub>. [Bernasconi and Paschelis J Am Chem Soc 108 2969 1986.]

3-Cyanopyridine [100-54-9] M 104.1, m 50°, pK<sup>25</sup> 1.38. Crystd to constant melting point from oxylene/hexane.

4-Cyanopyridine [100-48-1] M 104.1, m 76-79°, pK<sup>25</sup> 1.86. Crystd from dichloromethane/diethyl ether mixture.

Cyanuric acid (2,4,6-trichloro-1,3,5-triazine) [108-80-5] M 120.1, m >300°, pK 6.78. Crystd from water. Dried at room temperature in a desiccator under vacuum.

Cyanuric chloride (TCT, 2,4,6-trichloro-1,3,5-triazine) [108-77-0] M 184.4, m 146-149°, 154°, b 190°. Crystd from CCl<sub>4</sub> or pet ether (b 90-100°), and dried under vacuum. Recrystd twice from anhydrous \*benzene immediately before use [Abuchowski et al. J Biol Chem 252 3582 1977].

Cyclobutane carboxylic acid [3721-95-7] M 100.1, m 3-4°, -5.4°, b 84-84.5°/10 mm, 110°/25mm, 135-138°/110mm, 194°/760mm,  $d_4^{20}$  1.061,  $n_D^{20}$  1.453, pK<sup>25</sup> 4.79. Dissolve in aqueous HCO<sub>3</sub> and acidify with HCl and extract into Et<sub>2</sub>O, wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), concentrate to a small volume, then distil through a glass helices packed column. The S-benzylthiouronium salt has m 176° (from EtOH), and the anilide has m 112.5-113°, and the p-toluide has m 123°. [Payne and Smith J Org Chem 22 1680 1957; Kantaro and Gunning J Am Chem Soc 73 480 1951.]

*trans*-Cyclobutane-1,2-dicarboxylic acid [1124-13-6] M 144.1, m 131°,  $pK_1^{25}$  4.11,  $pK_2^{25}$  5.15. Crystd from \*benzene.

**Cyclobutanone** [1191-95-3] **M 70.1, b 96-97°, d 0.931, n<sup>52</sup> 1.4189.** Treated with dilute aqueous KMnO<sub>4</sub>, dried with molecular sieves and fractionally distd. Purified via the semicarbazone, then regenerated, dried with CaSO<sub>4</sub>, and distd in a spinning-band column. Alternatively, purified by preparative gas chromatography using a Carbowax 20-M column at 80°. (This treatment removes acetone).

Cyclobutylamine [2516-34-9] M 71.1, b 82-83°/atm, 83.2-84.2°/760mm,  $d_4^{20}$  0.839,  $n_D^{20}$  1.437, pK<sup>25</sup> 10.04 (9.34 in 50% aq EtOH). It has been purified by steam distn. The aqueous distillate (e.g. 2L) is acidified with 3N HCl (90mL) and evapd to dryness in a vacuum. The *hydrochloride* is treated with a few mL of H<sub>2</sub>O, cooled in ice and a slush of KOH pellets ground in a little H<sub>2</sub>O is added slowly in portions and keeping the soln very cold. The amine separates as an oil from the strongly alkaline soln. The oil is collected dried over solid KOH and distd using a vac jacketed Vigreux column and protected from CO<sub>2</sub> using a soda lime tube. The fraction boiling at 79-83° is collected, dried over solid KOH for 2 days and redistd over a few pellets of KOH (b 80.5-81.5°). Best distil in a dry N<sub>2</sub> atmosphere. The purity can be checked by GLC using a polyethylene glycol on Teflon column at 72°, 15 psi, flow rate of 102 mL/min of He. The sample can appear homogeneous but because of tailing it is not possible to tell if H<sub>2</sub>O is present. The NMR in CCl<sub>4</sub> should show no signals less than 1 ppm from TMS. The *hydrochloride* has a multiplet at *ca* 1.5-2.6ppm (H 2,2,4,3,3,4,4), a quintet at 3.8 ppm (H 1) and a singlet at 4.75 for NH<sub>2</sub> [Roberts and Chambers J Am Chem

Soc 73 2509 1951]. The benzenesulfonamide has m 85-86° (from aq MeOH) and the benzoyl derivative has m 120.6-121.6° [Roberts and Mazur J Am Chem Soc 73 2509 1951; Iffland et al. J Am Chem Soc 75 4044 1953; Org Synth Coll Vol V 273 1973.]

Cyclodecanone [1502-06-3] M 154.2, m 21-24°, b 100-102°/12mm. Purified by sublimation in a vac.

cis-Cyclodecene [935-31-9] M 138.3, m -3°, -1°, b 73°/15mm, 90.3°/33mm, 194-195°/740mm, 197-199°/atm,  $d_4^{20}$  0.8770,  $n_D^{20}$  1.4854. Purified by fractional distn. It forms an AgNO<sub>3</sub> complex which crystallises from MeOH, m 167-187° [Cope et al. J Am Chem Soc 77 1628 1955; IR: Blomqvist et al. J Am Chem Soc 74 3636 1952; Prelog et al. Helv Chim Acta 35 1598 1952].

 $\alpha$ -Cyclodextrin (H<sub>2</sub>O) [10016-20-3] M 972.9, m >280°(dec),  $[\alpha]_{546}^{20}$  +175° (c 10, H<sub>2</sub>O). See entry on p. 524 in Chapter 6.

 $\beta$ -Cyclodextrin (H<sub>2</sub>O) [7585-39-9, 68/68-23-0] M 1135.0, m >300°(dec),  $[\alpha]_{546}^{20}$  +170° (c 10, H<sub>2</sub>O). See entry on p. 524 in Chapter 6.

trans-cis-cis-1,5,9-Cyclododecatriene (cyclododec-1c,5c,9t-triene) [2765-29-9] M 162.3, m -9°, -8°, b 117.5°/2mm, 237-239°/atm, 244°/760mm,  $d_4^{20}$  0.907,  $n_D^{20}$  1.5129. Purified by fractional distn, preferably in a vacuum under N<sub>2</sub>, and forms an insoluble AgNO<sub>3</sub> complex. [Breil et al. Makromol Chemie 69 28 1963.]

Cyclododecylamine [1502-03-0] M 183.3, m 27-29°, b 140-150°/ca 18mm, 280°/atm, pK 9.62 (in 80% methyl cellosolve). It can be purified via the hydrochloride salt m 274-275° (from EtOH) or the picrate m 232-234°, and the free base is distd at water-pump vacuum [Prelog et al. Helv Chim Acta 33 365 1950].

**1,3-Cycloheptadiene** [4054-38-0] M 94.2, b 55°/75mm, 71.5°/150mm, 120-121°/atm,  $d_4^{20}$  0.868,  $n_D^{20}$  1.4972. It was purified by dissolving in Et<sub>2</sub>O, wash with 5% HCl, H<sub>2</sub>O, dry (MgSO<sub>4</sub>), evap and the residue is distd under dry N<sub>2</sub> through a semi-micro column (some foarning occurs) [Cope et al. J Am Chem Soc 79 6287 1957; UV: Pesch and Friess J Am Chem Soc 72 5756 1950].

Cycloheptane [291-64-5] M 98.2, b 114.4°, d 0.812, n 1.4588. Distd from sodium, under nitrogen.

Cycloheptanol [502-41-0] M 114.2, b 77-81°/11mm, 185°/atm, d 0.951, n 1.477. Purified as described for cyclohexanol.

Cycloheptanone [502-42-1] M 112.2, b 105°/80mm, 172.5°/760, d 0.952,  $n^{24}$  1.4607. Shaken with aq KMnO<sub>4</sub> to remove material absorbing around 230-240nm, then dried with Linde type 13X molecular sieves and fractionally distd.

Cycloheptatriene [544-25-2] M 92.1, b 114-115°, d 0.895, n 1.522. Washed with alkali, then fractionally distd.

Cycloheptylamine [5452-35-7] M 113.2, b 50-52°/11mm, 60°/18mm,  $d_4^{20}0.887$ ,  $n_D^{20}1.472$ , pK<sub>Est</sub> ~10.5 (H<sub>2</sub>O), pK<sup>24</sup> 9.99 (in 50% aq methyl cellosolve). It can be purified by conversion to the hydrochloride m 242-246°, and the free base is distd under dry N<sub>2</sub> in a vacuum [Cope et al. J Am Chem Soc 75 3212 1953; Prelog et al. Helv Chim Acta 33 365 1950].

**1,3-Cyclohexadiene** [592-57-4] **M 80.1, b 83-84°/atm, d\_4^{20} 0.840, n\_D^{20} 1.471. Distd from NaBH<sub>4</sub>.** 

1,4-Cyclohexadiene [628-41-1] M 80.1, b 83-86°/714mm, 88.3°/741mm, 86-88°/atm, 88.7-89°/760mm,  $d_4^{20}$  0.8573,  $n_4^{20}$  1.4725. Dry over CaCl<sub>2</sub> and distil in a vacuum under N<sub>2</sub>. [Hückel and Wörffel Chem Ber 88 338 1955; Giovannini and Wegmüller Helv Chim Acta 42 1142 1959.]

Cyclohexane //10-82-7/ M 84.2, f 6.6°, b 80.7°, d<sup>24</sup> 0.77410, n 1.42623, n<sup>25</sup> 1.42354. Commonly, washed with conc H<sub>2</sub>SO<sub>4</sub> until the washings are colourless, followed by water, aq Na<sub>2</sub>CO<sub>3</sub> or 5% NaOH, and again water until neutral. It is next dried with P2O5, Linde type 4A molecular sieves, CaCl2, or MgSO4 then Na and distd. Cyclohexane has been refluxed with, and distd from Na, CaH2, LiAlH4 (which also removes peroxides), sodium/potassium alloy, or  $P_2O_5$ . Traces of \*benzene can be removed by passage through a column of silica gel that has been freshly heated: this gives material suitable for ultraviolet and infrared spectroscopy. If there is much \*benzene in the cyclohexane, most of it can be removed by a preliminary treatment with nitrating acid (a cold mixture of 30mL conc HNO<sub>3</sub> and 70mL of conc H<sub>2</sub>SO<sub>4</sub>) which converts \*benzene into nitrobenzene. The impure cyclohexane and the nitrating acid are placed in an ice bath and stirred vigorously for 15min, after which the mixture is allowed to warm to 25° during 1h. The cyclohexane is decanted, washed several times with 25% NaOH, then water dried with CaCl<sub>2</sub>, and distd from sodium. Carbonyl-containing impurities can be removed as described for chloroform. Other purification procedures include passage through columns of activated alumina and repeated crystn by partial freezing. Small quantities may be purified by chromatography on a Dowex 710-Chromosorb W gas-liquid chromatographic column. Rapid purification: Distil, discarding the forerun. Stand distillate over Grade I alumina (5% w/v) or 4A molecular sieves.

Cyclohexane butyric acid [4441-63-8] M 170.3, m 31°, 26.5-28.5°, b 136-139°/4 mm. 169°/20mm, 188.8°/46mm, pK<sup>25</sup> 4.95. Distil through a Vigreux column, and the crystalline distillate is recrystd from pet ether. The S-benzylthiouronium salt has m 154-155° (from EtOH) [Acta Chem Scand 9 1425 1955; English and Dayan J Am Chem Soc 72 4187 1950].

Cyclohexane-1,2-diaminetetraacetic acid (H<sub>2</sub>O; CDTA) [13291-61-7] M 364.4, pK<sub>1</sub> 1.34, pK<sub>2</sub> 3.20, pK<sub>3</sub> 5.75 (6.12), pK<sub>4</sub> 9.26 (12.35). Dissolved in aq NaOH as its disodium salt, then pptd by adding HCl. The free acid was filtered off and boiled with distd water to remove traces of HCl [Bond and Jones *Trans Faraday Soc* 55 1310 1959]. Recrystd from water and dried under vacuum.

*trans*-Cyclohexane-1,2-dicarboxylic acid [2305-32-0] M 172.2, m 227.5-228°, 228-230.5°, pK<sub>1</sub><sup>25</sup> 4.30, pK<sub>2</sub><sup>25</sup> 6.06 [*cis*, pK<sub>1</sub><sup>25</sup> 4.25, pK<sub>2</sub><sup>25</sup> 6.74]. It is purified by recrystn from EtOH or H<sub>2</sub>O. The *dimethyl ester* has m 95-96° (from \*C<sub>6</sub>H<sub>6</sub>-pet ether). [Abell J Org Chem 22 769 1957; Smith and Byrne J Am Chem Soc 72 4406 1950; Linstead et al. J Am Chem Soc 64 2093 1942.]

(±)-trans-1,2-Cyclohexanediol [1460-57-7] M 116.2, m 104°, 105°, 120°/14mm. Crystd from  $Me_2CO$  and dried at 50° for several days. It can also be recrystd from  $CCl_4$  or EtOAc and can be distilled. The 2,4-dinitrobenzoyl derivative has m 179°. [Winstein and Buckles J Am Chem Soc 64 2780 1942.]

trans-1,2-Cyclohexanediol [1R,2R-(-)- 1072-86-2; 1S,2S-(+)- 57794-08-8] M 116.2, m 107-109°, 109-110.5°, 109-111°, 111-112°, 113-114°,  $[\alpha]_D^{22}$  (-) and (+) 46.5° (c 1, H<sub>2</sub>O). The enantiomers have been recryst from \*C<sub>6</sub>H<sub>6</sub> or EtOAc. The (±) diol has been resolved as the distrychnine salt of the hemisulfate [Hayward, Overton and Whitham J Chem Soc Perkin Trans 1 2413 1976]; or the 1-menthoxy acetates. {1-trans- diastereoisomer has m 64°,  $[\alpha]_D$  -91.7° (c 1.4 EtOH) from pet ether or aqueous EtOH and yields the (-)-trans-diol } and {d-trans-diastereoisomer has m 126-127°,  $[\alpha]_D$  -32.7° (c 0.8 EtOH) from pet ether or aq EtOH and yields the (+)-trans diol}. The bis-4-nitrobenzoate has m 126.5°  $[\alpha]_D$  (-) and (+) 25.5° (c 1.1 CHCl<sub>3</sub>), and the bis-3,5-dinitrobenzoate has m 160°  $[\alpha]_D \pm$  -83.0° (c 1.8 CHCl<sub>3</sub>) [Wilson and Read J Chem Soc 1269 1935].

cis-1,3-Cyclohexanediol [823-18-7] M 116.2, m 86°. Crystd from ethyl acetate and acetone.

trans-1,3-Cyclohexanediol [5515-64-0] M 116.2, m 117°. Crystd from ethyl acetate.

cis-1,4-Cyclohexanediol [556-58-9] M 116.2, m 102.5°. Crystd from acetone (charcoal), then dried and sublimed under vacuum.

Cyclohexane-1,3-dione [504-02-9] M 112.1, m 107-108°. Crystd from \*benzene.

Cyclohexane-1,4-dione [637.88-7] M 112.1, m 76-77°, 78°, 79.5°, 79-80°, b 130-133°/20mm,  $d_4^{91}$  1.0861,  $n_D^{10^2}$  1.4576. Crystd from water, then \*benzene. It can also be recrystd from CHCl<sub>3</sub>/pet ether or Et<sub>2</sub>O. It has been purified by distn in a vacuum and the pale yellow distillate which solidified is then recrystd from CCl<sub>4</sub> (14.3 g/100 mL) and has m 77-79°. The *di-semicarbazone* has m 231°, the *dioxime* HCl has m 150° (from MeOH-\*C<sub>6</sub>H<sub>6</sub>) and the bis-2,4-dinitrophenylhydrazone m 240° (from PhNO<sub>2</sub>). [Org Synth Coll Vol V 288 1973; IR: LeFevre and LeFevre J Chem Soc 3549 1956.]

Cyclohexane-1,2-dione dioxime (Nioxime) [492-99-9] M 142.2, m 189-190°,  $pK_1^{25} 10.68$ ,  $pK_2^{25} 11.92$ . Crystd from alcohol/water and dried in a vacuum at 40°.

1,4-Cyclohexanedione monoethylene acetal (1,4-dioxa-spiro[4.5]decan-8-one) [4746-97-8] M 156.2, m 70-73°, 73.5-74.5°. Recrystd from pet ether and sublimes slowly on attempted distillation. Also purified by dissolving in Et<sub>2</sub>O and adding pet ether (b 60-80°) until turbid and cool. [Gardner et al. J Am Chem Soc 22 1206 1957; Britten and Lockwood J Chem Soc Perkin Trans 1 1824 1974.]

cis, cis-1,3,5-Cyclohexane tricarboxylic acid [16526-68-4] M 216.2, m 216-218°, pK<sub>Est(1)</sub>~4.1, pK<sub>Est(2)</sub>~5.4, pK<sub>Est(3)</sub>~6.8. Purified by recrystn from toluene + EtOH or H<sub>2</sub>O. It forms a 1.5 hydrate with m 216-218°, and a dihydrate at 110°. Purified also by conversion to the triethyl ester b 217-218°/10mm, 151°/1mm and distillate solidifies on cooling, m 36-37° and is hydrolysed by boiling in aq HCl. The trimethyl ester can be distd and recrystd from Et<sub>2</sub>O, m 48-49°. [Newman and Lawrie J Am Chem Soc 76 4598 1954, Lukes and Galik Coll Czech Chem Comm 19 712 1954.]

Cyclohexanol [108-93-0] M 100.2, m 25.2°, b 161.1°, d 0.946, n 1.466,  $n^{25}$  1.437,  $n^{30}$  1.462. Refluxed with freshly ignited CaO, or dried with Na<sub>2</sub>CO<sub>3</sub>, then fractionally distd. Redistd from Na. Further purified by fractional crystn from the melt in dry air. Peroxides and aldehydes can be removed by prior washing with ferrous sulfate and water, followed by distillation under nitrogen from 2,4-dinitrophenylhydrazine, using a short fractionating column: water distils as the azeotrope. Dry cyclohexanol is very hygroscopic.

Cyclohexanone [108-94-1] M 98.2, f -16.4°, b 155.7°, d 0.947,  $n^{15}$  1.452. n 1.451,  $pK^{25}$ -6.8 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK^{25}$  11.3 (enol), 16.6 (keto). Dried with MgSO<sub>4</sub>, CaSO<sub>4</sub>, Na<sub>2</sub>SO<sub>4</sub> or Linde type 13X molecular sieves, then distd. Cyclohexanol and other oxidisable impurities can be removed by treatment with chromic acid or dil KMnO<sub>4</sub>. More thorough purification is possible by conversion to the bisulfite addition compound, or the semicarbazone, followed by decompn with Na<sub>2</sub>CO<sub>3</sub> and steam distn. [For example, equal weights of the bisulfite adduct (crystd from water) and Na<sub>2</sub>CO<sub>3</sub> are dissolved in hot water and, after steam distn, the distillate is saturated with NaCl and extracted with \*benzene which is then dried and the solvent evaporated prior to further distn.]

Cyclohexanone oxime [100-64-1] M 113.2, m 90°. Crystd from water or pet ether (b 60-80°).

Cyclohexanone phenylhydrazone [946-82-7] M 173.3, m 77°. Crystd from EtOH.

Cyclohexene [110-83-8] M 82.2, b 83°, d 0.810, n 1.4464,  $n^{25}$  1.4437. Freed from peroxides by washing with successive portions of dil acidified ferrous sulfate, or with NaHSO<sub>3</sub> soln then with distd water, dried with CaCl<sub>2</sub> or CaSO<sub>4</sub>, and distd under N<sub>2</sub>. Alternative methods of removing peroxides include passage through a column of alumina, refluxing with sodium wire or cupric stearate (then distilling from sodium). Diene is removed by refluxing with maleic anhydride before distg under vac. Treatment with 0.1moles of MeMgI in 40mL of diethyl ether removes traces of oxygenated impurities. Other purification procedures include washing with aq NaOH, drying and distg under N<sub>2</sub> through a spinning band column; redistg from CaH<sub>2</sub>; storage with sodium wire; and passage through a column of alumina, under N<sub>2</sub>, immediately before use. Stored in a

refrigerator under argon. [Woon et al. J Am Chem Soc 108 7990 1986; Wong et al. J Am Chem Soc 109 3428 1987.]

(±)-2-Cyclohexen-1-ol (3-hydroxycyclohex-1-ene) [822-67-3] M 242.2, b 63-65°/12mm, 65-66°/13mm, 67°/15mm, 74°/25mm, 85°/35mm, 166°/atm,  $d_4^{20}0.9865$ ,  $n_D^{20}1.4720$ . Purified by distillation through a short Vigreux column. The 2,4-dinitrobenzoyl derivative has m 120.5°, and the phenylurethane has m 107°. [Org Synth 48 18 1968, Cook J Chem Soc 1774 1938; Deiding and Hartman J Am Chem Soc 75 3725 1953.]

Cyclohexene oxide [286-20-4] M 98.2, b 131-133°/atm,  $d_4^{20}$  0.971,  $n_D^{20}$  1.452. Fractionated through an efficient column. The main impurity is probably H<sub>2</sub>O. Dry over MgSO<sub>4</sub>, filter and distil several times (b 129-134°/atm). The residue is sometimes hard to remove from the distilling flask. To avoid this difficulty, add a small amount of a mixture of ground NaCl and Celite (1:1) to help break the residue particularly if H<sub>2</sub>O is added. [Org Synth Coll Vol I 185 1948.]

Cycloheximide [68-81-9] M 281.4, m 119.5-121°,  $[\alpha]_{546}^{20}$  +9.5° (c 2, H<sub>2</sub>O). Crystd from water/MeOH (4:1), amyl acetate, isopropyl acetate/isopropyl ether or water.

Cyclohexylamine [108-91-8] M 99.2, b 134.5°, d 0.866,  $d^{25}$  0.863, n 1.4593,  $n^{25}$  1.456,  $pK^{25}$  10.63. Dried with CaCl<sub>2</sub> or LiAlH<sub>4</sub>, then distd from BaO, KOH or Na, under N<sub>2</sub>. Also purified by conversion to the hydrochloride, several crystns from water, then liberation of the amine with alkali and fractional distn under N<sub>2</sub>.

Cyclohexylbenzene [827-52-1] M 160.3, f 6.8°, b 237-239°, d 0.950, n 1.5258. Purified by fractional distn, and fractional freezing.

Cyclohexyl bromide [108-85-0] M 156.3, b 72°/29mm, d 0.902, n<sup>25</sup> 1.4935. Shaken with 60% aqueous HBr to remove the free alcohol. After separation from excess HBr, the sample was dried and fractionally distd.

Cyclohexyl chloride [542-18-7] M 118.6, b 142-142.5°, d 1.000, n 1.462. See chlorocyclohexane on p. 162.

**1-Cyclohexylethylamine** [S-(+): 17430-98-7; R-(-): 5913-13-3] M 127.2, b 177-178°/atm,  $d_4^{20}$  0.866,  $n_D^{20}$  1.446,  $[\alpha]_D^{15}$  (-) and (+) 3.2° (neat), pK<sub>Est</sub> ~10.6. Purified by conversion to the *bitartrate* salt (m 172°), then decomposing with strong alkali and extracting into Et<sub>2</sub>O, drying (KOH), filtering, evaporating and distilling. The hydrochloride salt has m 242° (from EtOH-Et<sub>2</sub>O),  $[\alpha]_D^{15}$  -5.0° (c 10 H<sub>2</sub>O; from (+) amine). The oxalate salt has m 132° (from H<sub>2</sub>O). The (±)-base has b 176-178°/760mm, and HCl has m 237-238°. [Reihlen, Knöpfle and Sapper Justus Liebigs Ann Chem 532 247 1938; Chem Ber 65 660 1932.]

Cyclohexylidene fulvene [3141-04-6] M 134.2. Purified by column chromatography and eluted with *n*-hexane [Abboud et al. J Am Chem Soc 109 1334 1987].

Cyclohexyl mercaptan (cyclohexane thiol) [1569-69-3] M 116.2, b 38-39°/12 mm, 57°/23mm, 90°/100mm, 157°/763mm,  $d_4^{20}$  0.949,  $n_D^{20}$  1.493, pK<sub>Est</sub> ~10.8. Possible impurities are the sulfide and the disulfide. Purified by conversion to the Na salt by dissolving in 10% aq NaOH, extract the sulfide and disulfide with Et<sub>2</sub>O, and then acidify the aq soln (with cooling and under N<sub>2</sub>) with HCl, extract with Et<sub>2</sub>O, dry MgSO<sub>4</sub>, evaporate and distil in a vacuum (b 41°/12mm). The sulfide has b 74°/0.2mm,  $n_D^{18.5}$  1.5162 and the disulfide has b 110-112°/0.2mm,  $n_D^{18.5}$  1.5557. The Hg-mercaptide has m 77-78° (needles from EtOH). [Naylor J Chem Soc 1532 1947.]

Cyclohexyl methacrylate [101-43-9] M 168.2, b 81-86°/0.1mm, d 0.964, n 1.458. Purification as for methyl methacrylate. 1-Cyclohexyl-5-methyltetrazole [7707-57-5] M 166.2, m 124-124.5°. Crystd from absolute EtOH, then sublimed at 115°/3mm.

Cyclononanone [3350-30-9] M 140.2, m 142.0-142.8°, b 220-222°. Repeatedly sublimed at 0.05-0.1mm pressure.

cis, cis-1,3-Cyclooctadiene [29965-97-7] M 108.2, m -5°, -49°, b 55°/34mm, 142-144°/760mm,  $d_4^{20}$  0.8690,  $n_D^{20}$  1.48921. Purified by GLC. Fractionally distd through a Widmer column [ as a mobile liquid and redistilled with a Claisen flask or through a semi-micro column [Gould, Holzman and Neiman Anal Chem 20 361 1948]. NB: It has a strong characteristic disagreeable odour detectable at low concentrations and causes headaches on prolonged exposure. [IR: Cope and Estes J Am Chem Soc 72 1128 1950; UV: Cope and Baumgardner J Am Chem Soc 78 2812 1956.] [Widmer column. A Dufton column, modified by enclosing within two concentric tubes the portion containing the glass spiral. Vapour passes up the outer tube and down the inner tube before entering the centre portion. In this way flooding of the column, especially at high temperatures, is greatly reduced (Widmer Helv Chim Acta 7 59 1924).]

cis-cis-1,5-cyclooctadiene, [1552-12-1] M 108.2, m -69.5°, -70°, b 51-52°/25 m m, 97°/144mm, 150.8°/757mm,  $d_4^{20}$  0.880,  $n_D^{20}$  1.4935, Purified by GLC. It has been purified via the AgNO<sub>3</sub> salt. This is prepared by shaking with a soln of 50% aq AgNO<sub>3</sub> w/w several times (e.g. 3 x 50 mL and 4 x 50 mL) at 70° for ca 20min to get a good separation of layers. The upper layers are combined and further extracted with AgNO<sub>3</sub> at 40° (2 x 20 mL). The upper layer (19 mL) of original hydrocarbon mixture gives colourless needles AgNO<sub>3</sub> complex on cooling. The adduct is recrystd from MeOH (and cooling to 0°). The hydrocarbon is recovered by steam distilling the salt. The distillate is extracted with Et<sub>2</sub>O, dried (MgSO<sub>4</sub>), evap and distd. [Jones J Chem Soc 312 1954.]

Cyclooctanone [502-49-8] M 126.2, m 42°. Purified by sublimation after drying with Linde type 13X molecular sieves.

1,3,5,7-Cyclooctatetraene [629-20-9] M 104.2, b 141-141.5°, d 1.537,  $n^{25}$  1.5350. Purified by shaking 3mL with 20mL of 10% aqueous AgNO<sub>3</sub> for 15min, then filtering off the silver nitrate complex as a ppte. The ppte was dissolved in water and added to cold conc ammonia to regenerate the cyclooctatetraene which was fractionally distd under vacuum onto molecular sieves and stored at 0°. It was passed through a dry alumina column before use [Broadley et al. J Chem Soc, Dalton Trans 373 1986].

cis-Cyclooctene [931-88-4] M 110.2, b 32-34º/12mm, 66.5-67º/60mm, 88º/141mm, 140°/170mm, 143°/760mm,  $d_4^{20}$  0.84843,  $n_D^{20}$  1.4702, . The cis-isomer was freed from the transisomer by fractional distn through a spinning-band column, followed by preparative gas chromatography on a Dowex 710-Chromosorb W GLC column. It was passed through a short alumina column immediately before use [Collman et al. J Am Chem Soc 108 2588 1986]. It has also been distd in a dry nitrogen glove box from powdered fused NaOH through a Vigreux column and then passed through activated neutral alumina before use [Wong et al. J Am Chem Soc 109 4328 1987]. Alternatively it can be purified via the AgNO3 salt. This salt is obtained from crude cyclooctene (40 mL) which is shaken at 70-80° with 50% w/w AgNO<sub>3</sub> (2 x 15 mL) to remove cyclooctadienes (ag layer). Extraction is repeated at 40° (4 x 20 mL, of 50% AgNO<sub>3</sub>). Three layers are formed each time. The middle layer contains the AgNO3 adduct of cyclooctene which crystallises on cooling the layer to room temperature. The adduct (complex 2:1) is highly soluble in MeOH (at least 1g/mL) from which it crystallises in large flat needles when cooled at 0°. It is dried under slight vacuum for 1 week in the presence of CaCl<sub>2</sub> and paraffin wax soaked in the cyclooctene. It has m 51° and loses hydrocarbon on exposure to air. cis-Cyclooctene can be recovered by steam distn of the salt, collected, dried (CaCl<sub>2</sub>) and distilled in vacuum. [Braude et al. J Chem Soc 4711 1957; AgNO3: Jones J Chem Soc 1808 1954; Cope and Estes J Am Chem Soc **72** 1128 *1950*.]

cis-Cyclooctene oxide {(1r,8c)-9-oxabicyclo[6.1.0]nonane} [286-62-4] M 126.7, m 56-57°, 57.5-57.8°,50-60°, b 85-88°/17mm, 82.5°/22mm, 90-93°/37mm, 189-190°/atm. It can be distd in vacuum and the solidified distillate can be sublimed in vacuum below 50°. It has a characteristic odour.

[IR: Cope et al. J Am Chem Soc 74 5884 1952, 79 3905 1957; Reppe et al. Justus Liebigs Ann Chem 560 1 1948].

Cyclopentadecanone [502-72-7] M 224.4, m 63°. Sublimation is better than crystn from aq EtOH.

Cyclopentadiene [542-92-7] M 66.1, b 41-42°. Dried with Mg(ClO<sub>4</sub>)<sub>2</sub> and distd.

Cyclopentane [287-92-3] M 70.1, b 49.3°, d 0.745, n 1.40645, n<sup>25</sup> 1.4340. Freed from cyclopentene by two passages through a column of carefully dried and degassed activated silica gel.

**Cyclopentane carbonitrile** [4254-02-8] M 95.2, m -75.2°, -76°, b 43-44°/7mm, 50-62°/10mm, 67-68°/14mm, 74.5-75°/30mm,  $d_4^{20}$  0.912,  $n_D^{20}$  1.441. Dissolve in Et<sub>2</sub>O, wash thoroughly with saturated aqueous K<sub>2</sub>CO<sub>3</sub>, dry (MgSO<sub>4</sub>) and distil through a 10 cm Vigreux column. [McElvain and Stern J Am Chem Soc 77 457 1955, Bailey and Daly J Am Chem Soc 81 5397 1959.]

Cyclopentane-1,1-dicarboxylic acid [5802-65-3] M 158.1, m 184°, pK<sub>1</sub> 3.23, pK<sub>2</sub> 4.08. Recrystd from water.

**1,3-Cyclopentanedione** [3859-41-4] **M 98.1, m 149-150°, 151-152.5°, 151-154°, 151-153°**. Purified by Soxhlet extraction with CHCl<sub>3</sub>. The CHCl<sub>3</sub> is evaporated and the residue is recrystd from EtOAc and/or sublimed at 120°/4mm. It has an acidic pKa of 4.5 in H<sub>2</sub>O. [IR: Boothe et al. J Am Chem Soc 75 1732 1953; DePuy and Zaweski J Am Chem Soc 81 4920 1959.]

**Cyclopentanone** [120-92-3] **M 84.1, b 130-130.5°, d 0.947, n 1.4370, n^{25} 1.4340.** Shaken with aq KMnO<sub>4</sub> to remove materials absorbing around 230 to 240nm. Dried with Linde type 13X molecular sieves and fractionally distd. Has also been purified by conversion to the NaHSO<sub>3</sub> adduct which, after crystallising four times from EtOH/water (4:1), was decomposed by adding to an equal weight of Na<sub>2</sub>CO<sub>3</sub> in hot H<sub>2</sub>O. The free cyclopentanone was steam distd from the soln. The distillate was saturated with NaCl and extracted with \*benzene which was then dried and evaporated; the residue was distd [Allen, Ellington and Meakins J Chem Soc 1909 1960].

Cyclopentene [142-29-0] M 68.1, b 45-46°, d 0.772, n 1.4228. Freed from hydroperoxide by refluxing with cupric stearate. Fractionally distd from Na. Chromatographed on a Dowex 710-Chromosorb W GLC column. Methods for cyclohexene should be applicable here. Also washed with 1M NaOH soln followed by water. It was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, distd over powdered NaOH under nitrogen, and passed through neutral alumina before use [Woon et al. J Am Chem Soc 108 7990 1986]. It was distd in a dry nitrogen atmosphere from powdered fused NaOH through a Vigreux column, and then passed through activated neutral alumina before use [Wong et al. J Am Chem Soc 109 3428 1987].

1-Cyclopentene-1,2-dicarboxylic anhydride [3205-94-5] M 138.1, m 42-54°, 46-47°, b 130°/5mm, 133-135°/5mm,  $n_D^{20}$  1.497. If IR has OH peaks then some hydrolysis to the diacid (m 178°) must have occurred. In this case reflux with an appropriate volume of Ac<sub>2</sub>O for 30min, evaporate the Ac<sub>2</sub>O and distil *in vacuo*. The distillate solidifies and can be recrystd from EtOAc-hexane (1:1). The diacid distils without dec due to formation of the anhydride. The *dimethyl ester* has m 120-125°/11mm. [Askain Chem Ber 98 2322 1965.]

Cyclopentylamine [1003-03-8] M 85.2, m -85.7°, b 106-108°/760mm, 108.5°/760mm,  $d_4^{20}$  0.869,  $n_D^{20}$  1.452, pK<sup>25</sup> 10.65, (pK<sup>25</sup> 4.05 in 50% aq EtOH). May contain H<sub>2</sub>O or CO<sub>2</sub> in the form of carbamate salt. Dry over KOH pellets and then distil from a few pellets of KOH. Store in a dark, dry CO<sub>2</sub>-free atmosphere. It is characterised as the *thiocyanate salt* m 94.5°. The *benzenesulfonyl derivative* has m 68.5-69.5°. [Roberts and Chambers J Am Chem Soc 73 5030 1951; Bollinger et al. J Am Chem Soc 75 17291953.]

Cyclopropane [75-19-4] M 42.1, b -34°. Washed with a soln of HgSO<sub>4</sub>, and dried with CaCl<sub>2</sub>, then  $Mg(ClO_4)_2$ .

Cyclopropanecarbonyl chloride [4023-34-1] M 104.5, b 117.9-118.0°/723mm, 119.5-119.6<sup>[0</sup>/760mm,  $d_4^{20}$  1.142,  $n_4^{20}$  1.453. If the IR shows OH bands then some hydrolysis to the free acid must have occurred. In this case heat with oxalyl chloride at 50° for 2h or SOCl<sub>2</sub> for 30min, then evap and distil three times using a Dufton column. Store in an inert atm, preferably in sealed tubes. Strong **IRRITANT.** If it is free from OH bands then just distil *in vacuo* and store as before. [Jeffrey and Vogel J Chem Soc 1804 1948.]

**Cyclopropane-1,1-dicarboxylic acid** [598-10-7] **M 130.1, m 140°, pK\_1^{25} 1.8, pK\_2^{25} 5.42.** Recrystd from CHCl<sub>3</sub>.

Cyclopropylamine [765-30-0] M 57.1, b 49-49.5°/760mm, 48-50°/atm, 49-50°/750mm,  $d_4^{20}0.816$ ,  $n_D^{20}1.421$ ,  $pK^{25}$  9.10 ( $pK^{25}$  5.33 in 40% aq EtOH). It has been isolated as the *benzamide* m 100.6-101.0° (from aqueous EtOH). It forms a *picrate* m 149° (from EtOH-pet ether) from which the free base can be recovered using a basic ion exchange resin and can then be distd through a Todd column (see p. 174) using an automatic still head which only collects products boiling below 51°/atm. Polymeric materials if present will boil above this temperature. The *hydrochloride* has m 85-86° [Roberts and Chambers J Am Chem Soc 73 5030 1951; Jones J Org Chem 9 484 1944; Emmons J Am Chem Soc 79 6522 1957].

Cyclopropyldiphenylcarbinol [5785-66-0] M 224.3, m 86-87°. Crystd from n-heptane.

Cyclopropyl methyl ketone [765-43-5] M 84.1, b 111.6-111.8°/752mm, d 0.850, n 1.4242. Stored with anhydrous CaSO<sub>4</sub>, distd under nitrogen. Redistd under vacuum.

Cyclotetradecane [295-17-0] M 192.3, m 56°. Recrystd twice from aq EtOH then sublimed in vacuo [Dretloff et al. J Am Chem Soc 109 7797 1987].

Cyclotetradecanone [3603-99-4] M 206.3, m 25°, b 145°/10mm, d 0.926, n 1.480. It was converted to the semicarbazone which was recrystd from EtOH and reconverted to the free cyclotetradecanone by hydrolysis [Dretloff et al. J Am Chem Soc 109 7797 1987].

Cyclotrimethylenetrinitramine (RDX, 1,3,5-trinitrohexahydro-1,3,5-triazine) [121-82-4] M 222.2, m 203.8°(dec). Crystd from acetone. EXPLOSIVE.

*p*-Cymene [99-87-6] M 134.2, b 177.1°, d 0.8569, n 1.4909,  $n^{25}$  1.4885. Washed with cold, conc H<sub>2</sub>SO<sub>4</sub> until there is no further colour change, then repeatedly with H<sub>2</sub>O, 10% aqueous Na<sub>2</sub>CO<sub>3</sub> and H<sub>2</sub>O again. Dried with Na<sub>2</sub>SO<sub>4</sub>, CaCl<sub>2</sub> or MgSO<sub>4</sub>, and distd. Further purification steps include steam distn from 3% NaOH, percolation through silica gel or activated alumina, and a preliminary refluxing for several days over powdered sulfur. Stored over CaH<sub>2</sub>.

Cystamine dihydrochloride, S, S-(L,L)-Cystathionine, Cysteamine, Cysteamine hydrochloride, (±)-Cysteic acid, S-Cysteic acid (H<sub>2</sub>O), L-Cysteine hydrochloride (H<sub>2</sub>O), (±)-Cysteine hydrochloride and L-Cystine, Cytidine, see entries in Chapter 6.

Cytisine (7R,9S-7,9,10,11,12,13-hexahydro-7,9-methano-12*H*-pyrido[1,2-a][1,5]diazocin-8-one, Laburnine, Ulexine) [485-35-8] M 190.3, m 152-153°, 155°, b 218°/2mm,  $[\alpha]_D^{17}$ -120° (H<sub>2</sub>O),  $[\alpha]_D^{25}$ -115° (c 1, H<sub>2</sub>O),  $pK_1^{15}$  1.20,  $pK_2^{15}$  8.12 [also stated are  $pK_1$  6.11,  $pK_2$ 13.08]. Crystd from acetone and sublimed in a vacuum. Its solubilities are: 77% (H<sub>2</sub>O), 7.7% (Me<sub>2</sub>CO), 28.6% (EtOH), 3.3% (\*C<sub>6</sub>H<sub>6</sub>), 50% (CHCl<sub>3</sub>) but is insoluble in pet ether. The *tartrate* has m 206-207°  $[\alpha]_D^{26}$ +45.9°, the *N*-tosylate has m 206-207°, and the *N*-acetate has m 208°. [Bohlmann et al. Angew Chem 67 708 1955; van Tamelen and Baran J Am Chem Soc 77 4944 1955; Isolation: Ing J Chem Soc 2200 1931; Govindachari et al. J Chem Soc 3839 1957; Abs config: Okuda et al. Chem Ind (London) 1751 1961.] TOXIC. Cytosine see entry in Chapter 6.

cis-Decahydroisoquinoline [2744-08-3] M 139.2, b 97-98°/15mm, 208-209º/730mm, pK<sup>20</sup> 11.32. The free base is treated with satd aq picric acid, allowed to stand for 12h, filtd, washed with MeOH to remove the more soluble trans isomer and recrystd from MeOH to give pure cis-picrate m 149-150°. The picrate ( $\sim$ 5g) is shaken with 5M aq NaOH (50mL) and Et<sub>2</sub>O (150mL) while H<sub>2</sub>O is added to the aq phase to dissolve insoluble Na picrate. The Et<sub>2</sub>O extract is dried over solid NaOH and then shaken with Al<sub>2</sub>O<sub>3</sub> (Merck for chromatography) until the yellow color of traces of picric acid disappears (this color cannot be removed by repeated shaking with 5-10 M aq NaOH). The extract is concentrated to 50mL and dry HCl is bubbled through until separatn of the white crysts of the cis-HCl is complete. These are washed with Et<sub>2</sub>O, dried at 100° and recrystd from EtOH + EtOAc to yield pure cis-Hydrochloride m 182-183° (dried in a vac desiccator over KOH) with IR (KBr)  $v_{max}$  2920, 2820, 1582, 1470, 1445, 1410, 1395, 1313, 1135, 1080, 990, 870 cm<sup>-1</sup>. The pure free base is prepared by dissolving the hydrochloride in 10 M aq NaOH, extracted with Et<sub>2</sub>O, dried over solid KOH, filtd and distd in vac. It has IR (film) v<sub>max</sub> 2920, 2820, 2720, 2560, 1584, 1470, 1445, 1415, 1395, 1315, 1300, 1135, 1080, 1020, 990, 873 cm<sup>-1</sup>. The <sup>1</sup>H NMR in CDCl<sub>3</sub> is characteristically different from that of the trans-isomer. [Armarego J Chem Soc (C) 377 1967; Gray and Heitmeier J Am Chem Soc 80 6274 1958; Witkop J Am Chem Soc 70 2617 1948; Skita Chem Ber 57 1982 1924; Helfer Helv Chim Acta 6 7991923.]

trans-Decahydroisoquinoline [2744-09-4] M 139.2, b 106°/15mm, pK<sup>20</sup> 11.32. This is purified as the cis-isomer above. The trans-picrate has m 175-176°, and the trans-hydrochloride has m 221-222° and has IR (KBr)  $v_{max}$  2930, 3800, 1589, 1450, 1400, 1070, 952, 837 cm<sup>-1</sup>. The pure free base was prepared as above and had IR (film)  $v_{max}$  2920, 2820, 2720, 2560, 1584, 1470, 1445, 1415, 1395, 1315, 1300, 1135, 1080, 1020, 990, 873 cm<sup>-1</sup>. The <sup>1</sup>H NMR in CDCl<sub>3</sub> is characteristically different from that of the cis-isomer. (references as above and Helfer Helv Chim Acta 9 818 1926).

**Decahydronaphthalene (decalin, mixed isomers)** [91-17-8] M 138.2, b 191.7°, d 0.886, n 1.476. Stirred with conc  $H_2SO_4$  for some hours. Then the organic phase was separated, washed with water, saturated aqueous  $Na_2CO_3$ , again with water, dried with CaSO<sub>4</sub> or CaH<sub>2</sub> (and perhaps dried further with Na), filtered and distd under reduced pressure (b 63-70°/10mm). Also purified by repeated passage through long columns of silica gel previously activated at 200-250°, followed by distn from LiAlH<sub>4</sub> and storage under N<sub>2</sub>. Type 4A molecular sieves can be used as a drying agent. Storage over silica gel removes water and other polar substances.

cis-Decahydronaphthalene [493-01-6] M 138.2, f -43.2°, b 195.7°, d 0.897, n 1.48113. Purification methods described for the mixed isomers are applicable. The individual isomers can be separated by very efficient fractional distn, followed by fractional crystn by partial freezing. The *cis*-isomer reacts preferentially with AlCl<sub>3</sub> and can be removed from the *trans*-isomer by stirring the mixture with a limited amount of AlCl<sub>3</sub> for 48h at room temperature, filtering and distilling.

trans-Decahydronaphthalene [493-02-7] M 138.2, f -30.6°, b 187.3°, d 0.870, n 1.46968. See purification of cis-isomer above.

cis-Decahydroquinoline [10343-99-4] M 139.2, b 207-208°/708mm , pK<sup>20</sup> 11.29. It is available as a cis-trans-mixture (b 70-73°/10mm, Aldrich, ~ 18% cis-isomer [2051-28-7]), but the isomers can be fractionated in a spinning band column (1~1.5 metre, type E) at atmospheric pressure and collecting 2mL fractions with a distillation rate of 1 drop in 8-10sec. The lower boiling fraction solidifies and contains the trans-isomer (see below, m 48°). The higher boiling fraction b 207-208°/708mm, remains liquid and is mostly the cis-isomer. This is reacted with PhCOCl and M aq NaOH to yield the N-benzoyl derivative m 96° after recrystn from pet ether (b 80-100°). It is hydrolysed with 20% aq HCl by refluxing overnight. PhCO<sub>2</sub>H is filtd off, the filtrate is basified with 5M aq NaOH and extracted with Et<sub>2</sub>O. The dried extract (Na<sub>2</sub>SO<sub>4</sub>) is satd with dry HCl gas and the cis-decahydroquinoline hydrochloride which separates has m 222-224° after washing with Et<sub>2</sub>O and drying at 100°; and has IR (KBr)  $v_{max}$  2900, 2780, 2560, 1580, 1445, 1432, 1403, 1165, 1080, 1036, 990, 867 cm<sup>-1</sup>. The *free base* is obtained by dissolving the *hydrchloride* salt in 5M aq NaOH, extracting with Et<sub>2</sub>O and drying the extract (Na<sub>2</sub>SO<sub>4</sub>), evaporating and distilling the residue; it has IR (film)  $v_{max}$  2900, 2840, 2770, 1445, 1357, 1330, 1305, 1140, 1125, 1109, 1068, 844 cm<sup>-1</sup>. The <sup>1</sup>H NMR in CDCl<sub>3</sub> is characteristically different from that of the *trans*-isomer. [Armarego J Chem Soc (C) 377 1967; Hückel and Stepf Justus Liebigs Ann Chem **453** 163 1927; Bailey and McElvain J Am Chem Soc **52** 4013 1930.]

trans-Decahydroquinoline [767-92-0] M 139.2, m 48°, b 205-206°/708mm , pK<sup>20</sup> 11.29. The lower boiling fraction from the preceding spinning band column fractionation of the commercial *cis-trans*mixture (~ 20:60; see the *cis*-isomer above) solidifies readily (m 48°) and the receiver has to be kept hot with warm water. It is further purified by conversion to the *Hydrochloride* m 285-286° after recrystn from EtOH/AcOEt. This has IR (KBr)  $v_{max}$  2920, 2760, 2578, 2520, 1580, 1455, 1070, 1050, 975, 950, 833 cm<sup>-1</sup>. The *free base* is prepared as for the *cis*-isomer above and distd; and has IR (film, at ca 50°)  $v_{max}$  2905, 2840, 2780, 1447, 1335, 1305, 1240, 1177, 1125, 987, 900, 835 cm<sup>-1</sup>. The <sup>1</sup>H NMR in CDCl<sub>3</sub> is characteristically different from that of the *cis*-isomer. [Armarego J Chem Soc (C) 377 1967; Hückel and Stepf Justus Liebigs Ann Chem 453 163 1927; Bailey and McElvain J Am Chem Soc 52 4013 1930; Prelog and Szpilfogel Helv Chim Acta 28 1684 1945.]

*n*-Decane [124-18-5] M 142.3, b 174.1°, d 0.770, n 1.41189,  $n^{25}$  1.40967. It can be purified by shaking with conc H<sub>2</sub>SO<sub>4</sub>, washing with water, aqueous NaHCO<sub>3</sub>, and more water, then drying with MgSO<sub>4</sub>, refluxing with Na and distilling. Passed through a column of silica gel or alumina. It can also be purified by azeotropic distn with 2-butoxyethanol, the alcohol being washed out of the distillate, using water; the decane is next dried and redistilled. It can be stored with NaH. Further purification can be achieved by preparative gas chromatography on a column packed with 30% SE-30 (General Electric methyl-silicone rubber) on 42/60 Chromosorb P at 150° and 40psig, using helium [Chu J Chem Phys 41 226 1964]. Also purified by zone refining.

Decan-1,10-diol [112-47-0] M 174.3, m 72.5-74°. Crystd from dry ethylene dichloride.

*n*-Decanol (*n*-decyl alcohol) [112-30-1] M 158.3, f 6.0°, b 110-119°/0.1mm, d 0.823, n 1.434. Fractionally distd in an all-glass unit at 10mm pressure (b 110°), then fractionally crystd by partial freezing. Also purified by preparative GLC, and by passage through alumina before use.

*n*-Decyl bromide [112-29-8] M 221.2, b 117-118°/15.5mm, d 1.066. Shaken with  $H_2SO_4$ , washed with water, dried with  $K_2CO_3$ , and fractionally distd.

**Decyltrimethylammonium bromide** [2082-84-0] **M 280.3, m 239-242°.** Crystd from 50% (v/v) EtOH/diethyl ether, or from acetone and washed with ether. Dried under vacuum at 60°. Also recrystd from EtOH and dried over silica gel. [McDonnell and Kraus J Am Chem Soc 73 2170 1952; Dearden and Wooley J Phys Chem 91 2404 1987.]

(+)-Dehydroabietylamine (abieta-8,11,13-triene-18-ylamine) [1446-61-3] M 285.5, m 41°, 42.5-45°, b 192-193°/1mm, 250°/12mm,  $n_D^{40}$  1.546,  $[\alpha]_{546}^{20}$  +51° (c 1, EtOH), pK<sub>Est</sub> ~10.3. The crude base is purified by converting 2g of base in toluene (3.3mL) into the acetate salt by heating at 65-70° with 0.46g of AcOH and the crystals are collected and dried (0.96g from two crops; m 141-143°). The acetate salt is dissolved in warm H<sub>2</sub>O, basified with aqueous NaOH and extracted with \*C<sub>6</sub>H<sub>6</sub>. The dried extract (MgSO<sub>4</sub>) is evaporated in vacuum leaving a viscous oil which crystallises and can be distd. [Gottstein and Cheney J Org Chem 30 2072 1965.] The picrate has m 234-236° (from aq MeOH), and the formate has m 147-148° (from heptane).

Dehydro-L(+)-ascorbic acid [490-83-5] M 174.1, m 196°(dec),  $[\alpha]_{546}^{20}$  +42.5° (c 1, H<sub>2</sub>O), pK 3.90. Crystd from MeOH

**7-Dehydrocholesterol** [434-16-2] M 384.7, m 142-143°,  $[\alpha]_D^{20}$ -122° (c 1, CHCl<sub>3</sub>). Crystd from MeOH.

Dehydrocholic acid [81-23-2] M 402.5, m 237°,  $[\alpha]_{546}^{20}$  -159° (c 1, in CHCl<sub>3</sub>), pK<sub>Est</sub> ~4.9. Crystd from acetone.

**Dehydroepiandrosterone** [54-43-0] M 288.4, m 140-141° and 152-153° (dimorphic),  $[\alpha]_D^{20}$  +13° (c 3, EtOH). Crystd from MeOH and sublimed in vacuum.

Delphinine [561-07-9] M 559.7, m 197-199°, [α]<sup>20</sup><sub>D</sub> +26° (EtOH). Crystd from EtOH.

**3-Deoxy-D-allose** [6605-21-6] M 164.2,  $[\alpha]_D^{20}$  +8° (c 0.25 in H<sub>2</sub>O). Obtained from diethyl ether as a colourless syrup.

Deoxybenzoin [451-40-1] M 196.3, m 60°, b 177°/12mm, 320°/760mm. Crystd from EtOH.

**Deoxycholic acid** [83-44-3] M 392.6, m 171-174°, 176°, 176-178°,  $[\alpha]_{546}^{20}$  +64° (c 1, EtOH),  $[\alpha]_D^{20}$  +55° (c 2.5, EtOH), pK 6.58. Refluxed with CCl<sub>4</sub> (50mL/g), filtered, evaporated under vacuum at 25°, recrystd from acetone and dried under vacuum at 155° [Trenner et al. *J Am Chem Soc* 76 1196 1954]. A soln of (cholic acid-free) material (100mL) in 500mL of hot EtOH was filtered, evaporated to less than 500mL on a hot plate, and poured into 1500mL of cold diethyl ether. The ppte, filtered by suction, was crystd twice from 1-2 parts of absolute EtOH, to give an alcoholate, m 118-120°, which was dissolved in EtOH (100mL for 60g) and poured into boiling water. After boiling for several hours the ppte was filtered off, dried, ground and dried to constant weight [Sobotka and Goldberg *Biochem J* 26 555 1932]. Deoxycholic acid was also freed from fatty acids and cholic acid by silica gel chromatography by elution with 0.5% acetic acid in ethyl acetate [Tang et al. *J Am Chem Soc* 107 4058 1985]. It can also be recrystd from butanone. Its solubility in H<sub>2</sub>O at 15° is 0.24g/L but in EtOH it is 22.07g/L.

11-Deoxycorticosterone (21-hydroxyprogesterone) [64-85-7] M 330.5, m 141-142°,  $[\alpha]_{546}^{20}$ +178° and  $[\alpha]_{546}$  +223° (c 1, EtOH). Crystd from diethyl ether.

**2-Deoxy-\beta-D-galactose** [1949-89-9] M 164.2, m 126-128°,  $[\alpha]_D^{20}$  +60° (c 4, H<sub>2</sub>O). Crystd from diethyl ether.

**2-Deoxy-\alpha-D-glucose** [154-17-6] M 164.2, m 146°,  $[\alpha]_D^{20}$  +46° (c 0.5, H<sub>2</sub>O after 45h). Crystd from MeOH/acetone.

6-Deoxy-D-glucose (D-quinovose) [7658-08-4] M 164.2, m 146°,  $[\alpha]_D^{20} + 73°$  (after 5 min) and +30° (final, after 3h) (c 8.3, H<sub>2</sub>O). It is purified by recrystn from EtOAc and is soluble in H<sub>2</sub>O, EtOH but almost insoluble in Et<sub>2</sub>O and Me<sub>2</sub>CO. [Srivastava and Lerner Carbohydr Res 64 263 1978; NMR: Angyal and Pickles Aust J Chem 25 1711 1972.]

**2-Deoxy-** $\beta$ -**L-ribose** [18546-37-7] **M** 134.1, **m** 77°, 80°,  $[\alpha]_D^{25}$  +91.7° (c 7, pyridine, 40° final). Crystd from diethyl ether.

**2-Deoxy-\beta-D-ribose** [533-67-5] M 134.1, m 86-87°, 87-90°,  $[\alpha]_D^{20}$ -56° (c 1, H<sub>2</sub>O after 24h). Crystd from diethyl ether.

Desyl bromide (α-bromo-desoxybenzoin, ω-bromo-ω-phenyl acetophenone) [484-50-0] M 275.2, m 57.1-57.5°. Crystd from 95% EtOH.

**Desyl chloride** ( $\alpha$ -chloro-desoxybenzoin,  $\omega$ -chloro- $\omega$ -phenyl acetophenone) [447-31-4] M 230.7, m 62-64°, 66-67°, 67.5°, 68°. For the purification of small quantities recrystallise from pet ether (b 40-60°), but use MeOH or EtOH for larger quantities. For the latter solvent, dissolve 12.5g of chloride in 45mL of boiling EtOH (95%), filter and the filtrate yields colourless crystals (7.5g) on cooling. A further crop (0.9g) can be obtained by cooling in an ice-salt bath. It turns brown on exposure to sunlight but it is

stable in sealed dark containers. [Henley and Turner J Chem Soc 1182 1931; Org Synth Coll Vol II 159 1943.]

**Dexamethasone**  $(9-\alpha-fluoro-16-\alpha-methylprednisolone)$  [50-02-2] M 392.5, m 262-264°, 268-271°,  $[\alpha]_D^{25}$  +77.5° (c 1, dioxane). It has been recrystallised from Et<sub>2</sub>O or small volumes of EtOAc. Its solubility in H<sub>2</sub>O in 10 mg/100mL at 25°; and is freely soluble in Me<sub>2</sub>CO, EtOH and CHCl<sub>3</sub>. [Arth et al. J Am Chem Soc 80 3161 1958; for the  $\beta$ -methyl isomer see Taub et al. J Am Chem Soc 82 4025 1960.]

**Dexamethasone 21-acetate** (9- $\alpha$ -fluoro-16- $\alpha$ -methylprednisolone-21-acetate) [1177-87-3] M 434.5, m 215-225°, 229-231°, [ $\alpha$ ]<sup>25</sup><sub>D</sub> +77.6° (c 1, dioxane), +73° (c 1, CHCl<sub>3</sub>). Purified on neutral Al<sub>2</sub>O<sub>3</sub> using CHCl<sub>3</sub> as eluent, fraction evaporated, and recrystd from CHCl<sub>3</sub>. UV has  $\lambda_{max}$  at 239nm. [Oliveto et al. J Am Chem Soc 80 4431 1958].

Diacetamide [625-77-4] M 101.1, m 75.5-76.5°, b 222-223°. Purified by crystn from MeOH [Arnett and Harrelson J Am Chem Soc 109 809 1987].

**Diacetoxyiodobenzene** (iodobenzenediacetate) [3240-34-4] M 322.1, m 163-165°. Purity can be checked by treatment with  $H_2SO_4$  then KI and the liberated  $I_2$  estimated with standard thiosulfate. It has been recrystd from 5M acetic acid and dried overnight in a vac desiccator over CaCl<sub>2</sub>. The surface of the crystals may become slightly yellow but this does not affect its usefulness. [Sharefkin and Saltzman Org Synth Coll Vol V 600 1973.]

1,2-Diacetyl benzene [704-00-7] M 162.2, m 39-41°, 41-42°, b 110°/0.1mm, 148°/20mm. Purified by distn and by recrystn from pet ether. The bis-2,4-dinitrophenyl hydrazone has m 221° dec. [Halford and Weissmann J Org Chem 17 1646 1952; Riemschneider and Kassahn Chem Ber 92 1705 1959.]

1,4-Diacetyl benzene [1009-61-6] M 162.2, m 113-5-114.2°. Crystd from \*benzene and vacuum dried over CaCl<sub>2</sub>. Also dissolved in acetone, treated with Norit, evapd and recrystd from MeOH [Wagner et al. J Am Chem Soc 108 7727 1986].

(+)-Di-O-acetyl-L-tartaric anhydride [(R,R)-2,3-diacetoxysuccinic anhydride] [6283-74-5] M 216.2, m 129-132°, 133-134°, 135°, 137.5°,  $[\alpha]_D^{20}$  +97.2° (c 0.5, dry CHCl<sub>3</sub>). If the IR is good, i.e. no OH bands, then keep in a vacuum desiccator overnight (over P<sub>2</sub>O<sub>5</sub>/paraffin) before use. If OH bands are present then reflux 4g in Ac<sub>2</sub>O (12.6mL) containing a few drops of conc H<sub>2</sub>SO<sub>4</sub> for 10min (use a relatively large flask), pour onto ice, collect the crystals, wash with dry \*C<sub>6</sub>H<sub>6</sub> (2 x 2mL), stir with 17mL of cold Et<sub>2</sub>O, filter and dry in a vacuum desiccator as above, and store in dark evacuated ampoules under N<sub>2</sub> in small aliquots. It is not very stable in air; the melting point of the crystals drop one degree in the first four days then remains constant (132-134°). If placed in a stoppered bottle it becomes gummy and the m falls 100° in three days. Recrystn leads to decomposition. If good quality anhydride is required it should be prepared fresh from tartaric acid. It sublimes in a CO<sub>2</sub> atmosphere. [Org Synth Coll Vol IV 242 1963.]

Diallyl amine (N-2-propenyl-2-propen-1-amine) [124-02-7] M 97.2, b 107-111°/760mm, 112°/760mm,  $d_4^{20}$  0.789,  $n_D^{20}$  1.440, pK<sup>20</sup> 9.42. Keep over KOH pellets overnight, decant and distil from a few pellets of KOH at atm pressure (b 108-111°), then fractionate through a Vigreux column. [Vliet J Am Chem Soc 46 1307 1924; Org Synth Coll Vol I 201 1941.] The hydrochloride has m 164-165° (from Me<sub>2</sub>CO + EtOH). [Butler and Angels J Am Chem Soc 79 3128 1957.]

(+)-N, N'-Diallyl tartrimide (DATD) [58477-85-3] M 228.3, m 184°, [ $\alpha$ ]<sub>546</sub> +141° (c 3, MeOH). Wash with Et<sub>2</sub>O containing 10% EtOH until the washings are clear and colourless, and dry *in vacuo*. [*FEBS Lett* 7 293 1970.]

**Diamantane** [2292-79-7] M 188.3, m 234-235°. Purified by repeated crystn from MeOH or pentane. Also dissolved in  $CH_2Cl_2$ , washed with 5% aq NaOH and water, and dried (MgSO<sub>4</sub>). The soln was concentrated to a small volume, an equal weight of alumina was added, and the solvent evaporated. The residue was placed on an activated alumina column (ca 4 x weight of diamantane) and eluted with pet ether (b 40-60°). Eight sublimations and twenty zone refining experiments gave material **m** 251° of 99.99% purity by differential analysis [*Tetrahedron Lett* 3877 1970; J Chem Soc (C) 2691 1972].

**3,6-Diaminoacridine hydrochloride** [952-23-8] M 245.7, m 270°(dec),  $\varepsilon_{456}$  4.3 x 10<sup>4</sup>, pK<sub>1</sub><sup>20</sup> 1.5, pK<sub>2</sub><sup>20</sup> 9.60 (9.65 free base). First purified by pptn of the free base by adding aq NH<sub>3</sub> soln to an aq soln of the hydrochloride or hydrogen sulfate, drying the ppte and subliming at 0.01mm Hg [Müller and Crothers *Eur J Biochem*, 54 267 1975].

**3,6-Diaminoacridine sulfate (proflavin sulfate)** [1811-28-5] M **516.6, m** >300°(dec),  $\lambda_{max}$ **456nm.** An aqueous soln, after treatment with charcoal, was concentrated, chilled overnight, filtered and the ppte was rinsed with a little diethyl ether. The ppte was dried in air, then overnight in a vacuum oven at 70°.

**1.3-Diaminoadamantane** [10303-95-4] M 164.3, m 52°, pK<sub>Est(1)</sub>~8.6, pK<sub>Est(2)</sub>~10.6. Purified by zone refining.

1,4-Diaminoanthraquinone [128-95-0] M 238.3, m 268°. Purified by thin-layer chromatography on silica gel using toluene/acetone (9:1) as eluent. The main band was scraped off and extracted with MeOH. The solvent was evaporated and the quinone was dried in a drying pistol [Land, McAlpine, Sinclair and Truscott J Chem Soc, Faraday Trans 1 72 2091 1976]. Crystd from EtOH in dark violet crystals.

1,5-Diaminoanthraquinone [129-44-2] M 238.3, m 319°. Recrystd from EtOH or acetic acid [Flom and Barbara J Phys Chem 89 4481 1985].

**2,6-Diaminoanthraquinone** [131-14-6] **M 238.3, m 310-320°.** Crystd from pyridine. Columnchromatographed on Al<sub>2</sub>O<sub>3</sub> / toluene to remove a fluorescent impurity, then recrystd from EtOH.

3,3'-Diaminobenzidine tetrahydrochloride  $(2H_2O)$  [7411-49-6] M 396.1, m >300°(dec), pK<sub>Est(1)</sub>~3.3, pK<sub>Est(2)</sub>~4.7 (free base). Dissolved in water and ppted by adding conc HCl, then dried over solid NaOH.

**3,4-Diaminobenzoic acid** [619-05-6] M **152.2, m 213°(dec), 228-229°, pK\_1^{25}2.57 (4-NH<sub>2</sub>), pK\_2^{25}3.39 (3-NH<sub>2</sub>), pK\_{Est(3)} \sim 5.1 (CO<sub>2</sub>H). Crystd from H<sub>2</sub>O or toluene.** 

**3,5-Diaminobenzoic acid** [535-87-5] **M 152.2, m 235-240°(dec), pK<sup>25</sup> 5.13 (CO<sub>2</sub>H).** Crystd from water. *Dihydrochloride* has **m** 226-228°(dec).

4,4'-Diaminobenzophenone [611-98-3] M 212.3, m 242-244°, 243-245°, 246.5-247.5° (after sublimation at 0.0006 mm),  $pK_1^{25}1.37$ ,  $pK_2^{25}2.92$ . Purified by recrystn from EtOH and by sublimation in high vacuum. The dihydrochloride has m 260° dec (from EtOH) and the thiosemicarbazone has m 207-207.5° dec (from aq EtOH). [Kuhn et al. Chem Ber 75 711 1942.]

1,4-Diaminobutane dihydrochloride (putrescine 2HCl) [333-93-7] M 161.1, m >290°,  $pK_1^{25}$ 9.63,  $pK_2^{25}$  10.80. Crystd from EtOH/water.

**1,2-Diamino-4,5-dichlorobenzene** [5348-42-5] M 177.0, m 163°,  $pK_{Est(1)} \sim 0$ ,  $pK_{Est(2)} \sim 2.9$ . Refluxed with activated charcoal in CH<sub>2</sub>Cl<sub>2</sub>, followed by recrystn from diethyl ether/pet ether or pet ether [Koolar and Kochi J Org Chem 52 4545 1987].

2,2'-Diaminodiethylamine (diethylenetriamine) [111-40-0] M 103.2, b 208°, d 0.95, n 1.483,  $pK_1^{25}$  4.34,  $pK_2^{25}$  9.13,  $pK_3^{25}$  9.94. Dried with Na and distd, preferably under reduced pressure, or in a stream of N<sub>2</sub>. § Polymer-bound diethylenetriamine is commercially available.

4,5-Diamino-2,6-dihydroxypyrimidine (diamino uracil) sulfate [32014-70-3] M 382.3, m >300°, pK<sub>1</sub><sup>2°</sup>1.7, pK<sub>2</sub><sup>2°</sup>3.20, pK<sub>3</sub><sup>2°</sup>4.56. The salt is quite insoluble in H<sub>2</sub>O but can be converted to the

free base which is recrystd from H<sub>2</sub>O and converted to the sulfate by addition of the required amount of H<sub>2</sub>SO<sub>4</sub>. The hydrochloride has **m** 300-305° dec and can be used to prepare the sulfate by addition of H<sub>2</sub>SO<sub>4</sub>; It is more soluble than the sulfate. The perchlorate has **m** 252-254°. The free base has  $\lambda_{max}$  260nm (log  $\varepsilon$  4.24) in 0.1M HCl. [Bogert and Davidson J Am Chem Soc **86** 1668 1933; Bredereck et al. Chem Ber **86** 850 1953; Org Synth Coll Vol IV 247 1963; Barlin and Pfleiderer J Chem Soc (B) 1425 1971.]

5,6-Diamino-1,3-dimethyluracil hydrate (5,6-diamino-1,3-dimethyl-2-pyrimidine-2,4-dione hydrate) [5440-00-6] M 188.2, m 205-208° dec, 209° dec, 210° dec, pK<sub>1</sub> 1.7, pK<sub>2</sub> 4.6. Recryst from EtOH. The hydrochloride has m 310° (from MeOH) and the perchlorate has m 246-248°. [UV: Bredereck et al. Chem Ber 92 583 1959; Taylor et al. J Am Chem Soc 77 2243 1955.]

4,4'-Diamino-3,3'-dinitrobiphenyl [6271-79-0] M 274.2, m 275°, pK<sub>Est</sub> ~-0.2. Crystd from aqueous EtOH.

4,4'-Diaminodiphenylamine [537-65-5] M 199.3, m 158°, pK<sub>Est</sub> ~5.0. Crystd from water.

**4,4'-Diaminodiphenylmethane** [101-77-9] **M 198.3, m 91.6-92°, pK<sub>Est</sub> ~4.9.** Crystd from water, 95% EtOH or \*benzene.

3,3'-Diaminodipropylamine [56-18-8] M 131.2, b 152°/50mm, d 0.938, n 1.481,  $pK_1^{25}7.72$ ,  $pK_2^{25}9,57$ ,  $pK_3^{25}$  10.65. Dried with Na and distd under vacuum.

**6,9-Diamino-2-ethoxyacridine** (Ethacridine) [442-16-0] M 257.3, m 226°, pK<sub>Est</sub> ~11.5. Crystd from 50% EtOH.

2,7-Diaminofluorene [524-64-4] M 196.3, m 165°, pK<sub>Est</sub> ~4.6. Recrystd from H<sub>2</sub>O.

**2,4-Diamino-6-hydroxypyrimidine** [56-06-4] M **126.1, m 260-270°(dec), pK\_1^{25} 1.34, pK\_2^{25} <b>3.27, pK\_3^{25} 10.83.** Recryst from H<sub>2</sub>O.

**4,5-Diamino-6-hydroxypyrimidine hemisulfate** [102783-18-6] **M 350.3, m 268°, 270°, pK\_1^{25} 1.34, pK\_2^{25} 3.57, pK\_3^{25} 9.86**. Recrystd from H<sub>2</sub>O. The free base also recrystallises from H<sub>2</sub>O (m 239°). [UV: Mason J Chem Soc 2071 1954; Elion et al. J Am Chem Soc 74 411 1952.]

**1,5-Diaminonaphthalene** [2243-62-1] **M 158.2, m 190°, pK^{25} 4.12.** Rerystd from boiling H<sub>2</sub>O, but is wasteful due to poor solubility. Boil in chlorobenzene (charcoal), filter hot and cool the filtrate. This gives colourless crystals. Dry in a vac till free from chlorobenzene (odour), and store away from light.

**1,8-Diaminonaphthalene** [479-27-6] **M 158.2, m 66.5°, b 205°/12mm, pK 4.44.** Crystd from water or aqueous EtOH, and sublimed in a vacuum. *N,N'-DiMe* deriv [20734-56-9] has **m** 103-104° and **pK** 5.61; *N,N,N'-TriMe* deriv [20734-57-0] has **m** 29-30° and **pK** 6.43. [Hodgson et al. J Chem Soc 202 1945.]

**2,3-Diaminonaphthalene** [771-97-1] **M 158.2, m 199°, pK<sup>21</sup> 3.54 (in 50% aq EtOH).** Crystd from water, or dissolved in 0.1M HCl, heated to 50°. After cooling, the soln was extracted with decalin to remove fluorescent impurities and centrifuged.

**1,8-Diaminooctane** [373-44-4] M 144.3, m 50-52°, 51-52°, 52-53°, b 121°/18 mm, 120°/24 mm, pK<sub>1</sub><sup>20</sup> 10.1, pK<sub>2</sub><sup>20</sup> 11.0. Distil under vacuum in an inert atmosphere(N<sub>2</sub>, Ar), cool and store distillate in an inert atmosphere in the dark. The *dihydrochloride* has m 273-274°. [Nae and Le *Helv Chim Acta* 15 55 1955.]

**2,4-Diamino-5-phenylthiazole** (Amiphenazole) [490-55-1] M 191.3, m 163-164°(dec). Crystd from aqueous EtOH or water. Stored in the dark under N<sub>2</sub>.

**1,5-Diaminopentane** [462-94-2] M 102.2, m 14-16°, b 78-80°/12mm, 101-103°/35mm, 178-180°/750mm,  $d_4^{20}$  0.869,  $n_D^{20}$  1.458,  $pK_1^{20}$  10.02,  $pK_2^{20}$  10.96. Purified by distn, after standing over KOH pellets (at room temp; i.e. liquid form). It has  $pKa^{20}$  values of 10.02 and 10.96 in H<sub>2</sub>O. Its dihydrochloride has m 275° (sublimes in vac), and its *tetraphenyl boronate* has m 164°. [Schwarzenbach et al. Helv Chim Acta 35 2333 1952.]

*d*,*l*-2,6-Diaminopimelic acid [583-93-7] M 190.2, m 313-315°(dec) pK<sub>Est(1)</sub> ~2.2, pK<sub>Est(2)</sub>~9.7. Crystd from water.

**1,3-Diaminopropane** dihydrochloride [10517-44-9] M 147.1, m 243°, pK<sub>1</sub><sup>25</sup> 8.29, pK<sub>2</sub><sup>25</sup> 10.30. Crystd from EtOH/water.

**1,3-Diaminopropan-2-ol** [616-29-5] M 90.1, m 38-40°,  $pK_1^{25}$  7.94,  $pK_2^{25}$  9.57. Dissolved in an equal amount of water, shaken with charcoal and vacuum distd at 68°/0.1mm. It is too viscous to be distd through a packed column.

L(S)-2,3-Diaminopropionic acid monohydrochloride (3-amino-L-alanine hydrochloride) [1482-97-9] M 140.6, m 132-133°dec, 237°dec,  $[\alpha]_D^{25}$  +26.1° (c 5.8, M HCl),  $pK_1^{25}1.30$ ,  $pK_2^{25}6.79$ ,  $pK_3^{25}$  9.51. Forms needles from H<sub>2</sub>O and can be recrystd from aqueous EtOH. [Gmelin et al. Z Physiol Chem. 314 28 1959; IR: Koegel et al. J Am Chem Soc 77 5708 1977.]

2,3-Diaminopyridine [452-58-4] M 109.1, m 116°, pK<sub>1</sub><sup>25</sup> -0.50, pK<sub>2</sub><sup>25</sup> 6.92. Crystd from \*benzene and sublimed *in vacuo*.

**2,6-Diaminopyridine** [141-86-6] M 109.1, m 121.5°  $pK_{Est(1)}$  <-6.0,  $pK_{Est(2)}$  ~7.3. Crystd from \*benzene and sublimed *in vacuo*.

**3,4-Diaminopyridine** [54-96-6] **M 109.1, m 218-219°, pK\_1^{20} 0.49, pK\_2^{20} 9.14.** Crystd from \*benzene and stored under H<sub>2</sub> because it is deliquescent and absorbs CO<sub>2</sub>.

*meso*-2,3-Diaminosuccinic acid [23220-52-2] M 148.1, m 305-306°(dec, and sublimes), pK<sub>Est(1)</sub>~3.6, pK<sub>Est(2)</sub>~9.8. Crystd from water.

Diaminotoluene see toluenediamine.

**3,5-Diamino-1,2,4-triazole** (Guanazole) [1455-77-2] M 99.1, m 206°  $pK_1^{20}$  4.43,  $pK_2^{20}$  12.12. Crystd from water or EtOH.

**2,5-Di-tert-amylhydroquinone** [79-74-3] **M 250.4, m 185.8-186.5°.** Crystd under N<sub>2</sub> from boiling glacial acetic acid (7mL/g) plus boiling water (2.5mL/g) [Stolow and Bonaventura J Am Chem Soc **85** 3636 1963].

**Di-n-amyl phthalate** [131-18-0] **M 306.4, b 204-206°/11mm, d<sup>25</sup> 1.023, n 1.489.** Washed with aqueous Na<sub>2</sub>CO<sub>3</sub>, then distilled water. Dried with CaCl<sub>2</sub> and distd under reduced pressure. Stored in a vacuum desiccator over  $P_2O_5$ .

1,3-Diazaazulene (cycloheptimidazole) [275-94-5] M 130.1, m 120°. Recrystd repeatedly from deaerated cyclohexane in the dark.

1,5-Diazabicyclo[4.3.0]non-5-ene (DBN, 2,3,4,,6,7,8-hexahydropyrrolo[1,2-a]-pyrimidine) [3001-72-7] M 124.2, b 96-98°/11mm, 100-102°/12mm, 118-121°/32mm,  $d_4^{20}$  1.040,  $n_D^{20}$ 1.520, pK >13.0. Distd from BaO. It forms a hydroiodide by addn of 47% HI, dry and dissolve in MeCN, evaporate and repeat, recrystallise from EtOH then dry at 25°/1mm for 5h, then at 80°/0.03mm for 12h and store and dispense in a dry box, m 154-156° [Jaeger et al. J Am Chem Soc 101 717 1979]. The methiodide is recrystd from CHCl<sub>3</sub> + Et<sub>2</sub>O, m 248-250°, and hydrogen fumarate has m 159-160° and is crystd from isoPrOH [Rokach et al. J Med Chem 22 237 1979; Oediger et al. Chem Ber 99 2012 1966; Reppe et al. Justus Liebigs Ann Chem 596 210 1955].

1,4-Diazabicyclo[2.2.2]octane (DABCO, triethylenediamine TED) [280-57-9] M 112.2, m 156-157° (sealed tube),  $pK_1^{25}$  2.97,  $pK_2^{25}$  8.82 Crystd from 95% EtOH, pet ether or MeOH/diethyl ether (1:1). Dried under vacuum over CaCl<sub>2</sub> and BaO. It can be sublimed *in vacuo*, and readily at room temperature. Also purified by removal of water during azeotropic distn of a \*benzene soln. It was then recrystd twice from anhydrous diethyl ether under argon, and stored under argon [Blackstock et al. J Org Chem 52 1451 1987].

**1,8-Diazabicyclo**[5.4.0]undec-7-ene (DBU, 2,3,4,6,7,8,9,10-octahydropyrimidino[1,2-a]-azepine) [6674-22-2] M 152.2, b 115°/11mm, d 1.023, n 1.522,  $pK_{Est} \sim >13$ . Fractionally dist under vac. Also purified by chromatography on Kieselgel and eluting with CHCl<sub>3</sub>/EtOH/25% aq NH<sub>3</sub> (15:5:2) and checked by IR and MS. [Oediger et al. Chem Ber 99 2012 1962; Angew Chem, Int Ed Engl 6 76 1967; Guggisberg et al. Helv Chim Acta 61 1057 1978.]

1,8-Diazabiphenylene [259-84-7] M 154.2, pK<sub>Est</sub> ~4.4. Recrystd from cyclohexane, then sublimed in a vacuum.

2,7-Diazabiphenylene [31857-42-8] M 154.2, pK<sub>Est</sub> ~4.5. Recrystd from cyclohexane, then sublimed in a vacuum.

**Diazoaminobenzene** (1,3-diphenyltriazene) [136-36-6] M 197.2, m 99°. Crystd from pet ether (b 60-80°), 60% MeOH/water or 50% aqueous EtOH (charcoal) containing a small amount of KOH. Also purified by chromatography on alumina/toluene and toluene-pet ether. Stored in the dark.

6-Diazo-5-oxo-L-norleucine [157-03-9] M 171.2, m 145-155°(dec),  $[\alpha]_D^{20} + 21°$  (c 5, EtOH), pK<sub>1</sub> 2.1, pK<sub>2</sub> 8.95. Crystd from EtOH, aq EtOH or MeOH.

Dibenzalacetone [538-58-9] M 234.3, m 112°. Crystd from hot ethyl acetate (2.5mL/g) or EtOH.

**Dibenz**[*a*,*h*]**anthracene** [53-70-3] **M 278.4, m 266-267°.** The yellow-green colour (due to other pentacyclic impurities) has been removed by crystn from \*benzene or by selective oxidation with lead tetraacetate in acetic acid [Moriconi et al. J Am Chem Soc 82 3441 1960].

Dibenzo-18-crown-6 [14187-32-7] M 360.4, m 163-164°. Crystd from \*benzene, n-heptane or toluene and dried under vacuum at room temperature for several days. [Szezygiel J Phys Chem 91 1252 1987.]

**Dibenzo-18-crown-8** [14174-09-5] **M 448.5, m 103-106°.** Recrystd from EtOH, and vacuum dried at  $60^\circ$  over  $P_2O_5$  for 16hours. [Delville et al. J Am Chem Soc 109 7293 1987.]

**Dibenzofuran** [132-64-9] **M 168.2, m 82.4**°. Dissolved in diethyl ether, then shaken with two portions of aqueous NaOH (2M), washed with water, separated and dried (MgSO<sub>4</sub>). After evaporating the ether, dibenzofuran was crystd from aq 80% EtOH and dried under vacuum. [Cass et al. J Chem Soc 1406 1958.] High purity material was obtained by zone refining.

Dibenzopyran (xanthene) [92-83-1] M 182.2, m 100.5°, b 310-312°. See entry on p. 386.

**Dibenzothiophene** [132-65-0] **M 184.3, m 99°.** Purified by chromatography on alumina with pet ether, in a darkened room. Crystd from water or EtOH.

*trans*-1,2-Dibenzoylethylene [959-28-4] M 236.3, m 109-112°, 111°. Recrystd from MeOH or EtOH as yellow needles [Koller et al. *Helv Chim Acta* 29 512 1946]. The *dioxime* has m 210-211°dec from AcOH. [IR: Kuhn et al. J Am Chem Soc 72 5058 1950; Yates J Am Chem Soc 74 5375 1952; Erickson et al. J Am Chem Soc 73 5301 1951.]

Dibenzoylmethane (1,3-diphenyl-1,3-propanedione) [120-46-7] M 224.3, m 80°. Crystd from pet ether or MeOH.

Di-O-benzoyl-(R and S)-tartaric acid (H<sub>2</sub>O) [R-(+)- 17026-42-5; S-(-)- 2743-38-6] M 376.3, m 88-89° (hydrate), 173° (anhydrous),  $[\alpha]_{546}^{20}$  (+) and (-) 136° (c 2, EtOH),  $[\alpha]_D^{20}$  (+) and (-) 117° (c 5, EtOH),  $pK_{Est(1)} \sim 2.9$ ,  $pK_{Est(2)} \sim 4.2$ . Crystd from water (18g from 400 mL boiling H<sub>2</sub>O) and stir vigorously while cooling in order to obtain crystals; otherwise an oil will separate which solidifies on cooling. Dry in a vacuum desiccator over KOH-H<sub>2</sub>SO<sub>4</sub> - yield 16.4g) as monohydrate, m 88-89°. It crystallises from xylene as the anhydrous acid, m 173° (150-153°). It does not cryst from \*C<sub>6</sub>H<sub>6</sub>, toluene, \*C<sub>6</sub>H<sub>6</sub>-pet ether (oil), or CHCl<sub>3</sub>-pet ether. [Butler and Cretcher J Am Chem Soc 55 2605 1933; Tetrahedron 41 2465 1085.]

2,3,6,7-Dibenzphenanthrene [222-93-5] M 276.3, m 257°. Crystd from xylene.

Dibenzyl amine [103.49.1] M 197.3, m -26°, b 113-114°/0.1mm, 174-175°/6 mm, 270°/250mm, 300° (partial dec),  $d_4^{20}$  1.027,  $n_D^{20}$  1.576, pK<sup>25</sup> 8.52. Purified by distn in a vacuum. It causes burns to the skin. The dihydrochloride has m 265-266° after recrystn from MeOH-HCl, and the tetraphenyl boronate has m 129-133°. [Bradley and Maisey J Chem Soc 247 1954; Hall J Phys Chem 60 63 1956; Donetti and Bellora J Org Chem 37 3352 1972.]

Dibenzyl disulfide [150-60-7] M 246.4, m 71-72°. Crystd from EtOH.

Dibenzylethylenediamine (benzathine, DBED) [140-28-3] M 240.4, m 26°, b 195°/4mm, d 1.02, n 1.563,  $pK_{Est(1)} \sim 5.9$ ,  $pK_{Est(2)} \sim 8.9$ . Dissolve in acid, extract with toluene, basify, extract with Et<sub>2</sub>O, dry over solid KOH, evap and fractionate *in vacuo*. The *diacetate* cryst from H<sub>2</sub>O by addn of EtOH, has m 111° (sol in H<sub>2</sub>O is ~25%). [Frost et al., J Am Chem Soc 71 3842 1949.]

**1,3,4,6-Di-O-benzylidene-D-mannitol** [28224-73-9] M **358.4, m 192-195°, 193°,**  $[\alpha]_D^{20}$ -**11.9° (c 0.7, Me<sub>2</sub>CO).** Recryst from Et<sub>2</sub>O in long fine needles.  $\lambda$ max 256nm ( $\epsilon$  435) in 95% EtOH, R<sub>F</sub> 0.21 (1:1 CCl<sub>4</sub>-EtOAc) on TLC Silica Gel G. [Sinclair Carbohydr Res **12** 150 1970; ORD, CD, NMR, IR, MS: Brecknell et al. Aust J Chem **29** 1749 1976.]

**Dibenzyl ketone (1,3-diphenyl-2-propanone)** [102-04-5] M 210.3, m 34.0°. Fractionally crystd from its melt, then crystd from pet ether. Stored in the dark.

**Dibenzyl malonate** [15014-25-2] **M 284.3, b 188-190°/0.2mm, 193-196°/1mm, d\_4^{20} 1.158, n\_D^{20} 1.5452. Dissolve in toluene, wash with aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and distil. [Ginsburg and Pappo J Am Chem Soc 75 1094 1953; Baker et al. J Org Chem 17 77 1952.]** 

**Dibenzyl sulfide** [538-74-9] **M 214.3, m 48.5°, 50°.** Crystd from EtOH/water (10:1), or repeatedly from  $Et_2O$ . Also chromatographed on  $Al_2O_3$  (pentane as eluent), then recrystd from EtOH [Kice and Bowers J Am Chem Soc 84 2390 1962]. Vacuum dried at 30° over  $P_2O_5$ , fused under nitrogen and re-dried.

2,4-Dibromoaniline [615-57-6] M 250.9, m 79-80°, pK<sup>25</sup> 1.87. Crystd from aqueous EtOH.

9,10-Dibromoanthracene [523-27-3] M 336.0, m 226°. Recrystd from xylene and vacuum sublimed [Johnston et al. J Am Chem Soc 109 1291 1987].

*p*-Dibromobenzene [106-37-6] M 235.9, m 87.8°. Steam distd, crystd from EtOH or MeOH and dried in the dark under vacuum. Purified by zone melting.

2,5-Dibromobenzoic acid [610-71-9] M 279.9, m 157°, pK<sub>Est</sub> ~1.5. Crystd from water or EtOH.

4,4'-Dibromobiphenyl [92-86-4] M 312.0, m 164°, b 355-360°/760mm. Crystd from MeOH.

trans-1,4-Dibromobut-2-ene [821-06-7] M 213.9, m 54°, b 85°/10mm. Crystd from ligroin.

α, α-Dibromodeoxybenzoin [15023-99-1] M 354.0, m 111.8-112.7°. Crystd from acetic acid.

**Dibromodichloromethane** [594-18-3] M 242.7, m 22°. Crystd repeatedly from its melt, after washing with aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and drying with BaO.

**1,3-Dibromo-5,5-dimethylhydantoin** [77-48-5] **M 285.9, m 190-192°dec, 190-193°dec**. Recrystd from H<sub>2</sub>O. Solubility in CCl<sub>4</sub> is 0.003 mol/L at 25° and 0.024 mol/L at 76.5°.

**1,2-Dibromoethane** [106-93-4] M 187.9, f 10.0°, b 29.1°/10mm, 131.7°/760mm, d 2.179,  $n^{15}$  1.54160. Washed with conc HCl or H<sub>2</sub>SO<sub>4</sub>, then water, aqueous NaHCO<sub>3</sub> or Na<sub>2</sub>CO<sub>3</sub>, more water, and dried with CaCl<sub>2</sub>. Fractionally distd. Alternatively, kept in daylight with excess bromine for 2hours, then extracted with aqueous Na<sub>2</sub>SO<sub>3</sub>, washed with water, dried with CaCl<sub>2</sub>, filtered and distd. It can also be purified by fractional crystn by partial freezing. Stored in the dark.

4',5'-Dibromofluorescein [596-03-2] M 490.1, m 285°. Crystd from aqueous 30% EtOH.

5,7-Dibromo-8-hydroxyquinoline [521-74-4] M 303.0, m 196°,  $pK_1^{25}$  5.84,  $pK_2^{25}$  9.56. Crystd from acetone/EtOH. It can be sublimed.

**Dibromomaleic acid** [608-37-7] **M 273.9, m 123.5°, 125°dec, pK\_1^{25} 1.45, pK\_2^{25} 4.62. It has been recrystd from Et<sub>2</sub>O or Et<sub>2</sub>O-CHCl<sub>3</sub>. It is slightly soluble in H<sub>2</sub>O, soluble also in AcOH but insoluble in \*C<sub>6</sub>H<sub>6</sub> and CHCl<sub>3</sub>. [Salmony and Simonis Chem Ber 38 2583 1905; Ruggli Helv Chim Acta 3 566 1929.]** 

2,5-Dibromonitrobenzene [3460-18-2] M 280.9, m 84°. Crystd from acetone.

2,6-Dibromo-4-nitrophenol [99-28-5] M 280.9, m 143-144°, pK<sup>25</sup> 3.39. Crystd from aq EtOH.

2,4-Dibromophenol [615-58-7] M 251.9, m 37°, 41-42°, b 154°/10mm, 239°/atm, pK<sup>25</sup> 7.79. Crystd from CHCl<sub>3</sub> at -40°.

**2,6-Dibromophenol** [608-33-3] **M 251.9, m 56-57°, b 138°/10mm, 255-256°/740mm, pK<sup>25</sup> 6.67.** Vacuum distd (at 18mm), then crystd from cold CHCl<sub>3</sub> or from EtOH/water.

1,3-Dibromopropane [109-64-8] M 201.9, f -34.4°, b  $63-63.5^{\circ}/26mm$ ,  $76-77^{\circ}/40mm$ , 90°/80mm, 165°/atm, d 1.977, n 1.522. Washed with dilute aqueous Na<sub>2</sub>CO<sub>3</sub>, then water. Dried and fractionally distd under reduced pressure.

2,6-Dibromopyridine [626-05-1] M 236.9, m 117-119°, 118.5-119°, b 249°/757.5mm, pK<sub>Est</sub> <0. Purified by steam distn then twice recrystd from EtOH. Does not form an HgCl<sub>2</sub> salt. [den Hertog and Wibaut *Rec Trav Chim Pays Bas* 51 381 1932.]

*meso*-2,3-Dibromosuccinic acid [526-78-3] M 275.9, m 288-290° (sealed tube, dec),  $pK_1^{20}$ 1.56,  $pK_2^{20}$ 2.71. Crystd from distilled water, keeping the temperature below 70°.

**1,2-Dibromotetrafluoroethane** [124-73-2] **M 259.8, b 47.3°/760mm.** Washed with water, then with weak alkali. Dried with CaCl<sub>2</sub> or H<sub>2</sub>SO<sub>4</sub> and distd. [Locke et al. J Am Chem Soc 56 1726 1934.] Also purified by gas chromatography on a silicone DC-200 column.

a,a'-Dibromo-o-xylene [91-13-4] M 264.0, m 95°, b 129-130°/4.5mm. Crystd from CHCl<sub>3</sub>

α,α'-Dibromo-m-xylene [626-15-3] M 264.0, m 77°, b 156-160°/12mm. Crystd from acetone.

α, α'-Dibromo-*p*-xylene [623-24-5] M 264.0, m 145-147°, b 155-158°/12-15 mm, 245°/760mm. Crystd from \*benzene or chloroform.

**Di-n-butylamine** [111-92-2] **M 129.3, b 159°, n 1.41766, d 0.761, pK^{25} 11.25.** Dried with LiAlH<sub>4</sub>, CaH<sub>2</sub> or KOH pellets, filtered and distd from BaO or CaH<sub>2</sub>.

 $\alpha$ -Dibutylamino- $\alpha$ -(*p*-methoxyphenyl)acetamide (Ambucetamide) [519-88-0] M 292.4, m 134°. Crystd from EtOH containing 10% diethyl ether.

2,5-Di-tert-butyl aniline [21860-03-7] M 205.4, m 103-104°, 103-106°,  $pK^{25}$  3.34 (50% aq MeOH), 3.58 (90% aq MeOH). Recrystd from EtOH in fine needles after steam distn. It has a  $pKa^{25}$  of 3.58 (50% aq EtOH) and 3.34 (90% aq MeOH). The tosylate has m 164° (from AcOH). [Bell and Wilson J Chem Soc 2340 1956; Carpenter et al. J Org Chem 16 586 1951; Bartlett et al. J Am Chem Soc 76 2349 1954.]

**Di-tert-butylazodicarboxylate** [870-50-8] **M 230.3, m 90-92°.** Cryst from ligroin. Best purified by covering the dry solid (22g) with pet ether (b 30-60°, 35-40 mL) and adding ligroin (b 60-90°) to the boiling soln until the solid dissolves. On cooling, large lemon yellow crystals of the ester separate (~ 20g), m 90.7-92°. Evapn of the filtrate gives a further crop of crystals [Carpino and Crowley Org Synth 44 18 1964].

*p*-Di-tert-butylbenzene [1012-72-2] M 190.3, m 80°. Crystd from diethyl ether, EtOH and dried under vacuum over P<sub>2</sub>O<sub>5</sub> at 55°. [Tanner et al. J Org Chem 52 2142 1987.]

2,6-Di-tert-butyl-1,4-benzoquinone [719-22-2] M 220.3, m 66-67°. It can be recrystd from MeOH and sublimed in a vaccum.

3,5-Di-tert-butyl-o-benzoquinone [3383-21-9] M 220.3, m 112-114°, 113-114°. It can be recrystd from MeOH or pet ether, and forms fine red plates or rhombs. [Flaig et al. Justus Liebigs Ann Chem 597 196 1955; IR: Ley and Müller Chem Ber 89 1402 1956.]

3,5-Di-tert-butyl catechol [1020-31-1] M 222.3, m 99°, 99-100°,  $pK_{Est(1)} \sim 11.0$ ,  $pK_{Est(2)} \sim 13.1$ . Recrystd from pet ether. [ Ley and Müller Chem Ber 89 1402 1956; UV Flaig et al. Z Naturforschung 10b 668 1955.] Also crystd three times from pentane [Funabiki et al. J Am Chem Soc 108 2921 1986].

**Dibutylcarbitol** [di(ethyleneglycol)dibutyl ether] [112-73-2] M 218.3, b 125-130°/0.1mm, d 0.883, n 1.424. Freed from peroxides by slow passage through a column of activated alumina. The eluate was shaken with Na<sub>2</sub>CO<sub>3</sub> (to remove any remaining acidic impurities), washed with water, and stored with CaCl<sub>2</sub> in a dark bottle [Tuck J Chem Soc 3202 1957].

2,6-Di-tert-butyl-p-cresol (2,6-di-tert-butyl-4-methylphenol, butylatedhydroxytoluene, BHT) [128-37-0] M 230.4, m 71.5°,  $pK^{25}$  12.23. Dissolved in *n*-hexane at room temperature, then cooled with rapid stirring, to -60°. The ppte was separated, redissolved in hexane, and the process was repeated until the mother liquor was no longer coloured. The final product was stored under N<sub>2</sub> at 0° [Blanchard J Am Chem Soc 82 2014 1960]. Also crystd from EtOH, MeOH, \*benzene, *n*-hexane, methylcyclohexane or pet ether (b 60-80°), and dried under vacuum.

**Di**-tert-butyl dicarbonate (di-tert-butyl pyrocarbonate) [24424-99-5] M 218.3, m 23° (21-22°), b 55-56°/0.15mm, 62-65°/0.4mm, d 0.950, n 1.409. Melt by heating at ~35°, and distil in vac. If IR and NMR (v 1810m 1765 cm<sup>-1</sup>,  $\delta$  in CCl<sub>4</sub> 1.50 singlet) suggest very impure then wash with equal vol of H<sub>2</sub>O containing citric acid to make the aqueous layer slightly acidic, collect the organic layer and dry over anhyd MgSO<sub>4</sub> and distil in vac. [Pope et al. Org Synth 57 45 1977.] FLAMMABLE.

2,6-Di-tert-butyl-4-dimethylaminomethylphenol [88-27-7] M 263.4, m 93-94°, b 172°/30mm, pK<sub>Est</sub> ~12.0. Crystd from *n*-hexane.

**Di**-tert-butyldiperphthalate [2155-71-7] M 310.3, m dec explosively, CARE. Crystd from diethyl ether. Dried over H<sub>2</sub>SO<sub>4</sub>.

**2,6-Di**-tert-butyl-4-ethylphenol [4]30-42-1] M 234.4, m 42-44°, pK<sub>Est</sub> ~12.3. Cryst from aqueous EtOH or *n*-hexane.

N, N-Dibutyl formamide [761-65-9] M 157.3, b 63°/0.1mm, 118-120°/15mm, 244-246°/760mm,  $d_4^{20}$  0.878,  $n_D^{20}$  1.445. Purified by fractn distn [Mandel and Hill J Am Chem Soc 76 3981 1954].

2,5-Di-tert-butylhydroquinone [88-58-4] M 222.3, m 222-223°. Crystd from \*C<sub>6</sub>H<sub>6</sub> or AcOH.

**2,4-Di**-*tert*-**butyl**-**4**-**isopropylphenol** [5427-03-2] **M 248.4**, **m 39-41°**, **pK**<sub>Est</sub> ~**12.3**. Crystd from *n*-hexane or aq EtOH.

2,6-Di-tert-butyl-4-methylpyridine [38222-83-2] M 205.4, m 31-32°, 33-36°, b 148-153°/ 95mm, 223°/760mm,  $n_4^{20}$  1.476, pK<sub>Est</sub> ~5.7. Possible impurity is 2,6-di-tert-butyl-4neopentylpyridine. Attempts to remove coloured impurities directly by distn, acid-base extraction or treatment with activated charcoal were unsuccessful. Pure material can be obtained by dissolving 0.3mole of the alkylpyridine in pentane (150mL) and introducing it at the top of a water jacketed chromatographic column (40 x 4.5cm) the cooling is necessary because the base in pentane reacts exothermically with alumina) containing activated and acidic alumina (300g). The column is eluted with pentane using a 1L constant pressure funnel fitted at the top of the column to provide slight press. All the pyridine is obtained in the first two litres of eluent (the progress of elution is monitored by spotting a fluorescent TLC plate and examining under short wave UV light - a dark blue spot is evidence for the presence of the alkylpyridine). Elution is complete in 1h. Pentane is removed on a rotovap with 90-93% recovery yielding a liquid which solidifies on cooling, m 31-32°, and the base can be distilled. The HPtCl<sub>6</sub> salt has m 213-314° (dec), and the CF<sub>3</sub>SO<sub>3</sub>H salt has m 202.5-203.5° (from CH<sub>2</sub>Cl<sub>2</sub>). [Org Synth **60** 34 1981.]

**Di-tert-butyl peroxide** (tert-butyl peroxide) [110-05-4] M 146.2, d 0.794, n 1.389. Washed with aqueous AgNO<sub>3</sub> to remove olefinic impurities, water and dried (MgSO<sub>4</sub>). Freed from tert-butyl hydroperoxide by passage through an alumina column [Jackson et al. J Am Chem Soc 107 208 1985], and if necessary two high vacuum distns from room temp to a liquid-air trap [Offenbach and Tobolsky J Am Chem Soc 79 278 1957]. The necessary protection from EXPLOSION should be used.

2,6-Di-tert-butylphenol [128-39-2] M 206.3, m 37-38°, pK<sup>25</sup> 11.70. Crystd from aqueous EtOH or *n*-hexane.

Dibutyl phthalate [84-74-2] M 278.4, b 206°/20mm, 340°/760mm, d 1.4929,  $d^5$  1.0426,  $n^{25}$  1.490. Washed with dilute NaOH (to remove any butyl hydrogen phthalate), aqueous NaHCO<sub>3</sub> (charcoal), then distd water. Dried with CaCl<sub>2</sub>, distd under vacuum, and stored in a desiccator over P<sub>2</sub>O<sub>5</sub>. (See also p. 151.)

2,6-Di-*tert*-butylpyridine [585-48-8] M 191.3, b 100-101°/23mm, d 0.852, n 1.474, pK<sup>25</sup> 5.02. Redistd from KOH pellets.

§ Polystyrene supported version is commercially available.

**Di-n-butyl sulfide** [544-40-1] **M 146.3**,  $\alpha$ -form b 182°,  $\beta$ -form 190-230°(dec). Washed with aq 5% NaOH, then water. Dried with CaCl<sub>2</sub> and distd from sodium.

Di-n-butyl sulfone [598-04-9] M 162.3, m 43.5°. Purified by zone melting.

N,N'-Di-tert-butylthiourea [4041-95-6] M 188.3, m 174-175° (evac capillary). Recrystd from H<sub>2</sub>O [Bortnick et al. J Am Chem Soc 78 4358 1956].

3,5-Dicarbethoxy-1,4-dihydrocollidine [632-93-9] M 267.3, m 131-132°. Crystd from hot EtOH/water.

**Dichloramine-T** (*N*,*N*-dichloro-*p*-toluenesulfonamide) [473-34-7] M 240.1, m 83°. Crystd from pet ether (b 60-80°) or CHCl<sub>3</sub>/pet ether. Dried in air. (see also chloramine-T in Chapter 5).

Dichloroacetic acid [79-43-6] M 128.9, m 13.5°, b 95.0-95.5°/17-18mm, d 1.563, n 1.466,  $pK^{25}$  1.35. Crystd from \*benzene or pet ether. Dried with MgSO<sub>4</sub> and fractionally distd. [Bernasconi et al. J Am Chem Soc 107 3612 1985.]

sym-Dichloroacetone (1,3-dichloropropan-2-one) [534-07-6] M 127.0, m 41-43°, 45°, b 86-88°/12mm, 75-77°/22mm, 172-172.5°/atm, 170-175° /atm, d 1.383. Crystd from CCl<sub>4</sub>, CHCl<sub>3</sub> and \*benzene. Distd under vacuum. [Conant and Quayle Org Synth Coll Vol 211 1941; Hall and Sirel J Am Chem Soc 74 836 1952]. It is dimorphic [Daasch and Kagarise J Am Chem Soc 77 6156 1955]. The oxime has m 130-131°, b 106°/25mm [Arzneimittel-Forsch 8 638 1958].

Dichloroacetonitrile [3018-12-0] M 110.0, b 110-112°, d 1.369, n 1.440. Purified by distn and by gas chromatography. FLAMMABLE.

**2,4-Dichloroaniline** [554-00-7] **M 162.0, m 63°, pK^{25} 2.02.** Crystd from EtOH/water. Also crystd from EtOH and dried *in vacuo* for 6h at 40° [Moore et al. J Am Chem Soc 108 2257 1986; Edidin et al. J Am Chem Soc 109 3945 1987].

3,4-Dichloroaniline [95-76-1] M 162.0, m 71.5°, pK<sup>25</sup> 2.97. Crystd from MeOH.

**9,10-Dichloroanthracene** [605-49-1] **M 247.1, m 214-215°.** Purified by crystn from MeOH or EtOH, followed by sublimation under reduced pressure. [Masnori and Kochi J Am Chem Soc 107 7880 1985.]

2,4-Dichlorobenzaldehyde [874-42-0] M 175.0, m 72°. Crystd from EtOH or ligroin.

2,6-Dichlorobenzaldehyde [83-38-5] M 175.0, m 70.5-71.5°. Crystd from EtOH/water or pet ether (b 30-60°).

o-Dichlorobenzene [95-50-1] M 147.0, b 81-82°/31-32mm, 180.5°/760mm, d 1.306, n 1.551,  $n^{25}$  1.549. Contaminants may include the *p*-isomer and trichlorobenzene [Suslick et al. J Am Chem Soc 106 4522 1984]. It was shaken with conc or fuming H<sub>2</sub>SO<sub>4</sub>, washed with water, dried with CaCl<sub>2</sub>, and distd from CaH<sub>2</sub> or sodium in a glass-packed column. Low conductivity material (*ca* 10<sup>-10</sup> mhos) has been obtained by refluxing with P<sub>2</sub>O<sub>5</sub>, fractionally distilled and passed through a column packed with silica gel or activated alumina: it was stored in a dry-box under N<sub>2</sub> or with activated alumina.

*m*-Dichlorobenzene [541-73-1] M 147.0, b 173.0°, d 1.289, n 1.54586,  $n^{25}$  1.54337. Washed with aqueous 10% NaOH, then with water until neutral, dried and distd. Conductivity material (*ca* 10<sup>-10</sup> mhos) has been prepared by refluxing over P<sub>2</sub>O<sub>5</sub> for 8h, then fractionally distilling, and storing with activated alumina. *m*-Dichlorobenzene dissolves rubber stoppers.

*p*-Dichlorobenzene [106-46-7] M 147.0, m 53.0°, b 174.1°, d 1.241, n<sup>60</sup> 1.52849. *o*-Dichlorobenzene is a common impurity. Has been purified by steam distn, crystn from EtOH or boiling MeOH, air-dried and dried in the dark under vacuum. Also purified by zone refining.

2,2'-Dichlorobenzidine [84-68-4] M 253.1, m 165°, pK<sub>Est(1)</sub> ~3.0, pK<sub>Est(2)</sub>~4.0. Crystd from EtOH.

**3,3'-Dichlorobenzidine** [91-94-1] **M 253.1, m 132-133°, pK**<sub>Est(1)</sub> ~4.8, pK<sub>Est(2)</sub>~5.7. Crystd from EtOH or \*benzene. CARCINOGEN.

**2,4-Dichlorobenzoic acid** [50-84-0] **M 191.0, m 163-164°, pK<sup>25</sup> 2.68.** Crystd from aqueous EtOH (charcoal), then \*benzene (charcoal). It can also be recrystd from water.

2,5-Dichlorobenzoic acid [50-79-3] M 191.0, m 154°, b 301°/760mm, pK<sup>25</sup> 2,47. Crystd from water.

2,6-Dichlorobenzoic acid [50-30-6] M 191.0, m 141-142°, pK<sup>25</sup> 1.59. Crystd from EtOH and sublimed in vacuo.

**3,4-Dichlorobenzoic acid** [51-44-5] M 191.0, m 206-207°, pK<sup>25</sup> 3.64. Crystd from aqueous EtOH (charcoal) or acetic acid.

3,5-Dichlorobenzoic acid [51-36-5] M 191.0, m 188°, pK<sup>25</sup> 3.54. Crystd from EtOH and sublimed in a vacuum.

2,6-Dichlorobenzonitrile [1194-65-6] M 172.0, m 145°. Crystd from acetone.

**4,4'-Dichlorobenzophenone** [90-98-2] M **251.1, m 145-146°.** Recrystd from EtOH [Wagner et al. J Am Chem Soc **108** 7727 1986].

**2,5-Dichloro-1,4-benzoquinone** [615-93-0] **M 177.0, m 161-162°.** Recrystd twice from 95% EtOH as yellow needles [Beck et al. J Am Chem Soc **108** 4018 1986].

**2,6-Dichloro-1,4-benzoquinone** [697-91-6] **M 177.0, m 122-124°.** Recrystd from pet ether (b 60-70°) [Carlson and Miller J Am Chem Soc **107** 479 1985].

**2,6-Dichlorobenzoyl chloride** [4659-45-4] M **209.5, m 15-17, b 122-124°/15mm, d 1.464.** Reflux for 2h with excess of acetyl chloride (3 vols), distil off AcCl followed by the benzoyl chloride. Store away from moisture. It is an **IRRITANT**.

3,4-Dichlorobenzyl alcohol [1805-32-9] M 177.0, m 38-39°. Crystd from water.

2,3-Dichloro-1,3-butadiene [1653-19-6] M 123.0, b 41-43°/85mm, 98°/760mm. Crystd from pentane to constant melting point about -40°. A mixture of *meso* and *d*,*l* forms was separated by gas chromatography on an 8m stainless steel column (8mm i.d.) with 20% DEGS (diethyleneglycolsilyl chloride) on Chromosorb W (60-80 mesh) at 60° and 80mL He/min. [Su and Ache J Phys Chem 80 659 1976.]

(+) and (-) (8,8-Dichlorocamphorylsulfonyl)oxaziridine [127184-05-8] M 298.2, m 178-180°, 183-186°,  $[\alpha]_D^{20}$  (+) and (-) 88.3° (c 1.3, CHCl<sub>3</sub>), (+) and (-) 91° (c 5, CHCl<sub>3</sub>). Recryst from EtOH [Davis and Weismiller *J Org Chem* 55 3715 1990].

cis-3,4-Dichlorocyclobutene [2957-95-1] M 123.0, b 70-71°/55mm, 74-76°/55mm,  $d_4^{20}$ 1.297,  $n_D^{20}$  1.499. Distd at 55mm through a 36-in platinum spinning band column, a fore-run b 58-62°/55mm is mainly 1,4-dichlorobutadiene. When the temperature reaches 70° the reflux ratio is reduced to 10:1 and the product is collected quickly. It is usually necessary to apply heat frequently with a sun lamp to prevent any dichlorobutadiene from clogging the exit in the early part of the distn [Pettit and Henery Org Synth 50 36 1970].

2,3-Dichloro-5,6-dicyano-p-benzoquinone (DDQ) [84-58-2] M 227.0, m 203° (dec). Crystd from CHCl<sub>3</sub>, CHCl<sub>3</sub>/\*benzene (4:1), or \*benzene and stored at 0°. [Pataki and Harvey J Org Chem 52 2226 1987.]

**β,β'-Dichlorodiethyl ether** [111-44-4] **M 143.0, b 79-80<sup>o</sup>/20mm, 176-177.0<sup>o</sup>/743mm, n 1.457, d 1.219.** See bis-(β-dichloroethyl)ether on p. 134.

1,2-Dichloro-1,2-difluoroethane [431-06-1] M 134.9, b 59°, n 1.376. Purified by fract dist [Hazeldine J Chem Soc 4258 1952]. For purification of diastereoisomeric mixture, with resolution into meso and rac forms, see Machulla and Stocklin [J Phys Chem 78 658 1974].

**Dichlorodifluoromethane** (Freon 12) [75-71-8] M 120.9, m -158°, b -29.8°/atm, 42.5°/10atm. Passage through saturated aqueous KOH then conc H<sub>2</sub>SO<sub>4</sub>, and a tower packed with activated copper on Kielselguhr at 200° removed CO<sub>2</sub> and O<sub>2</sub>. A trap cooled to -29° removed a trace of high boiling material. It is a non-flammable propellant.

**1,3-Dichloro-5,5'-dimethylhydantoin** [118-52-5] M **197.0**, m **132-134°**, **136°**. Purified by dissolving in conc  $H_2SO_4$  and diluting with ice  $H_2O$ , dry and rerystd from CHCl<sub>3</sub>. It sublimes at 100° in a vacuum. Exhibits time dependent hydrolysis at pH 9. [Petterson and Grzeskowiak J Org Chem 24 1414 1959.]

**4,5-Dichloro-3H-1,2-dithiol-3-one** [1192-52-5] **M 187.1, m 52-56°, 61°, b 87°/0.5 mm, 125°/11mm.** Distd *in vacuo* and then recrystd from pet ether. IR: v 1650 cm<sup>-1</sup> [Boberg Justus Liebigs Ann Chem 693 212 1966].

1,1-Dichloroethane (ethylidene dichloride) [75-34-3] M 99.0, b 57.3°, d<sup>15</sup> 1.18350, d 1.177,  $n^{15}$  1.41975. Shaken with conc H<sub>2</sub>SO<sub>4</sub> or aqueous KMnO<sub>4</sub>, then washed with water, saturated aqueous NaHCO<sub>3</sub>, again with water, dried with K<sub>2</sub>CO<sub>3</sub> and distd from CaH<sub>2</sub> or CaSO<sub>4</sub>. Stored over silica gel.

**1,2-Dichloroethane** [107-06-2] **M 99.0, b 83.4°, d 1.256, n^{15} 1.44759.** Usually prepared by chlorinating ethylene, so that likely impurities include higher chloro derivatives and other chloro compounds depending on the impurities originally present in the ethylene. It forms azeotropes with water, MeOH, EtOH, trichloroethylene, CCl<sub>4</sub> and isopropanol. Its azeotrope with water (containing 8.9% water, and b 77°) can be used to remove gross amounts of water prior to final drying. As a preliminary purification step, it can be steam distd, and the lower layer was treated as below.

Shaken with conc  $H_2SO_4$  (to remove alcohol added as an oxidation inhibitor), washed with water, then dilute KOH or aqueous  $Na_2CO_3$  and again with water. After an initial drying with CaCl<sub>2</sub>, MgSO<sub>4</sub> or by distn, it is refluxed with  $P_2O_5$ , CaSO<sub>4</sub> or CaH<sub>2</sub> and fractionally distd. Carbonyl-containing impurities can be removed as described for chloroform.

**1,2-Dichloroethylene** [cis + trans 540-59-0] **M 96.9, b 60°** (cis), d 1.284, b 48° (trans), d 1.257. Shaken successively with conc  $H_2SO_4$ , water, aqueous NaHCO<sub>3</sub> and water. Dried with MgSO<sub>4</sub> and distn separated the cis- and trans-isomers.

cis-1,2-Dichloroethylene [156-59-2] M 96.9, b 60.4°, d 1.2830,  $n^{15}$  1.44903, n 1.4495. Purified by careful fractional distn, followed by passage through neutral activated alumina. Also by shaking with mercury, drying with K<sub>2</sub>CO<sub>3</sub> and distn. from CaSO<sub>4</sub>.

trans-1,2-Dichloroethylene [156-60-5] M 96.9, b 47.7°, n<sup>15</sup> 1.45189, n 1.4462, d 1.2551. Dried with MgSO<sub>4</sub>, and fractionally distd under CO<sub>2</sub>. Fractional crystn at low temperatures has also been used.

**5,7-Dichloro-8-hydroxyquinoline** [773-76-2] **M 214.1, m 180-181°, pK<sub>1</sub> 1.89, pK<sub>2</sub> 7.62.** Crystd from acetone/EtOH.

**2,3-Dichloromaleic anhydride** [1122-17-4] M 167.0, m 105-115°, 120°, 121-121.5°. Purified by sublimation *in vacuo* [Katakis et al. J Chem Soc, Dalton Trans 1491 1986]. It has also been purified by Soxhlet extraction with hexane, recrystd from CHCl<sub>3</sub> and sublimed [MS, Relles J Org Chem 37 3630 1972].

**Dichloromethane** (methylene dichloride) [75-09-2] M 84.9, b 40.0°, d 1.325, n 1.42456, n<sup>25</sup>1.4201. Shaken with portions of conc H<sub>2</sub>SO<sub>4</sub> until the acid layer remained colourless, then washed with water, aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub> or NaOH, then water again. Pre-dried with CaCl<sub>2</sub>, and distd from CaSO<sub>4</sub>, CaH<sub>2</sub> or P<sub>2</sub>O<sub>5</sub>. Stored away from bright light in a brown bottle with Linde type 4A molecular sieves, in an atmosphere of dry N<sub>2</sub>. Other purification steps include washing with aq Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, passage through a column of silica gel, and removal of carbonyl-containing impurities as described under Chloroform. It has also been purified by treatment with basic alumina, distd, and stored over molecular sieves under nitrogen [Puchot et al. J Am Chem Soc 108 2353 1986].

Dichloromethane from Japanese sources contained MeOH as stabiliser which is not removed by distn. It can, however, be removed by standing over activated 3A Molecular Sieves (note that 4A Sieves cause the development of pressure in bottles), passed through activated  $Al_2O_3$  and distd [Gao et al. *J Am Chem Soc* 109 5771 1987]. It has been fractionated through a platinum spinning band column, degassed, and distd onto degassed molecular sieves, Linde 4A, heated under high vacuum at over 450° until the pressure readings reached the low values of  $10^{-6}$  mm —  $\sim 1-2h$  [Mohammad and Kosower *J Am Chem Soc* 93 2713 1971]. **Rapid purification:** Reflux over CaH<sub>2</sub> (5% w/v) and distil. Store over 4A molecular sieves.

3,9-Dichloro-7-methoxyacridine [86-38-4] M 278.1, m 160-161°. Crystd from \*benzene.

5,7-Dichloro-2-methyl-8-hydroxyquinoline (5,7-dichloro-8-hydroxyquinaldine) [72-80-0] M 228.1, m 114-115°, pK<sub>Est(1)</sub>~2.0, pK<sub>Est(2)</sub>~8.4. Crystd from EtOH.

**2,4-Dichloro-6-methylphenol** [1570-65-6] **M 177.0, m 55°, b 129-132°/40mm, pK<sup>20</sup> 8.14.** Crystd from water.

2,4-Dichloro-1-naphthol (2050-76-2) M 213.1, m 106-107°, pK<sub>Est</sub> ~7.7. Crystd from MeOH.

2,3-Dichloro-1,4-naphthoquinone [117-80-6] M 227.1, m 193°. Crystd from EtOH.

**2,5-Dichloro-4-nitroaniline** [6627-34-5] M **207.0**, m **157-158°**,  $pK^{25}$  -1.74 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH, then sublimed.

2,6-Dichloro-4-nitroaniline [99-30-9] M 207.0, m 193°. Crystd from aq EtOH or \*benzene/EtOH.

2,5-Dichloro-1-nitrobenzene [89-61-2] M 192.0, m 56°. Crystd from absolute EtOH.

3,4-Dichloro-1-nitrobenzene [99-54-7] M 192.0, m 43°. Crystd from absolute EtOH.

2,4-Dichloro-6-nitrophenol [609-89-2] M 208.0, m 122-123°, pK<sub>Est</sub> ~5.0. Crystd from AcOH.

2,6-Dichloro-4-nitrophenol [618-00-4] M 208.0, m 125°, pK<sup>25</sup> 3.55. Crystd from EtOH and dried in vacuo over anhydrous MgSO<sub>4</sub>.

**4,6-Dichloro-5-nitropyrimidine** [4316-93-2] M 194.0, m 100-103°, 101-102°,  $pK_{Est} < 0$ . If too impure then dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dry over MgSO<sub>4</sub>, evaporate to dryness and recrystallise from pet ether (b 85-105°) as a light tan solid. It is sol in *ca* 8 parts of MeOH [Boon et al, *J Chem Soc* 96 1951; Montgomery et al. in *Synthetic Procedures in Nucleic Acid Chemistry* (Zorbach and Tipson eds) Wiley & Sons, NY, p76 1968].

Dichlorophen [2,2'-methylenebis(4-chlorophenol)] [97-23-4] M 269.1, b 177-178°, pK<sub>Est</sub> ~9.7. Crystd from toluene.

2,3-Dichlorophenol [576-24-9] M 163.0, m 57°, pK<sup>25</sup> 7.70. Crystd from ether.

**2,4-Dichlorophenol** [120-83-2] **M 163.0, m 42-43°, pK^{25} 7.89.** Crystd from pet ether (b 30-40°). Purified by repeated zone melting, using a P<sub>2</sub>O<sub>5</sub> guard tube to exclude moisture. Very *hygroscopic* when dry.

2,5-Dichlorophenol [583-78-8] M 163.0, m 58°, b 211°/744mm, pK<sup>25</sup> 7.51. Crystd from ligroin and sublimed.

**3,4-Dichlorophenol** [95-77-2] **M 163.0, m 68°, b 253.5°/767mm, pK<sup>25</sup> 8.58.** Crystd from pet ether/\*benzene mixture.

**3,5-Dichlorophenol** [591-35-5] **M 163.0, m 68°, b 122-124°/8mm, 233-234°/760mm, pK<sup>25</sup> 8.81.** Crystd from pet ether/\*benzene mixture.

2,4-Dichlorophenoxyacetic acid (2,4-D) [94-75-7] M 221.0, m 146°, pK<sup>25</sup> 2.90. Crystd from MeOH. TOXIC.

 $\alpha$ -(2,4-Dichlorophenoxy)propionic acid (2,4-DP, Dichloroprop) [120-36-5] M 235.1, m 117°, pK<sup>20</sup> 2,86, Crystd from MeOH. TOXIC.

**2,4-Dichlorophenylacetic acid** [19719-28-9] **M 205.0, m 131°, 132-133°, pK**<sub>Est</sub> ~4.0. Crystd from aqueous EtOH.

2,6-Dichlorophenylacetic acid [6575-24-2] M 205.0, m 157-158°, pK<sub>Est</sub> ~3.8. Crystd from aqueous EtOH.

**3-(3,4-Dichlorophenyl)-1,1-dimethyl urea (Diuron)** [330-54-1] **M 233.1.** Crystd four times from 95% EtOH [Beck et al. J Am Chem Soc 108 4018 1986].

**4,5-Dichloro-***o***-phenylenediamine** [5348-42-5] **M 177.1, m 162°, 162-163°, pK**<sub>Est(1)</sub> ~-**1.0, pK**<sub>Est(2)</sub>~**2.9.** Recrystd from hexane, \*C<sub>6</sub>H<sub>6</sub>, pet ether or H<sub>2</sub>O (Na<sub>2</sub>SO<sub>4</sub>) and sublimed at 150%/15mm.

**4,5-Dichlorophthalic** acid [56962-08-4] M 235.0, m 200° (dec to anhydride),  $pK_{Est(1)}$  2.2,  $pK_{Est(2)}$ ~4.7. Crystd from water. Can be purified by converting to the anhydride, reacting with boiling EtOH to form the *monoethyl ester* (m 133-134°) and hydrolysing back to the diacid

**3,6-Dichlorophthalic anhydride** [4466-59-5] **M 189-191°, 191-191.5°, b 339°.** Boil in xylene (allowing any vapours which would contain  $H_2O$  to be removed, e.g. Dean and Stark trap), which causes the acid to dehydrate to the anhydride and cool. Recryst from xylene [Villiger Chem Ber 42 3539 1909; Fedoorow Izv Akad Nauk SSSR Otd Khim Nauk 397 1948, Chem Abstr 1585 1948].

1,2-Dichloropropane [78-87-5] M 113°, b 95.9-96.2°, d 1.158, n 1.439. Distd from CaH<sub>2</sub>.

2,2-Dichloropropane [594-20-7] M 113.0, b 69.3°, d 1.090, n 1.415. Washed with aqueous Na<sub>2</sub>CO<sub>3</sub> soln, then distilled water, dried over CaCl<sub>2</sub> and fractionally distd.

2,6-Dichloropurine [5451-40-1] M 189.0, m 180-181.5°, 181°, 185-195°(dec), 188-189°, pK<sub>1</sub><sup>20</sup> 1.16 (aq H<sub>2</sub>SO<sub>4</sub>), pK<sub>2</sub><sup>20</sup> 7.06. It can be recrystd from 150 parts of boiling H<sub>2</sub>O and dried at 100° to constant weight. Soluble in EtOAc. The HgCl<sub>2</sub> salt separates from EtOH soln. UV:  $\lambda$ max 275nm ( $\varepsilon$  8.9K) at pH 1; and 280nm ( $\varepsilon$  8.5K) at pH 11 [Elion and Hitchings J Am Chem Soc 78 3508 1956; Schaeffer and Thomas J Am Chem Soc 80 3738 1958; Beaman and Robins J Appl Chem (London) 12 432 1962; Montgomery J Am Chem Soc 78 1928 1956].

**2,6-Dichloropyridine** [2402-78-0] **M 148.0, m 87-88°, pK -2.86 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from EtOH.

3,5-Dichloropyridine [2457-47-8] M 148.0, m 64-65°, pK<sup>25</sup> 0.67. Crystd from EtOH.

**4,7-Dichloroquinoline** [86-98-6] **M** 198.1, **m** 86.4-87.4°, **b** 148°/10mm, **pK**<sup>25</sup> 2.80. Crystd from MeOH or 95% EtOH.

**2,3-Dichloroquinoxaline** [2213-63-0] **M 199.0, m 152-153°, 152-154°, pK<sub>Est</sub> <0.** Recrystd from \*C<sub>6</sub>H<sub>6</sub> and dried in a vacuum [Cheeseman J Chem Soc 1804 1955].

2,6-Dichlorostyrene [28469-92-3] M 173.0, b 72-73°/2mm, d 1.4045, n 1.5798. Purified by fractional crystn from the melt and by distn.

2,4-Dichlorotoluene [95-73-8] M 161.1, m -13.5°, b 61-62°/3mm, d 1.250, n 1.5513. Recrystd from EtOH at low temperature or fractionally distd.

2,6-Dichlorotoluene [118-69-4] M 161.1, b 199-200°/760mm, d 1.254, n 1.548. Fractionally distd and collecting the middle fraction.

**3,4-Dichlorotoluene** [95-75-0] **M 161.1, m -16°, b 205°/760mm, d 1.2541, n 1.549.** Recrystd from EtOH at very temperature or fractionally distd.

α,α'-Dichloro-p-xylene [623-25-6] M 175.1, m 100°. Crystd from \*benzene and dried under vacuum.

**Dicinnamalacetone** (1,9-diphenyl-1,3,6,8-nonatetraen-5-one) [622-21-9] M 314.4, m 146°. Crystd from \*benzene/isooctane (1:1).

**Dicumyl peroxide** [80-43-3] M 270.4, m 39-40°. Crystd from 95% EtOH (charcoal). Stored at 0°. *Potentially* EXPLOSIVE.

9,10-Dicyanoanthracene [1217-45-4] M 228.3, m 340°. Recrystd twice from pyridine [Mattes and Farid J Am Chem Soc 108 7356 1986].

1,2-Dicyanobenzene [91-15-6] M 128.1, m 141°. (See phthalonitrile on p. 334.)

1,4-Dicyanobenzene [623-26-7] M 128.1, m 222°. Crystd from EtOH.

1,4-Dicyanonaphthalene [3029-30-9] M 178.2, m 206°. Purified by crystn and sublimed in vacuo.

**1,3-Dicyclohexylcarbodimide** (DCC) [538-75-0] M 206.3, m 34-35°, b 95-97°/0.2mm, 120-121°/0.6mm, 155°/11mm. It is sampled as a liquid after melting in warm H<sub>2</sub>O. It is sensitive to air and *it is a potent skin irritant*. It can be distd in a vacuum and stored in a tightly stoppered flask in a freezer. It is very soluble in CH<sub>2</sub>Cl<sub>2</sub> and pyridine where the reaction product with H<sub>2</sub>O, after condensation, is dicyclohexyl urea which is insoluble and can be removed by filtration. Alternatively dissolve in CH<sub>2</sub>Cl<sub>2</sub> add powdered anhyd MgSO<sub>4</sub> shake 4h, filter, evaporate and distil at 0.6 mm press and oil bath temperature 145°. [Biochem Prep 10, 122 1963; Justus Liebigs Ann Chem 571 83 1951; Justus Liebigs Ann Chem 612 11 1958.]

cis-Dicyclohexyl-18-crown-6 [16069-36-6] M 372.5, m 47-50°. Purified by chromatography on neutral alumina and eluting with an ether/hexane mixture [see *Inorg Chem* 14 3132 1975]. Dissolved in ether at ca 40°, and spectroscopic grade MeCN was added to the soln which was then chilled. The crown ether ppted and was filtered off. It was dried *in vacuo* at room temperature [Wallace J Phys Chem 89 1357 1985]. SKIN IRRITANT.

**Di**-*n*-decylamine [1120-49-6] M 297.6, m 34°. b 153°/1mm, 359°/760mm,  $pK_{Est} \sim 11.0$ . Dissolved in \*benzene and ppted as its bisulfate by shaking with 4M H<sub>2</sub>SO<sub>4</sub>. Filtered, washed with \*benzene, separating by centrifugation, then the free base was liberated by treating with aqueous NaOH [McDowell and Allen J Phys Chem 65 1358 1961].

Didodecylamine [3007-31-6] M 353.7, m 51.8°, pK<sup>25</sup> 11.00. Crystd from EtOH/\*C<sub>6</sub>H<sub>6</sub> under N<sub>2</sub>.

**Didodecyldimethylammonium bromide** [3282-73-3] **M 463.6, m 157-162°.** Recrystd from acetone, acetone/ether mixture, then from ethyl acetate, washed with ether and dried in a vacuum oven at 60° [Chen et al. J Phys Chem 88 1631 1984; Rupert et al. J Am Chem Soc 107 2628 1985; Halpern et al. J Am Chem Soc 108 3920 1986; Allen et al. J Phys Chem 91 2320 1987].

Dienestrol [4,4'-(diethylidene-ethylene)diphenol, Dienol] [84-17-3] M 266.3, m 227-228°, 231-233°, pK<sub>Est</sub> ~9.8. Crystd from EtOH or dilute EtOH, sublimes at 130°/1mm. The diacetate has m 119-120° (from EtOH) [Hobday and Short J Chem Soc 609 1943].

Diethanolamine (2,2'-iminodiethanol) [111-42-2] M 105.1, m 28°, b 154-155°/10mm, 270°/760mm pK<sup>25</sup> 8.88. Fractionally distd twice, then fractionally crystd from its melt.

**3,4-Diethoxy-3-cyclobutene-1,2-dione** (diethyl squarate) [5321-87-8] M 170.2, b 89-91°/0.4mm, 88-92°/0.4mm,  $d_4^{20}$  1.162,  $n_D^{25}$  1.5000. Dissolve in Et<sub>2</sub>O, wash with Na<sub>2</sub>CO<sub>3</sub>, H<sub>2</sub>O and dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate and distil using a Kügelrohr or purify by chromatography. Use a Kieselgel column and elute with 20% Et<sub>2</sub>O-Pet ether (b 40-60°) then with Et<sub>2</sub>O-pet ether (1:1), evaporate and distil *in vacuo*. [Dehmlow and Schell Chem Ber 113 1 1980; Perri and Moore J Am Chem Soc 112 1897 1990; IR: Cohen and Cohen J Am Chem Soc 88 1533 1966.] It can cause severe dermatitis [Foland et al. J Am Chem Soc 111 975 1989].

*N*, *N*-Diethylacetamide [685-91-6] M 157.2, b 86-88°, n 1.474, d 0.994. Dissolved in cyclohexane, shaken with anhydrous BaO and then filtered. The procedure was repeated three times, and the cyclohexane was distd off at 1 atmosphere pressure. The crude amide was also fractionally distd three times from anhydrous BaO.

Diethyl acetamidomalonate [1068-90-2] M 217.2, m 96°. Crystd from \*benzene/pet ether.

**Diethyl acetylenedicarboxylate** [762-21-0] **M 170.2, b 60-62°/0.3mm, 107-110°/11mm, 118-120°/20mm, d<sub>4</sub><sup>20</sup> 1.0735, n<sub>D</sub><sup>20</sup> 1.4428.** Dissolve in  $*C_6H_6$ , wash with NaHCO<sub>3</sub>, H<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil in a vacuum [IR: Walton and Hughes *J Am Chem Soc* **79** 3985 1957; Truce and Kruse *J Am Chem Soc* **81** 5372 1959].

**Diethylamine** [109-89-7] M 73.1, b 55.5°, d 0.707, n 1.38637,  $pK^{15}$  11.38. Dried with LiAlH<sub>4</sub> or KOH pellets. Refluxed with, and distd from, BaO or KOH. Converted to the *p*-toluenesulfonamide and crystd to constant melting point from dry pet ether (b 90-120°), then hydrolysed with HCl, excess NaOH was added, and the amine passed through a tower of activated alumina, redistd and dried with activated alumina before use [Swift J Am Chem Soc 64 115 1942].

§ A polystyrene diethylaminomethyl supported version is commercially available.

Diethylamine hydrochloride [660-68-4] M 109.6, m 223.5°. Crystd from absolute EtOH. Also crystd from dichloroethane/MeOH. Hygroscopic.

trans-4-(Diethylamino)azobenzene [3588-91-8] M 320.5, m 171° pK<sub>Est(1)</sub> ~-5.4, pK<sub>Est(2)</sub>~3.0. Purified by column chromatography [Flamigni and Monti J Phys Chem 89 3702 1985].

N,N-Diethylaniline [91-66-7] M 149.2, b 216.5°, d 0.938, n 1.5409 pK<sup>25</sup> 6.57. Refluxed for 4h with half its weight of acetic anhydride, then fractionally distd under reduced pressure (b 92°/10mm).

Diethyl azodicarboxylate (DEAD) [1972-28-7] M 174.2, b 104.5°/12mm, 211-213°/atm,  $d_4^{20}$  1.110,  $n_D^{20}$  1.420. Dissolve in toluene, wash with 10% NaHCO<sub>3</sub> till neutral (may require several washes if too much hydrolysis had occurred (check IR for OH bands), then wash with H<sub>2</sub>O (2 x), dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate the toluene and distil through a short Vigreux column. Main portion boils at 107-111°/15mm [Org Synth Coll Vol III 376 1955].

§ A polystyrene supported DEAD version is commercially available.

**5,5-Diethylbarbituric acid** (Barbital) [57-44-3] M 184.2, m 188-192°,  $pK_1^{25}$  8.02,  $pK_2^{25}$  12.7. Crystd from water or EtOH. Dried in a vacuum over  $P_2O_5$ .

**Diethyl bromomalonate** [685-87-0] **M 239.1, b 116-118°/10mm, 122-123°/20mm, d\_4^{20} 1.420, n\_D^{20} 1.4507.** Purified by fractional distn in a vacuum. IR: 1800 and 1700cm<sup>-1</sup> [Abramovitch *Can J Chem* 37 1146 1959; Bretschneider and Karpitschka *Monatsh Chem* 84 1091 1053].

Diethyl tert-butylmalonate [759-24-0] M 216.3, b 40-42°/0.03, 102-104°/11mm, 109.5-110.5°/17mm, 205-210°/760mm,  $d_4^{20}$  0.980,  $n_D^{20}$  1.425. Dissolve in Et<sub>2</sub>O, wash with aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, dry (MgSO<sub>4</sub>), filter, evaporate and distil residue. Identified by hydrolysis to the acid and determining the neutralisation equiv (theor: 80.0). The acid has m 155-157° efferv [Hauser, Abramovitch and Adams J Am Chem Soc 64 2715 1942; Bush and Beauchamp J Am Chem Soc 75 2949 1953].

N,N'-Diethylcarbanilide (sym-Diethyldiphenylurea) [85-98-3] M 268.4, m 79°. Crystd from EtOH.

**Diethyl carbonate** [105-58-8] **M 118.1, b 126.8°, d 0.975, n^{25} 1.38287.** It was washed (100mL) with an aqueous 10% Na<sub>2</sub>CO<sub>3</sub> (20mL) solution, saturated CaCl<sub>2</sub> (20mL), then water (30mL). After drying by standing over solid CaCl<sub>2</sub> for 1h (note that prolonged contact should be avoided because slow combination with CaCl<sub>2</sub> occurs), it should be fractionally distd. Also dried over MgSO<sub>4</sub> and distd.

1,1'-Diethyl-2,2'-cyanine iodide [977-96-8] M 454.4, m 274°(dec). Crystd from EtOH and dried in a vacuum oven at 80° for 4h.

N,N-Diethylcyclohexylamine [91-65-6] M 155.3, b 193°/760mm, d 0.850, n 1.4562, pK<sup>25</sup> 10.72. Dried with BaO and fractionally distd.

Diethylene glycol [111-46-6] M 106.1, f -10.5°, b 244.3°, d 1.118, n<sup>15</sup> 1.4490, n 1.4475. Fractionally distd under reduced pressure (b 133°/14mm), then fractionally crystd by partial freezing.

Diethylene glycol diethyl ether [112-36-7] M 162.2, b 85-86°/10mm, 188.2-188.3°/751mm, d 0.909, n 1.412. Dried with MgSO<sub>4</sub>, then CaH<sub>2</sub> or LiAlH<sub>4</sub>, under N<sub>2</sub>. If sodium is used the ether should be redistd alone to remove any products which may be formed by the action of sodium on the ether. As a preliminary purification, the crude ether (2L) can be refluxed for 12h with 25mL of conc HCl in 200mL of water, under reduced pressure, with slow passage of N<sub>2</sub> to remove aldehydes and other volatile substances. After cooling, addn of sufficient solid KOH pellets (slowly and with shaking until no more dissolves) gives two liquid phases. The upper of these is decanted, dried with fresh KOH pellets, decanted, then refluxed over, and distd from, sodium. Can be passed through (alkaline) alumina prior to purification.

Diethylene glycol ditosylate [7460-82-4] M 414.5, m 86-87°, 87-88°, 88-89°. Purified by recrystn from Me<sub>2</sub>CO and dried in a vacuum.

**Diethylene glycol mono**-*n*-butyl ether (butyl carbitol) [112-34-5] M 162.2, b 69-70°/0.3mm, 230.5°/760mm, d 0.967, n 1.4286. Dried with anhydrous K<sub>2</sub>CO<sub>3</sub> or CaSO<sub>4</sub>, filtered and fractionally distd. Peroxides can be removed by refluxing with stannous chloride or a mixture of FeSO<sub>4</sub> and KHSO<sub>4</sub> (or, less completely, by filtration under slight pressure through a column of activated alumina).

Diethylene glycol monoethyl ether [111-90-0] M 134.2, b 201.9°, d 0.999, n 1.4273, n<sup>25</sup> 1.4254. Ethylene glycol can be removed by extracting 250g in 750mL of \*benzene with 5mL portions of water, allowing for phase separation, until successive aqueous portions show the same volume increase. Dried, and freed from peroxides, as described for diethylene glycol mono-*n*-butyl ether.

Diethylene glycol monomethyl ether [111-77-3] M 120.2, b 194°, d 1.010, n 1.423. Purified as for diethylene glycol mono-*n*-butyl ether.

Diethylenetriaminepenta-acetic acid (DTPA) [67-43-6] M 393.4, m 219-220°,  $pK_1^{25}1.79$ ,  $pK_2^{25}2.56$ ,  $pK_3^{25}$  4.42,  $pK_4^{25}$  8.76,  $pK_5^{25}$  10.42. Crystd from water. Dried under vacuum or at 110°. [Bielski and Thomas J Am Chem Soc 109 7761 1987].

**Diethyl ether** (ethyl ether) [60-29-7] M 74.1, b 34.6°/760mm, d 0.714, n<sup>15</sup> 1.3555, n 1.35272. Usual impurities are water, EtOH, diethyl peroxide (which is explosive when concentrated), and aldehydes. Peroxides [detected by liberation of iodine from weakly acid (HCl) solutions of KI, or by the blue colour in the ether layer when 1mg of Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and 1 drop of dil H<sub>2</sub>SO<sub>4</sub> in 1mL of water is shaken with 10mL of ether] can be removed in several different ways. The simplest method is to pass dry ether through a column of activated alumina (80g Al<sub>2</sub>O<sub>3</sub>/700mL of ether). More commonly, 1L of ether is shaken repeatedly with 5-10mL of a soln comprising 6.0g of ferrous sulfate and 6mL of conc H<sub>2</sub>SO<sub>4</sub> in 110mL of water. Aqueous 10% Na<sub>2</sub>SO<sub>3</sub> or stannous chloride can also be used. The ether is then washed with water, dried for 24h with CaCl<sub>2</sub>, filtered and dried further by adding sodium wire until it remains bright. The ether is stored in a dark cool place, until distd from sodium before use. Peroxides can also be removed by wetting the ether with a little water, then adding excess LiAlH<sub>4</sub> or CaH<sub>2</sub> and leaving to stand for several hours. (This also dried the ether.)

Werner [Analyst 58 335 1933] removed peroxides and aldehydes by adding 8g AgNO<sub>3</sub> in 60mL of water to 1L of ether, then 100mL of 4% NaOH and shaking for 6min. Fierz-David [Chimia 1 246 1947] shook 1L of ether with 10g of a zinc-copper couple. (This reagent was prepared by suspending zinc dust in 50mL of hot water, adding 5mL of 2M HCl and decanting after 20sec, washing twice with water, covering with 50mL of water and 5mL of 5% cuprous sulfate with swirling. The liquid was decanted and discarded, and the residue was washed three times with 20mL of ethanol and twice with 20mL of diethyl ether).

Aldehydes can be removed from diethyl ether by distn from hydrazine hydrogen sulfate, phenyl hydrazine or thiosemicarbazide. Peroxides and oxidisable impurities have also been removed by shaking with strongly alkaline satd KMnO<sub>4</sub> (with which the ether was left to stand in contact for 24h), followed by washing with water, conc  $H_2SO_4$ , water again, then drying (CaCl<sub>2</sub>) and distn from sodium, or sodium containing benzophenone to form the ketyl. Other purification procedures include distn from sodium triphenylmethide or butyl magnesium bromide, and drying with solid NaOH or  $P_2O_5$ .

Rapid purification: Same as for 1,4-dioxane.

Diethyl ethoxymethylene malonate [87-13-8] M 216.2, b 014°/0.2mm, 109°/0.5mm, 279-283°/atm,  $d_4^{20}$  1.079,  $n_D^{20}$  1.4623. Likely impurity is diethyl diethoxymethylene malonate which is difficult to separate from diethyl ethoxymethylene malonate by distn and it is necessary to follow the course of the distn by the change in refractive index instead of boiling point. After a low boiling fraction is collected, there is obtained an intermediate fraction  $(n_D^{20} 1.414-1.458)$  the size of which depends on the amount of diethoxymethylene compound. This fraction is fractionated through a 5-inch Vigreux column at low pressure avoiding interruption in heating. Fraction b 108-110°/0.25mm was ca 10° lower than the submitters' (b 97.2°/0.25mm ( $n_D^{20} 1.4612-1.4623$ ) [Org Synth Coll Vol III 395 1955; Fuson et al. J Org Chem 11 197 1946; Duff and Kendal J Chem Soc 893 1948].

N, N'-Diethylformamide [617-84-5] M 101.2, b 29°/0.5mm, 61-63°/10mm, 178.3-178.5°/760mm,  $d_4^{20}$  0.906,  $n_D^{25}$ 1.4313. Distd under reduced pressure then at atmospheric pressure [Wintcler et al. *Helv Chim Acta* 37 2370 1954; NMR: Hoffmann Z Anal Chem 170 177 1959].

**Diethyl fumarate** [623-91-6] **M 172.2, b 218°, d 1.052, n 1.441.** Washed with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, then with saturated CaCl<sub>2</sub> soln, dried with CaCl<sub>2</sub> and distd.

Di-(2-ethylhexyl)phthalate ('di-iso-octyl' phthalate) [117-81-7] M 390.6, b 384°, 256-257°/1mm, d 0.9803, n 1.4863. Washed with Na<sub>2</sub>CO<sub>3</sub> soln, then shaken with water. After the resulting emulsion had been broken by adding ether, the ethereal soln was washed twice with water, dried (CaCl<sub>2</sub>), and evaporated. The residual liquid was distd several times under reduced pressure, then stored in a vacuum desiccator over  $P_2O_5$  [French and Singer J Chem Soc 1424 1956]

**Diethyl ketone (3-pentanone)** [96-22-0] **M 86.1, b 102.1°, d 0.8099, n 1.392.** Dried with anhydrous CaSO<sub>4</sub> or CuSO<sub>4</sub>, and distd from P<sub>2</sub>O<sub>5</sub> under N<sub>2</sub> or under reduced pressure. Further purification by conversion to the semicarbazone (recrystd to constant **m** 139°, from EtOH) which, after drying under vacuun over CaCl<sub>2</sub> and paraffin wax, was refluxed for 30min with excess oxalic acid, then steam distd and salted out with K<sub>2</sub>CO<sub>3</sub>. Dried with Na<sub>2</sub>SO<sub>4</sub> and distd [Cowan, Jeffrey and Vogel J Chem Soc 171 1940].

**Diethyl malonate** [105-53-3] **M 160.2, b 92°/22mm, 198-199°/760mm, d 1.056, d<sup>25</sup> 1.0507, n 1.413.** If too impure (IR, NMR) the ester (250g) has been heated on a steam bath for 36h with absolute EtOH (125mL) and conc  $H_2SO_4$  (75mL), then fractionally distd under reduced pressure. Otherwise fractionally distil under reduced pressure and collect the steady boiling middle fraction.

Diethyl phenyl orthoformate (diethoxy phenoxy ethane) [14444-77-0] M 196.3, b 111°/11mm, 122°/13mm,  $d_4^{20}$  1.0099,  $n_D^{20}$  1.4799. Fractionated through an efficient column under vacuum [Smith Acta Chem Scand 10 1006 1956].

Diethyl phthalate [84-66-2] M 222.2. b 172°/12mm, b 295°/760mm, d<sup>25</sup> 1.1160, n 1.5022. Washed with aqueous Na<sub>2</sub>CO<sub>3</sub>, then distilled water, dried (CaCl<sub>2</sub>), and distd under reduced pressure. Stored in a vacuum desiccator over  $P_2O_5$ .

**Diethyl phthalimidomalonate** [56680-61-5] **M 305.3, m 72-74°, 73-74°, pK 9.17.** Dissolve in xylene and when the temperature is 30° add pet ether (b 40-60°) and cool to 20° whereby the malonate separates as a pale brown powder [Booth et al. J Chem Soc 666 1944]. Alternatively, dissolve in  $C_6H_6$ , dry over CaCl<sub>2</sub>, filter, evaporate and the residual oil solidifies. This is ground with Et<sub>2</sub>O, filter and wash with Et<sub>2</sub>O until white in colour, and dry in a vacuum. The anion has  $\lambda \max 254$ nm ( $\varepsilon 18.5$ K) [Clark and Murray Org Synth Coll Vol I 271 1941; UV of Na salt: Nnadi and Wang J Am Chem Soc 92 4421 1970].

2,2-Diethyl-1,3-propanediol [115-76-4] M 132.2, m 61.4-61.8°. Crystd from pet ether (b 65-70°).

**Diethyl pyrocarbonate** (DEP) [1609-47-8] M 162.1, b 38-40°/12mm, 160-163°/atm,  $d_4^{20}$  1.119,  $n_D^{20}$  1.398. Dissolve in Et<sub>2</sub>O, wash with dilute HCl, H<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil the residue first *in vacuo* then at atmospheric pressure. It is soluble in alcohols, esters, ketones and hydrocarbon solvents. A 50% w/w soln is usually prepared for general use. **Treat with great CAUTION** as DEP irritates the eyes, mucous membranes and skin. [Boehm and Mehta Chem Ber 71 1797 1938; Thoma and Rinke Justus Liebigs Ann Chem 624 30 1959.]

Diethylstilboesterol [56-23-1] M 268.4, m 169-172°. Crystd from \*benzene.

Diethyl succinate [123-25-1] M 174.2, b 105°/15mm, d 1.047, n 1.4199. Dried with MgSO<sub>4</sub>, and distd at 15mm pressure.

Diethyl sulfate [64-67-5] M 154.2, b 96°/15mm, 118°/40mm, d 1.177, n 1.399. Washed with aqueous 3% Na<sub>2</sub>CO<sub>3</sub> (to remove acidic material), then distilled water, dried (CaCl<sub>2</sub>), filtered and distd. *Causes blisters to the skin.* 

**Diethyl disulfide** [110-81-6] **M 122.3, b 154-155°, d 0.993, n 1.506.** Dried with silica gel or MgSO<sub>4</sub> and distd under reduced pressure (optionally from CaCl<sub>2</sub>).

**Diethyl sulfide** [352-93-2] **M 90.2, m 0°/15mm, 90.1°/760mm, d 0.837, n 1.443.** Washed with aq 5% NaOH, then water, dried with CaCl<sub>2</sub> and distd from sodium. Can also be dried with MgSO<sub>4</sub> or silica gel. Alternative purification is *via* the Hg(II) chloride complex [(Et)<sub>2</sub>S.2HgCl<sub>2</sub>] (see dimethyl sulfide).

Diethyl (-)-D- (from the non-natural) [13811-71-7] and (+)-L- (from the natural acid) [89-91-2] tartrate M 206.2, m 17°, b 80°/0.5mm, 162°/19mm, 278-282°/atm,  $d_4^{20}$  1.204,  $n_D^{20}$  1.4476,  $[\alpha]_D^{20}$  (-) and (+) 26.5° (c 1, H<sub>2</sub>O) and (-) and (+) 8.5° (neat),  $[\alpha]_{546}^{20}$  (-) and (+) 30° (c 1, H<sub>2</sub>O). Distd under high vacuum and stored under vacuum or in an inert atm in a desiccator in round bottomed flasks equiped with a vac stopcock. Have also been dist by Kügelrohr distn and/or by 'wiped-film' molecular distn. Slightly sol in H<sub>2</sub>O but miscible in EtOH and Et<sub>2</sub>O. [Gao et al. J Am Chem Soc 109 5770 (5771) 1987; IR: Pristera Anal Chem 25 844 1953.]

Diethyl terephthalate [636-09-0] M 222.2, m 44°, 142°/2mm, 302°/760mm. Crystd from toluene and distd under reduced pressure.

sym-Diethylthiourea [105-55-5] M 132.2, m 76-77°. Crystd from \*benzene.

**Difluoroacetic acid** [381-73-7] **M 96.0, m -0.35°, b 67-70°/20mm, 134°/760mm, d** $_{4}^{20}$  **1.530,**  $n_{D}^{20}$  **1.3428, pK** $^{25}$  **1.28.** Purified by distilling over P<sub>2</sub>O<sub>5</sub>. The *acid chloride* is a fuming liquid b 25°/atm, and the *amide* has b 108.6°/35mm, m 52° (from \*C<sub>6</sub>H<sub>6</sub>), and the *anilide* has b 90°/1mm, 114°/5mm, m 58° [Henne and Pelley J Am Chem Soc **74** 1426 1952, Coffman et al. J Org Chem **14** 749 1949; NMR: Meyer et al. J Am Chem Soc **75** 4567 1953; pK: Wegscheider Z Phys Chem **69** 614 1909].

Diglycolic acid (2-oxapentane-1,5-dioic acid) [110-99-6] M 134.1, m 148° (monohydrate),  $pK_1^{25}$  2.97,  $pK_2^{25}$  4.37. Crystd from water.

**Diglycyl glycine** [556-33-2] **M 189.2, m 246°(dec), pK\_1^{25} 3.30, pK\_2^{25} 7.96.** Crystd from H<sub>2</sub>O or H<sub>2</sub>O/EtOH and dried at 110°.

**Diglyme** [bis-(2-methoxyethyl) ether, diethylene glycol dimethyl ether] [111-96-6] M 134.2, b 62°/17mm, 75°/35mm, 160°/760mm, d 0.917, n 1.4087. Dried with NaOH pellets or CaH<sub>2</sub>, then refluxed with, and distd (under reduced pressure) from Na, CaH<sub>2</sub>, LiAlH<sub>4</sub>, NaBH<sub>4</sub> or NaH. These operations were carried out under N<sub>2</sub>. The amine-like odour of diglyme has been removed by shaking with a weakly acidic ion-exchange resin (Amberlite IR-120) before drying and distn. Addn of 0.01% NaBH<sub>4</sub> to the distillate inhibits peroxidation. Purification as for dioxane. Also passed through a 12-in column of molecular sieves to remove water and peroxides.

**Digoxin** [20830-75-5] **M 781.0, m 265°(dec),**  $[\alpha]_{546}^{20}$  +14.0° (c 10, pyridine). Crystd from aqueous EtOH or aqueous pyridine.

4,4'-Di-*n*-heptyloxyazoxybenzene [2635-26-9] M 426.6, m 75°, 95° (smectic  $\rightarrow$  nematic) and 127° (nematic  $\rightarrow$  liquid), pK<sub>Est</sub> ~-5. Purified by chromatography on Al<sub>2</sub>O<sub>3</sub> (\*benzene), recrystd from hexane or 95% EtOH and dried by heating under vacuum. The liquid crystals can be sublimed *in vacuo*. [Mellifiori et al. Spectrochim Acta Part A 37(A) 605 1981; Dewar and Schroeder J Am Chem Soc 86 5235 1964; Weygand and Glaber J Prakt Chem 155 332 1940].

**9,10-Dihydroanthracene** [613-31-0] **M 180.3, m 110-110.5°.** Crystd from EtOH [Rabideau et al. J Am Chem Soc 108 8130 1986].

**2,3-Dihydrobenzofuran** (coumaran) [496-16-2] M 120.2, m -21.5°, 72-73°/12 mm, **84°/17mm**, 188°/atm,  $d_4^{20}$  1.065,  $n_D^{20}$  1.5524. Suspend in aqueous NaOH and steam distil. Saturate the distillate with NaCl and extract with Et<sub>2</sub>O, dry extract (MgSO<sub>4</sub>), filter, evap and distil the residue. It gives a strong violet colour with FeCl<sub>3</sub> + H<sub>2</sub>SO<sub>4</sub> and forms a yellow *picrate*, m 76°, from EtOH or \*C<sub>6</sub>H<sub>6</sub> which loses coumaran in a desiccator [Bennett and Hafez J Chem Soc 287 1941; Baddeley et al. J Chem Soc 2455 1956].

Dihydrochloranil (tetrachloro-1,4-hydroquinone) [87-87-6] M 247.9, m 240.5°. Crystd from EtOH or AcOH+EtOH. Sublimes at 77°/0.6x10<sup>-3</sup>mm. The dibenzoyl derivative has m 233°. [Conant and Fieser J Am Chem Soc 45 2207 1923; Rabideau et al. J Am Chem Soc 108 8130 1986.]

Dihydrocodeine [125-28-0] M 301.4, m 112-113°, b 248/14mm°. Crystd from aqueous methanol.

**1,4-Dihydro-1,4-epoxynaphthalene** [573-57-9] M 144.2, m 53-54.5°, 53-56°, 55-56°. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dry over  $K_2CO_3$ , filter, evaporate and dry the residue at 15mm, then recrystallise from pet ether (b 40-60°), dry at 25°/0.005mm and sublime (sublimes slowly at room temp)[Wittig and Pohmer Chem Ber 89 1334 1956; Gilman and Gorsich J Am Chem Soc 79 2625 1957].

Dihydropyran (3,4-dihydro-2*H*-pyran) [110-87-2] M 84.1, b 84.4°/742mm, 85.4-85.6°/760mm,  $d_4^{20}$  0.9261,  $n_D^{20}$  1.4423, pK<sub>Est</sub> ~ 4.2. Partially dried with Na<sub>2</sub>CO<sub>3</sub>, then fractionally distd. The fraction b 84-85°, was refluxed with Na until hydrogen was no longer evolved when fresh Na was

added. It was then dried, and distd again through a 60 x 1.2cm column packed with glass rings [Brandon et al. J Am Chem Soc 72 2120 1950; UV: Elington et al. J Chem Soc 2873 1952, NMR: Bushweller and O'Neil Tetrahedron Lett 4713 1969]. It has been characterised as the 2,3,5-dinitrobenzoyloxy-tetrahydrofuran derivative, m 103° which forms pale yellow crystals from dihydropyran-Et<sub>2</sub>O [Woods and Kramer J Am Chem Soc 69 2246 1947].

**3,4-Dihydro-2H-pyrido**[1,2*a*]-pyrimidin-2-one [5439-14-5] M 148.2, m 185-187°, 187-188°, 191-191.5°. Dissolve in CHCl<sub>3</sub>, filter, evaporate then recrystallise the residue from EtOH-Me<sub>2</sub>CO (needles) which can be washed with Et<sub>2</sub>O and dried. It can also be recrystd from CHCl<sub>3</sub>-pet ether or CHCl<sub>3</sub>-hexane. The *hydrochloride* has m 295-295° (dec, from EtOH or MeOH-Et<sub>2</sub>O), the *hydrobromide* has m 299-300°(dec, from MeOH-Et<sub>2</sub>O) and the *picrate* has m 224-226°(corr), m 219-220° from EtOH. [Adams and Pachter J Am Chem Soc 74 4906 1952; Lappin J Org Chem 23 1358 1958; Hurd and Hayao J Am Chem Soc 77 115 1955.]

**Dihydrotachysterol** [67-96-9] **M 398.7, m 125-127°,**  $[\alpha]_D^{20} + 97°$  (CHCl<sub>3</sub>). Crystd from 90% MeOH.

1,8-Dihydroxyanthraquinone [117-10-2] M 240.1, m 193-197°,  $pK_1^{25}$  8.30,  $pK_2^{25}$  12.46. Crystd from EtOH and sublimed in a vacuum.

2,4-Dihydroxyazobenzene (Sudan orange G) [2051-85-6] M 214.2, m 228°, pK\S(,Est(1))<0, pK<sub>Est(2)</sub> ~7.3, pK<sub>Est(3)</sub> ~9.3. Crystd from hot EtOH (charcoal).

**2,3-Dihydroxybenzaldehyde** [24677-78-9] **M 138.1, m 135-136°, pK<sub>1</sub><sup>20</sup>7.73, pK<sub>2</sub><sup>20</sup>10.91.** Crystd from water.

2,4-Dihydroxybenzoic acid [89-86-]] M 154.1, m 226-227°(dec),  $pK_1^{25}$  3.30,  $pK_2^{25}9.12$ ,  $pK_3^{25}15.6$ . Crystd from water.

2,5-Dihydroxybenzoic acid [490-79-9] M 154.1, m 204.5-205°, pK<sup>25</sup> 2.95. Crystd from hot water or \*benzene/acetone. Dried in a vacuum desiccator over silica gel.

**2,6-Dihydroxybenzoic acid** [303-07-1] M 154.1, m 167°(dec), pK<sup>25</sup> 1.05. Dissolved in aqueous NaHCO<sub>3</sub> and the soln was washed with ether to remove non-acidic material. The acid was ppted by adding H<sub>2</sub>SO<sub>4</sub>, and recrystd from water. Dried under vacuum and stored in the dark [Lowe and Smith J Chem Soc, Faraday Trans 1 69 1934 1973].

2,4-Dihydroxybenzophenone [131-56-6] M 214.2, m 145.5-147° pK<sub>Est(1)</sub> ~7.0, pK<sub>Est(2)</sub>~12.0. Recrystd from MeOH.

2,5-Dihydroxybenzyl alcohol (Gentisyl alcohol) [495-08-9] M 140.1, m 100°  $pK_{Est(1)} \sim 9.3$ ,  $pK_{Est(2)} \sim 11.3$ . Crystd from CHCl<sub>3</sub>. Sublimes at ~70° under high vacuum.

**2,2'-Dihydroxybiphenyl** [1806-29-7] **M 186.2**, **m 108.5-109.5°**,  $pK_1^{25}$ **7.56**,  $pK_2^{25}$ **11.80**. Repeatedly crystd from toluene, then sublimed at 60°/10<sup>-4</sup>mm.

 $3\alpha$ , $7\alpha$ -Dihydroxycholanic acid (Chenodeoxycholic acid) [474-25-9] M 239.6, m 143°,  $[\alpha]_{546}^{20}$  +14° (c 2, EtOH), pK<sub>Est</sub> ~4.9. Crystd from ethyl acetate.

7,8-Dihydroxycoumarin (Daphnetin) [486-35-1] M 178.2, m 256°(dec),  $pK_{Est(1)} \sim 8.5$ , pK  $Est(2) \sim 12.3$ . Crystd from aqueous EtOH. Sublimed.

**2,2'-Dihydroxy-6,6'-dinaphthyl disulfide** [6088-51-3] M **350.5, m 220-223°.** See 6-hydroxy-2-naphthyl disulfide on p. 264.

trans-2,3-Dihydroxy-1,4-dioxane [4845-50-5] M 120.1, m 91-95°, 100°. Recryst from Me<sub>2</sub>CO. With phenylhydrazine it gives glyoxal phenylhydrazone m 175° (from Me<sub>2</sub>CO-pet ether). The diacetyl derivative has m 105-106° [Head J Chem Soc 1036 1955, Raudnitz Chem Ind (London) 166 1956].

2,5-Dihydroxy-1,4-dithiane [40018-26-6] M 152.2, m (142-147°?) 150-152°, 151°. Recrystd from EtOH. The 2,5-diethoxy-dithiane has m 91° (92-93°) crystallises from pet ether and can be sublimed at 60°/0.001mm [Hormatka and Haber Monatsh Chem 85 1088 1954; Thiel et al. Justus Liebigs Ann Chem 611 121 1958; Hesse and Jøeder Chem Ber 85 924 1952].

(N, N-Dihydroxyethyl)glycine (BICINE) [150-25-4] M 163.2, m 193°(dec), pK<sub>1</sub><sup>25</sup>1.81, pK<sub>2</sub><sup>25</sup> 8.27. Dissolved in a small volume of hot water and ppted with EtOH, twice. Repeated once more but with charcoal treatment of the aqueous soln, and filtered before addition of EtOH.

Dihydroxyfumaric (1,2-dihydroxybut-1-ene-1,2-dioic) acid dihydrate [133-38-0] M 184.1, m  $155^{\circ}(dec)$ ,  $pK_1^{25}$  1.57,  $pK_2^{25}$  3.36. Crystd from water.

3,4'-Dihydroxyisoflavone [578-86-9] M 256.3, m 234-236°. Crystd from aqueous 50% EtOH.

5,7-Dihydroxy-4'-methoxyflavone [480-44-4] M 284.3, m 261°. Crystd from 95% EtOH.

1,8-Dihydroxy-3-methylanthraquinone (chrysophanic acid) [481-74-3] M 245.3, m 196°, pK<sub>Est(1)</sub> ~8.2, pK<sub>Est(2)</sub>~12.4. Crystd from EtOH or \*benzene and sublimed in a vacuum.

1,5-Dihydroxynaphthalene [83-56-7] M 160.2, m 260°, 250-261°, pK<sub>Est</sub> ~9.6. Crystd from nitromethane.

**1,6-Dihydroxynaphthalene** [575-44-0] M **160.2, m 138-139°** (with previous softening), pK<sub>Est</sub>~9.4. Crystd from \*benzene or \*benzene/EtOH after treatment with charcoal.

2,5-Dihydroxyphenylacetic acid (homogentisic acid) [451-13-8] M 168.2, m 152°, 154-152°,  $pK^{20}$  4.14 (COOH). Crystd from EtOH/CHCl<sub>3</sub> or H<sub>2</sub>O (sol 85% at 25°).

**3,4-Dihydroxytoluene** [452-86-8] **M 124.1, m 65-66°, 68°, b 112°/3mm, 241°/760mm, pK\_1^{25} 9.44 (9.7), pK\_2^{25} 10.90 (11.9). Crystd from \*C<sub>6</sub>H<sub>6</sub>. Purity checked by TLC. Crystd from high-boiling pet ether and distd in a vacuum.** 

**1,3-Diiminoisoindoline** [3468-11-9] M 145.2, m 193-194° (dec), 196° (dec), pK 8.27. It crystallises from H<sub>2</sub>O, MeOH or MeOH-Et<sub>2</sub>O (charcoal) in colourless prisms that become green on heating. [Elvidge and Linstead J Chem Soc 5000 1952]. IR (nujol): 3150 and 690 cm<sup>-1</sup>, and UV:  $\lambda$ max 251nm ( $\epsilon$  12.5K), 256nm ( $\epsilon$  12.5K) and 303nm ( $\epsilon$  4.6K) [Elvidge and Golden J Chem Soc 700 1957; Clark et al. J Chem Soc 3593 1953]. The thiocyanate has m 250-255° (dec), the monohydrochloride has m 300-301° (turns green) and the dihydrochloride has m 326-328° (turns green) and the picrate cryst from EtOH has m 299° (dec).

1,4-Diiodobenzene [624-38-4] M 329.9, m 132-133°. Crystd from EtOH or boiling MeOH, then air dried.

**1,2-Diiodoethane** [624-73-7] **M 281.9, m 81-84°, d 2.134.** Dissolved in ether, washed with satd aq  $Na_2S_2O_3$ , drying it over MgSO<sub>4</sub> and evap the ether *in vacuo* [Molander et al. J Am Chem Soc 109 453 1987].

5,7-Diiodo-8-hydroxyquinoline [83-73-8] M 397.0, m 214-215°(dec)  $pK_{Est(1)}$ ~3.2,  $pK_{Est(2)}$ ~8.2. Crystd from xylene and dried at 70° in a vacuum.

Diiodomethane (methylene diiodide) [75-11-6] M 267.8, m 6.1°, b 66-70°/11-12mm, d 3.325. Fractionally distd under reduced pressure, then fractionally crystd by partial freezing, and stabilized

with silver wool if necessary. It has also been purified by drying over  $CaCl_2$  and fractionally distd from Cu powder.

S-3,5-Diiodotyrosine (iodogorgoic acid) [300-39-0] M 469.0, m 204°(dec),  $[\alpha]_D$  +1.5° (in 1M HCl) pK<sub>1</sub> 2.12, pK<sub>2</sub> 6.48, pK<sub>3</sub> 7.82. See 3,5-diiodo-L-tyrosine dihydrate on p. 530 in Chapter 6.

Diisopropanolamine [110-97-4] M 133.2, m 41-44°, d 1.004, pK<sub>Est</sub> ~10.7. Repeatedly crystd from dry diethyl ether.

**Diisopropylamine** [108-18-9] **M 101.2, b 83.5°/760mm, n 1.39236, d 0.720, pK^{25} 11.20.** Distd from NaOH, or refluxed over Na wire or NaH for three minutes and distd into a dry receiver under N<sub>2</sub>. § A polystyrene supported version of diisopropylamine is commercially available.

**Diisopropylethylamine** [7087-68-5] **M 129.3, b 127°, pK**<sub>Est</sub> ~10.9. Distd from ninhydrin, then from KOH [Dryland and Sheppard, *J Chem Soc, Faraday Trans 1* 125 1986]. It is a strong base and should be stored in the absence of carbon dioxide.

(-)-2,3:4,6-Di-O-isopropylidene-2-keto-L-gulonic acid monohydrate (- DAG) [18467-77-1] M 292.3, m 100-101°, 103°,  $[\alpha]_D^{25}$  -21.6° (c 2.3, MeOH). Dissolve in Et<sub>2</sub>O, filter, dry (MgSO<sub>4</sub>), filter, evaporate to give a yellow oil. Addition of one drop of H<sub>2</sub>O induces crystn to the monohydrate, which also forms rhombic crystals by recrystn from 95% EtOH-H<sub>2</sub>O at room tempereture. [Flatt et al. Synthesis 815 1979; Reichstein and Grussner Helv Chim Acta 17 311 1934; Takagi and Jeffrey Acta Crystallogr Sect B 34 2932 1978; cf Org Synth 55 80 1976.]

1,2:5,6-Di-O-isopropylidene-D-mannitol [1707-77-3] M 262.3, m 121-125°, 122°,  $[\alpha]_D^{25}$  +1.2° (c 3, H<sub>2</sub>O). Although quite soluble in H<sub>2</sub>O it gives a purer product from this solvent, forming needles [Baer J Am Chem Soc 67 338 1945; NMR: Curtis et al. J Chem Soc, Perkin Trans 1 1756 1977].

**Diisopropyl ketone** (2,4-dimethyl-3-pentanone) [565-80-0] M 114.2, b 124°, d 0.801, n 1.400. Dried with CaSO<sub>4</sub>, shaken with chromatographic alumina and fractionally distd from  $P_2O_5$  under  $N_2$ .

**Diketene** [674-82-8] **M 84.1, m -7°, b 66-68°/90mm, d 1.440, n 1.4376, n<sup>25</sup> 1.4348.** Diketene polymerizes violently in the presence of alkali. Distd at reduced pressure, then fractionally crystd by partial freezing (using as a cooling bath a 1:1 soln of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> in water, cooled with Dry-ice until slushy, and stored in a Dewar flask). Freezing proceeds slowly, and takes about a day for half completion. The crystals are separated and stored in a refrigerator under N<sub>2</sub>. See ketene on p. 276.

2,2'-Diketospirilloxanthin [24009-17-4] M 624.9, m 225-227°,  $\epsilon_{1cm}^{1\%}(\lambda max)$  550(349nm), 820(422nm), 2125(488nm), 2725(516nm), 2130(551nm) in hexane. Purified by chromatography on a column of partially deactivated alumina. Crystd from acetone/pet ether. Stored in the dark, in an inert atmosphere at 0°.

Dilauroyl peroxide [105-74-8] M 398.6, m 53-54°. See lauryl peroxide (dodecyl peroxide) on p. 278.

**Dimedone** (5,5-dimethylcyclohexane-1,3-dione) [126-81-8] M 140.2, m 148-149°, pK<sup>25</sup> 5.27. Crystd from acetone (*ca* 8mL/g), water or aqueous EtOH. Dried in air.

2,3-Dimercapto-1-propanol (BAL, British Anti-Lewisite) [59-52-9] M 124.2, b 82-84°/0.8mm, d 1.239, n 1.5732,  $pK_1^{25}$ 8.62,  $pK_2^{25}$ 10.75. Ppted as the Hg mercaptide [see Bjöberg Chem Ber 75 13 1942], regenerated with H<sub>2</sub>S, and distd at 2.7mm [Rosenblatt and Jean Anal Chem 951 1955].

1,3-Dimercapto-2-propanol [584-04-3] M 124.2, b 829/1.5mm. Purified as for 2,3-dimercapto-1-propanol above.

*meso*-2,3-Dimercaptosuccinic acid [304-55-2] M 182.2, m 191-192° (dec), 210° (dec), 210-211° (dec), pK<sub>1</sub><sup>25</sup> 2.71, pK<sub>2</sub><sup>25</sup> 3.48, pK<sub>3</sub><sup>25</sup> 8.89, pK<sub>4</sub><sup>25</sup> 10.75. Purified by dissolving in NaOH and precipitating with dilute HCl, dry and recrystallise from MeOH. IR has v at 2544 (SH) and 1689 (CO<sub>2</sub>H) cm<sup>-1</sup>. The *bis-S-acetyl* deriv has m 183-185° (from EtOAc or Me<sub>2</sub>CO) and its *Me ester* has m 119-120° (from pet ether) [Gerecke et al. *Helv Chim Acta* 44 957 1961; Owen and Sultanbawa J Chem Soc 3112 1949].

4,4'-Dimethoxyazobenzene [501-58-6] M 242.3, m 162.7-164.7°, pK<sub>Est</sub> ~0. Chromatographed on basic alumina, eluted with \*benzene. Crystd from 2:2:1 (v/v) methanol/ethanol/\*benzene.

4,4'-Dimethoxyazoxybenzene [1562-94-3] M 258.3, transition temp 118-121°. See p,p'-azoxyanisole on p. 118.

1,2-Dimethoxybenzene (veratrole) [91-16-7] M 137.2, m 23°, b 208.5-208.7, d 1.085, n<sup>25</sup> 1.53232. Steam distd. Fractionally distd from BaO, CaH<sub>2</sub> or Na. Crystd from \*benzene or low-boiling pet ether at 0°. Fractionally crystd from its melt. Stored over anhydrous Na<sub>2</sub>SO<sub>4</sub>.

1,3-Dimethoxybenzene [151-10-0] M 137.2, b 212-213°, d 1.056, n 1.5215. Extracted with aqueous NaOH, and water, then dried. Fractionally distd from BaO or Na.

1,4-Dimethoxybenzene [150-78-7] M 137.2, m 57.2-57.8°. Steam distd. Crystd from hexane or \*benzene, and from MeOH or EtOH but these are wasteful due to high solubilities. Dried under vacuum. Also sublimes under vacuum.

**2,4-Dimethoxybenzoic acid** [91-52-1] **M 182.2, m 109°, pK<sup>25</sup> 4.36.** Crystd from water and dried in a vacuum desiccator over  $H_2SO_4$ .

2,6-Dimethoxybenzoic acid [1466-76-8] M 182.2, m 186-187°, pK<sup>25</sup> 3.44. Crystd from water.

3,4-Dimethoxybenzoic acid (veratric acid) [93-07-2] M 182.2, m 181-182°, pK<sup>25</sup> 4.43. Crystd from water or aq acetic acid.

3,5-Dimethoxybenzoic acid [1132-21-4] M 182.2, m 185-186°, pK<sup>25</sup> 3.97. Crystd from water, EtOH or aq acetic acid.

p,p'-Dimethoxybenzophenone [90-96-0] M 242.3, m 144.5°. Crystd from absolute EtOH.

2,6-Dimethoxy-1,4-benzoquinone [530-55-2] M 168.1, m 256°. Crystd from acetic acid. Sublimes in a vacuum.

1,1-Dimethoxyethane (acetaldehyde dimethyl acetal) [534-15-6] M 90.1, b 212°/760mm, d 0.828, n 1.4140. Purification as for acetal on p. 81. Also purified by GLC.

1,2-Dimethoxyethane (glycol dimethyl ether, glyme) [110-71-4] M 90.1, b 84°, d 0.867, n 1.380. Traces of water and acidic materials have been removed by refluxing with Na, K or CaH<sub>2</sub>, decanting and distilling from Na, K, CaH<sub>2</sub> or LiAlH<sub>4</sub>. Reaction has been speeded up by using vigorous high-speed stirring and molten potassium. For virtually complete elimination of water, 1,2-dimethoxyethane has been dried with Na-K alloy until a characteristic blue colour was formed in the solvent at Dry-ice/cellosolve temperatures: the solvent was kept with the alloy until distd for use [Ward J Am Chem Soc 83 1296 1961]. Alternatively, glyme, refluxed with benzophenone and Na-K, was dry enough if, on distn, it gave a blue colour of the ketyl immediately on addition to benzophenone and sodium [Ayscough and Wilson J Chem Soc 5412 1963]. Also purified by distn under N<sub>2</sub> from sodium benzophenone ketyl (see above).

5,6-Dimethoxy-1-indanone [2107-69-9] M 192.2, m 118-120°. Crystd from MeOH, then sublimed in a vacuum.

**Dimethoxymethane (methylal)** [109-87-5] M 76.1, b 42-46°/atm,  $d_4^{20}$  0.8608,  $n_D^{20}$  1.35335. See formaldehyde dimethyl acetal on p. 245.

1,4-Dimethoxynaphthalene [10075-62-4] M 188.2, m 87-88°. Crystd from EtOH.

1,5-Dimethoxynaphthalene [10075-63-5] M 188.2, m 183-184°. Crystd from EtOH.

2,6-Dimethoxyphenol [91-10-1] M 154.2, m 54-56°, pK<sub>Est</sub> ~9.6. Purified by zone melting or sublimation in a vacuum.

**3,5-dimethoxyphenol** (phloroglucinol dimethylether) [500-99-2] M 154.2, m 42-43°, b 115°/0.04mm, pK<sup>25</sup> 9.35. Purified by distn followed by sublimation in a vacuum.

**3,4-Dimethoxyphenyl acetic acid (homoveratric acid)** [93-40-3] M 196.2, m 97-99°, pK<sup>25</sup> **4.33.** Crystd from water or \*benzene/ligroin.

**3,5-Dimethoxyphenylacetonitrile** [13388-75-5] **M 177.1, m 53°.** Crystd from MeOH or pet ether (b 90-110°). [Adams et al. J Am Chem Soc **70** 664 1948; Sankaraman et al. J Am Chem Soc **109** 5235 1987.]

4,4'-Dimethoxythiobenzophenone [958-80-5] M 258.3, m 120°. Recrystd from a mixture of cyclohexane/dichloromethane (4:1).

**2,6-Dimethoxytoluene** [5673-07-4] **M 152.2, m 39-41°.** Sublimed in vacuo [Sankaraman et al. J Am Chem Soc 109 5235 1987].

**4,4'-Dimethoxytrityl chloride** (DMT) [40615-36-9] M 338.8, m 114°. Crysts from cyclohexaneacetyl chloride as the hydrochloride and dry over KOH pellets in a desiccator. When dissolved in  $*C_6H_6$  and air is blown through, HCl is removed. It crystallises from Et<sub>2</sub>O. [Justus Liebigs Ann Chem 370 142 1909; Chem Ber 36 2774 1903; Smith et al. J Am Chem Soc 84 430 1962; Smith et al. J Am Chem Soc 85 3821 1963.] If it had hydrolysed considerably (see OH in IR) then repeat the crystallisation from cyclohexaneacetyl chloride — excess of AcCl is removed in vac over KOH.

N, N-Dimethylacetamide [127-19-5] M 87.1, b 58.0-58.5°/11.4mm, d 0.940, n 1.437. Shaken with BaO for several days, refluxed with BaO for 1h, then fractionally distd under reduced pressure, and stored over molecular sieves.

 $\beta$ ,  $\beta$ -Dimethylacrylic acid (senecioic acid) [541-47-9] M 100.1, m 68°, pK<sup>25</sup> -5.4 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from hot water or pet ether (b 60-80°).

Dimethyl adipate [627-93-0] M 174.2, m 9-11°, b 109°/10mm, 121-123°/20mm, 235°/760mm,  $d_4^{20}$  1.0642,  $n_D^{20}$  1.4292. Dissolve in Et<sub>2</sub>O, wash with NaHCO<sub>3</sub>, H<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and distil several times until the IR and NMR are consistent with the structure [Lorette and Brown J Org Chem 24 261 1959; Hoffmann and Weiss J Am Chem Soc 79 4759 1957].

**Dimethyl adipimidate dihydrochloride** [14620-72-5] M 245.1, m 218-220°, 222-224°. If the salt smells of HCl then wash with MeOH and dry  $Et_2O$  (1:3) under N<sub>2</sub> until the HCl is completely removed. Recryst from MeOH-Et<sub>2</sub>O (it is very important that the solvents are super dry) [Hartman and Wold *Biochemistry* 6 2439 1967; McElvain and Shroeder J Am Chem Soc 71 40 1949].

**Dimethylamine** [124-40-3] **M 45.1, f -92.2°, b 0°/563mm, 6.9°/760mm, pK<sup>25</sup> 10.73.** Dried by passage through a KOH-filled tower, or by standing with sodium pellets at 0° during 18h. § A dimethylaminomethyl polystyrene supported version is commercially available. **Dimethylamine hydrochloride** [506-59-2] M 81.6, m 171°. Crystd from hot CHCl<sub>3</sub> or abs EtOH. Also recrystd from MeOH/ether soln. Dried in a vacuum desiccator over  $H_2SO_4$ , then  $P_2O_5$ . *Hygroscopic*.

4-N,N'-Dimethylaminoazo-benzene-4'-isothiocyanate {DABITC, 4-[(4-isocyanatophenyl)-azo]-N,N'-dimethylaniline} [7612-98-8] M 282.4, m 170-171°, pK<sub>Est</sub>~ 2.5. Crystd by dissolving 1g in 150mL of boiling Me<sub>2</sub>CO, filtering hot and allowing to cool at -20° overnight collecting the solid and drying in vac. Solns in pyridine should be used immediately otherwise it dec. Moistue sensitive. [Chang Methods Enzymol 91 79, 455 1983.]

*p*-Dimethylaminoazobenzene (Methyl Yellow) [60-11-7] M 225.3, m 118-119°(dec),  $pK_1^{25}$ -5.34 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$ 2.96. Crystd from acetic acid or isooctane, or from 95% EtOH by adding hot water and cooling. Dried over KOH under vacuum at 50°. CARCINOGEN.

*p*-Dimethylaminobenzaldehyde (Ehrlich's Reagent) [100-10-7] M 149.2, m 74-75°, pK<sub>Est</sub> ~2.6. Crystd from water, hexane, or from EtOH (2mL/g), after charcoal treatment, by adding excess of water. Also dissolved in aqueous acetic acid, filtered, and ppted with ammonia. Finally recrystd from EtOH.

*p*-Dimethylaminobenzoic acid [619-84-1] M 165.2, m 242.5-243.5°(dec), pK<sub>1</sub> 2.51, pK<sub>2</sub> 6.03. Crystd from EtOH/water.

p-Dimethylaminobenzophenone [530-44-9] M 225.3, m 92-93°, pK<sub>Est</sub> ~2.7. Crystd from EtOH.

N,N-Dimethylamino-p-chlorobenzene (p-chloro-N,N-dimethylaniline) [698-69-1] M 155.6, m 32-33.5°, 35.5°, b 231°/atm. Purified by vacuum sublimation [Guarr et al. J Am Chem Soc 107 5104 1985]. The picrate has m 126-128° (from methanol).

25,3R-(+)-4-Dimethylamino-1,2-diphenyl-3-methyl-2-butanol [38345-66-3] M 283.4, m 55-57°,  $[\alpha]_{546}^{20}$  +9.3° (c 9.6, EtOH),  $[\alpha]_D^{20}$  +7.7° (c 9.6, EtOH), pK<sub>Est</sub> ~10.0. Purification of the hydrochloride by dissolving 1.5g in 13.5 mL of 5N HCl heating to boiling and evaporate in a vacuum. Recrystn of the hydrochloride three times from MeOH-EtOAc gives m 189-190°,  $[\alpha]_D$ -33.7° (c 1, H<sub>2</sub>O) {enantiomer has +34.2°}. The hydrochloride in the minimum volume of water is basified with aqueous 5N NaOH and extracted with Et<sub>2</sub>O. The extract is dried (K<sub>2</sub>CO<sub>3</sub>) and evap leaving a residue which is stored in a desiccator over solid KOH as a low melting solid. It can be recovered with these procedures from asymmetric reductions with LAH, and reused. [J Am Chem Soc 77 3400 1955; J Org Chem 28 2381 2483 1963.]

*dl*-4-Dimethylamino-2,2-diphenylvaleramide [60-46-8] M 296.4, m 183-184°, pK<sub>Est</sub> ~9.8. Crystd from aqueous EtOH.

(-)-L-4-Dimethylamino-2,2-diphenylvaleramide [6078-64-4] M 296.4, m 136.5-137.5°. Crystd from pet ether or EtOH.

**2-Dimethylaminoethanol** [108-01-0] M 89.1, b 134.5-135.5°, d 1.430, n 1.4362,  $pK^{25}$  9.23. Dried with anhydrous K<sub>2</sub>CO<sub>3</sub> or KOH, and fractionally distd.

1-(3-Dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (EDCI, DEC, 1-ethyl-3-(3dimethyl-aminopropyl) carbodiimide hydrochloride) [25952-53-8] M 191.7, m 113.5-114.5°, 114-116°,  $pK_{Est} \sim 10.3$ . An excellent H<sub>2</sub>O-soluble peptide coupling reagent. It is purified by dissolving (ca 1g) in CH<sub>2</sub>Cl<sub>2</sub> (10mL) at room temperature and then add dry Et<sub>2</sub>O (~110mL) dropwise and the crystals that separate are collected, washed with dry Et<sub>2</sub>O and recrystd from CH<sub>2</sub>Cl<sub>2</sub>-Et<sub>2</sub>O and dried in a vacuum over P<sub>2</sub>O<sub>5</sub>. It is important to work in a dry atmosphere or work rapidly and then dry the solid as soon as possible. Material is moderately hygroscopic but once it becomes wet it reacts slowly with H<sub>2</sub>O. Store away from moisture and at -20° to slow down the hydrolysis process. The free base has b 47-48°/0.27mm, 53-54°/0.6mm, n<sub>D</sub><sup>25</sup> 1.4582. The methiodide is recrystallised from CHCl<sub>3</sub>-EtOAc, the crystals are filtered off, washed with dry Et<sub>2</sub>O and recrystd from CHCl<sub>3</sub>-Et<sub>2</sub>O, and dried *in vacuo* over P<sub>2</sub>O<sub>5</sub>, m 93-95°, 94-95°. [Sheehan et al. J Am Chem Soc 87 2492 1965; Sheehan and Cruickshank Org Synth Coll Vol V 555 1973.] § A polymer bound version is commercially avaiable.

**6-Dimethylaminopurine** [938-55-6] **M** 163.1, **m** 257.5-258.5°, 259-262°, 263-264°,  $pK_1^{25}$ **3.87**,  $pK_2^{25}$  10.5. It is purified by recrystn from H<sub>2</sub>O, EtOH (0.32g in 10mL) or CHCl<sub>3</sub>. [Albert and Brown J Chem Soc 2060 1954; UV: Mason J Chem Soc 2071 1954.] The monohydrochloride crystallises from EtOH-Et<sub>2</sub>O, **m** 253° (dec) [Elion et al. J Am Chem Soc 74 411 1952], the dihydrochloride has **m** 225° (dec) and the picrate has **m** 245° (235-236.5°) [Fryth et al. J Am Chem Soc 80 2736 1958].

4-Dimethylaminopyridine (DMAP) [1122-58-3] M 122.2, m 108-109°, b 191°, pK<sup>25</sup> 9.61.
Recrystd from toluene [Sadownik et al. J Am Chem Soc 108 7789 1986].
§ A polystyrene supported version (PS-DMAP) is commercially available.

*N*, *N*-Dimethylaniline [121-69-7] M 121.2, f 2°, b 84°/15mm, 193°/760mm, d 0.956,  $n^{25}$  1.5556,  $pK^{25}$  5.07. Primary and secondary amines (including aniline and monomethylaniline) can be removed by refluxing for some hours with excess acetic anhydride, and then fractionally distilling. Crocker and Jones (*J Chem Soc* 1808 1959) used four volumes of acetic anhydride, then distd off the greater part of it, and took up the residue in ice-cold dil HCl. Non-basic materials were removed by ether extraction, then the dimethylaniline was liberated with ammonia, extracted with ether, dried, and distd under reduced pressure. Metzler and Tobolsky (*J Am Chem Soc* 76 5178 1954) refluxed with only 10% (w/w) of acetic anhydride, then cooled and poured into excess 20% HCl, which, after cooling, was extracted with diethyl ether. (The amine hydrochloride, remains in the aqueous phase.) The HCl soln was cautiously made alkaline to phenolphthalein, and the amine layer was drawn off, dried over KOH and fractionally distd under reduced pressure, under nitrogen. Suitable drying agents for dimethylaniline include NaOH, BaO, CaSO<sub>4</sub>, and CaH<sub>2</sub>.

Other purification procedures include the formation of the picrate, prepared in \*benzene soln and crystd to constant melting point, then decomposed with warm 10% NaOH and extracted into ether: the extract was washed with water, and distd under reduced pressure. The oxalate has also been used. The base has been fractionally crystd by partial freezing and also from aq 80% EtOH then from absolute EtOH. It has been distd from zinc dust, under nitrogen.

2,6-Dimethylaniline [87-62-7] M 121.2, m 11°, b 210-211°/736mm, d 0.974, n 1.5604, pK<sup>25</sup> 3.95. Converted to its hydrochloride which, after recrystn, was decomposed with alkali to give the free base. Dried over KOH and fractionally distd.

3,4-Dimethylaniline [95-64-7] M 121.2, m 51°, b 116-118°/25mm, b 226°/760mm,  $pK^{25}$  5.17. Crystd from ligroin and distilled under vacuum.

9,10-Dimethylanthracene [781-43-1] M 206.3, m 180-181°. Crystd from EtOH, and by recrystn from the melt.

1,3-Dimethylbarbituric acid [769-42-6] M 156.1, m 123°, pK<sup>25</sup> 4.56. Crystd from water and sublimed in a vacuum. Also purified by dissolving 10g in 100mL of boiling CCl<sub>4</sub>/CHCl<sub>3</sub> (8:2) (1g charcoal), filtered and cooled to 25°. Dried *in vacuo* [Kohn et al. Anal Chem 58 3184 1986].

7,12-Dimethylbenz[a]anthracene [57-97-6] M 256.4, m 122-123°. Purified by chromatography on alumina/toluene or \*benzene. Crystd from acetone/EtOH.

**5,6-Dimethylbenzimidazole** [582-60-5] **M 146.2, m 205-206°, pK\_1^{25} 5.96, pK\_2^{25} 12.52.** Crystd from diethyl ether. Sublimed at 140°/3mm.

2,3-Dimethylbenzoic acid [603-79-2] M 150.2, m 146°, pK<sup>25</sup> 3.72. Crystd from EtOH and is volatile in steam.

2,4-Dimethylbenzoic acid [6/1-0/8] M 150.2, m 126-127°, b 267°/727mm, pK<sup>25</sup> 4.22. Crystd from EtOH, and sublimed in a vacuum.

**2,5-Dimethylbenzoic acid** [610-72-0] **M 150.2, m 134°, b 268°/760mm, pK<sup>25</sup> 4.00.** Steam distd, and crystd from EtOH.

2,6-Dimethylbenzoic acid [632-46-2] M 150.2, m 117°, pK<sup>25</sup> 3.35. Steam distd, and crystd from EtOH.

3,4-Dimethylbenzoic acid [619-04-5] M 150.2, m 166°, pK<sup>25</sup> 4.50. Crystd from EtOH and sublimed in vacuo.

3,5-Dimethylbenzoic acid [499-06-9] M 150.2, m 170°, pK<sup>25</sup> 4.30. Distd in steam, crystd from water or EtOH and sublimed in a vacuum.

4,4'-Dimethylbenzophenone [611-97-2] M 210.3, m 95°, b 333-334°/725mm. Purified by zone refining.

2,5-Dimethyl-1,4-benzoquinone [137-18-8] M 136.1, m 124-125°. Crystd from EtOH.

**2,6-Dimethyl-1,4-benzoquinone** [527-61-7] **M 136.1, m 72° (sealed tube).** Crystd from water/EtOH (8:1).

2,3-Dimethylbenzothiophene [31317-17-6] M 212.3, b 123-124°/10mm, n<sup>19</sup> 1.6171. Fractionated through a 90cm Monel spiral column, or other efficient fractionating or spinning band column and collecting the middle fraction.

*N*,*N*-Dimethylbenzylamine [103-83-3] M 135.2, b 66-67°/15mm, 181°/760mm,  $d_4^{20}$  0.898,  $n_D^{20}$  1.516, pK<sup>25</sup> 8.91. See *N*-benzyl dimethylamine on p. 128.

**4,4'-Dimethyl-2,2'-bipyridine** [1134-35-6] **M 184.2, m 175-176°, pK**<sub>Est(1)</sub> ~0.2, pK<sub>Est(2)</sub>~4.9. Crystd from ethyl acetate. [Elliott et al. J Am Chem Soc 107 4647 1985.]

1,1'-Dimethyl-4,4'-bipyridylium dichloride (3H<sub>2</sub>O; Methyl Viologen Dichloride, paraquat dichloride) [1910-42-5] M 311.2, m >300°(dec). Recrystd from MeOH/acetone mixture. Also crystd three times from absolute EtOH [Bancroft et al. Anal Chem 53 1390 1981]. Dried at 80° in a vacuum.

N,N-Dimethylbiuret [7710-35-2] M 131.1, m 178°. Purified by repeated crystn from the melt, or H<sub>2</sub>O. [Bredereck and Richter Chem Ber 99 2461 1968; Dunning and Close J Am Chem Soc 75 3615 1953.]

2,3-Dimethyl-1,3-butadiene [513-81-5] M 82.2, m -69-70°, b 68-69°/760mm, d 0.727, n 1.4385. Distd from NaBH<sub>4</sub>, and purified by zone melting.

1,3-Dimethylbutadiene sulfone (1,3-dimethylsulfolene) [10033-92-8] M 145.2, m 40.4-41.0°. Crystd from diethyl ether.

2,2-Dimethylbutane [75-83-2] M 86.2, b 49.7°, d 0.649, n<sup>25</sup> 1.36595. Distd azeotropically with MeOH, then washed with water, dried and distd.

**2,3-Dimethylbutane** [79-29-8] **M 86.2, b 58.0°, d 1.375, n^{25} 1.37231.** Distd from sodium, passed through a column of silica gel (activated by heating in nitrogen to 350° before use) to remove unsaturated impurities, and again distd from sodium. Also distilled azeotropically with MeOH, then washed with water, dried and redistd.

2,3-Dimethylbut-2-ene [563-79-1] M 84.2, b 72-73°/760mm, d 0.708, n 1.41153. Purified by GLC on a column of 20% squalene on chromosorb P at 50° [Flowers and Rabinovitch J Phys Chem 89 563 1985]. Also washed with 1M NaOH soln followed by H<sub>2</sub>O. Dried over Na<sub>2</sub>SO<sub>4</sub>, distd over powdered KOH

under nitrogen and passed through activated alumina before use. [Woon et al. J Am Chem Soc 108 7990 1986; Wong et al. J Am Chem Soc 109 3428 1987.]

Dimethylcarbamoyl chloride [79-44-7] M 107.5, m -33°, b 34°/0.1mm, d 1.172, n 1.4511. Must distil under high vacuum to avoid decomposition.

3,3'-Dimethylcarbanilide [620-50-8] M 240.3, m 225°. Crystd from ethyl acetate.

**Dimethyl carbonate** [616-38-5] **M 90.1, m 4.65°, b 90-91°, d 1.070, n 1.369.** Contains small amounts of water and alcohol which form azeotropes. Stood for several days in contact with Linde type 4A molecular sieves, then fractionally distd. The middle fraction was frozen slowly at 2°, several times, retaining 80% of the solvent at each cycle.

*cis- and trans-***1**,**4**-**Dimethylcyclohexane** [589-90-2] **M 112.2**, **b 120°**, **d 0.788**, **n 1.427**. Freed from olefins by shaking with conc H<sub>2</sub>SO<sub>4</sub>, washing with water, drying and fractionally distilling.

1,2-Dimethylcyclohexene [1674-10-8] M 110.2, b 135-136°/760mm, d 0.826, n 1.4591. Passed through a column of basic alumina and distd.

**1,5-Dimethyl-1,5-diazaundecamethylene polymethobromide (Hexadimethrene, Polybrene)** [28728-55-4] M 5000—10,000 polymer Purified by chromatography on Dowex 50 and/or by filtration through alumina before use [Frank Hoppe-Seyler's Z Physiol Chemie 360 997 1979]. Hygroscopic, sol in H<sub>2</sub>O is 10%.

2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline (4733-39-5) M 360.5, m >280°, pK<sub>Est</sub> ~5.6. Purified by recrystn from \*benzene.

Dimethyl disulfide [624-92-0] M 94.2, f -98°, b 40°/12mm, 110°/760mm, d 1.0605, n 1.5260. Passed through neutral alumina before use.

2,2-Dimethylethyleneimine [2658-24-4] M 71.1, b 70.5-71.0°, pK<sup>25</sup> 8.64. Freshly distd from sodium before use.

N,N-Dimethylformamide (DMF) /68-12-2/ M 73.1, b 40º/10mm, 61º/30mm, 88º/100mm, 153°/760mm, d 0.948, n<sup>25</sup> 1.4269, pK -0.3. Decomposes slightly at its normal boiling point to give small amounts of dimethylamine and carbon monoxide. The decomposition is catalysed by acidic or basic materials, so that even at room temperature DMF is appreciably decomposed if allowed to stand for several hours with solid KOH, NaOH or CaH<sub>2</sub>. If these reagents are used as dehydrating agents, therefore, they should not be refluxed with the DMF. Use of CaSO<sub>4</sub>, MgSO<sub>4</sub>, silica gel or Linde type 4A molecular sieves is preferable, followed by distn under reduced pressure. This procedure is adequate for most laboratory purposes. Larger amounts of water can be removed by azeotropic distn with \*benzene (10% v/v, previously dried over CaH<sub>2</sub>), at atmospheric pressure: water and \*benzene distil below 80°. The liquid remaining in the distn flask is further dried by adding MgSO<sub>4</sub> (previously ignited overnight at 300-400<sup>o</sup>) to give 25g/L. After shaking for one day, a further quantity of MgSO<sub>4</sub> is added, and the DMF distd at 15-20mm pressure through a 3-ft vacuumjacketed column packed with steel helices. However, MgSO<sub>4</sub> is an inefficient drying agent, leaving about 0.01M water in the final DMF. More efficient drying (to around 0.001-0.007M water) is achieved by standing with powdered BaO, followed by decanting before distn, with alumina powder (50g/L; previously heated overnight to 500-600°), and distilling from more of the alumina; or by refluxing at 120-140° for 24h with triphenylchlorosilane (5-10g/L), then distilling at ca 5mm pressure [Thomas and Rochow J Am Chem Soc 79 1843 1957]. Free amine in DMF can be detected by colour reaction with 1-fluoro-2,4-dinitrobenzene. It has also been purified by drying overnight over KOH pellets and then distd from BaO through a 10 cm Vigreux column [Exp Cell Res 100 213 1976]. [For efficiency of desiccants in drying dimethylformamide see Burfield and Smithers [J Org Chem 43 3966 1978, and for a review on purification, tests of purity and physical properties, see Juillard Pure Appl Chem 49 885 1977].

It has been purified by distilling from  $K_2CO_3$  under high vac and fractionated in an all-glass apparatus. The middle fraction is collected, degassed (seven or eight freeze-thaw cycles) and redistd under as high a vacuum as possible [Mohammad and Kosower J Am Chem Soc 93 2713 1971].

**Rapid purification:** Stir over  $CaH_2$  (5% w/v) overnight, filter, then distil at 20mmHg. Store the distd DMF over 3A or 4A molecular sieves. For solid phase synthesis, the DMF used must be of high quality and free from amines.

*d*,*l*-2,4-Dimethylglutaric acid [2121-67-7] M 160.2, m 144-145°  $pK_{Est(1)}$ ~4.4,  $pK_{Est(2)}$ ~5.4. Distd in steam and crystd from ether/pet ether.

**3,3-Dimethylglutaric** acid [4839-46-7] M 160.2, m 103-104°, b 89-90°/2mm, 126-127°/4.5mm,  $pK_2^{15}$  3.85,  $pK_2^{25}$  6.45. Crystd from water, \*benzene or ether/pet ether. Dried in a vacuum.

3,3-Dimethylglutarimide [1123-40-6] M 141.2, m 144-146°. Recrystd from EtOH [Arnett and Harrelson J Am Chem Soc 109 809 1987].

*N*,*N*-Dimethylglycinehydrazide hydrochloride [539-64-0] M 153.6, m 181°. Crystd by adding EtOH to a conc aqueous soln.

**Dimethylglyoxime** [95-45-4] M 116.1, m 240°,  $pK_1^{25}$  10.60,  $pK_2^{25}$  11.85. Crystd from EtOH (10mL/g) or aqueous EtOH. TOXIC.

2,5-Dimethyl-2,4-hexadiene [764-13-6] M 110.2, f 14.5°, b 132-134°, d 0.773, n 1.4796. Distd, then repeatedly fractionally crystd by partial freezing. Immediately before use, the material was passed through a column containing Woelm silica gel (activity I) and Woelm alumina (neutral) in separate layers.

2,2-Dimethylhexane [590-73-8] M 114.2, m -121.2°, b 107°, d 0.695. Dried over type 4A molecular sieves and distd.

2,5-Dimethylhexane [592-13-2] M 114.2, m -91.2°, b 109°, d 0.694. Dried over type 4A molecular sieves and distd.

**2,5-Dimethylhexane-2,5-diol** [110-03-2] **M 146.2, m 88-90°.** Purified by fractional crystn. Then the diol was dissolved in hot acetone, treated with activated charcoal, and filtered while hot. The soln was cooled and the diol was filtered off and washed well with cold acetone. The crystn process was repeated several times and the crystals were dried under a vac in a freeze-drying apparatus [Goates et al. J Chem Soc, Faraday Trans 1 78 3045 1982].

5,5-Dimethylhydantoin [77-71-4] M 128.1, m 177-178° pK<sup>24</sup>9.19. Crystd from EtOH and sublimed in vacuo.

1,1-Dimethylhydrazine [57-14-7] M 60.1, b 60.1°/702mm, d 0.790, n 1.408 pK<sup>30</sup> 7.21. Fractionally distd through a 4-ft column packed with glass helices. Ppted as its oxalate from diethyl ether soln. After crystn from 95% EtOH, the salt was decomposed with aqueous saturated NaOH, and the free base was distd, dried over BaO and redistd [McBride and Kruse J Am Chem Soc 79 572 1957]. Distn and storage should be under nitrogen.

**4,6-Dimethyl-2-hydroxypyrimidine** [108-79-2] M **124.1**, m **198-199°**,  $pK_1^{20}$  **3.77**,  $pK_2^{20}$  **10.50**. Crystd from absolute EtOH (charcoal).

**1,2-Dimethylimidazole** [1739-84-0] **M 96.1, m 38-40°, b 206°/760mm, d 1.084, pK<sub>Est</sub> ~8.1.** Crystd from \*benzene and stored at 0-4°. [Gorun et al. J Am Chem Soc 109 4244 1987.]

1,1-Dimethyl-1*H*-indene [18636-55-0] M 144.2, b 57°/4.8mm, 115°/20mm. Purified by gas chromatography or by fractional distn.

Dimethyl itaconate [617-52-7] M 158.2, m 38°, b 208°, d 1.124. Crystd from MeOH by cooling to -78°.

**Dimethylmaleic** anhydride [766-39-2] M 126.1, m 96°, b 225°/760mm. Distd from \*benzene/ligroin and sublimed in a vacuum.

**Dimethylmalonic acid** [595-46-0] **M 132.1, m 192-193**°  $pK_1^{25}$  **3.03,**  $pK_2^{25}$  **5.73.** Crystd from \*benzene/pet ether and sublimed in a vacuum with slight decomposition.

1,5-Dimethylnaphthalene [571-61-9] M 156.2, m 81-82°, b 265-266°. Crystd from 85% aq EtOH.

2,3-Dimethylnaphthalene [581-40-8] M 156.2, m 104-104.5°. Steam distd and crystd from EtOH.

2,6-Dimethylnaphthalene [581-42-0] M 156.2, m 110-111°, b 122.5-123.5°/10mm, 261-262°/760mm. Distd in steam and crystd from EtOH.

3,3'-Dimethylnaphthidine (4,4'-diamino-3,3'-dimethyl-1,1'-binaphthyl) [13138-48-2] M 312.4, m 213°. Recrystd from EtOH or pet ether (b 60-80°).

N,N-Dimethyl-m-nitroaniline [619-31-8] M 166.1, m 60°, pK<sup>25</sup> 2.63. Crystd from EtOH.

N, N-Dimethyl-p-nitroaniline [100-23-2] M 166.1, m 164.5-165.2°, pK<sup>25</sup> 0.61 (0.92). Crystd from EtOH or aqueous EtOH. Dried under vacuum.

**Dimethylnitrosamine** (*N*-nitrosodimethylamine) [62-75-9] M 74.0, m -28°, b 149-150°/atm, 153°/774mm, d. 1.006, n 1.4370. Dry over anhyd K<sub>2</sub>CO<sub>3</sub> or dissolve in Et<sub>2</sub>O, dry over solid KOH, filter, evap Et<sub>2</sub>O and distil yellow oily residue through a 30cm fractionating column discarding the first fraction which may contain Me<sub>2</sub>N. Also dried over CaCl<sub>2</sub> and distd at atm pressure. All should be done in an efficient fume cupboard as the vapors are **TOXIC** and **CARCINOGENIC**. [Fischer Chem Ber 8 1588 1875; Romberg Recl Trav Chim, Pays-Bas 5 248 1886; Hatt Org Synth Coll Vol II 211 1961; Krebs and Mandt Chem Ber 108 1130 1975.]

N,N-Dimethyl-p-nitrosoaniline [138-89-6] M 150.2, m 86-87°. See 4-nitroso-N,N-dimethylaniline on p. 314.

*N*,*N*-Dimethyl-*p*-nitrosoaniline hydrochloride [42344-05-8] M 186.7, m 177°. Crystd from hot water in the presence of a little HCl.

**2,6-Dimethyl-2,4,6-octatriene** [7216-56-0; cis/trans mixt 673-84-7; trans, trans 3016-19-1] M 136.2, **b 80-82°/15mm**,  $\varepsilon_{278nm}$  42,870. Repeated distn at 15mm through a long column of glass helices, the final distn being from sodium under nitrogen. See *neo*-allocimene on p. 100.

Dimethylolurea [140-95-4] M 120.1, m 137-139°. Crystd from aqueous 75% EtOH.

Dimethyl oxalate [553-90-2] M 118.1, m 54°, b 163-165°, d 1.148. Crystd repeatedly from EtOH. Degassed under nitrogen high vacuum and distd.

3,3-Dimethyloxetane [6921-35-3] M 86.1, b 79.2-80.3<sup>o</sup>/760mm. Purified by gas chromatography using a 2m silicone oil column.

2,3-Dimethylpentane [565-59-3] M 100.2, b 89.8°, d 0.695, n 1.39197, n<sup>25</sup> 1.38946. Purified by azeotropic distn with EtOH, followed by washing out the EtOH with water, drying and distn [Streiff et al. J Res Nat Bur Stand 37 331 1946]. **2,4-Dimethylpentane** [108-08-7] **M 100.2, b 80.5°, d 0.763, n 1.3814, n^{25} 1.37882.** Extracted repeatedly with conc H<sub>2</sub>SO<sub>4</sub>, washed with water, dried and distd. Percolated through silica gel (previously heated in nitrogen to 350°). Purified by azeotropic distn with EtOH, followed by washing out the EtOH with water, drying and distn.

**4,4-Dimethyl-1-pentene** [762-62-9] **M 98.2, b 72.5°/760mm, d 0.6827, n 1.3918.** Purified by passage through alumina before use [Traylor et al. J Am Chem Soc 109 3625 1987].

**Dimethyl peroxide** [690-02-8] **M 62.1, b 13.5°/760mm, d 0.8677, n 1.3503.** Purified by repeated trap-to-trap fractionation until no impurities could be detected by gas IR spectroscopy [Haas and Oberhammer J Am Chem Soc 106 6146 1984]. All necessary precautions should be taken in case of **EXPLOSION.** 

2,9-Dimethyl-1,10-phenanthroline [484-11-7] M 208.3, m 162-164°, pK<sup>25</sup> 5.85. Purified as hemihydrate from water, and as anhydrous from \*benzene.

**R**-(+)-*N*, *N'*-Dimethyl-1-phenethylamine [19342-01-9] and S-(-)-*N*, *N'*-Dimethyl-1-phenethylamine [17279-31-1] M 149.2, b 81°/16mm,  $[\alpha]_{D}^{20}$  (+) and (-) 50.2° (c 1, MeOH),  $[\alpha]_{D}^{26}$ +61.8° and -64.4° (neat *l* 1), d 0.908, pK<sub>Est</sub> ~9.0 (for RS). The amine is mixed with aqueous 10N NaOH and extracted with toluene. The extract is washed with saturated aqueous NaCl and dried over K<sub>2</sub>CO<sub>3</sub>, and transfered to fresh K<sub>2</sub>CO<sub>3</sub> until the soln is clear, and filtered. The filtrate is distd. If a short column packed with glass helices is used, the yield is reduced but a purer product is obtained. [Org Synth 25 89 1945; J Am Chem Soc 71 291 3929 3931 4165 1949.] The (-)-picrate has m 140-141° (cryst from EtOH). The racemate [1126-71-2] has b 88-89°/16mm, 92-94°/30mm, 194-195°/atm, d<sup>20</sup> 0.908.

**2,3-Dimethylphenol** [526-75-0] **M 122.2, m 75°, b 120°/20mm, 218°/760mm, pK<sup>25</sup> 10.54.** Crystd from aqueous EtOH.

2,5-Dimethylphenol [95-87-1] M 122.2, m 73°, b 211.5°/762mm, pK<sup>25</sup> 10.41. Crystd from EtOH/ether.

**2,6-Dimethylphenol** [576-26-1] **M 122.2, m 49°, b 203°/760mm, pK<sup>25</sup> 10.61.** Fractionally distd under nitrogen, crystd from \*benzene or hexane, and sublimed at 38°/10mm.

**3,4-Dimethylphenol** [95-65-8] **M 122.2, m 65°, b 225°/757mm, pK<sup>25</sup> 10.36.** Heated with an equal weight of conc H<sub>2</sub>SO<sub>4</sub> at 103-105° for 2-3h, then diluted with four volumes of water, refluxed for 1h, and either steam distd or extracted repeatedly with diethyl ether after cooling to room temperature. The steam distillate was also extracted and evaporated to dryness. (The purification process depends on the much slower sulfonation of 3,5-dimethylphenol than most of its likely contaminants.). It can also be crystd from water, hexane or pet ether, and vacuum sublimed. [Kester Ind Eng Chem (Anal Ed) 24 770 1932; Bernasconi and Paschalis J Am Chem Soc 108 29691986.]

**3,5-Dimethylphenol** [108-68-9] **M 122.2, m 68°, b 219°, pK<sup>25</sup> 10.19.** Purification as for 3,4dimethylphenol.

**Dimethyl phthalate** [131-11-3] M 194.2, b 282°, n 1.5149, d 1.190, d<sup>25</sup> 1.1865. Washed with aqueous Na<sub>2</sub>CO<sub>3</sub>, then distilled water, dried (CaCl<sub>2</sub>) and distd under reduced pressure (b 151-152°/0.1mm).

2,2-Dimethyl-1,3-propanediol (neopentyl glycol) [126-30-7] M 104.2, m 128.4-129.4°, b 208°/760mm. Crystd from \*benzene or acetone/water (1:1).

**2,2-Dimethyl-1-propanol** (*neo-pentyl alcohol*) [75-84-3] M 88.2, m 52°, b 113.1°/760mm. Difficult to distil because it is a solid at ambient temperatures. Purified by fractional crystallisation and sublimation.

N, N-Dimethylpropionamide [758-96-3] M 101.2, b 175-178°, d 0.920, n 1.440. Shaken over BaO for 1-2 days, then distd at reduced pressure.

**2,5-Dimethylpyrazine** [123-32-0] **M 108.1, b 156°, d 0.990, n 1.502, pK\_1^{25}-4.6 (aq H<sub>2</sub>SO<sub>4</sub>), pK\_2^{25}<b>1.85.** Purified via its picrate (m 150°) [Wiggins and Wise J Chem Soc 4780 1956].

**3,5-Dimethylpyrazole** [67-51-6] **M 96.1, m 107-108°, pK<sup>20</sup> 4.16.** Crystd from cyclohexane or water. [Barszez et al. J Chem Soc, Dalton Trans 2025 1986.]

**2,3-Dimethylquinoxaline** [2379-55-7] M 158.2, m 106°,  $pK^{25}$  -3.84 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from distilled water.

**2,4-Dimethylresorcinol** [634-65-1] **M 138.1, m 149-150°**  $pK_{Est(1)} \sim 9.8$ ,  $pK_{Est(2)} \sim 11.7$ . Crystd from pet ether (b 60-80°).

*meso*- $\alpha$ , $\beta$ -Dimethylsuccinic acid [608-40-2] M 146.1, m 211°, pK<sub>1</sub><sup>25</sup> 3.77, pK<sup>25</sup> 5.36. Crystd from EtOH/ether or EtOH/chloroform.

**2,2-Dimethylsuccinic acid** [597-43-3] M 146.1, m 141°,  $pK_1^{20}$  4.15,  $pK_2^{20}$  6.40. Crystd from EtOH/ether or EtOH/chloroform.

 $(\pm)$ -2,3-Dimethylsuccinic acid [13545-04-5] M 146.1, m 129°,  $pK_1^{25}$  3.82,  $pK_2^{25}$  5.98. Crystd from water.

Dimethyl sulfide [75-18-3] M 62.1, f -98.27°, b 0°/172mm, 37.5-38°/760mm, d<sup>21</sup> 0.8458, n<sup>25</sup> 1.4319. Purified via the Hg(II) chloride complex by dissolving 1 mole of Hg(II)Cl<sub>2</sub> in 1250mL of EtOH and slowly adding the boiling alcoholic soln of dimethyl sulfide to give the right ratio for 2(CH<sub>3</sub>)<sub>2</sub>S.3HgCl<sub>2</sub>. After recrystn of the complex to constant melting point, 500g of complex is heated with 250mL conc HCl in 750mL of water. The sulfide is separated, washed with water, and dried with CaCl<sub>2</sub> and CaSO<sub>4</sub>. Finally, it is distd under reduced pressure from sodium. Precautions should be taken (*efficient fume hood*) because of its very UNPLEASANT ODOUR.

2,4-Dimethylsulfolane [1003-78-7] M 148.2, b 128º/77mm, d<sup>25</sup> 1.1314. Vacuum distd.

Dimethyl sulfone [67-71-0] M 94.1, m 109°. Crystd from water. Dried over P2O5.

**Dimethyl sulfoxide (DMSO)** [67-68-5] M 78.1, m 18.0-18.5°, b 75.6-75.8°/12 m m, 190°/760mm, d 1.100, n 1.479. Colourless, odourless, very hygroscopic liquid, synthesised from dimethyl sulfide. The main impurity is water, with a trace of dimethyl sulfone. The Karl-Fischer test is applicable. It is dried with Linde types 4A or 13X molecular sieves, by prolonged contact and passage through a column of the material, then distd under reduced pressure. Other drying agents include CaH<sub>2</sub>, CaO, BaO and CaSO<sub>4</sub>. It can also be fractionally crystd by partial freezing. More extensive purification is achieved by standing overnight with freshly heated and cooled chromatographic grade alumina. It is then refluxed for 4h over CaO, dried over CaH<sub>2</sub>, and then fractionally distd at low pressure. For efficiency of desiccants in drying dimethyl sulfoxide see Burfield and Smithers [J Org Chem 43 3966 1978; Sato et al. J Chem Soc, Dalton Trans 1949 1986].

**Rapid purification:** Stand over freshly activated alumina, BaO or  $CaSO_4$  overnight. Filter and distil over CaH<sub>2</sub> under reduced pressure (~ 12 mm Hg). Store over 4A molecular sieves.

Dimethyl terephthalate [120-61-6] M 194.2, m 150°. Purified by zone melting.

N, N-Dimethylthiocarbamoyl chloride [16420-13-6] M 123.6, m 42-43°, b 64-65°/0.1mm. Crystd twice from pentane. *N*,*N*-Dimethyl-o-toluidine [609-72-3] M 135.2, b 68°/10mm, 211-211.5°/760mm, d 0.937, n 1.53664,  $pK^{25}$  5.85. Isomers and other bases have been removed by heating in a water bath for 100h with two equivalents of 20% HCl and two and a half volumes of 40% aq formaldehyde, then making the soln alkaline and separating the free base. After washing well with water it was distd at 10mm pressure and redistd at ambient pressure [von Braun and Aust *Chem Ber* 47 260 1914]. Other procedures include drying with NaOH, distilling from zinc in an atmosphere of nitrogen under reduced pressure, and refluxing with excess of acetic anhydride in the presence of conc H<sub>2</sub>SO<sub>4</sub> as catalyst, followed by fractional distn under vacuum.

*N*,*N*-Dimethyl-*m*-toluidine [121-72-2] M 135.2, b 211.5-212.5°, d 0.93, pK<sup>25</sup> 5.22. See *m*-methyl-*N*,*N*-dimethylaniline on p. 291.

N,N-Dimethyl-p-toluidine [99-97-8] M 135.2, b 93-94°/11mm, b 211°, d 0.937, n 1.5469, pK<sup>25</sup> 4.76. See p-methyl-N,N-dimethylaniline on p. 291.

**1,3-Dimethyluracil** [874-14-6] M 140.1, m 121-122°, pK -3.25 (aq  $H_2SO_4$ ). Crystd from EtOH/ether.

sym-Dimethylurea [96-31-1] M 88.1, m 106°. Crystd from acetone/diethyl ether by cooling in an ice bath. Also crystd from EtOH and dried at 50° and 5mm for 24h [Bloemendahl and Somsen J Am Chem Soc 107 3426 1985].

2,2'-Dinaphthylamine [532-18-3] M 269.3, m 170.5°, pK<sub>Est</sub> <0. Crystd from \*benzene.

2,4-Dinitroaniline [97-02-9] M 183.1, m 180°,  $\varepsilon_{348}$  12,300 in dil aq HClO<sub>4</sub>, pK<sup>25</sup> -4.27 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from boiling EtOH by adding one-third volume of water and cooling slowly. Dried in a steam oven.

**2,6-Dinitroaniline** [606-22-4] M 183.1, m 139-140°,  $pK^{25}$  -5.37 (aq H<sub>2</sub>SO<sub>4</sub>). Purified by chromatography on alumina, then crystd from \*benzene or EtOH.

2,4-Dinitroanisole [5327-44-6] M 198.1, m 94-95°. Crystd from aq EtOH.

**3,5-Dinitroanisole** [119-27-7] M 198.1, m 105-106°. Purified by repeated crystn from water and dried in a vacuum desiccator over  $P_2O_5$ .

1,2-Dinitrobenzene [528-29-0] M 168.1, m 116.5°. Crystd from EtOH.

**1,3-Dinitrobenzene** [99-65-0] M **168.1, m 90.5-91°.** Crystd from alkaline EtOH soln (20g in 750mL 95% EtOH at 40°, plus 100mL of 2M NaOH) by cooling and adding 2.5L of water. The ppte, after filtering off, washing with water and sucking dry, was crystd from 120mL, then 80mL of absolute EtOH [Callow, Callow and Emmens *Biochem J* **32** 1312 *1938*]. Has also been crystd from MeOH, CCl4 and ethyl acetate. Can be sublimed in a vacuum. [Tanner *J Org Chem* **52** 2142 *1987*.]

**1,4-Dinitrobenzene** [100-25-4] M 168.1, m 173°. Crystd from EtOH or ethyl acetate. Dried under vacuum over  $P_2O_5$ . Can be sublimed in a vacuum.

2,4-Dinitrobenzenesulfenyl chloride [528-76-7] M 234.6, m 96°. Crystd from CCl<sub>4</sub>.

2,4-Dinitrobenzenesulfonyl chloride [1656-44-6] M 266.6, m 102°. Crystd from \*benzene or \*benzene/pet ether.

**2,4-Dinitrobenzoic acid** [610-30-3] **M 212.1, m 183°, pK<sup>25</sup> 1.42.** Crystd from aqueous 20% EtOH (10mL/g), dried at 100°.

2,5-Dinitrobenzoic acid [610-28-6] M 212.1, m 179.5-180°, pK<sup>25</sup> 1.62. Crystd from distd water. Dried in a vacuum desiccator.

2,6-Dinitrobenzoic acid [603-12-3] M 212.1, m 202-203°, pK<sup>25</sup> 1.14. Crystd from water.

3,4-Dinitrobenzoic acid [528-45-0] M 212.1, m 166°, pK<sup>25</sup> 2.81. Crystd from EtOH by addition of water.

**3,5-Dinitrobenzoic** acid [99-34-3] M 212.1, m 205°, pK<sup>25</sup> 2.73 (2.79). Crystd from distilled water or 50% EtOH (4mL/g). Dried in a vacuum desiccator or at 70° over BaO under vacuum for 6h.

4,4'-Dinitrobenzoic anhydride [902-47-6] M 406.2, m 189-190°. Crystd from acetone.

**3,5-Dinitrobenzoyl chloride** [99-33-2] M 230.6, m 69.5°. Crystd from CCl<sub>4</sub> or pet ether (b 40-60°). It reacts readily with water, and should be kept in sealed tubes or under dry pet ether.

2,2'-Dinitrobiphenyl [2436-96-6] M 244.2, m 123-124°. Crystd from EtOH.

2,4'-Dinitrobiphenyl [606-81-5] M 244.2, m 92.7-93.7°. Crystd from EtOH.

**4,4'-Dinitrobiphenyl** [1528-74-1] **M 244.2, m 240.9-241.8°.** Crystd from \*benzene, EtOH (charcoal) or acetone. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

2,6-Dinitro-p-cresol (2,6-dinitro-4-methylphenol) [609-93-3] M 198.1, m 78-79°, pK<sub>Est</sub>~3.7. Recrystd from EtOH and is steam volatile. TOXIC IRRITANT.

4,6-Dinitro-o-cresol [534-52-1] M 198.1, m 85-86°, 87°, pK<sup>25</sup>4.70. Crystd from aqueous EtOH.

2,4-Dinitrodiphenylamine [961-68-2] M 259.2, m 157°, pK<sub>Est</sub> <0. Crystd from aqueous EtOH.

4,4'-Dinitrodiphenylurea [587-90-6] M 302.2, m 312°(dec). Crystd from EtOH. Sublimes in vac.

2,4-Dinitrofluorobenzene (Sanger's reagent) [70-34-8] M 186.1, m 25-27°, b 133°/2mm, 140-141°/5mm, d 1.483. Crystd from ether or EtOH. Vacuum distd through a Todd Column (see p. 174). If it is to be purified by distn *in vacuo*, the distn unit must be allowed to cool before air is allowed into the apparatus otherwise the residue carbonises spontaneously and an EXPLOSION may occur. The material is a skin irritant and may cause serious dermatitis.

1,8-Dinitronaphthalene [602-38-0] M 218.2, m 170-171°. Crystd from \*benzene.

2,4-Dinitro-1-naphthol (Martius Yellow) [605-69-6] M 234.2, m 81-82°, pK<sub>Est</sub> ~3.7. Crystd from \*benzene or aqueous EtOH.

2,4-Dinitrophenetole [610-54-8] M 240.2, m 85-86°. Crystd from aqueous EtOH.

2,4-Dinitrophenol [51-28-5] M 184.1, m 114°, pK<sup>25</sup> 4.12. Crystd from \*benzene, EtOH, EtOH/water or water acidified with dil HCl, then recrystd from CCl<sub>4</sub>. Dried in an oven and stored in a vac desiccator over CaSO<sub>4</sub>.

2,5-Dinitrophenol [329-71-5] M 184.1, m 108°, pK<sup>25</sup> 5.20. Crystd from H<sub>2</sub>O with a little EtOH.

**2,6-Dinitrophenol** [573-56-8] **M** 184.1, **m** 63.0-63.7°,  $pK^{25}$  3.73. Crystd from \*benzene/cyclohexane, aqueous EtOH, water or \*benzene/pet ether (b 60-80°, 1:1).

**3,4-Dinitrophenol** [577-71-9] **M 184.1, m 138°, pK<sup>25</sup> 5.42.** Steam distd and crystd from water and air-dried. CAUTION - EXPLOSIVE when dry, store with 10% water.

**3,5-Dinitrophenol** [586-11-8] **M 184.1, m 126°, pK<sup>25</sup> 6.68.** Crystd from \*benzene or CHCl<sub>3</sub>/pet ether. Should be stored with 10% water because it is **EXPLOSIVE** when dry.

2,4-Dinitrophenylacetic acid [643-43-6] M 226.2, m 179°(dec), pK<sup>25</sup> 3.50. Crystd from water.

**2,4-Dinitrophenylhydrazine** (DNPH) [119-26-6] M 198.1, m 200°(dec),  $pK_{Est} \sim 2.0$ . Crystd from butan-1-ol, dioxane, EtOH, \*C<sub>6</sub>H<sub>6</sub> or ethyl acetate. *HCl* has m 186°(dec).

2,2-Dinitropropane [595-49-3] M 162.1, m 53.5°. Crystd from EtOH or MeOH. Dried over CaCl<sub>2</sub> or under vacuum for 1h just above the melting point.

2,4-Dinitroresorcinol [519-44-8] M 200.1, m 149°, pK<sup>25</sup> 3.05. Crystd from aq EtOH. Explosive.

**3,5-Dinitrosalicylic acid** [609-99-4] **M 228.1, m 173-174°, pK**<sup>25</sup><sub>1</sub>**0.70, pK**<sup>25</sup><sub>2</sub>**7.40.** Crystd from water.

2,6-Dinitrothymol [303-21-9] M 240.2, m 53-54°. Crystd from aq EtOH.

2,3-Dinitrotoluene [602-01-7] M 182.1, m 63°. Distd in steam and crystd from water or \*benzene/pet ether. Stored with 10% water. Could be EXPLOSIVE when dry.

**2,4-Dinitrotoluene** [121-14-2] **M 182.1, m 70.5-71.0°.** Crystd from acetone, isopropanol or MeOH. Dried under vacuum over H<sub>2</sub>SO<sub>4</sub>. Purified by zone melting. *Could be* **EXPLOSIVE** *when dry*.

2,5-Dinitrotoluene [619-15-8] M 182.1, m 51.2°. Crystd from \*benzene.

2,6-Dinitrotoluene [606-20-2] M 182.1, m 64.3°. Crystd from acetone.

**3,4-Dinitrotoluene** [610-39-9] **M 182.1, m 61°.** Distil in steam and cryst from \*benzene/pet ether. Store with 10% of water to avoid **EXPLOSION.** 

**3,5-Dinitro**-*o*-toluic acid [28169-46-2] M 226.2, m 206°, pK<sub>Est</sub> ~3.0. Crystd from H<sub>2</sub>O or aq EtOH.

2,4-Dinitro-m-xylene [603-02-1] M 196.2, m 83-84°. Crystd from EtOH.

Dinonyl phthalate (mainly 3,5,5-trimethylhexyl phthalate isomer) [28553-12-0; 14103-61-8]M 418.6, m 26-29°, b 170°/2mm, d 0.9640, n 1.4825. Washed with aqueous Na<sub>2</sub>CO<sub>3</sub>, then shaken with water. Ether was added to break the emulsion, and the soln was washed twice with water, and dried (CaCl<sub>2</sub>). After evaporating the ether, the residual liquid was distd three times under reduced pressure. It was stored in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>

**Dioctadecyldimethylammonium bromide** [3700-67-2] **M 630.9, m 161-163°.** Crystd from acetone then MeOH [Lukac J Am Chem Soc 106 4387 1984]. Also purified by chromatography on alumina by washing with  $*C_6H_6$  and eluting with Me<sub>2</sub>CO, evap and cryst from MeCN [Swain and Kreevoy J Am Chem Soc 77 1126 1955].

Diosgenin [5/2-04-9] M 294.5, m 204-207<sup>o</sup>, [α]<sup>25</sup><sub>D</sub> -129<sup>o</sup> (in Me<sub>2</sub>CO). Crystd from acetone.

1,3-Dioxane [505-22-6] M 88.1, b 104.5°/751mm, d 1.040, n 1.417. Dried with sodium and fractionally distd.

**1,4-Dioxane** [123-91-1] M 88.1, f 11.8°, b 101.3°, d<sup>25</sup> 1.0292, n<sup>15</sup> 1.4236, n<sup>25</sup> 1.42025. Prepared commercially either by dehydration of ethylene glycol with H<sub>2</sub>SO<sub>4</sub> and heating ethylene oxide or bis(ß-chloroethyl)ether with NaOH. Usual impurities are acetaldehyde, ethylene acetal, acetic acid, water and peroxides. Peroxides can be removed (and the aldehyde content decreased) by percolation through a column of activated alumina (80g per 100-200mL solvent), by refluxing with NaBH<sub>4</sub> or anhydrous stannous chloride and distilling, or by acidification with conc HCl, shaking with ferrous sulfate and leaving in contact with it for 24h before filtering and purifying further.

Hess and Frahm [Chem Ber 71 2627 1938] refluxed 2L of dioxane with 27mL conc HCl amd 200mL water for 12h with slow passage of nitrogen to remove acetaldehyde. After cooling the soln KOH pellets were added slowly and with shaking until no more would dissolve and a second layer had separated. The dioxane was decanted, treated with fresh KOH pellets to remove any aq phase, then transferred to a clean flask where it was refluxed for 6-12h with sodium, then distd from it. Alternatively, Kraus and Vingee [J Am Chem Soc 56 511 1934] heated on a steam bath with solid KOH until fresh addition of KOH gave no more resin (due to acetaldehyde). After filtering through paper, the dioxane was refluxed over sodium until the surface of the metal was not further discoloured during several hours. It was then distd from sodium.

The acetal (b  $82.5^{\circ}$ ) is removed during fractional distn. Traces of \*benzene, if present, can be removed as the \*benzene/MeOH azeotrope by distn in the presence of MeOH. Distn from LiAlH<sub>4</sub> removes aldehydes, peroxides and water. Dioxane can be dried using Linde type 4X molecular sieves. Other purification procedures include distn from excess C<sub>2</sub>H<sub>5</sub>MgBr, refluxing with PbO<sub>2</sub> to remove peroxides, fractional crystn by partial freezing and the addition of KI to dioxane acidified with aq HCl. Dioxane should be stored out of contact with air, preferably under N<sub>2</sub>.

A detailed purification procedure is as follows: Dioxane was stood over ferrous sulfate for at least 2 days, under nitrogen. Then water (100mL) and conc HCl (14mL) / litre of dioxane were added (giving a pale yellow colour). After refluxing for 8-12h with vigorous N<sub>2</sub> bubbling, pellets of KOH were added to the warm soln to form two layers and to discharge the colour. The soln was cooled rapidly with more KOH pellets being added (magnetic stirring) until no more dissolved in the cooled soln. After 4-12h, if the lower phase was not black, the upper phase was decanted rapidly into a clean flask containing sodium, and refluxed over sodium (until freshly added sodium remained bright) for 1h. The middle fraction was collected (and checked for minimum absorbency below 250nm). The distillate was fractionally frozen three times by cooling in a refrigerator, with occasional shaking or stirring. This material was stored in a refrigerator. For use it was thawed, refluxed over sodium for 48h, and distilled into a container for use. All joints were clad with Teflon tape.

Coetzee and Chang [*Pure Appl Chem* 57 633 1985] dried the solvent by passing it slowly through a column (20g/L) of 3A molecular sieves activated by heating at 250° for 24h. Impurities (including peroxides) were removed by passing the effluent slowly through a column packed with type NaX zeolite (pellets ground to 0.1mm size) activated by heating at 400° for 24h or chromatographic grade basic Al<sub>2</sub>O<sub>3</sub> activated by heating at 250° for 24h. After removal of peroxides the effluent was refluxed several hours over sodium wire, excluding moisture, distilled under nitrogen or argon and stored in the dark.

One of the best tests of purity of dioxane is the formation of the purple disodium benzophenone complex during reflux and its persistence on cooling. (Benzophenone is better than fluorenone for this purpose, and for the storing of the solvent.) [Carter, McClelland and Warhurst *Trans Faraday Soc* 56 343 1960]. TOXIC.

**Rapid purification:** Check for peroxides (see Chapter 1 and Chapter 2 for test under ethers). Pre-dry with  $CaCl_2$  or better over Na wire. Then reflux the pre-dried solvent over Na (1% w/v) and benzophenone (0.2% w/v) under an inert atmosphere until the blue colour of the benzophenone ketyl radical anion persists. Distil, and store over 4A molecular sieves in the dark.

**1,3-Dioxolane** [646-06-0] **M 74.1, b 75.0-75.2°, d 1.0600, n<sup>21</sup> 1.3997.** Dried with solid NaOH, KOH or CaSO<sub>4</sub>, and distd from sodium or sodium amalgam. Barker et al. [J Chem Soc 802 1959] heated 34mL of dioxalane under reflux with 3g of PbO<sub>2</sub> for 2h, then cooled and filtered. After adding xylene (40mL) and PbO<sub>2</sub> (2g) to the filtrate, the mixture was fractionally distd. Addition of xylene (20mL) and sodium wire to the main fraction (b 70-71°) led to vigorous reaction, following which the mixture was finally distd. Xylene and sodium additions were made to the main fraction (b 73-74°) before it was finally distd.

4,4'-Di-*n*-pentyloxyazoxybenzene [64242-26-8] M 370.5. Crystd from Me<sub>2</sub>CO, and dried by heating under vacuum.

Diphenic acid [482-05-3] M 242.2, m 228-229°, pK<sup>25</sup> 3.46. Crystd from water.

**Diphenic anhydride** [6050-13-1] **M 466.3, m 217°.** After removing free acid by extraction with cold aq Na<sub>2</sub>CO<sub>3</sub>, the residue has been crystd from acetic anhydride and dried at 100°. Acetic anhydride also converts the acid to the anhydride.

*N*,*N*-Diphenylacetamidine [621-09-0] M 210.3, m 131°. Crystd from EtOH, then sublimed under vacuum at ca 96° onto a "finger" cooled in solid CO<sub>2</sub>/MeOH, with continuous pumping to free it from occluded solvent.

Diphenylacetic acid [117-34-0] M 212.3, m 147.4-148.4°, pK<sup>25</sup> 3.94. Crystd from \*benzene, H<sub>2</sub>O or aq 50% EtOH.

Diphenylacetonitrile [86-29-3] M 193.3, m 73-75°. Crystd from EtOH or pet ether (b 90-100°).

Diphenylacetylene (tolan) [501-65-5] M 178.2, m 62.5°, b 90-97°/0.3mm. Crystd from EtOH.

**Diphenylamine** [122-39-4] M 169.2, m 62.0-62.5°,  $pK^{25}$  0.77 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from pet ether, MeOH, or EtOH/water. Dried under vacuum.

Diphenylamine-2-carboxylic acid [91-40-7] M 213.2, m 184°,  $pK_1^{25}$  -1.28 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$  3.86. See N-phenylanthranilic acid on p. 327.

Diphenylamine-2,2'-dicarboxylic acid (2,2'-iminodibenzoic acid) [579-92-0] M 257.2, m 298°(dec), pK<sub>Est</sub> ~3.7. Crystd from EtOH.

9,10-Diphenylanthracene [1499-10-1] M 330.4, m 248-249°. Crystd from acetic acid or xylene [Baumstark et al. J Org Chem 52 3308 1987].

N,N'-Diphenylbenzidine [531-91-9] M 336.4, m 245-247°, 251-252°, pK<sup>25</sup> 0.30. Crystd from toluene or ethyl acetate. Stored in the dark.

trans-trans-1,4-Diphenylbuta-1,3-diene [538-81-8] M 206.3, m 153-153.5°. Its soln in pet ether (b 60-70°) was chromatographed on an alumina-Celite column (4:1) and the column was washed with the same solvent. The main zone was cut out, eluted with ethanol and transferred to pet ether, which was then dried and evaporated [Pinckard, Wille and Zechmesiter J Am Chem Soc 70 1938 1948]. Recrystd from hexane.

sym-Diphenylcarbazide [140-22-7] M 242.3, m 172°. A common impurity is phenylsemicarbazide which can be removed by chromatography [Willems et al. Anal Chim Acta 51 544 1970]. Crystd from EtOH or glacial acetic acid.

**1,5-Diphenylcarbazone** [538-62-5] **M 240.3, m 124-127°.** Crystd from EtOH (*ca* 5mL/g), and dried at 50°. A commercial sample, nominally *sym*-diphenylcarbazone but of **m** 154-156°, was a mixture of diphenylcarbazide and diphenylcarbazone. The former was removed by dissolving 5g of the crude material in 75mL of warm EtOH, then adding 25g Na<sub>2</sub>CO<sub>3</sub> dissolved in 400mL of distd water. The alkaline soln was cooled and extracted six times with 50mL portions of diethyl ether (discarded). Diphenylcarbazone was then ppted by acidifying the alkaline soln with 3M HNO<sub>3</sub> or glacial acetic acid. It was filtered on a Büchner funnel, air dried, and stored in the dark [Gerlach and Frazier Anal Chem **30** 1142 1958]. Other impurities were phenylsemicarbazide and diphenylcarbodiazone. Impurities can be detected by chromatography [Willems et al. Anal Chim Acta **51** 544 1970].

Diphenyl carbonate [102-09-0] M 214.2, m 80°. Purified by sublimation, and by preparative gas chromatography with 20% Apiezon on Embacel, and crystn from EtOH.

Diphenylcyclopropenone (Diphencyprone) [886-38-4] M 206.2, m 87-90<sup>o</sup>(hydrate), 119-121<sup>o</sup>(anhydr). Crystd from cyclohexane. UV (MeCN): λmax 226, 282, 297nm.

**Diphenyl disulfide** (phenyl disulfide) [882-33-7] M 218.3, m 60.5°. Crystd from MeOH. [Alberti et al. J Am Chem Soc 108 3024 1986]. Crystd repeatedly from hot diethyl ether, then vac dried at 30° over P<sub>2</sub>O<sub>5</sub>, fused under nitrogen and re-dried, the whole procedure being repeated, with a final drying under vac for 24h. Also recrystd from hexane/EtOH soln. [Burkey and Griller J Am Chem Soc 107 246 1985.]

**1,1-Diphenylethanol** [599-67-7] **M 198.3, m 80-81°.** Crystd from *n*-heptane. [Bromberg et al. J Am Chem Soc **107** 83 1985.]

1,1-Diphenylethylene [530-48-3] M 180.3, b 268-270°, d 1.024, n 1.6088. Distd under reduced pressure from KOH. Dried with CaH<sub>2</sub> and redistd.

*N*,*N*'-Diphenylethylenediamine (Wanzlick's reagent) [150-61-8] M 212.3, m 67.5°, b 178-182°/2mm  $pK_{Est(1)} \sim 0.5$ ,  $pK_{Est(2)} \sim 3.8$ . Crystd from aqueous EtOH or MeOH.

N,N'-Diphenylformamidine [622-15-1] M 196.2, m 142°, 137°, 136-139°. Crystd from absolute EtOH, gives the hydrate with aqueous EtOH.

1,3-Diphenylguanidine [102-06-7] M 211.3, m 148°, pK<sup>25</sup> 10.12. Crystd from toluene, aqueous acetone or EtOH, and vacuum dried.

**1,6-Diphenyl-1,3,5-hexatriene** [1720-32-7] **M 232.3, m 200-203°.** Crystd from CHCl<sub>3</sub> or EtOH/CHCl<sub>3</sub> (1:1).

5,5-Diphenylhydantoin [57-41-0] M 252.3, m 293-295°. Crystd from EtOH.

**1,1-Diphenylhydrazine** (hydrazobenzene) [122-66-7] M 184.2, m 34°, 44°, 175°/10 mm, 222°/40 mm, pK<sub>Est</sub> ~1.7. Crystd from hot EtOH containing a little ammonium sulfide or H<sub>2</sub>SO<sub>3</sub> (to prevent atmospheric oxidation), preferably under nitrogen. Dried in a vacuum desiccator. Also crystd from pet ether (b 60-100°) to constant absorption spectrum. *HCl*, from EtOH has m 163-164°(dec). *Picrate*, from \*C<sub>6</sub>H<sub>6</sub>, has m 123°(dec).

**1,3-Diphenylisobenzofuran** [5471-63-6] **M** 270.3, **m** 129-130°. Recrystd from EtOH or EtOH/CHCl<sub>3</sub> (1:1) under red light (as in photographic dark rooms) or from \*benzene in the dark.

**Diphenylmethane** [101-81-5] **M 168.2, m 25.4°.** Sublimed under vacuum, or distd at 72-75°/4mm. Crystd from EtOH. Purified by fractional crystn of the melt.

1,1-Diphenylmethylamine [91-00-9] M 183.2, m 34°, pK<sub>Est</sub> ~9.1. Crystd from water.

Diphenylmethyl chloride (benzhydryl chloride) [90-99-3] M 202.7, m 17.0°, b 167°/17mm, n 1.5960. Dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd under reduced pressure.

*all-trans*-1,8-Diphenyl-1,3,5,8-octatetraene [3029-40-1] M 258.4, m 235-237°. Crystd from EtOH.

2,5-Diphenyl-1,3,4-oxadiazole (PPD) [725-12-2] M 222.3, m 70° (hydrate), 139-140° (anhydrous), b 231°/13mm, 248°/16mm. Crystd from EtOH and sublimed *in vacuo*.

2,5-Diphenyloxazole (PPO) [92-71-7] M 221.3, m 74°, b 360°/760mm. Distd in steam and crystd from ligroin.

N, N'-Diphenyl-p-phenylenediamine [74-31-7] M 260.3, m 148-149°, b 219-224°/0.7 mm, pK<sub>Est</sub> <0. Crystd from EtOH, chlorobenzene/pet ether or \*benzene. Has also been crystd from aniline, then extracted three times with absolute EtOH.

**1,1-Diphenyl-2-picrylhydrazine** [1707-75-1] M 395.3, m 174°(dec), 178-179.5°(dec). Crystd from CHCl<sub>3</sub>, or \*benzene/pet ether (1:1), then degassed at 100° and  $<10^{-5}$ mm Hg for *ca* 50h to decompose the 1:1 molar complex formed with \*benzene.

2,2-Diphenylpropionic acid [5558-66-7] M 226.3, m 173-174°, pK<sub>Est</sub> ~3.8. Crystd from EtOH.

3,3-Diphenylpropionic acid [606-83-7] M 226.3, m 155°, pK<sub>Est</sub> ~4.5. Crystd from EtOH.

**Diphenyl sulfide** [139-66-2] **M 186.3, b 145°/8mm, d 1.114, n 1.633.** Washed with aqueous 5% NaOH, then water. Dried with CaCl<sub>2</sub>, then with sodium. The sodium was filtered off and the diphenyl sulfide was distd under reduced pressure.

Diphenyl sulfone [127-63-9] M 218.3, m 125°, b 378°(dec). Crystd from diethyl ether. Purified by zone melting.

sym-Diphenylthiourea (thiocarbanilide) [102-08-9] M 228.3, m 154°. Crystd from boiling EtOH by adding hot water and allowing to cool.

1,1-Diphenylurea [603-54-3] M 212.3, m 238-239°. Crystd from MeOH.

Dipicolinic acid (pyridine-2,6-dicarboxylic acid) [499-83-2] M 167.1, m 255°(dec),  $\lambda_{max}$  270nm, pK<sub>1</sub><sup>20</sup> 2.10, pK<sub>2</sub><sup>20</sup> 4.68. Crystd from water, and sublimed in a vacuum.

N, N-Di-n-propylaniline [2217-07-4] M 177.3, b 127°/10mm, 238-241°/760mm, pK<sup>23</sup> 5.68. Refluxed for 3hr with acetic anhydride, then fractionally distd under reduced pressure.

Dipropylene glycol (octan-4,5-diol) [110-98-5] M 134.2, b 109-110°/8mm, d 1.022, n 1.441. Fractionally distd below 15mm pressure, using packed column and taking precautions to avoid absorption of water.

Di-n-propyl ketone [123-19-3] M 114.2, b 143.5°, d 0.8143, n 1.40732. Dried with CaSO<sub>4</sub>, then distd from P<sub>2</sub>O<sub>5</sub> under nitrogen.

Di-n-propyl sulfide [111-47-7] M 118.2, b 141-142°, d 0.870, n 1.449. Washed with aqueous 5% NaOH, then water. Dried with CaCl<sub>2</sub> and distd from Na [Dunstan and Griffiths J Chem Soc 1344 1962].

Di-(4-pyridoyl)hydrazine [4329-75-3] M 246.2, m 254-255°. Crystd from water.

2,2'-Dipyridylamine [1202-34-2] M 171.2, m 84° and remelts at 95° after solidifying, b 176-178°/13mm, 307-308°/760mm, pK 6.69 (in 20% EtOH). Crystd from \*benzene or toluene [Blakley and De Armond J Am Chem Soc 109 4895 1987].

**2,2'-Dipyridyl disulfide** (2,2'dithiopyridine) [2127-03-9] M 220.3, m 53°, 56-58°, 57-58°,  $pK_1^{25}$  0.35,  $pK_2^{25}$  2.45. Recrystd from \*C<sub>6</sub>H<sub>6</sub>/pet ether (6:7), ligroin or \*C<sub>6</sub>H<sub>6</sub>. Picrate has m 119° (from EtOH). [Walter et al. Justus Liebigs Ann Chem 695 7785 1966; Marckwald et al. Chem Ber 33 1556 1900; Brocklehurst and Little Biochem J 133 67,78 1973.]

1,2-Di-(4-pyridyl)-ethane [4916-57-8] M 184.2, pK<sub>Est(1)</sub> ~3.8, pK<sub>Est(2)</sub>~5.4. Crystd from cyclohexane/\*benzene (5:1).

*trans*-1,2-Di-(4-pyridyl)-ethylene [13362-78-2] M 182.2, m 153-154°, 155.5-156.5°,  $pK_1^{25}$ 3.65,  $pK_2^{25}$  5.6. Crystd from water (1.6g/100mL at 100°). Di-HCl has m 347°, from EtOH

**1,3-Di-(4-pyridyl)-propane** [17252-51-6] M **198.3, m 60.5-61.5°**,  $pK_{Est(1)} \sim 4.5$ ,  $pK_{Est(2)} \sim 5.5$ . Crystd from *n*-hexane/\*benzene (5:1).

S-1,2-Distearin [1188-58-5] M 625.0, m 76-77°,  $[\alpha]_D^{20}$ -2.8° (c 6.3, CHCl<sub>3</sub>),  $[\alpha]_{546}^{20}$ +1.4° (c 10, CHCl<sub>3</sub>/MeOH, 9:1). Crystd from chloroform/pet ether.

**2,5-Distyrylpyrazine** [14990-02-4] **M 284.3, m 219°.** Recryst from xylene; chromatographed on basic silica gel (60-80 mesh) using  $CH_2Cl_2$  as eluent, then vac sublimed on to a cold surface at  $10^{-3}$  torr [Ebied J Chem Soc, Faraday Trans 1 78 3213 1982]. Operations should be carried out in the dark.

**1,3-Dithiane** [505-23-7] **M 120.2, m 54°.** Crystd from 1.5 times its weight of MeOH at 0°, and sublimed at 40-50°/0.1mm.

2,2'-Dithiobis(benzothiazole) [120-78-8] M 332.2, m 180°. Crystd from \*benzene.

4,4'-Dithiodimorpholine [103-34-4] M 236.2, m 124-125°. Crystd from hot aq dimethylformamide.

1,4-Dithioerythritol (DTE, erythro-2,3-dihydroxy-1,4-dithiobutane) [6892-68-8] M 154.3, m 82-84°, pK<sub>1</sub> 9.0, pK<sub>2</sub> 9.9. Crystd from ether/hexane and stored in the dark at 0°.

Dithiooxamide (rubeanic acid) [79-40-3] M 120.2, m >300°. Crystd from EtOH and sublimed in a vacuum.

**RS-1,4-Dithiothreitol (DTT, Cleland's reagent)** [27565-41-9] M 154.3, m 42-43°, pK<sub>1</sub> 8.3, pK<sub>2</sub> 9.5. Crystd from ether and sublimed at  $37^{\circ}/0.005$ mm. Should be stored at  $0^{\circ}$ .

Dithizone (diphenylthiocarbazone) [60-10-6] M 256.3, ratio of  $\varepsilon_{620nm}/\varepsilon_{450nm}$  should be  $\ge 1.65$ ,  $\varepsilon_{620}$  3.4 x 10<sup>4</sup> (CHCl<sub>3</sub>), pK<sub>2</sub> 4.6. The crude material is dissolved in CCl<sub>4</sub> to give a concentrated soln. This is filtered through a sintered glass funnel and shaken with 0.8M aq ammonia to extract dithizonate ion. The aqueous layer is washed with several portions of CCl<sub>4</sub> to remove undesirable materials. The aqueous layer is acidified with dil H<sub>2</sub>SO<sub>4</sub> to precipitate pure dithizone. It is dried in a vacuum. When only small amounts of dithizone are required, purification by paper chromatography is convenient. [Cooper and Hibbits J Am Chem Soc 75 5084 1933.] Instead of CCl<sub>4</sub>, CHCl<sub>3</sub> can be used, and the final extract, after washing with water, can be evapd in air at 40-50° and dried in a desiccator. Complexes with Cd, Hg, Ni and Zn.

Di-p-tolyl carbonate [621-02-3] M 242.3, m 115°. Purified by GLC with 20% Apiezon on Embacel followed by sublimation *in vacuo*.

N,N'-Di-o-tolylguanidine [97-39-2] M 239.3, m 179° (175-176°), pK<sub>Est</sub> ~10.3. Crystd from aqueous EtOH.

Di-p-tolylphenylamine [20440-95-3] M 273.4, m 108.5°, pK<sub>Est</sub> ~-5.0. Crystd from EtOH.

Di-p-tolyl sulfone [599-66-6] M 278.3, m 158-159°, b 405°. Crystd repeatedly from diethyl ether. Purified by zone melting.

Djenkolic acid (S,S'-methylene-bis-L-cysteine) [498-59-9] M 254.3, m 300-350°(dec),  $[\alpha]_D^{20}$ -65° (c 2, HCl) [See pK of S-methyl-L-cysteine]. Crystd from a large volume of water (sol 0.5g%).

cis-4,7,10,13,16,19-Docosahexaenoic acid [6217-54-5] M 328.5, m -44/1°, -44.1°,  $n_D^{20}$ 1.5017, pK<sub>Est</sub> ~4.6. Its solubility in CHCl<sub>3</sub> is 5%. It has been purified from fish oil by GLC using Ar as mobile phase and EGA as stationary phase with an ionisation detector [UV: Stoffel and Ahrens J Lipid Res 1 139 1959], and via the ester by evaporative "molecular" distillation using a 'continuous molecular still' at  $10^{-4}$  mm with the highest temperature being 110°, and a total contact time with the hot surface being 60sec [Farmer and van den Heuvel J Chem Soc 427 1938]. The methyl ester has b 208-211°/2mm,  $d_4^{20}$  0.9398,  $n_D^{20}$  1.5035. With Br<sub>2</sub> it forms a dodecabromide m ca 240° dec. Also the acid was converted to the methyl ester and purified through a three stage molecular still [as described by Sutton Chem Ind (London) 11383 1953] at 96° with the rate adjusted so that one third of the material was removed each cycle of three distillations. The distillate (numbered 4) (13g) was dissolved in EtOH (100mL containing 8g of KOH) at -70° and set aside for 4h at 30° with occasional shaking under a vac. Water (100mL) is added and the soln is extracted with pentane, washed with HCl, dried (MgSO<sub>4</sub>), filtered and evapd to give a clear oil (11.5g) m -44.5° to -44.1°. In the catalytic hydrogenation of the oil six mols of H<sub>2</sub> were absorbed and docosanoic acid (behenic acid) was produced with m 79.0-79.3° undepressed with an authentic sample (see docosanoic acid below) [Whitcutt Biochem J 67 60 1957].

Docosane [629-97-0] M 310.6, m 47°, b 224°/15mm. Crystd from EtOH or ether.

Docosanoic acid (behenic acid) [112-85-6] M 340.6, m 81-82°, pK<sub>Est</sub> ~4.9. Crystd from ligroin. [Francis and Piper J Am Chem Soc 61 577 1939].

1-Docosanol (behenyl alcohol) [661-19-8] M 182.3, m 70.8°. Crystd from ether or chloroform/ether.

*n*-Dodecane [112-40-3] M 170.3, b 97.5-99.5°/5mm, 216°/760mm, d 0.748, n 1.42156. Passed through a column of Linde type 13X molecular sieves. Stored in contact with, and distd from, sodium. Passed through a column of activated silica gel. Has been crystd from diethyl ether at -60°. Unsaturated dry material which remained after passage through silica gel has been removed by catalytic hydrogenation (Pt<sub>2</sub>O) at 451b/in<sup>2</sup> (3.06 atmospheres), followed by fractional distn under reduced pressure [Zook and Goldey J Am Chem Soc 75 3975 1953]. Also purified by partial crystn from the melt.

Dodecane-1,10-dioic acid (decane-1,10-dicarboxylic acid) [693-23-2] M 230.3, m 129°, b 245°/10mm, pK<sub>Est</sub> ~4.8. Crystd from water, 75% or 95% EtOH (sol 10%), or glacial acetic acid.

1-Dodecanol (dodecyl alcohol) [112-53-8] M 186.3, m 24°, b 91°/1mm, 135°/10mm, 167°/40mm, 213°/200mm, 259°/atm, d<sup>24</sup> 0.8309 (liquid). Crystd from aqueous EtOH, and vacuum distd in a spinning-band column. [Ford and Marvel Org Synth 10 62 1930.]

1-Dodecanthiol [112-55-0] M 202.4, b 111-112°/3mm, 153-155°/24mm, d 0.844, n 1.458, pK<sub>Est</sub>~10.8. Dried with CaO for several days, then distd from CaO.

Dodecylammonium butyrate [17615-97-3] M 273.4, m 39-40°, pK<sup>25</sup> 10.63 (for free base). Recrystd from *n*-hexane.

**Dodecylammonium propionate** [17448-65-6] **M 259.4, m 55-56°.** Recrystd from hexanol/pet ether (b 60-80°).

Dodecyldimethylamine oxide [1643-20-5] M 229.4, m 102°. Crystd from acetone or ethyl acetate. [Bunton et al. J Org Chem 52 3832 1987].

Dodecyl ether [4542-57-8] M 354.6, m 33°. Vacuum distd, then crystd from MeOH/\*benzene.

1-Dodecylpyridinium chloride [104-74-5] M 301.9, m 68-70°. Purified by repeated crystn from acetone (charcoal); twice recrystd from EtOH [Chu and Thomas J Am Chem Soc 108 6270 1986].

**Dodecyltrimethylammonium bromide** [1119-94-4] **M 308.4, m 246°(dec).** Purified by repeated crystn from acetone. Washed with diethyl ether and dried in a vacuum oven at 60° [Dearden and Wooley J Phys Chem 91 2404 1987].

**Dodecyltrimethylammonium chloride** [112-00-5] **M 263.9, m 246°(dec).** Dissolved in MeOH, treated with active charcoal, filtered and dried *in vacuo* [Waldenburg J Phys Chem 88 1655 1984], or recrystd several times from 10% EtOH in acetone. Also repeatedly crystd from EtOH/ether or MeOH. [Cella et al. J Am Chem Soc 74 2062 1952.]

Dulcitol [608-66-2] M 182.2, m 188-189°, b 276-280°/1.1mm. Crystd from water by addition of EtOH.

**Duroquinone (tetramethylbenzoquinone)** [527-17-3] M 164.2, m 110-111°. Crystd from 95% EtOH. Dried under vacuum.

 $\alpha$ -Ecdyson [3604-87-3] M 464.7, m 239-242°, 242°,  $[\alpha]_D^{20}$  +72° (c 1, EtOH). Recrystd from tetrahydrofuran-pet ether, and from H<sub>2</sub>O as a hydrate. It has been purified by chromatogaphy on Al<sub>2</sub>O<sub>3</sub> and elution with EtOAc-MeOH. It has  $\lambda$ max at 242nm ( $\epsilon$  12.400). Its acetate has m 214-216° from EtOAc-pet ether, and the 2,4-dinitrophenylhydrazone has m 170-175° (dec) from EtOAc. [Karlson and Hoffmeister Justus Liebigs Ann Chem 662 1 1963; Karlson Pure Appl Chem 14 75 1967.]

β-Ecdyson (β-echdysterone) [5289-74-7] M 480.7, m 245-247°,  $[\alpha]_D^{20}$  +66° (c 1, MeOH). Crystd from water or tetrahydrofuran/pet ether.

Echinenone [432-68-8] M 550.8, m 178-179°,  $A_{1cm}^{\%}$  ( $\lambda$ max) 2160 (458nm) in pet ether. Purified by chromatography on partially deactivated alumina or magnesia, or by using a thin layer of silica gel G with 4:1 cyclohexane/diethyl ether as the developing solvent. Stored in the dark at -20°.

Eicosane [112-95-8] M 282.6, m 36-37°, b 205°/15mm, d <sup>36.7</sup> 0.7779, n<sup>40</sup> 1.43453. Crystd from EtOH.

Elaidic (trans-oleic) acid [112-79-8] M 282.5, m 44.5°, pK<sup>25</sup> 4.9. Crystd from acetic acid, then EtOH.

Ellagic acid (2H<sub>2</sub>O) [476-66-4] M 338.2, m >360°, pK<sub>Est(1)</sub>~8, pK<sub>Est(2)</sub>~11. Crystd from pyridine.

Elymoclavine (8,9-didehydro-6-methylergoline-8-methanol) [548-43-6] M 254.3, m 249-253°(dec),  $[\alpha]_D^{20}$ -59° (c 1, EtOH). Crystd from MeOH.

Embonic acid (Pamoic acid, 4,4'-methylene bis[3-hydroxy-2-naphthalenecarboxylic acid]) [130-85-8] M 388.4, m 295°, >300°,  $pK_{Est(1)} \sim 2.2$ ,  $pK_{Est(2)} \sim 13.2$ . Forms crystals from dilute pyridine which decomposition above 280° without melting. It is almost insoluble in H<sub>2</sub>O, EtOH, Et<sub>2</sub>O, \*C<sub>6</sub>H<sub>6</sub>, CH<sub>3</sub>CO<sub>2</sub>H, sparingly soluble in CHCl<sub>3</sub> but soluble in nitrobenzene, pyridine and alkalis [Barber and Gaimster J Appl Chem (London) 2 565 1952]. Used for making salts of organic bases.

Emetine hydrochloride hydrate [316-42-7] M 553.6 + aq, m 235-240°, 235-250°, 240-250°, 248-250° (depending on H<sub>2</sub>O content),  $[\alpha]_D^{20}$  -49.2° (free base, c 4, CHCl<sub>3</sub>), +18° (c 6, H<sub>2</sub>O, dry salt), pK<sub>1</sub> 5.77, pK<sub>2</sub> 6.64. It crystallises from MeOH-Et<sub>2</sub>O, MeOH or Et<sub>2</sub>O-EtOAc. The *free base* has m 104-105°, and the (-)-*phenyl thiourea derivative* has m 220-221° [from EtOAc-pet ether,  $[\alpha]_D^{25}$  - 29.3° (CHCl<sub>3</sub>)]. IR: 3413 (OH) and 2611 (NH<sup>+</sup>) cm<sup>-1</sup>; UV  $\lambda$ max 230nm ( $\epsilon$  16 200) and 282nm ( $\epsilon$  6 890) [Brossi et al. *Helv Chim Acta* 42 1515 1959; Barash et al. *J Chem Soc* 3530 1959].

Emodine (1,3,8-trihydroxy-6-methyl-9,10-anthracenedione, archin) [518-82-1] M 270.2, m 253-257°, 255-256°, 256-257°, 262°, 264° (phenolic pKs 7-10). Forms orange needles from EtOH,  $Et_2O$ ,  $*C_6H_6$ , toluene or pyridine. It sublimes above 200° at 12mm. [Tutin and Clewer J Chem Soc 99 946 1911; IR: Bloom et al. J Chem Soc 178 1959; UV: Birkinshaw Biochem J 59 495 1955; Raistrick Biochem J 34 159 1940.]

1*R*,2*S*-(-)Ephedrine [299-42-3] M 165.2, m 40°, b 225°,  $[\alpha]_{546}^{20}$  -47° and  $[\alpha]_D^{20}$  -40° (c 5, 2.2M HCl), pK<sup>25</sup> 9.57. See (-)-ephedrine (1*R*,2*S*-2-methylamino-1-phenylpropanol) on p. 533 in Chapter 6.

(-)Ephedrine hydrochloride [50-98-6] M 201.7, m 218°,  $[\alpha]_{546}^{20}$  -48° (c 5, 2M HCl). Crystd from water.

Epichlorohydrin [106-89-8] M 92.5, b 115.5°, n 1.438, d 1.180. Distd at atmospheric pressure, heated on a steam bath with one-quarter its weight of CaO, then decanted and fractionally distd.

R(-)Epinephrine (adrenalin) [51-43-4] M 183.2, m 215°(dec),  $[\alpha]_{546}^{20}$  -61° (c 5, 0.5M HCl),  $pK_1^{25}$  8.75,  $pK_2^{25}$  9.89,  $pK_3^{25}$  ~13. Dissolved in dilute aqueous acid, then ppted by addn of dilute aqueous ammonia or alkali carbonates. (Epinephrine readily oxidises in neutral alkaline soln. This can be diminished if a little sulfite is added).

1,2-Epoxybutane [106-88-7] M 72.1, b 66.4-66.6°, d 0.837, n 1.3841. Dried with CaSO<sub>4</sub>, and fractionally distd through a long (126cm) glass helices-packed column. The first fraction contains a water azeotrope.

(+)-Equilenine [517-09-9] M 266.3, m 258-259°,  $[\alpha]_D^{16}$  +87° (c 7.1, H<sub>2</sub>O). Crystd from EtOH and dried in a vacuum.

**Ergocornine** [564-36-3] **M 561.7, m 182-184°**,  $[\alpha]_D^{20}$  -176° (c 0.5, CHCl<sub>3</sub>). Crystd with solvent of crystn from MeOH.

Ergocristine [511-08-0] M 573.7, m 165-170°,  $[\alpha]_D^{20}$ -183° (c 0.5, CHCl<sub>3</sub>). Crystd with 2 moles of solvent of crystn, from \*benzene.

Ergocryptine [511-09-1] M 575.7, m 212-214°,  $[\alpha]_D^{20}$ -180° (c 0.5, CHCl<sub>3</sub>). Crystd with solvent of crystn, from acetone, \*benzene or methanol.

Ergosterol [57-87-4] M 396.7, m 165-166°,  $[\alpha]_{546}^{20}$  -171° (in CHCl<sub>3</sub>). Crystd from ethyl acetate, then from ethylene dichloride.

Ergotamine [113-15-5] M 581.6, m 212-214°(dec),  $[\alpha]_D^{20}$ -160° (c 0.5, CHCl<sub>3</sub>), pK<sup>25</sup> 6.40. Crystd from \*benzene, then dried by prolonged heating in high vacuum. Very hygroscopic.

Ergotamine tartrate [379-79-3] M 657.1, m 203°(dec). Crystd from MeOH.

Erucic acid (cis-13-docosenoic acid) [112-86-7] M 338.6, m 33.8°, b 358°/400mm, pK<sub>Est</sub> ~4.9. Crystd from MeOH.

meso-Erythritol [149-32-6] M 122.1, m 122°. Crystd from distd water and dried at 60° in a vac oven.

Erythrityl tetranitrate [7297-25-8] M 302.1, m 61°. Crystd from EtOH.

β-Erythroidine [466-81-9] M 273.3,  $[α]_D^{20}$  +89° (H<sub>2</sub>O). Crystd from EtOH.

**D-Erythronic acid** (3R-3,4-dihydroxyfuran-2-one) [15667-21-7] M 118.1, m 98-100°, 103-104°, 104-105°, 105°,  $[\alpha]_D^{20}$ -73.2° (c 0.5, H<sub>2</sub>O),  $[\alpha]_{546}^{20}$ -87.6° (c 4, H<sub>2</sub>O). Recrystd from EtOAc (20 parts) or isoPrOH (3 parts). [Baker and MacDonald J Am Chem Soc 82 230 1960; Glattfeld and

Forbrich J Am Chem Soc 56 1209 1934; Weidenhagen and Wegner Chem Ber 72 2010 1939, Musich and

Esculetin (cichorigenin, 6,7-dihydroxycoumarin) [305-01-1] M 178.2, m 272-275° (dec), 274° (dec), pK<sub>Est(1)</sub> ~8.7, pK<sub>Est(2)</sub> ~12.4. Forms prisms from AcOH or aq EtOH and provides leaflets on sublimation in a vacuum. [Sethna and Shah *Chem Rev*; Merz *Arch Pharm (Weinheim Ger)* 270 486 1932.] *Esculin (the 6-glucoside)* has m 215° (dec),  $[\alpha]_{D}^{20}$  -41° (c 5, pyridine).

Rapoport J Am Chem Soc 100 4865 1978.]

Eserine (Physostigmine, Physostol,  $[(3aS-cis)-1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethyl-pyrrolo[2,3-b]indol-5-ol methylcarbamate ester] [57-47-6] M 275.4, m 102-104°, 105-106°, <math>[\alpha]_D^{17}$  -67° (c 1.3, CHCl<sub>3</sub>),  $[\alpha]_D^{25}$  -120° (\*C<sub>6</sub>H<sub>6</sub>), pK<sub>1</sub><sup>15</sup> 1.96, pK<sub>2</sub><sup>15</sup> 8.08. Recrystallises form Et<sub>2</sub>O or \*C<sub>6</sub>H<sub>6</sub> and forms an unstable low melting form m 86-87° [Harley-Mason and Jackson J Chem Soc 3651 1954; Wijnberg and Speckamp Tetrahedron 34 2399 1978].

1,3,5-Estratrien-3-ol-17-one (Estrone, Folliculin) [53-16-7] M 270.4, m 260-261°, polymorphic also m 254° and 256°,  $[\alpha]_{546}^{20}$  +198° (c 1, dioxane), pK<sup>25</sup> 10.91. Crystd from EtOH.

1,3,5-Estratrien-3B,16a,17B-triol (Estriol) [50-27-1] M 288.4, m 283°,  $[\alpha]_{546}^{20}$  +66° (c 1, dioxane). Crystd from EtOH/ethyl acetate.

Ethane [74-84-0] M 30.1, f -172°, b -88°,  $d_4^0$  1.0493 (air = 1). Ethylene can be removed by passing the gas through a sintered-glass disc into fuming H<sub>2</sub>SO<sub>4</sub> then slowly through a column of charcoal satd with bromine. Bromine and HBr were removed by passage through firebrick coated with N,N-dimethyl-p-toluidine. The ethane was also passed over KOH pellets (to remove CO<sub>2</sub>) and dried with Mg(ClO<sub>4</sub>)<sub>2</sub>. Further purification was by several distns of liquified ethane, using a condensing temperature of -195°. Yang and Gant [J Phys Chem 65 1861 1961] treated ethane by standing it for 24h at room temperature in a steel bomb containing activated charcoal treated with bromine. They then immersed the bomb in a Dry-ice/acetone bath and transferred the ethane to an activated charcoal trap cooled in liquid nitrogen. (The charcoal had previously been degassed by pumping for 24h at 450°.) By allowing the trap to warm slowly, the ethane was distd, retaining only the middle third. Removal of methane was achieved using Linde type 13X molecular sieves (previously degassed by pumping for 24h at 450°) in a trap which, after cooling in Dry-ice/acetone, was satd with ethane. After pumping for 10min, the ethane was recovered by warming the trap to room temperature. (The final gas contained less than 10<sup>-4</sup> mole % of either ethylene or methane).

Ethanesulfonyl chloride [594-44-5] M 128.6, b 55°/9mm, 62°/12mm, 74°/19mm, 76-79°/22mm, 95-98°/50mm, 177°/760mm,  $d_4^{20}$  1.357,  $n_D^{20}$  1.4539. Purified by repeated distn to remove HCl formed from hydrolysis. Fuming, corrosive liquid, handle in a good fumehood. It is hydrolysed by aq N NaOH at room temperature and is best stored in aliquots in sealed ampules under N<sub>2</sub>. [Davies and Dick J Chem Soc 484 1932; Klamann and Drahowzal Monatsh Chem 83 463 1952; Saunders et al. Biochem J 36 372 1942.]

Ethanethiol (ethyl mercaptan) [75-08-1] M 62.1, b 32.9°/704mm, d<sup>52</sup> 0.83147, pK<sup>25</sup> 10.61. Dissolved in aqueous 20% NaOH, extracted with a small amount of \*benzene and then steam distd until clear. After cooling, the alkaline soln was acidified slightly with 15% H<sub>2</sub>SO<sub>4</sub> and the thiol was distd off, dried with CaSO<sub>4</sub>, CaCl<sub>2</sub> or 4A molecular sieves, and fractionally distd under nitrogen [Ellis and Reid *J Am Chem Soc* 54 1674 1932].

Ethanol [64-17-5] M 46.1, b 78.3°,  $d^{15}$  0.79360,  $d^5$  0.78506, n 1.36139,  $pK^{25}$  15.93. Usual impurities of fermentation alcohol are fusel oils (mainly higher alcohols, especially pentanols), aldehydes, esters, ketones and water. With synthetic alcohol, likely impurities are water, aldehydes, aliphatic esters, acetone and diethyl ether. Traces of \*benzene are present in ethanol that has been dehydrated by azeotropic distillation with \*benzene. Anhydrous ethanol is very *hygroscopic*. Water (down to 0.05%) can be detected by formation of a voluminous ppte when aluminium ethoxide in \*benzene is added to a test portion, Rectified

spirit (95% ethanol) is converted to *absolute* (99.5%) ethanol by refluxing with freshly ignited CaO (250g/L) for 6h, standing overnight and distilling with precautions to exclude moisture.

Numerous methods are available for further drying of *absolute* ethanol for making "Super dry ethanol". Lund and Bjerrum [Chem Ber 64 210 1931] used reaction with magnesium ethoxide, prepared by placing 5g of clean dry magnesium turnings and 0.5g of iodine (or a few drops of CCl<sub>4</sub>), to activate the Mg, in a 2L flask, followed by 50-75 mL of absolute ethanol, and warming the mixture until a vigorous reaction occurs. When this subsides, heating is continued until all the magnesium is converted to magnesium ethoxide. Up to 1L of ethanol is added and, after an hour's reflux, it is distd off. The water content should be below 0.05%. Walden, Ulich and Laun [Z Phys Chem 114 275 1925] used amalgamated aluminium chips, prepared by degreasing aluminium chips (by washing with Et<sub>2</sub>O and drying in a vac to remove grease from machining the Al), treating with alkali until hydrogen was vigorously evolved, washing with H<sub>2</sub>O until the washings were weakly alkaline and then stirring with 1% HgCl<sub>2</sub> soln. After 2min, the chips were washed quickly with H<sub>2</sub>O, then alcohol, then ether, and dried with filter paper. (The amalgam became warm.) These chips were added to the ethanol, which was then gently warmed for several hours until evolution of hydrogen ceased. The alcohol was distd and aspirated for some time with pure dry air. Smith [J Chem Soc 1288 1927] reacted 1L of absolute ethanol in a 2L flask with 7g of clean dry sodium, and added 25g of pure ethyl succinate 27g of pure ethyl phthalate was an alternative), and refluxed the mixture for 2h in a system protected from moisture, and then distd the ethanol. A modification used 40g of ethyl formate, instead, so that sodium formate separated out and, during reflux, the excess of ethyl formate decomposed to CO and ethanol.

Drying agents suitable for use with ethanol include Linde type 4A molecular sieves, calcium metal, and CaH<sub>2</sub>. The calcium hydride (2g) was crushed to a powder and dissolved in 100mL *absolute* ethanol by gently boiling. About 70mL of the ethanol were distd off to remove any dissolved gases before the remainder was poured into 1L of *ca* 99.9% ethanol in a still, where it was boiled under reflux for 20h, while a slow stream of pure, dry hydrogen (better use nitrogen or Ar) was passed through. It was then distd [Rüber Z *Elektrochem* 29 334 1923]. If calcium was used for drying, about ten times the theoretical amount should be taken, and traces of ammonia (from some calcium nitride in the Ca metal) would be removed by passing dry air into the vapour during reflux.

Ethanol can be freed from traces of basic materials by distn from a little 2,4,6-trinitrobenzoic acid or sulfanilic acid. \*Benzene can be removed by fractional distn after adding a little water (the \*benzene/water/ethanol azeotrope distils at 64.9°); the alcohol is then redried using one of the methods described above. Alternatively, careful fractional distn can separate \*benzene as the \*benzene/ethanol azeotrope (**b** 68.2°). Aldehydes can be removed from ethanol by digesting with 8-10g of dissolved KOH and 5-10g of aluminium or zinc per L, followed by distn. Another method is to heat under reflux with KOH (20g/L) and AgNO<sub>3</sub> (10g/L) or to add 2.5-3g of lead acetate in 5mL of water to 1L of ethanol, followed (slowly and without stirring) by 5g of KOH in 25mL of ethanol: after 1hr the flask is shaken thoroughly, then set aside overnight before filtering and distilling. The residual water can be removed by standing the distillate over activated aluminium amalgam for 1 week, then filtering and distilling. Distn of ethanol from Raney nickel eliminates catalyst poisons.

Other purification procedures include pre-treatment with conc  $H_2SO_4$  (3mL/L) to eliminate amines, and with KMnO<sub>4</sub> to oxidise aldehydes, followed by refluxing with KOH to resinify aldehydes, and distilling to remove traces of  $H_3PO_4$  and other acidic impurities after passage through silica gel, and drying over CaSO<sub>4</sub>. Water can be removed by azeotropic distn with dichloromethane (azeotrope boils at 38.1° and contains 1.8% water) or 2,2,4-trimethylpentane.

**Rapid purification:** Place degreased Mg turnings (grease from machining the turnings is removed by washing with dry EtOH then  $Et_2O$ , and drying in a vac) (5g) in a dry 2L round bottomed flask fitted with a reflux condenser (protect from air with a drying tube filled with  $CaCl_2$  or KOH pellets) and flush with dry N<sub>2</sub>. Then add iodine crystals (0.5g) and gently warm the flask until iodine vapour is formed and coats the turnings. Cool, then add EtOH (50mL) and carefully heat to reflux until the iodine disappears. Cool again then add more EtOH (to 1L) and reflux under N<sub>2</sub> for several hours. Distil and store over 3A molecular sieves (pre-heated at  $300^{\circ} - 350^{\circ}$  for several hours and cooled under dry N<sub>2</sub> or argon).

S-Ethionine [13073-35-3] M 163.2, m 282°(dec),  $[\alpha]_D^{25} + 23.7°$  (in 5M HCl), pK<sup>25</sup> 9.02 (for RS). Likely impurities are N-acetyl-(R and S)-ethionine, S-methionine, and R-ethionine. Crystd from water by adding 4 volumes of EtOH.

Ethoxycarbonyl isocyanate [19617-43-7] M 115.1, b 51-55°/13mm, 56°/18mm,  $d_4^{20}$  1.15. Fractionally distilled. [J Heterocycl Chem 5 837 1968.]

Ethoxycarbonyl isothiocyanate [16182-04-0] M 131.5, b  $43^{\circ}/14$ mm,  $51-55^{\circ}/13$ mm,  $56^{\circ}/18$ mm,  $d_4^{20}$  1.12. Fractionally distd through a short column. It also distils at 83°/30mm with some decomposition liberating CO<sub>2</sub> and sulfurous gases, best distil below 20mm vacuum. [J Chem Soc 93 697 1908; 1340, 1948; J Heterocycl Chem 5 837 1968.]

**3-Ethoxy-***N*,*N*-**diethylaniline** [1846-92-2] **M 193.3, b 141-142°**/15mm pK<sub>Est</sub> ~6.1. Refluxed for 3h with acetic anhydride, then fractionally distilled under reduced pressure.

**2-Ethoxyethanol** [110-80-5] **M 90.1, b 134.8°, d 0.931, n 1.40751.** Dried with CaSO<sub>4</sub> or  $K_2CO_3$ , filtered and fractionally distd. Peroxides can be removed by refluxing with anhydrous SnCl<sub>2</sub> or by filtration under slight pressure through a column of activated alumina.

**2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline** (EEDQ) [16357-59-8] M 247.3, m 63.5-65°, 66-67°. Dissolve ~180g in CHCl<sub>3</sub>, evap to dryness under vac. Add dry Et<sub>2</sub>O (20mL) when a white solid separates on standing. Set aside for a few hours, collect solid, wash thoroughly with cold Et<sub>2</sub>O and dry in vac (~140g, m 63.5-65°). A further crop of solid (~25g) is obtained from the filtrate on standing overnight. [Fieser and Fieser *Reagents for Organic Synthesis* 2 191 1969; Belleau et al. J Am Chem Soc 90 823 1968 and 90 1651 1968.]

2-Ethoxyethyl ether [bis-(2-ethoxyethyl) ether] [112-36-7] M 162.2, b 76°/32mm, d 0.910, n 1.412. See diethyleneglycol diethyl ether on p. 203.

2-Ethoxyethyl methacrylate [2370-63-0] M 158.2, b 91-93°/35mm, d 0.965, n 1.429. Purified as described under methyl methacrylate.

1-Ethoxynaphthalene [5328-01-8] M 172.2, b 136-138°/14mm, 282°/760mm, d 1.061, n 1.604. Fractionally distd (twice) under a vacuum, then dried with, and distd under a vacuum from, sodium.

2-Ethoxynaphthalene [93-18-5] M 172.2, m 35.6-36.0°, b 142-143°/12mm. Crystd from pet ether. Dried under vacuum or distd in a vacuum.

Ethyl acetimidate [1000-84-6] M 87.1, b 92-95°/atm, 89.7-90°/765mm, d 0.8671, n 1.4025,  $pK_{Est} \sim 5.5$ . It is best to prepare it freshly from the hydrochloride (see below). Dissolve the hydrochloride (123.5g) by adding it slowly to an ice-cold mixt of H<sub>2</sub>O (500mL), K<sub>2</sub>CO<sub>3</sub> (276g) and Et<sub>2</sub>O (200mL) and stirring rapidly. The Et<sub>2</sub>O layer was separated, the aq layer was extd with Et<sub>2</sub>O (100mL), the combined Et<sub>2</sub>O layers were dried (MgSO<sub>4</sub>), evapd and the residual oil distd through a glass helices packed column (70x1.2cm). The yield was 19g (22%). [Glickman and Cope J Am Chem Soc 67 1020 1945; Chaplin and Hunter J Chem Soc 1118 1937; Methods Enzymol 25 585 1972.]

Ethyl acetimidate hydrochloride [2208-07-3] M 123.6, m 98-100°(dec), 110-115° (dec), 112-113°(dec), m 112-114°(dec),  $pK_{Est} \sim 5.5$ . Recrystd by dissolving in the minimum volume of super dry EtOH and addition of dry Et<sub>2</sub>O or from dry Et<sub>2</sub>O. Dry in vacuum and store in a vacuum desiccator with P<sub>2</sub>O<sub>5</sub>. Alternatively it could be crystd from EtOH (containing a couple of drops of ethanolic HCl) and adding dry Et<sub>2</sub>O. Filter and dry in a vac desiccator over H<sub>2</sub>SO<sub>4</sub> and NaOH. [Pinner Chem Ber 16 1654 1883.] [Glickman and Cope J Am Chem Soc 67 1020 1945; Chaplin and Hunter J Chem Soc 1118 1937; McElvain and Schroeder J Am Chem Soc 71 40 1949; McElvain and Tate J Am Chem Soc 73 2233 1951; Methods Enzymol 25 585 1972.]

Ethyl acetate [141-78-6] M 88.1, b 77.1°, d 0.9003, n 1.37239,  $n^{25}$  1.36979,  $pK^{25}$  -6.93 (aq H<sub>2</sub>SO<sub>4</sub>). The commonest impurities are water, EtOH and acetic acid. These can be removed by washing with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, then with saturated aqueous CaCl<sub>2</sub> or NaCl, and drying with K<sub>2</sub>CO<sub>3</sub>, CaSO<sub>4</sub> or MgSO<sub>4</sub>. More efficient drying is achieved if the solvent is further dried with P<sub>2</sub>O<sub>5</sub>, CaH<sub>2</sub> or molecular sieves before

distn. CaO has also been used. Alternatively, ethanol can be converted to ethyl acetate by refluxing with acetic anhydride (*ca* 1mL per 10mL of ester); the liquid is then fractionally distd, dried with  $K_2CO_3$  and redistd. **Rapid purification:** Distil, dry over  $K_2CO_3$ , distil again and store over 4A molecular sieves.

Ethyl acetoacetate [141-97-9] M 130.1, b 71°/12mm, 100°/80mm, d 1.026, n 1.419, pK<sup>25</sup> 10.68. Shaken with small amounts of saturated aqueous NaHCO<sub>3</sub> (until no further effervescence), then with water. Dried with MgSO<sub>4</sub> or CaCl<sub>2</sub>. Distd under reduced pressure.

Ethyl acrylate [140-88-5] M 100.1, b 20°/40mm, 99.5°/atm, d 0.922, n 1.406. Washed repeatedly with aqueous NaOH until free from inhibitors such as hydroquinone, then washed with saturated aqueous CaCl<sub>2</sub> and distd under reduced pressure. Hydroquinone should be added if the ethyl acrylate is to be stored for extended periods. LACHRYMATORY.

Ethylamine [75-04-7] M 45.1, b 16.6°/760mm, d 1.3663, pK<sup>20</sup> 10.79. Condensed in an all-glass apparatus cooled by circulating ice-water, and stored with KOH pellets below 0°.

Ethylamine hydrochloride [557-66-4] M 81.5, m 109-110°. Crystd from absolute EtOH or MeOH/CHCl<sub>3</sub>.

Ethyl o-aminobenzoate [94-09-7] M 165.2, m 92°, pK<sup>25</sup> 2.39. Crystd from EtOH/H<sub>2</sub>O and air dried.

*p*-Ethylaniline [589-16-2] M 121.2, b 88°/8mm, d 0.975, n 1.554,  $pK^{25}$  5.00. Dissolved in \*benzene, then acetylated. The acetyl derivative was recrystallised from \*benzene/pet ether, and hydrolysed by refluxing 50g with 500mL of water and 115mL of conc H<sub>2</sub>SO<sub>4</sub> until the soln becomes clear. The amine sulfate was isolated, suspended in water and solid KOH was added to regenerate the free base, which was separated, dried and distd from zinc dust under a vacuum [Berliner and Berliner J Am Chem Soc 76 6179 1954].

Ethylbenzene [100-41-6] M 106.2, b 136.2°, d 0.867, n 1.49594,  $n^{25}$  1.49330. Shaken with cold conc H<sub>2</sub>SO<sub>4</sub> until a fresh portion of acid remained colourless, then washed with aqueous 10% NaOH or NaHCO<sub>3</sub>, followed by distilled water until neutral. Dried with MgSO<sub>4</sub> or CaSO<sub>4</sub>, then dried further with, and distd from, sodium, sodium hydride or CaH<sub>2</sub>. Can also be dried by passing through silica gel. Sulfur-containing impurities have been removed by prolonged shaking with mercury. Also purified by fractional freezing.

Ethyl benzoate [93-89-0] M 150.2, b 98°/19mm, 212.4°/760mm, d 1.046,  $n^{15}$  1.5074,  $n^{25}$  1.5043, pK -7.37 (aq H<sub>2</sub>SO<sub>4</sub>). Washed with aq 5% Na<sub>2</sub>CO<sub>3</sub>, then satd CaCl<sub>2</sub>, dried with CaSO<sub>4</sub> and distd under reduced pressure.

Ethyl bis-(2,4-dinitrophenyl)acetate [5833-18-1] M 358.3, m 150-153°. Crystd from toluene as pale yellow crystals.

Ethyl bixin [6895-43-8] M 436.6, m 138°. Crystd from EtOH.

Ethyl bromide [74-96-4] M 109.0, b 0°/165mm, 38°/745mm, d 1.460, n 1.4241. The main impurities are usually EtOH and water, with both of which it forms azeotropes. Ethanol and unsaturated compounds can be removed by washing with conc  $H_2SO_4$  until no further coloration is produced. The ethyl bromide is then washed with water, aq Na<sub>2</sub>CO<sub>3</sub>, and water again, then dried with CaCl<sub>2</sub>, MgSO<sub>4</sub> or CaH<sub>2</sub>, and distd. from  $P_2O_5$ . Olefinic impurities can also be removed by storing the ethyl bromide in daylight with elementary bromine, later removing the free bromine by extraction with dil aq Na<sub>2</sub>SO<sub>3</sub>, drying the ethyl bromide with CaCl<sub>2</sub> and fractionally distilling. Alternatively, unsaturated compounds can be removed by bubbling oxygen containing *ca* 5% ozone through the liquid for an hour, then washing with aqueous Na<sub>2</sub>SO<sub>3</sub> to hydrolyse ozonides and remove hydrolysis products, followed by drying and distn.

Ethyl bromoacetate [105-36-2] M 167.0, b 158-158.5°/758mm, d 1.50, n 1.450. Washed with saturated aqueous Na<sub>2</sub>CO<sub>3</sub> (three times), 50% aq CaCl<sub>2</sub> (three times) and saturated aqueous NaCl (twice). Dried with MgSO<sub>4</sub>, CaCl<sub>2</sub> or CaCO<sub>3</sub>, and distd. LACHRYMATORY.

Ethyl 2-(bromomethyl)acrylate [17435-72-2] M 193.1, b 38°/0.8mm, d 1.398, n 1.479. If it contains some free acid, add H<sub>2</sub>O, cool, and neutralise with NaHCO<sub>3</sub> until evolution of CO<sub>2</sub> ceases. Extract the mixt with Et<sub>2</sub>O (3x) and dry combined extracts (Na<sub>2</sub>SO<sub>4</sub>, 3h). Evap Et<sub>2</sub>O and dist ester collecting fraction b 39-40°/0.9mm and check spectra. [Prep and NMR: Ramarajan et al. Org Synth Coll Vol VII 211 1990.]

Ethyl  $\alpha$ -bromopropionate [535-11-5] M 181.0, b 69-70°/25mm, d 1.39, n 1.447. Washed with saturated aqueous Na<sub>2</sub>CO<sub>3</sub> (three times), 50% aq CaCl<sub>2</sub> (three times) and saturated aqueous NaCl (twice). Dried with MgSO<sub>4</sub>, CaCl<sub>2</sub> or CaCO<sub>3</sub>, and distd. LACHRYMATORY.

Ethyl bromopyruvate [70-23-5] M 195.0, b 47°/0.5mm, 71-73°/5mm, 87°/9mm, 89-104°/14mm,  $d_4^{20}$  1.561,  $n_D^{20}$  1.464. Most likely impurity is free carboxylic acid (bromopyruvic or bromoacetic acids). Dissolve in dry Et<sub>2</sub>O or dry CHCl<sub>3</sub>, stir with CaCO<sub>3</sub> until effectivescence ceases, filter, (may wash with a little H<sub>2</sub>O rapidly), dry (MgSO<sub>4</sub>) and distil at least twice. The 2,4-dinitrophenylhydrazone has m 144-145°. [Burros and Holland J Chem Soc 672 1947; Letsinger and Laco J Org Chem 21 764 1956; Kruse et al. J Am Chem Soc 76 5796 1954.] LACHRYMATORY.

**2-Ethyl-1-butanol** [97-95-0] **M 102.2, b 146.3°, n^{15} 1.4243, n^{25} 1.4205.** Dried with CaSO<sub>4</sub> for several weeks, filtered and fractionally distd.

**2-Ethylbut-1-ene** [760-21-4] **M 84.1, b 66.6°, d 0.833, n 1.423.** Washed with saturated aqueous NaOH, then water. Dried with CaCl<sub>2</sub>, filtered and fractionally distd.

Ethyl *n*-butyrate [105-54-4] M 116.2, b 49°/50mm, 119-120°/760mm, d 0.880, n 1.393. Dried with anhydrous CuSO<sub>4</sub> and distd under dry nitrogen.

Ethyl carbamate (urethane) [51-79-6] M 88.1, m 48.0-48.6°. Crystd from \*benzene.

Ethyl carbazate (N-ethoxycarbonyl hydrazine) [4114-31-2] M 104.1, m 44-48°, 51-52°, b 95.5°/10m, 92-95°/12mm, 100-102°/11mm. Fractionated using a Vigreux column until the distillate crystallises [Allen and Bell Org Synth Coll Vol III 404 1955.]

N-Ethylcarbazole [86-28-2] M 195.3, m 69-70°. Recrystd from EtOH, EtOH/water or isopropanol and dried below 55°.

Ethyl carbonate [105-58-8] M 118.1, b 124-125°, d 0.975, n 1.38287. See diethyl carbonate on p. 203.

Ethyl chloride [75-00-3] M 64.5, b 12.4°, d 0.8978, n 1.3676. Passed through absorption towers containing, successively, conc  $H_2SO_4$ , NaOH pellets,  $P_2O_5$  on glass wool, or soda-lime, CaCl<sub>2</sub>,  $P_2O_5$ . Condensed into a flask containing CaH<sub>2</sub> and fractionally distd. Has also been purified by illumination in the presence of bromine at 0° using a 1000W lamp, followed by washing, drying and distn.

Ethyl chloroacetate [105-39-5] M 122.6, b 143-143.2°, d 1.150,  $n^{25}$  1.4192. Shaken with satutated aqueous Na<sub>2</sub>CO<sub>3</sub> (three times), aqueous 50% CaCl<sub>2</sub> (three times) and saturated aqueous NaCl (twice). Dried with Na<sub>2</sub>SO<sub>4</sub> or MgSO<sub>4</sub> and distd. LACHRYMATORY.

Ethyl chloroformate [541-41-3] M 108.5, m -81°, b 94-95°, d 1.135, n 1.3974. Washed several times with water, redistd using an efficient fractionating column at atmospheric pressure and a CaCl<sub>2</sub> guard tube to keep free from moisture [Hamilton and Sly J Am Chem Soc 47 435 1925; Saunders, Slocombe and Hardy, J Am Chem Soc 73 3796 1951]. LACHRYMATORY AND TOXIC.

Ethyl chrysanthemate (ethyl  $\pm 2,2$ -dimethyl-3{c and t}-[2-methylpropenyl]-cyclopropane carboxylate) [97-41-6] M 196.3, b 98-102°/11mm, 117-121°/20mm. Purified by vacuum distn. The free trans-acid has m 54° (from, EtOAc) and the free cis-acid has m 113-116° (from EtOAc). The 4-nitrophenyl ester has m 44-45° (from pet ether) [Campbell and Harper J Chem Soc 283 1945; IR: Allen et al. J Org Chem 22 1291 1957].

Ethyl cinnamate [103-36-6] M 176.2, f 6.7°, b 127°/6mm, 272.7°/768mm, d 1.040, n 1.55983. Washed with aqueous 10% Na<sub>2</sub>CO<sub>3</sub>, then water, dried (MgSO<sub>4</sub>), and distd. The purified ester was saponified with aqueous KOH, and, after acidifying the soln, cinnamic acid was isolated, washed and dried. The ester was reformed by refluxing for 15h the cinnamic acid (25g) with abs EtOH (23g), conc H<sub>2</sub>SO<sub>4</sub> (4g) and dry \*benzene (100mL), after which it was isolated, washed, dried and distd under reduced pressure [Jeffery and Vogel J Chem Soc 658 1958].

Ethyl trans-crotonate [623-70-1] M 114.2, b 137°, d 0.917, n 1.425. Washed with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, washed with saturated aqueous CaCl<sub>2</sub>, dried with CaCl<sub>2</sub> and distd.

Ethyl cyanoacetate [105-56-6] M 113.1, b 206.0°, d 1.061, n 1.41751. Shaken several times with aqueous 10% Na<sub>2</sub>CO<sub>3</sub>, washed well with water, dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd.

Ethyl cyanoformate [623-49-4] M 99.1, b 113-114°/740mm, 116.5-116.8°/765.5mm,  $d_4^{20}$  1.0112,  $n_D^{20}$  1.3818. Dissolve in Et<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil [Malachowsky et al. Chem Ber 70 1016 1937; Adickes et al. J Prakt Chem [2] 133 313 1932; Grundmann et al. Justus Liebigs Ann Chem 577 77 1952].

Ethylcyclohexane [1678-91-7] M 112.2, b 131.8°, d 0.789, n 1.43304, n<sup>25</sup> 1.43073. Purified by azeotropic distn with 2-ethoxyethanol, then the alcohol was washed out with water and, after drying, the ethylcyclohexane was redistd.

Ethyl cyclohexanecarboxylate [3289-28-9] M 156.2, b 76-77°/10mm, 92-93°/34mm, d 0.960, n 1.420. Washed with M sodium hydroxide solution, then water, dried with Na<sub>2</sub>SO<sub>4</sub> and distd.

Ethyl diazoacetate [623-73-4] M 114.1, m -22°, b 42°/5mm, 45°/12mm, 85-86°/88mm, 140-141°/720mm, 140-143°/atm,  $d_4^{17.6}$  1.0852,  $n_D^{17.6}$  1.4588. A very volatile yellow oil with a strong pungent odour. EXPLOSIVE [distillation even under reduced pressure is dangerous and may result in an explosion — TAKE ALL THE NECESSARY PRECAUTIONS IF DISTILLATION IS TO BE CARRIED OUT]. It explodes in contact with conc H<sub>2</sub>SO<sub>4</sub> - trace acid causes rapid decomp. It is slightly sol in H<sub>2</sub>O, but is miscible with EtOH, \*C<sub>6</sub>H<sub>6</sub>, pet ether and Et<sub>2</sub>O. To purify dissolve in Et<sub>2</sub>O [using CH<sub>2</sub>Cl<sub>2</sub> instead of Et<sub>2</sub>O protects the ester from acid], wash with 10% aq Na<sub>2</sub>CO<sub>3</sub>, dry (MgSO<sub>4</sub>), filter and repeat as many times as possible until the Et<sub>2</sub>O layer loses its yellow colour, remove the solvent below 20° (vac). Note that prolonged heating may lead to rapid decomp and low yields. It can also be purified by steam distn under reduced pressure but with considerable loss in yield. Place the residual oil in a brown bottle and keep below 10°, and use as soon as possible without distilling. [Womack and Nelson Org Synth Coll Vol III 392 1955; UV: Miller and White J Am Chem Soc **79** 5974 1957; Fieser 1 367 1967.]

Ethyl dibromoacetate [617-33-4] M 245.9, b 81-82°/14.5mm,  $n^{22}$  1.4973. Washed briefly with conc aqueous NaHCO<sub>3</sub>, then with aqueous CaCl<sub>2</sub>. Dried with CaSO<sub>4</sub> and distd under reduced pressure.

Ethyl  $\alpha,\beta$ -dibromo- $\beta$ -phenylpropionate [5464-70-0, erythro 30983-70-1] M 336.0, m 75°. Crystd from pet ether (b 60-80°).

Ethyl dichloroacetate [535-15-9] M 157.0, b 131.0-131.5°/401mm, d 1.28, n 1.438. Shaken with aqueous 3% NaHCO<sub>3</sub> to remove free acid, washed with distd water, dried for 3 days with CaSO<sub>4</sub> and distd under reduced pressure.

Ethyl 3,3-diethoxypropionate [10601-80-6] M 190.2, b 58.5°/1.5mm, 65°/2mm, 95-96°/12mm,  $d_4^{20}$  0.78,  $n_D^{25}$  1.4101. Dissolve in dry Et<sub>2</sub>O, and dry with solid NaHCO<sub>3</sub>, filter and distil and carefully fractionate [Dyer and Johnson J Am Chem Soc 56 223 1934].

Ethyl 1,3-dithiane-2-carboxylate [20462-00-4] M 192.3, b 75-77°/0.2mm, 96°/0.4mm,  $d_4^{20}$  1.220,  $n_D^{25}$  1.5379. Dissolve in CHCl<sub>3</sub>, wash with aqueous K<sub>2</sub>CO<sub>3</sub>, 2 x with H<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and distil. [Eliel and Hartman J Org Chem 37 505 1972; Seebach Synthesis 1 17 1969.]

Ethyl 1,3-dithiolane-2-carboxylate [20461-99-8] M 178.3, b 85°/0.1mm,  $d_4^{20}$  1.250,  $n_D^{20}$  1.538. Dissolve in CHCl<sub>3</sub>, wash with aqueous K<sub>2</sub>CO<sub>3</sub>, 2 x with H<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and distil [Hermann et al *Tetrahedron Lett* 2599 1973; Corey and Erickson J Org Chem 36 3553 1971].

Ethylene (ethene) [74-85-1] M 28.0, m -169.4°, b -102°/700mm. Purified by passage through a series of towers containing molecular sieves or anhydrous CaSO<sub>4</sub> or a cuprous ammonia soln, then conc  $H_2SO_4$ , followed by KOH pellets. Alternatively, ethylene has been condensed in liquid nitrogen, with melting, freezing and pumping to remove air before passage through an activated charcoal trap, followed by a further condensation in liquid air. A sputtered sodium trap has also been used, to remove oxygen.

Ethylene N, N'-bis[(o-hydroxyphenyl)glycine] [1170-02-1] M 360.4, m 249°(dec), pK<sub>Est(1)</sub>~1.8, pK<sub>Est(2)</sub>~4.8, pK<sub>Est(3)</sub>~9.0. Purified by extensive Soxhlet extraction with acetone. [Bonadies and Carrano J Am Chem Soc 108 4088 1986].

Ethylene carbonate (1,3-dioxolan-2-one) [96-49-1] M 88.1, m 37°, d 1.32,  $n^{40}$  1.4199. Dried over  $P_2O_5$  then fractionally distd at 10mm pressure. Crystd from dry diethyl ether.

Ethylenediamine (1,2-diaminoethane) [107-15-3] M 60.1, f 11.0°, b 117.0°, d 0.897, n 1.45677,  $n^{30}$  1.4513,  $pK_1^{25}$  6.86,  $pK_2^{25}$  9.92. Forms a constant-boiling (b 118.5°) mixture with water (15%) [hygroscopic and miscible with water]. Recommended purification procedure [Asthana and Mukherjee in J.F.Coetzee (ed), Purification of Solvents, Pergamon Press, Oxford, 1982 cf p 53]: to 1L of ethylenediamine was added 70g of type 5A Linde molecular sieves and shaken for 12h. The liquid was decanted and shaken for a further 12h with a mixture of CaO (50g) and KOH (15g). The supernatant was fractionally distd (at 20:1 reflux ratio) in contact with freshly activated molecular sieves. The fraction distilling at 117.2° /760mm was collected. Finally it was fractionally distilled from sodium metal. All distns and storage of ethylenediamine should be carried out under nitrogen to prevent reaction with CO<sub>2</sub> and water. Material containing 30% water was dried with solid NaOH (600g/L), heated on a water bath for 10h. Above 60°, separation into two phases took place. The hot ethylenediamine layer was decanted off, refluxed with 40g of sodium for 2h and distd [Putnam and Kobe Trans Electrochem Soc 74 609 1938]. Ethylenediamine is usually distd under nitrogen. Type 5A Linde molecular sieves (70g/L), then a mixture of 50g of CaO and 15g of KOH/L, with further dehydration of the supernatant with molecular sieves has also been used for drying this diamine, followed by distn from molecular sieves and, finally, from sodium metal. A spectroscopically improved material was obtained by shaking with freshly baked alumina (20g/L) before distn.

*N*,*N'*-Ethylenediaminediacetic acid (EDDA) [5657-17-0] M 176.2, m 222-224°(dec),  $pK_1^{25}$ 6.48,  $pK_2^{25}$ 9.57 (for NH groups). Crystd from water.

Ethylenediamine dihydrochloride [333-18-6] M 133.0, pK<sub>1</sub><sup>25</sup>6.86, pK<sub>2</sub><sup>25</sup>9.92. Crystd from water.

Ethylenediaminetetraacetic acid (EDTA) [60-00-4] M 292.3, m 253°(dec),  $pK_1^{25} 0.26 pK_2^{25} 0.96$ ,  $pK_3^{25} 2.60$ ,  $pK_4^{25} 2.67$ ,  $pK_5^{25} 6.16$ ,  $pK_6^{25} 10.26$ . Dissolved in aqueous KOH or ammonium hydroxide, and ppted with dil HCl or HNO<sub>3</sub>, twice. Boiled twice with distd water to remove mineral acid, then recrystd from water or dimethylformamide. Dried at 110°. Also recrystd from boiling 1N HCl, wash crystals with distd H<sub>2</sub>O and dried *in vacuo*. [Ma and Ray *Biochemistry* 19 751 1980.]

Ethylene dimethacrylate [97-90-5] M 198.2, b 98-100°/5mm, d 1.053, n 1.456. Distd through a short Vigreux column at about 1mm pressure, in the presence of 3% (w/w) of phenyl-B-naphthylamine.

Ethylene dimyristate [627-84-9] M 482.8, m 61.7°. Crystd from \*benzene-MeOH or diethyl ether-MeOH, and dried in a vacuum desiccator.

Ethylene dipalmitate [624-03-3] M 538.9, m 69.1°. Crystd from \*benzene-MeOH or diethyl ether-MeOH and dried in a vacuum desiccator.

Ethylene distearate [627-83-8] M 595.0, m 75.3°. Crystd from \*benzene-MeOH or diethyl ether-MeOH and dried in a vacuum desiccator.

Ethylene glycol [107-21-1] M 62.1, b 68°/4mm, 197.9°/760mm, d 1.0986,  $n^{15}$  1.43312,  $n^{25}$  1.43056,  $pK^{25}$  10.6. Very hygroscopic, and also likely to contain higher diols. Dried with CaO, CaSO<sub>4</sub>, MgSO<sub>4</sub> or NaOH and distd under vacuum. Further dried by reaction with sodium under nitrogen, refluxed for several hours and distd. The distillate was then passed through a column of Linde type 4A molecular sieves and finally distd under nitrogen, from more molecular sieves. Fractionally distd.

Ethylene glycol bis(ß-aminoethylether)-N, N'-tetraacetic acid (EGTA) [67-42-5] M 380.4, m >245°(dec),  $pK_1^{2^0}$  1.15 (2.40),  $pK_2^{2^0}$  2.40 (2.50),  $pK_3^{2^0}$  8.40 (8.67),  $pK_4^{2^0}$  8.94 (9.22). Dissolved in aq NaOH, pptd by addn of aq HCl, washed with water and dried at 100° *in vacuo*.

Ethylene glycol diacetate [111-55-7] M 146.2, b 190.1°, 79-81°/11mm, d<sup>25</sup> 1.4188, n 1.4150. Dried with CaCl<sub>2</sub>, filtd (excluding moisture) fractionally distd under reduced pressure.

Ethylene glycol dibutyl ether [112-48-1] M 174.3, b 78-80°/0.2mm, d 1.105, n 1.42. Shaken with aq 5% Na<sub>2</sub>CO<sub>3</sub>, dried with MgSO<sub>4</sub> and stored with chromatographic alumina to prevent peroxide formation.

Ethylene glycol diethyl ether (1,2-diethoxyethane) [629-14-1] M 118.2, b 121.5°, d 0.842, n 1.392. After refluxing for 12h, a mixture of the ether (2L), conc HCl (27mL) and water (200mL), with slow passage of nitrogen, the soln was cooled, and KOH pellets were added slowly and with shaking until no more dissolved. The organic layer was decanted, treated with some KOH pellets and again decanted. It was refluxed with, and distd from sodium immediately before use. Alternatively, after removal of peroxides by treatment with activated alumina, the ether has been refluxed in the presence of the blue ketyl formed by sodium-potassium alloy with benzophenone, then distd.

Ethylene glycol dimethyl ether (monoglyme) [110-71-4] M 90.1. See 1,2-dimethoxyethane on p. 210.

Ethylene oxide [75-21-8] M 44.0, b  $13.5^{\circ}/746$ mm, d<sup>10</sup> 0.882, n<sup>7</sup> 1.3597. Dried with CaSO<sub>4</sub>, then distd from crushed NaOH. Has also been purified by its passage, as a gas, through towers containing solid NaOH.

Ethylene thiourea (2-imidazolidinethione) [96-45-7] M 102.2, m 203-204°. Crystd from EtOH or amyl alcohol.

Ethylene urea (2-imidazolidone) [120-93-4] M 86.1, m 131°. Crystd from MeOH (charcoal).

Ethylenimine (aziridine) [151-56-4] M 43.1, b 55.5°/760mm, d 0.8321, pK<sup>25</sup> 8.00. See aziridine on p. 117.

2-Ethylethylenimine [2549-67-9] M 71.1, b 88.5-89°, pK<sup>25</sup> 8.31. Freshly distd from sodium before use. TOXIC.

Ethyl formate [109-94-4] M 74.1, b 54.2°, d 0.921,  $d^{30}$  0.909, n 1.35994,  $n^{25}$  1.3565. Free acid or alcohol is removed by standing with anhydrous K<sub>2</sub>CO<sub>3</sub>, with occasional shaking, then decanting and

distilling from  $P_2O_5$ . Alternatively, the ester can be stood with  $CaH_2$  for several days, then distd from fresh  $CaH_2$ . Cannot be dried with  $CaCl_2$  because it reacts rapidly with the ester to form a crystalline compound.

**Ethyl gallate** [831-61-8] **M 198.2, m 150-151°, 163-165°.** Recryst from 1,2-dichloroethane, UV:  $\lambda$ max (neutral species) 275nm ( $\varepsilon$  10 000); (anion) 235nm ( $\varepsilon$  10 300), 279nm ( $\varepsilon$  11 400) and 324nm ( $\varepsilon$  8 500) [Campbell and Coppinger J Am Chem Soc 73 2708 1951].

2-Ethyl-1-hexanol [104-76-7] M 130.2, b 184.3°, d 0.833, n 1.431. Dried with sodium, then fractionally distd.

2-Ethylhexyl vinyl ether [37769-62-3, 103-44-6] M 156.3, b 177-178°/atm. Usually contains amines as polymerization inhibitors. These are removed by fractional distn.

Ethyl hydrocupreine hydrochloride (Optochin) [3413-58-9] M 376.9, m 249-251°, pK<sub>1</sub><sup>25</sup> 5.50, pK<sub>2</sub><sup>25</sup> 9.95. Recryst from H<sub>2</sub>O [UV: Heidt and Forbes J Am Chem Soc 55 2701 1933].

Ethyl iodide (iodoethane) [75-03-6] M 156.0, b 72.4°, d 1.933, n  $^{15}$  1.5682, n<sup>25</sup> 1.5104. Drying with P<sub>2</sub>O<sub>5</sub> is unsatisfactory, and with CaCl<sub>2</sub> is incomplete. It is probably best to dry with sodium wire and distil [Harmond et al. J Am Chem Soc 82 704 1960]. Exposure of ethyl iodide to light leads to rapid decomposition, with the liberation of iodine. Free iodine can be removed by shaking with several portions of dil aq Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (until the colour is discharged), followed by washing with water, drying (with CaCl<sub>2</sub>, then sodium), and distn. The distd ethyl iodide is stored, over mercury, in a dark bottle away from direct sunlight. Other purification procedures include passage through a 60cm column of silica gel, followed by distn; and treatment with elemental bromine, extraction of free halogen with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> soln, followed by washing with water, drying and distn. Free iodine and HI have also been removed by direct distn through a LeBel-Henninger column containing copper turnings. Purification by shaking with alkaline solns, and storage over silver, are reported to be unsatisfactory.

Ethyl isobutyrate [97-62-1] M 116.2, b 110°, d 0.867, n 1.388. Washed with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, then with saturated aqueous CaCl<sub>2</sub>. Dried with CaSO<sub>4</sub> and distd.

Ethyl isocyanate [109-90-0] M 71.1, b 559.8°/759mm, 59-61°/atm, 60-63°/atm,  $d_4^{20}$  0.9031,  $n_D^{20}$  1.3808. Fractionate through an efficient column preferably in an inert atmosphere and store in aliquots in sealed tubes [Bieber J Am Chem Soc 74 4700 1952; Slocombe et al. J Am Chem Soc 72 1888 1950].

3-Ethylisothionicotinamide [10605-12-6] M 166.2, m 164-166°(dec). Crystd from EtOH.

Ethyl isovalerate [108-64-5] M 130.2, b 134.7°, d 0.8664, n 1.39621,  $n^{25}$  1.3975. Washed with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, then saturated aqueous CaCl<sub>2</sub>. Dried with CaSO<sub>4</sub> and distd.

Ethyl levulinate (4-oxopentanoic acid ethyl ester) [539-88-8] M 144.2, m 37.2°, b 106-108°/2mm, 138.8°/8mm, 203-205°/atm,  $d_4^{20}$  1.012,  $n_D^{20}$  1.423. Stir ester with Na<sub>2</sub>CO<sub>3</sub> and charcoal, filter and distil. It is freely soluble in H<sub>2</sub>O and EtOH [IR, NMR: Sterk Monatsh Chem 99 1770 1968; Thomas and Schuette J Am Chem Soc 53 2328 1931; Cox and Dodds J Am Chem Soc 55 3392 1933].

Ethyl malonate monoamide [7597-56-0] M 131.1, m 47-50°, 49.5-50°, 50°, b 130-135°/2mm. Crystallise from Et<sub>2</sub>O or by slow evaporation of an aqueous soln as colourless crystals [Snyder and Elston J Am Chem Soc 76 3039 1954; McAlvain and Schroeder J Am Chem Soc 71 45 1949; Rising et al. J Biol Chem 89 20 1930].

Ethyl methacrylate [97-63-2] M 114.2, b 59°/100mm, d 0.915, n 1.515. Washed successively with 5% aqueous NaNO<sub>2</sub>, 5% NaHSO<sub>3</sub>, 5% NaOH, then water. Dried with MgSO<sub>4</sub>, added 0.2% (w/w) of phenyl-β-naphthylamine, and distd through a short Vigreux column [Schultz J Am Chem Soc 80 1854 1958].

Ethyl methyl ether [540-67-0] M 60.1, b 10.8°, d° 0.725. Dried with CaSO<sub>4</sub>, passed through an alumina column (to remove peroxides), then fractionally distd.

**3-Ethyl-2-methyl-2-pentene** [19780-67-7] **M 112.2, b 114.5°/760mm.** Purified by preparative GLC on a column of 20% squalene on Chromosorb P at 70°.

3-Ethyl-4-methylpyridine [529-21-5] M 121.2, b 76°/12mm, 194.5°/750mm, d 0.947, n 1.510, pK<sub>Est</sub> ~6.3. Dried with solid NaOH, and fractionally distd.

5-Ethyl-2-methylpyridine [104-90-5] M 121.2, b 178.5°/765mm, d 0.919, n 1.497, pK<sup>20</sup> 6.51. Purified by conversion to the picrate, crystn, and regeneration of the free base, then distn.

*N*-Ethylmorpholine [100-74-3] M 115.2, b 138-139°/763mm, d 0.912, n 1.445, pK<sup>25</sup> 7.67. Distd twice, then converted by HCl gas into the hydrochloride (extremely deliquescent) which was crystd from anhydrous EtOH-acetone (1:2) [Herries, Mathias and Rabin *Biochem J* 85 127 1962].

Ethyl nitroacetate [626-35-7] M 133.1, b 42-43°/0.2mm, 71-72°/3mm, 93-96°/9mm, 194-195°/atm,  $d_4^{20}$  1.1953,  $n_D^{20}$  1.4260, pK<sup>25</sup> 5.82. Purified by repeated distn. IR 1748 (CO<sub>2</sub>), 1570 and 1337 (NO<sub>2</sub>), and 800cm<sup>-1</sup> [Hazeldine J Chem Soc 2525 1953]. The hydrazine salt crystallises from 95% EtOH or MeOH as yellow crystals m 104-105° [Ungnade and Kissinger J Org Chem 22 1661 1957, Emmons and Freeman J Am Chem Soc 77 4391 1955].

Ethyl p-nitrobenzoate [99-77-4] M 195.2, m 56°. Dissolved in diethyl ether and washed with aqueous alkali, then the ether was evaporated and the solid recrystd from EtOH.

Ethyl orthoformate [122-51-0] M 148.2, b 144°/760mm, d 0.892, n 1.391. Shaken with aqueous 2% NaOH, dried with solid KOH andd distd from sodium through a 20cm Vigreux column.

o-Ethylphenol [90-00-6] M 122.2, f 45.1°, b 210-212°, d 1.020, n 1.537, pK<sup>25</sup> 10.20. Purified as for *p*-ethylphenol below.

*p*-Ethylphenol [123-07-9] M 122.2, m 47-48°, b 218.0°/762mm,  $n^{25}$  1.5239,  $pK^{25}$  10.21. Non-acidic impurities were removed by passing steam through a boiling soln containing 1 mole of the phenol and 1.75 moles of NaOH (as aq 10% soln). The residue was cooled and acidified with 30% (v/v) H<sub>2</sub>SO<sub>4</sub>, and the free phenol was extracted into diethyl ether. The extract was washed with water, dried with CaSO<sub>4</sub> and the ether was evapd. The phenol was distd at 100mm pressure through a **Stedman** gauze-packed column (see p. 441). It was further purified by fractional crystn by partial freezing, and by zone refining, under nitrogen [Biddiscombe et al. J Chem Soc 5764 1963]. Alternative purification is via the benzoate, as for phenol.

Ethyl phenylacetate [101-97-3] M 164.2, b 99-99.3°/14mm, d 1.030, n 1.499. Shaken with saturated aqueous Na<sub>2</sub>CO<sub>3</sub> (three times), aqueous 50% CaCl<sub>2</sub> (twice) and saturated aqueous NaCl (twice). Dried with CaCl<sub>2</sub> and distd under reduced pressure.

3-Ethyl-5-phenylhydantoin (Ethotoin) [86-35-1] M 204.2, m 94°. Crystd from water.

*N*-Ethyl-5-phenylisoxazolinium-3'-sulfonate [4156-16-5] M 253.3, m 220°(dec). Crystd from diethyl ether or ethyl acetate/pet ether. [Lamas et al. J Am Chem Soc 108 5543 1986.]

**3-Ethyl-3-phenyl-2,6-piperidinedione** (Glutethimide) [77-21-4] M 217.3, m 84°. Crystd from diethyl ether or ethyl acetate/pet ether.

Ethyl propionate [105-37-3] M 102.1, b 99.1°, d 0.891,  $n^{15}$  1.38643, n 1.38394. Treated with anhydrous CuSO<sub>4</sub> and distd under nitrogen.

**2-Ethylpyridine** [100-71-0] **M 107.2, b 148.6°, d 0.942, pK<sup>25</sup> 5.89.** Dried with BaO, and fractionally distd. Purified by conversion to the picrate, recrystn and regeneration of the free base followed by distn.

**4-Ethylpyridine** [536-75-4] **M 107.2, b 168.2-168.3°, d 0.942, pK<sup>25</sup> 6.02.** Dried with BaO, and fractionally distd. Also converted to the picrate, recrystd and the free base regenerated and distd.

4-Ethylpyridine-1-oxide [14906-55-9] M 123.1, m 109-110°, pK<sub>Est</sub>~1.1. Crystd from acetone/ether.

Ethyl pyruvate [617-35-6] M 116.1, m -50°, b 44-45°/10mm, 56°/20mm, 69-71°/42mm, 63°/23mm, 155.5°/760mm,  $d_4^{20}$  1.047,  $n_D^{20}$  1.4052. Shake the ester with 10mL portions of satd aq CaCl<sub>2</sub> soln (removes ethyl acetate) and the organic layer is removed by centrifugation, decantation and filtration, and is distilled under reduced pressure. Purification of small quantities is carried out *via* the bisulfite adduct: the ester (2.2mL) is shaken with saturated NaHSO<sub>3</sub> (3.6mL), chill in a freezing mixture when crystals separate rapidly (particularly if seeded). After 5min EtOH (10mL) is added and the crystals are filtered off, washed with EtOH and Et<sub>2</sub>O and dried. Yield *ca* 3g of *bisulfite adduct*. Then treat the adduct (16g) with saturated aqueous MgSO<sub>4</sub> (32mL) and 40% formaldehyde (5mL) and shake, whereby the ester separates as an oil which is extracted with Et<sub>2</sub>O, the extract is dried (MgSO<sub>4</sub>), filtered, evapd and the residue is distd (b 56°/20mm), and then redistd (b 147.5°/750mm) to give 5.5g of pure ester. [Cornforth Org Synth Coll Vol IV 467 1963.]

Ethyl Red [2-(4-diethylaminophenylazo)benzoic acid] [76058-33-8] M 197.4, m 150-152°, pK<sub>1</sub> 2.5, pK<sub>2</sub> 9.5. Crystd from EtOH/diethyl ether or toluene. Indicator: pH 4.4 (red) and 6.2 (yellow)

Ethyl stearate [111-61-5] M 312.5, m 33°, b 213-215°/15mm. The solid portion was separated from the partially solid starting material, then crystd twice from EtOH, dried by azeotropic distn with \*benzene, and fractionally distd in a spinning-band column at low pressure [Welsh *Trans Faraday Soc* 55 52 1959].

Ethyl thiocyanate (ethyl rhodanide) [542-90-5] M 87.1, b 144-145°, d 1.011, n 1.462. Fractionally distd at atmospheric pressure. (CARE LACHRYMATOR.)

Ethyl thioglycolate [623-51-8] M 120.2, b 50-51°/10mm, 55°/17mm, 62.5-64°/22mm, 67-68°/24mm, 155-158°/atm,  $d_4^{20}$  1.096,  $n_D^{20}$  1.457. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil the residue under reduced pressure [Bredereck et al. *Chem Ber* 90 1837 1957). The *Ni complex* [*Ni*(*SCH*<sub>2</sub>*CO*<sub>2</sub>*Et*)<sub>2</sub>] recrystallised twice from EtOH gives crystals which became black when dried in a vacuum over H<sub>2</sub>SO<sub>4</sub>, m 104-105° [Dranet and Cefola *J Am Chem Soc* 76 1975 1954].

N-Ethyl thiourea [625-53-6] M 104.2, m 110°. Crystd from EtOH, MeOH or ether.

Ethyl trichloroacetate [515-84-4] M 191.4, b 100-100.5°/30mm, d 1.383. Shaken with saturated aqueous Na<sub>2</sub>CO<sub>3</sub> (three times), aqueous 50% CaCl<sub>2</sub> (three times), saturated aqueous NaCl (twice), then distd with CaCl<sub>2</sub> and distd under reduced pressure.

Ethyl trifluoroacetate [383-63-1] M 142.1, b 61.3°/750, 60-62°/atm, 62-64°/755mm,  $d_4^{20}$  1.191,  $n_D^{20}$  1.30738. Fractionate through a long Vigreux column. IR has v at 1800 (CO<sub>2</sub>) and 1000 (OCO) cm<sup>-1</sup> [Fuson et al. J Chem Phys 20 1627 1952; Bergman J Org Chem 23 476 1958].

Ethyl trifluoromethanesulfonate [425-75-2] M 178.1, b 115°/atm, 118-120°/atm,  $d_4^{20}$  1.378,  $n_D^{20}$  1.336. The ester reacts slowly with H<sub>2</sub>O and aqueous alkali. If its IR has no OH bands (-3000 cm<sup>-1</sup>) then purify by redistillation. If OH bands are present then dilute with dry Et<sub>2</sub>O and shake (carefully) with aqueous NaHCO<sub>3</sub> until effervescence ceases, then wash with H<sub>2</sub>O and dry (MgSO<sub>4</sub>), filter, evaporate and distil the residue under slight vacuum then at atmospheric pressure in a N<sub>2</sub> atmosphere. IT IS A POWERFUL ALKYLATING AGENT, AND THE FUMES ARE VERY TOXIC - CARRY ALL OPERATIONS IN AN EFFICIENT FUME CUPBOARD. [Gramstad and Hazeldine J Chem Soc 173 1956; Howells and McCown Chem Rev 77 69 1977.]

S-Ethyl trifluorothioacetate [383-64-2] M 158.1, b 88-90°/atm, 90.5°/760mm,  $d_4^{20}$  1.255,  $n_D^{20}$  1.372. If IR is free of OH bands then fractionate, but if OH bands are present then dilute with dry Et<sub>2</sub>O, wash with 5% KOH and H<sub>2</sub>O, dry over MgSO<sub>4</sub> and fractionate through an efficient column [Hauptschein et al. J Am Chem Soc 74 4005 1952]. Powerful obnoxious odour.

Ethyl vinyl ether [109-92-2] M 72.1, b 35.5°, d 0.755. Contains polymerization inhibitors (usually amines, e.g. triethanolamine) which can be removed by fractional distn. Redistd from sodium. LACHRYMATORY.

**1-Ethynyl-1-cyclohexanol** [78-27-3] M **124.2, m 30-33°, 32-33°, b 74°/12mm, 76-78°/17mm, 171-172°/694mm, 180°/atm, d\_4^{25} 0.9734, n\_D^{25} 1.4801. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dilute NaHCO<sub>3</sub>, H<sub>2</sub>O again, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate and distil the residue. IR (CCl<sub>4</sub>): 3448 (OH), 2941 (CH), 1449-1123 and 956 cm<sup>-1</sup>; NMR (CCl<sub>4</sub>) \delta: 3.2 (OH), 2.5 (=CH), 1.70 (m 10H, CH<sub>2</sub>) [Hasbrouck and Kiessling J Org Chem <b>38** 2103 1972].

Ethynyl p-tolylsulfone [13894-21-8] M 180.2, m 73-74°. Recrystd from pet ether and dried in vac.

Etiocholane (5B-androsterone) [438-23-3] M 260.5, m 78-80°. Crystd from acetone.

Etiocholanic acid [438-08-4] M 304.5, m 228-229°,  $pK_{Est} \sim 4.7$ . Crystd from glacial acetic acid and sublimes at 160°/0.002mm. The methyl ester has m 99-101°. [Weiland et al. Z Physiol Chem 161 80 1926.]

Etioporphyrin I [448-71-5] M 478.7, m 360-363°. Crystd from pyridine or CHCl<sub>3</sub>-pet ether.

Eucaliptol (1,8-cineol, 1,8-epoxy-p-menthane, 1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane) [470-82-6] M 154.2, m 1.3°, 1.5°, b 39-39.3°/4mm, 176-176.4°/760mm,  $d_4^{20}$ 0.9232,  $n_D^{20}$  1.4575. Purified by dilution with an equal volume of pet ether, then saturated with dry HBr. The ppte was filtered off, washed with small vols of pet ether, then cineole was regenerated by stirring the crystals with H<sub>2</sub>O. It can also be purified via its o-cresol or resorcinol addition compds. Stored over Na until required. Purified by fractional distn. Insoluble in H<sub>2</sub>O but soluble in organic solvents. [IR: Kome et al. Nippon Kagaku Zasshi [J Chem Soc Japan (Pure Chem Sect)] 80 66 1959; Chem Abstr 603 1961.]

Eugenol (4-allyl-2-methoxyphenol) [97-53-0] M 164.2, b 253°/760mm, 255°/760mm,  $d_4^{20}$  1.066,  $n_D^{20}$  1.540, pK<sup>25</sup> 10.19. Fractional distn gives a pale yellow liquid which darkens and thickens on in air. Should store under N<sub>2</sub> at -20°. [Waterman and Priedster *Recl Trav Chim Pays-Bas* 48 1272 1929.]

Eugenol methyl ether (4-allyl-1,2-dimethoxybenzene) [93-15-2] M 178.2, m -4°, b 127-129°/11mm, 146°/30mm, 154.7°/760mm,  $d_4^{20}$  1.0354,  $n_D^{20}$  11.53411. Recryst from hexane at low temp and redistd (preferably *in vacuo*). [Hillmer and Schorning Z Phys Chem [A] 167 407 1934; Briner and Fliszár Helv Chim Acta 42 2063 1959.]

(+)- $\alpha$ -Fenchol (1R-1,3,3-trimethyl-norbornan-2-ol) [1632-73-1] M 154.3, m 40-43°, 47-47.5°, b 201-202°,  $[\alpha]_D^{20}$ +12.5° (c 10, EtOH). It is prepared by reduction of (-)-fenchone and is purified by recrystallisation from \*C<sub>6</sub>H<sub>6</sub>-pet ether, or distn, or both. The 2-carboxybenzoyl (monophthalate) derivative has m 146.5-147.5°  $[\alpha]_D^{20}$ -20.4° (EtOH), and the 2-phenylurethane has m 81°. [Beckmann and Metzger Chem Ber 89 2738 1956].

(+)- Fenchone (1S-1,3,3-trimethyl-norbornan-2-one) [4695-62-9] M 152.2, m 5-7°, 6.1°, b 63-65°/13mm, 66°/15mm, 122°/10mm,  $d_4^{20}$  0.9434,  $n_D^{20}$  1.4636,  $[\alpha]_D^{20}$ +66.9° (neat, or in c 1.5, EtOH),  $[\alpha]_{546}^{20}$ +60.4° (neat). The oily liquid is purified by distn in a vacuum, and is very soluble in EtOH and Et<sub>2</sub>O. [Boyle et al. J Chem Soc, Chem Commun 395 1971, Hückel Justus Liebigs Ann Chem 549 186 1941; (±)-isomer: Braun and Jacob Chem Ber 66 1461 1933.] It forms two oximes; cis-oxime: m

167° (cryst from pet ether)  $[\alpha]_D^{20}$  +46.5° (c 2, EtOH), O-benzoyloxime **m** 81°  $[\alpha]_D^{20}$  +49° (EtOH) and oxime-HCl **m** 136° (dec). The trans-oxime has **m** 123° (cryst from pet ether)  $[\alpha]_D^{18}$ +148° (c 2, EtOH) and the Obenzoyloxime has **m** 125°  $[\alpha]_D^{20}$  +128.5° (c 2, EtOH) [Hückel Justus Liebigs Ann Chem 549 186 1941; Hückel and Sachs Justus Liebigs Ann Chem 498 166 1932].

(-)- Fenchone (1*R*-1,3,3-trimethyl-norbornan-2-one) [7787-20-4] M 152.2, m 5.2°, b 67.2°/10mm, 191-195°/atm,  $d_4^{20}$  0.9484,  $n_D^{20}$  1.4630,  $[\alpha]_D^{20}$ -66.8° (neat). Purification as for the (+)-enantiomer above and should have the same physical properties except for the optical rotations. UV:  $\lambda$ max 285nm ( $\epsilon$  12.29). [Braun and Jacob Chem Ber 66 1461 1933; UV: Ohloff et al. Chem Ber 90 106 1957.]

Flavone (2-phenyl-4H-1-benzopyran-4-one) [525-82-6] M 222.3, m 100°. Crystd from pet ether.

Fluoranthene (benzo[*j*,*k*]fluorene) [206-44-0] M 202.3, m 110-111°. Purified by chromatography of CCl<sub>4</sub> solns on alumina, with \*benzene as eluent. Crystd from EtOH, MeOH or \*benzene. Purified by zone melting. [Gorman et al. J Am Chem Soc 107 4404 1985.]

2-Fluorenamine [153-78-6] M 181.2. See 2-aminofluorene on p. 106.

9-Fluorenamine [525-03-1] M 181.2, m 64-65°, pK<sub>Est</sub> ~3.5. Crystd from hexane.

Fluorene [86-73-7] M 166.2, m 114.7-115.1°, b 160°/15mm. Purified by chromatography of CCl<sub>4</sub> or pet ether (b 40-60°) soln on alumina, with \*benzene as eluent. Crystd from 95% EtOH, 90% acetic acid and again from EtOH. Crystn using glacial acetic acid retained an impurity which was removed by partial mercuration and pptn with LiBr [Brown, Dubeck and Goldman J Am Chem Soc 84 1229 1962]. Has also been crystd from hexane, or \*benzene/EtOH, distd under vacuum and purified by zone refining. [Gorman et al. J Am Chem Soc 107 4404 1985.]

**9-Fluorenone** [486-25-9] **M 180.2, m 82.5-83.0°, 85-86°, b 341°/760mm.** Crystd from absolute EtOH, MeOH or \*benzene/pentane. [Ikezawa J Am Chem Soc 108 1589 1986.] Also twice recrystd from toluene and sublimed in a vac [Saltiel J Am Chem Soc 108 2674 1986]. Can be distd under high vacuum.

Fluorene-2,7-diamine [525-64-4] M 196.3, m 165-166°. Crystd from hot H<sub>2</sub>O or aq EtOH, dried in a vac and stored in the dark.

**9-Fluorenylmethyl chloroformate (FMOC-Cl)** [28920-43-6] **M 258.7, m 61-63°, 61.4-63°**. The IR should contain no OH bands (at ~3000 cm<sup>-1</sup>) due to the hydrolysis product 9-fluorenylmethanol. Purify by recrystn from dry Et<sub>2</sub>O. IR (CHCl<sub>3</sub>) has band at 1770 cm<sup>-1</sup> (C=O) and the NMR (CDCl<sub>3</sub>) has  $\delta$  at 4-4.6 (m 2H, CHCH<sub>2</sub>) and 7.1-7.8 (m, 8 aromatic H). The *azide (FMOC-N<sub>3</sub>)* has **m** 89-90° (from hexane) and IR (CHCl<sub>3</sub>) at 2135 (N<sub>3</sub>) and 1730 (C=O) cm<sup>-1</sup>; and the *carbazate (FMOC-NHNH<sub>2</sub>)* has **m** 171° dec (from nitromethane), IR (KBr) 3310, 3202 (NH) and 1686 (CONH) cm<sup>-1</sup>. [Caprino and Han J Org Chem **37**, 3404 1972 and J Am Chem Soc **92** 5748 1970; Koole et al. J Org Chem **59** 1657 1989; Fürst et al. J Chromatogr **499** 537 1990.]

**9-Fluorenylmethyl succinimidyl carbonate** [82911-69-1] M 337.3, m 147-151° (dec), 151° (dec). Recrystd from CHCl<sub>3</sub>-Et<sub>2</sub>O, or from pet ether (b 40-60°). [Pauet Can J Chem 60 976 1982; Lapatsaris et al. Synthesis 671 1983.]

Fluorescein [9-(o-carboxyphenyl-6-hydroxy-3H-xanthene-3-one] [2321-07-5] M 320.0,  $\epsilon_{495nm}$ 7.84 x 10<sup>4</sup> (in 10<sup>-3</sup>M NaOH), pK<sub>1</sub> 2.2, pK<sub>2</sub> 4.4, pK<sub>3</sub> 6.7. Dissolved in dilute aqueous NaOH, filtered and ppted by adding dilute (1:1) HCl. The process was repeated twice more and the fluorescein was dried at 100°. Alternatively, it has been crystd from acetone by allowing the soln to evaporate at 37° in an open beaker. Also recrystd from EtOH and dried in a vacuum oven.

Fluoresceinamine (mixture of 5- and 6-aminofluorescein) [27599-63-9] M 347.3, m 314-316° (dec, 5-amino) and m >200° (dec). Dissolve in EtOH, treat with charcoal, filter, evaporate and dry residue in vacuum at 100° overnight. Also recrystallise from 6% HCl, then dissolve in 0.5% aqueous NaOH and ppte by acidifying with acetic acid. The separate amines are made from the respective nitro compounds which are best separated *via* their acetate salts. They have similar  $R_F$  of 0.26 on Silica Gel Merck  $F_{254}$  in 5 mL MeOH + 150 mL Et<sub>2</sub>O satd with H<sub>2</sub>O. IR (Me<sub>2</sub>SO) has a band at 1690 cm<sup>-1</sup> (CO<sub>2</sub><sup>-</sup>) and sometimes a weak band at 1750 cm<sup>-1</sup> due to lactone. UV (EtOH) of 6-isomer  $\lambda$ max 222 ( $\epsilon$  60 000) and 5-isomer  $\lambda$ max 222 ( $\epsilon$  60 000) and 285 ( $\epsilon$  20.600). [IR: McKinney and Churchill J Chem Soc (C) 654 1970; McKinney et al. J Org Chem 27 3986 1962; UV: Verbiscar J Org Chem 29 490 1964.]

Fluorescein isothiocyanate isomer I (5-isocyanato isomer) [3326-32-7; 27072-45-3 mixture of 5- and 6-isomers] M 389.4, m >160° (slow dec). It is made from the pure 5-amino isomer. Purified by dissolving in boiling Me<sub>2</sub>CO, filtering and adding pet ether (b 60-70°) until it becomes turbid. If an oil separates then decant and add more pet ether to the supernatant and cool. Orange-yellow crystals separate, collect and dry *in vacuo*. Should give one spot on TLC (silica gel) in EtOAc, pyridine, AcOH (50:1:1) and in Me<sub>2</sub>NCHO, CHCl<sub>3</sub>, 28% N<sub>4</sub>OH (10:5:4). IR (Me<sub>2</sub>SO): 2110 (NCS) and 1760 (C=O). The NMR spectra in Me<sub>2</sub>CO-d<sub>6</sub> of the 5- and 6-isomers are distinctly different for the protons in the \*benzene ring; the UV in phosphate buffer pH 8.0 shows a max at ~490nm. [Sinsheimer et al. Anal Biochem 57 227 1974; McKinney et al. Anal Biochem 7 74 1964.]

Fluoroacetamide [640-19-7] M 77.1, m 108°. Crystd from chloroform.

Fluorobenzene [462-06-6] M 96.1, b 84.8°, d 1.025, n 1.46573,  $n^{30}$  1.4610. Dried for several days with  $P_2O_5$ , then fractionally distd.

o-Fluorobenzoic acid [445-29-4] M 140.1, m 127°, pK<sup>25</sup> 3.27. Crystd from 50% aqueous EtOH, then zone melted or vacuum sublimed at 130-140°.

*m*-Fluorobenzoic acid [445-38-9] M 140.1, m 124°,  $pK^{25}$  3.86. Crystd from 50% aqueous EtOH, then vacuum sublimed at 130-140°.

*p*-Fluorobenzoic acid [456-22-4] M 140.1, m 182°,  $pK^{25}$  4.15. Crystd from 50% aqueous EtOH, then zone melted or vacuum sublimed at 130-140°.

3-Fluoro-4-hydroxyphenylacetic acid [458-09-3] M 170.1, m 33°,  $pK_{Est(1)}$ ~4.4,  $pK_{Est(2)}$ ~9.4. Crystd from water.

1-Fluoro-4-nitrobenzene [350-46-9] M 141.1, m 27° (stable form), 21.5° (unstable form), b 205.3°/735mm, 95-97.5°/22mm, 86.6°/14mm. Crystd from EtOH.

1-Fluoro-4-nitronaphthalene [341-92-4] M 191.2, m 80°. Recrystd from EtOH as yellow needles [Bunce et al. J Org Chem 52 4214 1987].

o-Fluorophenol [367-12-4] M 112.1, m 16°, b 53°/14mm, d 1.257, n 1.514, pK<sup>25</sup> 8.70. Passed at least twice through a gas chromatographic column for small quantities, or fractionally distd under reduced pressure.

p-Fluorophenoxyacetic acid [405-79-8] M 170.1, m 106°, pK<sup>25</sup> 3.13. Crystd from EtOH.

4-Fluorophenylacetic acid [405-50-5] M 154.1, m 86°, pK<sup>25</sup> 4.22. Crystd from heptane.

**4-Fluorophenyl isocyanate** [1195-45-5] **M 137.1, b 55°/8mm, n\_D^{20} 1.514.** Purify by repeated fractionation through an efficient column. If IR indicated that there is too much urea (in the presence of moisture the symmetrical urea is formed) then dissolve in dry EtOH-free CHCl<sub>3</sub>, filter, evaporate and distil. It is a pungent LACHRYMATORY liquid. [see Hardy J Chem Soc 2011 1934; and Hickinbottom Reactions of Organic Compounds Longmans p. 493 1957.]

**4-Fluorophenyl** isothiocyanate [1544-68-9] M 153.2, m 24-26°, 26-27°, b 66°/2 mm, 215°/atm, 228°/760mm,  $n_D^{20}$  1.6116. Likely impurity is the symmetrical thiourea. Dissolve the isothiocyanate in dry CHCl<sub>3</sub>, filter and distil the residue in a vacuum. It can also be steam distd, the oily layer separated, dried over CaCl<sub>2</sub> and distilled *in vacuo*. Bis-(4-fluorophenyl)thiourea has m 145° (from aq EtOH). [Browne and Dyson J Chem Soc 3285 1931; Buu Hoi et al. J Chem Soc 1573 1955; Olander Org Synth Coll Vol I 448 1941].

p-Fluorophenyl-o-nitrophenyl ether [448-37-3] M 247.2, m 62°. Crystd from EtOH.

o-Fluorotoluene [95-52-3] M 110.1, b 114.4°, d 1.005, n 1.475. Dried with  $P_2O_5$  or CaSO<sub>4</sub> and fractionally distd through a silvered vacuum-jacketed glass column with 1/8th-in glass helices. A high reflux ratio is necessary because of the closeness of the boiling points of the o-, m- and p- isomers [Potter and Saylor J Am Chem Soc 37 90 1951].

*m*-Fluorotoluene [352-70-5] M 110.1, b 116.5°, d 1.00,  $n^{27}$  1.46524. Purification as for *o*-fluorotoluene.

p-Fluorotoluene [352-32-9] M 116.0°, d 1.00, n 1.46884. Purification as for o-fluorotoluene.

Formaldehyde [50-00-0] M 30.0, m 92°, b -79.6°/20mm,  $d^{20}$  0.815, pK<sup>25</sup> 13.27 (hydrate). Commonly contains added MeOH. Addition of KOH soln (1 mole KOH: 100 moles HCHO) to 40% formaldehyde soln, or evaporation to dryness, gives paraformaldehyde polymer which, after washing with water, is dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> or H<sub>2</sub>SO<sub>4</sub>. Formaldehyde is regenerated by heating the paraformaldehyde to 120° under vacuum, or by decomposing it with barium peroxide. The monomer, a gas, is passed through a glass-wool filter cooled to -48° in CaCl<sub>2</sub>/ice mixture to remove particles of polymer, then dried by passage over P<sub>2</sub>O<sub>5</sub> and either condensed in a bulb immersed in liquid nitrogen or absorbed in ice-cold conductivity water.

Formaldehyde dimethyl acetal (dimethoxymethane, methylal, formal) [109-87-5] M 76.1, m -108°, b 41-42°/736mm, 41-43°/atm, 42-46°/atm,  $d_4^{20}$  0.8608,  $n_D^{20}$  1.35335. It is a volatile flammable liquid which is soluble in three parts of H<sub>2</sub>O, and is readily hydrolysed by acids. Purify by shaking with an equal vol of 20% aq NaOH, stand for 20min, dry over fused CaCl<sub>2</sub>, filter and fractionally distil through an efficient column, store over molecular sieves. [Buchler et al. Org Synth Coll Vol III 469 1955; Ind Eng Chem 18 1092 1926; Rambaud and Besserre Bull Soc Chim Fr 45 1955; IR: Can J Chem 36 285 1958.]

Formaldehyde dimethyl mercaptal (bis-[methylthio]methane) [1618-26-4] M 108.2, b 44-47°/13mm, 45.5°/18mm, 148-149°/atm,  $d_4^{20}$  1.0594,  $n_D^{20}$  1.5322. Work in an efficient fume cupboard as the substance may contain traces (or more) of methylmercaptan which has a very bad odour. Dissolve in Et<sub>2</sub>O, shake with aqueous alkalis then dry over anhydrous K<sub>2</sub>CO<sub>3</sub>, filter and distil over K<sub>2</sub>CO<sub>3</sub> under a stream of N<sub>2</sub>. If the odour is very strong then allow all gas effuents to bubble through 5% aqueous NaOH soln which is then treated with dilute KMnO<sub>4</sub> in order to oxidise MeSH to odourless products. UV:  $\lambda$ max 238 nm (log  $\varepsilon$  2.73) [Fehnel and Carmack J Am Chem Soc 71 90 1949; Fehér and Vogelbruch Chem Ber 91 996 1958; Bøhme and Marz Chem Ber 74 1672 1941]. Oxidation with aq KMnO<sub>4</sub> yields bis-(methylsulfonyl)methane which has m 142-143° [Fiecchi et al. Tetrahedron Lett 1681 1967].

Formamide [75-12-7] M 45.0, f 2.6°, b 103°/9mm, 210.5°/760mm(dec), d 1.13, n 1.44754,  $n^{25}$  1.44682. Formamide is easily hydrolysed by acids and bases. It also reacts with peroxides, acid halides, acid anhydrides, esters and (on heating) alcohols; while strong dehydrating agents convert it to a nitrile. It is very hygroscopic. Commercial material often contains acids and ammonium formate. Vorhoek [J Am Chem Soc 58 2577 1956] added some bromothymol blue to formamide and then neutralised it with NaOH before heating to 80-90° under reduced pressure to distil off ammonia and water. The amide was again neutralised and the formamide was reduced under reduced pressure at 80-90°. The distillate was again neutralised and redistd. It was then fractionally crystd in the absence of CO<sub>2</sub> and water by partial freezing.

## **Purification of Organic Chemicals**

Formamide (specific conductance  $2 \times 10^{-7}$  ohm<sup>-1</sup> cm<sup>-1</sup>) of low water content was dried by passage through a column of 3A molecular sieves, then deionized by treatment with a mixed-bed ion-exchange resin loaded with H<sup>+</sup> and HCONH<sup>-</sup> ions (using sodium formamide in formamide)[Notley and Spiro J Chem Soc (B) 362 1966].

Formamidine acetate [3473-63-0] M 104.1, m 159-161°(dec), 164°(dec), pK<sub>Est</sub> ~ 12. Unlike the hydrochloride, the acetate salt is not hygroscopic. It is recrystd from a small volume of acetic acid, by addition of EtOH and the crysts are washed with EtOH then Et<sub>2</sub>O and dried in a vac. [Taylor, Ehrhart and Karanisi Org Synth 46 39 1966.]

Formamidine sulfinic acid (thiourea-S-dioxide) [1758-73-2] M 108.1, m 124-126°(dec). Dissolved in five parts of aq 1:1% NaHSO<sub>3</sub> at 60-63° (charcoal), then crystd slowly, with agitation, at 10°. Filtered. Dried immediately at 60° [Koniecki and Linch Anal Chem 30 1134 1958].

Formanilide [103-70-8] M 121.1, m 50°, b 166°/14mm, 216°/120mm, d 1.14. Crystd from ligroin/xylene.

Formic acid [64-18-6] M 46.0 (anhydr), f 8.3°, b 25°/40mm, 100.7°/760mm, d 1.22, n 1.37140, n<sup>25</sup> 1.36938, pK<sup>25</sup> 3.74. Anhydrous formic acid can be obtained by direct fractional distillation under reduced pressure, the receiver being cooled in ice-water. The use of P<sub>2</sub>O<sub>5</sub> or CaCl<sub>2</sub> as dehydrating agents is unsatisfactory. Reagent grade 88% formic acid can be satisfactorily dried by refluxing with phthalic anhydride for 6h and then distilling. Alternatively, if it is left in contact with freshly prepared anhydrous CuSO<sub>4</sub> for several days about one half of the water is removed from 88% formic acid: distn removes the remainder. Boric anhydride (prepared by melting boric acid in an oven at a high temperature, cooling in a desiccator, and powdering) is a suitable dehydrating agent for 98% formic acid; after prolonged stirring with the anhydride the formic acid is distd under vacuum. Formic acid can be further purified by fractional crystn using partial freezing.

Forskolin (5-[acetyloxy]-3-ethenyldodecahydro-6,10,10b-trihydroxy-3,4a,7,7,10a-pentamethyl-[3R-{ $3\alpha$ -4a $\beta$ , 5 $\beta$ , 6 $\beta$ , 6a $\alpha$ ,10 $\alpha$ , 10a $\beta$ , 10b $\alpha$ }-1H-naphtho[2,1-b]pyran-1-one) [66575-29-9] M 410.5, m 229-232°, 228-233°. Recrystd from \*C<sub>6</sub>H<sub>6</sub>-pet ether. It is antihypertensive, positive ionotropic, platelet aggregation inhibitory and adenylate cyclase activating properties [Chem Abstr 89 1978 244150, de Souza et al. Med Res Rev 3 201 1983].

**D(-)-Fructose** [57-48-7] **M 180.2, m 103-106°**,  $[\alpha]_{546}^{20}$  -190° (after 1h, c 10, H<sub>2</sub>O), pK<sup>25</sup> 12.03. Dissolved in an equal weight of water (charcoal, previously washed with water to remove any soluble material), filtered and evaporated under reduced pressure at 45-50° to give a syrup containing 90% of fructose. After cooling to 40°, the syrup was seeded and kept at this temperature for 20-30h with occasional stirring. The crystals were removed by centrifugation, washed with a small quantity of water and dried to constant weight under a vacuum over conc H<sub>2</sub>SO<sub>4</sub>. For higher purity, this material was recrystd from 50% aqueous ethanol [Tsuzuki, Yamazaki and Kagami J Am Chem Soc 72 1071 1950].

D(+)-Fucose [36/5-37-0] M 164.2, m 144°,  $[\alpha]_{546}^{20}$  +89° (after 24h, c 10 in H<sub>2</sub>O). Crystd from EtOH.

Fullerene  $C_{60}$  (Buckminsterfullerene  $C_{60}$ , Footballene, Buckyball 60) [99685-96-8] M 720.66 and Fullerene  $C_{70}$  [115383-22-7] M 840.77. Purified from the soluble toluene extract (400mg) of the soot (Fullerite) formed from resistive heating of graphite by adsorption on neutral alumina (100g; Brockmann I; 60 x 8cm). Elution with toluene-hexane (5:95 v/v) gives *ca* 250mg of quite pure  $C_{60}$ . It has characteristic spectral properties (see below). Further elution with toluene-hexane (20:80 v/v; i.e. increased polarity of solvent) provides 50mg of "pure"  $C_{70}$  [J Am Chem Soc 113 1050 1991].

Chromatography on alumina can be improved by using conditions which favour adsorption rather than crystn. Thus the residue from toluene extraction (1g) in  $CS_2$  (*ca* 300mL) is adsorbed on alumina (375g, standard grade, neutral *ca* 150 mesh, Brockmann I) and loaded as a slurry in toluene-hexanes (5:95 v/v) to a 50 x 8cm column of alumina (1.5Kg) in the same solvent. To avoid crystn of the fullerenes, 10% of toluene in hexanes is added quickly followed by 5% of toluene in hexanes after the fullerenes had left the loading fraction (2-3h). With a flow rate of 15mL/min the purple C<sub>60</sub> fraction is eluted during a 3-4h period. Evapn of the eluates gives 550-

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630mg of product which, after recrystn from  $CS_2$ -cyclohexane yields 520-600mg of  $C_{60}$  which contains adsorbed solvent. On drying at 275°/10<sup>-3</sup>mm for 48h a 2% weight loss is observed although the  $C_{60}$  still contains traces of solvent. Further elution of the column with 20% of toluene in hexanes provides 130mg of  $C_{70}$  containing 10-14% of  $C_{60}$  (by <sup>13</sup>C NMR). This was rechromatographed as above using a half scale column and adsorbing the 130mg in  $CS_2$  (20mL) on alumina (24g) and gave 105mg of recrystd  $C_{70}$  (containing 2% of  $C_{60}$ ). The purity of  $C_{60}$  can be improved further by washing the crystalline product with Et<sub>2</sub>O and Me<sub>2</sub>CO followed by recrystn from \*C<sub>6</sub>H<sub>6</sub> and vacuum drying at high temperatures. [J Chem Soc, Chem Commun 956 1992.]

Carbon soot from resistive heating of a carbon rod in a partial helium atmosphere (0.3bar) under specified conditions is extracted with boiling  $C_6H_6$  or toluene, filtered and the red-brown soln evapd to give crystalline material in 14% yield which is mainly a mixture of fullerenes  $C_{60}$  and  $C_{70}$ . Chromatographic filtration of the 'crude' mixture with  $C_6H_6$  allows no separation of components, but some separation was observed on silica gel TLC with *n*-hexane or *n*-pentane, but not cyclohexane. Analytical HPLC with hexanes (5µm Econosphere silica) gave satisfactory separation of  $C_{60}$  and  $C_{70}$  (retention times of 6.64 and 6.93min respectively) at a flow rate of 0.5mL/min and using a detector at 256nm. HPLC indicated the presence of minor (<1.5% of total mass) unidentified  $C_n$  with species (retention times of 5.86 and 8.31min. Column chromatography on flash silica gel with hexanes gives a few fractions of  $C_{60}$  with  $\geq$ 95% purity but later fractions contain mixtures of  $C_{60}$  and  $C_{70}$ . These can be obtained in 99.85 and >99% purity respectively by column chromatography on neutral alumina. [*J Phys Chem* **94** 8630 *1990*].

Separation of  $C_{60}$  and  $C_{70}$  can be achieved by HPLC on a dinitroanilinopropyl (DNAP) silica (5µm pore size, 300Å pore diameter) column with a gradient from *n*-hexane to 50% CH<sub>2</sub>Cl<sub>2</sub> using a diode array detector at wavelengths 330nm (for  $C_{60}$ ) and 384nm (for  $C_{70}$ ). [J Am Chem Soc 113, 2940, 1991.]

Soxhlet extraction of the "soot" is a good preliminary procedure, or if material of only ca 98% purity is required. Soxhlet extraction with toluene is run (20min per cycle) until colourless solvent filled the upper part of the Soxhlet equipment (10h). One third of the toluene remained in the pot. After cooling, the solution was filtered through a glass frit. This solid (purple in toluene) was ca 98% C<sub>60</sub>. This powder was again extracted in a Soxhlet using identical conditions as before and the C<sub>60</sub> was recrystd from toluene to give 99.5% pure C<sub>60</sub>. C<sub>70</sub> has greater affinity than C<sub>h60</sub> for toluene. [J Chem Soc, Chem Commun 1402 1992.]

Purification of  $C_{60}$  from a  $C_{60}/C_{70}$  mixture was achieved by dissolving in an aqueous soln of  $\gamma$  (but not  $\beta$ ) cyclodextrin (0.02M) upon refluxing. The rate of dissolution (as can be followed by UV spectra) is quite slow and constant up to  $10^{-5}$ M of  $C_{60}$ . The highest concn of  $C_{60}$  in H<sub>2</sub>O obtained was 8 x  $10^{-5}$ M and a 2  $\gamma$ -cyclodextrin:1  $C_{60}$  clathrate is obtained.  $C_{60}$  is extracted from this aqueous soln by toluene and  $C_{60}$  of >99 purity is obtained by evaporation. With excess of  $\gamma$ -cyclodextrin more  $C_{60}$  dissolves and the complex precipitates. The ppte is insol in cold H<sub>2</sub>O but sol in boiling H<sub>2</sub>O to give a yellow soln. [J Chem Soc, Chem Commun 604 1922.]

 $C_{60}$  and  $C_{70}$  can also be readily purified by inclusion complexes with *p*-tert-butylcalix[6] and [8]arenes. Fresh carbon-arc soot (7.5g) is stirred with toluene (250mL) for 1h and filtered. To the filtrate is added *p*-tert-butylcalix[8]arene, refluxed for 10min and filtered. The filtrate is seeded and set aside overnight at 20°. The  $C_{60}$  complex separated as yellow-brown plates and recryst twice from toluene (1g from 80mL), 90% yield. Addition of CHCl<sub>3</sub> (5mL) to the complex (0.85g) gave  $C_{60}$  (0,28g, 92% from recryst complex).

*p-tert*-Butylcalix[6]arene- $(C_{60})_2$  complex is prepared by adding to a refluxing soln of  $C_{60}$  (5mg) in toluene (5mL), *p-tert*-butylcalix[6]arene (4.4mg). The hot soln was filtered rapidly and cooled overnight to give prisms (5.5mg, 77% yield). Pure  $C_{60}$  is obtained by decomposing the complex with CHCl<sub>3</sub> as above.

The *p*-tert-butylcalix[6]arene- $(C_{70})_2$  complex is obtained by adding *p*-tert-butylcalix[6]arene (5.8mg) to a refluxing soln of  $C_{70}$  (5mg) in toluene (2mL), filtering hot and slowly cooling. to give red-brown needles (2.5mg, 31% yield) of the complex. Pure  $C_{70}$  is then obtained by decomposing the complex with CHCl<sub>3</sub>.

Decomposition of these complexes can also be achieved by boiling a toluene soln over KOH pellets for *ca* 10min. The calixarenes form Na salts which do not complex with the fullerenes. These appear to be the most satisfactory means at present for preparing large quantities of relatively pure fullerene  $C_{60}$  and  $C_{70}$  and is considerably cheaper than previous methods. [*Nature* **368** 229 1994.]

Repeated chromatography on neutral alumina yields minor quantities of solid samples of  $C_{76}$ ,  $C_{84}$ ,  $C_{90}$  and  $C_{94}$  believed to be higher fullerenes. A stable oxide  $C_{70}O$  has been identified. Chromatographic procedures for the separation of these compounds are reported. [Science 252 548 1991.]

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Physical properties of Fullerene  $C_{60}$ : It does not melt below 360°, and starts to sublime at 300° in vacuo. It is a mustard coloured solid that appears brown or black with increasing film thickness. It is soluble in common organic solvents, particularly aromatic hydrocarbons which give a beautiful magenta colour. Toluene solutions are purple in colour. Sol in \*C<sub>6</sub>H<sub>6</sub> (5mg/mL), but dissolves slowly. Crysts of C<sub>60</sub> are both needles and plates. UV-Vis in hexanes:  $\lambda$ max nm(log  $\varepsilon$ ) 211(5.17), 227sh(4.91), 256(5.24), 328(4.71), 357sh(4.08), 368sh(3.91), 376sh(3.75), 390(3.52), 395sh(3.30), 403(3.48), 407(3.78), 492sh(2.72) < 540(2.85), 568(2.78), 590(2.86), 598(2.87) and 620(2.60).

IR (KBr): v 1429m, 1182m, 724m, 576m and 527s cm<sup>-1</sup>. <sup>13</sup>C NMR: one signal at 142.68ppm.

Physical properties of Fullerene  $C_{70}$ : It does not melt below 360°, and starts to sublime at 350° in vacuo. A reddish-brown solid, greenish black in thicker films. Solns are port-wine red in colour. Mixtures of  $C_{60}$  and  $C_{70}$  are red due to  $C_{70}$  being more intensely coloured. It is less soluble than  $C_{60}$  in  $*C_6H_6$  but also dissolves slowly.  $C_{70}$  gives orange coloured soln in toluene. Drying at 200-250° is not sufficient to remove All solvent. Samples need to be sublimed to be free from solvent.

UV-Vis in hexanes:  $\lambda max nm(\log \varepsilon) 214(5.05), 235(5.06), 249sh(4.95), 268sh(4.78), 313(4.23), 330(4.38), 359(4.29), 377(4.45), 468(4.16), 542(3.78), 590sh(3.47), 599sh(3.38), 609(3.32), 623sh(3.09), 635sh(3.13) and 646sh(2.80).$ 

IR (KBr): v 1430m, 1428m, 1420m, 1413m, 1133mw, 1087w, 795s, 674ms, 642ms, 5778s, 566m, 535ms and 458m cm<sup>-1</sup>.

<sup>13</sup>C NMR [run in the presence of Cr(pentan-2,4-dione)<sub>3</sub> which induces a ca 0.12ppm in the spectrum]: Five signals at 150.07, 147.52, 146.82, 144.77 and 130.28ppm, unaffected by proton decoupling.

[Further reading: Kroto, Fischer and Cox Fullerenes Pergamon Press, Oxford 1993 ISBN 0080421520; Kadish and Ruoff (Eds) Fullerenes: Recent Advances in the Chemistry and Physics of Fullerenes and Related Materials The Electrochemical Soc. Inc, Pennington, NJ, 1994 ISBN 1566770823]

Fumagillin {2,4,6.8-decatetraene-1,10-dioic acid mono[4-(1,2-epoxy-1,5-dimethyl-4hexenyl)-5-methoxy-1-oxaspiro[2.5]oct-6-yl] ester} [23110-15-8] M 458.5, m 194-195°,  $[\alpha]_D^{20}$  -26.2° (in 95% EtOH), pK<sub>Est</sub> ~4.5. Forty grams of a commercial sample containing 42% fumagillin, 45% sucrose, 10% antifoam agent and 3% of other impurities were digested with 150mL of CHCl<sub>3</sub>. The insoluble sucrose was filtered off and washed with CHCl<sub>3</sub>. The combined CHCl<sub>3</sub> extracts were evapd almost to dryness at room temperature under reduced pressure. The residue was triturated with 20mL of MeOH and the fumagillin was filtered off by suction. It was crystd twice from 500mL of hot MeOH by standing overnight in a refrigerator (yellow needles). (The long chain fatty ester used as antifoam agent was still present, but was then removed by repeated digestion, on a steam bath, with 100mL of diethyl ether.) For further purification, the fumagillin (10g) was dissolved in 150mL of 0.2M ammonia, and the insoluble residue was filtered off. The ammonia soln (cooled in running cold water) was then brought to pH 4 by careful addn of M HCl with constant shaking in the presence of 150mL of CHCl3. (Fumagillin is acid-labile and must be removed rapidly from the aq acid soln.) The CHCl<sub>3</sub> extract was washed several times with distd water, dried  $(Na_2SO_4)$  and evaporated under reduced pressure. The solid residue was washed with 20mL of MeOH. The fumagillin was filtered by suction, then crystd from 200mL of hot MeOH. [Tarbell et al. J Am Chem Soc 77 5610 1955.]

Alternatively, 10g of fumagillin in 100mL CHCl<sub>3</sub> was passed through a silica gel (5g) column to remove tarry material, and the CHCl<sub>3</sub> was evaporated to leave an oil which gave fumagillin on crystn from amyl acetate. It recrystallises from MeOH (charcoal). The fumagillin was stored in dark bottles in the absence of oxygen and at low temperatures. [Schenk, Hargie and Isarasena J Am Chem Soc 77 5606 1955.]

Fumaraldehyde bis-(dimethyl acetal) (trans-1,1,4,4-tetramethoxybut-2-ene) [6068-62-8] M 176.2, b 100-103°/15mm, 101-103°/25mm,  $d_4^{20}$  1.011,  $n_D^{20}$  1.425. Dry over fused CaCl<sub>2</sub> and dist in vacuo. The maleic (cis) isomer has b 112°/11mm, and d<sup>23</sup> 0.932 and  $n_D^{25}$ 1.4243. [Zeik and Heusner Chem Ber 90 1869 1957; Clauson-Kaas et al. Acta Chem Scand 9 111 1955; Clauson-Kaas Acta Chem Scand 6 569 1952.]

Fumaric (*trans*-but-2-ene-1,4-dioic) acid [110-17-8] M 116.1, m 289.5-291.5° (sealed tube),  $pK_1^{25}$  3.10,  $pK_2^{25}$  4.60 (4.38). Crystd from hot M HCl or water. Dried at 100°.

**Furan** [110-00-9] **M 68.1, b 31.3°, d 1.42, n 1.4214.** Shaken with aqueous 5% KOH, dried with  $CaSO_4$  or  $Na_2SO_4$ , then distd under nitrogen, from KOH or sodium, immediately before use. A trace of hydroquinone could be added as an inhibitor of oxidation.

3-(2-Furanayl)acrylic acid [539-47-9] M 138.1, m 141°,  $pK_{Est} \sim 3.8$ . Crystd from H<sub>2</sub>O or pet ether (b 80-100°)(charcoal).

**Furan-2-carboxylic** (2-furoic) acid [88-14-2] M 112.1, m 133-134°, b 141-144°/20mm, 230-232°/760mm,  $pK_1^{25}$  -7.3 (O-protonation),  $pK_2^{25}$ 3.32. Crystd from hot water (charcoal), dried at 120° for 2h, then recrystd from CHCl<sub>3</sub>, and again dried at 120° for 2h. For use as a standard in volumetric analysis, good quality commercial acid should be crystd from CHCl<sub>3</sub> and dried as above or sublimed at 130-140° at 50-60mm or less.

Furan-3-carboxylic (3-furoic) acid [488-93-7] M 112.1, m 122-123°, pK<sup>25</sup> 4.03 Crystd from water.

**Furan-3,4-dicarboxylic acid** [3387-26-6] **M 156.1, m 217-218°**  $pK_1^{25}$ **1.44,**  $pK_2^{25}$ **7.84.** Crystd from water.

Furfural (2-furfuraldehyde) [98-01-1] M 96.1, b 54-56°/11mm, 59-60°/15mm, 67.8°/20mm, 90°/65mm, 161°/760mm,  $d_4^{20}$  1.159,  $n_D^{20}$  1.52608, pK -6.5 (O-protonation). Unstable to air, light and acids. Impurities include formic acid, β-formylacrylic acid and furan-2-carboxylic acid. Distd over an oil bath from 7% (w/w) Na<sub>2</sub>CO<sub>3</sub> (added to neutralise acids, especially pyromucic acid). Redistd from 2% (w/w) Na<sub>2</sub>CO<sub>3</sub>, and then, finally fractionally distd under vacuum. It is stored in the dark. [Evans and Aylesworth Ind Eng Chem (Anal ed) 18 24 1926.]

Impurities resulting from storage can be removed by passage through chromatographic grade alumina. Furfural can be separated from impurities other than carbonyl compounds by the bisulfite addition compound. The aldehyde is steam volatile.

It has been purified by distn (using a Claisen head) under reduced pressure. This is essential as is the use of an oil bath with temperatures of no more than  $130^{\circ}$  are highly recommended. When furfural is distd at atm press (in a stream of N<sub>2</sub>), or under reduced pressure with a free flame (caution because the aldehyde is flammable) an almost colourless oil is obtained. After a few days and sometimes a few hours the oil gradually darkens and finally becomes black. This change is accelerated by light but occurs more slowly when kept in a brown bottle. However, when the aldehyde is distd under vacuum and the bath temperature kept below 130° during the distn, the oil develops only a slight colour when exposed to direct sunlight during several days. The distn of very impure material should NOT be attempted at atm pressure otherwise the product darkens rapidly. After one distn under vacuum a distn at atmospheric pressure can be carried out without too much decomposition and darkening. The liquid **irritates mucous membranes**. Store in dark containers under N<sub>2</sub>. [Adams and Voorhees *Org Synth* Coll Vol I 280 1941.]

Furfuryl alcohol (2-furylmethanol) [98-00-0] M 98.1, b 68-69°/20mm, 170.0°/750mm, d 1.132, n 1.4873,  $n^{30}$  1.4801,  $pK^{25}$  2.61. Distd under reduced pressure to remove tarry material, shaken with aqueous NaHCO<sub>3</sub>, dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd under reduced pressure from Na<sub>2</sub>CO<sub>3</sub>. Further dried by shaking with Linde 5A molecular sieves.

Furfurylamine (2-aminomethylfuran) [617-89-0] M 97.1, b 142.5-143°/735mm, d 1.059, n 1.489, pK<sup>30</sup> 8.89. Distd under nitrogen from KOH through a column packed with glass helices.

Furil [492-94-4] M 190.2, m 165-166°. Crystd from MeOH or \*benzene (charcoal).

Furoin [552-86-3] M 192.2, m 135-136°. Crystd from MeOH (charcoal).

**Galactaric** Acid (mucic acid) [526-99-6] M 210.1, m 212-213°(dec)  $pK_1^{25}3.09$ (3.29),  $pK_2^{25}3.63$  (4.41). Dissolved in the minimum volume of dil aq NaOH, and ppted by adding dil HCl. The temperature should be kept below 25°.

**D-Galactonic acid** [576-36-3] **M 196.2, m 148°, pK**<sub>Est</sub> ~3.5. Crystd from EtOH. Cyclises to *D*-galactonono-1,4-lactone, **m** 134-136°,  $[\alpha]_{546}^{30}$  mutarotates in 1h to -92° (c 5,H<sub>2</sub>O).

D(-)-Galactono-1,4-lactone [2782-07-2] M 178.1, m 134-137°,  $[\alpha]_D^{20}$  -78° (in H<sub>2</sub>O). Crystd from EtOH.

D(+)-Galactosamine hydrochloride [1772-03-8] M 215.6, m 181-185°,  $[\alpha]_D^{25}$  +96.4° (after 24h, c 3.2 in H<sub>2</sub>O), pK<sub>Est</sub> ~7.7 (free base). Dissolved in a small volume of H<sub>2</sub>O. Then added three volumes of EtOH, followed by acetone until faintly turbid and stood overnight in a refrigerator. [Roseman and Ludoweig J Am Chem Soc 76 301 1954.]

 $\alpha$ -D-Galactose [59-23-4] M 180.2, m 167-168°,  $[\alpha]_D^{20}$  +80.4° (after 24h, c 4 in H<sub>2</sub>O), pK<sup>25</sup> 12.48. Crystd twice from aqueous 80% EtOH at -10°, then dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

Gallic acid (H<sub>2</sub>O) (3,4,5-trihydroxybenzoic acid) [5995-86-8 (H<sub>2</sub>O), 149-91-7 (anhydr)] M 188.1, m 253°(dec),  $pK_1^{25}4.27$ ,  $pK_2^{25}8.68$ . Crystd from water.

**Galvinoxyl** [2,6-di-tert-butyl- $\alpha$ -(3,5-di-tert-butyl-4-oxo-2,5-cyclohexadiene-1-ylidene)-ptolyloxy] [2370-18-5] M 421.65, m 153.2-153.6°, 158-159°. A stable free radical scavanger of short-lived free radicals with odd electrons on C or O. Best prepared freshly by oxidation of 3,3',5,5'-tetra-tertbutyl-4,4'-dihydroxydiphenyl-methane [m 154°, 157.1-157.6°; obtained by gently heating for 10-15min 2,6-ditert-butylphenol, formaldehyde and NaOH in EtOH and recryst from EtOH (20g/100mL) as colorless plates, Karasch and Joshi J Org Chem 22 1435 1957; Bartlett et al. J Am Chem Soc 82 1756 1960 and 84 2596 1962.] Oxidation is carried out under N<sub>2</sub> with PbO<sub>2</sub> in Et<sub>2</sub>O or isooctane [Galvin A. Coppinger J Am Chem Soc 79 501 1957; Bartlett et al. above] or with alkaline potassium ferricyanide [Karasch and Joshi, above], whereby Galvinoxyl separates as deep blue crystals, and is recrystd twice under N<sub>2</sub> from \*C<sub>6</sub>H<sub>6</sub> soln by suction evaporation at 30°. The VIS spectrum has  $\lambda$ max 407nm ( $\varepsilon$  30,000), 431nm ( $\varepsilon$  154,000) and weak absorption at 772.5nm, and IR: v 1577 and 2967cm<sup>-1</sup>, and is estimated by iodometric titration. It is sensitive to O<sub>2</sub> in presence of OH<sup>-</sup> ions and to traces of strong acid in hydroxylic or hydrocarbon solvents. At 62.5° in a 0.62mM soln in \*C<sub>6</sub>H<sub>6</sub> the radical decays with a first order  $k = 4 \times 10^{-8} \sec^{-1}$  (half life 1.7 x 10<sup>17</sup> sec, ~200 days) as observed by the change in OD at 550nm [see also Green and Adam J Org Chem 28 3550 1963].

Genistein (4',5,7-trihydroxyisoflavone) [446-72-0] M 270.2, m 297-298°,  $[\alpha]_D^{20}$  -28° (c 0.6, 20mM NaOH), (phenolic pKs 8-10). Crystd from 60% aqueous EtOH or water.

Genistin (genistein-7-D-glucoside) [529-59-9] M 432.4, m 256°. Crystd from 80% EtOH/water.

 $\alpha$ -Gentiobiose (amygdalose, 6-O- $\alpha$ -D-glucopyranosyl-D-glucopyranose) [5995-99-5 (bipyranose)] M 342.3, m 86°,  $[\alpha]_{546}^{20}$  +11° (after 24h, c 4, H<sub>2</sub>O). Crystd from MeOH (retains solvent of crystn).

β-Gentiobiose (see above) [5996-00-9 (bi-pyranose); 554-91-6 (one open ring)] M 342.3, m 190-195°,  $[α]_{546}^{20}$  +8° (after 6h, c 3, H<sub>2</sub>O). Crystd from MeOH or EtOH.

**Geraniol** [106-24-1] **M 154.3, b 230°, d 0.879, n 1.4766.** Purified by ascending chromatography or by thin layer chromatography on plates of kieselguhr G with acetone/water/liquid paraffin (130:70:1) as solvent system. Hexane/ethyl acetate (1:4) is also suitable. Also purified by GLC on a silicone-treated column of Carbowax 20M (10%) on Chromosorb W (60-80 mesh). [Porter *Pure Appl Chem* **20** 499 1969.] Stored in full, tightly sealed containers in the cool, protected from light.

Gibberillic acid (GA<sub>3</sub>) [77-06-5] M 346.4, m 233-235°(dec),  $[\alpha]_{546}^{20}$  +92° (c 1, MeOH), pK 4.0. Crystd from ethyl acetate.

Girard Reagent T (2-hydrazino-N, N, N-trimethyl-2-oxo-ethanaminium chloride) [123-46-6] M 167.6, m 192<sup>o</sup>. Should be crystd from absolute EtOH (slight decomposition) when it has a slight odour, and stored in tightly stoppered containers because it is hygroscopic.

Glucamine [488-43-7] M 181.2, m 127°,  $[\alpha]_D^{20}$ -8° (c 10, H<sub>2</sub>O), pK<sub>Est</sub> ~9.0. Crystd from MeOH.

D-Gluconamide [3118-85-2] M 197.2, m 144°,  $[\alpha]_D^{23} + 31^\circ$  (c 2, H<sub>2</sub>O). Crystd from EtOH.

**D-Glucono-** $\delta$ **-lactone** [90-80-2] **M 178.1, m 152-153°**,  $[\alpha]_{546}^{20}$  +76° (c 4, H<sub>2</sub>O). Crystd from ethylene glycol monomethyl ether and dried for 1h at 110°.

**D-Glucosamine** [3416-24-8] **M 179.2, m 110°(dec),**  $[\alpha]_D^{20} + 28^\circ \rightarrow +48^\circ$  (c 5, H<sub>2</sub>O), pK<sup>24</sup> 7.71. Crystd from MeOH. *N-Acetyl deriv*, **m** 205° from MeOH/Et<sub>2</sub>O has  $[\alpha]_D^{20} + 64^\circ \rightarrow +41^\circ$  (c 5, H<sub>2</sub>O).

**D-Glucosamine hydrochloride** [66-84-2] M 215.6, m >300°,  $[\alpha]_D^{25}$  +71.8° (after 20h, c 4, H<sub>2</sub>O). Crystd from 3M HCl, water, and finally water/EtOH/acetone as for galactosamine hydrochloride.

 $\alpha$ -D-Glucose [492-62-6] M 180.2, m 146°,  $[\alpha]_D^{20}$ +52.5° (after 24h, c 4, H<sub>2</sub>O), pK<sup>25</sup> 12.46. Recrysts slowly from aqueous 80% EtOH, then vacuum dried over P<sub>2</sub>O<sub>5</sub>. Alternatively, crystd from water at 55°, then dried for 6h in a vacuum oven between 60-70° at 2mm.

β-D-Glucose [50-99-7] M 180.2, m 148-150°. Crystd from hot glacial acetic acid.

 $\alpha$ -D-Glucose pentaacetate [604-68-2] M 390.4, m 110-111°, 112°,  $[\alpha]_{546}^{20}$  +119° (c 5, CHCl<sub>3</sub>). Crystd from MeOH or EtOH.

β-D-Glucose pentaacetate [604-69-3] M 390.4, m 131-132°,  $[α]_{546}^{20}$  +5° (c 5, CHCl<sub>3</sub>). Crystd from MeOH or EtOH.

D-Glucose phenylhydrazone [534-97-4] M 358.4, m 208°. Crystd from aqueous EtOH.

**D-Glucuronic acid** [6556-12-3] **M 194.1, m 165°,**  $[\alpha]_D^{20}$  +36° (c 3, H<sub>2</sub>O), pK<sub>2</sub><sup>20</sup> 3.18. Crystd from EtOH or ethyl acetate.

**D-Glucuronolactone** [32449-92-6] **M 176.1, m 175-177°**,  $[\alpha]_{546}^{20}$  + 22° (after 24h, c 10, H<sub>2</sub>O). Crystd from water.

L-Glutamic acid [56-86-0] M 147.1, m 224-225°(dec),  $[\alpha]_D^{25}$  +31.4° (c 5, 5M HCl),  $pK_1^{20}$ , p  $K_2^{20}$  2.06,4.35,  $pK_3^{20}$  9.85. Crystd from H<sub>2</sub>O acidified to pH 3.2 by adding 4 volumes of EtOH, and dried at 110°. Likely impurities are aspartic acid and cysteine.

L-Glutamic acid- $\gamma$ -benzyl ester [1676-73-9] M 237.3, m 179-181°,  $[\alpha]_{589}^{20}$  19.3° (c 1, HOAc),  $pK_1^{25}$  2.17,  $pK_2^{25}$  9.00. Recrystd from H<sub>2</sub>O and stored at 0°. [Estrin *Biochem Prep* 13 25 1971.]

L-Glutamine [56-85-9] M 146.2, m 184-185°,  $[\alpha]_D^{25}$  +31.8° (M HCl),  $pK_1^{25}$  2.17,  $pK_2^{25}$  9.13. Likely impurities are glutamic acid, ammonium pyroglutamate, tyrosine, asparagine, isoglutamine, arginine. Crystd from water.

Glutaraldehyde [111-30-8] M 100.1, b 71°/10mm, as 50% aq soln. Likely impurities are oxidation products - acids, semialdehydes and polymers. It can be purified by repeated washing with activated charcoal (Norit) followed by vacuum filtration, using 15-20g charcoal/100mL of glutaraldehyde soln.

Vacuum distn at 60-65°/15mm, discarding the first 5-10%, was followed by dilution with an equal volume of freshly distilled water at 70-75°, using magnetic stirring under nitrogen. The soln is stored at low temp (3-4°),

in a tightly stoppered container, and protected from light. Standardised by titration with hydroxylamine. [Anderson J Histochem Cytochem 15 652 1967.]

Glutaric acid [110-94-1] M 132.1, m 97.5-98°,  $pK_1^{25}$  4.35,  $pK_2^{25}$  5.40. Crystd from \*benzene, CHCl<sub>3</sub>, distilled water or \*benzene containing 10% (w/w) of diethyl ether. Dried under vacuum.

dl-Glyceraldehyde [56-82-6] M 90.1, m 145°. Crystd from EtOH/diethyl ether.

Glycerol [56-81-5] M 92.1, m 18.2°, b 182°/20mm, 290°/760mm, d 1.261,  $n^{25}$  1.47352, pK 14.4. Glycerol was dissolved in an equal volume of *n*-butanol (or *n*-propanol, amyl alcohol or liquid ammonia) in a water-tight container, cooled and seeded while slowly revolving in an ice-water slurry. The crystals were collected by centrifugation, then washed with cold acetone or isopropyl ether. [Hass and Patterson *Ind Eng Chem (Anal Ed)* 33 615 1941.] Coloured impurities can be removed from substantially dry glycerol by extraction with 2,2,4-trimethylpentane. Alternatively, glycerol can be decolorised and dried by treatment with activated charcoal and alumina, followed by filtering. Glycerol can be distd at 15mm in a stream of dry nitrogen, and stored in a desiccator over P<sub>2</sub>O<sub>5</sub>. Crude glycerol can be purified by digestion with conc H<sub>2</sub>SO<sub>4</sub> and saponification with a lime paste, then re-acidified with H<sub>2</sub>SO<sub>4</sub>, filtered, treated with an anion exchange resin and fractionally distd under vacuum.

Glycidol (oxirane-2-methanol) [RS-(±)- 556-52-5; R-(+)- 57044-25-4; S-(-)- 60456-23-7] M 74.1, b 61-62°/15mm, d 1.117, n 1.433 (±), b 49-50°/7mm, 66-67°/19mm,  $[\alpha]_{D}^{20}$ -15° (neat) (Sisomer, § also available on polymer support), b 56-56.5°/11mm, d 1.117, n 1.429,  $[\alpha]_{D}^{20}$ +15° (neat). Purified by fractional distn. The 4-nitrobenzoates have m 56° (±); m 60-62°,  $[\alpha]_{D}^{20}$ -37.9° (c 3.38 CHCl<sub>3</sub>) for R-(-)-isomer [106268-95-5]; m 60-62°,  $[\alpha]_{D}^{20}$ +38° (c 1 CHCl<sub>3</sub>) for S-(+)-isomer m 60-62°,  $[\alpha]_{D}^{20}$ -38° (c 1 CHCl<sub>3</sub>) [115459-65-9], and are recrystd from Et<sub>2</sub>O or Et<sub>2</sub>O/pet ether (b 40-60°) [S-isomer: Burgos et al. J Org Chem 52 4973 1987; Sowden and Fischer J Am Chem Soc 64 1291 1942.]

Glycinamide hydrochloride [1668-10-6] M 110.5, m 186-189° (207-208°), pK<sub>1</sub><sup>25</sup>-6.10, pK<sub>2</sub><sup>25</sup> -1.78, pK<sub>3</sub><sup>25</sup> 7.95. Crystd from EtOH.

Glycine see aminoacetic acid.

Glycine ethyl ester hydrochloride [623-33-6] M 136.9, m 145-146°, pK<sup>25</sup> 7.69. Crystd from absolute EtOH.

Glycine hydrochloride [6000-43-7] M 111.5, m 176-178°. Crystd from absolute EtOH.

Glycine methyl ester hydrochloride [5680-79-5] M 125.6, m 174°(dec), pK<sup>25</sup> 7.66. Crystd from MeOH.

Glycine *p*-nitrophenyl ester hydrobromide. [7413-60-7] M 277.1, m 214° (dec). Recryst from MeOH by adding diethyl ether. [Alners et al. *Biochem Preps* 13 22 1971].

Glycocholic acid (*N*-cholylglycine) [475-31-0] M 465.6, m 154-155°, 165-168°,  $[\alpha]_{546}^{20}$ +37° (c 1, EtOH), pK 4.4. Crystd from hot water as sesquihydrate. Dried at 100°.

Glycolic (α-hydroxyacetic) acid [79-14-1] M 76.1, m 81°, pK<sup>25</sup> 3.62. Crystd from diethyl ether.

**N-Glycylanilide** [555-48-6] M 150.2, m 62°, pK<sub>Est</sub>~8.0. Crystd from water, sol in Et<sub>2</sub>O...

Glycylglycine [556-50-3] M 132.1, m 260-262°(dec),  $pK^{20}$  8.40,  $pK^{30}$  8.04. Crystd from aqueos 50% EtOH or water at 50-60° by addition of EtOH. Dried at 110°.

Glycylglycine hydrochloride [13059-60-4] M 168.6, m 215-220°, 235-236°, 260-262°, pK<sub>1</sub><sup>25</sup> 3.12, pK<sub>2</sub><sup>25</sup>8.17. Crystd from 95% EtOH.

Glycyl-L-proline [704-15-4] M 172.2, m 185°,  $pK_1^{25}$  2.81,  $pK_2^{25}$  8.65. Crystd from water at 50-60° by addition of EtOH.

*dl*-Glycylserine [687-38-7] M 162.2, m 207°(dec),  $pK_1^{25}$  2.92,  $pK_2^{25}$  8.10. Crystd from H<sub>2</sub>O (charcoal) by addition of EtOH.

Glycyrrhizic acid ammonium salt  $(3H_2O)$  [53956-04-0] M 823.0, m 210°(dec),  $[\alpha]_{546}^{20}$  +60° (c 1, 50% aq EtOH), pK<sub>Est</sub> ~4.0. Crystd from glacial acetic acid, then dissolved in ethanolic ammonia and evaporated.

**Glyoxal bis(2-hydroxyanil)** [1149-16-2] **M 240.3, m 210-213°**, ε<sub>294nm</sub> 9880. Crystd from MeOH or EtOH.

Glyoxylic acid [298-12-4] M 74.0, m 98°(anhydr), 50-52°(monohydrate), pK<sup>25</sup> 2.98. Crystd from water as the monohydrate.

Gramine (3-dimethylaminoethylindole) [87-52-5] M 174.3, m 134°, pK<sup>25</sup> 16.00 (NH acidic). Crystd from diethyl ether, ethanol or acetone.

Griseofulvin [126-07-8] M 352.8, m 220°,  $[\alpha]_{D}^{22}$  +365° (c 1, acetone). Crystd from \*benzene.

Guaiacic acid [4,4'-(2,3-dimethyl-1-butene-(1,4-diyl)-bis-(2-methoxyphenol)] [500-40-3] M 328.4, m 99-100.5°, pK<sub>Est</sub> ~10.0. Crystd from EtOH.

Guaiacol (2-methoxyphenol) [90-05-1] M 124.1, m 32°, b 106°/24mm, 205°/746mm, pK<sup>25</sup> 9.90. Crystd from \*benzene/pet ether or distd.

Guaiacol carbonate [553-17-3] M 274.3, m 88.1º. Crystd from EtOH.

Guanidine [113-00-8] M 59.1, m ~50°, pK<sup>25</sup> 13.6. Crystd from water/EtOH under nitrogen. Very deliquescent and absorbs CO<sub>2</sub> from the air readily.

Guanidine carbonate [593-85-1] M 180.2, m 197°. Crystd from MeOH.

**Guanidine hydrochloride** [50-01-1] M 95.5, m 181-183°. Crystd from hot methanol by chilling to about -10°, with vigorous stirring. The fine crystals were filtered through fritted glass, washed with cold (-10°) methanol, dried at 50° under vacuum for 5h. (The product is more pure than that obtained by crystn at room temperature from methanol by adding large amounts of diethyl ether.) [Kolthoff et al. J Am Chem Soc 79 5102 1957].

Guanosine (H<sub>2</sub>O) [118-00-3] M 283.2, m 240-250°(dec),  $[\alpha]_{546}^{20}$  -86° (c 1, 0.1M NaOH), pK<sub>1</sub><sup>25</sup> 1.9, pK<sub>2</sub><sup>25</sup> 9.24, pK<sub>3</sub><sup>25</sup> 12.33. Crystd from water. Dried at 110°.

Guanylic acid (guanosine-5'-monophosphoric acid) [85-32-5] M 363.2, m 208°(dec),  $pK_2^{25}$ 2.4,  $pK_3^{25}$  6.66 (6.1),  $pK_4^{25}$  9.4. Crystd from water. Dried at 110°.

Harmine [442-51-3] M 212.3, m 261°(dec), pK<sup>20</sup> 7.61. Crystd from MeOH.

Harmine hydrochloride (hydrate) [343-27-1] M 248.7, m 280°(dec). Crystd from water.

Hecogenine acetate [915-35-5] M 472.7, m 265-268°,  $[\alpha]_D^{23}$  -4.5° (c 1, CHCl<sub>3</sub>). Crystd from MeOH.

Heptadecanoic acid (margaric) [506-12-7] M 270.5, m 60-61°, b 227°/100mm,  $pK_{Est} \sim 4.9$ . Crystd from MeOH or pet ether.

1-Heptadecanol [1454-85-9] M 256.5, m 54°. Crystd from acetone.

**Heptafluoro-2-iodopropane** [677-69-0] **M 295.9, b 41°.** Purified by gas chromatography on a triacetin (glyceryl triacetate) column, followed by bulb-to-bulb distn at low temperature. Stored over Cu powder to stabilise it.

*n*-Heptaldehyde [111-71-7] M 114.2, b 40.5°/12mm, 152.8°/760mm, d 0.819,  $n^{25}$  1.4130. Dried with CaSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub> and fractionally distd under reduced pressure. More extensive purification by pptn as the bisulfite compound (formed by adding the aldehyde to saturated aqueous NaHSO<sub>3</sub>) which was filtered off and recrystd from hot H<sub>2</sub>O. The crystals, after being filtered and washed well with H<sub>2</sub>O, were hydrolysed by adding 700mL of aqueous Na<sub>2</sub>CO<sub>3</sub> (12.5% w/w of anhydrous Na<sub>2</sub>CO<sub>3</sub>) per 100g of aldehyde. The aldehyde was then steam distd, separated, dried with CuSO<sub>4</sub> and distd under reduced pressure in a slow stream of nitrogen. [McNesby and Davis J Am Chem Soc 76 2148 1954].

n-Heptaldoxime [629-31-2] M 129.2, m 53-55°. Crystd from 60% aqueous EtOH.

*n*-Heptane [142-18-5] M 100.2, b 98.4°, d 0.684, n 1.38765,  $n^{25}$  1.38512. Passage through a silica gel column greatly reduces the ultraviolet absorption of *n*-heptane. (The silica gel is previously heated to 350° before use.) For more extensive purification, heptane is shaken with successive small portions of conc H<sub>2</sub>SO<sub>4</sub> until the lower (acid) layer remains colourless. The heptane is then washed successively with water, aq 10% Na<sub>2</sub>CO<sub>3</sub>, water (twice), and dried with CaSO<sub>4</sub>, MgSO<sub>4</sub> or CaCl<sub>2</sub>. It is distd from sodium. *n*-Heptane can be distd azeotropically with methanol, then the methanol can be washed out with water and, after drying, the heptane is redistd. Other purification procedures include passage through activated basic alumina, drying with CaH<sub>2</sub>, storage with sodium, and stirring with 0.5N KMnO<sub>4</sub> in 6N H<sub>2</sub>SO<sub>4</sub> for 12h after treatment with conc H<sub>2</sub>SO<sub>4</sub>. Carbonyl-containing impurities have been removed by percolation through a column of impregnated Celite made by dissolving 0.5g of 2,4-dinitrophenylhydrazine in 6mL of 85% H<sub>3</sub>PO<sub>4</sub> by grinding together, then adding 4mL of distilled water and 10g Celite. [Schwartz and Parks Anal Chem 33 1396 1961].

Hept-1-ene [592-76-7] M 98.2, b 93°/771mm, d 0.698, n 1.400. Distd from sodium, then carefully fractionally distd using an 18-in gauze-packed column. Can be purified by azeotropic distn with EtOH. Contained the 2- and 3-isomers as impurities. These can be removed by gas chromatography using a Carbowax column at 70°.

*n*-Heptyl alcohol [111-70-6] M 116.2, b 175.6°, d 0.825, n 1.425. Shaken with successive lots of alkaline KMnO<sub>4</sub> until the colour persisted for 15min, then dried with  $K_2CO_3$  or CaO, and fractionally distd.

*n*-Heptylamine [111-68-2] M 115.2, b 155°, d 0.775, n 1.434, pK<sup>25</sup> 10.66. Dried in contact with KOH pellets for 24h, then decanted and fractionally distd.

*n*-Heptyl bromide [629-04-9] M 179.1, b 70.6°/19mm, 180°/760mm, d 1.140, n 1.45. Shaken with conc H<sub>2</sub>SO<sub>4</sub>, washed with water, dried with K<sub>2</sub>CO<sub>3</sub>, and fractionally distd.

Heptyl- $\beta$ -D-glucopyranoside [78617-12-6] M 278.4, m 74-77°, 76-77°,  $[\alpha]_D^{20}$ -34.2° (c 5, H<sub>2</sub>O). Purified by several recrystns from M<sub>2</sub>CO which is a better solvent than EtOAc. The *acetate* has m 66-68.5°,  $[\alpha]_D^{20}$ -20.5° (c 4, CHCl<sub>3</sub>) [Pigman and Richtmyer J Am Chem Soc 64 369 1942].

Heptyl- $\beta$ -D-1-thioglucopyranoside [85618-20-8] M 294.4, m 98-99°. The tetra-acetyl derivative is purified by silica gel column chromatography and eluted with a \*C<sub>6</sub>H<sub>6</sub>-Me<sub>2</sub>CO (gradient up to 5% of Me<sub>2</sub>CO) and recrystd from *n*-hexane as colourless needles m 72-74° (Erbing and Lindberg Acta Chem Scand

**B30** 611 1976 gave **m** 69-70°). Hydrolysis using an equivalent of base in methanol gave the desired glucoside. This is a non-ionic detergent for reconstituting membrane proteins and has a critical micelle concentration of 30 mM. [Shimamoto et al. J Biochem (Tokyo) 97 1807 1985; Saito and Tsuchiya Chem Pharm Bull Jpn 33 503 1985].

Hesperetin (3',5,7-trihydroxy-4'-methoxyflavanone) [520-33-2] M 302.3, m 227-228°, pK<sub>Est</sub> ~8.5-10.5 (phenolic). Crystd from EtOAc or ethanol. The natural (-) form has  $[\alpha]_D^{20}$  -38° (c 2, EtOH). Note that C2 is chiral.

Hesperidin (hesperetin 7-rhamnoside) [520-26-3] M 610.6, m 258-262°,  $[\alpha]_{546}^{20}$  -82° (c 2, pyridine). Dissolved in dilute aqueous alkali and ppted by adjusting the pH to 6-7.

Hexachlorobenzene [118-74-1] M 284.8, m 230.2-231.0°. Crystd repeatedly from \*benzene. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

Hexachloro-1,3-butadiene [87-68-3] M 260.8. See perchlorobutadiene on p. 323.

1,2,3,4,5,6-Hexachlorocyclohexane  $[\alpha-319-84-6; \gamma-58-89-9]$  M 290.8, m 158° ( $\alpha-$ ), 312° ( $\beta$ -), 112.5° ( $\gamma$ -isomer). Crystd from EtOH. Purified by zone melting. Possible CANCER AGENT, TOXIC.

Hexachlorocyclopentadiene [77-47-4] M 272.8, b 80°/1mm, d 1.702, n<sup>25</sup> 1.5628. Dried with MgSO<sub>4</sub>. Distd under vacuum in nitrogen.

Hexachloroethane [67-72-1] M 236.7, m 187°. Steam distd, then crystd from 95% EtOH. Dried in the dark under vacuum.

Hexacosane [630-01-3] M 366.7, m 56.4°, b 169°/0.05mm, 205°/1mm, 262°/15mm. Distd under vacuum and crystd from diethyl ether.

Hexacosanoic acid (cerotinic acid) [506-46-7] M 396.7, m 86-87°, 88-89°,  $pK_{Est} \sim 4.9$ . Crystd from EtOH, aq EtOH and pet ether+Me<sub>2</sub>CO.

1,14-Hexadecanedioic acid (thaspic acid). [505-54-4] M 286.4, m 126°,  $pK_{Est(1)}$ ~4.5,  $pK_{Est(2)}$ ~5.5. Crystd from EtOH, ethyl acetate or \*C<sub>6</sub>H<sub>6</sub>.

*n*-Hexadecane (Cetane) [544-76-3] M 226.5, m 18.2°, b 105°/0.1mm, d 0.773, n 1.4345,  $n^{25}$  1.4325. Passed through a column of silica gel and distd under vacuum in a column packed with Pyrex helices. Stored over silica gel. Crystd from acetone, or fractionally crystd by partial freezing.

Hexadecanoic acid (palmitic acid) [57-10-3] M 256.4, m 62-63°, b 215°/15mm, pK<sup>25</sup> 6.46 (50% aq EtOH), 5.0 (H<sub>2</sub>O). Purified by slow (overnight) recrystn from hexane. Some samples were also crystd from acetone, EtOH or EtOAc. Crystals were stood in air to lose solvent, or were pumped dry of solvent on a vacuum line. [Iwahashi et al. J Chem Soc, Faraday Trans 1 81 973 1985; pK: White J Am Chem Soc 72 1858 1950].

Hexadecyl 3-hydroxynaphthalene-2-carboxylate [531-84-0] M 412.6, m 73-74°. Recrystd from hot EtOH and sublimed in a vacuum. [Oshima and Hayashi J Soc Chem Ind Jpn 44 821 1941.]

1,5-Hexadiene [592-42-7] M 82.2, b 59.6°, d 0.694, n 1.4039. Distd from NaBH<sub>4</sub>.

Hexaethylbenzene [604-88-6] M 246.3, m 128.7-129.5°. Crystd from \*benzene or \*benzene/EtOH.

Hexafluoroacetone [684-16-2, 34202-69-2 (3 $H_2O$ )] M 166.1, m -129°, (trihydrate m 18-21°), b -28°. Dehydrated by passage of the vapour over  $P_2O_5$ . Ethylene was removed by passing the dried vapour

through a tube containing Pyrex glass wool moistened with conc  $H_2SO_4$ . Further purification was by low temperature distn using Warde-Le Roy stills. Stored in the dark at -78°. [Holmes and Kutschke *Trans Faraday Soc* 58 333 1962].

Hexafluoroacetylacetone (1,1,1,5,5,5-hexafluoro-2,4-pentanedione) [1522-22-1] M 208.1, b 68°/736mm, 70-70.2°/760mm, 68-71°/atm,  $d_4^{20}$  1.490,  $n_D^{20}$  1.333. It forms a dihydrate which has no UV spectrum compared with  $\lambda$ max (CHCl<sub>3</sub>) 273nm ( $\varepsilon$  7,800) for the anhydrous ketone. The dihydrate dec at ~90°. The hydrate (10g) plus anhyd CaSO<sub>4</sub> (Drierite, 30g) are heated and distd; the distillate is treated with more CaSO<sub>4</sub> and redist. When the distillate is treated with aqueous NaOH and heated, the dihydrate crystallises on cooling. The Cu complex has m 135° (after sublimation). [Gilman et al. J Am Chem Soc 78 2790 1956; Belford et al. J Inorg Nucl Chem 2 11 1956].

**Hexafluorobenzene** [392-56-3] **M 186.1, m 5.1°, b 79-80°, d 1.61, n 1.378.** Main impurities are incompletely fluorinated benzenes. Purified by standing in contact with oleum for 4h at room temperature, repeating until the oleum does not become coloured. Washed several times with water, then dried with  $P_2O_5$ . Final purification was by repeated fractional crystn.

**Hexafluoroethane** [76-16-4] **M 138.0, b -79°.** Purified for pyrolysis studies by passage through a copper vessel containing CoF<sub>3</sub> at *ca* 270°, and held for 3h in a bottle with a heated (1300°) platinum wire. It was then fractionally distd. [Steunenberg and Cady *J Am Chem Soc* 74 4165 1962.]

1,1,1,3,3,3-Hexafluoropropan-2-ol [920-66-1] M 168.1, b 57-58°/760mm, d 1.4563, n<sup>22</sup> 1.2750. Distd from 3A molecular sieves, retaining the middle fraction.

Hexahydro-1*H*-azepine (hexamethyleneimine, Azepane) [111-49-9] M 99.2, b 70-72°/30mm, 135-138°/atm, d 0.879, n 1.466,  $pK^{25}$  11.10 ( $pK^{\circ}$  9.71,  $pK^{75}$  9.71). Purified by dissolving in Et<sub>2</sub>O and adding ethanolic HCl until all the base separates as the white *hydrochloride*, filter, wash with Et<sub>2</sub>O and dry (m 236°). The salt is dissolved in the minimum vol of H<sub>2</sub>O and basified to pH ~ 14 with 10N KOH. The soln is extracted with Et<sub>2</sub>O, the extract is dried over KOH, evapd and distd. The base is a **FLAMMABLE** and **TOXIC** liquid, and best kept as the salt. The *nitrate* has m 120-123°, *Picrate* has m 145-147°, and the *Tosylate* has m 76.5° (ligroin). [Müller and Sauerwald Monatsh Chem 48 727 1027; Hjelt and Agback Acta Chem Scand 18 194 1964].

Hexahydromandelic acid [R-(-)-53585-93-6; S-(+)-61475-31-8] M 158.2, m 127-129°, 128-129°, 129.7°,  $[\alpha]_d^{20}(-)$  and (+) 25.5° (c 1, AcOH) and  $[\alpha]_d^{20}(-)$  and (+) 13.6° (c 7.6, EtOH). For hexagonal clusters by recrystallisation from CCl<sub>4</sub> or Et<sub>2</sub>O. [Wood and ComLey J Chem Soc 2638 1924; Lettré et al. Chem Ber 69 1594 1936]. The racemate has m 137.2-137.6° (134-135°) [Smith et al. J Am Chem Soc 71 3772 1949].

**Hexamethylbenzene** [87-85-4] **M 162.3, m 165-165.5**°. Sublimed, then crystd from abs EtOH, \*benzene, EtOH/\*benzene or EtOH/cyclohexane. Also purified by zone melting. Dried under vac over P<sub>2</sub>O<sub>5</sub>.

Hexamethyl(Dewar)benzene [7641-77-2] M 162.3, m 7°, b 60°/20mm, d 0.803, n 1.4480. Purified by passage through alumina [Traylor and Miksztal J Am Chem Soc 109 2770 1987].

Hexamethylenediamine [124-09-4] M 116.2, m 42°, b 46-47°/1mm, 84.9°/9 mm, 100°/20mm, 204-205°/760mm,  $pK_1^{25}$ 10.24,  $pK_2^{25}$ 11.02. Crystd in a stream of nitrogen. Sublimed in a vacuum.

Hexamethylenediamine dihydrochloride [6055-52-3] M 189.2, m 248°. Crystd from water or EtOH.

Hexamethylene glycol (1,6-hexanediol) [629-11-8] M 118.2, m 41.6°, 43-45°, b 134°/10mm, 250°, n 1.458. Fractionally crystd from its melt or from water. Distils in vacuo.

Hexamethylenetetramine (Urotropine, hexamine, HMTA) [100-97-0] M 140.1, m 280° (subln), 290-292° (sealed tube, CARE), d 1.331,  $pK^{25}$  4.85 (6.30). It is soluble in H<sub>2</sub>O (67%), CHCl<sub>3</sub> (10%), EtOH (8%) and Et<sub>2</sub>O (0.3%), and a 0.2M soln has a pH of 8.4. Dissolve in hot abs EtOH (reflux, Norite), filter using a heated funnel, cool at room temp first then in ice. Wash crysts with cold Et<sub>2</sub>O, dry in air or under a vacuum. A further crop can be obtained by adding Et<sub>2</sub>O to the filtrate. It sublimes above 260° without melting. The *picrate* has m 179° (dec). [pK 4.85:Reilley and Schmid Anal Chem 30 947 1958; pK 6.30: Pummerer and Hofmann Chem Ber 56 1255 1923.]

*n*-Hexane [110-54-3] M 86.2, b 68.7°, d 0.660, n 1.37486,  $n^{25}$  1.37226. Purification as for *n*-heptane. Modifications include the use of chlorosulfonic acid or 35% fuming H<sub>2</sub>SO<sub>4</sub> instead of conc H<sub>2</sub>SO<sub>4</sub> in washing the alkane, and final drying and distn from sodium hydride. Unsatd compounds can be removed by shaking the hexane with nitrating acid (58% H<sub>2</sub>SO<sub>4</sub>, 25% conc HNO<sub>3</sub>, 17% water, or 50% HNO<sub>3</sub>, 50% H<sub>2</sub>SO<sub>4</sub>), then washing the hydrocarbon layer with conc H<sub>2</sub>SO<sub>4</sub>, followed by H<sub>2</sub>O, drying, and distg over sodium or *n*-butyl lithium. Also purified by distn under nitrogen from sodium benzophenone ketyl solubilised with tetraglyme. Also purified by passage through a silica gel column followed by distn [Kajii et al. *J Phys Chem* 91 2791 1987]. FLAMMABLE liquid and possible nerve toxin.

Rapid purification: Distil, discarding the first forerun and stored over 4A molecular sieves.

1,2-Hexanediol [6920-22-5] M 118.2, b 214-215, d 0.951, n 1.442. Fractionally distd.

1-Hexene [592-41-6] M 84.2, b 63°, d 0.674, n 1.388. Purified by stirring over Na/K alloy for at least 6h, then fractionally distd from sodium under nitrogen.

cis-2-Hexene [7688-21-3] M 84.2, b 68-70°, d 0.699, n 1.399. Purification as for 1-hexene above.

trans-2-Hexene [4050-45-7] M 84.2, b 65-67°, n 1.390. Purifn as for 1-hexene above.

trans-3-Hexene [13269-52-8] M 84.2, b 67-69°, d 0.678, n 1.393. Purifn as for 1-hexene above.

meso-Hexoestrol [84-16-2] M 270.4, m 185-188°. Crystd from \*benzene or aqueous EtOH.

*n*-Hexyl alcohol (1-hexanol) [111-27-3] M 102.2, b  $157.5^{\circ}$ , d 0.818,  $n^{15}$  1.4198,  $n^{25}$  1.4158. Commercial material usually contains other alcohols which are difficult to remove. A suitable method is to esterify with hydroxybenzoic acid, recrystallise the ester and saponify. [Olivier *Recl Trav Chim, Pays-Bas* 55 1027 1936.] Drying agents include K<sub>2</sub>CO<sub>3</sub> and CaSO<sub>4</sub>, followed by filtration and distn. (Some decomposition to the olefin occurred when Al amalgam was used as drying agent at room temperature, even though the amalgam was removed prior to distn.) If the alcohol is required anhydrous, the redistd material can be refluxed with the appropriate alkyl phthalate or succinate, as described under *Ethanol*.

*n*-Hexylamine [111-26-2] M 101.2, b 131°, d 0.765, n 1.419,  $pK^{25}$  10.64. Dried with, and fractionally distd from, KOH or CaH<sub>2</sub>.

*n*-Hexyl bromide [111-25-1] M 165.1, b 87-88°/90mm,  $155^{\circ}/743$ mm, d 1.176, n 1.448. Shaken with H<sub>2</sub>SO<sub>4</sub>, washed with water, dried with K<sub>2</sub>CO<sub>3</sub> and fractionally distd.

*n*-Hexyl methacrylate [142-09-6] M 154.2, b 65-66°/4mm,88-88.5°/14mm, d 0.8849, n 1.4320. Purified as for *methyl methacrylate*. [IR: Hughes and Walton J Am Chem Soc 79 3985 1957.]

Hexyltrimethylammonium bromide [2650-53-5] M 224.3, m 186°. Recrystd from acetone. Extremely hygroscopic salt. [McDowell and Kraus J Am Chem Soc 73 2170 1951.]

**1-Hexyne** [693-02-7] **M 82.2, b 12.5°/75mm, 71°/760mm, d 0.7156, n 1.3989.** Distd from NaBH<sub>4</sub> to remove peroxides. Stood with sodium for 24h, then fractionally distd under reduced pressure. Also dried by repeated vac transfer into freshly activated 4A molecular sieves, followed by vacuum transfer into Na/K alloy and stirring for 1h before fractionally distilling.

2-Hexyne [764-35-2] M 82.2, b 83.8°/760mm, d 0.73146, n 1.41382. Purification as for 1-hexyne above.

**3-Hexyne** [928-49-4] **M 82.2, b 81°/760mm, d 0.7231, n 1.4115.** Purification as for 1-hexyne above.

Histamine [51-45-6] M 111.2, m 86° (sealed tube), b 167°/0.8mm, 209°/18mm,  $pK_1^{25}$  6.02,  $pK_2^{25}$  9.70. Crystd from \*benzene or chloroform.

Histamine dihydrochloride [56-92-8] M 184.1, m 249-252° (244-245°). Crystd from aq EtOH.

S-Histidine [71-00-1] M 155.2, m 287°(dec),  $[\alpha]_D^{25}$  -39.7° (c 1, H<sub>2</sub>O), +13.0° (6M HCl), pK<sub>1</sub><sup>25</sup> 1.96, pK<sub>2</sub><sup>25</sup> 6.12, pK<sub>3</sub><sup>25</sup> 9.17. Likely impurity is arginine. Adsorbed from aqueous soln on to Dowex 50-H<sup>+</sup> ion-exchange resin, washed with 1.5M HCl (to remove other amino acids), then eluted with 4M HCl as the dihydrochloride. Histidine is also purified as the dihydrochloride which is finally dissolved in water, the pH adjusted to 7.0, and the free zwitterionic base crystallises out on addition of EtOH. Sol in H<sub>2</sub>O is 4.2% at 25°.

S-Histidine dihydrochloride [1007-42-7] M 242.1, m 245°,  $[\alpha]_D^{20} + 47.5°$  (c 2, H<sub>2</sub>O). Crystd from water or aqueous EtOH, and washed with acetone, then diethyl ether. Converted to the histidine di-(3,4-dichlorobenzenesulfonate) salt by dissolving 3,4-dichlorobenzenesulfonic acid (1.5g/10mL) in the aqueous histidine soln with warming, and then the soln is cooled in ice. The resulting crystals (m 280° dec) can be recrystd from 5% aqueous 3,4-dichlorobenzenesulfonic acid, then dried over CaCl<sub>2</sub> under vacuum, and washed with diethyl ether to remove excess reagent. The dihydrochloride can be regenerated by passing the soln through a Dowex-1 (Cl<sup>-</sup> form) ion-exchange column. The solid is obtained by evapn of the soln on a steam bath or better in a vacuum. [Greenstein and Winitz, The Amino Acids Vol 3 p. 1976 1961.]

S-Histidine monohydrochloride (H<sub>2</sub>O) [5934-29-2 (H<sub>2</sub>O); 7048-02-4] M 209.6, m 80° monohydrate, 254°(dec, anhyd),  $[\alpha]_{D}^{25}$  +13.0° (6M HCl). Crystd from aqueous EtOH.

dl-Homocysteine [6027-13-0] M 135.2, pK<sub>2</sub><sup>25</sup>8.70, pK<sub>3</sub><sup>30</sup>10.46. Crystd from aqueous EtOH.

Homocystine [462-10-2] M 268.4, m 260-265°(dec),  $pK_1^{25}$  1.59,  $pK_2^{25}$  2.54,  $pK_3^{25}$  8.52,  $pK_4^{25}$  9.44. Crystd from water.

Homophthalic acid [89-51-0] M 180.2, m 182-183°, 189-190°, (depends on heating rate)  $pK_{Est(1)} \sim 3.5$ ,  $pK_{Est(2)} \sim 4.3$ . Crystd from boiling water (25mL/g). Dried at 100°.

Homopiperazine (1,4-diazepane) [505-66-8] M 100.2, m 38-40°, 43°, b 60°/10 mm, 92°/50mm, 169°/atm,  $pK_1^{20}$  6.70,  $pK_2^{20}$  10.41. Purified by fractionation through a column of 10 theoretical plates with a reflux ratio of 3:1. It boiled at 169° and the cool distillate crystallises in plates m 43°. [Poppelsdorf and Myerly J Org Chem 26 131 1961.] Its pKa values are 6.89 and 10.65 at 40°, and 6.28 and 9.86 at 40° [Pagano et al. J Phys Chem 65 1062 1961]. The 1,4-bis(4-bromobenzoyl derivative has m 194-198° (from EtOH); the hydrochloride has m 270-290° (from EtOH) and the picrate has m 265° (dec) [Lloyd et al. J Chem Soc (C) 780 1966].

L-Homoserine (2-amino-4-hydroxybutyric acid) [672-15-1] M 119.1, m 203°,  $[\alpha]_D^{26}$  +18.3° (in 2M HCl), pK<sub>Est(1)</sub> ~2.1, pK<sub>Est(2)</sub>~9.3. Likely impurities are N-chloroacetyl-L-homoserine, N-chloroacetyl-D-homoserine, L-homoserine, homoserine lactone, homoserine anhydride (formed in strong solns of homoserine if slightly acidic). Cyclises to the lactone in strongly acidic soln. Crystd from water by adding 9 volumes of EtOH.

Homoveratronitrile (3,4-dimethoxybenzylnitrile) [93-17-4] M 177.2, m 62-64°, 68°, b 184°/20mm, 195-196°/2mm, 208°/atm. Its solubility is 10% in MeOH. and has been recrystd from

EtOH or MeOH. Purified by distillation followed by recrystn. [Niederl and Ziering J Am Chem Soc 64 885 1952; Julian and Sturgis J Am Chem Soc 57 1126 1935.]

Homoveratrylamine (2-[3,4-dimethoxyphenyl]ethylamine) [120-20-7] M 181.2, b 99.3-101.3°/0.5mm, 168-170°/15mm,  $d_4^{20}$  1.091,  $n_D^{20}$  1.5460, pK<sub>Est</sub> ~9.8. Purified by fractionation through an efficient column in an inert atmosphere as it is a relatively strong base. [Horner and Sturm Justus Liebigs Ann Chem 608 12819 1957; Jung et al. J Am Chem Soc 75 4664 1953.] The hydrochloride has m 152°, 154°, 156° (from EtOH, Me<sub>2</sub>CO or EtOH/Et<sub>2</sub>O) and the picrate has m 165-167° dec, and the 4-nitrobenzoyl derivative has m 147° [Buck J Am Chem Soc 55 2593 1933].

Hordenine {4-[(2-dimethylamino)ethyl]phenol} [539-15-1] M 165.2, m 117-118°,  $pK^{25}$  9.46 (OH). Crystd from EtOH or water.

Humulon [26472-41-3] M 362.5, m 65-66.5°, [α]<sub>D</sub><sup>26</sup> -212° (95% EtOH). Crystd from Et<sub>2</sub>O.

Hyamine 1622 [(diisobutylphenoxyethoxyethyl)dimethylbenzylammonium chloride, benzethionium chloride] [121-54-0] M 448.1, m 164-166° (sinters at 120°, monohydrate). Crystd from boiling acetone after filtering, or from CHCl<sub>3</sub>-pet ether. The ppte was filtered off, washed with diethyl ether and dried for 24h in a vacuum desiccator.

Hydantoin (2,4-dihydroxyimidazole) [461-72-3] M 100.1, m 216°, 220°, pK<sup>25</sup> 9.15. Crystd from MeOH. The *diacetate* has m 104-105°.

Hydrazine N, N'-dicarboxylic acid diamide [110-21-4] M 116.1, m 248°. Crystd from water and dried in vac over  $P_2O_5$ .

4-Hydrazinobenzoic acid [619-67-0] M 152.2, m 217° (dec), pK<sup>25</sup> 4.13. Crystd from water.

1-Hydrazinophthalazine hydrochloride (hydralazine hydrochloride) [304-20-1] M 196.6, m 172-173°, pK<sup>20</sup> 6.57. Crystd from MeOH.

2-Hydrazinopyridine [4930-98-7] M 109.1, m 41-44°, 46-47°, 49-50°, b 105°/0.5mm, 128-135°/13mm. Purified by distn and by recrystn from  $Et_2O$ -hexane. [Kauffmann et al. Justus Liebigs Ann Chem 656 103 1962, Potts and Burton J Org Chem 31 251 1966.] The mono-hydrochloride has m 183° (dec) from aq HCl and the di-hydrochloride has m 214-215°.

Hydrazobenzene [122-66-7] M 184.2. See 1,1-diphenylhydrazine on p. 225.

Hydrobenzamide [1-phenyl-N, N'-bis(phenylmethylene)-methanediamine] [92-29-5] M 298.4, m 101-102°, 107-108°. Crystd from absolute EtOH or cyclohexane/\*benzene. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>. [Pirrone Gazz Chim Ital 67 534 1937.]

dl-Hydrobenzoin [492-70-6] M 214.3, m 120°. Crystd from diethyl ether/pet ether.

meso-Hydrobenzoin [579-43-1] M 214.3, m 139°. Crystd from EtOH or water.

Hydroquinone (1,4-dihydroxybenzene, quinol) [123-31-9] M 110.1, m 175.4, 176.6°,  $pK_1^{20}$ 9.91,  $p K_2^{20}$  11.56. Crystd from acetone, \*benzene, EtOH, EtOH/\*benzene, water or acetonitrile (25g in 30mL), preferably under nitrogen. Dried under vacuum. [Wolfenden et al. J Am Chem Soc 109 463 1987.]

4'-Hydroxyacetanilide [103-90-2] See 4-acetamidophenol on p. 83.

*p*-Hydroxyacetophenone [99-93-4] M 136.2, m 109°,  $pK^{25}$  8.01. Crystd from diethyl ether, aqueous EtOH or \*benzene/pet ether.

4-Hydroxyacridine [18123-20-1] M 195.2, m 116.5° pK<sub>1</sub><sup>15</sup> 5.28, pK<sub>2</sub><sup>15</sup> 9.75. Crystd from EtOH.

5-Hydroxyanthranilic acid [548-93-6] M 153.1, m >240°(dec),  $\lambda_{max}$  298nm, log  $\varepsilon$  3000 (0.1M HCl), pK<sub>1</sub><sup>20</sup> 2.7, pK<sub>2</sub><sup>20</sup> 5.37, pK<sub>3</sub><sup>20</sup> 10.12. Crystd from water. Sublimes below its melting point in a vacuum.

*erythro*-3-Hydroxy-*RS*-aspartic acid [6532-76-9] M 149.1,  $pK_1^{25}$  1.91,  $pK_2^{25}$  3.51,  $pK_3^{25}$  9.11. Likely impurities are 3-chloromalic acid, ammonium chloride, *threo*-3-hydroxyaspartic acid. Crystd from water.

*m*-Hydroxybenzaldehyde [100-83-4] M 122.1, m 108° pK<sub>1</sub><sup>25</sup> 8.98, pK<sub>2</sub><sup>25</sup> 15.81. Crystd from water.

*p*-Hydroxybenzaldehyde [123-08-0] M 122.1, m 115-116°,  $pK^{25}$  7.61. Crystd from water (containing some H<sub>2</sub>SO<sub>4</sub>). Dried over P<sub>2</sub>O<sub>5</sub> under vacuum.

*m*-Hydroxybenzoic acid [99-06-9] M 138.1, m 200.8°,  $pK_1^{25}$  4.08,  $pK_2^{25}$  9.98. Crystd from absolute EtOH.

*p*-Hydroxybenzoic acid [99-96-7] M 138.1, m 213-214°, pK<sub>1</sub><sup>25</sup> 4.50, pK<sub>2</sub><sup>25</sup> 9.11. Crystd from water.

p-Hydroxybenzonitrile [767-00-0] M 119.1, m 113-114°. See p-cyanophenol on p. 176.

**4-Hydroxybenzophenone** [1137-42-4] **M 198.2, m 133.4-133.8°, pK<sup>25</sup> 7.95.** See *p*-benzoylphenol on p. 126.

**2-Hydroxybenzothiazole** [934-34-9] **M 183.1, m 117-118°** Crystd from aqueous EtOH or water. [Dryland and Sheppard J Chem Soc Perkin Trans 1 125 1986.]

1-Hydroxybenzotriazole hydrate (HOBt) [2592-95-2] M 135.1, m 159-160°. Crystd from aqueous EtOH or water. [Dryland and Sheppard J Chem Soc Perkin Trans 1 125 1986.] § A polystyrene supported version is available.

2-Hydroxybenzyl alcohol [90-01-7] M 124.1, m 87°, pK<sup>25</sup> 9.84. Crystd from water or \*benzene.

3-Hydroxybenzyl alcohol [620-24-6] M 124.1, m 71°, pK<sub>Est</sub> ~9.8. Crystd from \*benzene.

4-Hydroxybenzyl alcohol [623-05-2] M 124.1, m 114-115°, pK<sup>25</sup> 9.73. Crystd from water.

**2-Hydroxybiphenyl** [90-43-7] **M 170.2, m 56°, b 145°/14mm, 275°/760mm, pK<sup>20</sup> 10.01.** Crystd from pet ether.

**4-Hydroxybiphenyl** (4-phenylphenol) [92-69-3] M 170.2, m 164-165°, b 305-308°/760mm, pK<sup>23</sup> 9.55. Crystd from aqueous EtOH, aq EtOH, \*C<sub>6</sub>H<sub>6</sub>, and vac dried over CaCl<sub>2</sub> [Buchanan et al. J Am Chem Soc 108 7703 1986].

**3-Hydroxy-2-butanone (acetoin)** [513-86-0] **M 88.1, b 144-145°, [m 100-105° dimer].** Washed with EtOH until colourless, then with diethyl ether or acetone to remove biacetyl. Air dried by suction and further dried in a vacuum desiccator.

(±)- $\alpha$ -Hydroxy- $\gamma$ -butyrolactone [19444-84-9] M 102.1, b 84°/0.2mm, 133°/10mm,  $d_4^{20}$  1.310,  $n_D^{20}$  1.4656. It has been purified by repeated fractionation, forms a colourless liquid. It has to be distd at high vacuum otherwise it will dehydrate. The *acetoxy* derivative has b 94°/0.2mm, [NMR: Daremon and Rambaud *Bull Soc Chim Fr* 294 1971; Schmitz et al. *Chem Ber* 108 1010 1975.]

4-Hydroxycinnamic acid (*p*-coumaric acid) [501-98-4] M 164.2, m 210-213°, 214-215°, 215°  $pK_1^{25}$  4.64,  $pK_2^{25}$  9.45. Crystd from H<sub>2</sub>O (charcoal). Needles from conc aqueous solutions as the *anhydrous acid*, but from hot dilute solutions the *monohydrate acid* separates on slow cooling. The acid (33g) has been recrystd from 2.5L of H<sub>2</sub>O (1.5g charcoal) yielding 28.4g of recrystd acid, m 207°. It is insol in \*C<sub>6</sub>H<sub>6</sub> or pet ether. The UV in 95% EtOH has  $\lambda_{max}$  223 and 286nm ( $\varepsilon$  14,450 and 19000 M<sup>-1</sup>cm<sup>-1</sup>). [UV Wheeler and Covarrubias J Org Chem 28 2015 1963; Corti Helv Chim Acta 32 681 1949.]

4-Hydroxycoumarin [1076-38-6] M 162.1, m 206°, pK<sub>Est</sub> ~9.0. Crystd from water and dried in a vacuum desiccator over Sicapent.

**3-(4-Hydroxy-3,5-dimethoxyphenyl)acrylic acid** [530-59-6] M 234.1, m 204-205°(dec), pK<sub>Est(1)</sub>~4.6, pK<sub>Est(2)</sub>~9.3. Crystd from water.

4-Hydroxydiphenylamine [122-37-2] M 185.2, m 72-73°, pK<sub>Est</sub> ~10.0. Crystd from chlorobenzene/pet ether.

12-Hydroxydodecanoic acid [505-95-3] M 216.3, m 86-88°, pK<sub>Est</sub> ~4.8. Crystd from toluene [Sadowik et al. J Am Chem Soc 108 7789 1986].

**2-Hydroxy-4**-(*n*-dodecyloxy)benzophenone [2985-59-3] M 382.5, m 50-52°,  $pK_{Est} \sim 7.1$ . Recryst from *n*-hexane and then 10% (v/v) EtOH in acetonitrile [Valenty et al. J Am Chem Soc 106 6155 1984].

*N*-[2-Hydroxyethyl]ethylenediamine [2-(2-aminoethylamino)ethanol] [111-41-1] M 104.1, b 91.2°/5mm, 238-240°/752mm, n 1.485, d 1.030,  $pK_1^{20}$  3.75,  $pK_2^{20}$  9.15. Distilled twice through a Vigreux column. Redistilled from solid NaOH, then from CaH<sub>2</sub>. Alternatively, it can be converted to the dihydrochloride and recrystallised from water. It is then dried, mixed with excess of solid NaOH and the free base distilled from the mixture. It is finally redistilled from CaH<sub>2</sub>. [Drinkard, Bauer and Bailar *J Am Chem Soc* 82 2992 1960.]

*N*-[2-Hydroxyethyl]ethylenediaminetriacetic acid (HEDTA) [150-39-0] M 278.3, m 212-214°(dec),  $pK_1^{20}2.51$ ,  $pK_2^{20}5.31$ ,  $pK_3^{20}9.86$ . Crystd from warm H<sub>2</sub>O, after filtering, by addition of 95% EtOH and allowing to cool. The crystals, collected on a sintered-glass funnel, were washed three times with cold absolute EtOH, then again crystd from H<sub>2</sub>O. After leaching with cold H<sub>2</sub>O, the crystals were dried at 100° under vacuum. [Spedding, Powell and Wheelwright J Am Chem Soc 78 34 1956.]

*N*-Hydroxyethyliminodiacetic acid (HIMDA) [93-62-9] M 177.2, m 181°(dec),  $pK_1^{25}2.16$ ,  $pK_2^{25}8.72$ ,  $pK_3^{25}13.7$  (OH). Crystd from water.

2-Hydroxyethylimino-tris(hydroxymethyl)methane (MONO-TRIS) [7343-51-3] M 165.2, m 91°, pK<sub>Est</sub> ~9.8. Crystd twice from EtOH. Dried under vacuum at 25°.

**2-Hydroxyethyl methacrylate** [868-77-9] M 130.1, b 67°/3.5mm, d 1.071, n 1.452. Dissolved in water and extracted with *n*-heptane to remove ethylene glycol dimethacrylate (checked by gas-liquid chromatography and by NMR) and distilled twice under reduced pressure [Strop, Mikes and Kalal J Phys Chem 80 694 1976].

N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES) [7365-45-9] M 238.3, pK<sup>20</sup> 7.55. Crystd from hot EtOH and water.

**3-Hydroxyflavone** [577-85-5] **M 238.2, m 169-170°, 171-172°.** Recrystd from MeOH, EtOH or hexane. Also purified by repeated sublimation under high vacuum, and dried by high vacuum pumping for at least one hour [Bruker and Kelly J Phys Chem **91** 2856 1987].

**B-Hydroxyglutamic acid** [533-62-0] **M 163.1, m 100°(dec), pK\_1^{25} 2.27, pK\_2^{25} 4.29, pK\_3^{25} 9.66. Crystd from water.** 

4-Hydroxyindane [1641-41-1] M 134.2, m 49-50°, b 120°/12mm, pK<sup>25</sup> 10.32. Crystd from pet ether. Acetyl deriv has m 30-32° (from EtOH), b 127°/14mm. [Dallacker et al. Chem Ber 105 2568 1972.]

5-Hydroxyindane [1470-94-6] M 134.2, m 55°, b 255°/760mm, pK<sub>Est</sub> ~10.4. Crystd from pet ether.

5-Hydroxy-L-lysine monohydrochloride [32685-69-1] M 198.7,  $[\alpha]_D^{25}$  +17.8° (6M HCl),  $pK_2^{25}$ 8.85,  $pK_3^{25}$  9.83. Likely impurities are 5-allo-hydroxy-(D and L)-lysine, histidine, lysine, ornithine. Crystd from water by adding 2-9 volumes of EtOH stepwise.

4-Hydroxy-3-methoxyacetophenone [498-02-2] M 166.2, m 115°, pK<sub>Est</sub> ~7.9. Crystd from water, or EtOH/pet ether.

**4-Hydroxy-3-methoxycinnamic acid (ferulic acid)** [1135-24-6] **M 194.2, m 174<sup>o</sup>, pK\_1^{25} 4.58,**  $pK_2^{25}$  9.39. Crystd from H<sub>2</sub>O.

**1-Hydroxymethyladamantane** [770-71-8] **M 166.3, m 115°.** Dissolve in  $Et_2O$ , wash with aqueous 0.1N NaOH and  $H_2O$ , dry over CaCl<sub>2</sub>, evaporate and recryst residue from aqueous MeOH. [*Chem Ber* **92** 1629 1959.]

17β-Hydroxy-17α-methyl-3-androsterone (Mestanolone) [521-11-9] M 304.5°, m 192-193°. Crystd from ethyl acetate.

**4-Hydroxy-2-methylazobenzene** [1435-88-7] **M 212.2, m 100-101°, pK<sub>Est</sub> ~9.5.** Crystd from hexane.

4-Hydroxy-3-methylazobenzene [621-66-9] M 212.2, m 125-126°. Crystd from hexane.

**3-Hydroxy-4-methylbenzaldehyde** [57295-30-4] M 136.1, m 116-117°, b 179°/15mm, pK<sub>Est</sub> ~10.2. Crystd from water.

*dl-2-Hydroxy-2-methylbutyric acid [3739-30-8]* M 118.1, m 72-73°, pK<sup>25</sup> 3.73. Crystd from \*benzene, and sublimed at 90°.

*dl*-2-Hydroxy-3-methylbutyric (α-hydroxyisovaleric) acid [600-37-3] M 118.1, m 86°, pK<sub>Est</sub> ~3.9. Crystd from ether/pentane.

**R**-γ-Hydroxymethyl-γ-butyrolactone [52813-63-5] M 116.1, b 101-102°/0.048mm,  $d_4^{20}$ 1.2238,  $n_D^{20}$  1.471,  $[\alpha]_{546}^{20}$  -38°,  $[\alpha]_D^{20}$  -33° (c 3, EtOH),  $[\alpha]_D^{30}$  -53.5° (c 3, EtOH). Purified by column chromatography in Silica gel 60 (Merck 70-230 mesh) and eluting with 7% EtOH-73% CHCl<sub>3</sub>. IR (film): 3400 (OH), 1765 (C=O) and 1180 (COC) cm<sup>-1</sup>. [Eguchi and Kakuta *Bull Chem Soc Jpn* 47 1704 1974; IR and NMR: Ravid et al. *Tetrahedron* 34 1449 1978.]

7-Hydroxy-4-methylcoumarin (4-methylumbelliferone) [90-33-5] M 176.2, m 185-186°, pK<sub>Est</sub>~10.0. Crystd from absolute EtOH. (See also entry on p. 548 in Chapter 6.)

**2-Hydroxymethyl-12-crown-4** [75507-26-5] **M 206.2**,  $d_4^{20}$  **1.186**,  $n_D^{20}$  **1.480**. Purified by chromatography on Al<sub>2</sub>O<sub>3</sub> with EtOAc as eluent to give a hygroscopic colourless oil with IR 3418 (OH) and 1103 (COC) cm<sup>-1</sup>, NMR  $\delta$  3.70 (s). [Pugia et al. J Org Chem **52** 2617 1987.]

 $S - (-) - 5 - Hydroxymethyl - 2(5H) - furanone [78508-96-0] M 114.1, 39-42°, 40-44°, b 130°/0.3mm, <math>[\alpha]_{546}^{20} - 180°, [\alpha]_D^{20} - 148°$  (c 1.4, H<sub>2</sub>O). It has been purified by chromatography on

Silica gel using hexane-EtOAc (1:1) to give a colourless oil which was distd using a Kügelrohr apparatus and the distillate crystallises on cooling. It has  $R_F 0.51$  on Whatman No 1 paper using pentan-1-ol and 85% formic acid (1:1) and developing with ammoniacal AgNO<sub>3</sub>. [Boll Acta Chem Scand 22 3245 1968; NMR: Oppolzer et al. Helv Chim Acta 68 2100 1985.]

5-(Hydroxymethyl)furfural [67-47-0] M 126.1, m 33.5°, b 114-116°/1mm. Crystd from diethyl ether/pet ether.

3-Hydroxy-3-methylglutaric acid (Meglutol) [503-49-1] M 162.1, m 99-102°, 108-109°, 100°,  $pK_{Est(1)} \sim 4.0$ ,  $pK_{Est(2)} \sim 5.0$ . Recrystd from diethyl ether/hexane and dried under vac at 60° for 1h.

*dl*-3-Hydroxy-N-methylmorphinan [297-90-5] M 257.4, m 251-253°. Crystd from anisole + aqueous EtOH.

6-Hydroxy-2-methyl-1,4-naphthaquinone [633-71-6] M 188.2, pK<sub>Est</sub> ~10.0. Crystd from aqueous EtOH. Sublimes on heating.

4-Hydroxy-4-methyl-2-pentanone [123-42-2] M 116.2, b 166°, d 0.932, n 1.4235, n<sup>25</sup> 1.4213. Loses water when heated. Can be dried with CaSO<sub>4</sub>, then fractionally distd under reduced pressure.

17α-Hydroxy-6α-methylprogesterone (Medroxyprogesterone) [520-85-4] M 344.5, m 220°,  $[\alpha]_D^{25}$  +75°. Crystd from chloroform.

2-Hydroxy-2-methylpropionic acid ( $\alpha$ -hydroxyisobutyric acid, 2-methyllactic acid)) [594-61-6] M 104.1, m 79°, b 114°/12mm, 212°/760mm, pK<sup>25</sup> 3.78. Distd in steam, crystd from diethyl ether or \*benzene, sublimed at 50° and dried under vacuum.

8-Hydroxy-2-methylquinoline [826-81-3] M 159.2, m 74-75°, b 266-267°, pK<sub>1</sub><sup>25</sup> 5.61, pK<sub>2</sub><sup>25</sup> 10.16. Crystd from EtOH or aqueous EtOH.

2-Hydroxy-1-naphthaldehyde [708-06-5] M 172.2, m 82°, b 192°/27mm, pK<sub>Est</sub> ~7.8. Crystd from EtOH (1.5mL/g), ethyl acetate or water.

**2-Hydroxy-1-naphthaleneacetic acid** [10441-45-9] **M 202.2, pK\_{Est(1)} \sim 4.2, pK\_{Est(2)} \sim 8.3.** Treated with activated charcoal and crystd from EtOH/water (1:9, v/v). Dried under vacuum, over silica gel, in the dark. Stored in the dark at -20° [Gafni, Modlin and Brand J Phys Chem 80 898 1976]. Forms a lactone (**m** 107°) readily.

6-Hydroxy-2-naphthalenepropionic acid [553-39-9] M 216.2, m 180-181°, pK<sub>Est(1)</sub> ~4.6, pK<sub>Est(2)</sub>~9.0 Crystd from aqueous EtOH or aqueous MeOH.

**3-Hydroxy-2-naphthalide** [92-77-3] **M 263.3, m 248.0-248.5°, CI 37505.** Crystd from xylene [Schnopper, Broussard and La Forgia Anal Chem **31** 1542 1959].

3-Hydroxy-2-naphtho-4'-chloro-o-toluidide [92-76-2] M 311.8, m 243.5-244.5°. Crystd from xylene [Schnopper, Broussard and La Forgia Anal Chem 31 1542 1959].

**3-Hydroxy-2-naphthoic-1'-naphthylamide** [123-68-3] **M 314.3, m 217-.5-218.0°.** Crystd from xylene [Schnopper, Broussard and La Forgia Anal Chem **31** 1542 1959].

**3-Hydroxy-2-naphthoic-2'-naphthylamide** [136-64-8] M 305.3, m 243.5-244.5°, and other naphthol AS derivatives. Crystd from xylene [Schnopper, Broussard and La Forgia Anal Chem 31 1542 1959].

**2-Hydroxy-1,4-naphthaquinone** [83-72-7] **M 174.2, m 192°(dec), pK\_1^{25}-5.6 (C=O protonation), pK\_2^{25}4.00 (phenolic OH). Crystd from \*benzene.** 

**5-Hydroxy-1,4-naphthaquinone** (Juglone) [481-39-0] M 174.2, m 155°, 164-165°, pK 8.7. Crystd from \*benzene/pet ether or pet ether.

**6-Hydroxy-2-naphthyl disulfide** [6088-51-3] M 350.5, m 221-222°, 226-227°,  $pK_{Est} \sim 9.0$ . Crystallises as leaflets from AcOH and is slightly soluble in EtOH, and AcOH, but is soluble in  $C_{6H_6}$  and in alkalis to give a yellow soln. [Zincke and Dereser *Chem Ber* 51 352 1918.] The acetoxy derivative has m 198-200° (from AcOH or dioxane-MeOH) and the diacetyl derivative has m 167-168° (from AcOH). A small amount of impure disulfide can be purified by dissolving in a small volume of Me<sub>2</sub>CO and adding a large volume of toluene, filter rapidly and concentrate to one third of its volume. The hot toluene soln is filtered rapidly from any tarry residue, and crystals separate on cooling. After recrystn from hot acetic acid gives crystals m 220-223° [Barrett and Seligman *Science* 116 323 1952].

2-Hydroxy-5-nitrobenzyl bromide [772-33-8] M 232.0, m 147°, pK<sub>Est</sub> ~8.0. Crystd from \*benzene or \*benzene/ligroin.

4-Hydroxy-2-*n*-nonylquinoline *N*-oxide [316-66-5] M 287.4, m 148-149°, pK<sub>Est</sub> ~6.0. Crystd from EtOH.

*N*-Hydroxy-5-norbornene-2,3-dicarboxylic acid imide [21715-90-2] M 179.2, m 165-166°, 166-169°,  $pK_{Est}\sim 6$  Dissolve in CHCl<sub>3</sub>, filter, evaporate and recrystallise from EtOAc. IR (nujol): 1695, 1710 and 1770 (C=O), and 3100 (OH) cm<sup>-1</sup>. *O*-Acetyl derivative has m 113-114° (from EtOH) with IR bands at 1730, 1770 and 1815 cm<sup>-1</sup> only, and the *O*-benzoyl derivative has m 143-144° (from propan-2-ol or \*C<sub>6</sub>H<sub>6</sub>). [Bauer and Miarka J Org Chem 24 1293 1959; Fujino et al. Chem Pharm Bull Jpn 22 1857 1974].

**DL-erythro-3-Hydroxynorvaline** (2-amino-3-hydroxypentanoic acid) [34042-00-7] M 133.2, m 257-259° (dec), 263° (dec), pK<sub>1</sub><sup>20</sup> 2.32, pK<sub>2</sub><sup>20</sup> 9.12. Purified by recrystn from aqueous EtOH. The *Cu salt* has m 255-256° (dec), the *benzoyl* derivative has m 181°, and the *N-phenylcarbamoyl* derivative has m 164°. [Buston et al. *J Biol Chem* 204 665 1953].

2-Hydroxyoctanoic acid (2-hydroxycaprylic acid) [617-73-2] M 160.2, m 69.5°, b 160-165°/10mm, pK<sub>Est</sub> ~3.7. Crystd from EtOH/pet ether or ether/ligroin.

1-Hydroxyphenazine (Hemipyocyanine) [528-71-2] M 196.2, m 157-158°,  $pK_1^{25}$  1.61,  $pK_2^{15}$ 8.33. Chromatographed on acidic alumina with \*benzene/ether. Crystd from \*benzene/heptane, and sublimed.

2-Hydroxyphenylacetic acid [614-75-5] M 152.2, m 148-149°, b 240-243°/760 mm, pK<sub>Est(1)</sub>~4.3, pK<sub>Est(2)</sub>~10.1. Crystd from ether or chloroform (m from latter is always lower).

3-Hydroxyphenylacetic acid [621-37-4] M 152.2, m 137°,  $pK_{Ext(1)}$ ~4.3,  $pK_{Ext(2)}$ ~10. Crystd from \*benzene/ligroin.

**4-Hydroxyphenylacetic acid** [156-38-7] **M 152.2, m 150-151°, 152°, pK<sub>1</sub> 4.28, pK<sub>2</sub> 10.1.** Crystd from water or Et<sub>2</sub>O/pet ether.

2-(2-Hydroxyphenyl)benzothiazole [3411-95-8] M 227.2, m 132-133°, b 173-179°/3 mm. Recrystd several times from aqueous EtOH and by sublimation. [Itoh and Fujiwara J Am Chem Soc 107 1561 1985.]

2-(2-Hydroxyphenyl)benzoxazole [835-64-3] M 211.2, m 127°, b 338°/760mm. Recrystd several times from aqueous EtOH and by sublimation. [Itoh and Fujiwara J Am Chem Soc 107 1561 1985.]

3-Hydroxy-2-phenylcinchoninic acid [485-89-2] M 265.3, m 206-207°(dec). Crystd from EtOH.

N-(p-Hydroxyphenyl)glycine [22818-40-2] M 167.2, m >240°(dec), pK<sub>Est(1)</sub>~2, pK<sub>Est(2)</sub>~4.5, pK<sub>Est(3)</sub>~10.3. Crystd from water.

N-(4-Hydroxyphenyl)-3-phenylsalicylamide [550-57-2] M 305.3, m 183-184°, pK<sub>Est</sub> ~9.5. Crystd from aqueous MeOH.

L-2-Hydroxy-3-phenylpropionic acid (3-phenyl lactic acid) [20312-36-1] M 166.2, m 125-126°,  $[\alpha]_D^{12}$ -18.7° (EtOH), pK see below. Crystd from water, MeOH, EtOH or \*benzene.

*dl*-2-Hydroxy-3-phenylpropionic acid [828-01-3] M 166.2, m 97-98°, b 148-150°/15mm, pK<sub>Est</sub> ~3.7. Crystd from \*benzene or chloroform.

3-p-Hydroxyphenylpropionic acid (phloretic acid) [501-97-3] M 166.2, m 129-130°, 131-133°,  $pK_{Est(1)}$ ~4.7,  $pK_{Est(2)}$ ~10.1. Crystd from ether or H<sub>2</sub>O.

*p*-Hydroxyphenylpyruvic acid [156-39-8] M 180.2, m 220°(dec), pK<sub>Est</sub> ~2.3. Crystd three times from 0.1M HCl/EtOH (4:1, v/v) immediately before use [Rose and Powell *Biochem J* 87 541 1963], or from Et<sub>2</sub>O. The 3,4-Dinitrophenylhydrazone has m 178°.

*N*-Hydroxyphthalimide [524-38-9] M 163.1, m 230°, ~235° (dec), 237-240°, pK<sup>30</sup> 7.0. Dissolve in H<sub>2</sub>O by adding Et<sub>3</sub>N to form the salt and while hot acidify, cool and pour into a large volume of H<sub>2</sub>O. Filter off the solid, wash with H<sub>2</sub>O, dry over P<sub>2</sub>O<sub>5</sub> in vacuum. [Nefken And Teser J Am Chem Soc 83 1263 1961; Fieser 1 485 1976; Nefkens et al. Recl Trav Chim Pays-Bas 81 683 1962] The O-acetyl derivative has m 178-180° (from EtOH).

3-β-Hydroxy-5-pregnen-20-one (pregnenolone) [145-13-1] M 316.5, m 189-190°,  $[\alpha]_D^{20}$  +30° (EtOH),  $[\alpha]_{546}$  +34° (c 1, EtOH). Crystd from MeOH.

17 $\alpha$ -Hydroxyprogesterone [604-09-1] M 330.5, m 222-223°,  $[\alpha]_{546}^{20}$  +141° (c 2, dioxane),  $\lambda_{max}$  240nm. Crystd from acetone or EtOH. Acetate: m 239-240° and caproate: m 119-121° crystallised from CHCl<sub>3</sub>/MeOH.

**R**-(+)-3-Hydroxyprolidine [2799-21-5] M 87.1, b 215-216°,  $d_4^{20}$  1.078,  $n_D^{20}$  1.490,  $[\alpha]_D^{20}$  +6.5° (c 1.5, MeOH), pK<sub>Est</sub> ~10.1. Purify by repeated distn. The hydrochloride has -ve rotation and the dimethiodide has m 230° and  $[\alpha]_D^{24}$  -8.02°. [Suyama and Kanno Yakugaku Zasshi (J Pharm Soc Japan) 85 531 1965; Uno et al. J Heterocycl Chem 24 1025 1987; Flanagan and Joullie Heterocycles 26 2247 1987.]

trans-L-4-Hydroxyproline [51-35-4] M 131.1, m 274°,  $[\alpha]_D^{20}$  -76.0° (c 5, H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup>1.86, pK<sub>2</sub><sup>25</sup>9.79. Crystd from MeOH/EtOH (1:1). Separation from normal *allo*-isomer can be achieved by crystn of the copper salts [see *Biochem Prep* 8 114 1961].

4'-Hydroxypropiophenone [70-70-2] M 150.2, m 149°, pK<sub>Est</sub> ~10. Crystd from water.

2-(α-Hydroxypropyl)piperidine (2-piperidinepropanol) [24448-89-3] M 143.2, m 121°, b 226°, pK<sub>Est</sub> ~10.2. Crystd from ether.

7-(2-Hydroxypropyl)theophylline (Proxyphylline) [603-00-9] M 238.2, m 135-136°. Crystd from EtOH.

6-Hydroxypurine (hypoxanthine) [68-94-0] M 136.1, m 150°(dec),  $pK_1^{20}8.96$ ,  $pK_2^{20}12.18$ . Crystd from hot water. Dried at 105°.

**2-Hydroxypyridine** (2-pyridone) [142-08-5] M 95.1, m 105-107°, b 181-185°/24mm,  $\varepsilon_{293nm}$  5900 (H<sub>2</sub>O) pK<sub>1</sub><sup>25</sup> 1.25, pK<sub>2</sub><sup>25</sup> 11.99. Distd under vacuum to remove coloured impurity, then crystd from

## **Purification of Organic Chemicals**

\*benzene, CCl<sub>4</sub>, EtOH or CHCl<sub>3</sub>/diethyl ether. It can be sublimed under high vacuum. [DePue et al. J Am Chem Soc 107 2131 1985.]

3-Hydroxypyridine [109-00-2] M 95.1, m 129° pK<sub>1</sub><sup>25</sup> 5.10, pK<sub>2</sub><sup>25</sup> 8.6. Crystd from water or EtOH.

4-Hydroxypyridine (4-pyridone) [626-64-2] M 95.1, m 65°(hydrate), 148.5° (anhydr), b >350°/760mm,  $pK_1^{20}$  3.20,  $pK_2^{20}$  11.12. Crystd from H<sub>2</sub>O. Loses H<sub>2</sub>O on drying *in vacuo* over H<sub>2</sub>SO<sub>4</sub>. Stored over KOH because it is *hygroscopic*.

2(6)-Hydroxypyridine-5(3)-carboxylic acid (6-hydroxynicotinic acid) [5006-66-6] M 139.1, m  $304^{\circ}(dec)$ , pK<sup>20</sup> 3.82. Crystd from water.

4-Hydroxypyridine-2,6-dicarboxylic acid (chelidamic acid) [138-60-3] M 183.1, m  $254^{\circ}(dec)$ ,  $pK_1^{22}$  1.9,  $pK_2^{22}$  3.18,  $pK_3^{22}$ 10.85. Crystd from water.

**2-Hydroxypyrimidine** [557-01-7] **M 96.1, m 179-180°, pK<sub>1</sub><sup>20</sup> 2.15, pK<sub>2</sub><sup>20</sup> 9.2.** Crystd from EtOH or ethyl acetate.

**4-Hydroxypyrimidine** [4562-27-0] **M 96.1, m 164-165°, pK<sub>1</sub><sup>20</sup> 1.66, pK<sub>2</sub><sup>20</sup> 8.63.** Crystd from \*benzene or ethyl acetate.

2-Hydroxypyrimidine hydrochloride [38353-09-2] M 132.5, m 205°(dec). Crystd from EtOH.

**2-Hydroxyquinoline** (carbostyril) [59-31-4] M 145.2, m 199-200°,  $pK_1^{20}$ -0.31,  $pK_2^{20}$ 11.76. Crystd from MeOH.

8-Hydroxyquinoline (oxine, 8-quinolinol) [148-24-3] M 145.2, m 71-73°, 75-76°, 76°, b ~ 267°  $pK_1^{25}$  4.91,  $pK_2^{25}$  9.81. Crystd from hot EtOH, acetone, pet ether (b 60-80°) or water. Crude oxine can be purified by pptn of copper oxinate, followed by liberation of free oxine with H<sub>2</sub>S or by steam distn after acidification with H<sub>2</sub>SO<sub>4</sub>. Stored in the dark. Forms metal complexes. [Manske et al. Can J Research 27F 359 1949; Phillips Chem Rev 56 271 1956.]

8-Hydroxyquinoline-5-sulfonic acid (H<sub>2</sub>O) [84-88-8] M 243.3, m >310°  $pK_1^{25}$  4.09,  $pK_2^{25}$  8.66. Crystd from water or dil HCl (*ca* 2% by weight).

5-Hydroxysalicylic acid [490-79-9] M 154.1. See 2,5-dihydroxybenzoic acid on p. 207.

trans-4-Hydroxystilbene [6554-98-9] M 196.3, m 189°. Crystd from \*benzene or acetic acid.

**N-Hydroxysuccinimide** [6066-82-6] M 115.1, m 96-98°, pK 6.0. Recrystd from EtOH/ethyl acetate [Manesis and Goodmen J Org Chem 52 5331 1987].

*dl-2-Hydroxytetradecanoic acid* [2507-55-3] M 244.4, m 81-82°, pK<sub>Est</sub> ~3.7. Crystd from chloroform.

*R***-2-Hydroxytetradecanoic acid** [26632-17-7] M 244.4, m 88-2-88.5°,  $[\alpha]_D^{20}$  -31° (CHCl<sub>3</sub>). Crystd from chloroform.

**4-Hydroxy-2,2,6,6-tetramethylpiperidine** [2403-88-5] **M** 157.3, **m** 130-131°, **pK** 10.05. Crystd from water as hydrate, and crystd from ether as the anhydrous base.

Hydroxy(tosyloxy)iodobenzene [phenyl(hydroxyl)tosyloxyiodine, hydroxy(4-methylbenzenesulfonato-O)phenyliodine, Koser's reagent] [27126-76-7] M 392.2, m 134-136°, 135-138°, 134-136°, 136-138.5°. Possible impurities are tosic acid (removed by washing with Me<sub>2</sub>CO) and acetic acid (removed by washing with Et<sub>2</sub>O). It is purified by dissolving in the minimum vol of MeOH, adding Et<sub>2</sub>O to cloud point and setting aside for the prisms to separate [Koser and Wettach J Org Chem 42 1476 1977; NMR: Koser et al. J Org Chem 41 3609 1976]. It has also been crystd from CH<sub>2</sub>Cl<sub>2</sub> (needles, m 140-142°) [Neiland and Karele J Org Chem, USSR (Engl Transl) 6 889 1970].

4(6)-Hydroxy-2,5,6(2,4,5)-triaminopyrimidine sulfate [35011-47-3] M 257.22, m >340°, pK<sub>1</sub> 2.0, pK<sub>2</sub> 5.1, pK<sub>3</sub> 10.1. This salt has very low solubility in H<sub>2</sub>O. It is best purified by conversion into the dihydrochloride salt which is then reconverted to the insoluble sulfate salt. The sulfate salt (2.57g, 10mmoles) is suspended in H<sub>2</sub>O (20mL) containing BaCl<sub>2</sub> (10mmoles) and stirred in a boiling water bath for 15min. After cooling the insoluble BaSO<sub>4</sub> is filtered off and washed with boiling H<sub>2</sub>O (10mL). The combined filtrate and washings are made acidic with HCl and evaporated to dryness. The residual hydrochloride salt is recrystd from H<sub>2</sub>O by adding conc HCl whereby the *dihydrochloride salt* separates as clusters which darken at 260° and dec > 300° [Baugh and Shaw J Org Chem 29 3610 1964; King and Spengley J Chem Soc 2144 1952]. The hydrochloride is then dissolved in H<sub>2</sub>O and while hot an equivalent of H<sub>2</sub>SO<sub>4</sub> is added when the sulfate separates as a white microcrystalline solid which is filtered off washed liberally with H<sub>2</sub>O and dried in vacuum over P<sub>2</sub>O<sub>5</sub>. [Albert and Wood J Appl Chem London 3 521 1953; UV: Cavalieri et al. J Am Chem Soc 70 3875 1948; see also Pfleiderer Chem Ber 90 2272 1957; Traube Chem Ber 33 1371 1900].

9-Hydroxytriptycene [73597-16-7] M 270.3, m 245-246.5°. Crystd from \*benzene/pet ether. Dried at 100° in a vacuum [Imashiro et al. J Am Chem Soc 109 729 1987].

5-Hydroxy-L-tryptophan [4350-09-8] M 220.2, m 273°(dec),  $[\alpha]_D^{22}$  -32.5°,  $[\alpha]_{546}^{20}$  -73.5° (c 1, H<sub>2</sub>O), pK<sub>Est(1)</sub>~2.4, pK<sub>Est(2)</sub>~9.0, pK<sub>Est(3)</sub>~9.4, pK<sub>Est(4)</sub> 16 (NH). Likely impurities are 5-hydroxy-D-tryptophan and 5-benzyloxytryptophan. Crystd under nitrogen from water by adding EtOH. Stored under nitrogen.

Hydroxyurea [127-07-1] M 76.1, m 70-72° (unstable form), m 135-140°, 141° (stable form). See hydroxyurea on p. 431 in Chapter 5.

**3-Hydroxyxanthone** [3722-51-8] **M 212.2, m 246°.** Purified by chromatography on SiO<sub>2</sub> gel with pet ether/\*benzene). Recrystd from \*benzene or EtOH [Itoh et al. J Am Chem Soc 107 4819 1985].

 $\alpha$ -Hyodeoxycholic acid [83-49-8] M 392.6, m 196-197°,  $[\alpha]_{546}^{20}$  +8° (c 2, EtOH), pK<sub>Est</sub> ~4.9. Crystd from ethyl acetate.

Hyoscine (scopolamine, atroscine) [51-34-3] M 321.4, m 59°,  $[\alpha]_D^{20}$  -18° (c 5, EtOH), -28° (c 2, H<sub>2</sub>O),  $[\alpha]_{546}^{20}$  -30° (c 5, CHCl<sub>3</sub>), pK<sup>25</sup> 7.55. Crystd from \*benzene/pet ether. Racemate has m 56-57° (H<sub>2</sub>O), 37-38° (2H<sub>2</sub>O), syrup (anhydr), *l* and *d* isomers can separate as syrups when anhydrous.

Hypericin [548-04-9] M 504.4, m 320°(dec). Crystd from pyridine by addition of methanolic HCl.

**Ibogaine** [83-74-9] M 300.3, m 152-153°,  $[\alpha]_D^{20}$  -54° (EtOH), pK 8.1 (80% aq MeOCH<sub>2</sub>CH<sub>2</sub>OH). Crystd from aqueous EtOH and sublimes at 150°/0.01mm.

**Imidazole (glyoxaline)** [288-32-4] M 68.1, m 89.5-91°, b 256°,  $pK_1^{25}6.99$ ,  $pK_2^{25}14.44$ . Crystd from \*benzene, CCl<sub>4</sub>, CH<sub>2</sub>Cl<sub>2</sub>, EtOH, pet ether, acetone/pet ether and distd deionized water. Dried at 40° under vacuum over P<sub>2</sub>O<sub>5</sub>. Distd at low pressure. Also purified by sublimation or by zone melting. [Caswell and Spiro J Am Chem Soc 108 6470 1986.] <sup>15</sup>N-imidazole was crystd from \*benzene [Scholes et al. J Am Chem Soc 108 1660 1986].

4'-(Imidazol-1-yl)acetophenone [10041-06-2] M 186.2, m 104-107°, pK 4.54. Twice recrystd from CH<sub>2</sub>Cl<sub>2</sub>/hexane [Collman et al. J Am Chem Soc 108 2588 1986].

Iminodiacetic acid [142-73-4] M 133.1, m 225°(dec), pK<sub>1</sub><sup>25</sup> 2.50, pK<sub>2</sub><sup>25</sup> 9.40. Crystd from water.

1,3-Indandione [606-23-5] M 146.2, m 129-132°, pK<sup>18</sup> 7.2 (1% aq EtOH). Recrystd from EtOH [Bernasconi and Paschalis J Am Chem Soc 108 2969 1986].

Indane [496-11-7] M 118.1, b 177°, d 0.960, n 1.538. Shaken with conc H<sub>2</sub>SO<sub>4</sub>, then water, dried and fractionally distd.

Indanthrene [81-77-6] M 442.4, m 470-500°. Crystd repeatedly from 1,2,4-trichlorobenzene.

Indazole [271-44-3] M 118.1, m 147°,  $pK_1^{20}$  1.32,  $pK_2^{25}$  13.80 (acidic NH). Crystd from water, sublimed under a vacuum, then pet ether (b 60-80°).

Indene [95-13-6] M 116.2, f -1.5°, b 114.5°/100mm, d 0.994, n 1.5763. Shaken with 6M HCl for 24h (to remove basic nitrogenous material), then refluxed with 40% NaOH for 2h (to remove benzonitrile). Fractionally distd, then fractionally crystd by partial freezing. The higher-melting portion was converted to its sodium salt by adding a quarter of its weight of sodamide under nitrogen and stirring for 3h at 120°. Unreacted organic material was distd off at 120°/1mm. The sodium salts were hydrolysed with water, and the organic fraction was separated by steam distn, followed by fractional distn. Before use, the distillate was passed, under nitrogen, through a column of activated silica gel. [Russell J Am Chem Soc 78 1041 1956.]

Indigo [482-89-3] M 262.3, sublimes at ~300°, m 390°(dec), and halogen-substituted indigo dyes. Reduced in alkaline soln with sodium hydrosulfite, and filtered. The filtrate was then oxidised by air, and the resulting ppte was filtered off, dried at 65-70°, ground to a fine powder, and extracted with CHCl<sub>3</sub> in a Soxhlet extractor. Evapn of the CHCl<sub>3</sub> gave the purified dye. [Brode, Pearson and Wyman J Am Chem Soc 76 1034 1954; spectral characteristics are listed.]

Indole [120-72-9] M 117.2, m 52°, b 124°/5mm, 253-254°/760mm,  $pK_1^{25}$ -2.47 (H<sub>o</sub> scale),  $pK_2^{25}$  16.97 (acidic NH). Crystd from \*benzene, hexane, water or EtOH/water (1:10). Further purified by sublimation in a vacuum or zone melting.

Indole-3-acetic acid [87-51-4] M 175.2, m 167-169°,  $pK_1^{25}$ -6.13 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$ 4.54 (CO<sub>2</sub>H). Recrystd from EtOH/water [James and Ware J Phys Chem 89 5450 1985].

**3-Indoleacetonitrile** [771-51-7] M **156.2, m 33-36°, 36-38°, b 157°/0.2mm, 158-160°/0.1mm, viscous oil n\_D^{20} <b>1.6097.** Distil in very high vacuum and the viscous distillate crystallises on standing after a few days; the *picrate* has m 127-128° (from EtOH) [Coker et al. J Org Chem **27** 850 1962; Thesing and Schülde Chem Ber **85** 324 1952]. The N-acetate has m 118° (from MeOH) and has  $R_F = 0.8$ , on Silica Gel F<sub>254</sub> in CHCl<sub>2</sub>-MeOH 19:1 [Buzas et al. Synthesis 129 1977].

Indole-3-butanoic acid [133-32-4] M 203.2, m 124-125°. See 3-indolylbutyric acid on p. 543 in Chapter 6.

Indole-3-propionic acid [830-96-6] M 189.2, m 134-135°, pK<sub>Est</sub> ~4.7. Recrystd from EtOH/water [James and Ware J Phys Chem 89 5450 1985].

Indolizine [pyrrocoline, pyrrolo(1,2-a)pyridine] [274-40-8] M 117, m 73-74°, 75°, pK<sup>20</sup> 3.94 (C-protonation). Purified through an alumina column in \*C<sub>6</sub>H<sub>6</sub> and eluted with \*C<sub>6</sub>H<sub>6</sub> (toluene could be used instead). The eluate contained in the fluorescent band (using UV light  $\lambda$  365mn) was collected, evapd and the cryst residues sublimed twice at 40-50°/0.2-0.5mm. The colourless crystals darkend on standing and should be stored in dark sealed containers. If the original sample is dark in color then is should be covered with water and steam distd. The crysts in the distillate are collected and, dried between filter paper and sublimed. It protonates on C3 in aqueous acid. It should give one fluorescent spot on paper chromatography (Whatman 1) in 3% aq ammonia and in *n*-BuOH, AcOH, H<sub>2</sub>O (4:1:1). The *picrate* has **m** 101° from EtOH. [Armarego J Chem Soc 226 1944; Armarego J Chem Soc (B) 191 1966; Scholtz Chem Ber **45** 734 1912.] (-)-Inosine [58-63-9] M 268.2, m 215°,  $[\alpha]_{546}^{20}$  -76° (c 1, 0.1M NaOH),  $pK_1^{25}$  1.06,  $pK_2^{25}$  8.96,  $pK_3^{25}$  11.36. Crystd from aqueous 80% EtOH.

*i*-Inositol (*myo*) [87-89-8] M 180.2, m 228°. See entry on p. 543 in Chapter 6.

Inositol monophosphate [15421-51-9] M 260.1, m 195-197°(dec). Crystd from water and EtOH.

Iodinin (1,6-phenazine-5,10-dioxide) [68-81-5] M 244.1, m 236°(dec), pK 12.5. Crystd from CHCl<sub>3</sub>.

Inulin [9005-80-5] M (162.14)<sub>n</sub>. Crystd from water.

Iodoacetamide [144-48-9] M 185.0, m ca 143°(dec). Crystd from water or CCl<sub>4</sub>.

Iodoacetic acid [64-69-7] M 160.6, m 78°, pK<sup>25</sup> 3.19. Crystd from pet ether (b 60-80°) or CHCl<sub>3</sub>/CCl.

2-Iodoaniline [615-43-0] M 219.0, m 60-61°, pK<sup>25</sup> 2.54. Distd with steam and crystd from \*benzene/pet ether.

**4-Iodoaniline** [540-37-4] **M 219.0, m 62-63°, pK<sup>25</sup> 3.81.** Crystd from pet ether (b 60-80°) by refluxing, then cooling in an ice-salt bath freezing mixture. Dried in air. Also crystd from EtOH and dried in a vacuum for 6h at 40° [Edidin et al. J Am Chem Soc 109 3945 1987].

4-Iodoanisole [696-62-8] M 234.0, m 51-52°, b 139°/35mm, 237°/726mm. Crystd from aqueous EtOH.

**Iodobenzene** [591-50-4] **M 204.0, b 63-65°/10mm, 188°/atm, d 1.829, n^{25} 1.6169.** Washed with dilute aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, then water. Dried with CaCl<sub>2</sub> or CaSO<sub>4</sub>. Decolorised with charcoal. Distd under reduced pressure and stored with mercury or silver powder to stabilise it.

o-Iodobenzoic acid [88-67-5] M 248.4, m 162°, pK<sup>2</sup>° 2.93. Crystd repeatedly from water and EtOH. Sublimed under vacuum at 100°.

*m*-Iodobenzoic acid [618-51-9] M 248.4, m 186.6-186.8°,  $pK^{25}$  3.85. Crystd repeatedly from water and EtOH. Sublimed under vacuum at 100°.

*p*-Iodobenzoic acid [619-58-9] M 248.4, m 271-272°,  $pK^{25}$  4.00. Crystd repeatedly from water and EtOH. Sublimed under vacuum at 100°.

4-Iodobiphenyl [1591-31-7] M 280.1, m 113.7-114.3°. Crystd from EtOH/\*benzene and dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

**2-Iodobutane** [513-48-4] **M 184.0, b 120.0, d 1.50, n^{25} 1.4973.** Purified by shaking with conc  $H_2SO_4$ , then washing with water, aq  $Na_2SO_3$  and again with water. Dried with  $MgSO_4$  and distd. Alternatively, passed through a column of activated alumina before distn, or treated with elemental bromine, followed by extraction of the free halogen with aqueous  $Na_2S_2O_3$ , thorough washing with water, drying and distilling. It is stored over silver powder and distd before use.

1-Iodo-2,4-dinitrobenzene [709-49-9] M 294.0, m 88°. Crystd from ethyl acetate.

Iodoform [75-47-8] M 393.7, m 119°. Crystd from MeOH, EtOH or EtOH/EtOAc. Steam volatile.

1-Iodo-4-nitrobenzene [636-98-6] M 249.0, m 171-172°. Ppted from acetone by addition of water, then recrystd from EtOH.

o-Iodophenol [533-58-4] M 280.1, m 42°, pK<sup>25</sup> 8.51. Crystd from CHCl<sub>3</sub> or diethyl ether.

*p*-Iodophenol [540-38-5] M 280.1, m 94°, 138-140°/5mm,  $pK^{25}$  9.30. Crystd from pet ether (b 80-100°) or distd *in vacuo*. If material has a brown or violet color, dissolve in CHCl<sub>3</sub>, shake with 5% sodium thiosulfate soln until the CHCl<sub>3</sub> is colorless. Dry (Na<sub>2</sub>SO<sub>4</sub>), extract, evap and dist residue *in vacuo*. [Dains and Eberly Org Synth Coll Vol II, 355 1948.]

5-Iodosalicylic acid (2-hydroxy-5-iodobenzoic acid) [119-30-2] M 264.0, m 197°  $pK_1^{25}$  2.65,  $pK_2^{25}$  13.05. Crystd from water.

o-Iodosobenzoic acid [304-91-6] M 264.0, m >200°, pK<sub>Est</sub> ~2.6. Crystd from EtOH.

N-Iodosuccinimide [516-12-1] M 225.0, m 200-201°. Crystd from dioxane/CCl<sub>4</sub>.

p-Iodotoluene [624-31-7] M 218.0, m 35°, b 211-212°. Crystd from EtOH.

**3-Iodo-L-tyrosine** [70-78-0] M **307.1, m 205-208°(dec),**  $[\alpha]_D^{25}$  -4.4° (c 5, 1M HCl), pK<sub>Est(2)</sub>~2.1, pK<sub>Est(3)</sub>~6.4, pK<sub>4</sub><sup>25</sup> 8.7. Likely impurities are tyrosine, diiodotyrosine and iodide. Crystd by soln in dilute ammonia, at room temperature, followed by addition of dilute acetic acid to pH 6. Stored at 0°.

 $\alpha$ -Ionone [127-41-3] M 192.3, b 131°/13mm, d 0.931, n 1.520,  $[\alpha]_D^{23}$  +347° (neat). Purified on a spinning band fractionating column.

 $\beta$ -Ionone [79-77-6] M 192.3, b 150-151°/24mm, d 0.945, n 1.5211,  $\epsilon_{296nm}$  10,700. Converted to the *semicarbazone* (m 149°) by adding 50g of semicarbazide hydrochloride and 44g of potassium acetate in 150mL of water to a soln of 85g of  $\beta$ -ionone in EtOH. (More EtOH was added to redissolve any  $\beta$ -ionone that ppted.) The semicarbazone crystallised on cooling in an ice-bath and was recrystallised from EtOH or 75% MeOH to constant m (148-149°). The semicarbazone (5g) was shaken at room temperature for several days with 20mL of pet ether and 48mL of M H<sub>2</sub>SO<sub>4</sub>, then the ether layer was washed with water and dilute aqueous NaHCO<sub>3</sub>, dried and the solvent was evaporated. The  $\beta$ -ionone was distilled under vacuum. (The customary steam distillation of  $\beta$ -ionone semicarbazone did not increase the purity.) [Young et al. J Am Chem Soc 66 855 1944].

Iproniazid (isonicotinic acid 2-isopropylhydrazide) phosphate [305-33-9] M 277.2, m 178-179°, 180-182°,  $pK_{Est} \sim 3.5$  (free base). Crystd from H<sub>2</sub>O and Me<sub>2</sub>CO. Free base has m 113-114° from \*C<sub>6</sub>H<sub>6</sub>/pet ether.

(±)-Irone (6-methyl-ionone, ±-trans-( $\alpha$ )-4t-[2,5,6,6-tetramethyl-cyclohex-2-yl]but-3t-en-2-one) [79-69-6] M 206.3, b 85-86°/0.05mm, 109°/0.7mm,  $d_4^{20}$  0.9340,  $n_D^{20}$  1.4998. If large amounts are available then fractionate through a Podbielniak column (see p. 141) or an efficient spinning band column, but small amounts are distilled using a Kügelrohr apparatus. The 4-phenyl-semicarbazone has m 174-175° (165-165.5°). [IR: Seidel and Ruzocka Helv Chim Acta 35 1826 1952; Naves Helv Chim Acta 31 1280 1948; Lecomte and Naves J Chim Phys 53 462 1956.]

Isatin (indole-2,3-dione) [91-56-5] M 147.1, m 201-203°, 205°, pK >12 (acidic NH). Crystd from amyl alcohol and sublimed at 180°/1mm. In aq NaOH the ring opens to yield sodium o-aminobenzoylformate.

Isatoic anhydride (3,1-benzoxazin-2,4[1-H]-dione) [118-48-9] M 163.1, m 235-240°, 240-243°, 243°, 243°, 243°, 243-245°. Recryst from EtOH or 95% EtOH (30mL/g) or dioxane (10mL/g) and dried in a vacuum. [Wagner and Fegley Org Synth Coll Vol III 488 1955; Ben-Ishai and Katchalski J Am Chem Soc 74 3688 1952; UV: Zentmyer and Wagner J Org Chem 14 967 1949.]

Isoamyl acetate (1-butyl-3-methyl acetate) [123-92-2] M 130.2, b 142.0°, d 0.871, n 1.40535. Dried with finely divided K<sub>2</sub>CO<sub>3</sub> and fractionally distd.

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Isoamyl alcohol (1-butyl-3-methyl alcohol) [123-51-3] M 88.2, b 132°/760mm, d<sup>15</sup> 0.8129, n<sup>15</sup> 1.4085. See 3-methyl-1-butanol on p. 290.

Isoamyl bromide (1-butyl-3-methyl bromide) [107-82-4] M 151.1, f -112°, b 119.2°/737mm, d 1.208, n 1.444. Shaken with conc  $H_2SO_4$ , washed with water, dried with  $K_2CO_3$  and fractionally distd.

Isoamyl chloride (1-butyl-3-methyl chloride) [513-36-0] M 106.6, b 99°/734mm, d 0.8704, n 1.4084. Shaken vigorously with 95% H<sub>2</sub>SO<sub>4</sub> until the acid layer no longer became coloured during 12h, then washed with water, saturated aq Na<sub>2</sub>CO<sub>3</sub>, and more water. Dried with MgSO<sub>4</sub>, filtered and fractionally distd. Alternatively, a stream of oxygen containing 5% of ozone was passed through the chloride for a time, three times longer than was necessary to cause the first coloration of starch iodide paper by the exit gas. Subsequent washing of the liquid with aqueous NaHCO<sub>3</sub> hydrolysed the ozonides and removed organic acids. After drying and filtering, the isoamyl chloride was distd. [Chien and Willard J Am Chem Soc 75 6160 1953.]

Isoamyl ether [diisopentyl ether, di-(1-butyl-3-methyl) ether] [544-01-4] M 158.3, b 173.4°, d 0.778, n 1.40850. This is a mixture of 2- and 3-methylbutyl ether. It is purified by refluxing with sodium for 5h, then distilled under reduced pressure, to remove alcohols. Isoamyl ether can also be dried with CaCl<sub>2</sub> and fractionally distd from P<sub>2</sub>O<sub>5</sub>.

D(-)-Isoascorbic acid (araboascorbic acid) [89-65-6] M 176.1, m 174°(dec),  $[\alpha]_D^{25}$  -16.8° (c 2, H<sub>2</sub>O), pK<sup>18</sup> 3.99. Crystd from H<sub>2</sub>O or dioxane.

*dl*-Isoborneol [124-76-5] M 154.3, m 212° (sealed tube). Crystd from EtOH or pet ether (b 60-80°). Sublimes in a vacuum.

**Isobutane** [75-28-5] **M 58.1, b -10.2°, d 0.557.** Olefines and moisture can be removed by passage at 65° through a bed of silica-alumina catalyst which has previously been evacuated at about 400°. Alternatively, water and CO<sub>2</sub> can be taken out by passage through  $P_2O_5$  then asbestos impregnated with NaOH. Treatment with anhydrous AlBr<sub>3</sub> at 0° then removes traces of olefins. Inert gases can be separated by freezing the isobutane at -195° and evacuating out the system.

**Isobutene** [115-11-7] **M 56.1, b -6.6°/760mm.** Dried by passage through anhydrous  $CaSO_4$  at  $0^\circ$ . Purified by freeze-pump-thaw cycles and trap-to-trap distn.

**Isobutyl alcohol (2-methyl-1-propanol)** [78-83-1] M 74.1, b 108°/760mm, d 0.801, n 1.396. Dried with  $K_2CO_3$ , CaSO<sub>4</sub> or CaCl<sub>2</sub>, filtered and fractionally distd. For further drying, the redistd alcohol can be refluxed with the appropriate alkyl phthalate or succinate as described under *ethanol* (see also p. 271).

**Isobutyl bromide** (1-bromo-2-methylpropane) [78-77-3] M 137.0, b 91.2°, d 1.260, n 1.437. Partially hydrolysed to remove any tertiary alkyl halide, then fractionally distd, washed with conc  $H_2SO_4$ , water and aqueous  $K_2CO_3$ , then redistd from dry  $K_2CO_3$ . [Dunbar and Hammett J Am Chem Soc 72 109 1950.]

Isobutyl chloride (1-chloro-2-methylpropane) [513-36-0] M 92.3, b 68.8°/760mm, d 0.877, n 1.398. Same methods as described under isoamyl chloride.

**Isobutyl chloroformate** [543-27-1] M 136.6, b 123-127°/atm, 128.8°/atm, d 1.053, n 1.4070. It can be dried over CaCl<sub>2</sub> and fractionated at atm press while keeping moisture out. Its purity can be checked by conversion to the *phenyl urethane derivative* with PhNCO [Saunders et al. J Am Chem Soc 73 3796 1951.] IR: v 1780cm<sup>-1</sup> [Thompson and Jameson Spectrochim Acta 13 236 1959; Röse Justus Liebigs Ann Chem 205 227 1880]. **Isobutyl formate** [542-55-2] **M 102.1, b 98.4°, d 0.885, n 1.38546.** Washed with saturated aqueous NaHCO<sub>3</sub> in the presence of saturatedd NaCl, until no further reaction occurred, then with saturated aqueous NaCl, dried (MgSO<sub>4</sub>) and fractionally distd.

**Isobutyl iodide (1-iodo-2-methylpropane)** [513-38-2] M 184.0, b 83°/250mm, 120°/760mm, d 1.60, n 1.495. Shaken with conc  $H_2SO_4$ , and washed with water, aqueous Na<sub>2</sub>SO<sub>3</sub>, and water, dried with MgSO<sub>4</sub> and distd. Alternatively, passed through a column of activated alumina before distn. Stored under nitrogen with mercury in a brown bottle or in the dark.

**Isobutyl vinyl ether** [109-53-5] M 100.2, b 108-110°, d 0.768, n 1.398. Washed three times with equal volumes of aqueous 1% NaOH, dried with CaH<sub>2</sub>, refluxed with sodium for several hours, then fractionally distd from sodium.

**Isobutyraldehyde** [78-84-2] M 72.1, b 62.0°, d 0.789, n 1.377. Dried with CaSO<sub>4</sub> and used immediately after distn under nitrogen because of the great difficulty in preventing oxidation. Can be purified through its acid bisulfite derivative.

Isobutyramide [563-83-7] M 87.1, m 128-129°, b 217-221°. Crystd from acetone, \*benzene, CHCl<sub>3</sub> or water, then dried under vacuum over P<sub>2</sub>O<sub>5</sub> or 99% H<sub>2</sub>SO<sub>4</sub>. Sublimed under vacuum.

**Isobutyric acid** [79-31-2] **M 88.1, b 154-154.5°, d 0.949, n 1.393, pK^{25} 4.60.** Distd from KMnO<sub>4</sub>, then redistd from P<sub>2</sub>O<sub>5</sub>.

**Isobutyronitrile (2-methylpropionitrile, isopropyl cyanide)** [78-82-0] M 69.1, b 103.6°,  $d^{25}$  0.7650, n 1.378. Shaken with conc HCl (to remove isonitriles), then with water and aq NaHCO<sub>3</sub>. After a preliminary drying with silica gel or Linde type 4A molecular sieves, it is shaken or stirred with CaH<sub>2</sub> until hydrogen evolution ceases, then decanted and distd from P<sub>2</sub>O<sub>5</sub> (not more than 5g/L, to minimize gel formation). Finally it is refluxed with, and slowly distd from CaH<sub>2</sub> (5g/L), taking precautions to exclude moisture.

(-)- $\gamma$ -Isocaryophyllene (8-methylene-4,11,11-trimethylbicyclo[7.2.0]undec-4-ene) [118-65-0] M 204.4, b 122-124°/12mm, 131-133°/16mm, 130-131°/24mm, 271-273°/atm, d<sub>4</sub><sup>20</sup> 0.8959, n<sub>D</sub><sup>20</sup> 1.496,  $[\alpha]_{546}^{20}$  -31°,  $[\alpha]_D^{20}$  -27° (neat). Purified by vac dist or GLC using a nitrile-silicone column [Corey et al. J Am Chem Soc 86 485 1964; Ramage and Simonsen J Chem Soc 741 1936; Kumar et al. Synthesis 461 1976].

L-Isoleucine [73-32-5] M 131.2, m 285-286°(dec),  $[\alpha]_D^{20}$  +40.6° (6M HCl)  $pK_1^{25}$  2.66,  $pK_2^{25}$  9.69. Crystd from water by addition of 4 volumes of EtOH.

(-)- $\beta$ -Isolongifolene (1-*R*-(-)- 2,2,7,7-tetramethyltricyclo[6.2.1.0<sup>1,6</sup>]undec-5-ene) [1135-66-6] M 204.4, b 82-83°/0.4mm, 144-146°/30mm, 255-256°/atm, d<sub>4</sub><sup>20</sup> 0.930, n<sub>D</sub><sup>20</sup> 1.4992, [ $\alpha$ ]<sub>546</sub><sup>20</sup> -166°, [ $\alpha$ ]<sub>D</sub><sup>20</sup> -138° (c 1, EtOH). Refluxed over and distd from Na. [Zeiss and Arakawa *J Am Chem Soc* 76 1653 1954; IR: Reinaecker and Graafe Angew Chem, Int Ed Engl 97 348 1985; UV and NMR: Ranganathan et al. *Tetrahedron* 26 621 1970.]

Isolysergic acid [478-95-5] M 268.3, m 218°(dec),  $[\alpha]_D^{20}$  +281° (c 1, pyridine)  $pK_1^{24} 3.33$ ,  $pK_2^{24} 8.46$ . Crystd from water.

Isonicotinamide [1453-82-3] M 122.1, m 155.5-156°,  $pK_1^{20}$ -1.0 (protonation of CONH<sub>2</sub>),  $pK_2^{20}$  3.61,  $pK_3^{25}$  11.47 (acidic CONH<sub>2</sub>). Recrystd from hot water.

**Isonicotinic acid (pyridine-4-carboxylic acid)** [55-22-1] M 123.1, m 320°, pK<sup>25</sup> 4.90. Crystd repeatedly from water. Dried under vac at 110°.

Isonicotinic acid hydrazide (isoniazide) [54-85-3] M 137.1, m 172°, pK<sub>1</sub> 1.75 (NHNH<sub>2</sub>), pK<sub>2</sub> 3.57 (=N-), pK<sub>3</sub> 10.75 (-NH). Crystd from 95% EtOH.

1-Isonicotinyl-2-isopropylhydrazide [54-92-2] M 179.2, m 112.5-113.5°. Crystd from \*benzene/pet ether.

1-Isonicotinyl-2-salicylidenehydrazide [495-84-1] M 241.2, m 232-233°. Crystd from EtOH.

Isonitrosoacetone (anti-pyruvic aldehyde-1-oxime) [31915-82-9] M 87.1, m 69°. Crystd from ether/pet ether or CCl<sub>4</sub>.

Isonitrosoacetophenone (phenylglyoxaldoxime) [532-54-7] M 149.2, m 126-128°. Crystd from water.

5-Isonitrosobarbituric acid (violuric acid) [26851-19-9] M 175.1, m 221-223°, 245-250°, pK<sub>1</sub> 4.41, pK<sub>2</sub> 9.66 (10.1). Crystd from water or EtOH. 1,1-Dimethylvioluric acid, m 144-147° has pK 4.72 [Taylor and Robinson Talanta 8 518 1961].

**Isononane** [34464-40-9] **M 128.3, b 142°/760mm.** Passed through columns of activated silica gel and basic alumina (activity 1). Distd under high vacuum from Na/K alloy.

Isopentyl formate [110-45-2] M 116.2, b 121-123°/atm, 123-123.6°/atm, 123-124°/atm,  $d_4^{20}$  0.8713,  $n_D^{20}$  1.391. Colourless liquid which is soluble in 300 volumes of H<sub>2</sub>O and is soluble in common organic solvents. It is purified by repeated distn using an efficient column at atmospheric pressure.

**Isophorone** [78-59-1] M 138.2, b 94°/16mm, d 0.921,  $n^{18}$  1.4778. Washed with aqueous 5% Na<sub>2</sub>CO<sub>3</sub> and then distd under reduced pressure, immediately before use. Alternatively, can be purified *via* the semicarbazone. [Erskine and Waight *J Chem Soc* 3425 1960.]

Isophthalic acid (benzene-1,3-dicarboxylic acid) [121-91-5] M 166.1, m 345-348°,  $pK_1^{25}$  3.70,  $pK_2^{25}$  4.60. Crystd from aqueous EtOH.

**Isopinocampheol** (pinan-3-ol, 2,6,6-trimethylbicyclo[3.1.1]heptan-3-ol) [1S,2S,3S,5R-(+)-27779-29-9; 1R,2R,3R,5S-(-)-25465-65-0] M 154.25, m 52-55°, 55-56°, 55-57°, b 103°/11mm,  $n_D^{20}$  1.4832,  $[\alpha]_{546}^{20}$  (+) and (-) 43°,  $[\alpha]_D^{20}$  (+) and (-) 36° (c 20, EtOH). Dissolve in Et<sub>2</sub>O, dry MgSO<sub>4</sub>, filter, evaporate, then recryst from pet ether. Also recryst from aqueous EtOH and has been distd in a vacuum. [Kergomard and Geneix Bull Soc Chim Fr 394 1958; Zweifel and Brown J Am Chem Soc 86 393 1964.] The 3,4-dinitrobenzoyl deriv has m 100-101°, the phenylcarbamoyl derivative has m 137-138° and the acid -phthalate has m 125-126°.

**Isoprene** (2-methyl-1,3-butadiene) [78-79-5] M 68.1, b 34.5-35°/762mm, d 0.681,  $n^{25}$  1.4225. Refluxed with sodium. Distd from sodium or NaBH<sub>4</sub> under nitrogen, then passed through a column containing KOH, CaSO<sub>4</sub> and silica gel. *tert*-Butylcatechol (0.02% w/w) was added, and the isoprene was stored in this way until redistd before use. The inhibitor (*tert*-butylcatechol) in isoprene can be removed by several washings with dil NaOH and water. The isoprene is then dried over CaH<sub>2</sub>, distd under nitrogen at atmospheric pressure, and the fraction distilling at 32° is collected. Stored under nitrogen at -15°.

**Isopropanol** [67-63-0] M 60.1, b 82.5°, d 0.783,  $n^{25.8}$  1.3739,  $pK^{25}$  17.1. Isopropyl alcohol is prepared commercially by dissolution of propene in H<sub>2</sub>SO<sub>4</sub>, followed by hydrolysis of the sulfate ester. Major impurities are water, lower alcohols and oxidation products such as aldehydes and ketones. Purification of isopropanol follows substantially the same procedure as for *n*-propyl alcohol.

Isopropanol forms a constant-boiling mixture, **b**  $80.3^{\circ}$ , with water. Most of the water can be removed from this 91% isopropanol by refluxing with CaO (200g/L) for several hours, then distilling. The distillate can be dried further with CaH<sub>2</sub>, magnesium ribbon, BaO, CaSO<sub>4</sub>, calcium, anhydrous CuSO<sub>4</sub> or Linde type 5A molecular sieves. Distn from sulfanilic acid removes ammonia and other basic impurities. Peroxides [indicated by liberation of iodine from weakly acid (HCl) solns of 2% KI] can be removed by refluxing with solid stannous chloride or with NaBH<sub>4</sub> then fractionally distilling. To obtain isopropanol containing only 0.002M of water, sodium (8g/L) has been dissolved in material dried by distn from CaSO<sub>4</sub>, 35mL of isopropyl benzoate has been

added and, after refluxing for 3h, the alcohol has been distd through a 50-cm Vigreux column. [Hine and Tanabe J Am Chem Soc 80 3002 1958.] Other purification steps for isopropanol include refluxing with solid aluminium isopropoxide, refluxing with NaBH<sub>4</sub> for 24h, and the removal of acetone by treatment with, and distn from 2,4-dinitrophenylhydrazine. Peroxides re-form in isopropanol if it is stood for several days.

Isopropenylcyclobutane [3019-22-5] M 98.1, b 98.7°, d 0.7743, n 1.438. Purified by preparative chromatography (silicon oil column), or fractionally distd. Dried with molecular sieves.

**Isopropyl acetate** [108-22-5] M 102.1, b 88.4°, d 0.873, n 1.3773. Washed with 50% aq  $K_2CO_3$  (to remove acid), then with saturated aq CaCl<sub>2</sub> (to remove any alcohol). Dried with CaCl<sub>2</sub> and fractionally distd.

**Isopropyl bromide (2-bromopropane)** [75-26-3] M 123.0, b 0°/69.2mm, 59.4°/760mm, d 1.31,  $n^{15}$  1.42847, n 1.4251. Washed with 95% H<sub>2</sub>SO<sub>4</sub> (conc acid partially oxidised it) until a fresh portion of acid did not become coloured after several hours, then with water, aq NaHSO<sub>3</sub>, aq 10% Na<sub>2</sub>CO<sub>3</sub> and again with water. (The H<sub>2</sub>SO<sub>4</sub> can be replaced by conc HCl.) Prior to this treatment, isopropyl bromide has been purified by bubbling a stream of oxygen containing 5% ozone through it for 1h, followed by shaking with 3% hydrogen peroxide soln, neutralising with aq Na<sub>2</sub>CO<sub>3</sub>, washing with distilled water and drying. Alternatively, it has been treated with elemental bromine and stored for 4 weeks, then extracted with aq NaHSO<sub>3</sub> and dried with MgSO<sub>4</sub>. After the acid treatment, isopropyl bromide can be dried with Na<sub>2</sub>SO<sub>4</sub>, MgSO<sub>4</sub> or CaH<sub>2</sub>, and fractionally distd.

**N-Isopropylcarbazole** [1484-09-9] **M 209.3, m 120°.** Crystd from isopropanol. Sublimed under vacuum. Zone refined. The *picrate* has **m** 143° after recrystn from EtOH.

**Isopropyl chloride (2-chloropropane)** [75-29-6] M 78.5, b 34.8°, d 0.864, n 1.3779,  $n^{25}$  1.3754. Purified with 95% H<sub>2</sub>SO<sub>4</sub> as described for *isopropyl bromide*, then dried with MgSO<sub>4</sub>, P<sub>2</sub>O<sub>5</sub> or CaH<sub>2</sub>, and fractionally distd from Na<sub>2</sub>CO<sub>3</sub> or CaH<sub>2</sub>. Alternatively, a stream of oxygen containing *ca* 5% ozone has been passed through the chloride for about three times as long as was necessary to obtain the first coloration of starch iodide paper by the exit gas, and the liquid was then washed with NaHCO<sub>3</sub> soln to hydrolyse ozonides and remove organic acids before drying and distilling.

Isopropyl ether (diisopropyl ether) [108-20-3] M 102.2, b 68.3°, d 0.719, n 1.3688, n<sup>25</sup> 1.36618. Common impurities are water and peroxides [detected by the liberation of iodine from weakly acid (HCl) solns of 2% KI]. Peroxides can be removed by shaking with aqueous Na<sub>2</sub>SO<sub>3</sub> or with acidified ferrous sulfate (0.6g FeSO<sub>4</sub> and 6mL conc H<sub>2</sub>SO<sub>4</sub> in 110mL of water, using 5-10g of soln per L of ether), or aqueous NaBH<sub>4</sub> soln. The ether is then washed with water, dried with CaCl<sub>2</sub> and distd. Alternatively, refluxing with LiAlH<sub>4</sub> or CaH<sub>2</sub>, or drying with CaSO<sub>4</sub>, then passage through an activated alumina column, can be used to remove water and peroxides. Other dehydrating agents used with isopropyl ether include P<sub>2</sub>O<sub>5</sub>, sodium amalgam and sodium wire. (The ether is often stored in brown bottles, or in the dark, with sodium wire.) Bonner and Goishi (J Am Chem Soc 83 85 1961) treated isopropyl ether with dil sodium dichromate/sulfuric acid soln, followed by repeated shaking with a 1:1 mixture of 6M NaOH and saturated KMnO4. The ether was washed several times with water, dilute aqueous HCl, and water, with a final washing with, and storage over, ferrous ammonium sulfate acidified with H<sub>2</sub>SO<sub>4</sub>. Blaustein and Gryder (J Am Chem Soc 79 540 1957), after washing with alkaline KMnO<sub>4</sub>, then water, treated the ether with ceric nitrate in nitric acid, and again washed with water. Hydroquinone was added before drying with CaCl<sub>2</sub> and MgSO<sub>4</sub>, and refluxing with sodium amalgam (108g Hg/100g Na) for 2h under nitrogen. The distillate (nitrogen atmosphere) was made 2 x 10<sup>-5</sup>M in hydroquinone to inhibit peroxide formation (which was negligible if the ether was stored in the dark). Catechol (pyrocatechol) and resorcinol are alternative inhibitors.

4,4'-Isopropylidenediphenol [80-05-7] M 228.3, m 158°, pK<sub>Est</sub> ~10.3. Crystd from acetic acid/water (1:1).

**Isopropyl iodide** (2-iodopropane) [75-30-9] M 170.0, b 88.9°, d 1.70, n 1.4987. Treated with bromine, followed by extraction of free halogen with aqueous  $Na_2S_2O_3$  or  $NaHSO_3$ , washing with water, drying (MgSO<sub>4</sub> or CaCl<sub>2</sub>) and distn. (The treatment with bromine is optional.) Other purification methods include

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passage through activated alumina, or shaking with copper powder or mercury to remove iodine, drying with  $P_2O_5$  and distn. Washing with conc  $H_2SO_4$  or conc HCl (to remove any alcohol), water, aqueous  $Na_2SO_3$ , water and aqueous  $Na_2CO_3$  has also been used. Treatment with silica gel causes some liberation of iodine. Distillations should be carried out at slightly reduced pressure. Purified isopropyl iodide is stored in the dark in the presence of a little mercury.

Isopropyl methyl ether [598-53-8] M 74.1, b 32.5°/777mm, d<sup>15</sup> 0.724, n 1.3576. Purified by drying with CaSO<sub>4</sub>, passage through a column of alumina (to remove peroxides) and fractional distn.

**Isopropyl** *p*-nitrobenzoate [13756-40-6] M 209.2, m 105-106°. Dissolved in diethyl ether, washed with aqueous alkali, then water and dried. Evapn of the ether and recrystn from EtOH gave pure material.

*p*-Isopropyl toluene (*p*-cymene) [99-87-6] M 134.2, b 176.9°/744mm, d 0.8569, n 1.4902. See entry on p. 183.

**Isoquinoline** [119-65-3] **M 129.2, m 24°, b 120°/18mm, d 1.0986, n 1.6148, pK^{25} 5.40.** Dried with Linde type 5A molecular sieves or Na<sub>2</sub>SO<sub>4</sub> and fractionally distd at reduced pressure. Alternatively, it was refluxed with, and distd from, BaO. Also purified by fractional crystn from the melt and distd from zinc dust. Converted to its *phosphate* (**m** 135°) or *picrate* (**m** 223°), which were purified by crystn and the free base recovered and distd. [Packer, Vaughn and Wong *J Am Chem Soc* 80 905 1958.] The procedure for purifying *via* the picrate comprises the addition of quinoline to picric acid dissolved in the minimum volume of 95% EtOH to yield yellow crystals which are washed with EtOH and air dried before recrystn from acetonitrile. The crystals are dissolved in dimethyl sulfoxide (previously dried over 4A molecular sieves) and passed through a basic alumina column, on which picric acid is adsorbed. The free base in the effluent is extracted with *n*-pentane and distd under vacuum. Traces of solvent are removed by vapour phase chromatography. [Mooman and Anton *J Phys Chem* 80 2243 1976.]

Isovaleric acid [502-74-2] M 102.1, b 176.5°/762mm, d 0.927, n<sup>15</sup> 1.4064, n 1.40331, pK<sup>25</sup> 4.77. Dried with Na<sub>2</sub>SO<sub>4</sub>, then fractionally distd.

L-Isovaline (2-amino-2-methylbutyric acid) [595-40-4] M 117.2, m ca 300° (sublimes in vac),  $[\alpha]_D^{25} + 10^\circ$  (5M HCl), pK<sub>Est(1)</sub>~2.4, pK<sub>Est(2)</sub>~9.7. Crystd from aqueous acetone.

Isovanillin (3-hydroxy-4-methoxybenzaldehyde) [62]-59-0] M 152.2, m 117°, b 175°/14mm, pK<sup>25</sup> 8.89. Cryst from H<sub>2</sub>O or \*C<sub>6</sub>H<sub>6</sub>. The oxime has m 147°.

**Isoviolanthrone** [128-64-3] M 456.5, m 510-511°(uncorrected). Dissolved in 98%  $H_2SO_4$  and ppted by adding water to reduce the acid concentration to about 90%. Sublimes *in vacuo*. [Parkyns and Ubblehode J Chem Soc 4188 1960.]

Itaconic acid (2-propen-1,2-dicarboxylic acid) [97-65-4] M 130.1, m 165-166°,  $pK_1^{25}3.63$ ,  $pK_2^{25}5.00$ . Crystd from EtOH, EtOH/water or EtOH/\*benzene.

Itaconic anhydride (2-propen-1,2-dicarboxylic anhydride) [2170-03-8] M 112.1, m 66-68°, 67-68°, 68°, b 139-140°/30mm. Crystd from CHCl<sub>3</sub>/pet ether. Can be distd under reduced press. Distn at atm press, or prolonged distn causes rearrangement to citraconic anhydride (2-methylmaleic anhydride). If the material (as seen in the IR spectrum) contains much free acid then heat with acetyl chloride or SOCl<sub>2</sub>, evaporate and distil at as high a vacuum as possible. The crude anhydride deposits crystals of itaconic acid on standing probably due to hydrolysis by  $H_2O$  — store in sealed ampoules under dry  $N_2$ . [Org Synth Coll Vol II 369 1943; IR: Nagai Bull Chem Soc Jpn 37 369 1964; Kelly and Segura J Am Chem Soc 56 2497 1934.]

**Janus Green B** (3-dimethylamino-7-[4-dimethylaminoazo]-5-phenylphenazonium chloride) [2869-83-2] M 511.1, m >200°. Dissolves in H<sub>2</sub>O to give a bluish violet soln which becomes colourless when made 10M in. NaOH. Dissolve in EtOH to give a blue-violet colour, filter from insoluble material then add dry  $Et_2O$  whereby the dye separates out leaving a small amount of blue colour in soln. Filter off the solid and dry in vacuum. Store in a dark bottle.

Janus Red B  $\{3-[(2-hydroxy-1-naphtholenyl)azo-2-methylphenylazo]N, N, N-trimethylbenzenaminium chloride\}$  [2636-31-9] M 460.0. Crystd from EtOH/H<sub>2</sub>O (1:1 v/v) and dry in vacuum. Store in a dark bottle.

Jervine  $(3\beta,23\beta-17,23$ -epoxy-2-hydroxyvertraman-11-one, a steroidal alkaloid) [469-59-0] M 425.6, m 243-245°,  $[\alpha]_D^{20}$ -150° (in EtOH), pK<sub>Est</sub>~9.4 Crystd from MeOH/H<sub>2</sub>O. The hydrochloride has m 300-302°. [Kutney et al. Can J Chem 53 1796 1975.]

Julolidine (2,3,6,7-tetrahydro-1H,5H-benzo[*ij*]quinolizidine) [479-59-4] M 173.3, m 34-36°, 40°, b 105-110°/1mm, 155-156°/17mm, 280° (dec), pK<sub>Est</sub> ~7.0. Purified by dissolving in dilute HCl, steam is bubbled through the soln and the residual acidic soln is basified with 10N NaOH, extracted with Et<sub>2</sub>O, washed with H<sub>2</sub>O, dried (NaOH pellets), filtered, evaporated and distd *in vacuo*. The distillate crystallises on standing (m 39-40°). On standing in contact with air for several days it develops a red colour. The colour can be removed by distilling or dissolving in 2-3 parts of hexane, adding charcoal, filtering and cooling in Me<sub>2</sub>CO-Dry-ice when julolidine crystallises (85-90% yield). The *hydrochloride* [83646-41-7] has m 218° (239-242°), the *picrate* has m 165° and the *methiodide* crystallises from MeOH, m 186° [Glass and Weisberger Org Synth Coll Vol III 304 1955.] Highly TOXIC.

**Kainic acid monohydrate** (25,35,45-2-carboxy-4-isoprenyl-3-pyrrolidineacetic acid) [487-79-6] M 231.4, m 235-245° (dec), 251° (dec),  $[\alpha]_D^{20}$  -14.6° (c 1.46, H<sub>2</sub>O), pK<sub>1</sub> 2.09, pK<sub>2</sub> 4.58, pK<sub>3</sub> 10.21. Purified by adsorbing on to a strongly acidic ion exchange resin (Merck), elution of the diacid with aqueous M NaOH, the eluate is evaporated, H<sub>2</sub>O is added, and filtered through a weakly acidic ion exchange resin (Merck). The filtrate is then evaporated and recrystd from EtOH. Its solubility is 0.1g in 1mL of 0.5N HCl. (±)- $\alpha$ -Kainic acid recryst from H<sub>2</sub>O, m 230-260°. UV (MeOH):  $\lambda$ max 219 (log  $\varepsilon$  3.9); <sup>1</sup>H NMR (CCl<sub>4</sub>, 100MHz, Me<sub>4</sub>Si standard)  $\delta$ : 1.64 (s 1H), 1.70 (s 3H), 3.24 (d J 7.5, 2H), 3.3-4.2 (1H), 3.70 (s 3H), 3.83 (s 3H), 4.35 (dd J 7.5, J 14.5, 1H), 5.21 (t J 7.5, 1H), 7.26 (t J 7.5, 1H). [Oppolzer and Andres Helv Chim Acta 62 2282 1979.]

**Kerosene** [8008-20-6] (mixture of hydrocarbons) b ~175-325°, d 0.75-0.82, n 1.443. Stirred with conc H<sub>2</sub>SO<sub>4</sub> until a fresh portion of acid remains colourless, then washed with water, dried with solid KOH and distd in a Claisen flask. For more complete drying, the kerosene can be refluxed with, and distd from Na.

Ketanserine [3(4-p-fluorobenzoylpiperidinyl-N-ethyl)quinazolin-2,4-dione] [74050-98-9] M 395.4, m 227-235°, pK 7.5. Solubility is 0.001% in H<sub>2</sub>O, 0.038% in EtOH and 2.34 in Me<sub>2</sub>NCHO. It has been purified by recrystn from 4-methyl-3-pentanone [Peeters et al. Cryst Structure Commun 11 375 1982; Kacprowicz et al. J Chromatogr 272 417 1983; Davies et al. J Chromatogr 275 232 1983].

**Ketene** [463-51-4] **M 42.0, b 127-130°, d 1.093, n 1.441.** Prepared by pyrolysis of acetic anhydride. Purified by passage through a trap at -75° and collected in a liquid-nitrogen-cooled trap. Ethylene was removed by evacuating the ethylene in an isopentane-liquid-nitrogen slush pack at -160°. Stored at room temperature in a suitable container in the dark. See diketene on p. 209.

2-Keto-L-gulonic acid [526-98-7] M 194.1, m 171°. Crystd from water and washed with acetone.

Ketone moschus (4-tert-butyl-2,6-dimethyl-3,5-dinitroacetophenone) [81-14-1] M 234.1, m 134-137°, 137-138°. Purified by recryst from MeOH. [Fuson et al. J Org Chem 12 587 1947.]

Khellin (4,9-dimethoxy-7-methyl-5-oxofuro[3,2-g]-1,2-chromene) [82-02-0] M 260.3, m 154-155°, b 180-200°/0.05mm. Crystd from MeOH or diethyl ether.

Kojic acid [(2-hydroxy-5-hydroxymethyl)-4H-pyran-4-one] [501-30-4] M 142.1, m 154-155°,  $pK_1^{25}$ -1.38,  $pK_2^{25}$ 7.66. Crystd from MeOH (charcoal) by adding Et<sub>2</sub>O. Sublimed at 0.1 torr.

Kynurenic acid (4-hydroxyquinoline-2-carboxylic acid) [492-27-3] M 189.1, m 282-283°, pK<sub>Est(1)</sub>~2, pK<sub>Est(2)</sub>~10. Crystd from absolute EtOH.

L-Kynurenine [343-65-7] M 208.2, m 190°(dec),  $210^{\circ}(dec)$ ,  $[\alpha]_{D}^{20}$  -30° (c 0.4, H<sub>2</sub>O), pK<sub>Est(1)</sub>~2.3, pK<sub>Est(2)</sub>~3.5, pK<sub>Est(3)</sub>~9.2. Crystd from H<sub>2</sub>O or aq AcOH. *Picrate* has m 188.5-189°(dec) after crystn from H<sub>2</sub>O.

L-Kynurenine sulfate [16055-80-4] M 306.3, m 194°, monohydrate m 178°,  $[\alpha]_D^{25}$ +9.6° (H<sub>2</sub>O). Crystd from water by addition of EtOH.

L(+)-Lactic acid [79-33-4] M 90.1, m 52.8°, b  $105^{\circ}/0.1$ mm,  $[\alpha]_D^{20}$  +3.82° (H<sub>2</sub>O), pK<sup>31</sup> 3.83. Purified by fractional distn at 0.1mm pressure, followed by fractional crystn from diethyl ether/isopropyl ether (1:1, dried with sodium). [Borsook, Huffman and Liu *J Biol Chem* 102 449 1933.] The solvent mixture, \*benzene/diethyl ether (1:1) containing 5% pet ether (b 60-80°) has also been used.

Lactobionic acid [96-82-2] M 358.3, m 128-130°,  $[\alpha]_{546}^{20}$  +28° (c 3, after 24h in H<sub>2</sub>O), pK<sub>Est</sub> ~3.6. Crystd from water by addition of EtOH.

 $\alpha$ -Lactose (H<sub>2</sub>O) [63-42-3] M 360.3, m 220°(dec),  $[\alpha]_D^{20}$  +52.3° (c 4.2, H<sub>2</sub>O), pK 12.2 (OH). Crystd from water below 93.5°.

Lactulose [4618-18-2] M 342.2, m 167-169°(dec), [a]<sup>20</sup><sub>546</sub> -57° (c 1, H<sub>2</sub>O). Crystd from MeOH.

Lanatoside A [17575-20-1] M 969.1, m 245-248°, [a]<sub>D</sub><sup>20</sup> +32° (EtOH). Crystd from MeOH.

Lanatoside B [17575-21-2] M 985.1, m 233°(dec),  $[\alpha]_D^{20}$  +35° (MeOH). Crystd from MeOH.

Lanatoside C [17575-22-3] M 297.1, m 246-248°, [a]<sub>D</sub><sup>20</sup> +34° (EtOH). Crystd from MeOH.

**Lanosterol** [79-63-0] **M 426.7, m 138-140°,**  $[\alpha]_D^{20}$ +62.0° (c 1, CHCl<sub>3</sub>). Recrystd from anhydrous MeOH. Dried *in vacuo* over P<sub>2</sub>O<sub>5</sub> for 3h at 90°. Purity checked by proton magnetic resonance.

Lanthanide shift reagents A variety of these reagents are available commercially and they are generally quite stable and should not deteriorate on long storage in a dry state and in the absence of light. [See G.R.Sullivan in *Top Stereochem* (Eliel and Allinger Eds) J Wiley & Sons Vol 10 287 1978; T.C.Morrill Ed. Lanthanide Shift Reagents Deerfield Beach Florida 1986, ISBN 0895731193.]

Lapachol [84-79-7] M 226.3, m 140°. Crystd from EtOH or diethyl ether.

*dl- and l-Laudanosine*  $[(\pm) 1699-51-0; (-) 2688-77-9]$  M 357.4, m 114-115°. Crystd from EtOH. The (-)-isomer has m 83-85° and  $[\alpha]_D^{20}$ -85° (c 0.5, EtOH).

Lauraldehyde (1-dodecanal) [112-54-9] M 184.3, b 99.5-100°/3.5mm,  $n^{24.7}$  1.4328. Converted to the addition compound by shaking with saturated aqueous NaHSO<sub>3</sub> for 1h. The ppte was filtered off, washed with ice cold water, EtOH and ether, then decomposed with aqueous Na<sub>2</sub>CO<sub>3</sub>. The aldehyde was extracted into diethyl ether which, after drying and evap, gave an oil which was fractionally distd under vacuum.

Lauric acid (1-dodecanoic acid) [143-07-7] M 200.3, m 44.1°, b 141-142°/0.6-0.7 mm, 225°/100 mm, pK<sup>20</sup> 5.3. Vacuum distd. Crystd from absolute EtOH, or from acetone at -25°.

Alternatively, purified via its methyl ester (b 140.0%/15mm), as described for capric acid. Also purified by zone melting.

Lauryl peroxide (dodecyl peroxide) [105-74-8] M 398.6, m 53-54°. Crystd from *n*-hexane or \*benzene and stored below 0°. Potentially EXPLOSIVE.

L-Leucine [61-90-5] M 131.2, m 293-295°(dec),  $[\alpha]_D^{25}$  +15.6° (5M HCl),  $pK_1^{25}$  2.33,  $pK_2^{25}$  9.74. Likely impurities are isoleucine, valine, and methionine. Crystd from water by adding 4 volumes of EtOH.

Leucomalachite Green [129-73-7] M 330.5, m 92-93°, pK<sup>25</sup> 6.90 (several pK's). Crystd from 95% EtOH (10mL/g), then from \*benzene/EtOH, and finally from pet ether.

Lithocholic acid [434-13-9] M 376.6, m 184-186°,  $[\alpha]_D^{23} + 35^\circ$  (c 1, EtOH), pK<sub>Est</sub> ~4.8. Crystd from EtOH or acetic acid.

Lumichrome [1086-80-2] M 242.2, m >290°,  $pK_{Est(1)}$ ~-0.1 (basic),  $pK_{Est(2)}$ ~9.9 (acidic), Recrystd twice from glacial AcOH and dried at 100° in a vacuum.

Luminol (5-aminophthalazin-1,4-dione) [521-31-3] M 177.2, m 329-332°, pK<sub>1</sub> 3.37, pK<sub>2</sub> 6.35. Dissolved in KOH soln, treated with Norit (charcoal), filtered and ppted with conc HCl. [Hardy, Sietz and Hercules *Talanta* 24 297 1977.] Stored in the dark in an inert atmosphere, because its structure changes during its luminescence. It has been recrystd from 0.1M KOH [Merenyi et al. J Am Chem Soc 108 77716 1986].

dl-Lupinane [10248-30-3] M 169.3, m 98-99°. Crystd from acetone.

Lupulon [468-28-0] M 414.6, m 92-94°. Crystd from 90% MeOH.

Lutein ( $\alpha$ -carotene-3,3'-diol, xanthophyll) [127-40-2] M 568.9, m 196°,  $\varepsilon_{1cm}^{1\%}$  1750 (423nm), 2560 (446nm), 2340 (477.5nm) in EtOH;  $\lambda_{max}$  in CS<sub>2</sub> 446, 479 and 511nm. Crystd from MeOH (copper-coloured prisms) or from diethyl ether by adding MeOH. Also purified by chromatography on columns of magnesia or calcium hydroxide, and crystd from CS<sub>2</sub>/EtOH. May be purified via the dipalmitate ester. Stored in the dark, in an inert atmosphere.

Lutidine (mixture). For the preparation of pure 2,3-, 2,4- and 2,5-lutidine from commercial "2,4- and 2,5-lutidine" see Coulson et al. J Chem Soc 1934 1959, and Kyte, Jeffery and Vogel J Chem Soc 4454 1960.

**2,3-Lutidine** [583-61-9] **M 107.2, f -14.8°, b 160.6°, d 0.9464, n 1.50857, pK^{25} 6.57.** Steam distd from a soln containing about 1.2 equivalents of 20% H<sub>2</sub>SO<sub>4</sub>, until *ca* 10% of the base has been carried over with the non-basic impurities. The acid soln was then made alkaline, and the base was separated, dried over NaOH or BaO, and fractionally distd. The distd lutidine was converted to its urea complex by stirring 100g with 40g of urea in 75mL of H<sub>2</sub>O, cooling to 5°, filtering at the pump, and washing with 75mL of H<sub>2</sub>O. The complex, dissolved in 300mL of H<sub>2</sub>O was steam distd until the distillate gave no turbidity with a little solid NaOH. The distillate was then treated with excess solid NaOH, and the upper layer was removed: the aqueous layer was then extracted with diethyl ether. The upper layer and the ether extract were combined, dried (K<sub>2</sub>CO<sub>3</sub>), and distd through a short column. Final purification was by fractional crystn using partial freezing. [Kyte, Jeffery and Vogel J Chem Soc 4454 1960].

**2,4-Lutidine** [108-47-4] M **107.2, b 157.8°, d 0.9305, n 1.50087, n^{25} 1.4985, pK^{25} 6.77. Dried with Linde type 5A molecular sieves, BaO or sodium, and fractionally distd. The distillate (200g) was heated with \*benzene (500mL) and conc HCl (150mL) in a Dean and Stark apparatus on a water bath until water no longer separated, and the temperature just below the liquid reached 80°. When cold, the supernatant \*benzene was decanted and the 2,4-lutidine hydrochloride, after washing with a little \*benzene, was dissolved in water (350mL). After removing any \*benzene by steam distn, an aqueous soln of NaOH (80g) was added, and the free** 

lutidine was steam distd. It was isolated by saturating the distillate with solid NaOH, and distd through a short column. The pptn cycle was repeated, then the final distillate was partly frozen in an apparatus at -67.8-68.5° (cooled by acetone/CO<sub>2</sub>). The crystals were then melted and distd. [Kyte, Jeffery and Vogel J Chem Soc 4454 1960.] Alternative purifications are via the picrate [Clarke and Rothwell J Chem Soc 1885 1960], or the hydrobromide [Warnhoff J Org Chem 27 4587 1962]. The latter is ppted from a soln of lutidine in \*benzene by passing dry HBr gas: the salt is recrystd from CHCl<sub>3</sub>/methyl ethyl ketone, then decomposed with NaOH, and the free base is extracted into diethyl ether, dried, evaporated and the residue distd.

**2,5-Lutidine** [589-93-5] **M 107.2, m -15.3°, b 156.7°/759mm, d 0.927, n^{25} 1.4982, pK^{25} 6.40. Steam distd from a soln containing 1-2 equivalents of 20% H<sub>2</sub>SO<sub>4</sub> until about 10% of the base had been carried over with the non-basic impurities, then the acid soln was made alkaline, and the base separated, dried with NaOH and fractionally distd twice.** Dried with Na and fractionally distd through a Todd column packed with glass helices (see p. 174).

**2,6-Lutidine** [108-48-5] **M 107.2, m -59°, b 144.0°, d 0.92257, n 1.49779, pK^{25} 6.72.** Likely contaminants include 3- and 4-picoline (similar boiling points). However, they are removed by using BF<sub>3</sub>, with which they react preferentially, by adding 4mL of BF<sub>3</sub> to 100mL of dry fractionally distd 2,6-lutidine and redistilling. Distn of commercial material from AlCl<sub>3</sub> (14g per 100mL) can also be used to remove picolines (and water). Alternatively, lutidine (100mL) can be refluxed with ethyl benzenesulfonate (20g) or ethyl *p*-toluenesulfonate (20g) for 1h, then the upper layer is cooled, separated and distd. The distillate is refluxed with BaO or CaH<sub>2</sub>, then fractionally distd, through a glass helices-packed column.

2,6-Lutidine can be dried with KOH or sodium, or by refluxing with (and distilling from) BaO, prior to distn. For purification via its picrate, 2,6-lutidine, dissolved in abs EtOH, is treated with an excess of warm ethanolic picric acid. The ppte is filtered off, recrystd from acetone (to give **m** 163-164.5°), and partitioned between ammonia and CHCl<sub>3</sub>/diethyl ether. The organic soln, after washing with dilute aqueous KOH, is dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd. [Warnhoff *J Org Chem* **27** 4587 1962.] Alternatively, 2,6-lutidine can be purified *via* its urea complex, as described under 2,3-lutidine. Other purification procedures include azeotropic distn with phenol [Coulson et al. *J Appl Chem (London)* **2** 71 1952], fractional crystn by partial freezing, and vapour-phase chromatography using a 180-cm column of polyethylene glycol-400 (Shell, 5%) on Embacel (May and Baker) at 100°, with argon as carrier gas [Bamford and Block *J Chem Soc* 4989 1961].

**3,5-Lutidine** [591-22-0] **M 107.2, f -6.3°, b 172.0°/767mm, d 0.9419, n 1.50613, n<sup>2 5</sup> 1.5035, pK<sup>2 5</sup> 6.15.** Dried with sodium and fractionally distd through a Todd column packed with glass helices (see p. 174). Dissolved (100mL) in dil HCl (1:4) and steam distd until 1L of distillate was collected. Excess conc NaOH was added to the residue which was again steam distd. The base was extracted from the distillate, using diethyl ether. The extract was dried with K<sub>2</sub>CO<sub>3</sub>, and distd. It was then fractionally crystd by partial freezing.

Lycopene [502-65-8] M 536.9, m 172-173°,  $\varepsilon_{1cm}^{1\%}$  2250 (446nm), 3450 (472nm), 3150 (505nm) in pet ether. Crystd from CS<sub>2</sub>/MeOH, diethyl ether/pet ether, or acetone/pet ether, and purified by column chromatography on deactivated alumina, CaCO<sub>3</sub>, calcium hydroxide or magnesia. Stored in the dark, in an inert atmosphere.

Lycorine [476-28-8] M 552.9, m 275-280°(dec)  $[\alpha]_D^{20}$  -130° (c 0.16, EtOH). Crystd from EtOH.

Lycoxanthin  $(\Psi, \Psi$ -carotene-16-ol) [19891-74-8] M 268.3, m 173-174°,  $\varepsilon_{1 \text{ cm}}^{1\%}$  3360 (472.5nm), also  $\lambda_{\text{max}}$  444 and 503nm in pet ether. Crystd from diethyl ether/light petroleum, \*benzene/pet ether or CS<sub>2</sub>. Purified by chromatography on columns of CaCO<sub>3</sub>, Ca(OH)<sub>2</sub> or deactivated alumina, washing with \*benzene and eluting with 3:1 \*benzene/MeOH. Stored in the dark, in an inert atmosphere, at -20°.

Lysergic acid [82-58-6] M 268.3, m 240°(dec),  $[\alpha]_D^{20}$  +40° (pyridine),  $pK_1^{25}3.32$ ,  $pK_2^{25}7.82$ . Crystd from water.

L-Lysine [56-87-1] M 146.2,  $m > 210^{\circ}(dec)$ ,  $pK_1 2.18$ ,  $pK_2 8.95$ ,  $pK_3 10.53$ . Crystd from aqueous EtOH.

**L-Lysine dihydrochloride** [657-26-1] **M 219.1, m 193°,**  $[\alpha]_D^{25}$  +25.9° (5M HCl). Crystd from MeOH, in the presence of excess HCl, by adding diethyl ether.

**L-Lysine monohydrochloride** [657-27-2] **M 182.7,**  $[\alpha]$  as above. Likely impurities are arginine, D-lysine, 2,6-diaminoheptanedioic acid and glutamic acid. Crystd from water at pH 4-6 by adding 4 volumes of EtOH. Above 60% relative humidity it forms a dihydrate.

 $\beta$ -D-Lyxose [1114-34-7] M 150.1, m 118-119°,  $[\alpha]_D^{20}$  -14° (c 4, H<sub>2</sub>O). Crystd from EtOH or aqueous 80% EtOH. Dried under vacuum at 60°, and stored in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> or CaSO<sub>4</sub>.

**Malachite Green (carbinol)** [510-13-4] M 346.4, m 112-114°, CI 42000,  $pK^{24}$  6.84. The oxalate was recrystd from hot water and dried in air. The carbinol was ppted from the oxalate (1g) in distd water (100mL) by adding M NaOH (10mL). The ppte was filtered off, recrystd from 95% EtOH containing a little dissolved KOH, then washed with ether, and crystd from pet ether. Dried in a vacuum at 40°. An acid soln (2 x 10<sup>-5</sup>M in 6 x 10<sup>-5</sup>M H<sub>2</sub>SO<sub>4</sub>) rapidly reverted to the dye. [Swain and Hedberg J Am Chem Soc 72 3373 1950.]

Z-Maleamic acid (cis-maleic acid monoamide) [557-24-4] M 115.1, m 158-161°, 172-173°(dec), pK<sub>Est</sub> ~2.65. Crystd from EtOH. IRRITANT.

Maleic acid [110-16-7] M 116.1, m 143.5°,  $pK_1^{25}$  1.91,  $pK_2^{25}$  6.33. Crystd from acetone/pet ether (b 60-80°) or hot water. Dried at 100°.

Maleic anhydride [108-31-6] M 98.1, m 54°, b 94-96°/20mm, 199°/760mm. Crystd from \*benzene, CHCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub> or CCl<sub>4</sub>. Sublimed under reduced pressure. [Skell et al. J Am Chem Soc 108 6300 1986.]

Maleic hydrazide [123-33-1] M 112.1, m 144°(dec), pK<sub>1</sub><sup>25</sup> 5.67, pK<sub>2</sub><sup>25</sup> 13.3. Crystd from water.

Maleimide (pyrrol-2,5-dione) [541-59-3] M 97.1, m 91-93°, 92.6-93°,  $d_D^{105.5}$  1.2493,  $n_D^{110.7}$  1.49256. Purified by sublimation in a vacuum. The UV has  $\lambda_{max}$  at 216 and 280nm in EtOH. [de Wolf and van de Straete *Bull Soc Chim Belg* 44 288 1935; UV: Rondestvedt et al. *J Am Chem Soc* 78 6115 1956; IR: Chiorboli and Mirone Ann Chim (Rome) 42 681 1952.]

Maleuric acid [105-61-3] M 158.1, m 167-168°(dec). Crystd from hot water.

*dl*-Malic acid [617-48-1 and 6915-15-7] M 134.1, m 128-129°. Crystd from acetone, then from acetone/CCl<sub>4</sub>, or from ethyl acetate by adding pet ether (b 60-70°). Dried at 35° under 1mm pressure to avoid formation of the anhydride.

L-Malic acid [97-67-6] M 134.1, m 104.5-106°,  $[\alpha]_D^{20}$  -2.3° (c 8.5, H<sub>2</sub>O),  $pK_1^{25}$  3.46,  $pK_2^{25}$  5.10. Crystd (charcoal) from ethyl acetate/pet ether (b 55-56°), keeping the temperature below 65°. Or, dissolved by refluxing in fifteen parts of anhydrous diethyl ether, decanted, concentrated to one-third volume and crystd at 0°, repeatedly to constant melting point.

Malonamide [108-13-4] M 102.1, m 170°. Crystd from water.

**Malonic acid** [141-82-2] **M 104.1, m 136°, pK\_1^{2^5} 2.58, pK\_2^{2^5} 5.69.** Crystd from \*benzene/diethyl ether (1:1) containing 5% of pet ether (b 60-80°), washed with diethyl ether, then recrystd from H<sub>2</sub>O or acetone. Dried under vac over conc H<sub>2</sub>SO<sub>4</sub>.

Malononitrile [109-77-3] M 66.1, m 32-34°, b 109°/20mm, 113-118°/25mm, 220°/760mm. Crystd from water, EtOH, \*benzene or chloroform. Distd in a vacuum from, and stored over,  $P_2O_5$ . [Bernasconi et al. J Am Chem Soc 107 7692 1985; Gratenhuis J Am Chem Soc 109 8044 1987].

Maltol (3-hydroxy-2-methyl-4-pyrone) [118-71-8] M 126.1, m 161-162°. Crystd from CHCl<sub>3</sub> or aqueous 50% EtOH. Volatile in steam. It can be readily sublimed in a vacuum.

**Maltose** (H<sub>2</sub>O) [6363-53-7] M **360.3, m 118°.** Purified by chromatography from aqueous soln on to a charcoal/Celite (1:1) column, washed with water to remove glucose and other monosaccharides, then eluted with aqueous 75% EtOH. Crystd from water, aqueous EtOH or EtOH containing 1% nitric acid. Dried as the monohydrate at room temperature under vacuum over  $H_2SO_4$  or  $P_2O_5$ .

Mandelic acid ( $\alpha$ -hydroxyphenylacetic acid) [S-(+)- 17199-29-0; R-(-)- 611-71-2] M 152.2, m 130-133°, 133°, 133.1° (evacuated capillary), 133-133.5°,  $[\alpha]_{546}^{20}$  (+) and (-) 188° (c 5, H<sub>2</sub>O),  $[\alpha]_D^{20}$  (+) and (-) 155° (c 5, H<sub>2</sub>O) and (+) and (-) 158° (c 5, Me<sub>2</sub>CO), pK<sup>25</sup> 3.41. Purified by recrystn from H<sub>2</sub>O, \*C<sub>6</sub>H<sub>6</sub> or CHCl<sub>3</sub> [Roger J Chem Soc 2168 1932; Jamison and Turner J Chem Soc 611 1942.] They have solubilities in H<sub>2</sub>O of ca 11% at 25°. [Banks and Davies J Chem Soc 73 1938.] The S-benzylisothiuronium salt has m 180° (from H<sub>2</sub>O) and  $[\alpha]_D^{25}$  (+) and (-) 57° (c 20, EtOH) [El Masri et al. Biochem J 68 199 1958].

**RS**-(±)-Mandelic acid [61-72-3] M 152.2, m 118°, 120-121°. Purified by Soxhlet extraction with \*benzene (about 6mL/g), allowing the extract to crystallise. Also crystallises from CHCl<sub>3</sub>. The *S*-benzylisothiuronium salt has m 169° (166°) (from H<sub>2</sub>O). Dry at room temperature under vacuum.

**D-Mannitol** [69-65-8] **M 182.2, m 166.1°,**  $[\alpha]_{546}^{20}$  + 29° (c 10, after 1h in 8% borax soln). Crystd from EtOH or distilled water and dried at 100°.

Mannitol hexanitrate [15825-70-4] M 452.2, m 112-113°. Crystd from EtOH. EXPLOSIVE (on detonation).

 $\alpha$ -D-Mannose [3458-28-4] M 180.2, m 132°,  $[\alpha]_D^{20}$  +14.1° (c 4, H<sub>2</sub>O). Crystd repeatedly from EtOH or aq 80% EtOH, then dried under vacuum over P<sub>2</sub>O<sub>5</sub> at 60°.

Meconic acid (3-hydroxy- $\gamma$ -pyrone-2,6-dicarboxylic acid) [497-59-6] M 200.1, m 100° (loses H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup> 1.83, pK<sub>2</sub><sup>25</sup> 2.3, pK<sub>3</sub><sup>25</sup> 10.10. Crystd from water and dried at 100° for 20min.

Melamine (2,4,6-triamino-1,3,5-triazine) [108-78-1] M 126.1, m 353°, pK<sup>25</sup> 5.00. Crystd from water or dilute aqueous NaOH.

D(+)-Melezitose (H<sub>2</sub>O) [597-12-6] M 540.5, m 153-154°(dec),  $2H_2O$  m 160°(dec),  $[\alpha]_D^{20}$ +88° (c 4, H<sub>2</sub>O). Crystallises from water as the dihydrate, then dried at 110° (anhydrous).

D(+)-Melibiose (2H<sub>2</sub>O) [585-99-9, 66009-10-7] M 360.3, m 84-85°,  $[\alpha]_D^{20}$ +135° (c 5, after 10h H<sub>2</sub>O). Crystallises as a hydrate from water or aqueous EtOH.

(±)-Mellein [(±)-3,4-dihydro-8-hydroxy-3-methyl-2-benzopyran-1-one] [1200-93-7] M 178.2, m 37-39°, 39°, pK<sub>Est</sub> ~9.5. Purified by recrystn from aqueous EtOH. It has UV max at 247 and 314nm. [Arakawa et al. Justus Liebigs Ann Chem 728 152 1969; Blair and Newbold Chem Ind (London) 93 1955, J Chem Soc 2871 1955.] The methyl ether has m 66-67° and UV:  $\lambda$ max 242nm ( $\varepsilon$  7,400) and 305nm ( $\varepsilon$  4,600).

Melphalan (4-[bis-{2-chloroethyl}amino]-L-phenylalanine) [148-82-3] M 305.2, m 182-183° (dec), 183-185°,  $[\alpha]_D^{25}$ +7.5° (c 1.33, 1.0 N HCl),  $[\alpha]_D^{20}$ -28° (c 0.8, MeOH), pK<sub>Est</sub> ~6.4. Purified by recrystn from MeOH and its solubility is 5% in 95% EtOH containing one drop of 6N HCl. It is soluble in EtOH and propylene glycol but is almost insoluble in H<sub>2</sub>O. The *RS-form* has **m** 180-181° and the *R-form* crystallises from MeOH with a **m** 181.5-182° and  $[\alpha]_D^{21}$  -7.5° (c 1.26, 1.0 N HCl). [Bergel and Stock *J Chem Soc* 2409 1954.]

(-)-Menthol [2216-51-5] M 156.3, m 44-46.5°,  $[\alpha]_D 50^\circ$  (c 10, EtOH). Crystd from CHCl<sub>3</sub>, pet ether or EtOH/water.

1*R*-(-)-Menthyl chloride (1*S*,2*R*,4*R*-2-chloro-1-isopropyl-1-methylcyclohexane) [16052-42-9] M 174.7, m -20.1° to -16.5°, b 88.5°/12.5mm, 101-105°/21mm,  $d_D^{2,0}$  0.936,  $n_D^{2,0}$ 1.463(neat). Dissolve in pet ether (b 40-60°), wash with H<sub>2</sub>O, conc H<sub>2</sub>SO<sub>4</sub> until no discoloration of the organic layer occurs (care with the use of conc H<sub>2</sub>SO<sub>4</sub> during shaking in a separating funnel), again with H<sub>2</sub>O and dry over MgSO<sub>4</sub>. Evaporate the pet ether and dist the residual oil through a Claisen head with a Vigreux neck (head) of *ca* 40 cm length. [Smith and Wright *J Org Chem* 17 1116 1952; Barton et al. *J Chem Soc* 453 1952.]

Meprobamate [2,2-di(carbamoyloxymethyl)pentane] [57-53-4] M 246.3, m 104-106°. Crystd from hot water. Could be an addictive drug.

**2-Mercaptobenzimidazole** [583-39-1] **M 150.2, m 302-304°, 312°, pK<sup>20</sup> 10.24.** Crystd from aq EtOH, AcOH or aq ammonia.

**2-Mercaptobenzothiazole** [149-30-4] M 167.2, m 182°,  $pK^{25}$  7.5 (50% aq AcOH). Crystd repeatedly from 95% EtOH, or purified by incomplete pptn by dilute H<sub>2</sub>SO<sub>4</sub> from a basic soln, followed by several crystns from acetone/H<sub>2</sub>O or \*benzene. Complexes with Ag, Au, Bi, Cd, Hg, Ir, Pt, and Tl.

2-Mercaptoethanol [60-24-2] M 78.1, b 44°/4mm, 53.5°/10mm, 58°/12mm, 68°/20mm, 78.5°/40mm, 96-97° (92°)/100mm, 157°/748mm,  $d_4^{20}$  1.114,  $n_D^{20}$  1.500,  $pK^{25}$  9.72 (9.43). Purified by distn in a vacuum. Distn at atmospheric pressure causes some oxidation and should be done in an inert atmosphere. [Woodward J Chem Soc 1892 1948.] It has a foul odour, is irritating to the eyes, nose and skin — should be handled in an efficient fume cupboard. It is miscible with H<sub>2</sub>O, EtOH, Et<sub>2</sub>O and \*C<sub>6</sub>H<sub>6</sub> and has a UV max at 235nm. The 2,4-dinitrophenyl thioether has m 101-102°(from EtOH or aq MeOH) [Grogen et al. J Org Chem 20 50 1955].

2-Mercaptoethylamine [60-23-1] M 77.2. See cysteamine p. 525 in Chapter 6.

2-Mercaptoimidazole [872-35-5] M 100.1, m 221-222°, pK<sub>1</sub><sup>20</sup>-1.6, p K<sub>2</sub><sup>20</sup>11.6. Crystd from H<sub>2</sub>O.

**2-Mercapto-1-methylimidazole** [60-56-0] **M 114.2, m 145-147°, pK\_1^{20}-2.0, p K \_2^{20} 11.9. Crystd from EtOH.** 

**6-Mercaptopurine** (H<sub>2</sub>O) [6112-76-1] M 170.2, m >315°(dec),  $pK_1^{20}$  0.5,  $pK_2^{20}$  7.77,  $pK_3^{20}$  10.8. Crystd from pyridine (30mL/g), washed with pyridine, then triturated with water (25mL/g), adjusting to pH 5 by adding M HCl. Recrystd by heating, then cooling, the soln. Filtered, washed with water and dried at 110°. Has also been crystd from water (charcoal).

8-Mercaptoquinoline (2H<sub>2</sub>O, thioxine) [491-33-8] M 197.3, m 58-59°,  $pK_1^{25}$  2.0,  $pK_2^{25}$  8.40. Easily oxidised in air to give diquinolyl-8,8'-disulfide (which is stable). It is more convenient to make 8-mercaptoquinoline by reduction of the material. [Nakamura and Sekido *Talanta* 17 515 1970.]

Mesaconic acid (methylfumaric acid) [498-24-8] M 130.1, m 204-205°, pK<sup>18</sup> 4.82. Crystd from water or EtOH [Katakis et al. J Chem Soc, Dalton Trans 1491 1986].

Mescaline sulfate [2-(3,4,5-trimethoxyphenyl)ethylamine sulfate] [5967-42-0] M 309.3, m 183-184°, pK<sub>Est</sub> ~9.7. Crystd from water.

Mesitylene (1,3,5-trimethylbenzene) [108-67-8] M 120.2, m -44.7°, b 99.0-99.8°/100 mm, 166.5-167°/760 mm,  $n^{25}$  1.4967, d 0.865. Dried with CaCl<sub>2</sub> and distd from Na in a glass helices packed column. Treated with silica gel and redistd. Alternative purifications include vapour-phase chromatography, or fractional distn followed by azeotropic distn with 2-methoxyethanol (which is subsequently washed out with H<sub>2</sub>O), drying and fractional distn. More exhaustive purification uses sulfonation by dissolving in two volumes of conc H<sub>2</sub>SO<sub>4</sub>, precipitating with four volumes of conc HCl at 0°, washing with conc HCl and recrystallising from CHCl<sub>3</sub>. The mesitylene sulfonic acid is hydrolysed with boiling 20% HCl and steam distd. The separated mesitylene is dried (MgSO<sub>4</sub> or CaSO<sub>4</sub>) and distilled. It can also be fractionally crystd from the melt at low temperatures.

Mesityl oxide [141-79-7] M 98.2, b 112°/760mm,  $n^{24}$  1.4412, d 0.854,  $pK^{20}$  -5.36 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). Purified via the semicarbazone (m 165°). [Erskine and Waight J Chem Soc 3425 1960.]

Metalphthalein (H<sub>2</sub>O) (o-cresolcomplexon) [2411-89-4] M 636.6, m 186<sup>o</sup>(dec). See ocresolphthalein complexone on p. 173.

Metanilic acid (3-aminobenzenesulfonic acid) [121-47-1] M 173.2, m <300°(dec),  $pK_1^{25} < 1$ ,  $pK_2^{25}$  3.74. Crystd from water (as the hydrate), under CO<sub>2</sub> in a semi-darkened room. (The soln is photosensitive.) Dried over 90% H<sub>2</sub>SO<sub>4</sub> in a vac desiccator.

α-Methacraldehyde [78-85-3] M 68.1, b 68.4°, d 0.849, n 1.416. Fractionally distd under nitrogen through a short Vigreux column. Stored in sealed ampoules. (Slight polymerisation may occur.)

Methacrylamide [79-39-0] M 85.1, m 111-112°. Crystd from \*benzene or ethyl acetate and dried under vacuum at room temperature.

Methacrylic acid [79-41-4] M 86.1, b 72°/14mm, 160°/760mm, d 1.015, n 1.431, pK 4.65. Aq methacrylic acid (90%) was satd with NaCl (to remove the bulk of the water), then the organic phase was dried with CaCl<sub>2</sub> and distd under vacuum. Polymerisation inhibitors include 0.25% *p*-methoxyphenol, 0.1% hydroquinone, or 0.05% *N*,N'-diphenyl-*p*-phenylenediamine.

Methacrylic anhydride [760-93-0] M 154.2, b 65°/2mm, d 1.040, n 1.454. Distd at 2mm pressure, immediately before use, in the presence of hydroquinone.

Methacrylonitrile [126-98-7] M 67.1, b 90.3°, d 0.800, n 1.4007,  $n^{30}$  1.3954. Washed (to remove inhibitors such as *p-tert*-butylcatechol) with satd aq NaHSO<sub>3</sub>, 1% NaOH in saturated NaCl and then with saturated NaCl. Dried with CaCl<sub>2</sub> and fractionally distd under nitrogen to separate from impurities such as methacrolein and acetone.

Methane [74-82-8] M 16.0, m -184°, b -164°/760mm, -130°/6.7atm, d<sup>-164</sup> 0.466 (air 1). Dried by passage over CaCl<sub>2</sub> and P<sub>2</sub>O<sub>5</sub>, then passed through a Dry-ice trap and fractionally distd from a liquidnitrogen trap. Oxygen can be removed by prior passage in a stream of hydrogen over reduced copper oxide at 500°, and higher hydrocarbons can be removed by chlorinating about 10% of the sample: the hydrocarbons, chlorides and HCl are readily separated from the methane by condensing the sample in the liquid-nitrogen trap and fractionally distilling it. Methane has also been washed with conc H<sub>2</sub>SO<sub>4</sub>, then solid NaOH and then 30% NaOH soln. It was dried with CaCl<sub>2</sub>, then P<sub>2</sub>O<sub>5</sub>, and condensed in a trap at liquid air temp, then transferred to another trap cooled in liquid nitrogen. CO<sub>2</sub>, O<sub>2</sub>, N<sub>2</sub> and higher hydrocarbons can be removed from methane by adsorption on charcoal. [Eiseman and Potter J Res Nat Bur Stand 58 213 1957.] HIGHLY FLAMMABLE.

Methanesulfonic acid [76-75-2] M 96.1, m 20°, b 134.5-135°/3mm, d 1.483, n 1.432,  $pK^{25}$ -1.86 (-1.2). Dried, either by azeotropic removal of water with \*benzene or toluene, or by stirring 20g of P<sub>2</sub>O<sub>5</sub> with 500mL of the acid at 100° for 0.5h. Then distd under vacuum and fractionally crystd by partial freezing. Sulfuric acid, if present, can be removed by prior addition of  $Ba(OH)_2$  to a dilute soln, filtering off the  $BaSO_4$  and concentrating under reduced pressure, and is sufficiently pure for most applications.

Methanesulfonyl chloride [124-63-0] M 114.5. b 55 $^{\circ}$ /11mmm, d 1.474, n 1.452. Distd from  $P_2O_5$  under vacuum.

[67-56-1] M 32.0, b 64.5°, d<sup>15</sup> 0.79609, d<sup>25</sup> 1.32663, n<sup>15</sup> 1.33057, n<sup>25</sup> 1.32663, Methanol pK<sup>25</sup> 15.5. Almost all methanol is now obtained synthetically. Likely impurities are water, acetone, formaldehyde, ethanol, methyl formate and traces of dimethyl ether, methylal, methyl acetate, acetaldehyde, carbon dioxide and ammonia. Most of the water (down to about 0.01%) can be removed by fractional distn. Drying with CaO is unnecessary and wasteful. Anhydrous methanol can be obtained from "absolute" material by passage through Linde type 4A molecular sieves, or by drying with CaH<sub>2</sub>, CaSO<sub>4</sub>, or with just a little more sodium than required to react with the water present; in all cases the methanol is then distd. Two treatments with sodium reduces the water content to about 5 x  $10^{-5}$ %. [Friedman, Gill and Doty J Am Chem Soc 83 4050 1961.] Lund and Bjerrum [Chem Ber 64 210 1931] warmed clean dry magnesium turnings (5g) and iodine (0.5g) with 50-75mL of "absolute" methanol in a flask until the iodine disappeared and all the magnesium was converted to methoxide. Up to 1L of methanol was added and, after refluxing for 2-3h, it was distd off, excluding moisture from the system. Redistn from tribromobenzoic acid removes basic impurities and traces of magnesium oxides, and leaves conductivity-quality material. The method of Hartley and Raikes [J Chem Soc 127 524 1925] gives a slightly better product. This consists of an initial fractional distn, followed by distn from aluminium methoxide, and then ammonia and other volatile impurities are removed by refluxing for 6h with freshly dehydrated CuSO<sub>4</sub> (2g/L) while dry air is passed through: the methanol is finally distd. (The aluminium methoxide is prepared by warming with aluminium amalgam (3g/L) until all the aluminium has reacted. The amalgam is obtained by warming pieces of sheet aluminium with a soln of HgCl<sub>2</sub> in dry methanol). This treatment also removes aldehydes.

If acetone is present in the methanol, it is usually removed prior to drying. Bates, Mullaly and Hartley [*J Chem* Soc 401 1923] dissolved 25g of iodine in 1L of methanol and then poured the soln, with constant stirring, into 500mL of M NaOH. Addition of 150mL of water ppted iodoform. The soln was stood overnight, filtered, then boiled under reflux until the odour of iodoform disappeared, and fractionally distd. (This treatment also removes formaldehyde.) Morton and Mark [*Ind Eng Chem* (Anal Edn) 6 151 1934] refluxed methanol (1L) with furfural (50mL) and 10% NaOH soln (120mL) for 6-12h, the refluxing resin carrying down with it the acetone and other carbonyl-containing impurities. The alcohol was then fractionally distd. Evers and Knox [*J Am Chem Soc* 73 1739 1951], after refluxing 4.5L of methanol for 24h with 50g of magnesium, distd off 4L of it, which they then refluxed with AgNO<sub>3</sub> for 24h in the absence of moisture or CO<sub>2</sub>. The methanol was again distd, shaken for 24h with activated alumina before being filtered through a glass sinter and distd under nitrogen in an all-glass still. Material suitable for conductivity work was obtained.

Variations of the above methods have also been used. For example, a sodium hydroxide soln containing iodine has been added to methanol and, after standing for 1day, the soln has been poured slowly into about a quarter of its volume of 10% AgNO<sub>3</sub>, shaken for several hours, then distd. Sulfanilic acid has been used instead of tribromobenzoic acid in Lund and Bjerrum's method. A soln of 15g of magnesium in 500mL of methanol has been heated under reflux, under nitrogen, with hydroquinone (30g), before degassing and distilling the methanol, which was subsequently stored with magnesium (2g) and hydroquinone (4g per 100mL). Refluxing for about 12h removes the bulk of the formaldehyde from methanol: further purification has been obtained by subsequent distn, refluxing for 12h with dinitrophenylhydrazine (5g) and H<sub>2</sub>SO<sub>4</sub> (2g/L), and again fractionally distilling. **Rapid purification:** Methanol purification is the same as for Ethanol.

Another simple purification procedure consists of adding 2g of NaBH<sub>4</sub> to 1.5L methanol, gently bubbling with argon and refluxing for a day at  $30^{\circ}$ , then adding 2g of freshly cut sodium (washed with methanol) and refluxing for 1day before distilling. The middle fraction is taken. [Jou and Freeman J Phys Chem **81** 909 1977.]

*dl*-Methionine (*RS*-α-aminohexanoic acid) [59-51-8] M 149.2, m 281°(dec). Crystd from hot water.

L-Methionine [63-68-3] M 149.2, m 283°(dec),  $[\alpha]_D^{25}$  +21.2° (0.2M HCl)  $pK_1^{25}$  2.13,  $pK_2^{25}$  9.73. Crystd from aqueous EtOH.

*dl*-Methionine sulfoxide [454-41-1, 62697-73-8] M 165.2, m >240°(dec). Likely impurities are *dl*-methionine sulfone and *dl*-methionine. Crystd from water by adding EtOH in excess.

Methoxyacetic acid [625-45-6] M 90.1, b 97°/13-14mm, d 1.175, n 1.417, pK<sup>25</sup> 3.57. Fractionally crystd by repeated partial freezing, then fractionally distd under vacuum through a vacuum-jacketed Vigreux column 20cm long.

*p*-Methoxyacetophenone [100-06-1] M 150.2, m 39°, b 139°/15mm, 264°/736mm. Crystd from diethyl ether/pet ether.

Methoxyamine hydrochloride [593-56-6] M 83.5, m 151-152°, pK<sup>25</sup> 4.60. Crystd from absolute EtOH or EtOH by addition of diethyl ether. [Kovach et al. J Am Chem Soc 107 7360 1985.]

p-Methoxyazobenzene [2396-60-3] M 212.3, m 54-56°. Crystd from EtOH.

**3-Methoxybenzanthrone** [3688-79-7] **M 274.3, m 173°.** Crystd from \*benzene, EtOH or Me<sub>2</sub>CO as yellow needles.

*m*-Methoxybenzoic acid (*m*-anisic acid) [586-38-9] M 152.2, m 110°,  $pK^{25}$  4.09. Crystd from EtOH/water.

*p*-Methoxybenzoic acid (*p*-anisic acid) [100-09-4] M 152.2, m 184.0-184.5°,  $pK^{25}$  4.51. Crystd from EtOH, water, EtOH/water or toluene.

4-Methoxybenzyl chloride (anisyl chloride) [824-94-2] M 156.6, m -1°, b 76°/0.1mm, 95°/5mm, 110°/10mm, 117-117/5°/14mm, 117°/18mm,  $d_4^{20}$  1.15491,  $n_D^{20}$  1.55478. Purified by fractional distn under vacuum and the middle fraction is redistd at 10<sup>-6</sup> mm at room temperature by intermittent cooling of the receiver in liquid N<sub>2</sub>, and the middle fraction is collected. [Mohammed and Kosower J Am Chem Soc 93 2709 1971.]

**3-Methoxycarbonyl-2,5-dihydrothiophen-1,1-dioxide** [67488-50-0] **M 176.1, m 57-58°, 60-62°.** If IR show CO bands then dissolve in CHCl<sub>2</sub>, wash with aqueous Na<sub>2</sub>CO<sub>3</sub> and H<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and wash the residue with cold Et<sub>2</sub>O and dry *in vacuo*. NMR (CDCl<sub>3</sub>):  $\delta$  7.00 (m 1H), 3.98 (bs 4H) and 3.80 (s Me). [Mcintoch and Sieber J Org Chem 43 4431 1978.]

"Methoxychlor", 1,1-Bis(p-methoxyphenyl)-2,2,2-trichloroethane (dimorphic) [72-43-5] M 345.7, m 78-78.2°, or 86-88°. Freed from 1,1-bis(p-chlorophenyl)-2,2,2-trichloroethane by crystn from EtOH.

*trans-p*-Methoxycinnamic acid [830-09-1, 943-89-5 (trans)] M 178.2, m 173.4-174.8°, pK<sup>25</sup> 4.54. Crystd from MeOH to constant melting point and UV spectrum.

**2-Methoxyethanol** (methylcellosolve) [109-86-4] M 76.1, b 124.4°, d 0.964, n 1.4017,  $pK^{25}$ 14.8. Peroxides can be removed by refluxing with stannous chloride or by filtration under slight pressure through a column of activated alumina. 2-Methoxyethanol can be dried with K<sub>2</sub>CO<sub>3</sub>, CaSO<sub>4</sub>, MgSO<sub>4</sub> or silica gel, with a final distn from sodium. Aliphatic ketones (and water) can be removed by making the solvent 0.1% in 2,4-dinitrophenylhydrazine and allowing to stand overnight with silica gel before fractionally distilling.

2-Methoxyethoxymethylchloride (MEMCl) [3970-21-6] M 124.6, b 50-52°/13mm, 140-145°(dec)/atm, d 1.092, n 1.427. Possible impurites are methoxyethanol (b 124°/atm), HCHO and HCl which can be removed below the b of MEMCl. Purify by fractional distn in a vacuum. If too impure, prepare from methoxyethanol (152g) and s-trioxane (66g) by bubbling a stream of dry HCl (with stirring) until a clear mixt is obtained. Dilute with pentane (900mL), dry (3h over 100g MgSO<sub>4</sub>, at 5°), evaporate and the residue is distd in a vac. It is MOISTURE SENSITIVE and TOXIC. The MEM.NEt<sub>3</sub>+Cl<sup>-</sup> salt, prepared by reactn with 1.3 equivs of  $Et_3N$  (16h/25°) and dried in vac has m 58-61°, and is moisture sensitive. [Corey et al. *Tetrahedron* Lett 809 1976.]

 $\beta$ -Methoxyethylamine [109-85-3] M 75.1, b 94°, d 0.874, n 1.407, pK<sup>25</sup> 9.40. An aqueous 70% soln was dehydrated by azeotropic distn with \*benzene or methylene chloride and the amine was distilled twice from zinc dust. Store in a tight container as it absorbs CO<sub>2</sub> from the atmosphere.

6-Methoxy-1-indanone [13623-25-1] M 162.2, m 151-153°. Crystd from MeOH, then sublimed in a high vacuum.

5-Methoxyindole [1006-94-6] M 147.2, m 55°, 57°, b 176-178°/17mm,  $pK_{Est} \sim 0$ . Crystd from cyclohexane pet ether or pet ether/Et<sub>2</sub>O.

**1-Methoxynaphthalene** [2216-69-5] M **158.2, b 268.4-268.5°.** See methyl 1-naphthyl ether on p. 295.

2-Methoxynaphthalene [93-04-9] M 158.2, m 73.0-73.6°, b 273°/760mm. Fractionally distd under vacuum. Crystd from absolute EtOH, aqueous EtOH, \*benzene or *n*-heptane, and dried under vacuum in an Abderhalden pistol or distd *in vacuo*. [Kikuchi et al. J Phys Chem 91 574 1987.]

1-Methoxy-4-nitronaphthalene [4900-63-4] M 203.2, m 85°. Purified by chromatography on silica gel and recrystd from MeOH. [Bunce et al. J Org Chem 52 4214 1987.]

*p*-Methoxyphenol [150-76-5] M 124.1, m 54-55°, b 243°,  $pK^{25}$  10.21. Crystd from \*benzene, pet ether or H<sub>2</sub>O, and dried under vacuum over P<sub>2</sub>O<sub>5</sub> at room temp. Sublimes *in vacuo*. [Wolfenden et al. J Am Chem Soc 109 463 1987.]

α-Methoxyphenylacetic acid (*O*-methyl mandelic acid), [R-(-)-3966-32-3; S-(+)-26164-26-1]M 166.2, m 62.9°, 62-65°, 65-66°,  $[α]_{546}^{20}$  (-) and (+) 179° (169.8°),  $[α]_D^{20}$  (-) and (+) 150.7° (148°) (c 0.5, EtOH), pK<sub>Est</sub> ~3.1. Purified by recrystn from \*C<sub>6</sub>H<sub>6</sub>-pet ether (b 80-100°). [Neilson and Peters J Chem Soc 1519 1962; Weizmann et al. J Am Chem Soc 70 1153 1948; Pirie and Smith J Chem Soc 338 1932; NMR: Dale and Mosher J Am Chem Soc 95 512 1973; for resolution: Roy and Deslongchamps Can J Chem 63 651 1985; Trost et al. J Am Chem Soc 108 4974 1986.] The racemic mixture has m 72°, b 121-122°/0.4mm, 165°/18mm (from pet ether) [Braun et al. Chem Ber 63 2847 1930].

o-Methoxyphenylacetic acid [93-25-4] M 166.2, m 71.0-71.2°, pK<sub>Est</sub> ~4.4. Crystd from H<sub>2</sub>O, EtOH or aq EtOH and dried in a vacuum desiccator over Sicapent.

*m*-Methoxyphenylacetic acid [1798-09-0] M 166.2, m 71.0-71.2°, pK<sub>Est</sub> ~4.3. Crystd from H<sub>2</sub>O, or aq EtOH.

*p*-Methoxyphenylacetic acid [104-01-8] M 166.2, m 85-87°,  $pK^{25}$  4.36. Crystd from EtOH/water.

5-(p-Methoxyphenyl)-1,2-dithiole-3-thione [42766-10-9] M 240.2, m 111°. Crystd from butyl acetate.

*N*-(*p*-Methoxyphenyl)-*p*-phenylenediamine [101-64-4] M 214.3, m 102°, b 238°/12mm, pK 6.6 (5.9). Crystd from ligroin.

8-Methoxypsoralen see xanthotoxin p. 577 in Chapter 6.

α-Methoxy-α-trifluoromethylphenylacetic acid (MTPA, Mosher's acid) [R-(+)- 20445-31-2; S-(-)- 17257-71-5] M 234.2, m 43-45°, 90°/0.1mm, 105-107°/1mm,  $[α]_{546}^{20}$  (+) and (-) 87°,  $[α]_D^{20}$  (+) and (-) 73° (c 2, MeOH), pK<sub>Est</sub> ~2.5. A likely impurity is phenylethylamine from the resolution. Dissolve acid in ether-\*benzene (3:1), wash with  $0.5N H_2SO_4$ , then water, dry over magnesium sulfate, filter, evaporate and distil. [Dale et al. J Org Chem 34 2543 1969, J Am Chem Soc 75 512 1973.]

α-Methoxy-α-trifluoromethylphenylacetyl chloride [R-(-)-39637-99-5; S-(+)-20445-33-4] M 252.6, b 54-56°/1mm, 213-214°/atm,  $d_4^{20}$  1.353,  $n_D^{20}$  1.468,  $[\alpha]_{546}^{20}$  (-) and (+) 167°,  $[\alpha]_D^{20}$  (-) and (+) 137° (c 4, CCl<sub>4</sub>),  $[\alpha]_D^{24}$  (-) and (+)10.0° (neat). The most likely impurity is the free acid due to hydrolysis and should be checked by IR. If free from acid then distil taking care to keep moisture out of the apparatus. Otherwise add SOCl<sub>2</sub> and reflux for 50h and distil. Note that shorter reflux times resulted in a higher boiling fraction (b 130-155°/1mm) which has been identified as the anhydride. [Dale et al. J Org Chem 34 2543 1969; for enantiomeric purity see J Am Chem Soc 97 512 1973.]

*N*-Methylacetamide [79-16-3] M 73.1, m 30°, b 70-71°/2.5-3mm,  $pK_1^{25}$ -3.70,  $pK_2^{25}$ -0.42. Fractionally distd under vacuum, then fractionally crystd twice from its melt. Impurities include acetic acid, methyl amine and H<sub>2</sub>O. For detailed purification procedure, see Knecht and Kolthoff, *Inorg Chem* 1 195 *1962*. Although *N*-methylacetamide is commercially available it is often extensively contaminated with acetic acid, methylamine, water and an unidentified impurity. The recommended procedure is to synthesise it in the laboratory by direct reaction. The gaseous amine is passed into hot glacial acetic acid, to give a partially aq soln of methylammonium acetate which is heated to *ca* 130° to expel water. Chemical methods of purificat such as extractn by pet ether, treatment with H<sub>2</sub>SO<sub>4</sub>, K<sub>2</sub>CO<sub>3</sub> or CaO can be used but are more laborious.

Tests for purity include the Karl Fischer titration for water; this can be applied directly. Acetic acid and methylamine can be detected polarographically.

In addition to the above, purification of N-methylacetamide can be achieved by fractional freezing, including zone melting, repeated many times, or by chemical treatment with vacuum distn under reduced pressures. For details of zone melting techniques, see Knecht in *Recommended Methods for Purification of Solvents and Tests for Impurities*, Coetzee Ed. Pergamon Press 1982.

*N*-Methylacetanilide [579-10-2] M 149.2, m 102-104°. Crystd from water, ether or pet ether (b 80-100°).

Methyl acetate [79-20-9] M 74.1, b 56.7-57.2°, d 0.934. n 1.36193,  $n^{25}$  1.3538,  $pK^{20}$  -7.28 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). Methanol in methyl acetate can be detected by measuring solubility in water. At 20°, the solubility of methyl acetate in water is *ca* 35g per 100mL, but 1% MeOH confers miscibility. Methanol can be removed by conversion to methyl acetate, using refluxing for 6h with acetic anhydride (85mL/L), followed by fractional distn. Acidic impurities can be removed by shaking with anhydrous K<sub>2</sub>CO<sub>3</sub> and distilling. An alternative treatment is with acetyl chloride, followed by washing with conc NaCl and drying with CaO or MgSO<sub>4</sub>. (Solid CaCl<sub>2</sub> cannot be used because it forms a crystalline addition compound.) Distn from copper stearate destroys peroxides. Free alcohol or acid can be eliminated from methyl acetate by shaking with strong aq Na<sub>2</sub>CO<sub>3</sub> or K<sub>2</sub>CO<sub>3</sub> (three times), then with aq 50% CaCl<sub>2</sub> (three times), satd aq NaCl (twice), drying with K<sub>2</sub>CO<sub>3</sub> and distn from P<sub>2</sub>O<sub>5</sub>.

Methyl acetimidate hydrochloride [14777-27-6] M 109.6, m 93-95°, 105°(dec),  $pK_{Est} \sim 5.5$ . Crystd from methanol by adding dry ether to a ratio of 1:1 and cooled at 0°. Filter off the crystals in a cold room, wash with methanol/ether (1:2), then dry in a vacuum. [Hunter and Ludwig J Am Chem Soc 84 3491 1962.] The free base has b 90-91°/765mm, d 0.867, n 1.403 [Hunter and Ludwig Methods Enzymol 25 585 1973.]

*p*-Methylacetophenone [122-00-9] M 134.2, m 22-24°, b 93.5°/7mm, 110°/14mm, d 1.000, n 1.5335. Impurities, including the *o*- and *m*-isomers, were removed by forming the semicarbazone which, after repeated crystn, was hydrolysed to the ketone. [Brown and Marino J Am Chem Soc 84 1236 1962.] Also purified by distn under reduced pressure, followed by low temperature crystn from isopentane.

Methyl acrylate [96-33-3] M 86.1, b 80°, d 0.9535, n 1.4040. Washed repeatedly with aqueous NaOH until free from inhibitors (such as hydroquinone), then washed with distd water, dried (CaCl<sub>2</sub>) and fractionally distd under reduced pressure in an all-glass apparatus. Sealed under nitrogen and stored at 0° in the dark. [Bamford and Han J Chem Soc, Faraday Trans 1 78 855 1982.]

1-Methyladamantane [768-91-2] M 150.2, m 103°. Purified by zone melting and sublimes at 90-95°/12mm.

2-Methyladamantane [700-56-1] M 150.2. Purified by zone melting.

Methylamine (gas) [74-89-5] M 31.1, b -7.55°/719mm, pK<sup>25</sup> 10.62. Dried with sodium or BaO.

Methylamine hydrochloride [593-51-1] M 67.5, m 231.8-233.4°, b 225-230°/15mm,  $pK^{25}$  10.62. Crystd from *n*-butanol, absolute EtOH or MeOH/CHCl<sub>3</sub>. Washed with CHCl<sub>3</sub> to remove traces of dimethylamine hydrochloride. Dried under vacuum first with H<sub>2</sub>SO<sub>4</sub> then P<sub>2</sub>O<sub>5</sub>. Deliquescent, stored in a desiccator over P<sub>2</sub>O<sub>5</sub>.

1-Methylaminoanthraquinone [82-38-2] M 237.3, m 166.5°, pK<sub>Est</sub>~2. Crystd to constant melting point from butan-1-ol, then crystd from EtOH. It can be sublimed under vacuum.

*N*-Methyl-*o*-aminobenzoic acid (*N*-methylanthranilic acid) [119-68-6] M 151.2, m 178.5°,  $pK_1^{25}$  1.97,  $pK_2^{25}$  5.34. Crystd from water or EtOH.

p-Methylaminophenol sulfate [55-55-0] M 344.4, m 260°(dec), pK<sup>25</sup> 5.9. Crystd from MeOH.

6-Methylaminopurine [443-72-1] M 149.2, m >300°, 312-314° (dec),  $pK_1^{20} < 1$ ,  $pK_2^{20} 4.15$ ,  $pK_3^{20} 10.02$ . Best purified by recrystallising 2g from 50mL of H<sub>2</sub>O and 1.2g of charcoal. [UV: Albert and Brown J Chem Soc 2060 1954; UV: Mason J Chem Soc 2071 1954; see also Elion et al. J Am Chem Soc 74 411 1952.] The picrate has m 265°(257°) [Bredereck et al. Chem Ber 81 307 1948].

Methyl 3-aminopyrazine-2-carboxylate [16298-03-6] M 153.1, m 169-172°, 172°. Forms yellow needles from H<sub>2</sub>O (100 parts using charcoal). If it contains the free acid then dissolve in CH<sub>2</sub>Cl<sub>2</sub> wash with saturated aqueous Na<sub>2</sub>CO<sub>3</sub>, brine, dry over MgSO<sub>4</sub> filter, evaporate and recrystallise the residue. The *free acid* has m 203-204° (dec) [UV: Brown and Mason J Chem Soc 3443 1956] and pK<sub>1</sub> <1 and pK<sub>2</sub> 3.70. The *ammonium salt* has m 232° (dec) (from aq Me<sub>2</sub>CO) and the *amide* has m 239.2° (from H<sub>2</sub>O) [Ellingson et al. J Am Chem Soc 67 1711 1945].

N-Methylaniline [100-61-8] M 107.2, b 57°/4mm, 81-82°/14mm, d 0.985, n 1.570, pK<sup>25</sup> 4.56. Dried with KOH pellets and fractionally distd under vacuum. Acetylated and the acetyl derivative was recrystd to constant melting point (m 101-102°), then hydrolysed with aqueous HCl and distd from zinc dust under reduced pressure. [Hammond and Parks J Am Chem Soc 77 340 1955.]

**N-Methylaniline hydrochloride** [2739-12-0] **M 143.7, m 123.0-123.1°.** Crystd from dry \*benzene/CHCl<sub>3</sub> and dried under vacuum.

Methyl p-anisate [121-98-2] M 166.2, m 48°. Crystd from EtOH.

**4-Methyl anisole** [104-93-8] **M 122.2, b 175-176°, d\_{15}^{15} 0.9757, n 1.512.** Dissolved in diethyl ether, washed with M NaOH, water, dried (Na<sub>2</sub>CO<sub>3</sub>), evaporated and the residue distd under vacuum.

2-Methylanthracene [613-12-7] M 192.3, m 204-206° Chromatographed on silica gel with cyclohexane as eluent and recrystd from EtOH [Werst J Am Chem Soc 109 32 1987].

4-Methylanthracene [779-02-2] M 192.3, m 77-79°, b 196-197°/12mm, d 1.066. Chromatographed on silica gel with cyclohexane as eluent and recrystd from EtOH [Werst J Am Chem Soc 109 32 1987].

2-Methylanthraquinone [84-54-8] M 222.3, m 176°. Crystd from EtOH, then sublimed.

Methylarenes (see also pentamethyl- and hexamethyl- benzenes). Recrystd from EtOH and sublimed in vacuum [Schlesener et al. J Am Chem Soc 106 7472 1984].

Methyl benzoate [93-58-3] M 136.2, b 104-105°/39mm, 199.5°/760mm, d 1.087, n<sup>15</sup> 1.52049, n 1.51701, pK<sup>20</sup> -8.11, -6.51 (H<sub>0</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). Washed with dilute aqueous NaHCO<sub>3</sub>, then water, dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally distd under reduced pressure.

p-Methylbenzophenone [134-84-9] M 196.3, m 57°. Crystd from MeOH and pet ether.

Methyl-1,4-benzoquinone [553-97-9] M 122.1, m 68-69°. Crystd from heptane or EtOH, dried rapidly (vacuum over P<sub>2</sub>O<sub>5</sub>) and stored under vacuum.

Methyl benzoylformate [15206-55-0] M 164.2, m 246-248°. Purified by radial chromatography (diethyl ether/hexane, 1:1), and dried at 110-112° at 6mm pressure. [Meyers and Oppenlaender J Am Chem Soc 108 1989 1986.]

2-Methyl-3,4-benzphenanthrene [652-04-0] M 242.3, m 70°. Crystd from EtOH.

dl- $\alpha$ -Methylbenzyl alcohol [13323-81-4] M 122.2, b 60.5-61.0°/3mm. See dl-1-phenylethanol on p. 330.

**R**-(+)- $\alpha$ -Methylbenzylamine [R(+) 3886-69-9, RS 618-36-0] M 121.2, b 187-188°/atm,  $[\alpha]_{546}^{20}$ +35° (c 10, EtOH),  $[\alpha]_{D}^{25}$ +39.7° (neat), pK 9.08 (for RS). Dissolve in toluene, dry over NaOH and distd, fraction boiling at 187-188°/atm is collected. Store under N<sub>2</sub> to avoid forming the carbamate and urea. Similarly for the S-(-) enantiomer [2627-86-3]. [Org Synth Coll Vol II 503 1943.]

*p*-Methylbenzyl bromide [104-81-4]. See  $\alpha$ -bromo-*p*-xylene on p. 143.

*p*-Methylbenzyl chloride [104-82-5] M 140.6, b 80°/2mm, d 1.085, n 1.543. Dried with CaSO<sub>4</sub> and fractionally distd under vacuum.

Methylbixin [26585-94-4] M 408.5, m 163°. Crystd from EtOH/CHCl<sub>3</sub>.

**Methyl bromide** [74-83-9] **M 94.9, b 3.6°.** Purified by bubbling through conc  $H_2SO_4$ , followed by passage through a tube containing glass beads coated with  $P_2O_5$ . Also purified by distn from AlBr<sub>3</sub> at -80°, by passage through a tower of KOH pellets and by partial condensation.

Methyl o-bromobenzoate [610-94-6] M 215.1, b 122°/17mm, 234-244°/760mm. Soln in ether is washed with 10% aqueous Na<sub>2</sub>CO<sub>3</sub>, water, then dried and distd.

Methyl p-bromobenzoate [619-42-1] M 215.1, m 79.5-80.5°. Crystd from MeOH.

**2-Methylbutane (isopentane)** [78-78-4] M 72.2, b 27.9°, d 0.621, n 1.35373,  $n^{25}$  1.35088. Stirred for several hours in the cold with conc H<sub>2</sub>SO<sub>4</sub> (to remove olefinic impurities), then washed with H<sub>2</sub>O, aqueous Na<sub>2</sub>CO<sub>3</sub> and H<sub>2</sub>O again. Dried with MgSO<sub>4</sub> and fractionally distd using a Todd column packed with glass helices (see p. 174). Material transparent down to 180nm was obtained by distilling from sodium wire, and passing through a column of silica gel which had previously been dried in place at 350° for 12h before use. [Potts J Phys Chem 20 809 1952].

**2-Methyl-1-butanol** [137-32-6; RS 34713-94-5; S(-)- 1565-80-6] **M 88.2, b 130°(RS), 128.6°(S),**  $[\alpha]_D^{25}$  -5.8° (neat), d 0.809,  $n^{52}$  1.4082. Refluxed with CaO, distd, refluxed with magnesium and again fractionally distd. A small sample of highly purified material was obtained by fractional crystn after conversion into a suitable ester such as the trinitrophthalate or the 3-nitrophthalate. The latter was converted to the cinchonine salt in acetone and recrystd from CHCl<sub>3</sub> by adding pentane. The salt was saponified, extracted with ether, and fractionally distd. [Terry et al. J Chem Eng Data 5 403 1960.]

**3-Methyl-1-butanol** [123-51-3] M 88.2, b 128°/750mm, 132°/760mm, d<sup>15</sup> 0.8129, n<sup>15</sup> 1.4085, n 1.4075. Dried by heating with CaO and fractionally distilling, then heating with BaO and redistilling. Alternatively, boiled with conc KOH, washed with dilute  $H_3PO_4$ , and dried with  $K_2CO_3$ , then anhydrous CuSO<sub>4</sub>, before fractionally distilling. If very dry alcohol is required, the distillate can be refluxed with the appropriate alkyl phthalate or succinate as described for *ethanol*. It is separated from 2-methyl-1-butanol by fractional distn, fractional crystn and preparative gas chromatography.

**3-Methyl-2-butanol** [598-75-4] **M 88.2, b 111.5°, d 0.807, n 1.4095, n<sup>25</sup> 1.4076.** Refluxed with magnesium, then fractionally distd.

3-Methyl-2-butanone (methyl isopropyl ketone) [563-80-4] M 86.1, b 93-94°/752mm, d 0.818, n 1.410,  $pK^{25}$  -7.1 (aq H<sub>2</sub>SO<sub>4</sub>). Refluxed with a little KMnO<sub>4</sub>. Fractionated on a spinning-band column, dried with CaSO<sub>4</sub> and distd.

2-Methyl-2-butene [513-35-9] M 70.1, f -133.8°, b 38.4°/760mm, d<sup>15</sup> 0.66708, d 0.6783, d<sup>25</sup> 0.65694, n<sup>15</sup> 1.3908. Distd from sodium.

Methyl *n*-butyrate [623-42-7] M 102.1, b 102.3°/760mm, d 0.898, n 1.389. Treated with anhydrous CuSO<sub>4</sub>, then distd under dry nitrogen.

S-(+)-2-Methylbutyric acid [1730-91-2] M 102.1, b 64°/2mm, 78°/15mm, 90-94°/23mm, 174-175°/atm,  $d_4^{20}$  0.938,  $n_D^{20}$  1.406,  $[\alpha]_{546}^{20} + 23°$ ,  $[\alpha]_D^{20} + 19.8°$  (neat),  $[\alpha]_D^{13} + 18.3°$  (c 6, EtOH), pK<sup>25</sup> 4.76 (for RS). Purified by distn *in vacuo* [Sax and Bergmann J Am Chem Soc 77 1910 1955; Doering and Aschner J Am Chem Soc 75 393 1953 ]. The methyl ester is formed by addition of diazomethane and has b 112-115°/atm,  $[\alpha]_D^{27} + 21.1°$  (c 1.7, MeOH).

Methyl carbamate [598-55-0] M 75.1, m 54.4-54.8°. Crystd from \*benzene.

9-Methylcarbazole [1484-12-4] M 181.2, m 89°. Purified by zone melting.

4-Methylcatechol [452-86-8] M 124.1. See 3,4-dihydroxytoluene on p. 208.

**Methyl chloride** [74-87-3] **M 50.5, b -24.1°.** Bubbled through a sintered-glass disc dipping into conc  $H_2SO_4$ , then washed with water, condensed at low temperature and fractionally distd. Has been distd from AlCl<sub>3</sub> at -80°. Alternatively, passed through towers containing AlCl<sub>3</sub>, soda-lime and P<sub>2</sub>O<sub>5</sub>, then condensed and fractionally distd. Stored as a gas.

Methyl chloroacetate [96-34-4] M 108.5, b 129-130°, d 1.230, n 1.423. Shaken with satd aq Na<sub>2</sub>CO<sub>3</sub> (three times), aq 50% CaCl<sub>2</sub> (three times), satd aq NaCl (twice), dried (Na<sub>2</sub>SO<sub>4</sub>) and fractionally distd.

**R**-(+) Methyl 2-chloropropionate [77287-29-7] M 122.6, b 49-50°/35mm, 78-80°/120mm, 132-134°/760mm,  $d_4^{20}$  1.152,  $n_D^{20}$  1.417,  $[\alpha]_D^{20}$  +26° (19.0°) (neat). Purified by repeated distillation [Walker J Chem Soc 67 916 1895; Walden Chem Ber 28 1293 1985; see also Gless Synth Commun 16 633 1986].

3-Methylcholanthrene [56-49-5] M 268.4, m 179-180°. Crystd from \*benzene and diethyl ether. CARCINOGEN.

Methyl cyanoacetate [105-34-0] M 99.1, f -13°, b 205°, d 1.128, n 1.420. Purified by shaking with 10% Na<sub>2</sub>CO<sub>3</sub> soln, washing well with water, drying with anhydrous Na<sub>2</sub>SO<sub>4</sub>, and distilling.

Methyl cyanoformate [17640-15-2] M 85.1, b 81°/47mm, 97°/751mm, 100-101°/760mm,  $d_4^{20}1.072$ ,  $n_D^{20}1.37378$ . Purified by fractionation through a 45cm glass helices packed column and with a 30cm spinning band column. [Sheppard J Org Chem 27 3756 1962.] It has been distd through a short Vigreux

column, and further purified by recrystn from  $Et_2O$  at -40° as white crystals which melt at room temperature. NMR:  $\delta$  4.0 (CH<sub>3</sub>), and IR: 2250 (CN) and 1750 (CO) cm<sup>-1</sup>. [Childes and Weber J Org Chem 41 3486 1976.]

**Methylcyclohexane** [108-87-2] **M** 98.2, **b** 100.9°,  $d^{25}$  0.7650, **n** 1.4231,  $n^{52}$  1.42058. Passage through a column of activated silica gel gives material transparent down to 220nm. Also purified by passage through a column of activated basic alumina, or by azeotropic distn with MeOH, followed by washing out the MeOH with H<sub>2</sub>O, drying and distilling. Methylcyclohexane can be dried with CaSO<sub>4</sub>, CaH<sub>2</sub> or sodium. Has also been purified by shaking with a mixture of conc H<sub>2</sub>SO<sub>4</sub> and HNO<sub>3</sub> in the cold, washing with H<sub>2</sub>O, drying with CaSO<sub>4</sub> and fractionally distilling from potassium. Percolation through a Celite column impregnated with 2,4-dinitrophenylhydrazine (DNPH), phosphoric acid and H<sub>2</sub>O (prepared by grinding 0.5g DNPH with 6mL 85% H<sub>3</sub>PO<sub>4</sub>, then mixing with 4mL of distilled H<sub>2</sub>O and 10g of Celite) removes carbonyl-containing impurities.

**2-Methylcyclohexanol** [583-59-5] **M 114.2, b 65°/20mm, 167.6°/760mm, d 0.922, n 1.46085.** Dried with Na<sub>2</sub>SO<sub>4</sub> and distd under vacuum.

*cis-* and *trans-3-*Methylcyclohexanol [591-23-1] M 114.2, b 69°/16mm, 172°/760mm, d 0.930, n 1.45757, n<sup>25.5</sup> 1.45444. Dried with Na<sub>2</sub>SO<sub>4</sub> and distd under vacuum.

4-Methylcyclohexanone [589-92-4] M 112.2, b 165.5°/743mm, d 0.914, n 1.44506. Dried with CaSO<sub>4</sub>, then fractionally distd.

1-Methylcyclohexene [591-49-1] M 96.2, b 107.4-108°/atm, 110-111°/760mm, d 0.813, n 1.451. Freed from hydroperoxides by passing through a column containing basic alumina or refluxing with cupric stearate, filtered and fractionally distd from sodium.

**Methylcyclopentane** [96-37-7] **M 84.2, b 71.8°, d 0.749, n 1.40970, n^{25} 1.40700.** Purification procedures include passage through columns of silica gel (prepared by heating in nitrogen to 350° prior to use) and activated basic alumina, distn from sodium-potassium alloy, and azeotropic distn with MeOH, followed by washing out the methanol with water, drying and distilling. It can be stored with CaH<sub>2</sub> or sodium.

3'-Methyl-1,2-cyclopentenophenanthrene [549-38-2] M 232.3, m 126-127°. Crystd from AcOH.

S-Methyl-L-cysteine [1187-84-4] M 135.2, m 207-211°,  $[\alpha]_D^{26}$ -32.0° (c 5, H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup>1.94 (COOH), pK<sub>2</sub><sup>25</sup>8.73 (NH<sub>2</sub>, 8.97). Likely impurities are cysteine and S-methyl-dl-cysteine. Crystd from water by adding 4 volumes of EtOH.

5-Methylcytosine [4-amino-5-methylpyrimidin-2(1*H*)-one] [554-01-8] M 125.1, m 270°(dec), pK<sub>1</sub> 4.6, pK<sub>2</sub> 12.4. Crystd from water (sol 3.4%).

Methyl decanoate [110-42-9] M 186.3, b 114°/15mm, 224°/760mm, d 0.874, n 1.426. Passed through alumina before use.

Methyl 2,4-dichlorophenoxyacetate [1928-38-7] M 235.1, m 43°, b 119°/11mm. Crystd from MeOH.

*m*-Methyl-*N*, *N*-dimethylaniline [121-72-2] M 135.2, b 72-74°/5mm, 215°/760mm,  $pK^{25}$  5.22. Refluxed for 3h with 2 molar equivalents of acetic anhydride, then fractionally distd under reduced pressure. Also dried over BaO, distd and stored over KOH. Methods described for *N*, *N*-dimethylaniline are applicable.

*p*-Methyl-*N*, *N*-dimethylaniline [99-97-8] M 135.2, b 76.5-77.5°/4mm, 211°/760mm,  $pK^{25}$  4.76. Refluxed for 3h with 2 molar equivalents of acetic anhydride, then fractionally distd under reduced pressure. Also dried over BaO, distd and stored over KOH. Methods described for *N*, *N*-dimethylaniline are applicable.

**2-Methyl-1,3-dithiane** [6007-26-7] **M 134.3, b 53-54°/1.1mm, 66°/5mm, 79-80°/8-10mm, 85°/12mm, d**<sup>20</sup><sub>4</sub>**1.121, n**<sup>20</sup><sub>D</sub>**1.560.** Wash with H<sub>2</sub>O, 2.5 M aqueous NaOH, H<sub>2</sub>O, brine, dried over K<sub>2</sub>CO<sub>3</sub> (use toluene as solvent if volume of reagent is small), filter, evaporate and distil the colourless residue. IR film: 1455, 1371 and 1060 (all medium and CH<sub>3</sub>), 1451m, 1422s, 1412m, 1275m, 1236m, 1190m, 1171w, 918m and 866w (all dithiane) cm<sup>-1</sup> [Corey and Erickson J Org Chem **36** 3553 1971; Seebach and Corey J Org Chem **40** 231 1975].

Methyl dodecanoate [111-82-0] M 214.4, m 5°, b 141°/15mm, d 0.870, n<sup>50</sup> 1.4199. Passed through alumina before use.

N-Methyleneaminoacetonitrile [109-82-0] M 68.1, m 129°. Crystd from EtOH or acetone.

p, p'-Methylene-bis-(N, N-dimethylaniline) [101-61-1] M 254.4, m 89.5°. See p, p'-tetramethyldiaminodiphenylmethane on p. 364.

Methylene Blue [3,7-bis-(dimethylamino)phenothiazin-5-ium chloride [61-73-4] M 319.9, CI 52015,  $\varepsilon_{654}$  94,000 (EtOH),  $\varepsilon_{664}$  81,000 (H<sub>2</sub>O), pK<sup>25</sup> 3.8. Crystd from 0.1M HCl (16mL/g), the crystals were separated by centrifugation, washed with chilled EtOH and diethyl ether and dried under vacuum. Crystd from 50% aqueous EtOH, washed with absolute EtOH, and dried at 50-55° for 24h. Also crystd from \*benzene-MeOH (3:1). Salted out with NaCl from a commercial conc aqueous soln, then crystd from water, dried at 100° in an oven for 8-10h.

**3,4-Methylenedioxyaniline** [14268-66-7] **M 137.1, m 45-46°, b 144°/14mm, pK<sub>Est</sub> ~3.8.** Crystd from pet ether.

3,4-Methylenedioxycinnamic acid [2373-80-0] M 192.2, m 243-244°(dec), pK<sub>Est</sub> ~4.6. Crystd from glacial acetic acid.

5,5'-Methylenedisalicylic acid [122-25-8] M 372.3, m 238°(dec). Crystd from acetone and \*benzene.

Methylene Green [3,7-bis-(dimethylamino)-4-nitrophenothiazin-5-ium chloride] [2679-01-8] M 364.9, m >200°(dec), CI 52020,  $pK^{25}$  3.2. Crystd three times from water (18mL/g).

N-Methylephedrine (2-dimethylamino-1-phenylpropanol) [1S,2R-(+)-42151-56-4; 1R,2S-(-)-552-79-4] M 179.3, m 85-86°, 87-87.5°, 90°, b 115°/2mm,  $[\alpha]_{546}^{20}$  (+) and (-) 35°,  $[\alpha]_D^{20}$  (+) and (-) 30° (c 4.5, MeOH), pK<sup>26</sup> 9.22. It has been recrystd from Et<sub>2</sub>O, pet ether, of aq EtOH or aq MeOH and has been distilled under reduced pressure. [Smith J Chem Soc 2056 1927; Tanaka and Sugawa Yakugaku Zasshi (J Pharm Soc Japan) 72 1548 1952 (Chem Abstr 47 8682 1953); Takamatsu Yakugaku Zasshi (J Pharm Soc Japan) 76 1227 1956, Chem Abstr 51 4304 1957.] The hydrochloride has m 192-193° and  $[\alpha]_D^{20} + 30^\circ$  (c 5,H<sub>2</sub>O)[Prelog and Hüfliger Helv Chim Acta 33 2021 1950].

Methyl ether (dimethyl ether) [115-10-6] M 46.1, b -63.5°/96.5mm. Dried by passing over alumina and then BaO, or over CaH<sub>2</sub>, followed by fractional distn at low temperatures.

N-Methyl ethylamine hydrochloride [624-60-2] M 95.6, m 126-130°, pK 10.9 (free base). Crystd from absolute EtOH or diethyl ether.

*N*-Methyl formamide [123-39-7] M 59.1, m -3.5°, b 100.5°/25mm, d 1.005.,  $n^{52}$  1.4306 Dried with molecular sieves for 2days, then distd under reduced pressure through a column packed with glass helices. Fractionally crystd by partial freezing and the solid portion was vac distd.

Methyl formate [107-31-3] M 60.1, b 31.5°, d 0.971,  $n^{15}$  1.34648, n 1.34332. Washed with strong aq Na<sub>2</sub>CO<sub>3</sub>, dried with solid Na<sub>2</sub>CO<sub>3</sub> and distd from P<sub>2</sub>O<sub>5</sub>. (Procedure removes free alcohol or acid.)

**2-Methylfuran** [534-22-5] **M 82.1, b 62.7-62.8º/731mm, d 0.917, n 1.436.** Washed with acidified satd ferrous sulfate soln (to remove peroxides), separated, dried with CaSO<sub>4</sub> or CaCl<sub>2</sub>, and fractionally distd from KOH immediately before use. To reduce the possibility of spontaneous polymerisation, addition of about one-third of its volume of heavy mineral oil to 2-methylfuran prior to distn has been recommended.

Methyl gallate [99-24-1] M 184.2, m 202°. Crystd from MeOH.

*N*-Methylglucamine [6284-40-8] M 195.2, m 128-129°,  $[\alpha]_{546}^{20}$  -19.5°(c 2, H<sub>2</sub>O), pK<sup>28</sup> 9.62. Crystd from MeOH.

Methyl  $\alpha$ -D-glucosamine [97-30-3] M 194.2, m 165°,  $[\alpha]_D^{25}$ +157.8° (c 3.0, H<sub>2</sub>O), pK<sup>30</sup> 7.1. Crystd from MeOH.

 $\alpha$ -Methylglutaric acid [18069-17-5] M 146.1, m 79°, pK<sub>1</sub><sup>25</sup> 4.36, pK<sub>2</sub><sup>25</sup> 5.37. Crystd from distd water, then dried under vacuum over conc H<sub>2</sub>SO<sub>4</sub>.

 $\beta$ -Methylglutaric acid [626-51-7] M 146.1, m 87°, pK<sub>1</sub><sup>25</sup> 4.35, pK<sub>2</sub><sup>25</sup> 5.44. Crystd from distd water, then dried under vacuum over conc H<sub>2</sub>SO<sub>4</sub>.

**Methylglyoxal** [78-98-8] **M 72.1, b** ca 72°/760mm. Commercial 30% (w/v) aqueous soln was diluted to about 10% and distd twice, taking the fraction boiling below 50°/20mm Hg. (This treatment does not remove lactic acid).

Methyl Green [82-94-0, 7114-03-6 (ZnCl<sub>2</sub> salt)] M 458.5, m >200°(dec). Crystd from hot water.

1-Methylguanine [938-85-2] M 165.2, m >300°(dec),  $pK_1^{20}$  3.13,  $pK_2^{20}$  10.54. Crystd from 50% aqueous acetic acid.

7-Methylguanine [578-76-7] M 165.2, pK<sub>1</sub><sup>20</sup> 3.50, pK<sub>2</sub><sup>20</sup> 9.95. Crystd from water.

2-Methylhexane [591-76-4] M 100.2, b 90.1°, d 0.678, n 1.38485, n<sup>25</sup> 1.38227. Purified by azeotropic distn with MeOH, then washed with water (to remove the MeOH), dried over type 4A molecular sieves and distd.

**3-Methylhexane** [589-34-4] **M 100.2, b 91.9°, d 0.687, n 1.38864, n<sup>25</sup> 1.38609.** Purification as for 2-methylhexene.

Methyl hexanoate [106-70-7] M 130.2, b 52°/15mm, 150°/760mm, d 0.885, n 1.410. Passed through alumina before use.

Methylhydrazine [60-34-4] M 46.1, b 87°/745mm, d 0.876, n 1.436,  $pK^{30}$  7.87. Dried with BaO, then vacuum distd. Stored under nitrogen.

Methyl hydrazinocarboxylate [6294-89-9] M 90.1, m 70-73°. To remove impurities, the material was melted and pumped under vacuum until the vapours were spectroscopically pure [Caminati et al. J Am Chem Soc 108 4364 1986].

Methyl 4-hydroxybenzoate [99-76-3] M 152.2, m 127.5°, pK<sub>Est</sub> ~9.3. Fractionally crystd from its melt, recrystd from \*benzene, then from \*benzene/MeOH and dried over CaCl<sub>2</sub> in a vacuum desiccator.

Methyl 3-hydroxy-2-naphthoate [883-99-8] M 202.2, m 73-74°, pK<sub>Est</sub> ~9.0. Crystd from MeOH (charcoal) containing a little water.

N-Methylimidazole [616-47-7] M 82.1, b 81-84°/27mm, 197-198°/760mm, d 1.032, n 1.496, pK<sup>25</sup> 7.25. Dried with sodium metal and then distd. Stored at 0° under dry argon.

2-Methylimidazole [693-98-1] M 82.1, m 140-141°, b 267°/760mm, pK<sup>25</sup> 7.86. Recrystd from \*benzene or pet ether.

**4-Methylimidazole** [822-36-6] **M 82.1, m 47-48°, b 263°/760mm, pK<sup>25</sup> 7.61.** Recrystd from \*benzene or pet ether.

2-Methylindole [95-20-5] M 131.2, m 61°,  $pK^{25}$  -0.28 (C-3 protonation, aq H<sub>2</sub>SO<sub>4</sub>). Crystd from \*benzene. Purified by zone melting.

**3-Methylindole** (skatole) [83-34-1] M 131.2, m 95°, pK<sup>25</sup> -4.55 (C-3-protonation, aq H<sub>2</sub>SO<sub>4</sub>). Crystd from \*benzene. Purified by zone melting.

Methyl iodide [74-88-4] M 141.9, b 42.8°, d 2.281, n 1.5315. Deteriorates rapidly with liberation of iodine if exposed to light. Usually purified by shaking with dilute aqueous  $Na_2S_2O_3$  or NaHSO<sub>3</sub> until colourless, then washed with water, dilute aqueous  $Na_2CO_3$ , and more water, dried with CaCl<sub>2</sub> and distd. It is stored in a brown bottle away from sunlight in contact with a small amount of mercury, powdered silver or copper. (Prolonged exposure of mercury to methyl iodide forms methylmercuric iodide.) Methyl iodide can be dried further using CaSO<sub>4</sub> or P<sub>2</sub>O<sub>5</sub>. An alternative purification is by percolation through a column of silica gel or activated alumina, then distn. The soln can be degassed by using a repeated freeze-pump-thaw cycle.

**O-Methylisourea hydrogen sulfate** (2-methylpseudourea sulfate) [29427-58-5] M 172.2, m 114-118°, 119°. Recrystd from MeOH-Et<sub>2</sub>O (327g of salt dissolved in 1L of MeOH and 2.5L of Et<sub>2</sub>O is added) [Fearing and Fox J Am Chem Soc 76 4382 1954]. The picrate has m 192° [Odo et al. J Org Chem 23 1319 1958].

N-Methyl maleimide [930-88-1] M 111.1, m 94-96°. Crystd three times from diethyl ether.

Methylmalonic acid [516-05-2] M 118.1, m 135°(dec),  $pK_1^{25}3.05$ ,  $pK_2^{25}5.76$ . Crystallises as the hydrate from water.

3-Methylmercaptoaniline [1783-81-9] M 139.2, b 101.5-102.5°/0.3mm, 163-165°/16mm,  $d_4^{20}$  1.147,  $n_D^{20}$  1.641, pK<sup>25</sup> 4.05. Purified by fractional distn in an inert atmost phere. It has UV max at 226 and 300. [Bordwell and Cooper J Am Chem Soc 74 10581952.] The N-acetyl derivative has m 78-78.5° (after recrystn from aq EtOH).

4-Methylmercaptoaniline [104-96-1] M 139.2, b 140°/15mm, 151°/25mm, 155°/23mm,  $d_4^{20}$ 1.137,  $n_D^{20}$  1.639, pK<sup>25</sup> 4.40. Purified by fractional distn in an inert atmosphere. [Lumbroso and Passerini Bull Soc Chim Fr 311 1957; Mangini and Passerini J Chem Soc 4954 1956.]

Methyl methacrylate [80-62-6] M 100.1, f -50°, b 46°/100mm, d 0.937, n 1.4144. Washed twice with aqueous 5% NaOH (to remove inhibitors such as hydroquinone) and twice with water. Dried with CaCl<sub>2</sub>, Na<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>SO<sub>4</sub> or MgSO<sub>4</sub>, then with CaH<sub>2</sub> under nitrogen at reduced pressure. The distillate is stored at low temperatures and redistd before use. Prior to distn, inhibitors such as β-naphthylamine (0.2%) or di-β-naphthol are sometimes added. Also purified by boiling aqueous H<sub>3</sub>PO<sub>4</sub> soln and finally with saturated NaCl soln. It was dried for 24h over anhydrous CaSO<sub>4</sub>, distd at 0.1mm Hg at room temperature and stored at -30° [Albeck et al. J Chem Soc, Faraday Trans 1 1 1488 1978].

Methyl methanesulfonate [66-27-3] M 110.3, b 59°/0.6mm, 96-98°/19mm, d 1.300, n 1.4140. Purified by careful fractionation and collecting the middle fraction. Suspected CARCINOGEN. Note that MeSO<sub>3</sub>H has b 134.5-135°, 167-167.5°/10mm and methanesulfonic anhydride has b 138°/10mm)— both are possible impurities.

Methyl methanethiolsulfonate [2949-92-0] M 126.2, b 69-71°/0.4mm, 96-97°/4.5mm, 104-105°/10mm, 119°/16mm, d 1.226, n 1.515. Purified by fractional distn uner reduced pressure, IR: v 1350, 750 cm<sup>-1</sup>. [Applegate et al. J Org Chem 38 943 1973.]

α-Methylmethionine [562-48-1] M 163.0, m 283-284°, pK<sup>30</sup> 9.45. Crystd from aqueous EtOH.

S-Methyl-L-methionine chloride (Vitamin U) [1115-84-0] M 199.5,  $[\alpha]_D^{23} + 33^\circ$  (0.2M HCl), pK<sub>1</sub> 1.9, pK<sub>2</sub> 7.9. Likely impurities are methionine, methionine sulfoxide and methionine sulfone. Crystd from water by adding a large excess of EtOH. Stored in a cool, dry place, protected from light.

*N*-Methylmorpholine [109-02-4] M 101.2, b 116-117°/764mm, d 0.919, n 1.436, pK<sup>25</sup> 7.38. Dried by refluxing with BaO or sodium, then fractionally distd through a helices-packed column.

**4-Methylmorpholine-4-oxide monohydrate** [7529-22-8] **M 135.2, m 71-73°.** When dried for 2-3h at high vacuum it dehydrates. Add MeOH to the oxide and distil off the solvent under vacuum until the temp is  $ca 95^\circ$ . Then add Me<sub>2</sub>CO at reflux then cool to 20°. The crystals are filtered off washed with Me<sub>2</sub>CO and dry. The degree of hydration may vary and may be important for the desired reactions. [van Rheenan et al. *Tetrahedron Lett* 1973 1076; Schneider and Hanze US Pat 2 769 823; see also Sharpless et al. Tetrahedron Lett 2503 1976.]

[90-12-0] M 142.2, f -30°, b 244.6°, d 1.021, n 1.6108. Dried for 1-Methylnaphthalene several days with CaCl<sub>2</sub> or by prolonged refluxing with BaO. Fractionally distd through a glass helices-packed column from sodium. Purified further by soln in MeOH and pptn of its picrate complex by adding to a saturated soln of picric acid in MeOH. The picrate, after crystn to constant melting point (m 140-141°) from MeOH, was dissolved in \*benzene and extracted with aqueous 10% LiOH until the extract was colourless. Evaporation of the \*benzene under vacuum gave 1-methylnaphthalene [Kloetzel and Herzog J Am Chem Soc 72 1991] 1950]. However, neither the picrate nor the styphnate complexes satisfactorily separates 1- and 2methylnaphthalenes. To achieve this, 2-methylnaphthalene (10.7g) in 95% EtOH (50mL) has been ppted with 1,3,5-trinitrobenzene (7.8g) and the complex has been crystd from MeOH to m 153-153.5° (m of the 2-methyl isomer is 124°). [Alternatively, 2,4,7-trinitrofluorenone in hot glacial acetic acid could be used, and the derivative (m 163-164°) recrystd from glacial acetic acid]. The 1-methylnaphthalene was regenerated by passing a soln of the complex in dry \*benzene through a 15-in column of activated alumina and washing with \*benzene/pet ether (b 35-60°) until the coloured band of the nitro compound had moved down near the end of the column. The complex can also be decomposed using tin and acetic-hydrochloric acids, followed by extraction with diethyl ether and \*benzene; the extracts were washed successively with dilute HCl, strongly alkaline sodium hypophosphite, water, dilute HCl and water. [Soffer and Stewart J Am Chem Soc 74 567 1952.] It can be purified from anthracene by zone melting.

**2-Methylnaphthalene** [91-57-6] **M 142.2, m 34.7-34.9°, b 129-130°/25mm.** Fractionally crystd repeatedly from its melt, then fractionally distd under reduced pressure. Crystd from \*benzene and dried under vacuum in an Abderhalden pistol. Purified via its picrate (m 114-115°) as described for 1-methylnaphthalene.

**6-Methyl-2-naphthol** [17579-79-2] **M 158.2, m 128-129°, pK<sub>Est</sub> ~9.8.** Crystd from EtOH or ligroin. Sublimed *in vacuo*.

7-Methyl-2-naphthol [26593-50-0] M 158.2, m 118°, pK<sub>Est</sub> ~9.7. Crystd from EtOH or ligroin. Sublimed *in vacuo*.

Methyl 1-naphthyl ether [2216-69-5] M 158.2, b 90-91°/2mm, d 1.095,  $n^{26}$  1.6210. Steam distd from alkali. The distillate was extracted with diethyl ether. After drying (MgSO<sub>4</sub>) the extract and evaporating diethyl ether, the methyl naphthyl ether was then fractionated under reduced pressure from CaH<sub>2</sub>.

Methyl nitrate [598-58-3] M 77.0, b 65°/760mm, d<sup>5</sup> 1.2322, d<sup>15</sup> 1.2167, d<sup>25</sup> 1.2032. Distd at -80°. The middle fraction was subjected to several freeze-pump-thaw cycles. VAPOUR EXPLODES ON HEATING.

Methyl nitrite [624-91-9] M 61.0, b -12°,  $d^{15}$  (liq) 0.991. Condensed in a liquid nitrogen trap. Distd under vacuum, first trap containing dry Na<sub>2</sub>CO<sub>3</sub> to free it from acid impurities then into further Na<sub>2</sub>CO<sub>3</sub> traps before collection.

N-Methyl-4-nitroaniline [100-15-2] M 152.2, m 152.2°, pK<sup>25</sup> 0.55. Crystd from aqueous EtOH.

**2-Methyl-5-nitroaniline** [99-55-8] **M 152.2, m 109°, pK^{25} 2.35.** Acetylated, and the acetyl derivative crystd to constant melting point, then hydrolysed with 70% H<sub>2</sub>SO<sub>4</sub> and the free base regenerated by treatment with ammonia [Bevan, Fayiga and Hirst *J Chem Soc* 4284 1956].

4-Methyl-3-nitroaniline [119-32-4] M 152.2, m 81.5°, pK<sup>25</sup> 3.02. Crystd from hot water (charcoal), then ethanol and dried in a vacuum desiccator.

Methyl 3-nitrobenzoate [618-95-1] M 181.2, m 78°. Crystd from MeOH (1g/mL).

Methyl 4-nitrobenzoate [619-50-1] M 181.2, m 95-95.5°. Dissolved in diethyl ether, then washed with aqueous alkali, the ether was evaporated and the ester was recrystd from EtOH.

2-Methyl-2-nitro-1,3-propanediol [77-49-6] M 135.1, m 145°. Crystd from n-butanol.

2-Methyl-2-nitro-1-propanol [76-39-1] M 119.1, m 87-88°. Crystd from pet ether.

N-Methyl-4-nitrosoaniline [10595-51-4] M 136.2, m 118°. Crystd from \*benzene.

*N*-Methyl-*N*-nitroso-*p*-toluenesulfonamide (diazald) [80-11-5] M 214.2, m 62°. Crystd from \*benzene by addition of pet ether, store in a refrigerator.

Methylnorbornene-2,3-dicarboxylic anhydride (5-methylnorborn-5-ene-2-endo-3-endo-dicarboxylic anhydride) [25134-21-8] M 178.2, m 88.5-89°. Purified by thin layer chromatography on Al<sub>2</sub>O<sub>3</sub> (previously boiled in EtOAc) and eluted with hexane-\*C<sub>6</sub>H<sub>6</sub> (1:2) then recrystd from \*C<sub>6</sub>H<sub>6</sub>-hexane. The free acid has m 118.5-119.5°. [Miranov et al. *Tetrahedron* 19 1939 1963.]

**3-Methyloctane** [2216-33-3] **M 128.3, b 142-144°/760mm, d 0.719, n 1.407.** Passed through a column of silica gel [Klassen and Ross J Phys Chem **91** 3668 1987].

Methyl octanoate (methyl caprylate) [111-11-5] M 158.2, b 83°/15mm, 193-194°/760mm, d 0.877, n 1.419. Passed through alumina before use.

Methyl oleate [112-62-9] M 296.5, f -19.9°, b 217°/16mm, d 0.874, n 1.4522. Purified by fractional distn under reduced pressure, and by low temperature crystn from acetone.

**3-Methyl-2-oxazolidone** [19836-78-3] M 101.1, m 15°, b 88-91°/1mm, d 1.172, n 1.455. Purified by successive fractional freezing, then dried in a dry-box over 4A molecular sieves for 2 days.

3-Methyl-3-oxetanemethanol (3-hydroxymethyl-3-methyloxetane) [3143-02-0] M 102.1, b 80°/4mm, 92-93°/12mm,  $d_4^{20}$  1.033,  $n_D^{25}$  1.4449. Purified by fractionation through a glass column [Pattison J Am Chem Soc 79 3455 1957].

Methylpentane (mixture of isomers). Passage through a long column of activated silica gel (or alumina) gave material transparent down to 200nm by UV.

**2-Methylpentane** [107-83-5] **M 86.2, b 60.3°, d 0.655, n 1.37145, n<sup>25</sup> 1.36873.** Purified by azeotropic distn with MeOH, followed by washing out the MeOH with water, drying (CaCl<sub>2</sub>, then sodium), and distn. [Forziati et al. J Res Nat Bur Stand 36 129 1946.]

**3-Methylpentane** [96-14-0] **M 86.2, b 63.3°, d 0.664, n 1.37652, n**<sup>25</sup> **1.37384.** Purified by azeotropic distn with MeOH, as for 2-methylpentane. Purified for ultraviolet spectroscopy by passage through columns of silica gel or alumina activated by heating for 8h at 210° under a stream of nitrogen. Has also been treated with conc (or fuming) H<sub>2</sub>SO<sub>4</sub>, then washed with water, aqueous 5% NaOH, water again, then dried (CaCl<sub>2</sub>, then sodium), and distd through a long, glass helices-packed column.

**2-Methyl-2,4-pentanediol** [107-41-5] M 118.2, b 107.5-108.5°/25mm, d 0.922, n<sup>25</sup> 1.4265. Dried with Na<sub>2</sub>SO<sub>4</sub>, then CaH<sub>2</sub> and fractionally distd under reduced pressure through a packed column, taking precautions to avoid absorption of water.

**2-Methyl-1-pentanol** [105-30-6] **M 102.2, b 65-66°/60mm, 146-147°/760mm, d 0.827, n 1.420.** Dried with Na<sub>2</sub>SO<sub>4</sub> and distd.

**4-Methyl-2-pentanol** [108-11-2] **M 102.2, b 131-132°, d 0.810, n 1.413.** Washed with aqueous NaHCO<sub>3</sub>, dried and distd. Further purified by conversion to the phthalate ester by adding 120mL of dry pyridine and 67g of phthalic anhydride per mole of alcohol, purifying the ester and steam distilling it in the presence of NaOH. The distillate was extracted with ether, and the extract was dried and fractionally distd. [Levine and Walti *J Biol Chem* **94** 367 1931].

**3-Methyl-3-pentanol carbamate (Emylcamate)** [78-28-4] **M 145.2, m 56-58.5°.** Crystd from 30% EtOH.

**4-Methyl-2-pentanone (methyl isobutyl ketone)** [108-10-1] **M 100.2, b 115.7°, d 0.801, n 1.3958, n^{25} 1.3938.** Refluxed with a little KMnO<sub>4</sub>, washed with aqueous NaHCO<sub>3</sub>, dried with CaSO<sub>4</sub> and distd. Acidic impurities were removed by passage through a small column of activated alumina.

2-Methyl-1-pentene [763-29-1] M 84.2, b 61.5-62°, d 0.680, n 1.395. Water was removed, and peroxide formation prevented by several vacuum distns from sodium, followed by storage with sodium-potassium alloy.

*cis*-4-Methyl-2-pentene [691-38-3] M 84.2, m -134.4°, b 57.7-58.5°, d 0.672, n 1.388. Dried with CaH<sub>2</sub>, and distd.

*trans*-4-Methyl-2-pentene [674-76-0] M 84.2, m -140.8°, b 58.5°, d 0.669, n 1.389. Dried with CaH<sub>2</sub>, and distd.

5-Methyl-1,10-phenanthroline [3002-78-6] M 194.2, m 113°(anhydr), pK<sup>25</sup> 5.28. Crystd from \*benzene/pet ether.

N-Methylphenazonium methosulfate see 5-methylphenazinium methyl sulfate on p. 547 in Chapter 6.

**N-Methylphenothiazine** [1207-72-3] M 213.2,  $\alpha$ -form m 99.3° and b 360-365°, ß-form m 78-79°. Recrystn (three times) from EtOH gave  $\alpha$ -form (prisms). Recrystn from EtOH/\*benzene gave the ß-form (needles). Also purified by vacuum sublimation and carefully dried in a vacuum line. Also crystd from toluene and stored in the dark [Guarr et al. J Am Chem Soc 107 5104 1985; Olmsted et al. J Am Chem Soc 109 3297 1987.]

4-Methylphenylacetic acid [622-47-9] M 150.2, m 94°, pK<sup>25</sup> 4.37. Crystd from heptane or water.

1-Methyl-1-phenylhydrazine sulfate [33008-18-3] M 218.2,  $pK^{25}$  4.98 (free base). Crystd from hot H<sub>2</sub>O by addition of hot EtOH.

**3-Methyl-1-phenyl-5-pyrazolone** [89-25-8] **M 174.2, m 127°.** Crystd from hot  $H_2O$ , or EtOH/water (1:1).

N-Methylphthalimide [550-44-7] M 161.1, m 133.8°. Recrystd from absolute EtOH.

**2-Methylpiperazine** [109-07-9] **M 100.2, m 61-62°, 66°, b 147-150°/739mm, pK\_1^{25} 5.46, pK\_2^{25} 9.90. Purified by zone melting and by distn.** 

**3-Methylpiperidine** [626-56-2] **M 99.2, b 125°/763mm, d 0.846, n<sup>25</sup> 1.4448, pK<sup>25</sup> 11.07.** Purified via the hydrochloride (m 172°). [Chapman, Isaacs and Parker J Chem Soc 1925 1959.]

**4-Methylpiperidine** [626-58-4] **M 99.2, b 124.4°/755mm, d 0.839, n^{25} 1.4430, pK^{25} 10.78. Purified via the hydrochloride (m 189°). Freed from 3-methylpyridine by zone melting.** 

1-Methyl-4-piperidone [1445-73-4] M 113.2, b 53-56°/0.5mm, 54-56°/9mm, 68-71°/17mm, 85-87°/45mm,  $d_4^{20}$  0.972,  $n_D^{25}$  1.4588,  $pK^{25}$  7.9. It is best purified by fractional distn. The hydrochloride of the hydrate (4-diol) has m 94.7-95.5°, but the anhydrous hydrochloride which crystallises from CHCl<sub>3</sub>-Et<sub>2</sub>O and has m 165-168° (164-167°) and can also be obtained by sublimation at 120°/2mm. The oxime has m 130-132° (from Me<sub>2</sub>CO). The methiodide crystallises from MeOH and the crystals with 1MeOH has m 189-190°, and the solvent-free *iodide* has m 202-204° dec. [Lyle et al. J Org Chem 24 342 1959; Bowden and Greeen J Chem Soc 1164 1952; Tomita Yakugaku Zasshi (J Pharm Soc Japan) 71 1053 1951.]

2-Methylpropane-1,2-diamine (1,2-diamino-2-methylpropane) [811-93-8] M 88.2, b 47-48°/17mm,  $pK_1^{25}$  6.25 (6.18),  $pK_2^{25}$  9.82 (9.42). Dried with sodium for 2 days, then distd under reduced pressure from sodium.

**2-Methylpropane-1-thiol** [513-44-0] M 90.2, b 41.2°/142mm,  $n^{25}$  1.43582,  $pK_{Est} \sim 10.8$ . Dissolved in EtOH, and added to 0.25M Pb(OAc)<sub>2</sub> in 50% aqueous EtOH. The ppted lead mercaptide was filtered off, washed with a little EtOH, and impurities were removed from the molten salt by steam distn. After cooling, dilute HCl was added dropwise to the residue, and the mercaptan was distd directly from the flask. Water was separated from the distillate, and the mercaptan was dried (Na<sub>2</sub>CO<sub>3</sub>) and distd under nitrogen. [Mathias J Am Chem Soc 72 1897 1950.]

2-Methylpropane-2-thiol [75-66-1] M 90.2, b 61.6°/701mm,  $d^{25}$  0.79426,  $n^{25}$  1.41984,  $pK^{25}$  11.22. Dried for several days with CaO, then distd from CaO. Purified as for 2-methylpropane-1-thiol.

**2-Methyl-1-propanol** (isobutanol) [78-83-1] M 74.1, b 107.9°, d 0.804,  $n^{15}$  1.39768,  $n^{25}$  1.3939. Dried by refluxing with CaO and BaO for several hours, followed by treatment with calcium or aluminium amalgam, then fractional distn from sulfanilic or tartaric acids. More exhaustive purifications involve formation of phthalate or borate esters. Heating with phthalic anhydride gives the *acid phthalate* which, after crystn to constant melting point (m 65°) from pet ether, is hydrolysed with aqueous 15% KOH. The alcohol is distd as the water azeotrope and dried with K<sub>2</sub>CO<sub>3</sub>, then anhydrous CuSO<sub>4</sub>, and finally magnesium turnings, followed by fractional distn. [Hückel and Ackermann J Prakt Chem 136 15 1933.] The borate ester is formed by heating the dried alcohol for 6h in an autoclave at 160-175° with a quarter of its weight of boric acid. After fractional distns under vac the ester is hydrolysed by heating for a short time with aq alkali and the alcohol is dried with CaO and distd. [Michael, Scharf and Voigt J Am Chem Soc 38 653 1916.] (see p. 271).

Methyl propiolate [922-67-8] M 84.1, b 100°/atm, 102°/atm, 103-105°/atm, d 0.945, n 1.4080. Purified by fractional distn and collecting the middle fraction; note that propiolic acid has a high b [144°(dec)/atm]. LACHRYMATORY.

**N-Methylpropionamide** [1187-58-2] **M 87.1, f -30.9°, b 103°/12-13mm, d 0.934, n^{25} 1.4356.** A colourless, odourless, neutral liquid at room temperature with a high dielectric constant. The amount of water present can be determined directly by Karl Fischer titration; GLC and NMR have been used to detect unreacted propionic acid. Commercial material of high quality is available, probably from the condensation of anhydrous methylamine with 50% excess of propionic acid. Rapid heating to 120-140° with stirring favours the reaction by removing water either directly or as the ternary xylene azeotrope. The quality of the distillate improves during the distn. The propionamide can be dried over CaO.  $H_2O$  and unreacted propionic acid were removed as their xylene azeotropes. It was vacuum dried. Material used as an electrolyte solvent (specific conductance less than  $10^{-6}$  ohm<sup>-1</sup> cm<sup>-1</sup>) was obtained by fractional distn under reduced pressure, and stored over BaO or molecular sieves because it readily absorbs moisture from the atmosphere on prolonged storage. [Hoover Pure Appl Chem 37 581 1974; Recommended Methods for Purification of Solvents and Tests for Impurities, Coetzee Ed., Pergamon Press, 1982.]

Methyl propionate [554-12-1] M 88.1, b 79.7°. Washed with satd aq NaCl, then dried with  $Na_2CO_3$  and distd from  $P_2O_5$ . (This removes any free acid and alcohol.) It has also been dried with anhydrous CuSO<sub>4</sub>.

Methyl *n*-propyl ether [557-17-5] M 74.1, b 39°, d 0.736,  $n^{14}$  1.3602,  $pK^{25}$  -3.79 (aq H<sub>2</sub>SO<sub>4</sub>). Dried with CaSO<sub>4</sub>, then passed through a column of alumina (to remove peroxides) and fractionally distd.

Methyl *n*-propyl ketone [107-87-9] M 86.1, b 102.4°, d 0.807, n 1.3903. Refluxed with a little KMnO<sub>4</sub>, dried with CaSO<sub>4</sub> and distd. It was converted to its bisulfite addition compound by shaking with excess saturated aqueous NaHSO<sub>3</sub> at room temperature, cooling to 0°, filtering, washing with diethyl ether and drying. Steam distillation gave a distillate from which the ketone was recovered, washed with aq NaHCO<sub>3</sub> and distd water, dried (K<sub>2</sub>CO<sub>3</sub>) and fractionally distd. [Waring and Garik J Am Chem Soc 78 5198 1956.]

3-Methyl-1-propyn-3-ol carbamate [302-66-9] M 141.2, m 55.8-57°. Crystd from ether/pet ether or cyclohexane.

**2-Methylpyrazine** [109-08-0] **M** 94.1, **b** 136-137°, **d** 1.025, **n** 1.505,  $pK_1^{25}$ -5.25 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$ 1.47. Purified via the picrate. [Wiggins and Wise J Chem Soc 4780 1956.]

**2-Methylpyridine** (2-picoline) [109-06-8] M 93.1, b 129.4°, d 0.9444, n 1.50102,  $pK^{25}$  5.96. Biddiscombe and Handley [J Chem Soc 1957 1954] steam distd a boiling soln of the base in 1.2 equivalents of 20% H<sub>2</sub>SO<sub>4</sub> until about 10% of the base had been carried over, along with non-basic impurities. Excess aqueous NaOH was then added to the residue, the free base was separated, dried with solid NaOH and fractionally distd.

2-Methylpyridine can also be dried with BaO, CaO, CaH<sub>2</sub>, LiAlH<sub>4</sub>, sodium or Linde type 5A molecular sieves. An alternative purification is *via* the ZnCl<sub>2</sub> adduct, which is formed by adding 2-methylpyridine (90mL) to a soln of anhydrous ZnCl<sub>2</sub> (168g) and 42mL conc HCl in absolute EtOH (200mL). Crystals of the complex are filtered off, recrystd twice from absolute EtOH (to give **m** 118.5-119.5°), and the free base is liberated by addition of excess aqueous NaOH. It is steam distd, and solid NaOH added to the distillate to form two layers, the upper one of which is then dried with KOH pellets, stored for several days with BaO and fractionally distd. Instead of ZnCl<sub>2</sub>, HgCl<sub>2</sub> (430g in 2.4L of hot water) can be used. The complex, which separates on cooling, can be dried at 110° and recrystd from 1% HCl (to **m** 156-157°).

**3-Methylpyridine** (3-picoline) [108-99-6] M 93.1, m -18.5°, b 144°/767mm, d 0.957, n 1.5069,  $pK^{25}$  5.70. In general, the same methods of purification that are described for 2-methylpyridine can be used. However, 3-methylpyridine often contains 4-methylpyridine and 2,6-lutidine, neither of which can be removed satisfactorily by drying and fractionation, or by using the ZnCl<sub>2</sub> complex. Biddiscombe and Handley [J Chem Soc 1957 1954], after steam distn as for 2-methylpyridine, treated the residue with urea to remove 2,6lutidine, then azeotropically distd with acetic acid (the azeotrope had b 114.5°/712mm), and recovered the base by adding excess of aqueous 30% NaOH, drying with solid NaOH and carefully fractionally distilling. The distillate was then fractionally crystd by slow partial freezing. An alternative treatment [Reithof et al. Ind Eng Chem (Anal Edn) 18 458 1946] is to reflux the crude base (500mL) for 20-24h with a mixture of acetic anhydride (125g) and phthalic anhydride (125g) followed by distn until phthalic anhydride begins to pass over. The distillate was treated with NaOH (250g in 1.5L of water) and then steam distd. Addition of solid NaOH (250g) to this distillate (ca 2L) led to the separation of 3-methylpyridine which was removed, dried (K<sub>2</sub>CO<sub>3</sub>, then BaO) and fractionally distd. (Subsequent fractional freezing would probably be advantageous.) 4-Methylpyridine (4-picoline) [108-89-4] M 93.1, m 4.25°, b 145.0°/765mm, d 0.955, n 1.5058,  $pK^{25}$  4.99. Can be purified as for 2-methylpyridine. Biddescombe and Handley's method for 3methylpyridine is also applicable. Lidstone [J Chem Soc 242 1940] purified via the oxalate (m 137-138°) by heating 100mL of 4-methylpyridine to 80° and adding slowly 110g of anhydrous oxalic acid, followed by 150mL of boiling EtOH. After cooling and filtering, the ppte was washed with a little EtOH, then recrystd from EtOH, dissolved in the minimum quantity of water and distd with excess 50% KOH. The distillate was dried with solid KOH and again distd. Hydrocarbons can be removed from 4-methylpyridine by converting the latter to its hydrochloride, crystallising from EtOH/diethyl ether, regenerating the free base by adding alkali and distilling. As a final purification step, 4-methylpyridine can be fractionally crystd by partial freezing to effect a separation from 3-methylpyridine. Contamination by 2,6-lutidine is detected by its strong absorption at 270nm.

4-Methylpyridine 1-oxide [1003-67-4] M 109.1, m 182-184°. See 4-picoline-N-oxide on p. 335.

N-Methylpyrrole [96-54-8] M 81.1, b 115-116<sup>o</sup>/756mm, d 0.908, n 1.487, pK -3.4 (-2.90). Dried with CaSO<sub>4</sub>, then fractionally distd from KOH immediately before use.

1-Methyl-2-pyrrolidinone [872-50-4] M 99.1, f -24.4, b 65-76°/1mm, 78-79°/12mm, 94-96°/20mm, 202°/760mm,  $d_4^{20}$  1.0328,  $n_D^{20}$  1.4678, pK -0.17 (also -0.92, and 0.2). Dried by removing water as \*benzene azeotrope. Fractionally distd at 10 torr through a 100-cm column packed with glass helices. [Adelman J Org Chem 29 1837 1964; McElvain and Vozza J Am Chem Soc 71 896 1949.] The hydrochloride has m 86-88° (from EtOH or Me<sub>2</sub>CO-EtOH) [Reppe et al. Justus Liebigs Ann Chem 596 1 1955].

**2-Methylquinoline** (quinaldine) [91-63-4] M 143.2, b 86-87°/1mm, 155°/14mm, 246-247°/760mm, d 1.058, n 1.6126,  $pK^{25}$  5.65. Dried with Na<sub>2</sub>SO<sub>4</sub> or by refluxing with BaO, then fractionally distd under reduced pressure. Redistd from zinc dust. Purified by conversion to its *phosphate* (m 220°) or *picrate* (m 192°) from which after recrystn, the free base was regenerated. [Packer, Vaughan and Wong *J Am Chem Soc* 80 905 1958.] Its ZnCl<sub>2</sub> complex can be used for the same purpose.

4-Methylquinoline (lepidine) [491-35-0] M 143.2, b 265.5°, d 1.084, n 1.61995, pK<sup>25</sup> 5.59. Refluxed with BaO, then fractionally distd. Purified via its recrystd dichromate salt (m 138°). [Cumper, Redford and Vogel J Chem Soc 1176 1962.]

**6-Methylquinoline** [91-62-3] **M 143.2, b 258.6°, d 1.067, n 1.61606, pK^{25} 4.92.** Refluxed with BaO, then fractionally distd. Purified via its recrystd  $ZnCl_2$  complex (m 190°). [Cumper, Redford and Vogel J Chem Soc 1176 1962.]

7-Methylquinoline [612-60-2] M 143.2, m 38°, b 255-260°, d 1.052, n 1.61481, pK<sup>25</sup> 5.29. Purified via its dichromate complex (m 149°, after five recrystns from water). [Cumper, Redford and Vogel J Chem Soc 1176 1962.]

8-Methylquinoline [611-32-5] M 143.2, b 122.5°/16mm, 247.8°/760mm, d 1.703, n 1.61631, pK<sup>25</sup> 4.60. Purified as for 2-methylquinoline. The *phosphate* and *picrate* have m 158° and m 201° respectively.

Methyl Red (4-dimethylaminoazobenzene-2'-carboxylic acid) [493-52-7] M 269.3, m 181-182°, CI 13020,  $pK_1^{25}$  2.30,  $pK_2^{25}$  4.82. The acid is extracted with boiling toluene using a Soxhlet apparatus. The crystals which separated on slow cooling to room temperature are filtered off, washed with a little toluene and recrystd from glacial acetic acid, \*benzene or toluene followed by pyridine/water. Alternatively, dissolved in aq 5% NaHCO<sub>3</sub> soln, and ppted from hot soln by dropwise addition of aq HCl. Repeated until the extinction coefficients did not increase.

Methyl salicylate (methyl 2-hydroxybenzoate) [119-36-8] M 152.2, m -8.6°, b 79°/6 mm, 104-105°/14 mm, 223.3°/atm,  $d_4^{20}$  1.1149,  $n_D^{20}$  1.5380, pK<sup>25</sup> 10.19. Dilute with Et<sub>2</sub>O, wash with satd NaHCO<sub>3</sub> (it may effervesce due to the presence of free acid), brine, dry MgSO<sub>4</sub>, filter, evaporate and distil.

Its solubility is 1g/1.5L of  $H_2O$ . The *benzoyl* derivative has  $m 92^\circ$  (b 270-280°/120mm), and the 3,5dinitrobenzoate has  $m 107.5^\circ$ , and the 3,5-dinitrocarbamoyl derivative has  $m 180-181^\circ$ . [Hallas J Chem Soc 5770 1965.]

Methyl stearate [122-61-8] M 298.5, m 41-43°, b 181-182°/4mm. Crystd from pet ether or distd.

 $\alpha$ -Methylstyrene (monomer) [98-83-9] M 118.2, b 57°/15mm, d 0.910, n 1.5368. Washed three times with aqueous 10% NaOH (to remove inhibitors such as quinol), then six times with distd water, dried with CaCl<sub>2</sub> and distd under vacuum. The distillate is kept under nitrogen, in the cold, and redistd if kept for more than 48h before use. It can also be dried with CaH<sub>2</sub>.

trans-B-Methylstyrene [873-66-5] M 118.2, b 176°/760mm, d 0.910, n 1.5496. Distd under nitrogen from powdered NaOH through a Vigreux column, and passed through activated neutral alumina before use [Wong et al. J Am Chem Soc 109 3428 1987].

4-Methylstyrene [622-97-9] M 118.2, b 60°/12mm, 106°/10mm,  $d_4^{20}$  0.9173,  $n_D^{20}$  1.542. Purified as the above styrenes and add a small amount of antioxidant if it is to be stored, UV in EtOH  $\lambda$ max 285nm (log  $\varepsilon$  3.07), and in EtOH + HCl 295nm (log  $\varepsilon$  2.84) and 252nm (log  $\varepsilon$  4.23). [Schwartzman and Carson J Am Chem Soc 78 322 1956; Joy and Orchin J Am Chem Soc 81 305 1959; Buck et al. J Chem Soc 23771949.]

Methylsuccinic acid [498-21-5] M 132.1, m 115.0°, pK<sub>1</sub><sup>25</sup> 3.88, pK<sub>2</sub><sup>25</sup> 5.35. Crystd from water.

(±)-3-Methylsulfolane (3-methyl-tetrahydrothiophene-1,1-dioxide) [872-93-5] M 134.2, m 0.5°, b 101°/2mm, 125-130°/12mm, 278-282°/763.5mm,  $d_4^{20}$  1.1885,  $n_D^{20}$  1.4770. Distil under vacuum and recryst from Et<sub>2</sub>O at -60° to -70°. IR film has strong bands at 570 and 500 cm<sup>-1</sup>. [Eigenberger J Prakt Chem [2] 131 289 1931; Freaheller and Katon Spectrochim Acta 20 10991964.]

17 $\alpha$ -Methyltestosterone [58-18-4] M 302.5, m 164-165°,  $[\alpha]_{546}^{20}$  +87° (c 1, dioxane). Crystd from hexane/\*benzene.

Methyl tetradecanoate (methyl myristate) [124-10-7] M 382.7, m 18.5°, b 155-157°/7 mm. Passed through alumina before use.

**2-Methyltetrahydrofuran** [96-47-9] **M 86.1, b 80.0°, d\_4^{20} 0.856, n\_D^{20} 1.4053.** Likely impurities are 2-methylfuran, methyldihydrofurans and hydroquinone (stabiliser, which is removed by distn under reduced pressures). It was washed with 10% aqueous NaOH, dried, vacuum distd from CaH<sub>2</sub>, passed through freshly activated alumina under nitrogen, and refluxed over sodium metal under vacuum. Stored over sodium. [Ling and Kevan J Phys Chem 80 592 1976.] Vacuum distd from sodium, and stored with sodium-potassium alloy. (Treatment removes water and prevents the formation of peroxides.) Alternatively, it can be freed from peroxides by treatment with ferrous sulfate and sodium bisulfate, then solid KOH, followed by drying with, and distilling from, sodium, or type 4A molecular sieves under argon. It may be difficult to remove \*benzene if it is present as an impurity (can be readily detected by its ultraviolet absorption in the 249-268nm region). [Ichikawa and Yoshida J Phys Chem 88 3199 1984.] It has also been purifed by percolating through Al<sub>2</sub>O<sub>3</sub> and fractionated collecting fraction b 79.5-80°. After degassing, the material was distd onto degassed molecular sieves, then distd onto anthracene and a sodium mirror. The solvent was distd from the green soln onto potassium mirror or sodium-potassium alloy, from which it was distilled again. [Mohammad and Kosower J Am Chem Soc 93 2713 1971.] It should be stored in the presence of 0.1% of hydroquinone as stabiliser. HARMFUL VAPOURS.

N-Methylthioacetamide [5310-10-1] M 89.1, m 59°. Recrystd from \*benzene.

**3-Methylthiophene** [6]6-44-4] **M 98.2, b 111-113°, d 1.024, n 1.531.** Dried with  $Na_2SO_4$ , then distd from sodium.

**6(4)-Methyl-2-thiouracil** [56-04-2] **M 142.2, m 330°(dec), 299-303°(dec), 323-324°(dec), pK 8.1.** Crystd from a large volume of H<sub>2</sub>O. Purified by dissolving in base adding charcoal, filtering and acidifying with AcOH. Suspend the wet solid (*ca* 100g) in boiling H<sub>2</sub>O (1L), stir and add AcOH (20mL), stir and refrigerate. Collect the product, wash with cold H<sub>2</sub>O (4 x 200mL), drain for several hours then place in an oven at 70° to constant weight. [IR: Short and Thompson *J Chem Soc* 168 1952; Foster and Snyder Org Synth Coll Vol IV 638 1063.]

Methyl 4-toluenesulfonate [80-48-8] M 186.2, m 25-28°, 28°, b 144.6-145.2°/5mm, 168-170°/13mm,  $d_4^{20}$  1.23. It is purified by distn *in vacuo* and could be crystd from pet ether or Et<sub>2</sub>O-pet ether at low temperature. It is a powerful methylating agent and is TOXIC and a skin irritant, so it is better to purify by repeated distn. [IR: Schreiber Anal Chem 21 1168 1949; Buehler et al. J Org Chem 2 167 1937; Roos et al. Org Synth Coll Vol I 145 1948.]

**4-Methyl-1,2,4-triazoline-3,5-dione** (MTAD) [13274-43-6] M 113.1, m 103-104°, m 107-109°. Obtained as pink needles by sublimation at 40-50°/0.1mm (see 4-phenyl-1,2,4-triazoline-3,5-dione, PTAD below). [Cookson et al. Org Synth 51 121 1971; Cheng et al. J Org Chem 49 2910 1984.]

2-Methyltricycloquinazoline [2642-52-6] M 334.4, m >300°. Purified by vac sublimation. CARCINOGEN.

Methyl trifluoromethanesulfonate (methyl triflate) [333-27-7] M 164.1, b 97-97.5°/736mm, 99°/atm, 100-102°/atm,  $d_4^{20}$  1.496,  $n_D^{25}$  1.3238. It is a strong methylating agent but is corrosive and POISONOUS. Fractionate carefully and collecting the middle fraction (use efficient fume cupboard) and keep away from moisture. It is POWERFUL ALKYLATING AGENT and a strong IRRITANT. [IR: Gramstad and Haszeldine J Chem Soc 173 1956, 4069 1957.] Trifluoromethanesulfonic acid (triflic acid) [1493-13-6] M 151.1, boils higher (b 162°/atm), has a pKa of 3.10, and is TOXIC and hygroscopic. [Hansen J Org Chem 30 4322 1965; Kurz and El-Nasr J Am Chem Soc 104 5823 1982.]

*N*-Methyltryptophan (L-abrine) [526-31-8] M 218.3, m 295°(dec),  $[\alpha]_D^{21}$ +44.4° (c 2.8, 0.5M HCl), pK<sub>Est(1)</sub>~2.3, pK<sub>Est(2)</sub>~9.7. Crystd from water.

*dl-5-Methyltryptophan* [951-55-3] M 218.3, m 275°(dec) [pK see tryptophan]. Crystd from aqueous EtOH. *Picrate* has m 202° (dec).

**6-Methyluracil** [626-48-2] **M 126.1, m 270-280°(dec),**  $\lambda_{max}$  260<sub>nm</sub> loge 3.97, pK<sub>1</sub> ~1.1, pK<sub>2</sub> **9.8.** Crystd from EtOH or acetic acid.

**3-Methyluric acid** [39717-48-1] **M 182.1, m >350°, pK\_1 5.75 (6.2), pK\_2 >12. Crystd from water.** 

7-Methyluric acid [30409-21-3] M 182.1, m >380°, pK<sub>1</sub> 5.6, pK<sub>2</sub> 10.3. Crystd from water.

9-Methyluric acid [30345-24-5] M 182.1, m >400°. Crystd from water.

Methyl vinyl ketone [78-94-4] M 70.1, b  $62-68^{\circ}/400$  mm, 79-80°/760 mm, d 0.845, n 1.413. Forms an 85% azeotrope with water. After drying with K<sub>2</sub>CO<sub>3</sub> and CaCl<sub>2</sub> (with cooling), the ketone is distd at low pressures.

Methyl vinyl sulfone [3680-02-2] M 106.1, b 116-118°/20mm, d 1.215, n 1.461. Passed through a column of alumina, then degassed and distd on a vacuum line and stored at -190° until required.

Methyl Violet 2B [4,4'-bis-(diethylamino)-4"-methyliminotriphenylmethyl hydrochloride) [8004-87-3] M 394.0, m 137°(dec), CI 42535, max ~580nm. Crystd from absolute EtOH by pptn with diethyl ether during cooling in an ice-bath. Filtered off and dried at 105°.

1-Methylxanthine [6136-37-4] M 166.1, m >360° pK<sub>1</sub><sup>20</sup> 7.90, pK<sub>2</sub><sup>20</sup> 12.23. Crystd from water.

3-Methylxanthine [1076-22-8] M 166.1, m >360° pK<sub>1</sub><sup>20</sup>8.45, pK<sub>2</sub><sup>20</sup>11.92. Crystd from water.

7-Methylxanthine [552-62-5] M 166.1, m >380°(dec) pK<sub>1</sub><sup>20</sup> 8.42, pK<sub>2</sub><sup>20</sup>>13. Crystd from water.

8-Methylxanthine [17338-96-4] M 166.1, m 292-293°(dec). Crystd from water.

**9-Methylxanthine** [1198-33-0] **M 166.1, m 384°(dec), pK<sub>1</sub><sup>20</sup> 2.0, pK<sub>2</sub><sup>20</sup> 6.12, pK<sub>3</sub><sup>20</sup> 10.5 (>13).** Crystd from water.

Metrazol (Cardiazol, Leptazol, 3a,4,5,6,7,8-hexahydro-1,2,3,3a-tetraaza-azulene, 1,5pentamethylene-1,2,3,4-tetrazole) [54-95-5] M 138.2, m 61°, b 194°/12mm, pK<sub>Est</sub> ~<0. Crystd from diethyl ether. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

Michler's ketone [4,4'-bis(dimethylamino)benzophenone] [90-94-8] M 268.4, m 179°, pK<sup>25</sup> 9.84. Dissolved in dilute HCl, filtered and ppted by adding ammonia (to remove water-insoluble impurities such as benzophenone). Then crystd from EtOH or pet ether. [Suppan J Chem Soc, Faraday Trans1 71 539 1975.] It was also purified by dissolving in \*benzene, then washed with water until the aqueous phase was colourless. The \*benzene was evaporated off and the residue recrystd three times from \*benzene and EtOH [Hoshino and Kogure J Phys Chem 72 417 1988].

Monensin [17090-79-8] M 670.9, m 103-105° (1  $H_2O$ ),  $[\alpha]_D + 47.7°$ ,  $pK_{Est} \sim 4.6$ , pK 6.6 (66% Me<sub>2</sub>NCHO). Purified by chromatography, stable in aq alkaline soln. Slightly sol in  $H_2O$  but sol in EtOH, EtOAc and Et<sub>2</sub>O.

**N-Monobutyl urea** [592-31-4] M 116.2, m 96-98°. Crystd from EtOH/water, then dried under vacuum at room temperature.

*N*-Monoethyl urea [625-52-5] M 88.1, m 92-95°. Crystd from EtOH/water, then dried under vacuum at room temperature.

**N-Monomethyl urea** [598-50-5] M 74.1, m 93-95°. Crystd from EtOH/water, then dried under vacuum at room temperature.

Monopropyl urea [627-06-5] M 102.1, m 110°. Crystd from EtOH.

Morin (hydrate) (2',3,4',5,7-pentahydroxyflavone) [480-16-0] M 302.2, m 289-292°, pK<sub>1</sub> 5.3, pK<sub>2</sub> 8.74. Stirred at room temperature with ten times its weight of absolute EtOH, then left overnight to settle. Filtered, and evaporated under a heat lamp to one-tenth its volume. An equal volume of water was added, and the ppted morin was filtered off, dissolved in the minimum amount of EtOH and again ppted with an equal volume of water. The ppte was filtered, washed with water and dried at 110° for 1h. (Yield *ca* 2.5%.) [Perkins and Kalkwarf *Anal Chem* 28 1989 1956.] Complexes with W and Zr.

Morphine (H<sub>2</sub>O) [57-27-2] M 302.2, m 230°(dec),  $[\alpha]_D^{23}$ -130.9° (MeOH), pK<sub>1</sub> 8.31, pK<sub>2</sub> 9.51. Crystd from MeOH.

Morpholine [110-91-8] M 87.1, f -4.9°, b 128.9°, d 1.0007, n 1.4540,  $n^{25}$  1.4533,  $pK^{25}$  8.33. Dried with KOH, fractionally distd, then refluxed with Na, and again fractionally distd. Dermer and Dermer [J Am Chem Soc 59 1148 1937] ppted as the oxalate by adding slowly to slightly more than 1 molar equivalent of oxalic acid in EtOH. The ppte was filtered and recrystd twice from 60% EtOH. Addition of the oxalate to conc aq NaOH regenerated the base, which was separated and dried with solid KOH, then sodium, before being fractionally distd.

§ A polystyrene supported morpholine is commercially available.

2-(N-Morpholino)ethanesulfonic acid (MES) [4432-31-9] M 213.3, m >300°(dec), pK<sup>20</sup> 6.15. Crystd from hot EtOH containing a little water.

Mucochloric acid (2,3-dichloro-4-oxo-2-butenoic acid) [87-56-9] M 169.0, m 124-126°, pK<sup>25</sup> 4.20. Crystd twice from water (charcoal).

trans, trans-Muconic acid (hexa-2,4-dienedioic acid) [3588-17-8] M 142.1, m 300°,  $pK^{25}$  4.51, for cis, cis  $pK^{25}$  4.49. Cryst from H<sub>2</sub>O.

Muramic acid (H<sub>2</sub>O) (3-O- $\alpha$ -carboxyethyl-D-glucosamine) [1114-41-6] M 251.2, m 152-154°(dec). See muramic acid on p. 549 in Chapter 6.

Murexide (ammonium purpurate) [3051-09-0] M 284.2, m >300°,  $\lambda_{max}$  520nm ( $\epsilon$  12,000), pK<sub>2</sub> 9.2, pK<sub>3</sub> 10.9. The sample may be grossly contaminated with uramil, alloxanthine, etc. Difficult to purify. It is better to synthesise it from pure alloxanthine [Davidson J Am Chem Soc 58 1821 1936]. Crystd from water.

Myristic acid (tetradecanoic acid) [544-63-8] M 228.4, m 58°,  $pK^{20}$  6.3 (50% EtOH),  $pK_{Est}$  ~4.9 (H<sub>2</sub>O). Purified via the methyl ester (b 153-154°/10mm, n<sup>25</sup> 1.4350), as for capric acid. [Trachtman and Miller J Am Chem Soc 84 4828 1962.] Also purified by zone melting. Crystd from pet ether and dried in a vacuum desiccator containing shredded wax.

**Naphthacene** (benz[b]anthracene, 2,3-benzanthracene, rubene) [92-24-0] M 228.3, m >300°, 341° (open capillary), 349°, 357°. Crystd from EtOH or \*benzene. Dissolved in sodiumdried \*benzene and passed through a column of alumina. The \*benzene was evaporated under vacuum, and the chromatography was repeated using fresh \*benzene. Finally, the naphthacene was sublimed under vacuum. [Martin and Ubblehode J Chem Soc 4948 1961.] Also recrysts in orange needles from xylene and sublimes *in vacuo* at 186°. [UV: Chem Ber 65 517 1932, 69 607 1936; IR: Spectrochim Acta 4 373 1951.]

**2-Naphthaldehyde** [66-99-9] M 156.2, m 59°, b 260°/19mm,  $pK^{20}$  -7.04 (aq H<sub>2</sub>SO<sub>4</sub>). Distilled with steam and crystd from water or EtOH.

Naphthalene [91-20-3] M 128.2, m 80.3°, b 87.5°/10mm, 218.0°/atm, d 1.0253, d<sup>100</sup> 0.9625, n<sup>85</sup> 1.5590. Crystd one or more times from the following solvents: EtOH, MeOH, CCl<sub>4</sub>, \*benzene, glacial acetic acid, acetone or diethyl ether, followed by drying at 60° in an Abderhalden drying apparatus. Also purified by vacuum sublimation and by fractional crystn from its melt. Other purification procedures include refluxing in EtOH over Raney Ni, and chromatography of a CCl<sub>4</sub> soln on alumina with \*benzene as eluting solvent. Baly and Tuck [*J Chem Soc* 1902 *1908*] purified naphthalene for spectroscopy by heating with conc H<sub>2</sub>SO<sub>4</sub> and MnO<sub>2</sub>, followed by steam distn (repeating the process), and formation of the picrate which, after recrystallisation, was decomposed and the naphthalene was steam distd. It was then crystd from dilute EtOH. It can be dried over P<sub>2</sub>O<sub>5</sub> under vacuum. Also purified by sublimation and subsequent crystn from cyclohexane. Alternatively, it has been washed at 85° with 10% NaOH to remove phenols, with 50% NaOH to remove nitriles, with 10% H<sub>2</sub>SO<sub>4</sub> to remove organic bases, and with 0.8g AlCl<sub>3</sub> to remove thianaphthalenes and various alkyl derivatives. Then it was treated with 20% H<sub>2</sub>SO<sub>4</sub>, 15% Na<sub>2</sub>CO<sub>3</sub> and finally distd. [Gorman et al. *J Am Chem Soc* 107 4404 *1985*.]

Zone refining purified naphthalene from anthracene, 2,4-dinitrophenylhydrazine, methyl violet, benzoic acid, methyl red, chrysene, pentacene and indoline.

Naphthalene-2,5-disulfonic acid [92-41-1] M 288.2, pK<sub>Est</sub> <0. Crystd from conc HCl.

Naphthalene-1-sulfonic acid [85-47-2] M 208.2, m (2H<sub>2</sub>O) 90°, (anhydrous) 139-140°,  $pK^{20}$ -0.17. Crystd from conc HCl and twice from water.

Naphthalene-2-sulfonic acid [120-18-3] M 208.2, m 91°, pK<sub>Est</sub> <1. Crystd from conc HCl.

Naphthalene-1-sulfonyl chloride [85-46-1] M 226.7, m 64-67°, 68°, b 147.5°/0.9 mm, 147.5°/13mm. If the IR indicates the presence of OH then treat with an equal weight of PCl<sub>5</sub> and heat at *ca* 100° for 3h, cool and pour into ice + H<sub>2</sub>O, stir well and filter off the solid. Wash the solid with cold H<sub>2</sub>O and dry the solid in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> + solid KOH. Extract the solid with pet ether (b 40-60°) filter off any insoluble solid and cool. Collect the crystalline sulfonyl chloride and recryst from pet ether or \*C<sub>6</sub>H<sub>6</sub> pet ether. If large quantities are available then it can be distd under high vacuum. [Fierz-Davaid and Weissenbach *Helv Chim Acta* 3 2312 1920.] The sulfonamide has m 150° (from EtOH or H<sub>2</sub>O).

Naphthalene-2-sulfonyl chloride [93-11-8] M 226.7, m 74-76°, 78°, 79°, b 148°/0.6mm, 201°/13mm. Crystd (twice) from \*benzene/pet ether (1:1 v/v). Purified as the 2-sulfonyl chloride. [Fierz-Davaid and Weissenbach Helv Chim Acta 3 2312 1920.] The sulfonamide has m 217° (from EtOH).

1,8-Naphthalic acid (naphthalene-1,8-dicarboxylic acid) [518-05-8] M 216.9, m 270°,  $pK_{Est(1)} \sim 2.1$ ,  $pK_{Est(2)} \sim 4.5$ . Crystd from EtOH or aq EtOH.

**1,8-Naphthalic anhydride** [81-84-5] M **198.2, m 274°.** Extracted with cold aqueous  $Na_2CO_3$  to remove free acid, then crystd from acetic anhydride.

Naphthamide [2243-82-5] M 171.2, m 195°, pK<sup>20</sup> -2.30 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH.

Naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) [475-38-7] M 190.2, m ~ 220-230°(dec), m 225-230°,  $pK_{Est(1)}$ ~9.5,  $pK_{Est(2)}$ ~11.1. Red-brown needles with a green shine from EtOH. Also recrystd from hexane and purified by vacuum sublimation. [Huppert et al. J Phys Chem 89 5811 1985.] It is sparingly soluble in H<sub>2</sub>O but soluble in alkalis. It sublimes at 2-10mm. The diacetate forms golden yellow prisms from CHCl<sub>3</sub>, m 192-193° and the 5,8-dimethoxy derivative has m 157° (155°) (from pet ether) [Bruce and Thompson J Chem Soc 1089 1955; IR: Schmand and Boldt J Am Chem Soc 97 447 1975; NMR: Brockmann and Zeeck Chem Ber 101 4221 1968]. The monothiosemicarbazone has m 168°(dec) from EtOH [Gardner et al. J Am Chem Soc 74 2106 1952].

Naphthionic acid (4-aminonaphthalene-1-sulfonic acid) [84-86-6] M 223.3,  $m > 300^{\circ}(dec)$ ,  $pK^{25}$  2.68. It crystallises from H<sub>2</sub>O as needles of the 0.5 hydrate . Salt solns fluoresce strongly blue.

1-Naphthoic acid [86-55-5] M 172.2, m 162.5-163.0°, pK<sup>25</sup> 3.60. Crystd from toluene (3mL/g) (charcoal), pet ether (b 80-100°), or aqueous 50% EtOH.

2-Naphthoic acid [93-09-4] M 172.2, m 184-185°, pK<sup>25</sup> 4.14. Crystd from EtOH (4mL/g), or aqueous 50% EtOH. Dried at 100°.

1-Naphthol [90-15-3] M 144.2, m 95.5-96°,  $pK^{25}$  9.34. Sublimed, then crystd from aqueous MeOH (charcoal), aq 25% or 50% EtOH, \*benzene, cyclohexane, heptane, CCl<sub>4</sub> or boiling water. Dried over P<sub>2</sub>O<sub>5</sub> under vacuum. [Shizuka et al. J Am Chem Soc 107 7816 1985.]

2-Naphthol [135-19-3] M 144.2, m 122.5-123.5°,  $pK^{25}$  9.57. Crystd from aqueous 25% EtOH (charcoal), water, \*benzene, toluene or CCl<sub>4</sub>, e.g. by repeated extraction with small amounts of EtOH, followed by dissolution in a minimum amount of EtOH and pptn with distilled water, then drying over P<sub>2</sub>O<sub>5</sub> under vacuum. Has also been dissolved in aqueous NaOH, and ppted by adding acid (repeated several times), then ppted from \*benzene by addition of heptane. Final purification can be by zone melting or sublimation *in vacuo*. [Bardez et al. J Phys Chem **89** 5031 1985; Kikuchi et al. J Phys Chem **91** 574 1987.]

Naphthol AS-D (3-hydroxy-2-naphthoic-o-toluide) [135-61-5] M 277.3, m 1196-198°. Purified by recrystn from xylene. Gives yellow-green fluorescent solutions at pH 8.2-9.5, [IR: Schnopper et al. Anal Chem 31 1542 1959.] With AcCl naphthol AS-D acetate is obtained m 168-169°, and with

## **Purification of Organic Chemicals**

chloroacetyl chloride naphthol AS-D-chloroacetate is obtained [Moloney et al. J Histochem Cytochem 8 200 1960; Burstone Arch Pathology 63 164 1957].

α-Naphtholbenzein [bis-(α-{4-hydroxynaphth-1-yl})-benzyl alcohol] [6948-88-5] M 392.5, m 122-125°, pK<sub>Est</sub> ~ 9.3. Crystd from EtOH, aqueous EtOH or glacial acetic acid.

1-Naphthol-2-carboxylic acid (1-hydroxy-2-naphthoic acid) [86-48-6] M 188.2, m 203-204°,  $pK_{Est(1)}$ ~2.5,  $pK_{Est(2)}$ ~12. Successively crystd from EtOH/water, diethyl ether and acetonitrile, with filtration through a column of charcoal and Celite. [Tong and Glesmann J Am Chem Soc 79 583 1957.]

2-Naphthol-3-carboxylic acid (2-hydroxy-3-naphthoic acid) [92-70-6] M 188.2, m 222-223°,  $pK_1^{25}$  2.79,  $pK_2^{25}$  12.84. Crystd from water or acetic acid.

**1,2-Naphthoquinone** [524-42-5] **M 158.2, m 140-142°(dec).** Crystd from ether (red needles) or \*benzene (orange leaflets).

**1,4-Naphthoquinone** [130-15-4] M **158.2, m 125-125.5°.** Crystd from diethyl ether (charcoal). Steam distd. Crystd from \*benzene or aqueous EtOH. Sublimed in a vacuum.

β-Naphthoxyacetic acid [120-23-0] M 202.2, m 156°, pK<sub>Est</sub> ~3.0. Crystd from hot water or \*benzene.

 $\beta$ -Naphthoyltrifluoroacetone (4,4,4-trifluoro-2-naphthylbutan-1,3-dione) [893-33-4] M 266.2, m 70-71°, 74-76°, pK<sup>20</sup> 6.35. Crystd from EtOH. The mono oxime crystd from H<sub>2</sub>O or aq EtOH has m 137-138°. [Reid and Calvin J Am Chem Soc 72 2948 1950.]

Naphthvalene [34305-47-0] M 104.1, m dec at 175° to benzvalene. Purified by chromatography on alumina and eluting with pentane It is stable at room temp [Abelt et al. J Am Chem Soc 107 4148 1985]. The <sup>1</sup>H NMR in CCl<sub>4</sub> has  $\tau$  3.18 (4H), 6.17 (t J 1.5Hz, 2H), 7.60 (t J 1.5Hz 2H).

1-Naphthyl acetate [830-81-9] M 186.2, m 45-46°. Chromatographed on silica gel and crystd as the 2-isomer below.

2-Naphthyl acetate [1523-11-1] M 186.2, m 71°. Crystd from pet ether (b 60-80°) or dilute aq EtOH.

1-Naphthylacetic acid [86-87-3] M 186.2, m 132°, pK<sup>25</sup> 4.23. Crystd from EtOH or water.

**2-Naphthylacetic acid** [581-96-4] **M 186.2, m 143.1-143.4°, pK<sup>25</sup> 4.30.** Crystd from water or \*benzene.

1-Naphthylamine [134-32-7] M 143.2, m 50.8-51.2°, b 160°, pK<sup>25</sup> 3.94. Sublimed at 120° in a stream of nitrogen, then crystd from pet ether (b 60-80°), or abs EtOH then diethyl ether. Dried under vacuum in an Abderhalden pistol. Has also been purified by crystn of its hydrochloride from water, followed by liberation of the free base and distn; finally purified by zone melting. CARCINOGEN.

1-Naphthylamine hydrochloride [552-46-5] M 179.7, m sublimes on heating. Crystd from water (charcoal).

2-Naphthylamine [91-59-8] M 143.2, m 113°, pK<sup>25</sup> 4.20. Sublimed at 180° in a stream of nitrogen. Crystd from hot water (charcoal) or \*benzene. Dried under vacuum in an Abderhalden pistol. CARCINOGEN.

1-Naphthylamine-5-sulfonic acid [84-89-9] M 223.3, m >200°(dec),  $pK_{Est(1)}<1$ ,  $pK_2^{25}3.69$  (NH<sub>2</sub>) Crystd under nitrogen from boiling water and dried in a steam oven [Bryson Trans Faraday Soc 47 522, 527 1951].

**2-Naphthylamine-1-sulfonic acid** [81-16-3] M 223.3, m >200°(dec),  $pK_1^{25} < 1$ ,  $pK_2^{25} 2.35$  (NH<sub>2</sub>). Crystd under nitrogen from boiling water and dried in a steam oven [Bryson *Trans Faraday Soc* 47 522, 527 1951].

2-Naphthylamine-6-sulfonic acid [93-00-5] M 223.3, m >200°(dec). Crystd from a large volume of hot water.

1-(1-naphthyl) ethanol [R-(+)-42177-25-3; S-(-)-15914-84-8] M 172.2, m 46°, 45-47.5°, 48°,  $[\alpha]_{546}^{20}$  (+) and (-) 94°,  $[\alpha]_D^{20}$  (+) and (-) 78° (c 1, MeOH). Purified by recrystn from Et<sub>2</sub>O-pet ether, Et<sub>2</sub>O, hexane [Balfe et al. *J Chem Soc* 797 1946; IR, NMR: Theisen and Heathcock *J Org Chem* 53 2374 1988; see also Fredga et al. *Acta Chem Scand* 11 1609 1957]. The RS-alcohol [57605-95-5] has m 63-65,°, 65-66° from hexane.

1-(1-Naphthyl)ethylamine [R-(+)-3886-70-2; S-(-)-10420-89-0] M 171.2, b 153°/11mm, 178-181°/20mm,  $d_4^{20}$  1.067,  $n_D^{20}$  1.624,  $[\alpha]_{546}^{20}$  (+) and (-) 65°,  $[\alpha]_D^{20}$  (+) and (-) 55° (c 2, MeOH);  $[\alpha]_D^{17}$  (+) and (-) 82.8° (neat), pK<sub>Est</sub> ~9.3. Purified by distn in a good vacuum. [Mori et al. *Tetrahedron* 37 1343 1981; cf Wilson in *Top Stereochem* (Allinger and Eliel eds) vol 6 135 1971; Fredga et al. *Acta Chem Scand* 11 1609 1957.] The hydrochlorides crystallises from H<sub>2</sub>O  $[\alpha]_D^{18} \pm 3.9°$  (c 3, H<sub>2</sub>O) and the sulfates recrystallises from H<sub>2</sub>O as *tetrahydrates* m 230-232°. The *RS-amine* has b 153°/11mm, 156°/15mm, 183.5°/41mm [Blicke and Maxwell *J Am Chem Soc* 61 1780 1939].

2-Naphthylethylene (2-vinylnaphthalene) [827-54-3] M 154.2, m 66°, b 95-96°/2.1mm, 135-137°/18mm. Crystd from aqueous EtOH.

N-(α-Naphthyl)ethylenediamine dihydrochloride [1465-25-4] M 291.2, m 188-190°, pK<sub>Est(1)</sub>~3.8, pK<sub>Est(2)</sub>~9.4. Crystd from water.

1-Naphthyl isocyanate [86-84-0] M 169.2, m 3-5°, b 269-270°/atm,  $d_4^{20}$  1.18. Distd at atmospheric pressure or in a vacuum. Can be crystd from pet ether (b 60-70°) at low temperature. It has a pungent odour, is TOXIC and is absorbed through the skin.

1-Naphthyl isothiocyanate [551-06-4] M 185.3, m 58-59°. Crystd from hexane (1g in 9 mL). White needles soluble in most organic solvents but is insoluble in H<sub>2</sub>O. It is absorbed through the skin and may cause dermatitis. [Org Synth Coll Vol IV 700 1963.]

2-Naphthyl lactate [93-43-6] M 216.2. Crystd from EtOH.

2-(2-Naphthyloxy)ethanol [93-20-9] M 188.2, m 76.7°. Crystd from \*benzene/pet ether.

N-1-Naphthylphthalamic acid [132-66-1] M 291.3, m 203°. Crystd from EtOH.

2-Naphthyl salicylate [613-78-5] M 264.3, m 95°, pK<sub>Est</sub> ~10.0. Crystd from EtOH.

1-Naphthyl thiourea (ANTU) [86-88-4] M 202.2, m 198°. Crystd from EtOH.

1-Naphthyl urea [6950-84-1] M 186.2, m 215-220°. Crystd from EtOH.

2-Naphthyl urea [13114-62-0] M 186.2, m 219-220°. Crystd from EtOH.

**1,5-Naphthyridine** [254-79-5] **M 130.1, m 75°, b 112°/15mm, pK<sup>20</sup> 2.84.** Purified by repeated sublimation.

Narcein {6-[6-(2-dimethylaminoethyl)]-2-methoxy-3,4-(methylenedioxy)phenylacetyl]-2,3dimethoxybenzoic acid} [131-28-2] M 445.4, m 176-177° (145° anhydrous),  $pK_1^{15}$  3.5,  $pK_2^{15}$ 9.3. Crystd from water (as trihydrate).

Naringenin (4',5,7-trihydroxyflavanone) [480-41-1] M 272.3, m 251° (phenolic pKs~ 8-11). Crystd from aqueous EtOH.

Naringin (naringenin 7-rhamnoglucoside) [10236-47-2] M 580.5, m 171° (2H<sub>2</sub>O),  $[\alpha]_D^{19}$  -90° (c 1, EtOH),  $[\alpha]_{546}^{20}$  -107° (c 1, EtOH). Crystd from water. Dried at 110°(to give the dihydrate).

Neopentane (2,2-dimethylpropane) [463-82-1] M 72.2, b 79.3°, d 0.6737, n 1.38273. Purified from isobutene by passage over conc  $H_2SO_4$  or  $P_2O_5$ , and through silica gel.

Neostigmine [(3-dimethylcarbamoylphenyl)trimethylammonium] bromide [114-80-7] M 303.2, m 176°(dec). Crystd from EtOH/diethyl ether. (Highly TOXIC).

Neostigmine methyl sulfate [51-60-5] M 334.4, m 142-145°. Crystd from EtOH. (Highly TOXIC.]

Nerolidol (3,7,11-trimethyl-1,6,10-dodecatrien-3-ol) M 222.4 [cis/trans 7212-44-4] b 122°/3mm, n 1.477, d 0.73, [cis 3790-78-1] b 70°/0.1mm, [trans 40716-66-3] b 78°/0.2mm, 145-146°/2mm. Purified by TLC on plates of Kieselguhr G [McSweeney J Chromatogr 17 183 1965] or silica gel impregnated with AgNO<sub>3</sub>, using 1,2-CH<sub>2</sub>Cl<sub>2</sub>/CHCl<sub>3</sub>/EtOAc/PrOH (10:10:1:1) as solvent system. Also by GLC on butanediol succinate (20%) on Chromosorb W. Stored under N<sub>2</sub> at ~5° in the dark.

Neutral Red (2-amino-8-dimethylamino-3-methylphenazine HCl, Basic Red 5, CI 50040) [553-24-2] M 288.8, m 290°(dec), pK<sup>25</sup> 6.5. Crystd from \*benzene/MeOH (1:1). In aq sol it is red at pH 6.8 and yellow at pH 8.0.

Nicotinaldehyde thiosemicarbazone [3608-75-1] M 180.2, m 222-223°. Crystd from water.

Nicotinamide [98-92-0] M 122.1, m 128-131°, pK<sub>1</sub><sup>20</sup>0.5, pK<sub>2</sub><sup>20</sup>3.33. Crystd from \*benzene.

Nicotinic acid (niacin, 2-yridine-3-carboxylic acid) [59-67-6] M 123.1, m 232-234°,  $pK_1^{25}$ 2.00,  $pK_2^{25}$ 4.82. Crystd from \*benzene.

Nicotinic acid hydrazide [553-53-7] M 137.1, m 158-159°,  $pK_1^{20}3.3$ ,  $pK_2^{20}11.49(NH)$ . Crystd from aqueous EtOH or \*benzene.

Nile Blue A (a benzophenoxazinium sulfate dye) [3625-57-8] M 415.5, m >300°(dec), CI 51180, pK<sup>25</sup> 2.4. Crystd from pet ether.

Ninhydrin (1,2,3-triketohydrindene hydrate) [485-47-2] M 178.1, m 241-243°(dec), pK<sup>30</sup> 8.82. Crystd from hot water (charcoal). Dried under vacuum and stored in a sealed brown container.

Nitrilotriacetic acid [tris(carboxymethyl)amine, NTA, Complexone 1] [139-13-9] M 191.1, m 247°(dec), pK<sub>1</sub> 0.8, pK<sub>2</sub> 1.71, pK<sub>3</sub> 2.47, pK<sub>4</sub> 9.71. Crystd from water. Dried at 110°.

2-Nitroacetanilide [ 552-32-9] M 180.2, m 93-94°, pK<sub>Est</sub> <0. Crystd from water.

**4-Nitroacetanilide** [104-04-1] **M 180.2, m 217°, pK**<sub>Est</sub> <0. Ppted from 80% H<sub>2</sub>SO<sub>4</sub> by adding ice, then washed with water, and crystd from EtOH. Dried in air.

3-Nitroacetophenone [121-89-1] M 165.2, m 81°, b 167°/18mm, 202°/760mm. Distilled in steam and crystd from EtOH.

**4-Nitroacetophenone** [100-19-6] **M 165.2, m 80-81°, b 145-152°/760mm.** Crystd from EtOH or aqueous EtOH.

3-Nitroalizarin (1,2-dihydroxy-3-nitro-9,10-anthraquinone, Alizarin Orange) [568-93-4] M 285.2, m 244° (dec), pK<sub>Est(1)</sub>~4.6, pK<sub>Est(2)</sub>~9.6. Crystd from acetic acid.

*o*-Nitroaniline [88-74-4] M 138.1, m 72.5-73.0°,  $pK^{25}$  -0.25 (-0.31). Crystd from hot water (charcoal), then crystd from water, aqueous 50% EtOH, or EtOH, and dried in a vacuum desiccator. Has also been chromatographed on alumina, then recrystd from \*benzene.

*m*-Nitroaniline [99-09-2] M 138.1, m 114°, pK<sup>25</sup> 2.46. Purified as for *o*-nitroaniline. Warning: it is absorbed through the skin.

*p*-Nitroaniline [100-01-6] M 138.1, m 148-148.5°, pK<sup>25</sup> 1.02. Purified as for *o*-nitroaniline. Also crystd from acetone. Freed from *o*- and *m*-isomers by zone melting and sublimation.

o-Nitroanisole (2-methoxynitrobenzene) [91-23-6] M 153.1, f 9.4°, b 265°/737mm, d 1.251, n 1.563. Purified by repeated vacuum distn in the absence of oxygen.

*p*-Nitroanisole (4-methoxynitrobenzene) [100-17-4] M 153.1, m 54°. Crystd from pet ether or hexane and dried *in vacuo*.

**9-Nitroanthracene** [602-60-8] **M 223.2, m 142-143°.** Purified by recrystn from EtOH or MeOH. Further purified by sublimation or TLC.

5-Nitrobarbituric acid (dilituric acid) [480-68-2] M 173.1, m 176°, 176-183°, pK<sup>20</sup> 10.25. Crystd from water.

o-Nitrobenzaldehyde [552-89-6] M 151.1, m 44-45°, b 120-144°/3-6mm. Crystd from toluene (2-2.5mL/g) by addition of 7mL pet ether (b 40-60°) for 1mL of soln. Can also be distd at reduced pressures.

*m*-Nitrobenzaldehyde [99-61-6] M 151.1, m 58°. Crystd from water or EtOH/water, then sublimed twice at 2mm pressure at a temperature slightly above its melting point.

p-Nitrobenzaldehyde [555-16-8] M 151.1, m 106°. Purification as for m-nitrobenzaldehyde above.

Nitrobenzene [98-95-3] M 123.1, f 5.8°, b 84-86.5°/6.5-8mm, 210.8°/760mm, d 1.206,  $n^{15}$  1.55457, n 1.55257, pK<sup>18</sup> -11.26 (aq H<sub>2</sub>SO<sub>4</sub>). Common impurities include nitrotoluene, dinitrothiophene, dinitrobenzene and aniline. Most impurities can be removed by steam distn in the presence of dilute H<sub>2</sub>SO<sub>4</sub>, followed by drying with CaCl<sub>2</sub>, and shaking with, then distilling at low pressure from BaO, P<sub>2</sub>O<sub>5</sub>, AlCl<sub>3</sub> or activated alumina. It can also be purified by fractional crystn from absolute EtOH (by refrigeration). Another purification process includes extraction with aqueous 2M NaOH, then water, dilute HCl, and water, followed by drying (CaCl<sub>2</sub>, MgSO<sub>4</sub> or CaSO<sub>4</sub>) and fractional distn under reduced pressure. The pure material is stored in a brown bottle, in contact with silica gel or CaH<sub>2</sub>. It is very hygroscopic.

4-Nitrobenzene-azo-resorcinol (magneson II) [74-39-5] M 259.2, m 199-200°. Crystd from EtOH.

2-Nitrobenzenesulfenyl chloride (NPS-Cl) [7669-54-7] M 189.6, m 73-74.5°, 74-575°, 74-76°. Recrystd from CCl<sub>4</sub> (2mL/g), filter off the soln at 5° (recovery 75%). Also recrystd from pet ether (b 40-60°), dried rapidly at 50° and stored in a brown glass bottle, sealed well and stored away from moisture. [Hubacher Org Synth Coll Vol II 455 1943; Ito et al. Chem Pharm Bull (Jpn) 26 296 1978.]

4-Nitrobenzhydrazide [606-26-8] M 181.1, m 213-214°. Crystd from EtOH.

4'-Nitrobenzo-15-crown-5 [60835-69-0] M 313.3, m 84-85°, 93-95°. Recrystd from EtOH, MeOH or  $C_{6}H_{6}$ -hexane as for the 18-crown-6 compound below. It complexes with Na<sup>+</sup>, K<sup>+</sup>, NH<sub>4</sub><sup>+</sup>, Ca<sup>2+</sup>, Mg<sup>2+</sup> and Cd<sup>2+</sup>. NMR (CDCl<sub>3</sub>) has  $\delta$ : 3.6-4.4 (m 16CH<sub>2</sub>), 6.8 (d 1H arom), 7.65 (d 1H arom), 7.80 (dd 1H arom  $J_{ab}$  9Hz and  $J_{bc}$  3Hz) [Shmid et al. J Am Chem Soc 98 5198 1976; Kikukawa et al. Bull Chem Soc Jpn 50 2207 1977; Toke et al. Justus Liebigs Ann Chem 349 349, 761 1988; Lindner et al. Z Anal Chem 322 157 1985].

4'-Nitrobenzo-18-crown-6 [53408-96-1] M 357.4, m 83-84°, 83-84°. If impure and discoloured then chromatograph on  $Al_2O_3$  and eluting with  $*C_6H_6$  (1:1) with 1% MeOH added. The fractions are followed by TLC on  $Al_2O_3$  (using detection with Dragendorff's reagent  $R_F$  0.6 in the above solvent system). Recrystallise the residues from the fractions containing the product from  $*C_6H_6$ -hexane to give yellowish leaflets. It complexes with Na or K ions with  $logK_{Na}$  3.95 and  $logK_K$  4.71. [Petranek and Ryba Collect Chem Czech Chem Commun 39 2033 1974.]

**2-Nitrobenzoic acid** [552-16-9] **M 167.1, m 146-148°, pK<sup>25</sup> 2.21.** Crystd from \*benzene (twice), *n*-butyl ether (twice), then water (twice). Dried and stored in a vacuum desiccator. [Le Noble and Wheland J Am Chem Soc 80 5397 1958.] Has also been crystd from EtOH/water.

**3-Nitrobenzoic acid** [121-92-6] **M 167.1, m 143-143.5°, pK<sup>25</sup> 3.46.** Crystd from \*benzene, water, EtOH (charcoal), glacial acetic acid or MeOH/water. Dried and stored in a vacuum desiccator.

4-Nitrobenzoic acid [62-23-7] M 167.1, m 241-242°, pK<sup>25</sup> 3.43. Purification as for 3nitrobenzoic acid above.

4-Nitrobenzoyl chloride [122-04-3] M 185.6, m 75°, b 155°/20mm. Crystd from dry pet ether (b 60-80°) or CCl<sub>4</sub>. Distilled under vacuum. Irritant.

**4-Nitrobenzyl alcohol** [619-73-8] **M 153.1, m 93°.** Crystd from EtOH and sublimed in a vacuum. Purity should be at least 99.5%. Sublimed samples should be stored in the dark over anhydrous CaSO<sub>4</sub> (Drierite). It the IR contains OH bands then the sample should be resublimed before use. [Mohammed and Kosower J Am Chem Soc 93 2709 1979.]

**4-Nitrobenzyl bromide** [100-11-8] **M 216.0, m 98.5-99.0°.** Recrystd four times from abs EtOH, then twice from cyclohexane/hexane/\*benzene (1:1:1), followed by vac sublimation at 0.1mm and a final recrystn from the same solvent mixture. [Lichtin and Rao J Am Chem Soc 83 2417 1961.] Has also been crystd from pet ether (b 80-100°, 10mL/g, charcoal). It slowly decomposes even when stored in a desiccator in the dark. IRRITANT.

*m*-Nitrobenzyl chloride [619-23-8] M 171.6, m 45°. Crystd from pet ether (b 90-120°). IRRITANT.

*p*-Nitrobenzyl chloride [100-14-1] M 171.6, m 72.5-73°. Crystd from CCl<sub>4</sub>, dry diethyl ether, 95% EtOH or *n*-heptane, and dried under vacuum. IRRITANT.

p-Nitrobenzyl cyanide [555-21-5] M 162.2, m 117º. Crystd from EtOH. TOXIC.

4-(4-Nitrobenzyl)pyridine (PNBP) [1083-48-3] M 214.2, m 70-71°, pK<sub>Est</sub> ~5.0. Crystd from cyclohexane.

2-Nitrobiphenyl [86-00-0] M 199.2, m 36.7°. Crystd from EtOH (seeding required). Sublimed under vacuum.

**3-Nitrocinnamic acid** [555-68-0] **M 193.2, m 200-201°, pK<sup>25</sup> 2.58** (*trans*). Crystd from \*benzene or EtOH.

4-Nitrocinnamic acid [882-06-4] M 193.2, m 143° (cis), 286°(trans), pK<sub>Est</sub> ~2.6 (trans). Crystd from water.

4-Nitrodiphenylamine [836-30-6] M 214.2, m 133-134°, pK<sup>25</sup> -2.5. Crystd from EtOH.

**2-Nitrodiphenyl ether** [2216-12-8] **M 215.2, b 106-108°/0.01mm, 137-138°/0.5mm, 161-162°/4mm, 188-189°/12mm, 195-200°/25mm, d\_4^{20} 1.241, n\_D^{25} 1.600. Purified by fractional distn. UV (EtOH): 255, 315mm (\varepsilon 6200 and 2800); IR (CS<sub>2</sub>): 1350 (NO<sub>2</sub>) and 1245, 1265 (COC) cm<sup>-1</sup> [UV, IR: Dahlgard and Brewster J Am Chem Soc 80 5861 1958; Tomita and Takase Yakugaku Zasshi (J Pharm Soc Japan) 75 1077 1955; Fox and Turner J Chem Soc 1115 1930, Henley J Chem Soc 1222 1930**].

Nitrodurene (1-nitro-2,3,5,6-tetramethylbenzene) [3463-36-3] M 179.2, m 53-55°, b 143-144°/10mm. Crystd from EtOH, MeOH, acetic acid, pet ether or chloroform.

Nitroethane [79-24-3] M 75.1, b 115°, d 1.049, n 1.3920, n<sup>25</sup> 1.39015, pK<sup>25</sup> 8.60 (8.46, pH equilibrium requires ca 5 min). Purified as described for *nitromethane*. A spectroscopic impurity has been removed by shaking with activated alumina, decanting and rapidly distilling.

2-Nitrofluorene [607-57-8] M 211.2, m 156°. Crystd from aqueous acetic acid.

Nitroguanidine [556-88-7] M 104.1, m 246-246.5°(dec), 257°,  $pK_1^{25}$ -0.55,  $pK_2^{25}$ 12.20. Crystd from water (20mL/g).

5-Nitroindole [6146-52-7] M 162.1, m 141-142°,  $pK^{25}$  -7.4 (aq H<sub>2</sub>SO<sub>4</sub>). Decolorised (charcoal) and recrystd twice from aqueous EtOH.

Nitromesitylene (2-nitro-1,3,5-trimethylbenzene) [603-71-4] M 165.2, m 44°, b 255°. Crystd from EtOH.

Nitromethane [75-52-5] M 61.0, f -28.5°, b 101.3°, d 1.13749, d<sup>30</sup> 1.12398, n 1.3819, n<sup>30</sup> 1.37730, pK<sup>25</sup> 10.21. Nitromethane is generally manufactured by gas-phase nitration of methane. The usual impurities include aldehydes, nitroethane, water and small amounts of alcohols. Most of these can be removed by drying with CaCl<sub>2</sub> or by distn to remove the water/nitromethane azeotrope, followed by drying with CaSO<sub>4</sub>. Phosphorus pentoxide is not suitable as a drying agent. [Wright et al. J Chem Soc 199 1936.] The purified material should be stored by dark bottles, away from strong light, in a cool place. Purifications using extraction are commonly used. For example, Van Looy and Hammett [J Am Chem Soc 81 3872 1959] mixed about 150mL of conc  $H_2SO_4$  with 1L of nitromethane and allowed it to stand for 1 or 2days. The solvent was washed with water, aqueous Na<sub>2</sub>CO<sub>3</sub>, and again with water, then dried for several days with MgSO<sub>4</sub>, filtered again with CaSO<sub>4</sub>. It was fractionally distd before use. Smith, Fainberg and Winstein [J Am Chem Soc 83 618 1961] washed successively with aqueous NaHCO<sub>3</sub>, aqueous NaHSO<sub>3</sub>, water, 5% H<sub>2</sub>SO<sub>4</sub>, water and dilute NaHCO<sub>3</sub>. The solvent was dried with CaSO<sub>4</sub>, then percolated through a column of Linde type 4A molecular sieves, followed by distn from some of this material (in powdered form). Buffagni and Dunn [J Chem Soc 5105] 1961] refluxed for 24h with activated charcoal while bubbling a stream of nitrogen through the liquid. The suspension was filtered, dried (Na<sub>2</sub>SO<sub>4</sub>) and distd, then passed through an alumina column and redistd. It has also been refluxed over CaH<sub>2</sub>, distd and kept under argon over 4A molecular sieves.

Can be purified by zone melting or by distn under vacuum at  $0^\circ$ , subjecting the middle fraction to several freezepump-thaw cycles. An impure sample containing higher nitroalkanes and traces of cyanoalkanes was purified (on the basis of its NMR spectrum) by crystn from diethyl ether at -60° (cooling in Dry-ice)[Parrett and Sun J Chem Educ 54 448 1977].

Fractional crystn was more effective than fractional distn from Drierite in purifying nitromethane for conductivity measurements. [Coetzee and Cunningham J Am Chem Soc 87 2529 1965.] Specific conductivities around 5 x  $10^{-9}$  ohm<sup>-1</sup> cm<sup>-1</sup> were obtained.

Nitron [1,4-diphenyl-3-phenylamino-(1H)-1,2,4-triazolium (hydroxide) inner salt] [2218-94-2] M 312.4, m 189°(dec). Crystd from EtOH, chloroform or EtOH/\*C<sub>6</sub>H<sub>6</sub>.

1-Nitronaphthalene [86-57-7] M 173.2, m 57.3-58.3°, b 30-40°/0.01mm. Fractionally distd under reduced pressure, then crystd from EtOH, aqueous EtOH or heptane. Chromatographed on alumina from \*benzene/pet ether. Sublimes *in vacuo*.

2-Nitronaphthalene [581-89-5] M 173.2, m 79°, b 165°/15mm. Crystd from aqueous EtOH and sublimed in a vacuum.

1-Nitro-2-naphthol [550-60-7] M 189.2, m 103°, pK<sup>25</sup> 5.93. Crystd (repeatedly) from \*benzenepet ether (b 60-80°)(1:1).

2-Nitro-1-naphthol [607-24-9] M 189.2, m 127-128°, pK<sup>25</sup> 5.89. Crystd (repeatedly) from EtOH.

5-Nitro-1,10-phenanthroline [4199-88-6] M 225.2, m 197-198°, pK<sup>25</sup> 3.33. Crystd from \*benzene/pet ether, until anhydrous.

**2-Nitrophenol** [88-75-5] **M 139.1, m 44.5-45.5°, pK<sup>25</sup> 7.23.** Crystd from EtOH/water, water, EtOH, \*benzene or MeOH/pet ether (b 70-90°). Can be steam distd. Petrucci and Weygandt [Anal Chem 33 275 1961] crystd from hot water (twice), then EtOH (twice), followed by fractional crystn from the melt (twice), drying over CaCl<sub>2</sub> in a vacuum desiccator and then in an Abderhalden drying pistol.

**3-Nitrophenol** [554-84-7] **M 139.1, m 96°, b 160-165°/12mm, pK<sup>25</sup> 8.36.** Crystd from water, CHCl<sub>3</sub>, CS<sub>2</sub>, EtOH or pet ether (b 80-100°), and dried under vacuum over  $P_2O_5$  at room temperature. Can also be disted at low pressure.

**4-Nitrophenol** [100-02-7] **M 139.1, m 113-114°, pK^{25} 7.16.** Crystd from water (which may be acidified, e.g. N H<sub>2</sub>SO<sub>4</sub> or 0.5N HCl), EtOH, aqueous MeOH, CHCl<sub>3</sub>, \*benzene or pet ether, then dried under vacuum over P<sub>2</sub>O<sub>5</sub> at room temperature. Can be sublimed at 60°/10<sup>-4</sup>mm.

**2-Nitrophenoxyacetic acid** [1878-87-1] **M 197.2, m 150-159°, pK^{25} 2.90.** Crystd from water, and dried over  $P_2O_5$  under vacuum.

*p*-Nitrophenyl acetate [830-03-5] M 181.2, m 78-79°. Recrystd from absolute EtOH [Moss et al. J Am Chem Soc 108 5520 1986].

2-Nitrophenylacetic acid [3740-52-1] M 181.2, m 120°, pK<sup>25</sup> 3.95. Crystd from EtOH/water and dried over P<sub>2</sub>O<sub>5</sub> under vacuum.

**4-Nitrophenylacetic acid** [104-03-0] **M 181.2, m 80.5°, pK<sup>25</sup> 3.92.** Crystd from EtOH/water (1:1), then from sodium-dried diethyl ether and dried over  $P_2O_5$  under vacuum.

4-Nitro-1,2-phenylenediamine [99-56-9] M 153.1, m 201°, pK<sub>1</sub><sup>25</sup>1.39 (1-NH<sub>2</sub>), pK<sub>2</sub><sup>25</sup>2.61 (2-NH<sub>2</sub>). Crystd from water.

1-(4-Nitrophenyl)ethylamine hydrochloride [R-(+)-57233-86-0; S-(-)-132873-57-5] M 202.6, m 225°, 240-242° (dec), 243-245° (dec), 248-250°,  $[\alpha]_D^{20}$  (+) and (-) 72° (c 1, 0.05 M NaOH), (+) and (-) 0.3° (H<sub>2</sub>O), pK<sub>Est</sub> ~8.6. To ensure dryness the hydrochloride (ca 175 g) is extracted with EtOH (3x100mL) and evaporated to dryness (any residual H<sub>2</sub>O increases the solubility in EtOH and lowers the yield). The hydrochloride residue is triturated with absolute EtOH and dried *in vacuo*. The product is further purified by refluxing with absolute EtOH (200 mL for 83g) for 1h, cool to 10° to give 76.6g of hydrochloride m 243-245° (dec). The *free base* is prepd by dissolving in N NaOH, extract with CH<sub>2</sub>Cl<sub>2</sub> (3 x 500mL), dry (Na<sub>2</sub>CO<sub>3</sub>), filter, evaporate and distil, m 27°, b 119-120°/0.5mm (105-107°/0.5mm, 157-159°/9mm, d<sub>4</sub><sup>20</sup> 1.1764, n  $_{D}^{20}$  1.5688,  $[\alpha]_{D}^{24} \pm 17.7^{\circ}$  (neat)[Perry et al. Synthesis 492 1977; ORD: Nerdel and Liebig Justus Liebigs Ann Chem 621 142 1959].

**4-Nitrophenylhydrazine** [100-16-3] **M 153.1, m 158°(dec), pK\_1^{25}-9.2 (aq H<sub>2</sub>SO<sub>4</sub>), pK\_2^{25}3.70. Crystd from EtOH.** 

3-Nitrophenyl isocyanate [3320-87-4] M 164.1, m 52-54°. Crystd from pet ether (b 28-38°).

4-Nitrophenyl isocyanate [100-28-7] M 164.1, m 53°. Crystd from pet ether (b 28-38°).

2-Nitrophenylpropiolic acid [530-85-8] M 191.1, m 157º(dec), pK<sup>25</sup> 2.83. Crystd from water.

**4-Nitrophenyl trifluoroacetate** [658-78-6] **M 235.1, m 37-39°, b 120°/12mm.** Recrystd from CHCl<sub>3</sub>/hexane [Margolis et al. J Biol Chem **253** 7891 1078].

4-Nitrophenyl urea [556-10-5] M 181.2, m 238°. Crystd from EtOH and hot water.

**3-Nitrophthalic acid** [603-11-2] **M 211.1, m 216-218°, pK<sup>25</sup> 3.93.** Crystd from hot water (1.5mL/g). Air dried.

4-Nitrophthalic acid [610-27-5] M 211.1, m 165°, pK<sup>25</sup> 4.12. Crystd from ether or ethyl acetate.

3-Nitrophthalic anhydride [641-70-3] M 193.1, m 164°. Crystd from \*benzene, \*benzene/pet ether, acetic actic or acetone. Dried at 100°.

1-Nitropropane [108-03-2] M 89.1, b 131.4°, d 1.004, n 1.40161, n<sup>25</sup> 1.39936, pK<sup>25</sup> 8.98. Purified as *nitromethane*.

**2-Nitropropane** [79-46-9] **M 89.1, b 120.3°, d 0.989, n 1.3949, n<sup>25</sup> 1.39206, pK<sup>25</sup> 7.68.** Purified as *nitromethane*.

5-Nitro-2-*n*-propoxyaniline [553-79-7] M 196.2, m 47.5-48.5°, pK<sub>Est</sub> ~2.32. Crystd from *n*-propyl alcohol/pet ether.

3-Nitro-2-pyridinesulfenyl chloride [68206-45-1] M 190.2, m 217-222°(dec). Crystallises as yellow needles from CH<sub>2</sub>Cl<sub>2</sub>. When pure it is stable for several weeks at room temperature, and no decomposition was observed after 6 months at <0°. UV (MeCN) has  $\lambda$ max at 231nm ( $\epsilon$  12,988), 264nm ( $\epsilon$  5,784) and 372nm ( $\epsilon$  3,117). [NMR and UV: Matsuda and Aiba Chem Lett 951 1978; Wagner et al. Chem Ber 75 935 1942.]

5-Nitroquinoline [607-34-1] M 174.2, m 70°, pK<sup>20</sup> 2.69. Crystd from pentane, then from \*benzene.

8-Nitroquinoline [706-35-2] M 174.2, m 88-89°, pK<sup>20</sup> 2.55. Crystd from hot water, MeOH, EtOH or EtOH/diethyl ether (3:1).

4-Nitroquinoline 1-oxide [56-57-5] M 190.2, m 157°. Recrystd from aqueous acetone [Seki et al. J Phys Chem 91 126 1987].

2-Nitroresorcinol [601-89-8] M 155.1, m 81-81°, pK<sub>1</sub><sup>20</sup> 6.37, pK<sub>2</sub><sup>20</sup> 9.46. Crystd from aq EtOH.

4-Nitrosalicylic acid [619-19-1] M 183.1, m 277-288°, pK<sup>25</sup> 2.23. Crystd from water.

5-Nitrosalicylic acid [96-97-9] M 183.1, m 233°,  $pK_1^{25}$  2.32,  $pK_2^{25}$  10.34. Crystd from acetone (charcoal), then twice more from acetone alone.

**Nitrosobenzene** [586-96-9] **M 107.1, m 67.5-68°, b 57-59°/18mm.** Steam distd, then cryst from a small volume of EtOH with cooling below 0°, dried over CaCl<sub>2</sub> in a dessicator at atm pressure, and stored under N<sub>2</sub> at 0°. Alternatively it can be distd onto a cold finger cooled with brine at ~-10° in a vac at 17mm (water pump), while heating in a water bath at 65-70° [Robertson and Vaughan J Chem Educ 27 605 1950].

**N-Nitrosodiethanolamine** [1116-54-7] **M 134.4, b 125°/0.01mm, n 1.485.** Purified by dissolving the amine (0.5g) in 1-propanol (10mL) and 5g of anhydrous Na<sub>2</sub>SO<sub>4</sub> added with stirring. After standing for 1-2h, it was filtered and passed through a chromatographic column packed with AG 50W x 8 (H<sup>+</sup>form, a strongly acidic cation exchanger). The eluent and washings were combined and evapd to dryness at 35°. [Fukuda et al. Anal Chem 53 2000 1981.] Possible CARCINOGEN.

**4-Nitroso-***N*, *N*-**dimethylaniline** [138-89-6] **M 150.2**, **m 86-87°**, **92.5-93.5°**, **b 191-192°/100mm**, **pK**<sup>25</sup> **4.54**. Recryst from pet ether or CHCl<sub>3</sub>-CCl<sub>4</sub> and dried in air. Alternatively suspend in H<sub>2</sub>O, heat to boiling and add HCl until it dissolves. Filter, cool and collect the *hydrochloride* [42344-05-8], **m** 177° after recrystn from H<sub>2</sub>O containing a small amount of HCl. The *hydrochloride* (e.g. 30g) is made into a paste with H<sub>2</sub>O (100mL) in a separating funnel. Add cold aq 2.5 NaOH or Na<sub>2</sub>CO<sub>3</sub> to a pH of ~ 8.0 (green color due to free base) and extracted with toluene, CHCl<sub>3</sub> or Et<sub>2</sub>O. Dry extract (K<sub>2</sub>CO<sub>3</sub>), filter, distil off the solvent, cool residue and collect the crystalline free base. Recryst as above and dried in air.

N-Nitrosodiphenylamine [156-10-5] M 198.2, m 144-145°(dec). Crystd from \*benzene.

1-Nitroso-2-naphthol [131-91-9] M 173.2, m 110.4-110.8°, pK<sup>25</sup> 7.63. Crystd from pet ether (b 60-80°, 7.5mL/g).

2-Nitroso-1-naphthol [132-53-6] M 173.2, m 158°(dec), pK<sup>25</sup> 7.24. Purified by recrystn from pet ether (b 60-80°) or by dissolving in hot EtOH, followed by successive addition of small volumes of water.

4-Nitroso-1-naphthol [605-60-7] M 173.2, m 198°, pK<sup>25</sup> 8.18. Crystd from \*benzene.

2-Nitroso-1-naphthol-4-sulfonic acid  $(3H_2O)$  [3682-32-4] M 316.3, m 142-146°(dec), pK<sub>Est</sub> ~6.3 (OH). Crystd from dilute HCl soln. Crystals were dried over CaCl<sub>2</sub> in a vacuum desiccator. Also purified by dissolution in aqueous alkali and pptn by addition of water. Reagent for cobalt.

4-Nitrosophenol [104-91-6] M 123.1, m >124°(dec), pK<sup>25</sup> 6.36. Crystd from xylene.

N-Nitroso-N-phenylbenzylamine [612-98-6] M 212.2, m 58°. Crystd from absolute EtOH and dried in air.

*trans*-β-Nitrostyrene [5153-67-3] M 149.2, m 60°. Crystd from absolute EtOH, or three times from \*benzene/pet ether (b 60-80°) (1:1).

**4-Nitrostyrene** [100-13-0] **M 149.2, m 20.5-21°.** Crystd from CHCl<sub>3</sub>/hexane. Purified by addition of MeOH to ppte the polymer, then crystd at -40° from MeOH. Also crystd from EtOH. [Bernasconi et al. J Am Chem Soc 108 4541 1986.]

2-Nitro-4-sulfobenzoic acid [552-23-8] M 247.1, m 111°, pK<sub>Est</sub> ~1.65. Crystd from dilute HCl. Hygroscopic.

2-Nitrotoluene [88-72-2] M 137.1, m -9.55° ( $\alpha$ -form), -3.85° ( $\beta$ -form), b 118°/16mm, d 1.163, 222.3°/760mm, n 1.545. Crystd (repeatedly) from absolute EtOH by cooling in a Dry-ice/alcohol mixture, Further purified by passage of an alcoholic soln through a column of alumina.

**3-Nitrotoluene** [99-08-1] **M 137.1, m 16°, b 113-114°/15mm, 232.6°, d 1.156, n 1.544.** Dried with  $P_2O_5$  for 24h, then fractionally distd under reduced pressure. [Org. Synth Coll Vol I 416 1948.]

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**4-Nitrotoluene** [99-99-0] **M 137.1, m 52°.** Crystd from EtOH, MeOH/water, EtOH/water (1:1) or MeOH. Air dried, then dried in a vac desiccator over H<sub>2</sub>SO<sub>4</sub>. [Wright and Grilliom J Am Chem Soc **108** 2340 1986.]

5-Nitrouracil (2,4-dihydroxy-5-nitropyrimidine) [611-08-5] M 157.1, m 280-285°, >300°,  $pK_1^{20}$  0.03,  $pK_2^{20}$  5.55,  $pK_3^{20}$  11.3. Recrystallises as prisms from boiling H<sub>2</sub>O as the monohydrate and loses H<sub>2</sub>O on drying *in vacuo*. [UV: Brown J Chem Soc 3647 1959; Brown J Appl Chem 2 239 1952; Johnson J Am Chem Soc 63 263 1941.]

Nitrourea [556-89-8] M 105.1, m 158.4-158.8°(dec). Crystd from EtOH/pet ether.

5-Nitrovanillin (nitroveratric aldehyde) [6635-20-7] M 197.2, m 172-175°, 176°, 178°. Forms yellow plates from AcOH, and needles from EtOH [Slotta and Szyszke Chem Ber 68 184 1935]. With diazomethane, 5-nitro-3,4-dimethoxyacetophenone is formed [Brady and Manjunath J Chem Soc 125 1067 1924]. The methyl ether crystallises from EtOAc or AcOH, m 88°, 90-91°, and the phenylhydrazone has m 108-110° (from aqueous EtOH). [Finger and Schott J Prakt Chem [2] 115 288 1927.] For oxime m 216° (from EtOH or AcOH) and the oxime acetate has m 147° (from aq EtOH) [Vogel Monatsh Chem 20 384 1899; Brady and Dunn J Chem Soc 107 1861 1915].

*n*-Nonane [111-84-2] M 126.3, b 150.8°, d 0.719, n 1.40542,  $n^{25}$  1.40311. Fractionally distd, then stirred with successive volumes of conc H<sub>2</sub>SO<sub>4</sub> for 12h each until no further colouration was observed in the acid layer. Then washed with water, dried with MgSO<sub>4</sub> and fractionally distd. Alternatively, it was purified by azeotropic distn with 2-ethoxyethanol, followed by washing out the alcohol with water, drying and distilling. [Forziati et al. J Res Nat Bur Stand 36 129 1946].

2,5-Norbornadiene [121-46-0] M 92.1, b 89°, d 0.854, n 1.4707. Purified by distn from activated alumina [Landis and Halpern J Am Chem Soc 109 1746 1987].

cis-endo-5-Norbornene-2,3-dicarboxylic anhydride (carbic anhydride,  $3a\alpha,4,7,7,\alpha\alpha$ -tetrahydro-4 $\alpha,7\alpha$ -methanoisobenzofuran-1,3-dione) [129-64-6] M 164.2, m 164.1°, 164-165°, 164-167°, d 1.417. Forms crystals from pet ether, hexane or cyclohexane. It is hydrolysed by H<sub>2</sub>O to form the acid [Diels and Alder Justus Liebigs Ann Chem 460 98 1928; Maitte Bull Soc Chim Fr 499 1959]. The exo-exo-isomer has m 142-143° (from \*C<sub>6</sub>H<sub>6</sub>-pet ether) [Alder and Stein Justus Liebigs Ann Chem 504 216 1933].

Norbornylene [498-66-8] M 94.2, m 44-46°, b 96°. Refluxed over Na, and distd [Gilliom and Grubbs J Am Chem Soc 108 733 1986]. Also purified by sublimation *in vacuo* onto an ice-cold finger [Woon et al. J Am Chem Soc 108 7990 1986].

Norcamphor (bicyclo[2.2.1]heptan-2-one) [497-38-1] M 110.2, m 94-95°. Crystd from water.

**Norcholanic acid** [511-18-2] **M 346.5, m 177°, 186°,**  $[\alpha]_D^{20}$  + 32° (EtOH), pK<sub>Est</sub> ~4.8. Crystd from acetic acid.

Norcodeine [467-15-2] M 285.3, m 185°, 186°, pK 9.10. Crystd from acetone or ethyl acetate.

Nordihydroguaiaretic [1,4-bis(3,4-dihydroxyphenyl)-2,3-dimethylbutane] acid [500-38-9] M 302.4, m 184-185°, pK<sub>Est(1)</sub>~9.7, pK<sub>Est(2)</sub>~12. Crystd from dilute acetic acid.

Norleucine ( $\alpha$ -amino-*n*-caproic acid) [R(+)- 327-56-0; S(-)- 327-57-1] M 117.2, m 301°  $[\alpha]_{546}^{20}$ (+) and (-) 28° (c 5, 5M HCl); [RS: 616-06-8] m 297-300° (sublimes partially at ~280°), pK<sub>1</sub> 2.39, pK<sub>2</sub> 9.76 (for RS). Crystd from water. Norvaline (R- $\alpha$ -amino-*n*-valeric acid) [R(+)- 2031-12-9; S(-)- 6600-40-4] M 117.2, m 305°(dec),  $[\alpha]_{546}^{20}(+)$  and (-) 25° (c 10, 5M HCl),  $pK_1^{25}$  2.36,  $pK_2^{25}$  9.87 (9.72). Crystd from aqueous EtOH or water.

Nylon powder. Pellets were dissolved in ethylene glycol under reflux. Then ppted as a white powder on addition of EtOH at room temperature. This was washed with EtOH and dried at 100° under vacuum.

**n-Octacosane** [630-02-4] M 394.8, m 62.5°. Purified by forming its adduct with urea, washing and crystallising from acetone/water. [McCubbin *Trans Faraday Soc* 58 2307 1962.] Crystd from hot, filtered isopropyl ether soln (10mL/g).

*n*-Octacosanol (octacosyl alcohol) [557-61-9] M 410.8, m 83.4°, 84°. Recryst from large vols of Me<sub>2</sub>CO. It sublimes at 200-250°/1mm instead of distilling.

*n*-Octadecane [593-45-3] M 254.5, m 28.1°, b 173.5°/10mm, 316.1°/760mm,  $d_4^{20}$  0.7768, n 1.4390. Crystd from acetone and distd under reduced pressure from sodium.

Octadecyl acetate [822-23-1] M 312.5, m 32.6°. Distd under vac, then crystd from diethyl ether/MeOH.

**n-Octadecyl alcohol** (stearyl alcohol) [112-92-5] M 270.5, m 61°, b 153-154°/0.3 mm. Crystd from MeOH, or dry diethyl ether and \*benzene, then fractionally distd under reduced pressure. Purified by column chromatography. Freed from cetyl alcohol by zone melting.

Octadecyl ether (dioctadecyl ether) [6297-03-6] M 523.0, m 59.4°. Vacuum distd, then crystd from MeOH/\*benzene.

Octadecyltrimethylammonium bromide [1120-02-1] M 392.5, m 250°(dec). See entry on p. 446 in Chapter 6.

**2,3,7,8,12,13,17,18-Octaethyl-21H,23H-porphine** [2683-82-1] M **534.8, m 322°, 326°.** Chromatographed on SiO<sub>2</sub> using CHCl<sub>3</sub> as eluent. It crystallises from CHCl<sub>3</sub> (dark red), MeOH (blue violet), pyridine (m 318°) and  $*C_6H_6$  (deep red). [Fischer and Bämler Justus Liebigs Ann Chem **468** 58, 85 1929.]

**Octafluoropropane** (profluorane) [76-19-7] M 188.0, m -183°, b -38°. Purified for pyrolysis studies by passage through a copper vessel containing  $CoF_3$  at about 270°, then fractionally distd. [Steunenberg and Cady J Am Chem Soc 74 4165 1952.] Also purified by several trap-to-trap distns at low temperatures [Simons and Block J Am Chem Soc 59 1407 1937].

1,2,3,4,6,7,8,9-Octahydroanthracene [1079-71-6] M 186.3, m 78°. Crystd from EtOH, then purified by zone melting.

Octamethylcyclotetrasiloxane [556-67-2] M 296.6, m 17.3°, b 175-176°,  $d_4^{20}$  0.957, n 1.396. Purified by zone melting.

Octan-1,8-diol (octamethylene glycol) [629-41-4] M 146.2, m 59-61°, b 172°/20mm. Recrystd from EtOH and distd in a vac.

*n*-Octane [111-65-9] M 114.2, b 126.5°,  $d_4^{20}$  0.704, n 1.39743,  $n^{25}$  1.39505. Extracted repeatedly with conc H<sub>2</sub>SO<sub>4</sub> or chlorosulfonic acid, then washed with water, dried and distd. Also purified by azeotropic distn with EtOH, followed by washing with water to remove the EtOH, drying and distilling. For further details, see n-heptane. Also purified by zone melting.

**1-Octanethiol** [111-88-6] **M 146.3, b 86°/15mm, 197-200°/760mm, d\_4^{20} 0.8433, n 1.4540, pK<sup>25</sup> 10.72 (dil** *t***-BuOH). Passed through a column of alumina [Battacharyya et al. J Chem Soc, Faraday Trans 1 82 135 1986; Fletcher J Am Chem Soc 68 2727 1946].** 

1-Octene [111-66-0] M 112.2, b 121°/742mm,  $d_4^{20}$  0.716, n 1.4087. Distd under nitrogen from sodium which removes water and peroxides. Peroxides can also be removed by percolation through dried, acid washed alumina. Stored under nitrogen in the dark. [Strukul and Michelin J Am Chem Soc 107 7563 1985.]

(trans)-2-Octene [13389-42-9] M 112.2, b 124-124.5°/760mm,  $d_4^{20}$  0.722, n 1.4132. Purification as for 1-octene above.

*n*-Octyl alcohol [111-87-5] M 130.2, b 98°/19mm, 195.3°/760mm, d 0.828, n 1.43018. Fractionally distd under reduced pressure. Dried with sodium and again fractionally distd or refluxed with boric anhydride and distd (b 195-205°/5mm), the distillate being neutralised with NaOH and again fractionally distd. Also purified by distn from Raney nickel and by preparative GLC.

*n*-Octylammonium 9-anthranilate [88020-99-9] M 351.5, m 134-135°, pK<sup>25</sup> 10.65 (for octylamine). Recrystd several times from ethyl acetate.

*n*-Octylammonium hexadecanoate [88020-97-7] M 385.7, m 52-53°. Purified by several recrystns from *n*-hexane or ethyl acetate. The solid was then washed with cold anhydrous diethyl ether, and dried *in vacuo* over  $P_2O_5$ .

*n*-Octylammonium octadecanoate [32580-92-0] M 413.7, m 56-57°. Purified as for the *hexadecanoate* above.

*n*-Octylammonium tetradecanoate [17463-35-3] M 358.6, m 46-48°. Purified as for the *hexadecanoate* above.

4-Octylbenzoic acid [3575-31-3] M 234.3, m 99-100°,  $pK^{25}$  6.5 (80% aq EtOH),  $pK_{Est} \sim 4.5$  (H<sub>2</sub>O). Crystd from EtOH has m 139°; crystd from aq EtOH has m 99-100°. Forms liquid crystals.

*n*-Octyl bromide [111-83-1] M 193.1, b 201.5°,  $d_4^{20}$  1.118,  $n^{25}$  1.4503. Shaken with  $H_2SO_4$ , washed with water, dried with  $K_2CO_3$  and fractionally distd.

4-(*tert*-Octyl)phenol [140-66-9] M 206.3, m 85-86°, b 166°/20mm, pK<sub>Est</sub> ~ 10.4. Crystd from *n*-hexane.

**1-Octyne** [629-05-0] **M 110.2, b 126.2°/760mm, d\_4^{20} 0.717, n^{25} 1.4159. Distd from NaBH<sub>4</sub> to remove peroxides.** 

 $\alpha$ -Oestradiol [57-91-0] M 272.4, m 220-230°,  $[\alpha]_D^{20}$ +55° (c 1, dioxane). Crystd from aq EtOH.

β-Oestradiol-3-benzoate [50-50-0] M 376.5, m 194-195°,  $[\alpha]_{546}^{20}$  +70° (c 2, dioxane). Crystd from EtOH

Oleic acid [112-80-1] M 282.5, m 16°, b 360°(dec),  $d_4^{20}$  0.891,  $n^{30}$  1.4571,  $pK^{25}$  6.42 (50% aq EtOH),  $pK_{Est} \sim 4.8$  (H<sub>2</sub>O). Purified by fractional crystn from its melt, followed by molecular distn at 10<sup>-3</sup>mm, or by conversion to its methyl ester, the free acid can be crystd from acetone at -40° to -45° (12mL/g). For purification by the use of lead and lithium salts, see Keffler and McLean [J Soc Chem Ind (London) 54 176T 1935]. Purification based on direct crystn from acetone is described by Brown and Shinowara [J Am Chem Soc 59 6 1937; pK White J Am Chem Soc 72 1857 1950].

Oleyl alcohol [143-28-2] M 268.5, b 182-184°/1.5mm,  $d_4^{20}$  0.847,  $n^{27.5}$  1.4582. Purified by fractional crystn at -40° from acetone, then distd under vacuum.

**Opianic acid (2-formyl-4,5-dimethylbenzoic acid)** [519-05-1] **M 210.2, m 150°, pK<sup>25</sup> 3.07.** Crystd from water.

Orcinol (5-methylresorcinol) [504-15-4] M 124.2, m 107.5°, m 59-61° (hydrate), pK<sub>1</sub><sup>20</sup>9.36 (9.48), pK<sub>2</sub><sup>20</sup>11.6 (11.20). Crystd from CHCl<sub>3</sub>/\*benzene (2:3).

**L-Ornithine** [70-26-8] **M 132.2, m 140°**,  $[\alpha]_D^{25} + 16°$  (c 0.5,  $H_2O$ ),  $pK_2^{20} 8.75$ ,  $pK_3^{25} 10.73$ . Crystd from water containing 1mM EDTA (to remove metal ions).

**L-Ornithine monohydrochloride** [3184-13-2] **M 168.6, m 233°(dec),**  $[\alpha]_D^{25}$  +28.3° (5M HCl). Likely impurities are citrulline, arginine and D-ornithine. Crystd from water by adding 4 volumes of EtOH and dried in a vacuum desiccator over fused CaCl<sub>2</sub>.

Orotic acid (H<sub>2</sub>O) [50887-69-9] M 174.1, m 235-346°(dec),  $pK_1^{25}$  1.8,  $pK_2^{25}$  9.55. Crystd from water.

Orthanilic acid (2-aminobenzenesulfonic acid) [88-21-1] M 173.2,  $m > 300^{\circ}(dec)$ ,  $pK^{25}$  2.49. Crystd from aqueous soln, containing 20mL of conc HCl per L, then crystd from distilled water, and dried in a vacuum desiccator over Sicapent.

Ouabain {3-[(6-deoxy- $\alpha$ -L-mannopyranosyl)oxy]-1,5,11a,14,19-pentahydroxycard-20(22)enolide} [630-60-4] M 728.8, m 180°(dec),  $[\alpha]_{546}^{20}$  -30° (c 1, H<sub>2</sub>O). Crystd from water as the octahydrate. Dried at 130°. Stored in the dark.

Oxalic acid  $(2H_2O)$  [6153-56-6] M 90.0, m 101.5°; [anhydrous 144-62 -7] m 189.5°,  $pK_1^{25}$ 1.08 (1.37),  $pK_2^{25}$  3.55 (3.80). Crystd from distilled water. Dried in vacuum over  $H_2SO_4$ . The anhydrous acid can be obtained by drying at 100° overnight.

**Oxaloacetic acid** [328-42-7] **M 132.1, m 160°(decarboxylates),**  $pK_1^{25}2.22$ ,  $pK_2^{25}3.89$ ,  $pK_3^{25}$ **13.0.** Crystd from boiling ethyl acetate, or from hot acetone by addition of hot \*benzene.

**2-Oxoglutaric acid (2-oxopentane-1,5-dioic,**  $\alpha$ -ketoglutaric acid) [328-50-7] M 146.1, m 114°, 115-117°, (pK<sub>Est</sub> see oxaloacetic acid above). Crystd repeatedly from Me<sub>2</sub>CO/\*benzene, EtOAc or ethyl propionate.

Oxalylindigo [2533-00-8] M 316.3. Recrystd twice from nitrobenzene and dried by heating *in vacuo* for several hours. [Sehanze et al. J Am Chem Soc 108 2646 1986.]

Oxamide [471-46-5] M 88.1, m >320°(dec). Crystd from water, ground and dried in an oven at 150°.

2-Oxazolidinone [497-25-6] M 87.1, m 89-90°, 91°, b 152°/0.4mm. Crystd from \*benzene or dichloroethane.

**Oxetane** (1.3-trimethylene oxide) [503-30-0] M 58.1, b 45-46°/736mm, 47-49°/atm, 48°/760mm,  $d_4^{20}$  0.892,  $n_D^{20}$ 1.395. Distd twice from sodium metal and then fractionated through a small column at atmospheric pressure, b 47.0-47.2°. Also purified by preparative gas chromatography using a 2m silica gel column. Alternatively add KOH pellets (50g for 100g of oxetane) and distil through an efficient column or a column packed with 1/4in Berl Saddles and the main portion boiling at 45-50° is collected and redistilled over fused KOH. [Noller Org Synth Coll Vol III 835 1955; Dittmer et al. J Am Chem Soc 79 4431 1957.]

Oxine Blue [3-(4-hydroxyphenyl)-3-(8-hydroxy-6-quinilinyl)-1(3H)-isobenzofuranone] [3733-85-5] M 369.4, m 134-135°. Recrystd from EtOH. Dried over H<sub>2</sub>SO<sub>4</sub>.

**Palmitic acid anhydride** (hexadecanoic anhydride) [623-65-4] M 494.9, m 63-64°, 64°, d<sup>82</sup> 0.838, n<sup>68</sup> 1.436. It is moisture sensitive and hydrolyses in water. Purified by refluxing with acetic anhydride for 1hr, evaporating and freeing the residue of acetic acid and anhydride by drying the residue at high vac and crystallising from pet ether at low temperature.

[2.2]-Paracyclophane (tricyclo[8.2.2.2<sup>4,7</sup>]hexadeca-4,6,10,12,13,15-hexaene) [1633-22-3] M 208.3, m 284°, 285-287°, 286-288°, 288-290°. Purified by recrystn from AcOH. <sup>1</sup>H-NMR  $\delta$ : 1.62 (Ar-H) and -1.71 (CH<sub>2</sub>) [Waugh and Fessenden J Am Chem Soc 79 846 1957; IR and UV: Cram et al. J Am Chem Soc 76 6132 1954, Cram and Steinberg J Am Chem Soc 73 5691 1951; complex with unsaturated compounds: Cram and Bauer J Am Chem Soc 81 5971 1959; Syntheses: Brink Synthesis 807 1975, Givens et al. J Org Chem 44 16087 1979, Kaplan et al. Tetrahedron Lett 3665 1976].

**Paraffin** (oil) [8012-95-1] d 0.880, n 1.482. Treated with fuming  $H_2SO_4$ , then washed with water and dilute aqueous NaOH, then percolated through activated silica gel.

**Paraffin Wax.** Melted in the presence of NaOH, washed with water until all of the base had been removed. The paraffin was allowed to solidify after each wash. Finally, 5g of paraffin was melted by heating on a waterbath, then shaken for 20-30min with 100mL of boiling water and fractionally crystd.

**Parafuchsin** (4,4',4"-triaminotrityllium [triphenylmethane] carbonium ion, pararosaniline, paramagenta) [467-62-9] M 305.4, pK 7.57 and free base has pK >13. Dissolve in EtOH (1.16g in 30mL), filter and add aqueous NH<sub>3</sub> till neutral and ppte by adding H<sub>2</sub>O giving 0.8g m 247° dec (sintering at 230°). Dissolve in EtOH neutralise with NH<sub>3</sub> add 0.1g of charcoal filter, and repeat, then add H<sub>2</sub>O (100mL) to ppte the colourless *carbinol* dry, m 257° dec (sintering at 232°). [Weissberger and Theile J Chem Soc 148 1934.] The carbinol (pseudo-base) was said to have m 232° (186° dec), and is slightly sol in H<sub>2</sub>O but sol in acids and EtOH [pK: Goldacre and Phillips J Chem Soc 172 1949]. The perchlorate (dark red with a green shine) has m 300° and explodes at 317° [Dilthey and Diaklage J Prakt Chem [2] 129 1931].

Paraldehyde (acetaldehyde trimer, 2,4,6-trimethyl-1,3,5-trioxane) [123-63-7] M 132.2, m 12.5°, 124°, d 0.995, n 1.407. Washed with water and fractionally distd.

Patulin {4-hydroxy-4H-furo[3.2-c]pyran-2(6H)-one} [149-29-1] M 154.1, m 110°. Crystd from diethyl ether or chloroform. (Highly TOXIC).

**Pavatrine hydrochloride** [548-65-2] M 333.7, m 143-144°. Recrystd from isopropanol, and dried over  $P_2O_5$  under vacuum.

**Pelargonic acid (nonanoic acid)** [112-05-0] **M 158, m 15°, b 98.9°/1mm, 225°/760mm, pK<sup>25</sup> 4.96.** Esterified with ethylene glycol and distd. (This removes dibasic acids as undistillable residues.) The acid was regenerated by hydrolysing the ester.

Pelargononitrile (octyl cyanide) [2243-27-8] M 139.2, m -34°, b 92°/10mm, 224°, d 0.818, n 1.4255. Stirred with  $P_2O_5(\sim 5\%)$ , distd from it and redistd under vac. IR should have CN but no OH bands.

Pelargonyl chloride (nonanoyl chloride) [764-85-2] M 176.7, b 88°/12mm, d 0.941, n 1.436. Refluxed with acetyl chloride (~ 3 vols) for 1h, then distil off the AcCl followed by the nanoyl chloride under reduced pressure. It is moisture sensitive and should be stored in sealed ampules.

**Penicillic acid** [90-65-3] **M 158.2, m 58-64° (monohydrate), 83-84° (anhydrous, lactone).** Crystd from water as the monohydrate, or from pet ether. Free acid is in equilibrium with the lactone. Pentabromoacetone [79-49-2] M 452.6, m 76°, pK 8.0 (MeOH),  $pK_{Est} \sim 4.6$  (H<sub>2</sub>O). Crystd from diethyl ether or EtOH and sublimes.

**Pentabromophenol** [608-71-9] **M 488.7, m 229°, pK\_{Est} \sim 4.5.** Purified by crystn (charcoal) from toluene then from CCl<sub>4</sub>. Dried for 2 weeks at *ca* 75°.

1-Pentacene [135-48-8] M 278.4, m 300°. Crystd from \*benzene.

**Pentachloroethane** (pentalin) [76-01-7] M 202.3, b 69°/37mm, 152.2°/64mm, 162.0°, d 1.678,  $n^{15}$  1.50542. Usual impurities include trichloroethylene. Partially decomposes if distd at atmospheric pressure. Drying with CaO, KOH or sodium is unsatisfactory because of the elimination of the elements of HCl. It can be purified by steam distn, or by washing with conc H<sub>2</sub>SO<sub>4</sub>, water, and then aqueous K<sub>2</sub>CO<sub>3</sub>, drying with solid K<sub>2</sub>CO<sub>3</sub> or CaSO<sub>4</sub>, and fractionally distd under reduced pressure.

Pentachloronitrobenzene [82-68-8] M 295.3, m 146°. Crystd from EtOH.

**Pentachlorophenol** [87-86-5] M 266.3, m 190-191°, pK<sup>25</sup> 4.8. Twice crystd from toluene/EtOH. Sublimed *in vacuo*.

**Pentachloropyridine** [2176-62-7] M 251.3, m 122-124°, 123°, 124°, 124-125°, 125-126°, b 279-280°/atm, pK -6.02 (aq H<sub>2</sub>SO<sub>4</sub>). Purified by recryst from EtOH or aqueous EtOH. It sublimes at 150°/3mm. [den Hertog et al. *Recl Trav Chim Pays-Bas* 69 673 1950; Schikh et al. *Chem Ber* 69 2604 1936.]

Pentachlorothiophenol [133-49-3] M 282.4, m between 228° and 235°, pK<sub>Est</sub> ~1.1. Crystd from \*benzene.

Pentadecafluoro octanoic acid (perfluorocaprylic acid) [335-67-1] M 414.1, m 54.9-55.6°, b 189°/736mm, pK<sub>Est</sub> <0. Recrystd from CCl<sub>4</sub> and toluene, and can be distd. It forms micelles in H<sub>2</sub>O and the solubility is 1% in H<sub>2</sub>O. [Bernett and Zisman J Phys Chem 63 1911 1959; IR: Bro and Sperati J Polym Sci 38 289 1959.]

Pentadecanoic acid [1002-84-2] M 242.4, m 51-53°, 80°, b 158°/1mm, 257°/760mm, d<sup>80</sup> 0.8424, pK<sub>Est</sub> ~5.0. Cryst from Et<sub>2</sub>O and distd. Very hygroscopic. See purification of palmitic acid.

Pentadecanolide (1-oxacyclohexadecan-2-one, pentadecanoic- $\omega$ -lactone, 15-hydroxypentadecanoic lactone, exaltolide, Tibetolide) [106-02-5] M 240.4, m 34-36°, 37-37.5°, 37-38°, b 102-103°/0.03mm, 112-114°/0.2mm, 137°/2mm, 169°/10-11mm, d<sup>40</sup><sub>4</sub> 0.9401. It has been recrystd from MeOH (4 parts) at -15°. [Hundiecker and Erlbach *Chem Ber* 80 135 1947; Galli and Mandolini *Org Synth* 58 100 1978; Demole and Enggist *Helv Chim Acta* 11 2318 1978.]

**Penta-1,3-diene** [cis: 1574-41-0; trans: 2004-70-8] **M 68.1, b 42°, d 0.680, n 1.4316.** Distd from NaBH<sub>4</sub>. Purified by preparative gas chromatography. [Reimann et al. J Am Chem Soc 108 5527 1986.]

Penta-1,4-diene [591-93-5] M 68.1, b 25.8-26.2°/756mm, d 0.645, n 1.3890. Distd from NaBH<sub>4</sub>. Purified by preparative gas chromatography. [Reimann et al. J Am Chem Soc 108 5527 1986.]

**Pentaerythritol** [115-77-5] **M 136.2, m 260.5°.** Refluxed with an equal volume of MeOH, then cooled and the ppte dried at 90°. Crystd from dil aq HCl. Sublimed under vacuum at 200°.

Pentaerythritol tetraacetate [597-71-7] M 304.3, m 78-79°. Crystd from hot water, then leached with cold water until the odour of acetic acid was no longer detectable.

Pentaerythrityl laurate [13057-50-6] M 864.6, m 50°. Crystd from pet ether.

Pentaerythritol tetranitrate. [78-11-5] M 316.2, m 140.1°. Crystd from acetone or acetone/EtOH. EXPLOSIVE.

**Pentaethylenehexamine** [4067-16-7] M 232.4, d 0.950,  $n_D^{20}$  1.510,  $pK_1$  1.2,  $pK_2$  2.7,  $pK_3$  4.3,  $pK_4$  7.8,  $pK_5$  9.1,  $pK_6$  9.9 (all estimated). Fractionally distd twice at 10-20mm, the fraction boiling at 220-250° being collected. Its soln in MeOH (40mL in 250mL) was cooled in an ice-bath and conc HCl was added dropwise with stirring. About 50mL was added, and the ppted hydrochloride was filtered off, washed with acetone and diethyl ether, then dried in a vacuum desiccator. [Jonassen et al. J Am Chem Soc 79 4279 1957.]

**Pentafluorobenzene** [363-72-4] **M 168.1, b 85°/atm, 85-86<sup>c</sup>/atm, 88-89°/atm, d\_4^{20} 1.524, n\_D^{20} 1.3931. Purified by distn and by gas chromatography. IR film: 1535 and 1512 cm<sup>-1</sup> (\*benzene ring). [UV: Stephen and Tatlow** *Chem Ind (London)* **821 1957; Nield et al. J Chem Soc 166 1959.] See triethylenepentamine** 

2,3,4,5,6-Pentafluorobenzoic acid [602-94-8] M 212.1, m 101-103°, 103-104°, 104-105°, 106-107°,  $pK^{25}1.75$ . Dissolve in Et<sub>2</sub>O, treat with charcoal, filter, dry (CaSO<sub>4</sub>), filter, evaporate and recrystallise residue from pet ether (b 90-100°) after adding a little toluene to give large colourless plates. UV (H<sub>2</sub>O):  $\lambda$ max 265nm ( $\epsilon$  761). The S-benzylisothiuronium salt has m 187° after recrystn from H<sub>2</sub>O. [McBee and Rapkin J Am Chem Soc 73 1366 1951; Nield et al. J Chem Soc 166, 170 1959.]

**O**-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine hydrochloride (PFBHA) [57981-02-9] M 249.6, m 215°, 215-216°, pK<sub>Est</sub> ~1.1. Recrystd from EtOH to form colourless leaflets. Drying the compound at high vacuum and elevated temperature will result in losses by sublimation. [Youngdale J Pharm Sci 65 625 1976; Wehner and Handke J Chromatog 177 237 1979; Nambara et al. give incorrect m as 115-116° J Chromatogr 114 81 1975.]

2,3,4,5,6-Pentafluorophenol [771-61-9] M 184.1, m 33-35°, 38.5-39.5°, b 72-74°/48 mm, 142-144°/atm, 143°/atm,  $n_D^{20}$ 1.4270 (liquid prep), pK<sup>25</sup> 5.53. A hygroscopic low melting solid not freely soluble in H<sub>2</sub>O. Purified by distn, preferably in a vacuum [Forbes et al. J Chem Soc 2019 1959; IR and pKa: Birchall and Haszeldine J Chem Soc 13 1959]. IR film: 3600 (OH) and 1575 (fluoroaromatic breathing) cm<sup>-1</sup>. The benzoyl derivative has m 74-75°, 3,4-dinitrobenzoyl derivative has m 107°, the tosylate has m 64-65° (from EtOH) and the K salt crystallises from Me<sub>2</sub>CO, m 242° dec, with 1H<sub>2</sub>O salt the m is 248° dec and the 2H<sub>2</sub>O salt has m 245° dec.

1-(Pentafluorophenyl)ethanol [R-(+)-104371-21-3; S-(-)-104371-20-2] M 212.1, m 41-42°,42°, 42.5-43°,  $[\alpha]_{546}^{20}$  (+) and (-) 9°,  $[\alpha]_D^{20}$  (+) and (-) 7.5° (c 1, *n*-pentane). Recryst from *n*-pentane at -40° and vacuum sublimed at room temp at 0.3mm (use ice cooled cold finger). It has also been purified by column chromatography through Kieselgel 60 (0.063-0.2mm mesh, Merck), eluted with EtOAc-*n*-hexane (1:5), then recryst from *n*-pentane and vacuum sublimed. It has R<sub>F</sub> on Kieselgel 60 F<sub>254</sub> TLC foil and eluting with EtOAc-*n*-hexane (1:5). [Meese Justus Liebigs Ann Chem 2004 1986.] The racemate [75853-08-6] has m 32-34°, b 77-79°/8mm, 80-82°/37mm,  $n_D^{20}$  1.4426 and the 3,4-dinitrobenzoate has m 83° [Nield et al. J Chem Soc 166 1959].

**2,2,3,3,3-Pentafluoropropan-1-ol** [422-05-9] M 150.1, b 80°, d 1.507, n 1.288,  $pK^{25}$  12.74. Shaken with alumina for 24h, dried with anhydrous  $K_2CO_3$ , and distd, collecting the middle fraction (b 80-81°) and redistilling.

Pentafluoropyridine [700-16-3] M 169.1, m -41.5°, b 83.5°, 84°, 83-85°,  $d_4^{20}$  1.609,  $n_D^{20}$  1.3818, pK<sub>Est</sub> ~<0. Distd through a concentric tube column; has  $\lambda$  max in cyclohexane at 256.8nm. [Chambers et al. J Chem Soc 3573 1964]; <sup>19</sup>F NMR: Bell et al. J Fluorine Chem 1 51 1971.] The hexafluoroantimonate has m 98-102° dec.

**Pentamethylbenzene** [700-12-9] **M 148.3, m 53.5-55.1°.** Successively crystd from absolute EtOH, toluene and MeOH, and dried under vacuum. [Rader and Smith J Am Chem Soc 84 1443 1962.] It has also been crystd from \*benzene or aqueous EtOH, and sublimed.

*n*-Pentane [109-66-0] M 72.2, b 36.1°, d 0.626,  $n^{25}$  1.35472. Stirred with successive portions of conc H<sub>2</sub>SO<sub>4</sub> until there was no further coloration during 12h, then with 0.5N KMnO<sub>4</sub> in 3M H<sub>2</sub>SO<sub>4</sub> for 12h, washed with water and aqueous NaHCO<sub>3</sub>. Dried with MgSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>, then P<sub>2</sub>O<sub>5</sub> and fractionally distd through a column packed with glass helices. It was also purified by passage through a column of silica gel, followed by distn and storage with sodium hydride. An alternative purification is by azeotropic distn with MeOH, which is subsequently washed out from the distillate (using water), followed by drying and distn. For removal of carbonyl-containing impurities, see n-heptane. Also purified by fractional freezing (*ca* 40%) on a copper coil through which cold air was passed, then washed with conc H<sub>2</sub>SO<sub>4</sub> and fractionally distd.

**Pentane-1-thiol** [110-66-7] M 104.2, m -76°, b 122.9°/697.5mm, d<sup>25</sup> 0.8375, pK<sub>Est</sub> ~10.1. Dissolved in aqueous 20% NaOH, then extracted with a small amount of diethyl ether. The soln was acidified slightly with 15% H<sub>2</sub>SO<sub>4</sub>, and the thiol was distd out, dried with CaSO<sub>4</sub> or CaCl<sub>2</sub>, and fractionally distd under nitrogen. [Ellis and Reid J Am Chem Soc 54 1674 1932.]

Pentan-2-ol [6032-29-7] M 88.2, b 119.9°, d 0.810, n 1.41787, n<sup>25</sup> 1.4052. Refluxed with CaO, distd, refluxed with magnesium and again fractionally distd.

Pentan-3-ol [584-02-1] M 88.2, b 116.2°, d 0.819, n<sup>25</sup> 1.4072. Refluxed with CaO, distd, refluxed with magnesium and again fractionally distd.

**Pentan-3-one (diethyl ketone)** [96-22-0] **M 86.1, b 102.1°, d 0.8099, n 1.392.** See diethyl ketone on p. 204.

Pentaquine monophosphate [5428-64-8] M 395.6, m 189-190°, pK<sup>70</sup> 8.22. Crystd from 95% EtOH.

Pent-2-ene (mixed isomers) [109-68-2] M 70.1, b 36.4°, d 0.650, n 1.38003, n<sup>25</sup> 1.3839. Refluxed with sodium wire, then fractionally distd twice through a Fenske (glass helices packing) column.

*cis*-Pent-2-ene [627-20-3] M 70.1, b 37.1°, d 0.657, n<sup>25</sup> 1.3798. Dried with sodium wire and fractionally distd, or purified by azeotropic distn with MeOH, followed by washing out the MeOH with water, drying and distilling. Also purified by chromatography through silica gel and alumina [Klassen and Ross J Phys Chem 91 3668 1987].

trans-Pent-2-ene [646-04-8] M 70.1, b 36.5°, d 0.6482, n 1.3793. It was treated as above and washed with water, dried over anhydrous Na<sub>2</sub>CO<sub>3</sub>, and fractionally distd. The middle cut was purified by two passes of fractional melting.

**Pentobarbital** (5-ethyl-5-1'-methylbutyl barbituric acid, Nembutal) [76-74-4] M 226.4, m  $\sim 127^{\circ}(dec)$ , pK<sub>Est(1)</sub>~ 8.0, pK<sub>Est(2)</sub>~12.7. Soln of the sodium salt in 10% HCl was prepared and the acid was extracted by addition of ether. Then purified by repeated crystn from CHCl<sub>3</sub>. [Bucket and Sandorfy J Phys Chem 88 3274 1984.]

Pentyl acetate (*n*-amyl acetate) [628-63-7] M 130.2, b 147-149°/atm, 149.55°, 149.2°/atm,  $d_4^{20}$  0.8753,  $n_D^{20}$  1.4028. Purified by repeated fractional distn through an efficient column or spinning band column. [Timmermann and Hennant-Roland J Chim Phys 52 223 1955; Mumford and Phillips J Chem Soc 75 1950; <sup>1</sup>H NMR: Crawford and Foster Can J Phys 34 653 1956.]

**Pent-2-yne** [627-21-4] **M 68.1, b 26°/2.4mm, d 0.710, n<sup>25</sup> 1.4005.** Stood with, then distd at low pressure from, sodium or NaBH<sub>4</sub>.

**Perbenzoic acid** [93-59-4] **M 138.1, m 41-43°, b 97-110°/13-15mm, pK**<sub>Est</sub> ~7.7. Crystd from \*benzene or pet ether. Readily sublimed and is steam volatile. Sol in CHCl<sub>3</sub>, CCl<sub>4</sub> and Et<sub>2</sub>O. [Org Synth Coll Vol I (2nd Edn) 431 1948.] **EXPLOSIVE.** 

**Perchlorobutadiene** [87-68-3] M 260.8, b 144.1°/100mm, 210-212°/760mm, d 1.683, n 1.5556. Washed with four or five 1/10th volumes of MeOH (or until the yellow colour has been extracted), then stirred for 2h with  $H_2SO_4$ , washed with distilled water until neutral and filtered through a column of  $P_2O_5$ . Distd under reduced pressure through a packed column. [Rytner and Bauer J Am Chem Soc 82 298 1960.]

**Perfluorobutyric acid** [375-22-4] M 214.0, m -17.5°, b 120°/735mm, d 1.651,  $n^{16}$  1.295,  $pK^{25}$  -0.17. Fractionally distd twice in an Oldershaw column with an automatic vapour-dividing head, the first distn in the presence of conc H<sub>2</sub>SO<sub>4</sub> as a drying agent.

**Perfluorocyclobutane** [115-25-3] **M 200.0, m -40°, b -5°, d<sup>-20</sup> 1.654, d° 1.72.** Purified by trapto-trap distn, retaining the middle portion.

**Perfluorocyclohexane** [355-68-0] **M 300.1, m 51° (sublimes), b 52°.** Extracted repeatedly with MeOH, then passed through a column of silica gel (previously activated by heating at 250°).

**Perfluoro-1,3-dimethylcyclohexane** [335-27-3] **M 400.1, b 101°, d 1.829, n 1.300.** Fractionally distd, then 35mL was sealed with about 7g KOH pellets in a borosilicate glass ampoule and heated at 135° for 48h. The ampoule was cooled and opened, and the liquid was resealed with fresh KOH in another ampoule and heated as before. This process was continued until no further decomposition was observed. The substance was then washed with distilled water, dried (CaSO<sub>4</sub>) and distd. [Grafstein Anal Chem **26** 523 1954.]

**Perfluoroheptane** [335-57-9] **M** 388.1, **b** 99-101°,  $d^{25}$  1.7200. Purified as for *perfluorodimethylhexane*. Other procedures include shaking with H<sub>2</sub>SO<sub>4</sub>, washing with water, drying with P<sub>2</sub>O<sub>5</sub> for 48h and fractionally distilling. Alternatively, it has been refluxed for 24h with saturated acid KMnO<sub>4</sub> (to oxidise and remove hydrocarbons), then neutralised, steam distd, dried with P<sub>2</sub>O<sub>5</sub>, and passed slowly through a column of dry silica gel. It has been purified by fractional crystn, using partial freezing.

**Perfluoro**-*n*-hexane [355-42-0] M 338.1, m -4°, b 58-60°, d 1.684. Purified by fractional freezing. The methods described for *perfluoroheptane* should be applicable here.

**Perfluoro**(methylcyclohexane) [355-02-2] M 350.1, b 76.3°,  $d^{25}$  1.7878. Refluxed for 24h with saturated acid KMnO<sub>4</sub> (to oxidise and remove hydrocarbons), then neutralised, steam distd, dried with P<sub>2</sub>O<sub>5</sub> and passed slowly through a column of dry silica gel. [Glew and Reeves J Phys Chem 60 615 1956.] Also purified by percolation through a 1m neutral activated alumina column, and <sup>1</sup>H-impurities checked by NMR.

Perfluorononane [375-96-2] M 488.1, b 126-127°, d 1.80, n 1.275. Purified as for perfluorodimethylcyclohexane.

Perfluoropropyl iodide [754-34-7] M 295.9, b 41°, d 2.13, n 1.339. Purified by fractional distn.

Perfluorotributylamine (heptacosafluorotributylamine) [311-89-7] M 671.1, b 177.6°/760mm, d 1.881, n 1.291, pK<sub>Est</sub> ~5.0. Purified as for perfluorodimethylcyclopropane, see also perfluorotripropylamine [Hazeldine J Chem Soc 102 1951].

Perfluorotripropylamine (heneicosafluorotripropylamine) [338-83-0] M 521.1, b 130°/atm, 129.5-130.5°/atm, d 1.822, n 1.279, pK<sub>Est</sub> ~5.6. Purified as for *perfluorodimethylcyclopropane*. [Hazeldine J Chem Soc 102 1951, for azeotropes see Simons and Linevsky J Am Chem Soc 74 4750 1972.] IRRITANT.

**Pericyazine** [10-{3-(4-hydroxy-1-piperidinyl)-propyl}-10H-phenothiazine-2-carbonitrile] [2622-26-6] M 365.4, m 116-117°. Recrystd from a saturated soln in cyclohexane. Antipsychotic and is a reagent for Pd and Rh. **Perylene** [198-55-0] **M 252.3, m 273-274°.** Purified by silica-gel chromatography of its recrystd picrate. [Ware J Am Chem Soc 83 4374 1961.] Crystd from \*benzene, toluene or EtOH and sublimed in a flow of oxygen-free nitrogen. [Gorman et al. J Am Chem Soc 107 4404 1985; Johansson et al. J Am Chem Soc 109 7374 1987.]

**Petroleum ether** [8032-32-4] **b** 35-60°, **d** 0.640, **n** 1.363. Shaken several times with conc  $H_2SO_4$ , then 10%  $H_2SO_4$  and conc KMnO<sub>4</sub> (to remove unsatd, including aromatic, hydrocarbons) until the permanganate colour persists. Washed with water, aqueous Na<sub>2</sub>CO<sub>3</sub> and again with water. Dried with CaCl<sub>2</sub> or Na<sub>2</sub>SO<sub>4</sub>, and distd. It can be dried further using CaH<sub>2</sub> or sodium wire. Passage through a column of activated alumina, or treatment with CaH<sub>2</sub> or sodium, removes peroxides. For the elimination of carbonyl-containing impurities without using permanganate, see *n*-heptane. These procedures could be used for all fractions of pet ethers. **Rapid purification:** Pass through an alumina column and fractionally distilling, collecting the desired

R(-)-α-Phellandrene (p-menta-1,5-diene) [4221-98-1] M 136.2, b 61°/11mm, 175-176°/760mm, d 0.838, n 1.471. Purified by gas chromatography on an Apiezon column.

**Phenacylamine hydrochloride** [5468-37-1] **M 171.6, m 194**°(dec). See 2-aminoacetophenone hydrochloride on p. 103.

**Phenanthrene** [85-01-8] **M 178.2, m 98°.** Likely contaminants include, anthracene, carbazole, fluorene and other polycyclic hydrocarbons. Purified by distn from sodium, boiling with maleic anhydride in xylene, crystn from acetic acid, sublimation and zone melting. Has also been recrystd repeatedly from EtOH, \*benzene or pet ether (b 60-70°), with subsequent drying under vacuum over  $P_2O_5$  in an Abderhalden pistol. Feldman, Pantages and Orchin [J Am Chem Soc 73 4341 1951] separated from most of the anthracene impurity by refluxing phenanthrene (671g) with maleic anhydride (194g) in xylene (1.25L) under nitrogen for 22h, then filtered. The filtrate was extracted with aqueous 10% NaOH, the organic phase was separated, and the solvent was evaporated. The residue, after stirring for 2h with 7g of sodium, was vacuum distd, then recrystd twice from 30% \*benzene in EtOH, then dissolved in hot glacial acetic acid (2.2mL/g), slowly adding an aqueous soln of CrO<sub>3</sub> (60g in 72mL H<sub>2</sub>O added to 2.2L of acetic acid), followed by slow addition of conc H<sub>2</sub>SO<sub>4</sub> (30mL). The mixture was refluxed for 15min, diluted with an equal volume of water and cooled. The ppte was filtered off, washed with water, dried and distd, then recrystd twice from EtOH. Further purification is possible by chromatography from CHCl<sub>3</sub> soln on activated alumina, with \*benzene as eluent, and by zone refining.

Phenanthrene-9-aldehyde [4707-71-5] M 206.3, m 102-103°, pK -6.39 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH and sublimed at 95-98°/0.07mm.

**9,10-Phenanthrenequinone** [84-11-7] **M 208.2, m 208°, pK -7.1 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from dioxane or 95% EtOH and dried under vacuum.

**Phenanthridine** [229-87-8] M 179.2, m 106.5°, 108-109°, b 350°,  $pK^{20}$  4.61 (4.48). Purified via the HgCl<sub>2</sub> addition compound formed when phenanthridine (20g) in 1:1 HCl (100mL) was added to aq HgCl<sub>2</sub> (60g in 3L), and the mixture was heated to boiling. Conc HCl was then added until all of the solid had dissolved. The compound separated on cooling, and was dec with aq NaOH (ca 5M). Phenanthridine was extracted with Et<sub>2</sub>O and crystd from pet ether (b 80-100°) or EtOAc. [Cumper et al. J Chem Soc 45218 1962.] Also purified by zone melting; sublimes in vac. [Slough and Ubbelhode J Chem Soc 911 1957.] See p. 124.

**1,10-Phenanthroline** (*o*-phenanthroline) [66-71-7 (anhydr); 5144-89-8 (H<sub>2</sub>O)] M **198.2, m 98-101°, 108-110° (hydr), 118° (anhydr), b** >300°,  $pK_1^{25}$ -0.7 (aq HClO<sub>4</sub>),  $pK_2^{25}$  4.86 (4.96). Crystd as its *picrate* (m 191°) from EtOH, then the free base was liberated, dried at 78°/8mm over P<sub>2</sub>O<sub>5</sub> and crystd from pet ether (b 80-100°). [Cumper, Ginman and Vogel J Chem Soc 1188 1962.] It can be purified by zone melting. Also crystd from hexane, \*benzene/pet ether (b 40-60°) or sodium-dried \*benzene, dried and stored over H<sub>2</sub>SO<sub>4</sub>. The monohydrate is obtained by crystn from aqueous EtOH or ethyl acetate. It has been crystd from H<sub>2</sub>O (300 parts) to give the monohydrate m 102-103° and sublimes at 10<sup>-3</sup>mm [Fielding and LeFevre J

boiling fraction.

Chem Soc 1811 1951.] The anhydrous compound has **m** 118° (after drying at high vacuum at 80°), also after recrystn from pet ether or  $C_6H_6$  (70 parts) and drying at 78°/8mm. [UV: Badger et al. J Chem Soc 3199 1951.] It has a pKa in H<sub>2</sub>O of 4.857 (25°) or 5.02 (20°) and 4.27 in 50% aq EtOH (20°) [Albert et al. J Chem Soc 2240 1948].

1,10-Phenanthroline hydrochloride (o-phenanthroline hydrochloride) [3829-86-5] M 243.7, m 212-219°. It crystallises from 95% EtOH, m 212-219° as the monohydrate, the half hydrate has m 217°. The 3HCl has m 143-145° (sinters at 128°) [Thevenet et al. Acta Cryst Sect B 33 2526 1977].

4,7-Phenanthroline-5,6-dione [84-12-8] M 210.2, m 295°(dec). Crystd from MeOH.

**Phenazine** [92-82-0] **M 180.2, m 171°, pK\_1^{20} -4.9 (aq H<sub>2</sub>SO<sub>4</sub>), pK\_2^{20} 1.21. Crystd from EtOH, CHCl<sub>3</sub> or ethyl acetate, after pre-treatment with activated charcoal. It can be sublimed** *in vacuo***, and zone refined.** 

Phenazine methosulfate [299-11-6] M 306.3. See 5-methylphenazinium methyl sulfate on p. 547 in Chapter 6.

Phenethylamine [64-04-0] M 121.2, b 87°/13mm, d 0.962, n 1.535, pK<sup>25</sup> 9.88. Distd from CaH<sub>2</sub>, under reduced pressure, just before use.

**Phenethyl bromide** [103-63-9] **M 185.1, b 92°/11mm, d 1.368, n 1.557**. Washed with conc H<sub>2</sub>SO<sub>4</sub>, water, aq 10% Na<sub>2</sub>CO<sub>3</sub> and water again, then dried with CaCl<sub>2</sub> and fractionally distd just before use.

N-2-Phenethyl urea [2158-04-5] M 164.2, m 173-174°. Crystd from water.

Phenetole [103-73-1] M 122.2, b 60°/9mm, 77.5°/31mm, 170.0°/760mm, d 0.967, n 1.50735, n<sup>25</sup> 1.50485. Small quantities of phenol can be removed by shaking with NaOH, but this is not a very likely contaminant of commercial material. Fractional distn from sodium, at low pressures, probably gives adequate purification. It can be dissolved in diethyl ether and washed with 10% NaOH (to remove phenols), then water. The ethereal soln was evaporated and the phenetole fractionally distd under vacuum.

Phenocoll hydrochloride (4-ethoxyaniline, p-phenetidine HCl) [536-10-6] M 230.7, m 234°, pK<sup>28</sup> 5.20. Crystd from water. Sublimes *in vacuo*.

**Phenol** [108-95-2] M 94.1, m 40.9°, b 85.5-86.0°/20mm, 180.8°/760mm, d 1.06,  $n^{4.1}$  1.54178,  $n^{4.6}$  1.53957,  $pK^{2.5}$  9.86 (10.02). Steam was passed through a boiling soln containing 1mole of phenol and 1.5-2.0moles of NaOH in 5L of H<sub>2</sub>O until all non-acidic material had distd. The residue was cooled, acidified with 20% (v/v) H<sub>2</sub>SO<sub>4</sub>, and the phenol was separated, dried with CaSO<sub>4</sub> and fractionally distd under reduced pressure. It was then fractionally crystd several times from its melt [Andon et al. J Chem Soc 5246 1960]. Purification via the benzoate has been used by Berliner, Berliner and Nelidow [J Am Chem Soc 76 507 1954]. The benzoate was crystd from 95% EtOH, then hydrolysed to the free phenol by refluxing with two equivalents of KOH in aq EtOH until the soln became homogeneous. It was acidified with HCl and extracted with diethyl ether. The ether layer was freed from benzoic acid by thorough extraction with aqueous NaHCO<sub>3</sub>, and, after drying and removing the ether, the phenol was distd.

Phenol has also been crystd from a 75% w/w soln in water by cooling to  $11^{\circ}$  and seeding with a crystal of the hydrate. The crystals were centrifuged off, rinsed with cold water (0-2°) satd with phenol, and dried. It can be crystd from pet ether [Berasconi and Paschalis J Am Chem Soc 108 2969 1986].

Draper and Pollard [Science 109 448 1949] added 12% water, 0.1% aluminium (can also use zinc), and 0.05% NaHCO<sub>3</sub> to phenol, and distd at atmospheric pressure until the azeotrope was removed. The phenol was then distd at 25mm. Phenol has also been dried by distn from the \*benzene soln to remove the water-\*benzene azeotrope and the excess \*benzene, followed by distn of the phenol at reduced pressure under nitrogen. Processes such as this are probably adequate for analytical grade phenol which has as its main impurity water. Phenol has also been crystd from pet ether/\*benzene or pet ether (b 40-60°). Purified material is stored in a vacuum desiccator over  $P_2O_5$  or CaSO<sub>4</sub>.

**Phenol-2,4-disulfonic acid** [96-77-5] **M 254.2, pK\_1 < 1, pK\_2 < 1, pK\_3 \sim 8.3. Crystd from EtOH/diethyl ether.** 

**Phenolphthalein** [77-09-8] **M 319.2, m 263°, pK**<sub>Est(1)</sub>~ **4.2, pK**<sub>Est(2)</sub>~ **9.8.** Dissolved in EtOH (7mL/g), then diluted with eight volumes of cold water. Filtered. Heated on a water-bath to remove most of the alcohol and the pptd phenolphthalein was filtered off and dried under vacuum.

Phenolphthalol [81-92-5] M 306.3, m 201-202°, pK<sub>Est</sub> ~ 9.8. Crystd from aqueous EtOH.

Phenosafranine (3,7-diamino-5-phenylphenazinium chloride) [81-93-6] M 322.8, m >300°,  $\lambda_{max}$  530nm (H<sub>2</sub>O). Crystd from dilute HCl.

**Phenothiazine** [92-84-2] **M 199.3, m 184-185°.** Crystd from \*benzene or toluene (charcoal) after boiling for 10min under reflux. Filtered on a suction filter. Dried in an oven at 100°, then in a vacuum desiccator over paraffin chips. Also twice recrystd from water and dried in an oven at 100° for 8-10h.

**Phenoxazine** [135-67-1] **M 199.2, m 156°, 156-158°, 158-159°, b 215°/4mm.** Crystd from EtOH and sublimed *in vacuo*. If too impure then extract in a Soxhlet using toluene. Evaporate the solvent and dissolve residue (*ca* 100g) in  $C_{6}H_{6}$  (1L) **CARCINOGEN**, use an efficient fume cupboard) and chromatograph through an Al<sub>2</sub>O<sub>3</sub> column (50 x 450 mm). The eluent (*ca* 3L) is evaporated to *ca* 150mL and cooled when *ca* 103g of phenoxazine **m** 149-153° is obtained. Sublimation yields platelets **m** 158-159°. It forms a green *picrate* **m** 141.5-142°. [Gilman and Moore *J Am Chem Soc* 79 3485 1957; Müller et al. *J Org Chem* 24 37 1959.]

Phenoxyacetic acid [122-59-8] M 152.2, m 98-99°, pK<sup>25</sup> 3.18. Crystd from water or aq EtOH.

**Phenoxyacetyl chloride** [701-99-5] **M 170.6, b 112°/10mm, 102°/16mm, 225-226°/atm, d\_4^{20} 1.235, n\_D^{20} 1.534. If it has no OH band in the IR then distil in a vacuum, taking precautions for the moisture-sensitive compound. If it contains free acid (due to hydrolysis, OH bands in the IR) then add an equal volume of redistilled SOCl<sub>2</sub>, reflux for 2-3h, evaporate and distil the residue in a vacuum as before. The** *amide* **has <b>m** 101°. [McElvain and Carney J Am Chem Soc **68** 2592 1946.]

4-Phenoxyaniline [139-59-3] M 185.2, m 95°, pK<sup>20</sup> 4.44 (50% aq EtOH). Crystd from water.

Phenoxybenzamine [N-(2-chloroethyl)-N-(1-methyl-2-phenoxyethyl)benzylamine] [59-96-1] M 303.5, m 38-40°, hydrochloride [63-92-3] M 340.0, m 137.5-140°, pK<sub>Est</sub> ~4.2. The free base is crystd from pet ether and the *HCl* is crystd from EtOH/diethyl ether.

**2-Phenoxybenzoic acid** [2243-42-7] **M 214.2, m 113°, b 355°/760mm, pK<sup>15</sup> 3.53.** Crystd from aqueous EtOH.

3-Phenoxybenzoic acid [3739-38-6] M 214.2, m 145°, pK 3.59. Crystd from aqueous EtOH.

**Phenoxybutyric acid** [6303-58-8] **M 180.2, m 64°, 65-66°, 82-83°, 99°, b 180-185°/12mm, pK 3.17.** It has been purified by recrystn from pet ether,  $*C_6H_6$ ,  $Et_2O$ -pet ether, EtOH and from  $H_2O$ . It can be steam distd or distd in a good vac. [UV: Ramart-Lucas and Hoch Bull Soc Chim Fr [4] 51 824 1932; Dann and Arndt Justus Liebigs Ann Chem 587 38 1954.] The acid chloride has b 154-156°/20mm [Hamford and Adams J Am Chem Soc 57 921 1935]; and the amide crystallises from  $*C_6H_6$  as needles m 113°.

2-Phenoxypropionic acid (lactic acid O-phenylether) [940-31-8] M 166.2, m 115-116°, b 105-106°/5mm, 265-266°/758mm, pK 3.11. Crystd from water.

Phensuximide (N-methyl-2-phenylsuccinimide) [86-34-0] M 189.2, m 71-73°. Crystd from hot 95% EtOH.

Phenylacetamide [103-81-1] M 135.2, m 158.5°. Crystd repeatedly from absolute EtOH. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

**Phenyl acetate** [122-79-2] **M 136.2, b 78°/10mm, d 1.079, n^{22} 1.5039.** Freed from phenol and acetic acid by washing (either directly or as a soln in pentane) with aqueous 5% Na<sub>2</sub>CO<sub>3</sub>, then with saturated aqueous CaCl<sub>2</sub>, drying with CaSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>, and fractional distn at reduced pressure.

Phenylacetic acid [103-82-2] M 136.2, m 76-77°, b 140-150°/20mm,  $pK_1$  -7.59 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2$  4.31. Crystd from pet ether (b 40-60°), isopropyl alcohol, aq 50% EtOH or hot water. Dried under vac. It can be distd under reduced pressure.

Phenylacetone (1-phenylpropan-2-one) [103-79-9] M 134.2, b 69-71°/3mm, d 1.00, n 1.516. Converted to the semicarbazone and crystd three times from EtOH (m 186-187°). The semicarbazone was hydrolysed with 10% phosphoric acid and the ketone was distd. [Kumler, Strait and Alpen J Am Chem Soc 72 1463 1950.]

4'-Phenylacetophenone [92-91-1] M 196.3, m 120.3-121.2°, b 196-210°/18mm, 325-327°/760mm. Crystd from EtOH or acetone. Can also be distd under reduced or atmospheric pressure.

**Phenylacetylene** [536-74-3] **M 102.1, b 75°/80mm, d 0.930, n<sup>25</sup> 1.5463, pK ~19.** Distd through a spinning band column. Should be filtered through a short column of alumina before use [Collman et al. J Am Chem Soc 108 2988 1986; for pK see Brandsma Preparative Acetylenic Chemistry, 1st Edn Elsevier 1971, p. 15, ISBN 0444409475].

*dl*-Phenylalanine [150-30-1] M 165.2, m 162°,  $pK_1^{25}$  2.58,  $pK_2^{25}$  9.24. Crystd from water and dried under vacuum over P<sub>2</sub>O<sub>5</sub>.

L-Phenylalanine [63-91-2] M 165.2, m 280°(dec),  $[\alpha]_D^{25}$ -34.0° (c 2, H<sub>2</sub>O). Likely impurities are leucine, valine, methionine and tyrosine. Crystd from water by adding 4 volumes of EtOH. Dried under vac over P<sub>2</sub>O<sub>5</sub>. Also crystd from satd refluxing aq solns at neutral pH, or 1:1 (v/v) EtOH/water soln, or conc HCl.

Phenylalaninol (2-amino-3-phenylpropan-1-ol) [R-(+)-5267-64-1; S-(-)-3182-95-4] M 151.2, m 91-92°, 91.5°, 92-94°, b 80°/11mm (Kügelrohr),  $[\alpha]_{546}^{20}$  (+) and (-) 28°,  $[\alpha]_D^{20-25}$  (+) and (-) 23-28.7° (c 1-5, EtOH), pK<sub>Est</sub> ~9.3. It can be recrystd from Et<sub>2</sub>O, \*C<sub>6</sub>H<sub>6</sub>-pet ether (b 40-60°) or toluene and distd in a vacuum. Has been purified by dissolving in Et<sub>2</sub>O, drying over K<sub>2</sub>CO<sub>3</sub>, filtering, evaporating to a small volume, cooling in ice and collecting the plates. Store in the presence of KOH (i.e. CO<sub>2</sub>—free atm). [Karrer and Ehrhardt *Helv Chim Acta* 34 3203 1951; Oeda Bull Chem Soc Jpn 13 465 1938.] The picrate has m 141-141.5° (from EtOH-pet ether). The hydrogen oxalate has m 177°, 161-162° [Hunt and McHale J Chem Soc 2073 1957]. The racemate has m 87-88° from \*C<sub>6</sub>H<sub>6</sub>-pet ether (75-77° from Et<sub>2</sub>O), and the hydrochloride has m 139-141° [Fodor et al. J Chem Soc 1858 1951].

**3-Phenylallyl chloride** (cinnamyl chloride) [E: 18685-01-3; Z: 39199-93-4] M 152.6, b 92-93°/3mm. Distd under vacuum three times from K<sub>2</sub>CO<sub>3</sub>.

Phenyl 4-aminosalicylate [133-11-9] M 229.2, m 153°,  $pK_{Est(1)}$ ~2.0 (NH<sub>2</sub>),  $pK_{Est(2)}$ ~9.7 (OH). Crystd from isopropanol.

**4-Phenylanisole** (4-methoxybiphenyl) [361-37-6] M 184.2, m 89.9-90.1°. Crystd from \*benzene/pet ether. Dried under vacuum in an Abderhalden pistol.

9-Phenylanthracene [602-55-1] M 254.3, m 153-154°, b 417°. Chromatographed on alumina in \*benzene and crystd from acetic acid.

*N*-Phenylanthranilic acid [91-40-7] M 213.2, m 182-183°,  $pK_1^{25}$  -1.28 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$  3.86 (CO<sub>2</sub>H). Crystd from EtOH (5mL/g) or acetic acid (2mL/g) by adding hot water (1mL/g).

2-Phenyl-1-azaindolizine [56983-95-0] M 194.2, m 140°, pK<sub>Est</sub> ~1.9. Crystd from EtOH or \*benzene/pet ether.

p-Phenylazobenzoyl chloride [104-24-5] M 244.7, m 93°. Crystd from pet ether (b 60-80°).

4-Phenylazo-1-naphthylamine [131-22-6] M 247.3, m 125-125.5°. Crystd from cyclohexane or aq EtOH. [Brode et al. J Am Chem Soc 74 4641 1952.]

1-Phenylazo-2-naphthylamine [85-84-7] M 247.3, m 102-104°. See 1-benzeneazo-2-naphthylamine on p. 120.

**4-Phenylazophenacyl bromide** [62625-24-5] **M 317.3, m 103-104°.** Purified on a column of silica gel, using pet ether/diethyl ether (9:1 v/v) as solvent.

**4-Phenylazophenol** (4-hydroxyazobenzene) [1689-82-3] M 198.2, m 155°,  $pK_1^{25}$ -0.93,  $pK_2^{25}$ 8.2. Crystd from \*benzene or 95% EtOH.

**Phenyl benzenethiosulfonate** (diphenyldisulfoxide) [1212-08-4] M 250.3, m 36-37°, 45-46°, 45-47°. Recrystd from EtOH or MeOH. Also purified from phenylsulfide impurities by dissolving in CHCl<sub>3</sub>, washing with aq satd NaHCO<sub>3</sub>, drying (Na<sub>2</sub>SO<sub>4</sub>) evaporating and the residual oil was passed through a silica gel column (600g) and eluted with hexane-\*C<sub>6</sub>H<sub>6</sub> (1L, 4:1, eluting PhSSPh) then \*C<sub>6</sub>H<sub>6</sub> (1L) which elutes PhSSO<sub>2</sub>Ph. [Trost and Massiot J Am Chem Soc 99 4405 1977; Knoevenagel and Römer Chem Ber 56 215 1923.]

**Phenyl benzoate** [93-99-2] **M 198.2, m 69.5°, b 198-199°.** Crystd from EtOH using *ca* twice the volume needed for complete soln at 69°.

Phenyl-1,4-benzoquinone [363-03-1] M 184.2, m 114-115°. Crystd from heptane or pet ether (b 60-70°) and sublimed *in vacuo*. [Carlson and Miller J Am Chem Soc 107 479 1985.]

1-Phenylbiguanide [102-02-3] M 177.2, m 144-146°,  $pK_1^{32}$  2.16,  $pK_2^{32}$  10.74. Crystd from water or toluene.

S-(-)-1-Phenylbutanol [22135-49-5] M 150.2, m 46-47°, 46-48°, 49°, b 90-92°/2mm.  $[\alpha]_D^{18}$ -51.4° (c 5, CHCl<sub>3</sub>), -44.7° (c 5.13, \*C<sub>6</sub>H<sub>6</sub>). Purified by distn and crystallises on cooling. The hydrochloride has  $[\alpha]_D^{20}$  +45.1° (c 4.8, \*C<sub>6</sub>H<sub>6</sub>). The (-)-hydroperoxide has b 58°/0.005mm,  $n_D^{20}$  1.5123,  $\alpha_D^{18}$ -2.14°, (l = 0.5 dcm, neat). [Holding and Ross J Chem Soc 145 1954; Davies and Feld J Chem Soc 4637 1958.] The (±)-racemate has b 73°/0.05mm, and its 4-nitrophenylhydrazone has m 58°.

Phenylbutazone (4-butyl-1,2-diphenylpyrazolidin-3,5-dione) [50-33-9] M 308.4, m 105°, 106-108°. Crystd from EtOH.

2-Phenylbutyramide [90-26-6] M 163.2, m 86°. Crystd from water.

**2-Phenylbutyric acid** [R-(-)-938-79-4; S-(+)-4286-15-1] M 164.2, b 102-104°/atm,  $d_4^{20}$  1.056,  $n_D^{20}$  1.521,  $[\alpha]_D^{20}(-)$  and (+) 96° (c 2.5, \*C<sub>6</sub>H<sub>6</sub>),  $[\alpha]_D^{23}(-)$  and (+) 5.8° (neat), pK<sub>Est</sub> ~4.3. Purified by distn at atmospheric pressure using an efficient column. The *acid chlorides* have b 106-107°/20mm,  $[\alpha]_D^{18}(-)$  and (+) 108° (c 2, \*C<sub>6</sub>H<sub>6</sub>). [Levene et al. J Biol Chem 100 589 1933, Gold and Aubert Helv Chim Acta 41 1512 1958; ORD in heptane: Rothen and Levene J Chem Phys 7 975 1939.]

**3-Phenylbutyric** acid [R-(-)- 772-14-5; S-(+)- 772-15-6] M 164.2, b 94-95°/3mm, 134°/4mm,  $d_4^{26}$  1.066,  $n_D^{25}$  1.5167,  $[\alpha]_D^{20}$  (-) and (+) 57° (c 1, \*C<sub>6</sub>H<sub>6</sub>), pK<sup>25</sup> 4.40. Purified as the 2-isomer above, i.e. by distn, but under a good vacuum. [Prelog and Scherrer Helv Chim Acta 42 2227 1959; Levene and Marker J Biol Chem 93 761 1932, 100 685 1933; Cram J Am Chem Soc 74 2137 1952.] The *R*-amide

crystallises from H<sub>2</sub>O, **m** 101.5-102°,  $[\alpha]_D^{20}$  -16.5° (c 1.2, EtOH). The racemic acid has **m** 39-40°, **b** 134-136°/6mm, 158°/12mm [Marvel et al. J Am Chem Soc 62 3499 1940].

4-Phenylbutyric acid [1821-12-1] M 164.2, m 50°, pK<sup>25</sup> 4.76. Crystd from pet ether (b 40-60°).

o-(Phenylcarbamoyl)-1-scopolamine methobromide [138-10-3] M 518.4, m 200.5-201.5° (dec). Crystd from 95% EtOH.

9-Phenylcarbazole [1150-62-5] M 243.3, m 94-95°. Crystd from EtOH or isopropanol and sublimed in vacuo.

**O-Phenyl chlorothionoformate** [1005-56-7] **M 172.6, b 81-83°/6mm, 91°/10mm, d\_4^{20} 1.276, n\_D^{20} 1.585.** Purified by dissolving in CHCl<sub>3</sub>, washing with H<sub>2</sub>O, drying (CaCl<sub>3</sub>), filtering, evaporating and distilling twice under vacuum to give a clear yellow liquid. It is reactive and POISONOUS - work in a fume cupboard. Store in sealed ampoules under N<sub>2</sub>. Possible impurity is O,O'-diphenyl thiocarbonate which has m 106° which remains behind in the distilling flask. [Bögemann et al. in Methoden Der Organischen Chemie (Houben-Weyl) 4th edn (E. Müller Ed.) Vol 9 Schwefel-Selen-Tellur Verbindungen pp. 807-808 1955; Rivier and Schalch Helv Chim Acta 6 612 1932; Kalson Chem Ber 20, 2384 1987; Rivier and Richard Helv Chim Acta 8 490 1925; Schönberg and Varga Justus Liebigs Ann Chem 483 176 1930; Chem Ber 64 1390 1931.]

Phenyl cinnamate [2757-04-2] M 224.3, m 75-76°, b 205-207°/15mm. Crystd from EtOH (2mL/g). It can also be distd under reduced pressure.

 $\alpha$ -Phenylcinnamic acid [91-48-5] M 224.3, m 174°(cis), m 138-139°(trans), pK 4.8 (60% aq EtOH). Crystd from ether/pet ether.

o-Phenylenediamine [95-54-5] M 108.1, m 100-101°,  $pK_1^{25}$  0.67 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$  4.47 (4.85). Crystd from aqueous 1% sodium hydrosulfite (charcoal), washed with ice-water and dried in a vacuum desiccator, or sublimed *in vacuo*. It has been purified by recrystn from toluene and zone refined [Anson et al. J Am Chem Soc 108 6593 1986]. Purification by refluxing a CH<sub>2</sub>Cl<sub>2</sub> solution containing charcoal was also carried out followed by evaporation and recrystn [Koola and Kochi J Org Chem 52 4545 1987], protect from light.

*m*-Phenylenediamine [108-45-2] M 108.1, m 61-63°, 62-63°, 62.5°, 63-64°, b 146°/22mm, 282-284°/760mm, 284-287°/atm,  $d_{10}^{10}$  1.1422,  $n_D^{57.7}$  1.6340,  $pK_1^{25}$  2.41,  $pK_2^{25}$  4.98. Purified by distn under vac followed by recryst from EtOH (rhombs) and if necessary redistn. It should be protected from light otherwise it darkens rapidly. [Neilson et al. J Chem Soc 371 1962; IR: Katritzky and Jones J Chem Soc 3674, 2058 1959; UV: Forbes and Leckie Can J Chem 36 1371 1958.] The hydrochloride has m 277-278°, and the bis-4-chlorobenzenesulfonyl derivative has m 220-221° from H<sub>2</sub>O (214-215°, from MeOH-H<sub>2</sub>O) [Runge and Pfeiffer Chem Ber 90 1737 1957].

*p*-Phenylenediamine [106-50-3] M 108.1, m 140°,  $pK_1^{25}$  2.89,  $pK_2^{25}$  6.16. Crystd from EtOH or \*benzene, and sublimed *in vacuo*, protect from light.

o-Phenylenediamine dihydrochloride [615-28-1] M 181.1, m 180°. Crystd from dilute HCl (60mL conc HCl, 40mL water, with 2g stannous chloride), after treatment of the hot soln with charcoal by adding an equal volume of conc HCl and cooling in an ice-salt mixture. The crystals were washed with a small amount of conc HCl and dried in a vacuum desiccator over NaOH.

2-Phenyl-1,3-diazahexahydroazulene [2161-31-1] M 212.3. Recrystd three times from de-aerated cyclohexane in the dark.

1,4-Phenylene diisothiocyanate (bitoscanate) [4044-65-9] M 192.3, m 129-131°, 130-131°, 132°. Purified by recrystn from AcOH, pet ether (b 40-60°), Me<sub>2</sub>CO or aq Me<sub>2</sub>CO. [van der Kerk et al. Recl Trav Chim Pays-Bas 74 1262 1955; Leiber and Slutkin J Org Chem 27 2214 1962.]

**1-Phenyl-1,2-ethanediol** [*R*-(-)- 16355-00-3; *S*-(+)- 25779-13-9] **M** 138.2, **m** 64-67°, 65-66°,  $[\alpha]_D^{24}$  (-) and (+) 40.5° (c 2.8, H<sub>2</sub>O),  $[\alpha]_D^{20}$  (-) and (+) 39° (c 3, EtOH). Purified by recryst from \*C<sub>6</sub>H<sub>6</sub>-ligroin and sublimed at 1-2mm. [Arpesella et al. Gazetta 85 1354 1955; Prelog et al. Helv Chim Acta 37 221 1954.]

*dl*-1-Phenylethanol [13323-81-4] M 122.2, b 60.5-61.0°/3mm, 106-107°/22-23mm, d 1.01,  $n^{25}$  1.5254. Purified via its hydrogen phthalate. [See Houssa and Kenyon J Chem Soc 2260 1930.] Shaken with a soln of ferrous sulfate, and the alcohol layer was washed with distilled H<sub>2</sub>O, dried (MgSO<sub>4</sub>) and fractionally distd.

2-Phenylethanol [60-12-8] M 122.2, b 215-217°, d 1.020. Purified by shaking with a soln of ferrous sulfate, and the alcohol layer was washed with distd water and fractionally distd.

**Phenyl ether (diphenyl ether)** [101-84-8] M 170.2, m 27.0°, d 1.074,  $n^{30.7}$  1.57596. Crystd from 90% EtOH. Melted, washed with 3M NaOH and water, dried with CaCl<sub>2</sub> and fractionally distd under reduced pressure. Fractionally crystd from its melt and stored over P<sub>2</sub>O<sub>5</sub>.

**1-Phenylethyl isocyanate** ( $\alpha$ -methylphenyl isocyanate) [R-(+)-33375-06-3; S(-)-14649-03-7]M 147.2, b 82-83°/12-14mm,  $d_4^{20}$  1.045,  $n_D^{20}$  1.513,  $[\alpha]_D^{24}$  (+) and (-) 2° (c 3.5, \*C<sub>6</sub>H<sub>6</sub>), (+) and (-) 10.5° (neat). Purified by fractional distn under vacuum. With ammonia it gives the *ureido* derivative which crystallises from H<sub>2</sub>O, m 121-122°,  $[\alpha]_D^{25}$  (+) and (-) 48.8°. [Cairns J Am Chem Soc 63 870 1941.] The racemate has b 90-94°/3mm, 96°/18mm [Seiftan Justus Liebigs Ann Chem 562 75 1949].

p-α-Phenylethylphenol [1988-89-2] M 198.3, m 56.0-56.3°, pK<sub>Est</sub> ~10.3. Crystd from pet ether.

5-(α-Phenylethyl)semioxamazide [93-95-8] M 207.1, m 167-168° (l-), 157° (dl-). Crystd from EtOH.

**9-Phenyl-3-fluorone** [975-17-7] M **320.3**, m >300°(dec),  $\lambda_{max}$  462nm ( $\epsilon$  4.06 x 10<sup>4</sup>, in 1M HCl aq EtOH). Recrystd from warm, acidified EtOH by addition of ammonia. The crude material (1g) can be extracted with EtOH (50mL) in a Soxhlet apparatus for 10h to remove impurities. Impurities can be detected by paper electrophoresis. [Petrova et al. Anal Lett 5 695 1972.]

L- $\alpha$ -Phenylglycine [2935-35-5] M 151.2, m 305-310°,  $[\alpha]_{546}$  +185° (c 1, M HCl),  $pK_1^{25}$ 1.83,  $pK_2^{25}$  4.39 (for *dl*). Crystd from EtOH.

Phenylglycine-o-carboxylic acid [612-42-0] M 195.2, m 208°. Crystd from hot water (charcoal).

Phenylhydrazine [100-63-0] M 108.1, m 23°, b 137-138°/18mm, 241-242°/760mm, d 1.10, n 1.607,  $pK_1^{20}$  -5.2 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$  5.27. Purified by chromatography, then crystd from pet ether (b 60-80°)/\*benzene. [Shaw and Stratton J Chem Soc 5004 1962.]

**Phenylhydrazine hydrochloride** [59-88-1] M 144.5, m 244°. One litre of boiling EtOH was added to 100g of phenylhydrazine hydrochloride dissolved during 1-3h (without heating) in 200mL of warm water (60-70°). The soln was filtered off, while still hot, through Whatman No 2 filter paper and cooled in a refrigerator. The ppte was collected on a medium sintered-glass filter and recrystd twice this way, then washed with cold EtOH, dried thoroughly and stored in a stoppered brown bottle. [Peterson, Karrer and Guerra Anal Chem 29 144 1957.] Hough, Powell and Woods [J Chem Soc 4799 1956] boiled the hydrochloride with three times its weight of water, filtered hot (charcoal), added one-third volume of conc HCl and cooled to 0°. The crystals were washed with acetone, and dried over  $P_2O_5$  under vacuum. The salt has also been crystd from 95% EtOH.

**Phenylhydroxylamine** (*N*-hydroxyaniline) [100-65-2] M 109.1, m 82°, pK 3.2. Impure base deteriorates rapidly. Crystd from H<sub>2</sub>O,  $*C_6H_6$  or  $*C_6H_6$ /pet ether (40-60°). *Picrate* has m 186°.

2-Phenyl-1,3-indandione [83-12-5] M 222.2, m 149-151°, pK<sup>20</sup> 4.12 (1% aq MeOH). Crystd from EtOH.

2-Phenylindolizine [25379-20-8] M 193.2, m 214°(dec), pK<sub>Est</sub> ~4.4. Crystd from EtOH.

**Phenylisocyanate** [103-71-9] **M 119.1, b 45-47°/10mm, d 1.093, n 1.536.** Distd under reduced pressure from  $P_2O_5$ .

**Phenylisothiocyanate** (phenyl mustard oil) [103-72-0] M 135.2, m -21°, b 95°/12 mm, 117.1°/33mm, 221°/760mm,  $d_4^{25}$  1.1288,  $n_D^{23.4}$  1.64918. It is insol in H<sub>2</sub>O, but sol in Et<sub>2</sub>O and EtOH. If impure (due to formation of thiourea) then steam dist into a receiver containing 5-10mL of N H<sub>2</sub>SO<sub>4</sub>. Separate the oil, dry over CaCl<sub>2</sub> and distil under vacuum. [Dains et al. Org Synth Coll Vol I 447 1941.]

**8-Phenylmenthol** [1R, 2S, 5R-(-)-65253-04-5; 1S, 2R, 5S-(+)-57707-91-2] **M 232.4**,  $[\alpha]_{D}^{20}(-)$  and (+) **26°** (c 2, EtOH). Dissolve in toluene, dry (Na<sub>2</sub>SO<sub>4</sub>), evap and chromatograph on a silica gel column and eluting with 5% Et<sub>2</sub>O in pet ether to give an oil with the desired rotation. IR has v 3420cm<sup>-1</sup> (OH) with consistent <sup>1</sup>H NMR [Corey and Ensley J Org Chem 43 1610 1978; Whitesell et al. Tetrahedron 42 2993 1986; Bednarski and Danishefsky J Am Chem Soc 108 7060 1986.]

**1-Phenyl-5-mercaptotetrazole** [86-93-1] M **178.2, m 150°** (dec), **155°** (dec), **157-158°**,  $pK^{25}$ **3.65** (5% aq EtOH). Purified by recryst from EtOH or CHCl<sub>3</sub> (m 152°) [Tautomerism: Kauer and Sheppard J Org Chem **32** 3580 1967; UV: Leiber et al. Can J Chem **37** 563 1959]. The ammonium salt crystallises from EtOH and dec at 176°, and the sodium salt crystallises from EtOH-\*C<sub>6</sub>H<sub>6</sub>, melts at 96° and dec at 145° [Stollé J Prakt Chem [2] **133** 60 1932].

Phenyl methanesulfonate [16156-59-5] M 172.1, m 61-62°. Crystd from MeOH.

2-Phenylnaphthalene [612-94-2] M 204.3, m 103-104°. Chromatographed on alumina in \*benzene and crystd from aqueous EtOH.

*N*-Phenyl-1-naphthylamine [90-30-2] M 219.3, m 63.7-64.0°, pK<sub>Est</sub> ~0.1. Crystd from EtOH, pet ether or \*benzene/EtOH. Dried under vacuum in an Abderhalden pistol.

*N*-Phenyl-2-naphthylamine [135-88-6] M 219.3, m 107.5-108.5°, 110°, pK<sub>Est</sub> ~0.5. Crystd from EtOH, MeOH, glacial acetic acid or \*benzene/hexane.

**4-Phenylphenacyl bromide** [135-73-9] **M 275.2, m 126°.** Crystd (charcoal) from EtOH (15mL/g), or ethyl acetate/pet ether (b 90-100°).

**2-Phenylpropanal** [93-53-8] M 134.2, b 206°/760mm, d 1.001, n 1.5183. May contain up to 15% of acetophenone. Purified via the bisulfite addition compound [Lodge and Heathcock J Am Chem Soc 109 3353 1987] and see Chapter 2 for prepn, and decompn, of bisulfite adduct.

Phenylpropiolic acid [637-44-5] M 146.2, m 137.8-138.4°, pK<sup>25</sup> 2.23. Crystd from \*benzene, CCl<sub>4</sub> or aqueous EtOH.

**RS-2-Phenylpropionic acid** [492-37-5] **M 150.2, m 16-16.5°, b 153-155°/20 mm, 189°/48mm, 260-262°/atm, d 1.10, n 1.522, pK^{25} 4.3.** Fractionally distd, or recrystd from pet ether (b 40-60°) strong cooling (see references below).

**2-Phenylpropionic acid** [*R*-(-)- 7782-26-5; *S*-(+)- 7782-24-3] M 150.2, m 30.3-31°, 30-32°, b 115°/1-2mm, 142°/12mm,  $[\alpha]_{\rm D}^{20}$ (-) and (+) 99.7° (l = 1 dcm, neat), (-) and (+) 89.1° (c

1.7, EtOH), (-) and (+) 75° (c 1.6, CHCl<sub>3</sub>). Purified by vacuum distn and by recrystn from pet ether. The S-anilide has m 103-104° (from H<sub>2</sub>O or CHCl<sub>3</sub>/\*C<sub>6</sub>H<sub>6</sub>),  $[\alpha]_D^{25}$  +47° (c 9, Me<sub>3</sub>CO) [Argus and Kenyon J Chem Soc 916 1939; Campbell and Kenyon J Chem Soc 25 1946; Levene et al. J Biol Chem 88 27, 34 1930; Beilstein 9, 3rd Suppl p 2417].

**3-Phenylpropionic acid (hydrocinnamic acid)** [501-52-0] **M 150.2, m 48-48.5°, pK<sup>25</sup> 4.56.** Crystd from \*benzene, CHCl<sub>3</sub> or pet ether (b 40-60°). Dried in a vacuum.

**3-Phenylpropyl bromide** [637-59-2] **M 199.1, b 110°/12mm, 128-129°/29mm, d 1.31.** Washed successively with conc  $H_2SO_4$ , water, 10% aqueous  $Na_2CO_3$  and again with water, then dried with CaCl<sub>2</sub> and fractionally distd just before use.

Phenyl 2-pyridyl ketoxime [1826-28-4] M 198.2, m 151-152°. Crystd from EtOH (charcoal).

**Phenylpyruvic acid** [156-06-9] **M 164.2, m 150-154°, 158-159°, pK**<sub>Est</sub> ~2.1. Recrystd from  $*C_6H_6$ . The phenylhydrazone has **m** 173° [Zeller Helv Chim Acta 26 1614 1943; Hopkins and Chisholm Can J Research [B] 24 89 1946]. The 2,4-dinitrophenylhydrazone has **m** 162-164° (189°, 192-194°) [Fones J Org Chem 17 1952].

6-Phenylquinoline [612-95-3] M 205.3, m 110.5-111.5°, pK<sub>Est</sub> ~5.2. Crystd from EtOH (charcoal).

2-Phenylquinoline-4-carboxylic acid (cinchophen) [132-60-5] M 249.3, m 215°,  $pK_{Est(1)}\sim 0.5$  (CO<sub>2</sub>H),  $pK_{Est(2)}\sim 5.1$  (N). Crystd from EtOH (ca 20mL/g).

Phenyl salicylate (Salol) [118-55-8] M 214.2, m 41.8-42.6°, pK<sub>Est</sub> ~9.9. Fractionally crystd from its melt, then crystd from \*benzene.

3-Phenylsalicylic acid [304-06-3] M 214.3, m 186-187.5°,  $pK_{Est(1)} \sim 2.8$  (CO<sub>2</sub>H),  $pK_{Est(2)} \sim 11.0$  (OH). Dissolved in *ca* l equivalent of saturated aqueous Na<sub>2</sub>CO<sub>3</sub>, filtered and ppted by adding 0.8 equivalents of M HCl. Crystd from ethylene dichloride (charcoal), and sublimed at 0.1mm. [Brooks, Eglington and Norman J Chem Soc 661 1961.]

1-Phenylsemicarbazide [103-03-7] M 151.2, m 172°. Crystd from water and dried in vac over KOH.

4-Phenylsemicarbazide [537-47-3] M 151.2, m 122°. Crystd from water and dried in vac over KOH.

Phenylsuccinic acid [R-(-)-46292-93-7; S-(+)-4036-30-1] M 194.2, m 173-176°, 178.5-179°, 179-180°,  $[\alpha]_D^{25}(-)$  and (+) 171° (c 2, Me<sub>2</sub>CO),  $[\alpha]_D^{26-30}(-)$  and (+) 148° (c 0.27-5, EtOH),  $pK_1^{25}$  3.78,  $pK_2^{25}$  5.55. Purified by repptn from alkali and recrystn from H<sub>2</sub>O. [Naps and Johns J Am Chem Soc 62 2450 1940; Fredga and Matell Bull Soc Chim Belg 62 47 1953; Wren and Williams J Chem Soc 109 572 1916.] The racemate [635-51-8] has m 166-168°, 168° after recrystn from H<sub>2</sub>O or MeCN; its S-benzylthiouronium salt has m 164-165° (from EtOH) [Griediger and Pedersen Acta Chem Scand 9 1425 1955].

1-Phenyl-5-sulfanilamidopyrazole [526-08-9] M 314.3, m 179-183°. Crystd from EtOH.

1-Phenylthiosemicarbazide [645-48-7] M 167.2, m 200-201°(dec). Crystd from EtOH.

4-Phenylthiosemicarbazide [5351-69-9] M 167.2, m 140°. Crystd from EtOH.

1-Phenyl-2-thiourea [103-85-5] M 152.1, m 154°. Crystd from water and dried at 100° in air.

Phenyltoloxamine [2-(2-dimethylaminoethoxy)-diphenylmethane] hydrochloride [6152-43-8] M 291.8, m 119-120<sup>o</sup>, pK<sup>25</sup> 9.3 (free base). Crystd from isobutyl methyl ketone. Phenyl 4-toluenesulfonate [640-60-8] M 248.2, m 94.5-95.5°. Crystd from MeOH or glacial acetic acid.

**Phenyl 4-tolylcarbonate** [13183-20-5] **M 228.2, m 67°.** Purified by preparative GLC with 20% Apiezon on Embacel, and sublimed *in vacuo*.

**4-Phenyl-1,2,4-triazole-3,5-diol (4-phenylurazole)** [15988-11-1] **M 175.2, m 207-209°.** Crystd from water.

**4-Phenyl-1,2,4-triazoline-3,5-dione** (PTAD) [4233-33-4] M 175.2, m 165-170°(dec), 170-177°(dec). Carmine red needles obtained by sublimation (ice cold finger) at 100°/0.1mm, and/or by recrystn from EtOH. IR: v 1760, 1780 cm<sup>-1</sup>. [Cookson et al. Org Synth 51 121 1971; Moore et al. J Org Chem 39 3700 1974.]

**1-Phenyl-2,2,2-trifluoroethanol** [*R*-(-)- 10531-50-7; *S*-(+)- 340-06-7] M **176.1, b 74-76°/10mm, 125-127°/760mm, d<sub>4</sub><sup>20</sup> 1.301, n<sub>D</sub><sup>20</sup> 1.4632, [\alpha]\_D^{20} (-) and (+) 31° (neat). Purified by fractional distn preferably in a vacuum. [Morrison and Ridgeway** *Tetrahedron Lett* **573 1969; NMR: Pirkle and Beare** *J Am Chem Soc* **<b>90** 6250 1968.] The racemate [340-05-6] has b 52-54°/2mm, 57-59°/2mm, 64-65°/5mm, d<sub>4</sub><sup>20</sup> 1.293, n<sub>D</sub><sup>20</sup> 1.457, and the 2-carbobenzoyl derivative has m 137-138° [Mosher et al. *J Am Chem Soc* **78** 4374 1956].

**Phenylurea** [64-10-8] **M 136.2, m 148°, pK^{25} -1.45 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from boiling water (10mL/g). Dried in a steam oven at 100°.

**9-Phenyl-9-xanthenol (hydroxypixyl)** [596-38-3] **M 274.3, m 158-161°, 158.5-159°, 159°.** Dissolve in AcOH and add H<sub>2</sub>O whereby it separates as colourless prisms. It is slightly soluble in CHCl<sub>3</sub>, soluble in  $C_{6}H_{6}$  but insoluble in pet ether. It sublimes on heating. UV in H<sub>2</sub>SO<sub>4</sub>:  $\lambda$ max 450nm ( $\epsilon$  5620) and 370nm ( $\epsilon$  24,900) and the HClO<sub>4</sub> salt in CHCl<sub>3</sub> has  $\lambda$ max 450 ( $\epsilon$  404) and 375nm ( $\epsilon$  2420). [Sharp J Chem Soc 2558 1958; Bünzly and Decker Chem Ber 37 2983 1904; Chattopadhyaya and Reece J Chem Soc, Chem Commun 639 1978; Gomberg and Cone Justus Liebigs Ann Chem 370 142 1909.]

Phloretin [2',4',6'-trihydroxy-3-(p-hydroxyphenyl)propiophenone] [60-82-2] M 274.3, m 264-271°(dec),  $pK_{Est(1)}$ ~7.5,  $pK_{Est(2)}$ ~8.0,  $pK_{Est(3)}$ ~10,  $pK_{Est(4)}$ ~12 (phenolic OH's). Crystd from aqueous EtOH.

Phloridzin (2H<sub>2</sub>O) [phloretin 2'-O- $\beta$ -D-glucoside] [60-81-1] M 472.5, m 110°, [ $\alpha$ ]<sup>20</sup><sub>546</sub>-62° (c 3.2, EtOH). Crystd as dihydrate from water.

Phloroacetophenone (2H<sub>2</sub>O) (2',4',6'-trihydroxyacetophenone) [480-66-0] M 186.2, m 218-219°, pK<sub>Est(1)</sub>~7.9, pK<sub>Est(2)</sub>~12.0. Crystd from hot water (35mL/g).

Phloroglucinol (2H<sub>2</sub>O) (benzene-1,3,5-triol) [6099-90-7 (2H<sub>2</sub>O); 108-73-6 (anhydr)] M 126.1, m 217-219°, 117° (anhydrous),  $pK_1^{25}$ -7.74 (HClO<sub>4</sub>),  $pK_2^{20}$ 7.97,  $pK_3^{20}$ 9.23. Crystd from water, and stored in the dark under nitrogen.

Phorone (2,6-dimethylhepta-2,5-dien-4-one) [504-20-1] M 138.2, m 28°, b 197°/743 mm. Crystd repeatedly from EtOH.

"Phosphine" [dye CI 793, Chrysaniline mononitrate, 3-amino-9-(4-aminophenyl)acridinium mononitrate) [10181-37-0] M 348.4, m >250°(dec), pK<sub>Est</sub> ~8.0. Crystd from \*benzene/EtOH.

Phthalaldehyde [643-79-8] M 134.1, m 54-56°, 55.5-56°, 58°, b 83-84°/0.8mm. Purified by steam distillation better by using super heated steam (at 175-180°) and efficient cooling. The distillate is saturated with Na<sub>2</sub>SO<sub>4</sub> extracted exhaustively with EtOAc, dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and evaporated. The residue

is recrystd from pet ether (b 90-100°) [Beill and Tarbell Org Synth Coll Vol IV 808 1963]. It can be distd under vacuum. The bis-2,4-dinitrophenylhydrazone has m 278-280° [Hatt and Stephenson J Chem Soc 199 1952].

Phthalazine [253-52-1] M 130.2, m 90-91°, pK<sup>20</sup> 3.47. Crystd from diethyl ether or \*benzene, and sublimed under vacuum.

Phthalazine-1,4-dione (phthalhydrazide) [1445-69-8] M 162.2, m 330-333°, 336°, 346°,  $pK_1^{20}$ -3.29  $pK_2^{20}$ -0.99,  $pK_3^{20}$ 5.67,  $pK_4^{20}$ 13.0. Twice recrystd from 0.1M KOH [Merenyi et al. J Am Chem Soc 108 7716 1986], EtOH or dimethylformamide and sublimes >300°.

Phthalazone (1-hydroxyphthalazine) [119-39-1] M 146.2, m 183-184°, 186-188°, b  $337^{\circ}/760$  mm,  $pK_1^{20}$  -2.2,  $pK_2^{20}$  -1.4,  $pK_3^{20}$  11.99. Crystd from H<sub>2</sub>O or EtOH and sublimed *in vacuo*.

*o*-Phthalic acid [88-99-3] M 166.1, m 211-211.5°,  $pK_1^{25}$  2.76 (3.05),  $pK_2^{25}$  4.92 (4.73). Crystd from water.

**Phthalic anhydride** [85-44-9] **M 148.1, m 132°, b 295°.** Distd under reduced pressure. Purified from the acid by extracting with hot CHCl<sub>3</sub>, filtering and evaporating. The residue was crystd from CHCl<sub>3</sub>, CCl<sub>4</sub> or \*benzene, or sublimed. Fractionally crystd from its melt. Dried under vacuum at 100°. [Saltiel J Am Chem Soc 108 2674 1986.]

Phthalide [87-41-2] M 134.1, m 72-73°, pK -7.98 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from water (75mL/g) and dried in air on filter paper.

Phthalimide [85-41-6] M 147.1, m 235°, 238°, pK 8.30. Crystd from EtOH (20mL/g) (charcoal), or by sublimation. For potassium phthalimide see entry in Chapter 5.

Phthalimidoglycine [4702-13-0] M 205.2, m 192-193°, pK<sub>Est</sub> ~3. Crystd from water or EtOH.

Phthalonitrile [91-15-6] M 128.1, m 141°. Crystd from EtOH, toluene or \*benzene. Can also be distd under high vacuum.

Phthalylsulfacetamide [131-69-1] M 362.3, m 196°. Crystd from water.

Phthiocol (2-hydroxy-3-methylnaphthaquinone) [483-55-6] M 188.1, m 173-174°, pK<sub>Est</sub> ~4.2. Crystd from diethyl ether/pet ether.

Physalien (all trans  $\beta$ -carotene-3,3'-diol dipalmitate) [144-67-2] M 1044, m 98.5-99.5°,  $A_{1m}^{1\%}$  ( $\lambda$ max) 1410 (449nm), 1255 (478nm) in hexane. Purified by chromatography on water-deactivated alumina, using hexane/diethyl ether (19:1) to develop the column. Crystd from \*benzene/EtOH. Stored in the dark, in inert atmosphere, at 0°.

Physodic acid [4,4',6'-trihydroxy-6-(2-oxoheptyl)-2'-pentyl-2,3'-oxydibenzoic acid 1,5lactone] [84-24-2] M 470.5, m 205°,  $pK_{Est(1)}$ ~3.0,  $pK_{Est(2)}$ ~10,  $pK_{Est(3)}$ ~13. Crystd from MeOH. The diacetate has m 155-156° (from Me<sub>2</sub>CO/CS<sub>2</sub>).

Phytoene (7,7',8,8',11,11',12,12'-octahydro- $\psi,\psi$ -carotene) [540-04-5] M 544.9,  $A_{1m}^{1\%}$  ( $\lambda$ max) 850 (287nm) in hexane,  $\lambda_{max}$  275, 287 and 297nm nm. Purified by chromatography on columns of magnesium oxide-Supercel (a diatomaceous filter aid) or alumina [Rabourn et al. Arch Biochem Biophys 48 267 1954]. Stored as a solution in pet ether under nitrogen at -20°.

Phytofluene [540-05-6] M 549.0, b 140-185°(bath temp)/0.0001m  $A_{1m}^{1\%}(\lambda \max)$  1350 (348nm) in pet ether,  $\lambda_{\max}$  331, 348, 267. Purified by chromatography on partially deactivated alumina [Kushwaha et al. J Biol Chem 245 4708 1970]. Stored as a soln in pet ether under nitrogen at -20°.

Picein (*p*-acetylphenyl- $\beta$ -D-glucopyranoside) [530-14-3] M 298.3, m 195-196°,  $[\alpha]_D^{20}$ -88° (c 1, H<sub>2</sub>O). Crystd from MeOH or (as monohydrate) from water.

Picene [213-14-3] M 278.3, m 364°. Crystd from isopropylbenzene/xylene. Can also be sublimed.

2-Picoline-N-oxide (2-methylpyridine-1-oxide) [931-19-1] M 109.1, m 41-45°, b 89-90°/0.8-0.9mm, 90-100°/1mm, 110°/4mm, 135°/5mm, 123°/9mm, 123-124°/15mm, 259-261°/atm,  $n_D^{25}$  1.5854 (supercooled), pK<sup>25</sup> 1.10. Purified by fractional distillation and could be recrystd from \*C<sub>6</sub>H<sub>6</sub>-hexane but is hygroscopic. [Bullitt and Maynard J Am Chem Soc 76 1370 1954; Ross et al. J Am Chem Soc 78 3625 1956; IR: Wiley and SlaymAker J Am Chem Soc 79 2233 1957.] The picrate has m 125-126.5° (from EtOH) [Boekelheide and Linn J Am Chem Soc 76 1286 1954]. The phthalate has m 115-116° (from EtOH) [den Hertog et al. Recl Trav Chim Pays-Bas 70 591 1951.]

**3-Picoline-N-oxide** (3-methylpyridine-1-oxide) [1003-73-2] M 109.1, m 37-39°, 37-38° (evac capillary), 84-85°/0.3mm, 101-103°/0.7-0.8mm, 114-115°/1.5mm, 118°/2mm, pK<sup>25</sup> 1.08. Purified by careful fractionation *in vacuo*. The distillate remains supercooled for several days before solidifying. It is a slightly *hygroscopic* solid which could melt in the hand. The *picrate* has m 149-151° (from EtOH). [Taylor and Corvetti Org Synth Coll Vol IV 654 1963; IR: Katritzky et al. J Chem Soc 3680 1959; Jaffé and Doak J Am Chem Soc 77 4441, 4481 1955; Boekelheide and Linn J Am Chem Soc 76 1286 1954].

**4-Picoline-***N***-oxide** (4-methylpyridine-1-oxide) [1003-67-4] M 109.1, m 182-184°, 185-186°, 186-188°,  $pK^{25}$  1.29. Recryst from EtOH-EtOAc, Me<sub>2</sub>CO-Et<sub>2</sub>O or \*C<sub>6</sub>H<sub>6</sub>. [Bullitt and Maynard J Am Chem Soc 76 1370 1954; Boekelheide and Linn J Am Chem Soc 76 1286 1954].

Picolinic acid (pyridine-2-carboxylic acid) [98-98-6] M 123.1, m 138°,  $pK_1^{25}$  1.03 (1.36),  $pK_2^{25}$  5.30 (5.80). Crystd from water or \*benzene.

 $\alpha$ -Picolinium chloride [14401-91-3] M 129.6, m 200°. 1:1 Mixture of  $\alpha$ -picoline and HCl, distd at 275°. Then vacuum sublimed at 91-91.5°.

*N*-Picolinoylbenzimidazole [100312-29-6] M 173.3, m 105-107°. Recrystd three times from hexane [Fife and Przystas J Am Chem Soc 108 4631 1986].

**Picric acid** [88-89-1] **M 229.1, m 122-123°, pK^{25} 0.33 (0.37).** Crystd first from acetic acid then acetone, toluene, CHCl<sub>3</sub>, aqueous 30% EtOH, 95% EtOH, MeOH or H<sub>2</sub>O. Dried in a vacuum oven at 80° for 2h. Alternatively, dried over Mg(ClO<sub>4</sub>)<sub>2</sub> or fused and allowed to freeze under vacuum three times. Because it is **EXPLOSIVE**, picric acid should be stored moistened with H<sub>2</sub>O, and only small portions should be dried at any one time. The dried acid should **NOT** be heated.

**Picrolic acid** [3-methyl-4-nitro-1-(4-nitrophenyl)-2-pyrazolin-5-one, picrolonic acid] [550-74-3] M 264.2, m 120°(dec),116.5° (dec at 125°) 125°. Crystd from water or EtOH (Solubility is 0.123% at 15° and 1.203% at 100° in H<sub>2</sub>O; and 1.107% at 0° and 11.68% at 81° in EtOH). It forms Ca, Cu Hg, Mg, Na, Sr, and Pb complexes [Maquestian et al *Bull Soc Chim Belg* 82 233 1973; Isaki et al. *Chem Ber* 74 1420 1941].

Picrotoxin [124-87-8] M 602.6, m 203°, [α]<sup>20</sup><sub>546</sub> -40° (c 1, EtOH). Crystd from water.

Picryl chloride [88-88-0] M 226.3, m 83°. Crystd from CHCl3 or EtOH.

Picryl iodide [4436-27-5] M 340.0, m 164-165°. Crystd from \*benzene.

Pimelic acid (heptane-1,7-dioic acid) [111-16-0] M 160.2, m 105-106°,  $pK_1^{25}$  4.46,  $pK_2^{25}$  5.58. Crystd from water or from \*benzene containing 5% diethyl ether.

**Pinacol (hexahydrate)** [6091-58-3 (6 $H_2O$ ); 76-09-5 (anhydr)] M 194.3, m 46.5°, b 59°/4mm. Distd then crystd repeatedly from water.

**Pinacol** (anhydrous) [76-09-5] M 118.1, m 41.1°, b 172°. The hydrate is rendered anhydrous by azeotropic distn of water with \*benzene. Recrystd from \*benzene or toluene/pet ether, absolute EtOH or dry diethyl ether. Recrystn from water gives the hexahydrate.

Pinacolone oxime [2475-93-6] M 115.2, m 78°. Crystd from aqueous EtOH.

Pinacyanol chloride [2768-90-3] M 388.9, m 270°(dec). Crystd from EtOH/diethyl ether.

**R**- $\alpha$ -Pinene [7785-70-8] **M** 136.2, **b** 61°/30mm, 156.2°/760mm, **d** 0.858, **n**<sup>15</sup> 1.4634, **n** 1.4658,  $[\alpha]_D^{25}$ +47.3°. Isomerised by heat, acids and certain solvents. Should be distd under reduced pressure under nitrogen and stored in the dark. Purified *via* the nitrosochloride [Waterman et al. *Recl Trav Chim Pays-Bas* 48 1191 1929]. For purification of optically active forms see Lynn [J Am Chem Soc 91 361 1919]. Small quantities (0.5mL) have been purified by GLC using helium as carrier gas and a column at 90° packed with 20 wt% of polypropylene sebacate on a Chromosorb support. Larger quantities were fractionally distd under reduced pressure in a column packed with stainless steel gauze spirals. Material could be dried with CaH<sub>2</sub> or sodium, and stored in a refrigerator: CaSO<sub>4</sub> and silica gel were not satisfactory because they induced spontaneous isomerisation. [Bates, Best and Williams J Chem Soc 1521 1962.]

S- $\alpha$ -Pinene [7785-26-4] M 136.2, b 155-156°/760mm, d 0.858, n 1.4634,  $[\alpha]_D^{20}$ -47.2°. Purification as for *R*- $\alpha$ -Pinene above.

*dl*-Pipecolinic acid (piperidine-2-carboxylic acid) [4043-87-2] M 129.1, m 264°,  $pK_1^{25}2.29$ ,  $pK_2^{25}10.77$ . Crystd from water.

**Piperazine** [110-85-0] **M 86.1, m 110-112°, 44° (hexahydrate** 142-63-2) **b 125-130°/760mm,**  $pK_1^{25}$  5.33,  $pK_2^{25}$  9.73. Crystd from EtOH or anhydrous \*benzene, and dried at 0.01mm. It can be sublimed under vacuum and purified by zone melting.

§ Piperazine on polystyrene support is commercially available.

**Piperazine-**N, N'-**bis(2-ethanesulfonic acid) (PIPES)** [5625-37-6] M 302.4,  $pK_1^{25} < 3$ ,  $pK_2^{25} < 6.82$  (7.82). Crystd from boiling water (maximum solubility is about 1g/L) or as described for ADA [N-(2-acetamido)iminodiacetic acid, see above].

**Piperazine dihydrochloride (H<sub>2</sub>O)** [142-64-3 (2HCl); 6094-40-2 (xHCl)] M 177.1, m 82.5-83.5°. Crystd from aqueous EtOH. Dried at  $110^{\circ}$ .

**Piperazine phosphate (H<sub>2</sub>O)** [18534-18-4] **M 197.6.** Crystd twice from water, air-dried and stored for several days over Drierite. The salt dehydrates slowly if heated at  $70^{\circ}$ .

Piperic acid [trans, trans-5-(3,4-methylenedioxyphenyl)-2,4-pentadieneoic acid] [136-72-1] M 218.2, m 217°, pK<sub>Est</sub> ~4.7. Crystd from EtOH. Turns yellow in light. Sublimes with partial dec.

**Piperidine** [110-89-4] M 85.2, f -9°, b 35.4°/40mm, 106°/760mm, d 0.862, n 1.4535, n<sup>25</sup> 1.4500, pK<sup>25</sup> 11.20. Dried with BaO, KOH, CaH<sub>2</sub>, or sodium, and fractionally distd (optionally from sodium, CaH<sub>2</sub>, or P<sub>2</sub>O<sub>5</sub>). Purified from pyridine by zone melting. § Piperidine on polystyrene support is commercially available.

**Piperidinium chloride** [6091-44-7] **M 121.6, m 244-245°.** Crystd from EtOH/diethyl ether in the presence of a small amount of HCl.

Piperidinium nitrate [6091-45-8] M 145.2, m 110°. Crystd from acetone/ethyl acetate.

Piperine (1-piperoylpiperidine) [94-62-2] M 285.4, m 129-129.5°, pK<sup>15</sup> 1.98. Crystd from EtOH or \*benzene/ligroin.

**Piperonal** [120-57-0] **M 150.1, m 37°, b 140°/15mm, 263°/760mm.** Crystd from aqueous 70% EtOH or EtOH/water.

Piperonylic acid [94-53-1] M 166.1, m 229°, pK<sup>25</sup> 4.50. Crystd from EtOH or water.

**Pivalic acid** (trimethylacetic acid) [75-98-9] M 102.1, m 35.4°, b 71-73°/0.1mm, pK<sup>25</sup> 5.03. Fractionally distd under reduced pressure, then fractionally crystd from its melt. Recrystd from \*benzene.

**Pivaloyl chloride** (trimethylacetyl chloride) [3282-30-2] M 120.6, b 57.6°/150mm, 70.5-71/250mm, 104°/754mm, 104-105°/atm, 105-108°/atm,  $d_4^{20}$  1.003,  $n_D^{20}$  1.4142. First check the IR to see if OH bands are present. If absent, or present in small amounts, then redistil under moderate vac. If present in large amounts then treat with oxalyl chloride or thionyl chloride and reflux for 2-3h, evap and distil residue. Strongly LACHRYMATORY - work in a fumecupboard. Store in sealed ampoules under N<sub>2</sub>. [Traynham and Battiste J Org Chem 22 1551 1957; Grignard reactns: Whitmore et al. J Am Chem Soc 63 647 1941.]

Plumbagin (5-hydroxy-2-methyl-1,4-naphthaquinone) [481-42-5] M 188.1, m 78-79°, pK<sub>Est(1)</sub>~9.5, pK<sub>Est(2)</sub>~11.0. Crystd from aqueous EtOH and sublimed in a vac. Steam distils.

Polyacrylonitrile [25014-41-9]. Ppted from dimethylformamide by addition of MeOH.

**Poly(diallyldimethylammonium) chloride** [26062-79-3]. Ppted from water in acetone, and dried in vacuum for 24h. [Hardy and Shriner J Am Chem Soc 107 3822 1985.]

**Polyethylene** [9002-88-4]. Crystd from thiophen-free \*benzene and dried over  $P_2O_5$  under vacuum.

Polymethyl acrylate [9003-21-8]. Ppted from a 2% soln in acetone by addition of water.

**Polystyrene** [9003-53-6]. Ppted repeatedly from CHCl<sub>3</sub> or toluene soln by addition of MeOH. Dried *in vacuo* [Miyasaka et al. J Phys Chem 92 249 1988].

Polyvinyl acetate [9003-20-7]. Ppted from acetone by addition of *n*-hexane.

**Poly**(*N*-vinylcarbazole) [25067-59-8]. Ppted seven times from tetrahydrofuran with MeOH, with a final freeze-drying from \*benzene. Dried under vacuum.

Polyvinyl chloride [9002-81-2]. Ppted from cyclohexanone by addition of MeOH.

**Poly(4-vinylpyridine)** [25232-41-1] M (105.1)<sub>n</sub>. Purified by repeated pptn from solns in EtOH and dioxane, and then EtOH and ethyl acetate. Finally, freeze-dried from *tert*-butanol.

**Poly**(*N*-vinylpyrrolidone) [9003-39-8] M (111.1)<sub>n</sub>, crosslinked [25249-54-1] m >300°. Purified by dialysis, and freeze-dried. Also by pptn from CHCl<sub>3</sub> soln by pouring into ether. Dried in a vacuum over  $P_2O_5$ . For the crosslinked polymer purification is by boiling for 10min in 10% HCl and then washing with glass-distilled water until free from Cl ions. Final Cl ions were removed more readily by neutralising with KOH and continued washing.

Prednisone [53-03-2] M 358.5, m 238°(dec),  $[\alpha]_D^{20}$ +168° (c 1, dioxane),  $\lambda_{max}$  238nm (log  $\epsilon$  4.18) in MeOH. Crystd from acetone/hexane.

Pregnane [481-26-5] M 300.5, m 83.5°, [α]<sup>20</sup><sub>D</sub>+21° (CHCl<sub>3</sub>). Crystd from MeOH.

5 $\beta$ -Pregnane-3 $\alpha$ ,20 $\alpha$ -diol [80-92-2] M 320.5, m 243-244°,  $[\alpha]_{546}^{20}$  +31° (c 1, EtOH). Crystd from acetone.

5β-Pregnane-3α,20β-diol [80-91-1] M 320.5, m 244-246°,  $[\alpha]_{546}^{20}$  +22° (c 1, EtOH). Crystd from EtOH.

**Procaine** [4-(2-diethylaminomethoxycarbonyl)aniline] [59-46-1] M 236.3, m 51° (dihydrate), 61° (anhydrous),  $pK_1^{15}$  2.45,  $pK_2^{15}$  8.91. Crystd as the dihydrate from aqueous EtOH and as anhydrous material from pet ether or diethyl ether. The latter is *hygroscopic*.

**Proclavine** (3,6-diaminoacridine) [92-62-6] M 209.2, m 284-286°, pK<sup>25</sup> 9.60. Crystd from aqueous MeOH. For proflavin see 3,6-diaminoacridine hydrochloride

**Progesterone** [57-83-0] **M 314.5, m 128.5°,**  $[α]_{546}^{20}$  +220° (c 2, dioxane). Crystd from EtOH. When crystd from pet ether **m** is 121°,  $λ_{max}$  240nm, log ε 4.25 (EtOH).

**L-Proline** [147-85-3] **M** 115.1, **m** 215-220°(dec)(D-isomer), 220-222°(dec) (L-form), 205°(dec)(DL-isomer),  $[\alpha]_D^{25}$  (H<sub>2</sub>O, L-isomer),  $pK_1^{25}$  1.95,  $pK_2^{25}$  10.64. Likely impurity are hydroxyproline. Purified via its picrate which was crystd twice from water, then decomposed with 40% H<sub>2</sub>SO<sub>4</sub>. The picric acid was extracted with diethyl ether, the H<sub>2</sub>SO<sub>4</sub> was pptd with Ba(OH)<sub>2</sub>, and the filtrate evapd. The residue was crystd from hot absolute EtOH [Mellan and Hoover J Am Chem Soc 73 3879 1951] or EtOH/ether. Hygroscopic. Stored in a desiccator.

**Prolycopene** (all Z- $\psi$ , $\psi$ -carotene) [2361-24-2] M 536.5, m 111°,  $\lambda_{max}$  443.5, 470nm in pet ether. Purified by chromatography on deactivated alumina [Kushwaha et al. J Biol Chem 245 4708 1970]. Crystd from pet ether. Stored in the dark, in an inert atmosphere at -20°.

**L-Prolylglycine** [2578-57-6] M 172.2, m 236°,  $[\alpha]_D^{20} + 21.1^\circ$  (c 4, H<sub>2</sub>O),  $pK_1^{25} 3.19$ ,  $pK_2^{25} 8.97$ . Crystd from water at 50-60° by addition of EtOH.

Proneurosporene (3,4,7',8'-tetrahydrolycopene) [10467-46-6] M 538.9,  $\lambda_{max}$  408, 432, 461 nm,  $\epsilon_{1cm}^{1\%}$  2040 (432nm) in hexane. Purified by chromatography on deactivated alumina [Kushwaha et al. J Biol Chem 245 4708 1970]. Stored in the dark, in an inert atmosphere at 0°.

**Propane** [74-98-6] **M 44.1, m -189.7, b -42.1°/760mm, d 0.5005, n 1.2898.** Purified by bromination of the olefinic contaminants. Propane was treated with bromine for 30min at 0°. Unreacted bromine was quenched, and the propane was distd through two -78° traps and collected at -196° [Skell et al. J Am Chem Soc 108 6300 1986].

**Propane-1,2-diamine** (propylenediamine) [78-90-0] M 74.1, b 120.5°, d 0.868, n 1.446,  $pK_1^{25}$  6.61,  $pK_2^{25}$  9.82. Purified by azeotropic distn with toluene. [Horton, Thomason and Kelly Anal Chem 27 269 1955.]

**Propane-1,2-diol** (propyleneglycol) [57-55-6] M 76.1, b 104°/32mm, d 1.040, n 1.433. Dried with Na<sub>2</sub>SO<sub>4</sub>, decanted and distd under reduced pressure.

**Propane-1,3-diol** [504-63-2] **M 76.1, b 110-122°/12mm, d 1.053, n<sup>18.5</sup> 1.4398.** Dried with  $K_2CO_3$  and distd under reduced pressure. More extensive purification involved conversion with benzaldehyde to 2-phenyl-1,3-dioxane (m 47-48°) which was subsequently decomposed by shaking with 0.5M HCl (3mL/g) for 15min and standing overnight at room temperature. After neutralisation with  $K_2CO_3$ , the benzaldehyde was removed by distn and the diol was recovered from the remaining aqueous soln by continuous extraction with CHCl<sub>3</sub> for 1day. The extract was dried with  $K_2CO_3$ , the CHCl<sub>3</sub> was evaporated and the diol was distd. [Foster, Haines and Stacey *Tetrahedron* 6 177 1961.]

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**Propane-1-thiol** [107-03-9] M 76.1, b 65.3°/702mm,  $d^{25}$  0.83598,  $n^{25}$  1.43511,  $pK^{20}$  10.82. Purified by soln in aqueous 20% NaOH, extraction with a small amount of \*benzene and steam distn until clear. After cooling, the soln was acidified slightly with 15% H<sub>2</sub>SO<sub>4</sub>, and the thiol was distd out, dried with anhydrous CaSO<sub>4</sub> or CaCl<sub>2</sub>, and fractionally distd under nitrogen. [Mathias and Filho J Phys Chem 62 1427 1958.] Also purified by liberation of the mercaptan by adding dilute HCl to the residue remaining after steam distn. After direct distn from the flask, and separation of the water, the mercaptan was dried (Na<sub>2</sub>SO<sub>4</sub>) and distd under nitrogen.

**Propane-2-thiol (Isopropyl mercaptan)** [75-33-2] **M 76.1, b 49.8°/696mm, d<sup>25</sup> 0.80895, n<sup>25</sup> 1.42154, pK<sup>25</sup> 10.86.** Purification as for propane-1-thiol above.

**Propargyl alcohol (2-propyn-1-ol)** [107-19-7] M 56.1, b 54°/57mm, 113.6°/760mm, d 0.947, n 1.432. Commercial material contains a stabiliser. An aqueous soln of propargyl alcohol can be concentrated by azeotropic distn with butanol or butyl acetate. Dried with  $K_2CO_3$  and distd under reduced pressure, in the presence of about 1% succinic acid, through a glass helices-packed column.

**Propargyl chloride (3-chloropropyne)** [624-65-7] M 74.5, b 58°/760mm, 65°/760mm, d 1.03, n 1.435. Purified by fractional distn at atm press. Note that a possible impurity propargyl alcohol has b 114-115°/atm. [Henry Chem Ber 8 398 1875.] HIGHLY TOXIC and FLAMMABLE.

**Propene** [115-07-1] **M 42.1, m -185.2°, b -47.8°/750mm, d 0.519, n<sup>-71</sup> 1.357.** Purified by freeze-pump-thaw cycles and trap-to-trap distn.

*p*-(1-Propenyl)phenol [cis/trans 6380-21-8; 539-12-8] M 134.2, m 93-94°, pK<sub>Est</sub> ~10.2. Crystd from water.

β-Propiolactone [57-57-8] M 72.1, b 83°/45mm, d 1.150, n<sup>25</sup> 1.4117. Fractionally distd under reduced pressure, from sodium. CARCINOGEN.

**Propionaldehyde** [123-38-6] **M 58.1, b 48.5-48.7°, d 0.804, n 1.3733, n^{25} 1.37115.** Dried with CaSO<sub>4</sub> or CaCl<sub>2</sub>, and fractionally distd under nitrogen or in the presence of a trace of hydroquinone (to retard oxidation). Blacet and Pitts [*J Am Chem Soc* 74 3382 1952] repeatedly vacuum distd the middle fraction until no longer gave a solid polymer when cooled to -80°. It was stored with CaSO<sub>4</sub>.

**Propionamide** [79-05-0] **M 73.1, m 79.8-80.8°, pK<sup>24</sup> -0.9** ( $H_0$  scale, aq H<sub>2</sub>SO<sub>4</sub>). Crystd from acetone, \*benzene, CHCl<sub>3</sub>, water or acetone/water, then dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> or conc H<sub>2</sub>SO<sub>4</sub>.

**Propionic acid** [79-09-4] M 74.1, b 141°, d 0.992, n 1.3865,  $n^{25}$  1.3843,  $pK_1^{25}$ -6.8 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{25}$  4.88. Dried with Na<sub>2</sub>SO<sub>4</sub> or by fractional distn, then redistd after refluxing with a few crystals of KMnO<sub>4</sub>. An alternative purification uses the conversion to the ethyl ester, fractional distn and hydrolysis. [Bradbury J Am Chem Soc 74 2709 1952.] Propionic acid can also be heated for 0.5h with an amount of benzoic anhydride equivalent to the amount of water present (in the presence of CrO<sub>3</sub> as catalyst), followed by fractional distn. [Cham and Israel J Chem Soc 196 1960.]

**Propionic anhydride** [123-62-6] M 130.2, b 67°/18mm, 168°/780mm, d 1.407, n 1.012. Shaken with  $P_2O_5$  for several minutes, then distd.

**Propionitrile** [107-12-0] **M 55.1, b 97.2°, d 1.407, n<sup>15</sup> 1.36812, n<sup>30</sup> 1.36132.** Shaken with dil HCl (20%), or with conc HCl until the odour of isonitrile has gone, then washed with water, and aqueous  $K_2CO_3$ . After a preliminary drying with silica gel or Linde type 4A molecular sieves, it is stirred with CaH<sub>2</sub> until hydrogen evolution ceases, then decanted and distd from P<sub>2</sub>O<sub>5</sub> (not more than 5g/L, to minimise gel formation). Finally, it is refluxed with, and slowly distd from CaH<sub>2</sub> (5g/L), taking precautions to exclude moisture.

*n*-Propyl acetate [109-60-4] M 102.1, b 101.5°, d 0.887, n 1.38442,  $pK^{25}$  -7.18 (H<sub>o</sub> scale, aq H<sub>2</sub>SO<sub>4</sub>). Washed with satd aqueous NaHCO<sub>3</sub> until neutral, then with satd aqueous NaCl. Dried with MgSO<sub>4</sub> and fractionally distd.

*n*-Propyl alcohol (1-propanol) [71-23-8] M 60.1, b 97.2°, d<sup>25</sup> 0.79995, n 1.385, pK<sup>25</sup> 16.1. The main impurities in n-propyl alcohol are usually water and 2-propen-1-ol, reflecting the commercial production by hydration of propene. Water can be removed by azeotropic distn either directly (azeotrope contains 28% water) or by using a ternary system, e.g. by adding \*benzene. Alternatively, for gross amounts of water, refluxing over CaO for several hours is suitable, followed by distn and a further drying. To obtain more nearly anhydrous alcohol, suitable drying agents are firstly NaOH, CaSO<sub>4</sub> or K<sub>2</sub>CO<sub>3</sub>, then CaH<sub>2</sub>, aluminium amalgam, magnesium activated with iodine, or a small amount of sodium. Alternatively, the alcohol can be refluxed with n-propylsuccinate or phthalate in a method similar to the one described under EtOH. Allyl alcohol is removed by adding bromine (15 mL/L) and then fractionally distilling from a small amount of  $K_2CO_3$ . Propionaldehyde, also formed in the bromination, is removed as the 2,4-dinitrophenylhydrazone. *n*-Propyl alcohol can be dried down to 20ppm of water by passage through a column of pre-dried molecular sieves (type 3 or 4A, heated for 3h at 300°) in a current of nitrogen. Distn from sulfanilic or tartaric acids removes impurities. Albrecht [J Am Chem Soc 82 3813 1960] obtained spectroscopically pure material by heating with charcoal to 50-60°, filtering and adding 2,4-dinitrophenylhydrazine and a few drops of conc H<sub>2</sub>SO<sub>4</sub>. After standing for several hours, the mixture was cooled to 0°, filtered and vac distd. Gold and Satchell [J Chem Soc 1938 1963] heated n-propyl alcohol with 3-nitrophthalic anhydride at 76-110° for 15h, then recrystd the resulting ester from  $H_2O$ , \*benzene/pet ether (b 100-120°)(3:1), and \*benzene. The ester was hydrolysed under reflux with aq 7.5M NaOH for 45min under nitrogen, followed by distn (also under nitrogen). The fraction (b 87-92°) was dried with K<sub>2</sub>CO<sub>3</sub> and stirred under reduced pressure in the dark over 2,4-dinitrophenylhydrazine, then freshly distilled. Also purified by adding 2g NaBH<sub>4</sub> to 1.5L alcohol, gently bubbling with argon and refluxing for 1day at 50°. Then added 2g of freshly cut sodium (washed with propanol) and refluxed for one day. Distd, taking the middle fraction [Jou and Freeman J Phys Chem 81 909 1977].

*n*-Propylamine [107-10-8] M 59.1, b 48.5°, d 0.716, n 1.38815,  $pK^{25}$  10.69. Distd from zinc dust, at reduced pressure, in an atmosphere of nitrogen.

*n*-Propyl bromide. [106-94-5] M 123.0, b 71.0°, d 1.354.,  $n^{15}$  1.43695,  $n^{25}$  1.43123. Likely contaminants include *n*-propyl alcohol and isopropyl bromide. The simplest purification procedure uses drying with MgSO<sub>4</sub> or CaCl<sub>2</sub> (with or without a preliminary washed of the bromide with aq NaHCO<sub>3</sub>, then water), followed by fractional distn away from bright light. Chien and Willard [*J Am Chem Soc* **79** 4872 1957] bubbled a stream of oxygen containing 5% ozone through *n*-propyl bromide for 1h, then shook with 3% hydrogen peroxide soln, neutralised with aq Na<sub>2</sub>CO<sub>3</sub>, washed with distilled water and dried. Then followed vigorous stirring with 95% H<sub>2</sub>SO<sub>4</sub> until fresh acid did not discolour within 12h. The propyl bromide was separated, neutralised, washed dried with MgSO<sub>4</sub> and fractionally distd. The centre cut was stored in the dark. Instead of ozone, Schuler and McCauley [*J Am Chem Soc* **79** 821 1957] added bromine and stored for 4 weeks, the bromine then being extracted with aq NaHSO<sub>3</sub> before the sulfuric acid treatment was applied. Distd. Further purified by preparative gas chromatography on a column packed with 30% SE-30 (General Electric ethylsilicone rubber) on 42/60 Chromosorb P at 150° and 40psi, using helium. [Chu *J Phys Chem* **41** 226 1964.]

*n*-Propyl chloride [540-54-5] M 78.5, b 46.6°, d 0.890, n 1.3880. Dried with MgSO<sub>4</sub> and fractionally distd. More extensively purified using extraction with  $H_2SO_4$  as for *n*-propyl bromide. Alternatively, Chien and Willard [*J Am Chem Soc* 75 6160 1953] passed a stream of oxygen containing about 5% ozone through the *n*-propyl chloride for three times as long as was needed to cause the first coloration of starch iodide paper by the exit gas. After washing with aqueous NaHCO<sub>3</sub> to hydrolyse ozonides and remove organic acids, the chloride was dried with MgSO<sub>4</sub> and fractionally distd.

1-Propyl-3-(p-chlorobenzenesulfonyl) urea [94-20-2] M 260.7, m 127-129°. Crystd from aqueous EtOH.

Propylene carbonate [108-32-7] M 102.1, b 110°/0.5-1mm, 238-239°/760mm, d 1.204, n 1.423. Manufactured by reaction of 1,2-propylene oxide with CO<sub>2</sub> in the presence of a catalyst (quaternary

ammonium halide). Contaminants include propylene oxide, carbon dioxide, 1,2- and 1,3-propanediols, allyl alcohol and ethylene carbonate. It can be purified by percolation through molecular sieves (Linde 5A, dried at  $350^{\circ}$  for 14h under a stream of argon), followed by distn under vac. [Jasinski and Kirkland Anal Chem **39** 163 1967.] It can be stored over molecular sieves under an inert gas atmosphere. When purified in this way it contains less than 2ppm water. Activated alumina and dried CaO have been also used as drying agents prior to fractional distn under reduced pressure. It has been dried with 3A molecular sieves and distd under nitrogen in the presence of *p*-toluenesulfonic acid. Then redistilled and the middle fraction collected.

*dl*-Propylene oxide [75-56-9] M 58.1, b 34.5°, d 0.829, n 1.3664. Dried with Na<sub>2</sub>SO<sub>4</sub> or CaH<sub>2</sub>, and fractionally distilled through a packed column (glass helices), after refluxing with Na, CaH<sub>2</sub>, or KOH pellets.

*n*-Propyl ether (dipropyl ether) [111-43-3] M 102.2, b 90.1°, d 0.740,  $n^{15}$  1.38296, n 1.3803, pK -4.40 (aq H<sub>2</sub>SO<sub>4</sub>). Purified by drying with CaSO<sub>4</sub>, by passage through an alumina column (to remove peroxides), and by fractional distn.

**Propyl formate** [110-74-7] M 88.1, b 81.3°, d 0.9058, n 1.3779. Distd, then washed with satd aq NaCl, and with satd aq NaHCO<sub>3</sub> in the presence of solid NaCl, dried with MgSO<sub>4</sub> and fractionally distd.

n-Propyl gallate [121-79-9] M 212.2, m 150°. Crystd from aqueous EtOH.

*n*-Propyl iodide (1-iodopropane) [107-08-4] M 170.0, b 102.5°, d 1.745, n 1.5041. Should be distd at reduced pressure to avoid decomposition. Dried with MgSO<sub>4</sub> or silica gel and fractionally distd. Stored under nitrogen with mercury in a brown bottle. Prior to distn, free iodine can be removed by shaking with copper powder or by washing with aq Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and drying. Alternatively, the *n*-propyl iodide can be treated with bromine, then washed with aq Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and dried. See also *n*-butyl iodide.

*n*-Propyl propionate [106-36-5] M 120.2, b 122°, d 0.881, n 1.393. Treated with anhydrous CuSO<sub>4</sub>, then distd under nitrogen.

6-Propyl-2-thiouracil (propacil, propyail) [51-52-5] M 170.2, m 218-220°, 218-220°,  $pK_1^{21}$ -6.54 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{21}$  -4.22 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_3^{21}$  8.25 (4% aq EtOH). Purified by recrystn from H<sub>2</sub>O (sol in 900 parts at 20°, and 100 parts at 100°). UV, MeOH:  $\lambda$ max 277nm. [Anderson et al. J Am Chem Soc 67 2197 1945; Vanderhaegue Bull Soc Chim Belg 59 689 1950.]

**Propyne** [74-99-7] **M 40.1, m -101.5°, b -23.2°/760mm, d<sup>-50</sup> 0.7062, n<sup>-40</sup> 1.3863.** Purified by preparative gas chromatography.

Protocatechualdehyde [139-85-5] M 138.1, m 153°. Crystd from water or toluene and dried in a vacuum desiccator over KOH pellets or shredded wax respectively.

Protopine [fumarine, macleyine, 4,6,7,14-tetrahydro-5-methyl-bis[1,3]-benzodioxolo[4,5c:5',6'-g]azecine-13(5H)-one] [130-86-9] M 353.4, m 208°, pK 5.99. Crystd from EtOH/CHCl<sub>3</sub>.

*IS*,2*S*-Pseudoephedrine (1-hydroxy-1-phenyl-2-methylaminopropane) [90-82-4] M 165.2, m 118-119°,  $[\alpha]_D^{20}$ +53.0° (EtOH), +40.0° (H<sub>2</sub>O), pK<sup>25</sup> 9.71. Crystd from dry diethyl ether, or from water and dried in a vacuum desiccator.

*IS*, 2*S*-Pseudoephedrine hydrochloride [345-78-8] M 210.7, m 181-182°, 185-188°,  $[\alpha]_{D}^{20}$  +61° (c 1 H<sub>2</sub>O). Crystd from EtOH.

Pteridine [91-18-9] M 132.2, m 139.5-140°,  $pK_1^{20}$  4.05 (equilibrium, hydrate),  $pK_2^{20}$  11,90 (OH of hydrate). Crystd from EtOH, \*benzene, *n*-hexane, *n*-heptane or pet ether. It sublimes at 120-130°/20mm. Stored at 0°, in the dark; turns green in the presence of light and on long standing in the dark.

**2,4-(1***H***,3***H***)-Pteridinedione H<sub>2</sub>O (lumazine) [487-21-8] M 182.1, m >350°, pK\_1^{20} < 1.0, pK\_2^{20} 7.94. Crystd from water.** 

Pterin (2-aminopteridin-4(3H)-one) [2236-60-4] M 163.1, m >300°,  $pK_1^{20}$  2.27 (basic),  $pK_2^{20}$  7.96 (acidic). It was dissolved in hot 1% aqueous ammonia, filtered, and an equal volume of hot 1M aqueous formic acid was added. The soln was allowed to cool at 0-2° overnight. The solid was collected and washed with distilled water several times by centrifugation and dried *in vacuo* over P<sub>2</sub>O<sub>5</sub> overnight, and then at 100° overnight.

Pterocarpin {(6aR - cis)-6a, 12a - dihydro - 3 - methoxy - 6H - [1,3]dioxolo[5,6]benzofuro[3,2c][1] $benzopyran} [524-97-0] M 298.3, m 165°, <math>[\alpha]_{546}^{20}$  -215° (c 0.5, CHCl<sub>3</sub>). Crystd from EtOH, or pet ether.

Pteroic acid (2-amino-6-p-carboxyanilinomethylpteridin-4(3H)-one) [119-24-4] M 312.3, m >300°(dec),  $pK_{Est(1)}$ ~ 2.3 (basic, N1),  $pK_{Est(2)}$ ~ 2.6 (basic, CH<sub>2</sub>NH),  $pK_{Est(3)}$ ~ 4.5 (COOH),  $pK_{Est(4)}$ ~ 7.9 (acidic 4-OH). Crystd from dilute HCl. Hygroscopic IRRITANT

R(+)-Pulegone [89-82-7] M 152.2, b 69.5°/5mm, n 1.4849, d 0.935,  $[\alpha]_{546}^{20}$  +23.5°(neat). Purified via the semicarbazone. [Erskine and Waight J Chem Soc 3425 1960.]

Purine [120-73-0] M 120.1, m 216-217°, pK<sub>1</sub><sup>20</sup> 2.30, pK<sub>2</sub><sup>20</sup> 9.86. Crystd from toluene or EtOH.

Purpurin (1,2,4-trihydroxy-5,10-anthraquinone) [81-54-9] M 256.2, m 253-256°, pK<sub>Est(1)</sub>~7.0 (2-OH), pK<sub>Est(2)</sub>~9.0 (4-OH), pK<sub>Est(3)</sub>~11.1 (1-OH). Cryst from aq EtOH, dry at 100°.

Purpurogallin (2,3,4,6-tetrahydroxy-5H-benzocyclohepten-5-one) [569-77-7] M 220.2, m 274° (rapid heating) (pK 7—10, phenolic OH). Crystd from acetic acid.

**Pyocyanine** (1-hydroxy-5-methylphenazinium zwitterion) [85-66-5] M 210.2, m 133° (sublimes and dec on further heating). Crystd from H<sub>2</sub>O as dark blue needles. *Picrate* has m 190° dec.

**Pyrazine** [290-37-9] **M 80.1, m 47°, b 115.5-115.8°, pK\_1^{20} -6.25 (aq H<sub>2</sub>SO<sub>4</sub>), pK\_2^{25}1.1 (0.51 at 20°). Distd in steam and crystd from water. Purified by zone melting.** 

Pyrazinecarboxamide [98-96-4] M 123.1, m 189-191° (sublimes slowly at 159°), pK -0.5. Crystd from water or EtOH.

Pyrazinecarboxylic acid [98-97-5] M 124.1, m 225-229°(dec), pK<sup>25</sup> 2.92. Crystd from water.

**Pyrazine-2,3-dicarboxylic acid** [89-01-0] **M 168.1, m 183-185°(dec), pK<sub>1</sub> <-2.0, pK<sub>2</sub> 0.9, pK<sub>3</sub> 2.77 (2.20).** Crystd from water. Dried at 100°.

**Pyrazole** [288-13-1] **M 68.1, m 70°, pK<sup>25</sup> 2.48.** Crystd from pet ether, cyclohexane, or water. [Barszcz et al. J Chem Soc, Dalton Trans 2025 1986.]

Pyrazole-3,5-dicarboxylic acid [3112-31-0] M 174.1, m 287-289°(dec),  $pK_{Est(1)}$ ~1.2 (CO<sub>2</sub>H),  $pK_{Est(2)}$ ~3.7 (CO<sub>2</sub>H),  $pK_{Est(3)}$ ~12 (NH). Crystd from water or EtOH.

**Pyrene** [129-00-0] **M 202.3, m 149-150°.** Crystd from EtOH, glacial acetic acid, \*benzene or toluene. Purified by chromatography of CCl<sub>4</sub> solns on alumina, with \*benzene or *n*-hexane as eluent. [Backer and Whitten J Phys Chem **91** 865 1987.] Also zone refined, and purified by sublimation. Marvel and Anderson [J Am Chem Soc **76** 5434 1954] refluxed pyrene (35g) in toluene (400mL) with maleic anhydride (5g) for 4days, then added 150mL of aqueous 5% KOH and refluxed for 5h with occasional shaking. The toluene layer was separated, washed thoroughly with H<sub>2</sub>O, concentrated to about 100mL and allowed to cool. Crystalline pyrene was filtered off and recrystd three times from EtOH or acetonitrile. [Chu and Thomas J Am Chem Soc **108**  6270 1986; Russell et al. Anal Chem 50 2961 1986.] The material was free from anthracene derivatives. Another purification step involved passage of pyrene in cyclohexane through a column of silica gel. It can be sublimed in a vacuum and zone refined. [Kano et al. J Phys Chem 89 3748 1985.]

Pyrene-1-aldehyde [3029-19-4] M 230.3, m 125-126°. Recrystd three times from aqueous EtOH.

1-Pyrenebutyric acid [3443-45-6] M 288.4, m 184-186°, pK<sub>Est</sub> ~4.1. Crystd from \*benzene, EtOH, EtOH/water (7:3 v/v) or  $C_6H_6/AcOH$ . Dried over  $P_2O_5$ . [Chu and Thomas J Am Chem Soc 108 6270 1986.]

**1-Pyrenecarboxylic acid** [19694-02-1] **M 230.3, m 126-127°, pK\_{Est} \sim 3,2.** Crystd from \*C<sub>6</sub>H<sub>6</sub> or 95% EtOH.

1-Pyrenesulfonic acid [26651-23-0] M 202.2, m >350°, pK<sub>Est</sub> <0. Crystd from EtOH/water. The tetra-Na salt cryst from H<sub>2</sub>O and the sulfonyl chloride has m 120°(dec). [Vollmann et al. Justus Liebigs Ann Chem 531 32 1937 and Justus Liebigs Ann Chem 540 189 1939.]

1,3,6,8-Pyrenetetrasulfonic acid [6528-53-6] M 522.2, m >400°, pK<sub>Est</sub> <0 Crystd from water [Tietz and Bayer Justus Liebigs Ann Chem 540 189 1939.]

**Pyridine** [110-86-1] **M 79.1, f -41.8°, b 115.6°, d 0.9831, n 1.51021, pK^{25} 5.23.** Likely impurities are H<sub>2</sub>O and amines such as the picolines and lutidines. Pyridine is *hygroscopic* and is miscible with H<sub>2</sub>O and organic solvents. It can be dried with solid KOH, NaOH, CaO, BaO or sodium, followed by fractional distn. Other methods of drying include standing with Linde type 4A molecular sieves, CaH<sub>2</sub> or LiAlH<sub>4</sub>, azeotropic distn of the H<sub>2</sub>O with toluene or \*benzene, or treated with phenylmagnesium bromide in ether, followed by evaporation of the ether and distn of the pyridine. A recommended [Lindauer and Mukherjee *Pure Appl Chem* **27** 267 1971] method dries pyridine over solid KOH (20g/Kg) for 2weeks, and fractionally distils the supernatant over Linde type 5A molecular sieves and solid KOH. The product is stored under CO<sub>2</sub>-free nitrogen. Pyridine can be stored in contact with BaO, CaH<sub>2</sub> or molecular sieves. Non-basic materials can be removed by steam distilling a soln containing 1.2 equivalents of 20% H<sub>2</sub>SO<sub>4</sub> or 17% HCl until about 10% of the base has been carried over along with the non-basic impurities. The residue is then made alkaline, and the base is separated, dried with NaOH and fractionally distd.

Alternatively, pyridine can be treated with oxidising agents. Thus pyridine (800mL) has been stirred for 24h with a mixture of ceric sulfate (20g) and anhydrous  $K_2CO_3$  (15g), then filtered and fractionally distd. Hurd and Simon [*J Am Chem Soc* 84 4519 1962] stirred pyridine (135mL), water (2.5L) and KMnO<sub>4</sub> (90g) for 2h at 100°, then stood for 15h before filtering off the ppted manganese oxides. Addition of solid KOH (*ca* 500g) caused pyridine to separate. It was decanted, refluxed with CaO for 3h and distd.

Separation of pyridine from some of its homologues can be achieved by crystn of the oxalates. Pyridine is ppted as its oxalate by adding it to the stirred soln of oxalic acid in acetone. The ppte is filtered, washed with cold acetone, and pyridine is regenerated and isolated. Other methods are based on complex formation with  $ZnCl_2$  or HgCl<sub>2</sub>. Heap, Jones and Speakman [*J Am Chem Soc* **43** 1936 *1921*] added crude pyridine (1L) to a soln of  $ZnCl_2$  (848g) in 730mL of water, 346mL of conc HCl and 690mL of 95% EtOH. The crystalline ppte of  $ZnCl_2$ .(pyridine)<sub>2</sub> was filtered off, recrystd twice from absolute EtOH, then treated with a conc NaOH soln, using 26.7g of solid NaOH to 100g of the complex. The ppte was filtered off, and the pyridine (60mL) in 300mL of 10% (v/v) HCl to a soln of HgCl<sub>2</sub> (405g) in hot water (2.3L). On cooling, crystals of pyridine-HgCl<sub>2</sub> (1:1) complex separated and were filtered off, crystd from 1% HCl (to **m** 178.5-179°), washed with a little EtOH and dried at 110°. The free base was liberated by addition of excess aq NaOH and separated by steam distn. The distillate was saturated with solid KOH, and the upper layer was removed, dried further with KOH, then BaO and distd. Another possible purification step is fractional crystn by partial freezing.

Small amounts of pyridine have been purified by vapour-phase chromatography, using a 180-cm column of polyethyleneglycol-400 (Shell 5%) on Embacel (May and Baker) at 100°, with argon as carrier gas. The Karl Fischer titration can be used for determining water content. A colour test for pyrrole as a contaminant is described by Biddiscombe et al. [J Chem Soc 1957 1954].

§ Polystyrene supported pyridine is commercially available.

**Pyridine-2-aldehyde** [1121-60-4] **M 107.1, b 81.5°/25mm, d 1.121, n 1.535, pK\_1^{25}3.84, pK\_2^{25}12.68.** Sulfur dioxide was bubbled into a soln of 50g in 250mL of boiled water, under nitrogen, at 0°, until pptn was complete. The addition compound was filtered off rapidly and, after washing with a little water, it was refluxed in 17% HCl (200mL) under nitrogen until a clear soln was obtained. Neutralisation with NaHCO<sub>3</sub> and extraction with ether separated the aldehyde which was recovered by drying the extract, then distilling twice, under nitrogen. [Kyte, Jeffery and Vogel J Chem Soc 4454 1960.]

**Pyridine-3-aldehyde** [500-22-1] **M 107.1, b 89.5°/14mm, d 1.141, n 1.549, pK\_1^{20} 3.80, pK\_2^{20} 13.10. Purification as for pyridine-2-aldehyde.** 

**Pyridine-4-aldehyde** [872-85-5] **M 107.1, b 79.5°/12mm, d 1.137, n 1.544, pK<sub>1</sub><sup>20</sup>4,77, pK<sub>2</sub><sup>20</sup>12.20.** Purification as for pyridine-2-aldehyde.

**Pyridine-2-aldoxime** (pyridine-2-carboxaldoxime) [873-69-8] M 122.1, m 111-113°, 114°, pK<sub>1</sub><sup>25</sup> 3.56, pK<sub>2</sub><sup>25</sup> 10.17. Recrystd from Et<sub>2</sub>O-pet ether or H<sub>2</sub>O. The *picrate* has m 169-171° (from aqueous EtOH). It is used in peptide synthesis. [UV: Grammaticakis *Bull Chem Soc Fr* 109, 116 1956; Ginsberg and Wilson J Am Chem Soc 79 481 1957; Hanania and Irvine Nature 183 40 1959; Green and Saville J Chem Soc 3887 1956.]

Pyridine-3-aldoxime [1193-92-6] M 122.1, m 150°, pK<sub>1</sub><sup>20</sup> 4.07, pK<sub>2</sub><sup>20</sup> 10.39. Crystd from water.

Pyridine-4-aldoxime [696-54-8] M 122.1, m 129°, pK<sub>1</sub><sup>20</sup>4.73, pK<sub>2</sub><sup>20</sup>10.03. Crystd from water.

**2,6-Pyridinedialdoxime** [2851-68-5] M 165.1, m 212°, pK<sub>Est(1)</sub>~3.0, pK<sub>Est(2)</sub>~10. Crystd from water.

**Pyridine-2,5-dicarboxylic acid** [100-26-5] **M 167.1, m 254°, pK\_2^{25} 2.49, pK\_3^{25} 5.12.** Crystd from dil HCl.

**Pyridine-3,4-dicarboxylic acid** [490-11-9] **M 167.1, m 256°, pK\_1^{25} 2.43, pK\_2^{25} 4.78.** Crystd from dilute aqueous HCl.

**Pyridine hydrobromide perbromide (pyridinium bromide perbromide)** [39416-48-3] M 319.9, m 130° (dec), 132-134° (dec). It is a very good brominating agent - liberating one mol. of Br<sub>2</sub>. Purified by recrystn from glacial acetic acid (33g from 100mL of AcOH). [Fieser and Fieser Reagents for Organic Chemistry Vol 1 967 1967.]

**Pyridine hydrochloride** [628-13-7] M 115.6, m 144°, b 218°. Crystd from CHCl<sub>3</sub>/ethyl acetate and washed with diethyl ether.

Pyridine N-oxide [694-59-7] M 95.1, m 67°, pK<sup>24</sup> 0.79. Purified by vacuum sublimation.

**Pyridine 3-sulfonic acid** [636-73-7] M 159.2, m 365-366° (dec), 357°,  $pK^{25}$  2.89 (12% aq EtOH), 3.22 (H<sub>2</sub>O)(protonation on N). Purified by recrystn from H<sub>2</sub>O or aqueous EtOH as needles or plates. [pKa: Evans and Brown J Org Chem 27 3127 1962; IR: Arnett and Chawla J Am Chem Soc 100 214 1978.] UV in 50% aqueous EtOH:  $\lambda$ max at 208 and 262nm. The ammonium salt has m 243° (from H<sub>2</sub>O), the sulfonyl chloride has m 133-134° (from pet ether), the amide has m 110-111° (from H<sub>2</sub>O), the hydrochloride has m > 300° (dec), and the N-methyl betaine has m 130° (from H<sub>2</sub>O). [Gastel and Wibaut Recl Trav Chim Pays Bas 53 1031 1934; McIlvain and Goese J Am Chem Soc 65 2233 1943; Machek Monatsh Chem 72 77 1938.]

**2-Pyridinethiol** (2-mercaptopyridine) [2637-34-5] M 111.2, m 127.4°, 127-130°, 130-132°,  $pK_1^{20}$  -1.07,  $pK_2^{20}$  9.97, If impure, dissolve in CHCl<sub>3</sub>, wash with dil AcOH, H<sub>2</sub>O, dry (MgSO<sub>4</sub>), evaporate under reduced press and recryst residue from\*C<sub>6</sub>H<sub>6</sub> or H<sub>2</sub>O. 2-Methylmercaptopyridine (b 100-104°/33mm) was

Pyridoxal hydrochloride, pyridoxamine hydrochloride and pyridoxine hydrochloride (vitamin  $B_6$ ) see entries in Chapter 6.

1-(2-Pyridylazo)-2-naphthol (PAN) [85-85-8] M 249.3, m 140-142°,  $pK_1^{30-36}$  2.9,  $pK_2^{30-36}$ 11.2. Purified by repeated crystn from MeOH. It can also be purified by sublimation under vacuum. Purity can be checked by TLC using a mixed solvent (pet ether, diethyl ether, EtOH; 10:10:1) on a silica gel plate.

4-(2-Pyridylazo)resorcinol (PAR) [1141-59-9] M 215.2, m >195°(dec),  $\lambda_{max}$  415nm,  $\varepsilon$  2.59 x 10<sup>4</sup> (pH 6-12), pK<sub>1</sub><sup>25</sup> 2.69, pK<sub>2</sub><sup>25</sup> 5.50. Purified as the sodium salt by recrystn from 1:1 EtOH/water. Purity can be checked by TLC using a silica gel plate and a mixed solvent (*n*-BuOH:EtOH:2M NH<sub>3</sub>; 6:2:2).

Pyridyldiphenyltriazine [1046-56-6] M 310.4, m 191-192°. Purified by repeated recrystn from EtOH/dimethylformamide.

1-(4-pyridyl)ethanol [R-(+)- 27854-88-2; S-(-)- 54656-96-1] M 123.2, m 63-65°, 67-69°,  $[\alpha]_D^{20}$  (+) and (-) 49.8° (c 0.5, EtOH), pK<sub>Est</sub> ~5.4. Purified by recrystn from pet ether. The (-)-di-O-benzoyl tartrate salt has m 146-148° (from EtOH). [UV, ORD: Harelli and Samori J Chem Soc Perkin Trans 2 1462 1974.] The racemate recrystallises from Et<sub>2</sub>O m 74-76°, b 90-94°/1mm [Ferles and Attia Collect Czech Chem Commun 38 611 1973; UV, NMR: Nielson et al. J Org Chem 29 2898 1964.]

**Pyrogallol** [87-66-1] **M 126.1, m 136°, pK\_1^{20}9,05, pK\_2^{20}11.19, pK\_3^{20}14. Crystd from EtOH/\*benzene.** 

*R*-pyroglutamic acid (5-oxo-D-proline, *R*-2-Pyrrolidone-5-carboxylic acid) [4042-36-8] M 129.1, m 156-158°,  $[\alpha]_{546}^{20}$  +11° (c 5, H<sub>2</sub>O). Crystd from EtOH/pet ether.

S-Pyroglutamic acid (5-oxo-L-proline) [98-79-3] M 129.1, m 156-158°, 162-164°,  $[\alpha]_{546}^{20}$ -11° (c 5, H<sub>2</sub>O), pK 12.7 (by electron spin resonance). Crystd from EtOH by addition of pet ether. NH<sub>4</sub> salt has m 184-186° (from EtOH).

**Pyromellitic acid (benzene-1,2,4,5-tetracarboxylic acid)** [89-05-4] M 254.2, m 276°, 281-284°,  $pK_1^{25}$  1.87,  $pK_2^{25}$  2.72,  $pK_3^{25}$  4.30,  $pK_4^{25}$  5.52. Dissolved in 5.7 parts of hot dimethylformamide, decolorised and filtered. The ppte obtained on cooling was separated and air dried, the solvent being removed by heating in an oven at 150-170° for several hours. Crystd from water.

**Pyromellitic dianhydride** [89-32-7] **M 218.1, m 286°.** Crystd from ethyl methyl ketone or dioxane. Dried, and sublimed *in vacuo*.

 $\alpha$ -Pyrone (2*H*-pyran-2-one) [504-31-4] M 96.1, m 5°, 8-9°, b 103-111°/19-22 mm, 110°/26mm, 104°/ 30mm, 115-118°/37mm, 206-207°/atm,  $d_4^{20}$  1.1972,  $n_D^{20}$  1.5298, pK -1.14 (aq H<sub>2</sub>SO<sub>4</sub>). Dissolve in Et<sub>2</sub>O, wash with brine, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate, distil residue under vacuum and redistil. It is a colourless liquid. [Zimmermann et al. Org Synth Coll Vol V 982 1973; Nakagawa and Saegusa Org Synth 56 49 1977; Elderfield J Org Chem 6 566 1941.] The picrate has m 106-107° (from EtOH).

 $\gamma$ -Pyrone (4*H*-pyran-4-one) [108-97-4] M 96.1, m 32.5-32.6°, 33°, 32-34°, b 88.5°/7 mm, 91-91.5°/9mm, 95-97°/13mm, 105°/23mm, 215°/atm, pK<sup>25</sup> 0.10. Purified by vacuum distn, the distillate crystallises and is hygroscopic. It is non-steam volatile. The hydrochoride has m 139° (from EtOH), and the picrate has m 130.2-130.3° (from EtOH or H<sub>2</sub>O). [Mayer Chem Ber 90 2362 1957; IR: Jones et al. Can J Chem 37 2007 1959; Neelakatan J Org Chem 22 1584 1957.]

**Pyronin Y** [3,6-bis(dimethylamino)xanthylium chloride] [92-32-0] M 302.8, m 250-260°, CI 45005,  $\lambda$ max 522nm, pK<sub>Est</sub> ~7.6. Commercial material contained a large quantity of zinc. Purified by dissolving 1g in 50mL of hot water containing 5g NaEDTA. Cooled to 0°, filtered, evapd to dryness and the residue extracted with EtOH. The soln was evaporated to 5-10mL, filtered, and the dye pptd by addition of excess dry diethyl ether. It was centrifuged and the crystals were washed with dry ether. The procedure was repeated, then the product was dissolved in CHCl<sub>3</sub>, filtered and evapd. The dye was stored in a vacuum.

**Pyrrole** [109-97-7] M 67.1, m 23.4°, b 66°/80mm, 129-130°/atm, d 0.966, n 1.5097,  $pK_1^{25}$  -4.4 (Protonation on carbon),  $pK_2^{25}$  17.51 (aq KOH, H. scale). Dried with NaOH, CaH<sub>2</sub> or CaSO<sub>4</sub>. Fractionally distd under reduced pressure from CaH<sub>2</sub>. Stored under nitrogen, turns brown in air. Redistd immediately before use.

**Pyrrolidine** [123-75-1] **M 71.1, b 87.5-88.5°, d 0.860, n 1.443, pK^{25} 11.31.** Dried with BaO or sodium, then fractionally distd, under N<sub>2</sub>, through a Todd column packed with glass helices (see p. 174).

**Pyrrolidine-1-carbodithioic acid ammonium salt** [5108-96-3] M 164.3, m 128-130°, pK<sup>25</sup> 3.25 (free acid). Purified by recryst twice by dissolving in MeOH and adding Et<sub>2</sub>O. Also by recrystn from EtOH. [Synth and Polarography: Kitagawa and Taku *Bull Chem Soc Jpn* 64 2151 1973; Malissa and Schöffmann *Mikrochim Acta* 187 1955.]

**Pyruvic acid** [127-17-3] **M 88.1, m 13°, b 65°/10mm, pK^{25} 2.39 (2.60).** Distd twice, then fractionally crystd by partial freezing.

*p*-Quaterphenyl [135-70-6] M 306.4, m 312-314°. Recrystd from dimethyl sulfoxide at *ca* 50°.

Quercetin (2H<sub>2</sub>O) (3,3',4',5,6-pentahydroxyflavone) [6151-25-3 (2H<sub>2</sub>O); 117-39-3 (anhydr)] M 338.3, m ca 315°(dec), (phenolic pKs 7—10). Crystd from aq EtOH and dried at 100°.

Quercitrin (quercetin glycoside) [522-12-3] M 302.2, m 168°, 176-178°. Crystd from aq EtOH and dried at 135° to give the higher melting form.

Quinaldic (quinoline-2-carboxylic) acid [93-10-7] M 173.2, m 156-157°, pK<sub>1</sub><sup>25</sup> 1.45, pK<sub>2</sub><sup>25</sup> 2.49 (2.97). Crystd from \*benzene.

Quinalizarin(1,2,5,8-tetrahydroxy-9,10-anthraquinone)[81-61-8]M 272.2, m 275°, $pK_{Est(1)} \sim 7.1$ (1-OH),  $pK_{Est(2)} \sim 9.9$ (8-OH),  $pK_{Est(3)} \sim 11.1$ (5-OH),  $pK_{Est(4)} \sim 11.8$ (2-OH). Crystdfrom acetic acid or nitrobenzene. It can be sublimed *in vacuo*.m vacuo.m vacuo.

Quinazoline [253-82-7] M 130.2, m 48.0-48.5°, b 120-121°/17-18mm,  $pK_1^{20}$ -4.51 (aq H<sub>2</sub>SO<sub>4</sub>, anhydrous dication),  $pK_2^{20}$ 2.01 (anhydrous monocation),  $pK_3^{20}$ 4.3 (equilibrium with 3,4-hydrated species),  $pK_4^{20}$  12.1 (hydrated anion). Purified by passage through an activated alumina column in \*benzene or pet ether (b 40-60°). Distd under reduced pressure, sublimed under vacuum and crystd from pet ether. [Armarego J Appl Chem 11 70 1961.]

Quinhydrone [106-34-3] M 218.2, m 168°. Crystd from H<sub>2</sub>O at 65°, then dried in a vac desiccator.

1*R*,3*R*,4*R*,5*R*-Quinic acid (1,3,4,5-tetrahydroxy-cyclohexane-carboxylic acid) [77-95-2] M 192.3, m 172°(dec),  $[\alpha]_{546}^{20}$  -51° (c 20, H<sub>2</sub>O), pK<sup>25</sup> 3.58. Crystd from water.

Quinidine [56-54-2] M 324.4, m 171°,  $[\alpha]_{546}^{20}$  +301.1° (CHCl<sub>3</sub> contg 2.5% (v/v) EtOH), pK<sub>1</sub><sup>15</sup> 4.13, pK<sub>2</sub><sup>15</sup> 8.77. Crystd from \*benzene or dry CHCl<sub>3</sub>/pet ether (b 40-60°), discarding the initial, oily crop of crystals. Dried under vacuum at 100° over P<sub>2</sub>O<sub>5</sub>.

Quinine [130-95-0] M 324.4, m 177°(dec),  $[\alpha]_{546}^{20}$  -160° (c 1, CHCl<sub>3</sub>), pK<sub>1</sub><sup>20</sup> 4.13 (quinoline N), pK<sub>2</sub><sup>20</sup> 8.52 (piperidine N). Crystd from abs EtOH.

Quinine bisulfate  $[6183-68-2 (7H_2O); 549-56-4 (anhydr)]$  M 422.4, m 160° (anhydrous). Crystd from 0.1M H<sub>2</sub>SO<sub>4</sub>, forms heptahydrate when crystd from water

Quinine sulfate  $(2H_2O)$  [6119-70-6  $(H_2O)$ ; 804-63-7 (anhydr)] M 783.0, m 205°. Crystd from water, dried at 110°.

Quinizarin (1,4-dihydroxy-9,10-anthraquinone) [81-64-1] M 240.2, m 200-202°, pK<sub>1</sub><sup>25</sup> 9.90 (9.5), pK<sub>2</sub><sup>25</sup> 11.18. Crystd from glacial acetic acid.

[91-22-5] M 129.2, m -16°, b 111.5°, 236°/758mm, d 1.0937, n 1.625, pK<sup>25</sup> Quinoline 4.80 (4.93). Dried with Na<sub>2</sub>SO<sub>4</sub> and vac distd from zinc dust. Also dried by boiling with acetic anhydride, then fractionally distilling. Calvin and Wilmarth [J Am Chem Soc 78 1301 1956] cooled redistd quinoline in ice and added enough HCl to form its hydrochloride. Diazotization removed aniline, the diazo compound being broken down by warming the soln to 60°. Non-basic impurities were removed by ether extraction. Quinoline was liberated by neutralising the hydrochloride with NaOH, then dried with KOH and fractionally distd at low pressure. Addition of cuprous acetate (7g/L of quinoline) and shaking under hydrogen for 12h at 100° removed impurities due to the nitrous acid treatment. Finally the hydrogen was pumped off and the quinoline was distd. Other purification procedures depend on conversion to the phosphate (m 159°, pptd from MeOH soln, filtered, washed with MeOH, then dried at 55°) or the picrate (m 201°) which, after crystn were reconverted to the amine. The method using the picrate [Packer, Vaughan and Wong J Am Chem Soc 80 905 1958] is as follows: quinoline is added to picric acid dissolved in the minimum volume of 95% EtOH, giving yellow crystals which were washed with EtOH, air-dried and crystd from acetonitrile. These were dissolved in dimethyl sulfoxide (previously dried over 4A molecular sieves) and passed through basic alumina, on which the picric acid is adsorbed. The free base in the effluent is extracted with n-pentane and distd under vacuum. Traces of solvent can be removed by vapour-phase chromatography. [Moonaw and Anton J Phys Chem 80 2243 1976.] The ZnCl<sub>2</sub> and dichromate complexes have also been used. [Cumper, Redford and Vogel J Chem Soc 1176 1962.]

2-Quinolinealdehyde [5470-96-2] M 157.2, m 71°, pK<sub>Est</sub> ~3.3. Steam distd. Crystd from H<sub>2</sub>O. Protected from light.

8-Quinolinecarboxylic acid [86-59-9] M 173.2, m 186-187.5°, pK<sub>1</sub><sup>25</sup> 1.82, pK<sub>2</sub><sup>25</sup> 6.87. Crystd from water.

Quinoline ethiodide (1-ethylquinolinium iodide) [634-35-5] M 285.1, m 158-159°. Crystd from aqueous EtOH.

Quinoxaline [9/-19-0] M 130.2, m 28° (anhydr), 37°(H<sub>2</sub>O), b 108-110°/0.1 mm, 140°/40mm, pK<sub>1</sub><sup>20</sup>-5.52 (-5.8, dication), pK<sub>2</sub><sup>25</sup>2.08 (monocation). Crystd from pet ether. Crystallises as the monohydrate on addition of water to a pet ether soln.

Quinoxaline-2,3-dithiol [1199-03-7] M 194.1, m 345°(dec), pK<sub>1</sub> 6.9, pK<sub>2</sub> 9.9. Purified by repeated dissolution in alkali and re-pptn by acetic acid.

p-Quinquephenyl (p-pentaphenyl) [61537-20-0] M 382.5, m 388.5°. Recrystd from boiling dimethyl sulfoxide (b 189°, lowered to 110°). The solid obtained on cooling was filtered off and washed repeatedly with toluene, then with conc HCl. The final material was washed repeatedly with hot EtOH. It was also recrystd from pyridine, then sublimed *in vacuo*.

Quinuclidine (1-azabicyclo[2.2.2]octane) [100-76-5] M 111.2, m 158 $^{\circ}$ (sublimes), pK<sup>25</sup> 10.95. Crystd from diethyl ether.

**D-Raffinose** (5H<sub>2</sub>O) [17629-30-0 (5H<sub>2</sub>O); 512-69-6 (anhydr)] M 594.5, m 80°,  $[\alpha]_{546}^{20}$  +124° (c 10, H<sub>2</sub>O). Crystd from aqueous EtOH.

Rauwolscine hydrochloride [6211-32-1] M 390.0, m 278-280°. Crystd from water.

Reductic acid (1,2-dihydroxycyclopent-1,2-en-3-one) [80-72-8] M 114.1, m 213°, pK<sup>20</sup> 4.72. Crystd from ethyl acetate.

Rescinnamine [24815-24-5] M 634.7, m 238-239°(vac),  $[\alpha]_D^{20}$ -97° (c 1, CHCl<sub>3</sub>), pK<sub>Est(1)</sub>~<0 (carbazole N), pK<sub>Est(2)</sub>~7.0 (quinolizidine N). Crystd from \*benzene or MeOH.

**Reservic acid** [83-60-3] **M 400.5, m 241-243°, pK**<sub>Est(1)</sub>~<0 (carbazole N), pK<sub>Est(2)</sub>~4.0 (CO<sub>2</sub>H), pK<sub>Est(3)</sub>~7.4 (quinolizidine N). Crystd from MeOH. The hydrochloride 0.5H<sub>2</sub>O has m 257-259°,  $[\alpha]_D^{23}$ -81° (H<sub>2</sub>O).

Reservine [50-55-5] M 608.7, m 262-263°,  $[\alpha]_{546}^{20}$ -148° (c 1, CHCl<sub>3</sub>), pK<sub>Est(1)</sub>~<0 (carbazole N), pK<sub>2</sub> 6.6 (7.4)(quinolizidine N). Crystd from aq acetone.

**Resorcinol** [108-46-3] **M** 110.1, **m** 111.2-111.6°,  $pK_1^{25}$  9.23,  $pK_2^{25}$  13.05. Crystd from \*benzene, toluene or \*benzene/diethyl ether.

Retene [483-65-8] M 234.3, m 99°. Crystd from EtOH.

Retinal (vitamin A aldehyde), Retinoic acid (vitamin A acid), Retinol (vitamin A alcohol) see entries in Chapter 6.

**Retinyl acetate** [127-47-9] **M 328.5, m 57°.** Separated from retinol by column chromatography, then crystd from MeOH. See Kofler and Rubin [*Vitamins and Hormones (NY)* **18** 315 1960] for review of purification methods. Stored in the dark, under  $N_2$  or Ar, at 0°. See Vitamin A acetate p. 574 in Chapter 6.

**Retinyl palmitate** [79-81-2] M 524.9, m 28-29°,  $\epsilon_{1cm}^{1\%}$  (all-trans) 1000 (325 nm) in EtOH. Separated from retinol by column chromatography on water-deactivated alumina with hexane containing a very small percentage of acetone. Also chromatographed on TLC silica gel G, using pet ether/isopropyl ether/acetic acid/water (180:20:2:5) or pet ether/acetonitrile/acetic acid/water (190:10:1:15) to develop the chromatogram. Then recrystd from propylene at low temperature.

Rhamnetin (3,3'-4',5-tetrahydroxy-7-methoxy flavone, 7-methyl quercitin) [90-19-7] M 316.3, m >300°(dec), several phenolic pKs ~7-10.5. Crystd from EtOH.

L- $\alpha$ -Rhamnose (H<sub>2</sub>O) [10030-85-0 (H<sub>2</sub>O); 3615-41-6 (anhydr)] M 182.2, m 105°,  $[\alpha]_D^{15}$  +9.1° (c 5, H<sub>2</sub>O). Crystd from water or EtOH.

**Rhodamine B chloride [3,5-bis-(diethylamino)-9-(2-carboxyphenyl)xanthylium chloride]** [81-88-9] M 479.0, m 210-211°(dec), CI 45170,  $\lambda$ max 543nm, {Free base [509-34-2] CI 749}, pK 5.53. Major impurities are partially dealkylated compounds not removed by crystn. Purified by chromatography, using ethyl acetate/isopropanol/ammonia (conc)(9:7:4, R<sub>F</sub> 0.75 on Kieselgel G). Also crystd from conc soln in MeOH by slow addition of dry diethyl ether; or from EtOH containing a drop of conc HCl by slow addition of ten volumes of dry diethyl ether. The solid was washed with ether and air dried. The dried material has also been extracted with \*benzene to remove oil-soluble material prior to recrystn. Store in the dark.

**Rhodamine 6G** [Basic Red 1, 3,5-bis-(ethylamino)-9-(2-ethoxycarbonylphenyl)-2,7dimethylxanthylium chloride] [989-38-8] M 479.3, CI 45160,  $\lambda$  max 524nm, pK 5.58. Crystd from MeOH or EtOH, and dried in a vac oven. Rhodanine (2-mercaptothiazolidin-4-one) [141-84-4] M 133.2, m 168.5° (capillary), pK<sup>20</sup> 5.18. Crystd from glacial acetic acid or water.

**Riboflavin, riboflavin-5'-phosphate** (Na salt,  $2H_2O$ ) and ribonucleic acid see entries in Chapter 6.

 $\alpha$ -D-Ribose [50-69-1] M 150.1, m 90°,  $[\alpha]_{546}^{20}$  -24° (after 24h, c 10, H<sub>2</sub>O), pK<sup>25</sup> 12.22. Crystd from aqueous 80% EtOH, dried under vacuum at 60° over P<sub>2</sub>O<sub>5</sub> and stored in a vacuum desiccator.

Ricinoleic acid (*dl* 12-hydroxyoleic acid) [141-22-0] M 298.5, m 7-8° ( $\alpha$ -form), 5.0° ( $\gamma$ -form), n 1.4717, pK<sub>Est</sub> ~4.5. Purified as methyl acetylricinoleate [Rider J Am Chem Soc 53 4130 1931], fractionally distilling at 180-185°/0.3mm, then 87g of this ester was refluxed with KOH (56g), water (25mL), and MeOH (250mL) for 10min. The free acid was separated, crystd from acetone at -50°, and distd in small batches, b 180°/0.005mm. [Bailey et al. J Chem Soc 3027 1957.]

**Rosaniline HCl (Magenta I, Fuschin)** [632-99-5] **M 337.9, m >200°(dec).** Purified by dissolving in EtOH, filtering and adding H<sub>2</sub>O. Filter or centrifuge and wash the ppte with Et<sub>2</sub>O and dry in air. Could be crystd from H<sub>2</sub>O. Also recrystd from water and dried *in vacuo* at 40°. Crystals have a metallic green lustre. UV max in EtOH is at 543nm ( $\epsilon$  93,000). Solubility in H<sub>2</sub>O is 0.26%. A carmine red colour is produced in EtOH. [Scalan J Am Chem Soc 57 887 1937.]

(4-[bis-{4-hydroxyphenyl}methylene]-2,5-cyclohexadien-one, 4',4"-dip-Rosolic acid [603-45-2] M 290.3, m 292°, 295-300° (dec with hydroxy-fuschson, aurin, corallin) liberation of phenol), 308-310°(dec), pK<sub>1</sub> 3.11, pK<sub>2</sub> 8.62. It forms green crystals with a metallic lustre but the colour depends on the solvent used. When recrystd from brine (satd aqueous NaCl) acidified with HCl it forms red needles, but when recrystd from EtOH-AcOH the crystals have a beetle iridescent green colour. It has been recrystd from Me<sub>2</sub>CO (although it dissolves slowly), methyl ethyl ketone, 80-95% AcOH and from AcOH-\*C<sub>6</sub>H<sub>6</sub>. An aq KOH soln is golden yellow and a 70%  $H_2SO_4$  soln is deep red in colour. An alternative purification is to dissolve this triphenylmethane dye in 1.5% of aq NH<sub>3</sub>, filter, and heat to 70-80°, then acidify with dilute AcOH by adding it slowly with vigorous stirring, whereby the aurin separates as a brick-red powder or as purplish crystals depending on the temperature and period of heating. Filter off the solid, wash with  $H_2O$ and a little dilute AcOH then H<sub>2</sub>O again. Stir this solid with Et<sub>2</sub>O to remove any ketones and allow to stand overnight in the Et<sub>2</sub>O, then fiter and dry in air then in a vacuum. [Gomberg and Snow J Am Chem Soc 47 202 1925; Baines and Driver J Chem Soc 123 1216 1923; UV: Burawoy Chem Ber 64 462 1941; Neuk and Schmid J Prakt Chem [2] 23 549 1881.]

**Rubijervine** (slanid-5-ene-3 $\beta$ -12 $\alpha$ -diol) [79-58-3] M 413.6, m 240-246°,  $[\alpha]_D^{20}$ +19° (EtOH), pK<sub>Est</sub>~7.0. Crystd from EtOH. It has solvent of crystn.

Rubrene [517-51-1] M 532.7, m >315°. See 5,6,11,12-tetraphenylnaphthacene on p. 366.

(+)-Rutin (quercetin-3-rubinoside) [153-18-4] M 610.5, m 188-189,  $[\alpha]_{546}^{20}$  +13° (c 5, EtOH) (polyphenolic flavone pKs 7—10). Crystd from MeOH or water/EtOH, air dried, then dried for several hours at 110°.

**Saccharic acid** (D-glucaric acid) [87-73-0] M 210.1, m 125-126°,  $[\alpha]_D^{20} + 6.9^\circ \rightarrow +20.6^\circ$  (H<sub>2</sub>O), pK<sub>1</sub> 3.01, pK<sub>2</sub> 3.94 (D-isomer). Crystd from 95% EtOH.

Safranine O [477-73-6] M 350.9,  $\lambda_{max}$  530nm, pK<sup>25</sup> 6.4. Crystd from \*benzene/MeOH (1:1) or water. Dried under vacuum over H<sub>2</sub>SO<sub>4</sub>.

Safrole (5-allyl-1,3-benzodioxole, 4-allyl-1,2-methylenedioxybenzene) [94-59-7] M 162.1, m~ 11°, b 69-70°/1.5mm, 104-105°/6mm, 231.5-232°/atm, 235-237°/atm,  $d_4^{2°}$  1.0993,  $n_D^{2°}$  1.53738. It has been purified by fractional distn, although it has also been recrystd from low boiling pet ether at low temperatures. [IR: Briggs et al. Anal Chem 29 904 1957; UV: Patterson and Hibbert J Am Chem Soc 65 1962 1943.] The maleic anhydride adduct forms yellow crystals from toluene m 257° [Hickey J Org Chem 13 443 1948], and the picrate forms orange-red crystals from CHCl<sub>3</sub> [Baril and Magrdichian J Am Chem Soc 58 1415 1936].

D(-)-Salicin [138-52-3] M 286.3, m 204-208°, [α]<sub>D</sub><sup>25</sup> -63.5° (c ca 3, H<sub>2</sub>O). Crystd from EtOH.

Salicylaldehyde (o-hydroxybenzaldehyde) [90-02-8] M 122.1, b 93°/25mm, 195-197°/760mm, d 1.167, n 1.574,  $pK^{25}$  8.37. Ppted as the bisulfite addition compound by pouring the aldehyde slowly and with stirring into a 25% soln of NaHSO<sub>3</sub> in 30% EtOH, then standing for 30min. The ppte, after filtering at the pump, and washing with EtOH, was decomposed with aq 10% NaHCO<sub>3</sub>, and the aldehyde was extracted into diethyl ether, dried with Na<sub>2</sub>SO<sub>4</sub> or MgSO<sub>4</sub>, and distd, under reduced pressure. Alternatively, salicylaldehyde can be pptd as its copper complex by adding it to warm, satd soln of copper acetate, shaking and then standing in ice. The ppte was filtered off, washed thoroughly with EtOH, then with diethyl ether, and decomposed with 10% H<sub>2</sub>SO<sub>4</sub>, the aldehyde was extracted into diethyl ether, dried and distd. It has also been purified by repeated vacuum distn, and by dry column chromatography on Kieselgel G [Nishiya et al. J Am Chem Soc 108 3880 1986]. The acetyl derivative has m 38-39° (from pet ether or EtOH) and b 142°/18mm, 253°/atm.

Salicylaldoxime [94-67-7] M 137.1, m 57°, pK<sub>Est</sub> ~ 8.3. Crystd from CHCl<sub>3</sub>/pet ether (b 40-60°).

Salicylamide [65-45-2] M 137.1, m 142-144°, pK<sup>20</sup> 8.37. Crystd from water or repeatedly from chloroform [Nishiya et al. J Am Chem Soc 108 3880 1986].

Salicylanilide [87-17-2] M 213.2, m 135°, pK<sub>Est</sub> ~8.3. Crystd from water.

Salicylhydroxamic acid [89-73-6] M 153.1, m 179-180°(dec),  $pK_1^{30}$  2.15,  $pK_2^{30}$  7.46,  $pK_3^{30}$  9.72. Crystd from acetic acid.

Salicyclic acid (2-hydroxybenzoic acid) [69-72-7] M 138.1, m 157-159°, 158-160°, 159.5°, 159-160°, 162°, b 211°/20mm,  $pK_1^{25}$  3.01,  $pK_2^{25}$  13.43 (13.01). It has been purified by steam distn, by recrystn from H<sub>2</sub>O (solubility is 0.22% at room temp and 6.7% at 100°), absolute MeOH, or cyclohexane and by sublimation in a vacuum at 76°. The *acid chloride* (needles) has m 19-19.5°, b 92°/15mm, *amide* m 133° (yellow needles from H<sub>2</sub>O), and *anilide* (prisms fron H<sub>2</sub>O) m 135°. The *O-acetyl* derivative has m 135° (rapid heating and the liquid resolidifies at 118°) and the *o-benzoyl* derivative has m 132° (aq EtOH). [IR: Hales et al. J Chem Soc 3145 1954; UV: Bergmann et al. J Chem Soc 2351 1950].

Sarcosine [107-97-1] M 89.1, m 212-213°(dec), pK<sub>1</sub><sup>20</sup> 2.12, pK<sub>2</sub><sup>20</sup> 10.19. Crystd from abs EtOH.

Scopoletin (7-hydroxy-6-methoxycoumarin) [92-61-5] M 192.2, m 206°, 208-209°, pK 8.96 (70% aq EtOH). Crystd from water, acetic acid or  $*C_6H_6/MeOH$ .

Sebacic acid [111-20-6] M 202.3, m 134.5°,  $pK_1^{25}$  4.58,  $pK_2^{25}$  5.54. Purified via the disodium salt which, after crystn from boiling water (charcoal), was again converted to the free acid. The free acid was crystd repeatedly from hot distd water or from Me<sub>2</sub>CO+pet ether and dried under vacuum.

Sebacic acid monomethyl ester [818-88-2] M 216.3, m 42-43°, b 169-171°/4mm. Recrystd from Me<sub>3</sub>CO+pet ether or pet ether at low temperature and distd in a vacuum.

Sebaconitrile (decanedinitrile) [1871-96-1] M 164.3, m 8°, b 199-200°. Mix with  $P_2O_5$  (10% by wt) and distilled from it, then redistilled.

Secobarbital (5-allyl-5-1'-methylbutylbarbituric acid) [76-73-3] M 260.3, m 100°,  $pK_{Est(1)}\sim3.5$ ,  $pK_{Est(2)}\sim12.0$ . A soln of the salt in 10% HCl was ppted and the acid form was extracted by the addition of ether. Then purified by repeated crystn from CHCl<sub>3</sub>. [Buchet and Sandorfy J Phys Chem 88 3274 1984.]

Semicarbazide hydrochloride (hydrazine carboxamide hydrochloride) [563-41-7] M 111.5, m 173°(dec), 175°(dec),  $pK^{24}$  3.66. Crystd from aqueous 75% EtOH and dried under vacuum over CaSO<sub>4</sub>. Also crystd from a mixture of 3.6 mole % MeOH and 6.4 mole % of water. [Kovach et al. J Am Chem Soc 107 7360 1985.] IR: v 700, 3500 cm<sup>-1</sup> [Org Synth Coll Vol I 485 1941; Davison and Christie J Chem Soc 3389 1955; Thiele and Stange Chem Ber 27 33 1894; pK: Bartlett J Am Chem Soc 54 2853 1923]. The free base crystd as prisms from abs EtOH, m 96° [Curtius and Heidenreich Chem Ber 27 55 1894]. TOXIC ORALLY, possible CARCINOGEN and TERATOGEN.

Sennoside A [81-27-6] M 862.7, m 220-240°(dec),  $[\alpha]_D^{20}$  -147° (c 5, Me<sub>2</sub>CO/H<sub>2</sub>O 7:1). Crystd from aq acetone or large vols of H<sub>2</sub>O.

Sennoside B [128-57-4] M 962.7, m 182-190°(dec),  $[\alpha]_D^{20}$  -100° (c 2, Me<sub>2</sub>CO/H<sub>2</sub>O 7:3). Crystd from aq acetone or large vols of H<sub>2</sub>O.

L-Serine [56-45-1] M 105.1, m 228°(dec),  $[\alpha]_D^{25}$ +14.5° (1M HCl),  $[\alpha]_{546}^{20}$ +16° (c 5, 5M HCl),  $pK_1^{25}$  2.15,  $pK_2^{25}$ 9.21. Likely impurity is glycine. Crystd from water by adding 4 volumes of EtOH. Dried. Stored in a desiccator.

Serotonin creatinine sulfate  $(H_2O)$  [971-74-4] M 405.4, m 220°(dec), pK<sub>1</sub> 10.1, pK<sub>2</sub> 11.1, pK<sub>3</sub> 18.25 (NH) for serotonin, pK 4.9 for creatinine. Crystd (as monohydrate) from water.

Shikimic acid [138-59-0] M 174.2, m 183-184.5°, 190°,  $[\alpha]_{546}^{20}$  -210° (c 2, H<sub>2</sub>O), pK<sup>14</sup> 4.15. Crystd from water or MeOH/AcOEt and sublimes in a vac.

β-Sitosterol [83-46-5] M 414.7, m 136-137°,  $[α]_{546}^{20}$  -42° (c 2, CHCl<sub>3</sub>). Crystd from MeOH. Also purified by zone melting.

- Skellysolve A is essentially *n*-pentane, b 28-30°,
- **Skellysolve A** is essentially *n*-hexane, **b** 60-68°,
- Skellysolve C is essentially *n*-heptane, **b** 90-100°,
- Skellysolve D is mixed heptanes, b 75-115°,
- Skellysolve E is mixed octanes, b 100-140°,
- **Skellysolve F** is pet ether, **b** 30-60°,
- Skellysolve G is pet ether, b 40-75°,
- Skellysolve H is hexanes and heptanes, b 69-96°,
- Skellysolve L is essentially octanes, b 95-127°. For methods of purification, see petroleum ether.

Smilagenin [126-18-1] M 416.6, m 185°,  $[\alpha]_D^{25}$ -69° (c 0.5, CHCl<sub>3</sub>). Crystd from acetone.

Solanidine [80-78-4] M 397.6, m 218-219°,  $[\alpha]_D^{20}$ -29° (c 0.5, CHCl<sub>3</sub>), pK<sup>15</sup> 6.66. Crystd from CHCl<sub>3</sub>/MeOH.

α-Solanine [20562-02-1] M 868.1, m 286°(dec),  $[\alpha]_D^{20}$ -58° (c 0.8, pyridine), pK<sup>15</sup> 6.66. See α-solanine on p. 566 in Chapter 6. Solanone [S(+)-trans-2-methyl-5-isopropyl-1,3-nonan-8-one] [1937-54-8] M 194.3, b 60°/1mm,  $[\alpha]_D^{20} + 14^\circ$  (neat). Purified by high vacuum distillation and stored in sealed ampules [Kohda and Sato J Chem Soc, Chem Commun 951 1981]. It has UV (hexane) at  $\lambda \max 230$ nm ( $\varepsilon 11,800$ ).

Solasodine [126-17-0] M 413.6, m 202°,  $[\alpha]_D^{25}$  -100° (c 2, MeOH), pK 7.7. Crystd (as monohydrate) from MeOH or aq 80% EtOH, and sublimes in a vac.

Solasonine (solasodine-3-O-mannoglucoside) [19121-58-5] M 884.0, m 279°,  $[\alpha]_D^{20}$ -75° (c 0.5, MeOH), pK<sub>Est</sub> ~ 7.7. Crystd from aq 80% dioxane or MeOH.

Solochrome Violet R [4-hydroxy-3-(2-hydroxynaphthyl-1-ylazo)benzenesulfonic acid] [2092-55-9] M 367.3, CI 15670,  $\lambda$ max 501nm, pK<sub>2</sub><sup>25</sup>7.22 (OH), pK<sub>3</sub><sup>25</sup> 13.39 (OH). Converted to the monosodium salt by pptn with NaOAc/AcOH buffer of pH 4, then purified by pptn of the free acid from aq soln with conc HCl, washing and extracting with EtOH in a Soxhlet extractor. The acid ppted on evaporating the EtOH and was reconverted to the sodium salt as described for *Chlorazole Sky Blue FF*. Dried at 110°. It is *hygroscopic*. [Coates and Rigg *Trans Faraday Soc* 57 1088 1961.]

Sorbic acid (2,4-hexadienoic acid) [110-44-1] M 112.1, m 134°, pK<sup>25</sup> 4.76. Crystd from water.

Sorbitol [50-70-4] M 182.2, m 89-93° (hemihydrate), 110-111° (anhydrous),  $[\alpha]_{546}^{20}$ -1.8° (c 10, H<sub>2</sub>O), pK<sup>6°</sup> 13.00. Crystd (as hemihydrate) several times from EtOH/water (1:1), then dried by fusing and storing over MgSO<sub>4</sub>.

(-)-Sparteine sulfate pentahydrate [6160-12-9] M 422.5, m loses H<sub>2</sub>O at 100° and turns brown at 136° (dec),  $[\alpha]_D^{20}-22°$  (c 5, H<sub>2</sub>O),  $[\alpha]_D^{21}-16°$  (c 10, EtOH for free base), pK<sub>1</sub><sup>20</sup> 2.24, pK<sub>2</sub><sup>20</sup>9.46. Recrystd from aq EtOH or H<sub>2</sub>O although the solubility in the latter is high. The *free* (-)base has b 173°/8mm and is steam volatile but resinifies in air. The *dipicrate* forms yellow needles from EtOH-Me<sub>2</sub>CO, m 205-206° [Clemo et al. J Chem Soc 429 1931; see also Bolnmann and Schuman The Alkaloids (Ed Manske) Vol 9 175 1967]. The *free* (±)-base has m 71-72.5° [van Tamelen and Foltz J Am Chem Soc 82 2400 1960].

Spermidine [N-(3-aminopropyl)-1,4-diaminobutane] [124-20-9] M 145.3, m 23-25°, b 128-131°/15mm, d 0.918, n 1.482,  $pK_1^{25}$ 8.25,  $pK_2^{25}$ 9.64,  $pK_3^{25}$  10.43. It is a strong base with an alkylamine odour and absorbs CO<sub>2</sub> from the atmosphere. It is purified by shaking with solid K<sub>2</sub>CO<sub>3</sub> or NaOH, decanting and distilling from K<sub>2</sub>CO<sub>3</sub> in a vacuum. Store in the dark under N<sub>2</sub>.

Spermidine trihydrochloride [334-50-9] M 245.3, m ~250°(dec), 256-258°, for pKa see free base above. Recrystd from dry 3% HCl in ethanol adding dry  $Et_2O$  if necessary. Filter rapidly and dry in a vac desiccator. Alternatively centrifuge the crystals off wash them with dry  $Et_2O$  and dry in a vacuum.

Spermine 4HCl (N,N-bis(3-aminopropyl)-1,4-butanediamine 4HCl) [306-67-2] M 348.2, m 313-315°. The pKs are similar to spermidine above. Purification as for spermidine trihydrochloride above.

Squalene (all-trans- 2,6,10,15,19,23-hexamethyltetracosahexa-2,6,10,14,18,22-ene, spinacen) [111-02-4] M 410.7, m ~75°, b 203°/0.15mm. See squalene on p. 567 in Chapter 6.

Squaric acid (3,4-dihydroxy-3-cyclobutene-1,2-dione) [2892-51-5] M 114.1, m 293°(dec), 294°(dec), >300°,  $pK_1^{20}$ 1,50,  $pK_2^{20}$ 2.93. Purified by recryst from H<sub>2</sub>O — this is quite simple because the acid is ~ 7% soluble in boiling H<sub>2</sub>O and only 2% at room temperature. It is not soluble in Me<sub>2</sub>CO or Et<sub>2</sub>O hence it can be rinsed with these solvents and dried in air or a vacuum. It is not hygroscopic and gives an intense purple colour with FeCl<sub>3</sub>. It has IR v at 1820 (C=O) and 1640 (C=C) cm<sup>-1</sup>; and UV  $\lambda$ max at 269.5nm ( $\epsilon$  37K M<sup>-1</sup>cm<sup>-1</sup>).) [Cohn et al. J Am Chem Soc 81 3480 1959; Park et al. J Am Chem Soc 84 2919 1962] See also pKa values of 0.59 ±0.09 and 3.48 ±0.023 [Scwartz and Howard J Phys Chem 74 4374 1970].

Starch [9005-84-9] M (162.1)n. See entry on p. 567 in Chapter 6.

Stearic acid (octadecanoic acid) [57-11-4] M 284.5, m 71.4°, 72°, b 144-145°/27 mm, 383°/760mm, d 0.911, n 1.428,  $pK_{Est} \sim 5.0$ . Crystd from acetone, acetonitrile, EtOH (5 times), aq MeOH, ethyl methyl ketone or pet ether (b 60-90°), or by fractional pptn by dissolving in hot 95% EtOH and pouring into distd water, with stirring. The ppte, after washing with distd water, was dried under vacuum over P<sub>2</sub>O<sub>5</sub>. It has also been purified by zone melting and partial freezing. [Tamai et al. J Phys Chem 91 541 1987.]

**Stigmasterol** [83-48-7] **M 412.7, m 170°,**  $[\alpha]_D^{22}$ -51° (CHCl<sub>3</sub>),  $[\alpha]_{546}^{20}$ -59° (c 2, CHCl<sub>3</sub>). Crystd from hot EtOH. Dried in vacuum over P<sub>2</sub>O<sub>5</sub> for 3h at 90°. Purity was checked by NMR.

cis-Stilbene [645-49-8] M 180.3, b 145°/12mm. Purified by chromatography on alumina using hexane and distd under vacuum. (The final product contains ca 0.1% of the trans-isomer). [Lewis et al. J Am Chem Soc 107 203 1985; Saltiel J Phys Chem 91 2755 1987.]

trans-Stilbene [103-30-0] M 180.3, m 125.9°, b 305-307°/744mm, d 0.970. Purified by vac distn. (The final product contains about 1% of the *cis* isomer). Crystd from EtOH. Purified by zone melting. [Lewis et al. J Am Chem Soc 107 203 1985; Bollucci et al. J Am Chem Soc 109 515 1987; Saltiel J Phys Chem 91 2755 1987.]

(-)-Strychnine [57-24-9] M 334.4, m 268°,  $[\alpha]_{546}^{20}$  -139° (c 1, CHCl<sub>3</sub>),  $pK_1^{20}$  2,50,  $pK_2^{20}$  8.2. Crystd as the hydrochloride from water, then neutralised with ammonia.

Styphnic acid (2,4,6-trinitroresorcinol) [82-71-3] M 245.1, m 177-178°, 179-180°,  $pK_1^{25}$  0.06 (1.74),  $pK_2^{25}$  4.23 (4.86). Crystd from ethyl acetate or water containing HCl [EXPLODES violently on rapid heating.]

Styrene [100-42-5] M 104.2, b 41-42°/18mm, 145.2°/760mm, d 0.907, n 1.5469,  $n^{2.5}$  1.5441. Styrene is difficult to purify and keep pure. Usually contains added inhibitors (such as a trace of hydroquinone). Washed with aqueous NaOH to remove inhibitors (e.g. tert-butanol), then with water, dried for several hours with MgSO<sub>4</sub> and distd at 25° under reduced pressure in the presence of an inhibitor (such as 0.005% p-tert-butylcatechol). It can be stored at -78°. It can also be stored and kept anhydrous with Linde type 5A molecular sieves, CaH<sub>2</sub>, CaSO<sub>4</sub>, BaO or sodium, being fractionally distd, and distd in a vacuum line just before use. Alternatively styrene (and its deuterated derivative) were passed through a neutral alumina column before use [Woon et al. J Am Chem Soc 108 7990 1986; Collman J Am Chem Soc 108 2588 1986].

(±)-Styrene glycol (±-1-phenyl-1,2-ethanediol) [93-56-1] M 138.2, m 67-68°. Crystd from pet ether.

Styrene oxide [96-09-3] M 120.2, b 84-86°/16.5mm, d 1.053, n 1.535. Fractional distn at reduced pressure does not remove phenylacetaldehyde. If this material is present, the styrene oxide is treated with hydrogen under 3 atmospheres pressure in the presence of platinum oxide. The aldehyde, but not the oxide, is reduced to  $\beta$ -phenylethanol) and separation is now readily achieved by fractional distn. [Schenck and Kaizermen J Am Chem Soc 75 1636 1953.]

Suberic acid (hexane-1,6-dicarboxylic acid) [505-48-6] M 174.2, m 141-142°,  $pK_1^{25}$  4.12,  $pK_2^{25}$  5.40. Crystd from acetone and sublimes at 300° without dec.

Succinamic acid (succinic acid amide) [638-32-4] M 117.1, m 155°, 156-157°,  $pK^{25}$  4.54. Crystd from Me<sub>2</sub>CO or H<sub>2</sub>O and dried in vac. Not v sol in MeOH. Converted to succinimide above 200°.

Succinamide [110-14-5] M 116.1, m 262-265°(dec). Crystd from hot water.

Succinic acid [110-15-6] M 118.1, m 185-185.5°,  $pK_1^{25}$  4.21,  $pK_2^{25}$  5.72. Washed with diethyl ether. Crystd from acetone, distd water, or *tert*-butanol. Dried under vacuum over P<sub>2</sub>O<sub>5</sub> or conc H<sub>2</sub>SO<sub>4</sub>. Also

purified by conversion to the disodium salt which, after crystn from boiling water (charcoal), is treated with mineral acid to regenerate the succinic acid. The acid is then recrystd and vacuum dried.

Succinic anhydride [108-30-5] M 100.1, m 119-120°. Crystd from redistd acetic anhydride or CHCl<sub>3</sub>, then filtered, washed with diethyl ether and dried under vacuum.

Succinimide [123-56-8] M 99.1, m 124-125°, pK<sup>25</sup> 9.62. Crystd from EtOH (1mL/g) or water.

Succinonitrile [110-61-2] M 80.1, m 57.9°, b 108°/1mm, 267°/760mm. Purified by vacuum sublimation, also crystd from acetone.

D(+)-Sucrose ( $\beta$ -D-fructofuranosyl- $\alpha$ -D-glucopyranoside) [57-50-1] M 342.3, m 160-186°, 186-188°,  $[\alpha]_{546}^{20}$  +78° (c 10, H<sub>2</sub>O),  $[\alpha]_D^{20}$  + 66° (c 26, H<sub>2</sub>O), pK 12.62. Crystd from water (solubility: 1g in 0.5mL H<sub>2</sub>O at 20°, 1g in 0.2mL in boiling H<sub>2</sub>O). Sol in EtOH (0.6%) and MeOH (1%). Sucrose diacetate hexaisobutyrate is purified by melting and, while molten, treated with NaHCO<sub>3</sub> and charcoal, then filtered.

**D-Sucrose octaacetate** [126-14-7] **M 678.6, m 83-85°,**  $[\alpha]_{546}^{20}$  +70° (c 1, CHCl<sub>3</sub>). Crystd from EtOH.

Sudan I (Solvent Yellow 14, 1-phenylazo-2-naphthol) [824-07-9] M 248.3, m 135°, CI 12055, λmax 476nm, pK<sub>Est</sub> ~9.0. Crystd from EtOH.

Sudan III [Solvent Red 23, 1-(p-phenylazo-phenylazo)-2-naphthol] [85-86-9] M 352.4, m 199°(dec), CI 26100,  $\lambda_{max}$  354, 508 nm, pK<sub>Est</sub> ~9.0. Crystd from EtOH, EtOH/water or \*benzene/abs EtOH (1:1).

Sudan IV [Solvent Red 24, 1-(4-o-tolylazo-o-tolylazo)-2-naphthol] [85-83-6] M 380.5, m  $\sim 184^{\circ}(dec)$ , CI 26105,  $\lambda max$  520nm, pK<sub>Est</sub> ~9.0. Crystd from EtOH/water or acetone/water.

Sulfaguanidine [57-67-0] M 214.2, m 189-190°, pK<sub>1</sub> 0.48, pK<sub>2</sub> 2.75. Crystd from hot water (7mL/g).

Sulfamethazine [57-68-1] M 278.3, m 198-200°, pK1 2.65, pK2 7.4. Crystd from dioxane.

Sulfanilamide (*p*-aminobenzenesulfonamide) [63-74-1] M 172.2, m 166°,  $pK_1^{20}$  2.30,  $pK_2^{20}$  10.26. Crystd from water or EtOH.

Sulfanilic acid (4-aminobenzenesulfonic acid) [121-57-3] M 173.2,  $pK_1^{25} < 1$ ,  $pK_2^{25} 3.23$ . Crystd (as dihydrate) from boiling water. Dried at 105° for 2-3h, then over 90% H<sub>2</sub>SO<sub>4</sub> in a vacuum desiccator.

Sulfapyridine [144-83-2] M 349.2, m 193°, pK<sup>20</sup> 8.64. Crystd from 90% acetone and dried at 90°.

o-Sulfobenzoic acid (H<sub>2</sub>O) [123333-68-6 (H<sub>2</sub>O); 632-25-7] M 202.2, m 68-69°,  $pK_{Est(1)} < 1$ ,  $pK_{Est(2)} \sim 3.1$  (CO<sub>2</sub>H). Crystd from water.

o-Sulfobenzoic acid (monoammonium salt) [6939-89-5] M 219.5. Crystd from water.

o-Sulfobenzoic anhydride [81-08-3] M 184.2, m 128°, b 184-186°/18mm. See also 2,1benzoxathiol-3-one-1,1-dioxide on p. 126.

Sulfolane (tetramethylenesulfone) [126-33-0] M 120.2, m 28.5°, b 153-154°/18 mm, 285°/760 mm, d 1.263, n<sup>30</sup> 1.4820. Prepared commercially by Diels-Alder reaction of 1,3-butadiene and sulfur dioxide, followed by Raney nickel hydrogenation. The principle impurities are water, 3-sulfolene, 2-sulfolene and 2-isopropyl sulfolanyl ether. It is dried by passage through a column of molecular sieves. Distd

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under reduced pressure through a column packed with stainless steel helices. Again dried with molecular sieves and distd. [Cram et al. J Am Chem Soc 83 3678 1961; Coetzee Pure Appl Chem 49 211 1977.]

Also, it was stirred at  $50^{\circ}$  and small portions of solid KMnO<sub>4</sub> were added until the colour persisted during 1h. Dropwise addition of MeOH then destroyed the excess KMnO<sub>4</sub>, the soln was filtered, freed from potassium ions by passage through an ion-exchange column and dried under vacuum. It has also been vacuum distd from KOH pellets. It is hygroscopic. [See Sacco et al. J Phys Chem 80 749 1976; J Chem Soc, Faraday Trans 1 73 1936 1977; 74 2070 1978; Trans Faraday Soc 62 2738 1966.] Coetzee has reviewed the methods of purification of sulfolane, and also the removal of impurities. [Coetzee in Recommended Methods of Purification of Solvents and Tests for Impurities, Coetzee Ed. Pergamon Press, 1982.]

5-Sulfosalicylic acid [5965-83-3] M 254.2, m 108-110°,  $pK_1^{25} < 0$ ,  $pK_2^{25} 2.67$ ,  $pK_3^{25} 11.67$ . Crystd from water. Alternatively, it was converted to the monosodium salt which was crystd from water and washed with a little water, EtOH and then diethyl ether. The free acid was recovered by acidification.

Syringaldehyde (3,5-dimethoxy-4-hydroxybenzaldehyde) [134-96-3] M 182.2, m 113°, pK<sub>Est</sub> ~8. Crystd from pet ether.

Syringic acid (3,5-dimethoxy-4-hydroxybenzoic acid) [530-57-4] M 198.2, m 204-205°, 206.5°, 206-209°, 209-210°,  $pK_1^{25}$  4.34,  $pK_2^{25}$  9.49. Recrystd from H<sub>2</sub>O using charcoal [Bogert and Coyne J Am Chem Soc 51 571 1929; Anderson and Nabenhauer J Am Chem Soc 48 3001 1926.] The methyl ester has m 107° (from MeOH), the 4-acetyl derivative has m 190° and the 4-benzoyl derivative has m 229-232°. [Hahn and Wassmuth Chem Ber 67 2050 1934; UV: Lemon J Am Chem Soc 69 2998 1947 and Pearl and Beyer J Am Chem Soc 72 1743 1950.]

**D(-)-Tagatose** [87-81-0] **M 180.2, m 134-135°, [α]<sub>546</sub> -6.5° (c 1, H<sub>2</sub>O).** Crystd from aqueous EtOH.

*d*- Tartaric acid [147-71-7] M 150.1, m 169.5-170° (2S,3S-form, natural)  $[\alpha]_{546}^{20}$  -15° (c 10, H<sub>2</sub>O); m 208° (2RS,3RS-form), pK<sub>1</sub><sup>25</sup> 3.03, pK<sub>2</sub><sup>25</sup> 4.46, pK<sub>3</sub><sup>25</sup> 14.4. Crystd from distilled H<sub>2</sub>O or \*benzene/diethyl ether containing 5% of pet ether (b 60-80°) (1:1). Soxhlet extraction with diethyl ether has been used to remove an impurity absorbing at 265nm. It has also been crystd from absolute EtOH/hexane, and dried in a vacuum for 18h [Kornblum and Wade J Org Chem 52 5301 1987].

*meso*-Tartaric acid [147-73-9] M 150.1, m 139-141°,  $pK_1^{25}$  3.17,  $pK_2^{25}$  4.91. Crystd from water, washed with cold MeOH and dried at 60° under vacuum.

**Taurocholic acid** [81-24-3] M 515.6, m 125°(dec),  $[\alpha]_D$  +38.8 (c 2, EtOH), pK 1.4. Crystd from EtOH/diethyl ether.

Terephalaldehyde [623-27-8] M 134.1, m 116°, b 245-248°/771mm. Crystd from water.

Terephthalic acid (benzene-1,4-dicarboxylic acid) [100-21-0] M 166.1, m sublimes >300° without melting,  $pK_1^{20}$  3.4,  $pK_2^{20}$  4.34. Purified via the sodium salt which, after crystn from water, was reconverted to the acid by acidification with mineral acid.

Terephthaloyl chloride [100-20-9] M 203.0, m 80-82°. Crystd from dry hexane.

o-Terphenyl [84-15-1] M 230.3, m 57-58°. Crystd from EtOH. Purified by chromatography of  $CCl_4$  solns on alumina, with pet ether as eluent, followed by crystn from pet ether (b 40-60°) or pet ether/\*benzene. They can also be distd under vacuum.

m-Terphenyl [92-06-8] M 230.3, m 88-89°. Purification as for o-terphenyl above.

*p*-Terphenyl [92-94-4] M 230.3, m 212.7°. Crystd from nitrobenzene or trichlorobenzene. It was purified by chromatography on alumina in a darkened room, using pet ether, and then crystallizing from pet ether (b 40-60°) or pet ether/\*benzene.

**Terpin hydrate** [2451-01-6] **M 190.3, m 105.5°** (cis), 156-158° (trans). Crystd from H<sub>2</sub>O or EtOH.

2,2':6',2"-Terpyridyl (2,2':6',2"-terpyridyl) [1148-79-4] M 233.3, m 91-92°,  $pK_1^{23}$  2.64,  $pK_2^{23}$  4.33. Crystd from diethyl ether, toluene or from pet ether, then aqueous MeOH, followed by vacuum sublimation at 90°.

Terreic acid (2-hydroxy-3-methyl-1,4-benzoquinone-5,6-epoxide) [121-40-4] M 154.1, m 127-127.5°,  $[\alpha]_D^{22}$ +74° (pH 4, phosphate buffer), -17° (CHCl<sub>3</sub>), pK 4.5. Crystd from \*benzene or hexane. Sublimed *in vacuo*.

**Terthiophene** (2,5-di[thienyl]thiophene;  $\alpha$ -terthienyl) [1081-34-1] M 248.4, m 94-95.5°, 94-96°. Possible impurities are bithienyl and polythienyls. Suspend in H<sub>2</sub>O and steam distil to remove bithienyl. The residue is cooled and extracted with CHCl<sub>3</sub>, dried (MgSO<sub>4</sub>), filtered, evaporated and the residue chromatographed on Al<sub>2</sub>O<sub>3</sub> using pet ether-3% Me<sub>2</sub>CO as eluant. The terphenyl zone is then eluted from the Al<sub>2</sub>O<sub>3</sub> with Et<sub>2</sub>O, the extract is evaporated and the residue is recrystd from MeOH (40mL per g). The platelets are washed with cold MeOH and dried in air. [UV: Sease and Zechmeister J Am Chem Soc 69 270 1947; Uhlenbroek and Bijloo Recl Trav Chim Pays-Bas 79 1181 1960.] See also entry on p. 568 in Chapter 6.

**Testosterone** [58-22-0] **M 288.4, m 155°,**  $[\alpha]_{546}^{20}$  +130° (c 1, dioxane). Crystd from aq acetone.

**Testosterone propionate** [57-85-2] **M 344.5, m 118-122°,**  $[\alpha]_{546}^{20}$  +100° (c 1, dioxane). Crystd from aqueous EtOH.

2,4,5,6-Tetraaminopyrimidine sulfate [5392-28-9] M 238.2, m 255° (dec), >300°, >350° (dec), pK<sup>20</sup> 6.82. Purified by recrystn from H<sub>2</sub>O, 2N H<sub>2</sub>SO<sub>4</sub> (20 parts, 67% recovery) or 0.1N H<sub>2</sub>SO<sub>4</sub> (40 parts, 62% recovery), and dried in air. [UV: Konrad and Pfleiderer Chem Ber 103 722 1970; Malletta et al. J Am Chem Soc 69 1814 1947; Cavalieri et al. J Am Chem Soc 70 3875 1948.]

Tetra-*n*-amylammonium bromide [866-97-7] M 378.5, m 100-101°. Crystd from pet ether, \*benzene or acetone/ether mixtures and dried in vacuum at 40-50° for 2 days.

**Tetra-***n***-amylammonium iodide** [2498-20-6] **M 425.5, m 135-137°.** Crystd from EtOH and dried at 35° under vac. Also purified by dissolving in acetone and pptd by adding diethyl ether; and dried at 50° for 2 days.

1,4,8,11-Tetraazacyclotetradecane [295-37-4] M 200.33, m 173° (closed capillary and sublimes at 125°), 183-185°,  $pK_{Est(1)}$ ~3.8,  $pK_{Est(2)}$ ~6.0,  $pK_{Est(3)}$ ~9.0,  $pK_{Est(4)}$ ~9.6. Purified by recrystn from dioxane (white needles) and sublimes above 120°. It has been distilled, b 132-140°/4-8mm. It forms complexes with metals and gives a sparingly soluble nitrate salt, m 205° (dec), which crystallises from H<sub>2</sub>O and is dried at 150°. [UV: Bosnich et al. *Inorg Chem* 4 1102 *1963*, van Alphen *Recl Trav Chim Pays-Bas* 56 343 *1937*.]

Tetrabenazine(2-0x0-3-isobutyl-9,10-dimethoxy-1,2,3,4,6,7,-hexahydro-11bH-benzo[a]-quinolizine)[58-46-8]M 317.4, m 127-128°, pK<sub>Est</sub> ~ 8. Crystd from MeOH. The hydrochloridehas m 208-210° and the oxime has m 158° (from EtOH).

**1,1,2,2,-Tetrabromoethane** [79-27-6] M 345.7, f 0.0°, b 243.5°, d 2.965, n 1.63533. Washed successively with conc  $H_2SO_4$  (three times) and  $H_2O$  (three times), dried with  $K_2CO_3$  and CaSO<sub>4</sub> and distd.

**Tetra-n-butylammonium bromide** [1643-19-2] M 322.4, m 119.6°. Crystd from \*benzene (5mL/g) at 80° by adding hot *n*-hexane (three volumes) and allowing to cool. Dried over  $P_2O_5$  or Mg(ClO<sub>4</sub>)<sub>2</sub>, under vacuum. The salt is very hygroscopic. It can also be crystd from ethyl acetate or dry acetone by adding diethyl ether and dried *in vacuo* at 60° for 2 days. It has been crystd from acetone by addition of diethyl ether. So hygroscopic that all manipulations should be carried out in a dry-box. Purified by precipitation of a saturated solution in dry CCl<sub>4</sub> by addition of cyclohexane or by recrystallisation from ethyl acetate, then heating in vacuum to 75° in the presence of  $P_2O_5$ . [Symons et al. J Chem Soc, Faraday Trans 1 76 2251 1908.] Also recrystallised from CH<sub>2</sub>Cl<sub>2</sub>/diethyl ether and dried in a vacuum desiccator over  $P_2O_5$ . [Blau and Espenson J Am Chem Soc 108 1962 1986.]

**Tetra**-*n*-butylammonium chloride [1112-67-0] M 277.9, m 15.7°. Crystd from acetone by addition of diethyl ether. Very hygroscopic and forms crystals with  $34H_2O$ .

Tetra-*n*-butylammonium fluoroborate [429-42-5] M 329.3, m 161-163°. See tetrabutylammonium fluoroborate on p. 480 in Chapter 5.

**Tetra-n-butylammonium hexafluorophosphate** [3109-63-5] **M 387.5, m 239-241°.** Recrystd from satd EtOH/water and dried for 10h in vac at 70°. It was also recrystd three times from abs EtOH and dried for 2 days in a drying pistol under vac at boiling toluene temperature [Bedard and Dahl J Am Chem Soc 108 5933 1986].

Tetra-n-butylammonium hydrogen sulfate [32503-27-8] M 339.5, m 171-172°. Crystd from acetone.

**Tetra-***n***-butylammonium iodide** [311-28-4] M 369.4, m 146°. Crystd from toluene/pet ether (see entry for the corresponding bromide), acetone, ethyl acetate, EtOH/diethyl ether, nitromethane, aq EtOH or water. Dried at room temperature under vac. It has also been dissolved in MeOH/acetone (1:3, 10mL/g), filtered and allowed to stand at room temperature to evaporate to *ca* half its original volume. Distilled water (1mL/g) was then added, and the ppte was filtered off and dried. It was also dissolved in acetone, ppted by adding ether and dried in vac at 90° for 2 days. It has also been recrystallised from CH<sub>2</sub>Cl<sub>2</sub>/pet ether or hexane, or anhydrous methanol and stored in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub>. [Chau and Espenson J Am Chem Soc 108 1962 1986.]

**Tetra-***n***-butylammonium nitrate** [1941-27-1] **M 304.5, m 119°.** Crystd from \*benzene (7mL/g) or EtOH, dried in a vacuum over  $P_2O_5$  at 60° for 2 days.

**Tetra-n-butylammonium perchlorate** [1923-70-2] **M 341.9°, m 210°(dec).** Crystd from EtOH, ethyl acetate, from *n*-hexane or diethyl ether/acetone mixture, ethyl acetate or hot  $CH_2Cl_2$ . Dried in vacuum at room temperature over  $P_2O_5$  for 24h. [Anson et al. J Am Chem Soc 106 4460 1984; Ohst and Kochi J Am Chem Soc 108 2877 1986; Collman et al. J Am Chem Soc 108 2916 1986; Blau and Espenson J Am Chem Soc 108 1962 1986; Gustowski et al. J Am Chem Soc 108 1986; Ikezawa and Kutal J Org Chem 52 3299 1987.]

**Tetra-***n***-butylammonium picrate** [914-45-4] **M 490.6, m 89°.** Crystd from EtOH. Dried in a vacuum desiccator over  $P_2O_5$ .

**Tetra-n-butylammonium tetrabutylborate**  $(Bu_4N^+ Bu_4B^-)$  [23231-91-6] M 481.7, m 109.5°. Dissolved in MeOH or acetone, and crystd by adding distd water. Dried in vacuum at 70°. It has also been successively recrystd from isopropyl ether, isopropyl ether/acetone (50:1) and isopropyl ether/EtOH (50:1) for 10h, then isopropyl ether/acetone for 1h, and dried at 65° under reduced pressure for 1 week. [Kondo et al. J Chem Soc, Faraday Trans 1 76 812 1980.]

2,3,4,5-Tetrachloroaniline [634-83-3] M 230.9, m 119-120°, pK<sub>Est</sub> ~-0.26. Crystd from EtOH.

2,3,5,6-Tetrachloroaniline [3481-20-7] M 230.9, m 107-108°, pK<sub>Est</sub> ~-1.8. Crystd from EtOH.

**1,2,3,4-Tetrachlorobenzene** [634-66-2] **M 215.9, m 45-46°, b 254°/760mm.** Crystd from EtOH.

1,2,3,5-Tetrachlorobenzene [634-90-2] M 215.9, m 51°, b 246°/760mm. Crystd from EtOH.

1,2,4,5-Tetrachlorobenzene [95-94-3] M 215.9, m 139.5-140.5°, b 240°/760mm. Crystd from EtOH, ether, \*benzene, \*benzene/EtOH or carbon disulfide.

3,4,5,6-Tetrachloro-1,2-benzoquinone [2435-53-2] M 245.9, m 130°. Crystd from AcOH. Dry in vacuum desiccator over KOH.

1,1,2,2-Tetrachloro-1,2-difluoroethane [72-12-0] M 203.8, f 26.0°, b 92.8°/760 mm. Purified as for trichlorotrifluoroethane.

sym-Tetrachloroethane [79-34-5] M 167.9, b  $62^{\circ}/100$  mm, 146.2°/atm, d 1.588, n<sup>15</sup> 1.49678. Stirred, on a steam-bath, with conc H<sub>2</sub>SO<sub>4</sub> until a fresh portion of acid remained colourless. The organic phase was then separated, distd in steam, dried (CaCl<sub>2</sub> or K<sub>2</sub>CO<sub>3</sub>), and fractionally distd in a vac.

**Tetrachloroethylene** [127-18-4] M 165.8, b 62°/80mm, 121.2°, d<sup>15</sup> 1.63109, d 1.623, n<sup>15</sup> 1.50759, n 1.50566 It decomposes under similar conditions to CHCl<sub>3</sub>, to give phosgene and trichloroacetic acid. Inhibitors of this reaction include EtOH, diethyl ether and thymol (effective at 2-5ppm). Tetrachloroethylene should be distd under a vac (to avoid phosgene formation), and stored in the dark out of contact with air. It can be purified by washing with 2M HCl until the aq phase no longer becomes coloured, then with water, drying with Na<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>SO<sub>4</sub>, CaCl<sub>2</sub> or P<sub>2</sub>O<sub>5</sub>, and fractionally distilling just before use. 1,1,2-Trichloroethane and 1,1,1,2-tetrachloroethane can be removed by counter-current extraction with EtOH/water.

Tetrachloro-N-methylphthalimide [14737-80-5] M 298.9, m 209.7°. Crystd from absolute EtOH.

2,3,4,6-Tetrachloronitrobenzene [879-39-0] M 260.9, m 42°. Crystd from aqueous EtOH.

2,3,5,6-Tetrachloronitrobenzene [117-18-0] M 260.9, m 99-100°. Crystd from aqueous EtOH.

2,3,4,5-Tetrachlorophenol [4901-51-3] M 231.9, m 116-117°, pK<sub>Est</sub> ~6.2. Crystd from pet ether.

2,3,4,6-Tetrachlorophenol [58-90-2] M 231.9, m 70°, b 150°/15mm, pK<sub>Est</sub> ~5.4. Crystd from pet ether.

2,3,5,6-Tetrachlorophenol [935-95-5] M 231.9, m 115°, pK<sub>Est</sub> ~5.0. Crystd from pet ethers.

**Tetrachlorophthalic anhydride** [117-08-8] **M 285.9, m 255-257°.** Crystd from chloroform or \*benzene, then sublimed.

2,3,4,6-Tetrachloropyridine [14121-36-9] M 216.9, m 74-75°, b 130-135°/16-20mm, pK<sub>Est</sub> ~-5.7. Crystd from 50% EtOH.

Tetracosane [646-31-1] M 338.7, m 54°, b 243-244°/15mm. Crystd from diethyl ether.

Tetracosanoic (lignoceric) acid [557-59-5] M 368.7, m 84°, 87.5-88°,  $pK_{Est}$  ~5.0. Crystd from acetic acid, Me<sub>2</sub>CO, toluene, pet ether/Me<sub>2</sub>CO, \*C<sub>6</sub>H<sub>6</sub>/Me<sub>2</sub>CO.

**1,2,4,5-Tetracyanobenzene** [712-74-3] **M 178.1, m 270-272° (280°).** Crystd from EtOH and sublimed *in vacuo*. [Lawton and McRitchie J Org Chem **24** 26 1959; Bailey et al. Tetrahedron **19** 161 1963.]

**Tetracyanoethylene** [670-54-2] **M 128.1, m 199-200**<sup>o</sup> (sealed tube). Crystd from chlorobenzene, dichloroethane, or dichloromethane [Hall et al. J Org Chem 52 5528 1987]. Stored at 0<sup>o</sup> in a desiccator over NaOH pellets. (It slowly evolves HCN on exposure to moist air.) It can also be sublimed at 120<sup>o</sup> under vacuum. Also purified by repeated sublimation at 120-130<sup>o</sup>/0.5mm. [Frey et al. J Am Chem Soc 107 748 1985; Traylor and Miksztal J Am Chem Soc 109 2778 1987.]

7,7,8,8-Tetracyanoquinodimethane [1518-16-7] M 204.2, m 287-290°(dec). Recrystd from distd, dried, acetonitrile.

**Tetradecane** [629-59-4] **M 198.4, m 6°, b 122°/10mm, 252-254°, d 0.763, n 1.429.** Washed successively with 4M  $H_2SO_4$  and water. Dried over MgSO<sub>4</sub> and distd several times under reduced pressure [Poë et al. J Am Chem Soc 108 5459 1986].

1-Tetradecanol [112-72-1] M 214.4, m 39-39.5°, b 160°/10mm, 170-173°/20mm. Crystd from aq EtOH. Purified by zone melting.

**Tetradecyl ether (di-tetradecyl ether)** [5412-98-6] **M 410.7.** Distd under vac and then crystd repeatedly from MeOH/\*benzene.

**Tetradecyltrimethylammonium bromide** [1119-97-7] **M 336.4, m 244-249°.** Crystd from acetone or a mixture of acetone and >5% MeOH. Washed with diethyl ether and dried in a vacuum oven at 60°. [Dearden and Wooley J Phys Chem **91** 2404 1987.]

Tetraethoxymethane [78-09-1] M 192.3, b 159°. See tetraethyl orthocarbonate on p. 360.

**Tetraethylammonium bromide** [71-91-0] **M 210.2, m 269°(dec), 284°(dec).** Recrystd from EtOH, CHCl<sub>3</sub> or diethyl ether, or, recrystd from acetonitrile, and dried over  $P_2O_5$  under reduced pressure for several days. Also recrystd from EtOH/diethyl ether (1:2), EtOAc, water or boiling MeOH/acetone (1:3) or by adding equal volume of acetone and allowing to cool. Dried at 100° in vacuo for 12 days, and stored over  $P_2O_5$ .

**Tetraethylammonium chloride hydrate** [56-34-8] **M 165.7, m dec>200°.** Crystd from EtOH by adding diethyl ether, from warm water by adding EtOH and diethyl ether, from dimethylacetamide or from  $CH_2Cl_2$  by addition of diethyl ether. Dried over  $P_2O_5$  in vacuum for several days. Also crystd from acetone/ $CH_2Cl_2$ /hexane (2:2:1) [Blau and Espenson J Am Chem Soc 108 1962 1986; White and Murray J Am Chem Soc 109 2576 1987].

**Tetraethylammonium iodide** [68-05-3] **M 257.2, m 302°,** >**300°(dec).** Crystd from acetone/MeOH, EtOH/water, dimethylacetamide or ethyl acetate/EtOH (19:1). Dried under vacuum at 50° and stored over  $P_2O_5$ .

**Tetraethylammonium perchlorate** [2567-83-1] **M 229.7, m 345°(dec).** Crystd repeatedly from water, aqueous MeOH, acetonitrile or acetone, and dried at 70° under vacuum for 24h. [Cox et al. J Am Chem Soc 106 5965 1984; Liu et al. J Am Chem Soc 108 1740 1986; White and Murray J Am Chem Soc 109 2576 1987.] Also twice crystd from ethyl acetate/95% EtOH (2:1) [Lexa et al. J Am Chem Soc 109 6464 1987].

**Tetraethylammonium picrate** [741-03-7] **M 342.1, m >300°(dec).** Purified by successive crystns from water or 95% EtOH followed by drying in vacuum at 70°.

Tetraethylammonium tetrafluoroborate [429-06-1] M 217.1, m 235°, 275-277°, 289-291°. Recrystd three times from a mixture of ethyl acetate/hexane (5:1) or MeOH/pet ether, then stored at 95° for 48h under vacuum [Henry and Faulkner J Am Chem Soc 107 3436 1985; Huang et al. Anal Chem 58 2889 1986]. See entry on p. 481 in Chapter 5.

**Tetraethylammonium tetraphenylborate** [12099-10-4] **M 449.4.** Recrystd from aqueous acetone. Dried in a vacuum oven at 60° for several days. Similarly for the propyl and butyl homologues.

**Tetraethyl 1,1,2,2-ethanetetracarboxylate** [632-56-4] **M 318.3, m 73-74°.** Twice recrystd from EtOH by cooling to 0°.

Tetraethylene glycol dimethyl ether [143-24-8] M 222.3, b 105°/1mm, d 1.010, n 1.435. Stood with CaH<sub>2</sub>, LiAlH<sub>4</sub> or sodium, and distd when required.

**Tetraethylenepentamine** [112-57-2] M 189.3, b 169-171°/0.05mm, d 0.999, n 1.506,  $pK_1^{25}$ 2.98,  $pK_2^{25}$  4.72,  $pK_3^{25}$  8.08,  $pK_4^{25}$  9.10,  $pK_5^{25}$  9.68. Distd under vacuum. Purified via its pentachloride, nitrate or sulfate. Jonassen, Frey and Schaafsma [J Phys Chem 61 504 1957] cooled a soln of 150g of the base in 300mL of 95% EtOH, and added dropwise 180mL of conc HCl, keeping the temperature below 20°. The white ppte was filtered, crystd three times from EtOH/water, then washed with diethyl ether and dried by suction. Reilley and Holloway [J Am Chem Soc 80 2917 1958], starting with a similar soln cooled to 0°, added slowly (keeping the temperature below 10°) a soln of 4.5g-moles of HNO<sub>3</sub> in 600mL of aqueous 50% EtOH (also cooled to 0°). The ppte was filtered by suction, recrystd five times from aqueous 5% HNO<sub>3</sub>, then washed with acetone and absolute EtOH and dried at 50°. [For purification via the sulfate see Reilley and Vavoulis (Anal Chem 31 243 1959), and for an additional purification step using the Schiff base with benzaldehyde see Jonassen et al. J Am Chem Soc 79 4279 1957].

Tetraethyl orthocarbonate (ethyl orthocarbonate, tetraethoxy ethane) [78-09-1] M 192.3, b 59.6-60°/14mm, 158°/atm, 159°/atm, 160-161°/atm,  $d_4^{20}$  0.9186,  $n_D^{20}$  1.3932. Likely impurities are hydrolysis products. Shake with brine (satd NaCl; dilute with a little Et<sub>2</sub>O if amount of material is small) and dry (MgSO<sub>4</sub>). The organic layer is filtered off and evaporated, and the residue is distd through a helices packed fractionating column with a total reflux partial take-off head. All distns can be done at atmospheric pressure in an inert atmosphere (e.g. N<sub>2</sub>). [Roberts and McMahon Org Synth Coll Vol IV 457 1963; Connolly and Dyson J Chem Soc 828 1937; Tieckelmann and Post J Org Chem 13 266 1948.]

1,1,2,2-Tetrafluorocyclobutane [374-12-9] M 128.1, b 50-50.7°, d 1.275, n 1.3046. Purified distn or by preparative gas chromatography using a 2m x 6mm(i.d.) column packed with B,B'oxydipropionitrile on Chromosorb P at 33°. [Conlin and Fey J Chem Soc, Faraday Trans 1 76 322 1980; Coffmann et al. J Am Chem Soc 71 490 1949.]

**Tetrafluoro-1,3-dithietane** [1717-50-6] **M 164.1, m -6°, b 47-48°/760mm, d<sup>25</sup> 1.6036, n<sup>25</sup> 1.3908.** Purified by preparative gas chromatography or by distn through an 18in spinning band column. Also purified by shaking vigorously *ca* 40mL with 25mL of 10% NaOH, 5mL of 30% H<sub>2</sub>O<sub>2</sub> until the yellow colour disappeared The larger layer was separated, dried over silica gel to give a colourless liquid boiling at 48°. It had a singlet at -1.77ppm in the NMR spectrum. [Middleton, Howard and Sharkey, *J Org Chem* **30** 1375 *1965.*]

**2,2,3,3-Tetrafluoropropanol** [76-37-9] **M** 132.1, **b** 106-106.5°,  $pK^{25}$  12.74. Tetrafluoropropanol (450mL) was added to a soln of 2.25g of NaHSO<sub>3</sub> in 90mL of water, shaken vigorously and stood for 24h. The fraction distilling at or above 99° was refluxed for 4h with 5-6g of KOH and rapidly distd, followed by a final fractional distn. [Kosower and Wu *J Am Chem Soc* 83 3142 *1961.*] Alternatively, shaken with alumina for 24h, dried overnight with anhydrous K<sub>2</sub>CO<sub>3</sub> and distd, taking the middle fraction (b 107-108°).

**Tetera-n-heptylammonium bromide** [4368-51-8] **M 490.7, m 89-91°.** Crystd from *n*-hexane, then dried in a vacuum oven at 70°.

Tetra-n-heptylammonium iodide [3535-83-9] M 537.7. Crystd from EtOH.

Tetra-*n*-hexylammonium bromide [4328-13-6] M 434.6, m 99-100°. Washed with ether, and dried in a vacuum at room temperature for 3 days.

Tetra-n-hexylammonium chloride [5922-92-9] M 390.1. Crystd from EtOH.

Tetra-*n*-hexylammonium iodide [2138-24-1] M 481.6, m 99-101°. Washed with diethyl ether and dried at room temperature *in vacuo* for 3 days.

Tetrahexylammonium perchlorate [4656-81-9] M 454.1, m 104-106°. Crystd from acetone and dried *in vacuo* at 80° for 24h.

**Tetrahydrofuran** [109-99-9] M 72.1, b 25°/176mm, 66°/760mm,  $d_4^{20}$  0.889,  $n_D^{20}$  1.4070, pK -2.48 (aq H<sub>2</sub>SO<sub>4</sub>). It is obtained commercially by catalytic hydrogenation of furan from pentosancontaining agricultural residues. It was purified by refluxing with, and distilling from LiAlH<sub>4</sub> which removes water, peroxides, inhibitors and other impurities [Jaeger et al. J Am Chem Soc 101 717 1979]. Peroxides can also be removed by passage through a column of activated alumina, or by treatment with aq ferrous sulfate and sodium bisulfate, followed by solid KOH. In both cases, the solvent is then dried and fractionally distd from sodium. Lithium wire or vigorously stirred molten potassium have also been used for this purpose. CaH<sub>2</sub> has also been used as a drying agent.

Several methods are available for obtaining the solvent almost anhydrous. Ware [J Am Chem Soc 83 1296 1961] dried vigorously with sodium-potassium alloy until a characteristic blue colour was evident in the solvent at Dry-ice/cellosolve temperatures. The solvent was kept in contact with the alloy until distd for use. Worsfold and Bywater [J Chem Soc 5234 1960], after refluxing and distilling from P<sub>2</sub>O<sub>5</sub> and KOH, in turn, refluxed the solvent with sodium-potassium alloy and fluorenone until the green colour of the disodium salt of fluorenone was well established. [Alternatively, instead of fluorenone, benzophenone, which forms a blue ketyl, can be used.] The tetrahydrofuran was then fractionally distd, degassed and stored above CaH<sub>2</sub>. *p*-Cresol or hydroquinone inhibit peroxide formation. The method described by Coetzee and Chang [*Pure Appl Chem* 57 633 1985] for 1,4-dioxane also applies here. Distns should always be done in the presence of a reducing agent, e.g. FeSO<sub>4</sub>. It irritates the skin, eyes and mucous membranes and the vapour should never be inhaled. It is HIGHLY FLAMMABLE and the necessary precautions should be taken. Rapid purification: Purification as for diethyl ether.

*l*-Tetrahydropalmatine (2,3,9,10-tetramethoxy-6*H*-dibenzo[a,g]quinolizidine) [10097-84-4] M 355.4, m 148-149°,  $[\alpha]_D^{20}$ -291° (EtOH). Crystd from MeOH by addition of water [see *J Chem Soc* (*C*) 530 1967].

**Tetrahydropyran** [142-68-7] **M 86.1, b 88.0°, n 1.4202, d 0.885, pK -2.79 (aq H\_2SO\_4).** Dried with CaH<sub>2</sub>, then passed through a column of silica gel to remove olefinic impurities and fractionally distd. Freed from peroxides and moisture by refluxing with sodium, then distilling from LiAlH<sub>4</sub>. Alternatively, peroxides can be removed by treatment with aqueous ferrous sulfate and sodium bisulfate, followed by solid KOH, and fractional distn from sodium.

**Tetrahydro-4***H***-pyran-4-one**  $\{29943-42-8\}$  **M 100.1, b 57-59°/11mm, 65-66°/15mm, 67-68°/18mm, 73°/20mm, 164.7°/atm, 166-166.5°/atm, d<sup>20</sup><sub>4</sub> 1.0844, n<sup>20</sup><sub>D</sub> 1.4551.** Purified by repeated distn preferably in a vacuum. [Baker *J Chem Soc* 296 *1944*; IR: Olsen and Bredoch *Chem Ber* **91** 1589 *1958*.] The oxime has **m** 87-88° and **b** 110-111°/13mm [Cornubert et al. *Bull Soc Chim Fr* 36 *1950*]. The 4-nitrophenylhydrazone forms orange-brown needles from EtOH, **m** 186° [Cawley and Plant *J Chem Soc* 1214 *1938*].

**Tetrahydrothiophene** [110-01-0] M 88.2, m -96°, b 14.5°/10mm, 120.9°/760mm, d 0.997, n 1.5289. Crude material was purified by crystn of the mercuric chloride complex to a constant melting point. It was then regenerated, washed, dried, and fractionally distd. [Whitehead et al. J Am Chem Soc 73 3632 1951.] It has been dried over Na<sub>2</sub>SO<sub>4</sub> and distd in a vacuum [Roberts and Friend J Am Chem Soc 108 7204 1986].

**Tetrahydro-4H-thiopyran-4-one** [1072-72-6] **M** 116.2, **m** 60-62°, 61-62°, 64-65°, 65-67°. Purified by recrystn from diisopropyl ether or pet ether and dried in air. If too impure then dissolve in Et<sub>2</sub>O, wash with aq NaHCO<sub>3</sub>, then H<sub>2</sub>O, dried (MgSO<sub>4</sub>), filtd, evapd and the residue recrystd as before. [Cardwell J Chem Soc 715 1949.] The oxime can be recrystd from CHCl<sub>3</sub>-pet ether (at -20°) and has **m** 84-85° [Barkenbus et al. J Org Chem 20 871 1955]. The 2,4-dinitrophenylhydrazone has **m** 186° (from EtOAc) [Barkenbus et al. J Org Chem 16 232 1951]. The S-dioxide is recrystd from AcOH, **m** 173-174° [Fehnel and Carmack J Am Chem Soc 70 1813 1948].

**Tetrahydroxy-***p***-benzoquinone (2H<sub>2</sub>O)** [5676-48-2] **M 208.1, pK\_1^{30} 4,80, pK\_2^{30} 6.8.** Crystd from water.

Tetrakis(dimethylamino)ethylene [996-70-3] M 300.2, b 60°/1mm, d 0.861, n 1.4817,  $pK_{Est(1)}<0$ ,  $pK_{Est(2)}<0$ ,  $pK_{Est(3)}\sim 1.5$ ,  $pK_{Est(4)}$  5.1. Impurities include tetramethylurea, dimethylamine, tetramethylethanediamine and tetramethyloxamide. It was washed with water while being flushed with nitrogen to remove dimethylamine, dried over molecular sieves, then passed through a silica gel column (previously activated at 400°) under nitrogen. Degassed on a vacuum line by distn from a trap at 50° to one at -70°. Finally, it was stirred over sodium-potassium alloy for several days. [Holroyd et al. J Phys Chem 89 4244 1985; Wiberg Angew Chem Int Ed Engl 7 766 1968.]

**Tetralin** (1,2,3,4-tetrahydronaphthalene) [119-64-2] M 132.2, b 65-66°/5mm, 207.6°/760 mm, d 0.968, n 1.5413. It was washed with successive portions of conc  $H_2SO_4$  until the acid layer no longer became coloured, then washed with aq 10% Na<sub>2</sub>CO<sub>3</sub>, and then distd water. Dried (CaSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>), filtered, refluxed and fractionally distd at under reduced pressure from sodium or BaO. It can also be purified by repeated fractional freezing.

Bass [J Chem Soc 3498 1964] freed tetralin, purified as above, from naphthalene and other impurities by conversion to ammonium tetralin-6-sulfonate. Conc  $H_2SO_4$  (150mL) was added slowly to stirred tetralin (272mL) which was then heated on a water bath for about 2h to give complete soln. The warm mixture, when poured into aq NH<sub>4</sub>Cl soln (120g in 400mL water), gave a white ppte which, after filtering off, was crystd from boiling water, washed with 50% aq EtOH and dried at 100°. Evapn of its boiling aq soln on a steam bath removed traces of naphthalene. The pure salt (229g) was mixed with conc  $H_2SO_4$  (266mL) and steam distd from an oil bath at 165-170°. An ether extract of the distillate was washed with aq Na<sub>2</sub>SO<sub>4</sub>, and the ether was evapd, prior to distilling the tetralin from sodium. Tetralin has also been purified *via* barium tetralin-6-sulfonate, conversion to the sodium salt and decomposition in 60%  $H_2SO_4$  using superheated steam.

Tetralin hydroperoxide [771-29-9] M 164.2, m 56°. Crystd from hexane.

 $\alpha$ -Tetralone (1,2,3,4-tetrahydro-1-oxonaphthalene) [529-34-0] M 146.2, m 2-7°, 7.8-8.0°, b 75-85°/0.3mm, 89°/0.5mm, 94-95°/2mm, 132-134°/15mm, 143-145°/20mm,  $d_4^{20}$  1.0695,  $n_D^{20}$  1.5665. Check the IR first. Purify by dissolving 20mL in Et<sub>2</sub>O (200mL), washing with H<sub>2</sub>O (100mL), 5% aq NaOH (100mL), H<sub>2</sub>O (100mL), 3% aq AcOH (100mL), 5% NaHCO<sub>3</sub> (100mL) then H<sub>2</sub>O (100mL) and dry the ethereal layer over MgSO<sub>4</sub>. Filter, evap and fractionate the residue through a 6in Vigreux column under reduced pres to give a colourless oil (~17g) with b 90-91°/0.5-0.7mm. [Snyder and Werber Org Synth Coll Vol III 798 1955.] It has also been fractionated through a 0.5metre packed column with a heated jacket under reflux using a partial take-off head. [Olson and Bader Org Synth Coll Vol IV 898 1963.]

β-Tetralone (1,2,3,4-tetrahydro-2-oxonaphthalene) [530-93-8] M 146.2, m 17-18°, ~18°, b 93-95°/2mm, 104-105°/4mm, 114-115°/4-5mm, 140°/18mm,  $d_4^{20}$  1.1000,  $n_D^{20}$  1.5598. If reasonably pure then fractionate through an efficient column. Otherwise purify via the bisulfite adduct. To a soln of NaHSO<sub>3</sub> (32.5g, 0.31mol) in H<sub>2</sub>O (57mL) is added 95% EtOH (18mL) and set aside overnight. Any bisulfite-sulfate that separated is removed by filtration and the filtrate is added to the tetralone (14.6g, 0.1mol) and shaken vigorously. The adduct separates in a few minutes as a white ppte and kept on ice for ~3.5h with occasional shaking. The ppte is collected, washed with 95% EtOH (13mL), then with Et<sub>2</sub>O (4 x 15mL, by stirring the suspension in the solvent, filtering and repeating the process). The colourless product is dried in air and stored in air tight containers in which it is stable for extended periods (yield is ~17g). This bisulfite (5g) is suspended in H<sub>2</sub>O (25mL) and Na<sub>2</sub>CO<sub>3</sub>.H<sub>2</sub>O (7.5g) is added (pH of soln is ~10). The mixture is then extracted

with Et<sub>2</sub>O (5 x 10mL, i.e. until the aqueous phase does not test for tetralone — see below). Wash the combined extracts with 10% aqueous HCl (10mL), H<sub>2</sub>O (10mL, i.e. until the washings are neutral), dry (MgSO<sub>4</sub>), filter, evaporate and distil the residual oil using Claisen flask under reduced pressure and in a N<sub>2</sub> atm. The pure tetralone is a colourless liquid b 70-71°/0.25mm (see also above). The yield is ~2g. Tetralone test: Dissolve a few drops of the tetralone soln (ethereal or aqueous) in 95% EtOH in a test tube and add 10 drops of 25% NaOH down the side of the tube. A deep blue colour develops at the interface with air. [Soffer Org Synth Coll Vol IV 903 1963; Cornforth et al. J Chem Soc 689 1942; UV: Soffer et al. J Am Chem Soc 1556 1952.] The phenylhydrazone has m 108° [Crawley and Robinson J Chem Soc 2001 1938].

Tetramethylammonium bromide [64-20-0] M 154.1, sublimes with dec >230°. Crystd from EtOH, EtOH/diethyl ether, MeOH/acetone, water or from acetone/MeOH (4:1) by adding an equal volume of acetone. It was dried at  $110^{\circ}$  under reduced pressure or at  $140^{\circ}$  for 24h.

**Tetramethylammonium chloride** [75-57-0] **M 109.6, m >230°(dec).** Crystd from EtOH, EtOH/CHCl<sub>3</sub>, EtOH/diethyl ether, acetone/EtOH (1:1), isopropanol or water. Traces of the free amine can be removed by washing with CHCl<sub>3</sub>.

**Tetramethylammonium hydroxide (5H<sub>2</sub>O)** [10424-65-4 (5H<sub>2</sub>O); 75-59-2 (aq soln) ] M **181.2, m** 63°, 65-68°. Freed from chloride ions by passage through an ion-exchange column (Amberlite IRA-400, prepared in its OH<sup>-</sup> form by passing 2M NaOH until the effluent was free from chloride ions, then washed with distilled H<sub>2</sub>O until neutral). A modification, to obtain carbonate-free hydroxide, uses the method of Davies and Nancollas [*Nature* **165** 237 1950].

**Tetramethylammonium iodide** [75-58-1] **M 201.1, m >230°(dec).** Crystd from water or 50% EtOH, EtOH/diethyl ether, ethyl acetate, or from acetone/MeOH (4:1) by adding an equal volume of acetone. Dried in a vacuum desiccator.

**Tetramethylammonium perchlorate** [2537-36-2] **M 173.6, m >300 °(dec).** Crystd from acetone and dried *in vacuo* at 60° for several days.

**Tetramethylammonium tetraphenylborate** [15525-13-0] **M 393.3.** Recrystd from acetone, acetone/CCl<sub>4</sub> and from acetone/1,2-dichloroethane. Dried over  $P_2O_5$  in vacuum, or in a vacuum oven at 60° for several days.

1,2,3,4-Teteramethylbenzene (prehnitine) [488-23-3] M 134.2, m -6.3°, b 79.4°/10 mm, 204-205°/760mm, d 0.905, n 1.5203. Dried over sodium and distd under reduced pressure.

1,2,3,5-Tetramethylbenzene (isodurene) [527-53-7] M 134.2, m -23.7°, b 74.4°/10 mm, 198°/760mm, d 0.890, n 1.5130. Refluxed over sodium and distd under reduced pressure.

1,2,4,5-tetramethylbenzene (durene) [95-93-2] M 134.2, m 79.5-80.5°. Chromatographed on alumina, and recrystd from aqueous EtOH or \*benzene. Zone-refining removes duroaldehydes. Dried under vacuum. [Yamauchi et al. J Phys Chem 89 4804 1985.] It has also been sublimed *in vacuo* [Johnston et al. J Am Chem Soc 109 1291 1987].

N, N, N', N'-Tetramethylbenzidine [366-29-0] M 240.4, m 195.4-195.6°, pK<sub>Est(1)</sub>~3.4, pK<sub>Est(2)</sub>~4.5. Crystd from EtOH or pet ether, then from pet ether/\*benzene, and sublimed in a vacuum. [Guarr et al. J Am Chem Soc 107 5104 1985.] Dried under vac in an Abderhalden pistol, or carefully on a vacuum line.

**2,2,4,4-Tetramethylcyclobutan-1,3-dione** [933-52-8] **M 140.2, m 114.5-114.9°.** Crystd from \*benzene and dried under vacuum over P<sub>2</sub>O<sub>5</sub> in an Abderhalden pistol.

3,3,5,5-Tetramethylcyclohexanone [14376-79-5] M 154.3, m 11-12°, 13.2°, b 59-61°, 80-82°/13mm, 196°/760mm, 203.8-204.8°/760mm,  $d_D^{20}$  0.8954,  $n_D^{20}$  1.4515. Purified first through a

24in column packed with Raschig rings then a 40cm Vigreux colum under reduced pressure (b 69-69.3°/7mm, see above). The oxime has m 144-145° (from 60% EtOH) and the semicarbazone has m 196-197°, 197-198° (214.5°, 217-218°) [Karasch and Tawney J Am Chem Soc 63 2308 1941; UV: Sandris and Ourisson Bull Soc Chim Fr 958 1956].

p, p'-Tetramethyldiaminodiphenylmethane [bis(p-dimethylaminophenyl)methane, Michler's base] [101-61-1] M 254.4, m 89-90°, b 155-157°/0.1mm, pK<sub>Est(1)</sub>~5.8, pK<sub>Est(2)</sub>~5.1. Crystd from EtOH (2mL/g) or 95% EtOH (*ca* 12mL/g). It sublimes on heating.

**Tetramethylene sulfoxide (tetrahydrothiophen 1-oxide)** [1600-44-8] M 104.2, b 235-237°, d 1.175, n 1.525. Shaken with BaO for 4 days, then distd from CaH<sub>2</sub> under reduced pressure.

*N*,*N*,*N'*,*N'*-**Tetramethylethylenediamine (TMEDA, TEMED)** [110-18-9] **M** 116.2, b 122°, d 1.175,  $n^{25}$  1.4153,  $pK_1^{25}$  5.90,  $pK_2^{25}$  9.14. Partially dried with molecular sieves (Linde type 4A), and distd in vacuum from butyl lithium. This treatment removes all traces of primary and secondary amines and water. [Hay, McCabe and Robb *J Chem Soc, Faraday Trans 1* 68 1 1972.] Or, dried with KOH pellets. Refluxed for 2h with one-sixth its weight of *n*-butyric anhydride (to remove primary and secondary amines) and fractionally distd. Refluxed with fresh KOH, and distd under nitrogen. [Cram and Wilson *J Am Chem Soc* 85 1245 1963.] Also distd from sodium.

Tetramethylethylenediamine dihydrochloride [7677-21-8] M 198.2, m ~300°. Crystd from 98% EtOH/conc HCl. Hygroscopic. [Knorr Chem Ber 37 3510 1904.]

1,1,3,3-Tetramethylguanidine [80-70-6] M 115.2, b 159-160°, d 0.917 n 1.470,  $pK^{25}$  13.6. Refluxed over granulated BaO, then fractionally distd.

*N*,*N*,*N*',*N*'-**Tetramethyl-1,8-naphthalenediamine** [20734-58-1] M 214.3, m 45-48°, 47-48°, b 144-145°/4mm, pK<sub>1</sub> -10.5 (aq H<sub>2</sub>SO<sub>4</sub>, diprotonation), pK<sub>2</sub> 12.34 (monoprotonation). It is prepared by methylating 1,8-diaminonaphthalene and likely impurities are methylated products. The tetramethyl compound is a stronger base than the unmethylated, di and trimethylated derivatives. The pKa values are: 1,8-(NH<sub>2</sub>)<sub>2</sub> = 4.61, 1,8-(NHMe)<sub>2</sub> = 5.61, 1-NHMe-8-NHMe<sub>2</sub> = 6.43 and 1,8-(NMe<sub>2</sub>)<sub>2</sub> = 12.34. The mixture is then treated H<sub>2</sub>O at pH 8 (where all but the required base are protonated) and extracted with Et<sub>2</sub>O or CHCl<sub>3</sub>. The dried extract (K<sub>2</sub>CO<sub>3</sub>) yields the tetramethyldiamine on evapn which can be distd. It is a strong base with weak nucleophilic properties, e.g. it could not be alkylated by refluxing with EtI in MeCN for 4 days and on treatment with methyl fluorosulfonate only the fluorosulfonate salt of the base is obtained. [NMR: Adler et al. *J Chem Soc, Chem Commun* 723 1968; *J Am Chem Soc* 63 358 1941.] See Proton sponge p. 134.

Tetramethyl orthocarbonate (methyl orthocarbonate, tetramethoxy methane) [1850-14-2] M 136.2, m -5.6°, -5°, -2°, b 113.5°/760mm, 113.5-114°/755mm, 112-114°/atm,  $d_4^{20}$  1.0202,  $n_D^{20}$  1.3860. Purified in the same way as for tetraethyl orthocarbonate. [Smith Acta Chem Scand 10 1006 1956; Tiekelmann and Post J Org Chem 13 266 1948.]

2,6,10,14-Tetramethylpentadecane (pristane, norphytane) [1921-70-6] M 268.5, b 68° (bath temp)/0.004mm, 158°/10mm, 296°/atm,  $d_4^{20}$  0.7827,  $n_D^{20}$  1.4385. Purified by shaking with conc H<sub>2</sub>SO<sub>4</sub> (care with this acid, if amount of pristane is too small then it should be diluted with pet ether *not* Et<sub>2</sub>O which is quite sol in the acid), the H<sub>2</sub>O (care as it may heat up if in contact with conc H<sub>2</sub>SO<sub>4</sub>), dried (MgSO<sub>4</sub>) evaporated and distd over Na metal. [Sörensen and Sörensen Acta Chem Scand 3 939 1949.]

N, N, N', N'-Tetramethyl-1,4-phenylenediamine [100-22-1] M 164.3, m 51°, b 260°/760mm, pK<sub>1</sub><sup>20</sup> 2.29, pK<sub>2</sub><sup>20</sup> 6.35. Crystd from pet ether or water. It can be sublimed or dried carefully in a vacuum line, and stored in the dark under nitrogen. Also recrystd from its melt.

N, N, N', N'-Tetramethyl-1,4-phenylenediamine dihydrochloride [637-01-4] M 237.2, m 222-224°. Crystd from isopropyl or *n*-butyl alcohols, satd with HCl. Treated with aq NaOH to give the free base which was filtered, dried and sublimed in a vacuum. [Guarr et al. J Am Chem Soc 107 5104 1985.]

2,2,6,6-Tetramethylpiperidinyl-1-oxy (TEMPO) [2564-83-2] M 156.3, m 36-38°. Purified by sublimation (33°, water aspirator) [Hay and Fincke J Am Chem Soc 109 8012 1987].

**2,2,6,6-Tetramethyl-4-piperidone hydrochloride** (triacetoneamine) [33973-59-0] M 191.7, m 190° (dec), 198-199° (dec),  $pK^{25}$  7.90. Purified by recrystn from EtOH/Et<sub>2</sub>O, MeCN or Me<sub>2</sub>CO/MeOH. The free base has m 37-39° (after sublimation), b 102-105°/18mm, and hydrate m 56-58° (wet Et<sub>2</sub>O); the hydrobromide has m 203° (from EtOH-Et<sub>2</sub>O) and the picrate has m 196° (from aq EtOH). [Sandris and Ourisson Bull Soc Chim Fr 345 1958.]

**Tetramethylthiuram disulfide [bis-(dimethylthiocarbamyl)-disulfide]** [137-26-8] **M 240.4, m 146-148°, 155-156°.** Crystd (three times) from boiling CHCl<sub>3</sub>, then recrystd from boiling CHCl<sub>3</sub> by adding EtOH dropwise to initiate pptn, and allowed to cool. Finally it was ppted from cold CHCl<sub>3</sub> by adding EtOH (which retained the monosulfide in soln). [Ferington and Tobolsky J Am Chem Soc 77 4510 1955.]

**1,1,3,3-Tetramethyl urea** [632-22-4] M **116.2, f -1.2°, b 175.2°/760mm, d 0.969, n 1.453.** Dried over BaO and distd under nitrogen.

**Tetramethyl uric acid** [2309-49-1] **M 224.2, m 225°, 228°, pK\_{Est}<0.** Crystd from H<sub>2</sub>O or MeOH.

**1,3,5,5-Tetranitrohexahydropyrimidine** [81360-42-1] **M 270.1, m 153-154°.** Crystd from EtOH (5x), and sublimed (~65°/0.05mm) [J Org Chem 47 2474 1982; J Labelled Comp Radiopharm 29 1197 1991].

**Tetranitromethane** [509-14-8] M 196.0, m 14.2°, b 21-23°/23mm, 126°/760mm, d 1.640, n 1.438. Shaken with dilute NaOH, washed, steam distd, dried with Na<sub>2</sub>SO<sub>4</sub> and fractionally crystd by partial freezing. The melted crystals were dried with MgSO<sub>4</sub> and fractionally distd under reduced pressure. Shaken with a large volume of dilute NaOH until no absorption attributable to the *aci*-nitro anion (from mono- di- and trinitromethanes) is observable in the water. Then washed with distilled water, and distilled at room temperature by passing a stream of air or nitrogen through the liquid and condensing in a trap at -80°. It can be dried with MgSO<sub>4</sub> or Na<sub>2</sub>SO<sub>4</sub>, fractionally crystd from the melt, and fractionally distd under reduced pressure.

Tetra(*p*-nitrophenyl)ethylene [47797-98-8] M 512.4, m 306-307°. Crystd from dioxane or AcOH and dried at 150°/0.1mm. [Gorvin J Chem Soc 678 1959.]

4,7,13,18-Tetraoxa-1,10-diazabicyclo[8.5.5]eicosane (Cryptand 211) [31250-06-3] M 288.1,  $pK_{Est} \sim 7.9$ . Redistd, dried under high vacuum over 24h, and stored under nitrogen.

1,7,10,16-Tetraoxa-4,13-diazacyclooctadecane (4,13-diaza-18-crown-6) [23978-55-4] M 262.3, m 118-116°, pK<sub>Est</sub> ~ 8.8. Twice recrystd from \*benzene/n-heptane, and dried for 24h under high vacuum [E.Weber and F.Vögtle *Top Curr Chem* (Springer Verlag, Berlin) 98 1 1981; D'Aprano and Sesta J Phys Chem 91 2415 1987].

**Tetrapentylammonium bromide** [866-97-7] M 378.5, m 100-101°. See tetra-*n*-amylammonium bromide on p. 356.

Tetraphenylethylene [632-51-9] M 332.4, m 223-224°, b 415-425°/760mm. Crystd from dioxane or from EtOH/\*benzene. Sublimed under high vacuum.

**Tetraphenylhydrazine** [632-52-0] **M 336.4, m 147°, pK**<sub>Est</sub> ~0. Crystd from 1:1 CHCl<sub>3</sub>/toluene or CHCl<sub>3</sub>/EtOH. Stored in a refrigerator, in the dark.

trans-1,1,4,4-Tetraphenyl-2-methylbutadiene [20411-57-8] M 372.5. Crystd from EtOH.

**1,2,3,4-Tetraphenylnaphthalene** [751-38-2] **M 432.6, m 199-201°, 204-204.5°.** Crystd from MeOH or as EtOH. [Fieser and Haddadin Org Synth **46** 107 1966.]

5,6,11,12-Tetraphenylnaphthacene (Rubrene) [517-51-1] M 532.7, m>315°, 322°, d 1.255 Orange crysts by sublimation at 250-260°/3-4mm [UV Badger and Pearce Spectrochim Acta 4 280 1950]. Also recrystd from \*benzene under red light because it is chemiluminescent and light sensitive.

**5,10,15,20-Tetraphenylporphyrin** (**TPP**) [917-23-7] **M 614.7**,  $\lambda_{max}$  **482nm.** Purified by chromatography on neutral (Grade I) alumina, and recrystd from CH<sub>2</sub>Cl<sub>2</sub>/MeOH [Yamashita et al. *J Phys Chem* **91** 3055 1987].

**Tetra-n-propylammonium bromide** [1941-30-6] **M 266.3, m >280°(dec).** Crystd from e thyl acetate/EtOH (9:1), acetone or MeOH. Dried at 110° under reduced pressure.

**Tetra-***n***-propylammonium iodide** [631-40-3] **M 313.3, m >280°(dec).** Purified by crystn from EtOH, EtOH/diethyl ether (1:1), EtOH/water or aqueous acetone. Dried at 50° under vacuum. Stored over  $P_2O_5$  in a vacuum desiccator.

Tetra-*n*-propylammonium perchlorate [15780-02-6] M 285.8, m 239-241°. See tetrapropylammonium perchlorate on p. 483 in Chapter 5.

**5,10,15,20-Tetra-4'-pyridinylporphyrin** [16834-13-2] **M 618.7, m >300°(dec).** Purified by chromatography on alumina (neutral, Grade I), followed by recrystn from CH<sub>2</sub>Cl<sub>2</sub>/MeOH [Yamashita et al. J Phys Chem **91** 3055 1987].

Tetrathiafulvalene [31366-25-3] M 204.4, m 122-124°. Recrystd from cyclohexane/hexane under an argon atmosphere [Kauzlarich et al. J Am Chem Soc 109 4561 1987].

**1,2,3,4-Tetrazole** [288-94-8] **M 70.1, m 156°, pK 4.89 (acidic).** Crystd from EtOH, sublimed under high vacuum at ca 120° (care should be taken due to possible **EXPLOSION**).

**Thebaine** [115-37-7] M 311.4, m 193°,  $[\alpha]_D^{25}$ -219° (EtOH), pK<sup>15</sup> 8.15. Sublimed at 170-180°.

2-Thenoyltrifluoroacetone [326-91-0] M 222.2, m 42-44°, b 96-98°/9mm. Crystd from hexane or \*benzene. (Aqueous solns slowly decompose).

2-Thenylamine [27757-85-3] M 113.1, b 78.5°/15mm, pK<sup>30</sup> 8.92. Distd under reduced pressure (nitrogen), from BaO, through a column packed with glass helices.

Theobromine [83-67-0] M 180.2, m 337°, pK<sup>40</sup> -0.16, pK<sup>25</sup> 9.96. Crystd from water.

**Theophylline** [58-55-9] **M 180.2, m 270-274°, pK\_1^{40} -0.24, pK\_2 2.5, pK\_3^{40} 8.79. Crystd from H<sub>2</sub>O.** 

Thevetin [11018-93-2] M 858.9, m softens at 194°, m 210°. Crystd (as trihydrate) from isopropanol. Dried at 100°/10mm to give the hemihydrate (very hygroscopic).

Thianthrene [92-85-3] M 216.3, m 158°. Crystd from Me<sub>2</sub>CO (charcoal), AcOH or EtOH. Sublimes in a vacuum.

 $\epsilon$ -[2-(4-Thiazolidone)]hexanoic acid [539-35-5] M 215.3, m 140°, pK<sub>Est</sub> ~4.7. Crystd from H<sub>2</sub>O, Me<sub>2</sub>CO or MeOH.

**Thiazoline-2-thiol** [96-53-7] **M** 119.2, m 106-107°, 106-108°,  $pK_{Est} \sim 13.0$ . Purified by dissolution in alkali, pptn by addition of HCl and then recrystd from H<sub>2</sub>O as needles. [IR: Flett J Chem Soc 347 1953 and Mecke et al. Chem Ber 90 975; Gabriel and Stelzner Chem Ber 28 2931 1895.]

4-(2-Thiazolylazo)resorcinol [2246-46-0] M 221.2, m 200-202°(dec),  $\lambda_{max}$  500 nm, pK<sub>1</sub><sup>25</sup> 1.25, pK<sub>2</sub><sup>25</sup>6.53, pK<sub>3</sub><sup>25</sup>10.76. Dissolved in alkali, extracted with diethyl ether, and re-ppted with dil HCl. The purity was checked by TLC on silica gel using pet ether/diethyl ether/EtOH (10:10:1) as the mobile phase.

Thietane (trimethylene sulfide) [287-27-4] M 74.1, m -64°, -73.2°, b 93.8-94.2°/752mm, 95°/atm,  $d_4^{20}$  1.0200,  $n_D^{20}$  1.5020. Purified by preparative gas chromatography on a dinonyl phthalate column. It has also been purified by drying over anhydrous K<sub>2</sub>CO<sub>3</sub>, and distd through a 25 cm glass helices packed column (for 14g of thietane), then dried over CaSO<sub>4</sub> before sealing in a vac. [Haines et al. J Phys Chem 58 270 1954.] It is characterised as the dimethylsulfonium iodide m 97-98° [Bennett and Hock J Chem Soc 2496 1927]. The S-oxide has b 102°/25mm,  $n_D^{21}$  1.5075 [Tamres and Searles J Am Chem Soc 81 2100 1959].

**Thioacetamide** [62-55-5] **M 75.1, m 112-113°, pK<sup>25</sup> 13.4.** Crystd from absolute diethyl ether or \*benzene. Dried at 70° in vacuum and stored over  $P_2O_5$  at 0° under nitrogen. (*Develops an obnoxious odour on storage*, and absorption at 269nm decreases, hence it should be freshly crystd before use).

Thioacetanilide [677-53-6] M 151.2, m 75-76°, pK<sub>Est</sub> ~13.1. Crystd from H<sub>2</sub>O and dried in vacuo.

Thiobarbituric acid [504-17-6] M 144.2, m 235°(dec),  $pK_1^{25}$  2.25,  $pK_2^{25}$ 10.72 (2% aq ETOH). Crystd from water.

Thiobenzanilide [636-04-4] M 213.2, m 101.5-102°, pK<sub>Est</sub> ~12.6. Crystd from MeOH at Dry-ice temperature.

(1*R*)-(-)-Thiocamphor (1*R*-bornane-2-thione, 1*R*-(-)-1,7,7-trimethylbicyclo[2.2.1]heptane-2-thione) [53402-10-1] M 168.3, m 136-138°, 146°,  $[\alpha]_D^{22}$ -22° (c 3, EtOAc). Forms red prisms from EtOH and sublimes under vacuum. It possesses a sulfurous odour and is volatile as camphor. [Sen J Indian Chem Soc 12 647 1935; 18 76 1941.] The racemate crystallises from \*C<sub>6</sub>H<sub>6</sub> and has m 145° [138.6-139°, White and Bishop J Am Chem Soc 62 10 1940].

**1,1'-Thiocarbonyldiimidazole** [6160-65-2] M **178.1, m 100-102°, 105-106°.** It forms yellow crystals by recrystn from tetrahydrofuran or by sublimation at 10<sup>-3</sup>Torr (bath temp 70-80°). Hydrolysed by H<sub>2</sub>O, store dry. [Staab and Walther Justus Liebigs Ann Chem **657** 98 1962; Pullukat et al. Tetrahedron Lett 1953 1967.]

Thiochrome {2,7-dimethyl-5*H*-thiachromine-8-ethanol; 3,8-dimethyl-2-hydroxyethyl-5*H*-thiazolo[2,3:1',2']pyrimido[4',5'-d]pyrimidine} [92-35-3] M 262.3, m 227-228°, pK<sub>Est</sub> ~ 5.8 (thiazol-N protonation). Crystd from chloroform.

Thiodiglycollic acid [123-93-3] M 150.2, m 129°,  $pK_1^{25}$  3.15 (3.24),  $pK_2^{25}$  4.13 (4.56). Crystd from water.

3,3'-Thiodipropionic acid [111-17-1] M 178.2, pK<sub>1</sub><sup>25</sup> 3.84, pK<sub>2</sub><sup>25</sup> 4.66. Crystd from water.

Thioflavine T [2390-54-7] M 318.9, pK<sup>25</sup> 2.7. Crystd from \*benzene/EtOH (1:1).

Thioformamide [115-08-2] M 61.0, m 29°, pK<sub>Est</sub> ~12.4. Crystd from ethyl acetate or ether/pet ether.

**Thioglycollic acid** [68-11-1] **M 92.1, b 95-96°/8mm, d 1.326, n 1.505, pK\_1^{25} 3.42, pK\_2^{25} <b>10.20.** Mixed with an equal volume of \*benzene, the \*benzene is then distd to dehydrate the acid. After heating to 100° to remove most of the \*benzene, the residue was distd under vacuum and stored in sealed ampoules at 3°. [Eshelman et al. Anal Chem 22 844 1960.]

Thioguanosine (2-amino-6-mercapto-9- $\beta$ -D-ribofuranosylpurine) [85-31-4] M 299.3, m 230-231°(dec),  $[\alpha]_D^{20}$ -64° (c 1.3, 0.1N NaOH), pK 8.33. Crystd (as hemihydrate) from water.

**Thioindigo** [522-75-8] **M 296.2, m >280°.** Adsorbed on silica gel from  $CCl_4/*$ benzene (3:1), eluted with \*benzene, crystd from CHCl<sub>3</sub> and dried at 60-65°. [Wyman and Brode J Am Chem Soc 73 1487 1951.] This paper also gives details of purification of other thioindigo dyes.

Thiomalic (mercaptosuccinic) acid [70-49-5] M 150.2, m 153-154°,  $pK_1^{25}$  3.64 (3.17),  $pK_2^{25}$  4.64 (4.67),  $pK_3^{25}$  10.37 (10.52). Extracted from aqueous soln several times with diethyl ether, and the aqueous soln freeze-dried.

**Thio-Michler's Ketone** [1226-46-6] M 284.6,  $\lambda_{max}$  457 nm ( $\varepsilon$  2.92 x 10<sup>4</sup> in 30% aq *n*-**propanol**). Purified by recrystn from hot EtOH or by triturating with a small volume of CHCl<sub>3</sub>, followed by filtration and washing with hot EtOH [Terbell and Wystrade *J Phys Chem* 68 2110 1964].

**Thionanthone (thioxanthone)** [492-22-8] **M 212.3, m 212-213°, b 371-373°/712mm.** See 9*H*-thioxanthene-9-one on p. 369.

**2-Thionaphthol** [91-60-1] **M 160.2, m 81°, 82°, b 153.5°/15mm, 286°/760mm, pK<sub>Est</sub> ~6.1.** Crystd from EtOH.

Thionine (3,7-diaminophenothiazine) [135-59-1; 581-64-6 (HCl)] M 263.7,  $\varepsilon_{590}$  6.2 x 10<sup>4</sup> M<sup>-1</sup> cm<sup>-1</sup>, pK<sup>15</sup> 6.9. The standard biological stain is highly pure. It can be crystd from water or 50% EtOH, then chromatographed on alumina using CHCl<sub>3</sub> as eluent [Shepp, Chaberek and McNeil J Phys Chem 66 2563 1962]. Dried overnight at 100° and stored in a vacuum. The hydrochloride can be crystd from 50% EtOH or dilute HCl and aqueous *n*-butanol. Purified also by column chromatography and washed with CHCl<sub>3</sub> and acetone. Dried *in vacuo* at room temperature.

**Thiooxine hydrochloride** (8-mercaptoquinoline hydrochloride) [34006-16-1] M 197.7, m 170-175° (dec),  $pK_1^{25}$  2.16,  $pK_2^{25}$  8.38. Crystallises from EtOH and the crystals are yellow in colour. It has  $pKa^{20}$  values of 2.05 and 8.29 in H<sub>2</sub>O. [UV: Albert and Barlin J Chem Soc 2384 1959.]

Thiophane (tetrahydrothiophene) [110-01-0] M 88.2, b 40.3°/39.7mm. See tetrahydrothiophene on p. 361.

**Thiophene** [110-02-1] M 84.1, f -38.5°, b 84.2°, d 1.525, n 1.52890,  $n^{30}$  1.5223. The simplest purification procedure is to dry with solid KOH, or reflux with sodium, and fractionally distd through a glass-helices packed column. More extensive treatments include an initial wash with aq HCl, then water, drying with CaSO<sub>4</sub> or KOH, and passage through columns of activated silica gel or alumina. Fawcett and Rasmussen [J Am Chem Soc 67 1705 1945] washed thiophene successively with 7M HCl, 4M NaOH, and distd water, dried with CaCl<sub>2</sub> and fractionally distd. \*Benzene was removed by fractional crystn by partial freezing, and the thiophene was degassed and sealed in Pyrex flasks. [Also a method is described for recovering the thiophene from the \*benzene-enriched portion.]

Thiophene-2-acetic acid [1918-77-0] M 142.2, m 76°, pK<sup>25</sup> 3.89. Crystd from ligroin.

Thiophene-3-acetic acid [6964-21-2] M 142.2, m 79-80°, pKEst ~3.1. Crystd from ligroin.

2-Thiophenecarboxaldehyde [98-03-3] M 112.2, b 106°/30mm, d 1.593, n 1.222. Washed with 50% HCl and distd under reduced pressure just before use.

Thiophene-2-carboxylic acid [527-72-0] M 128.2, m 129-130°, pK<sup>25</sup> 3.89. Crystd from water.

Thiophene-3-carboxylic acid [88-31-1] M 128.1, m 137-138°, pK<sup>25</sup> 6.23. Crystd from water.

**Thiophenol (benzenethiol)** [108-98-5] M **110.2, f -14.9°, b 46.4°/10mm, 168.0°/760mm, d 1.073, n 1.5897, pK^{25} 6.62.** Dried with CaCl<sub>2</sub> or CaSO<sub>4</sub>, and distd at 10mm pressure or at 100mm (b 103.5°) in a stream of nitrogen. Thiopyronine (2,7-dimethylaminothiaxanthane) [2412-14-8] M 318.9,  $\lambda_{max}$  564nm ( $\epsilon$  78,500) H<sub>2</sub>O, pK<sub>Est</sub> ~ 7. Purified as the hydrochloride by recrystn from hydrochloric acid. [Fanghanel et al. J Phys Chem 91 3700 1987.]

**Thiosalicylic (2-mercaptobenzoic) acid** [147-93-3] M 154.2, m 164-165°,  $pK_1^{25}$  3.54,  $pK_2^{25}$  8.80. Crystd from hot EtOH (4mL/g), after adding hot distd water (8mL/g) and boiling with charcoal. The hot soln was filtered, cooled, the solid collected and dried *in vacuo* (P<sub>2</sub>O<sub>5</sub>). Cryst from AcOH and sublimes *in vacuo*.

Thiosemicarbazide [79-19-6] M 91.1, m 181-183°, pK<sub>1</sub><sup>25</sup> 1.88, pK<sub>2</sub><sup>25</sup> 12.81. Crystd from water.

**Thiothienoyltrifluoroacetone** [4552-64-1] **M 228.2, m 61-62°.** Easily oxidised and has to be purified before use. This may be by recrystd from \*benzene or by dissolution in pet ether, extraction into 1M NaOH soln, acidification of the aqueous phase with 1-6M HCl soln, back extraction into pet ether and final evapn of the solvent. The purity can be checked by TLC. It was stored in ampoules under nitrogen at 0° in the dark. [Muller and Rother Anal Chim Acta 66 49 1973.]

Thiouracil [141-90-2] M 128.2, m 240°(dec), pK<sup>25</sup> 7.52. Crystd from water or EtOH.

Thiourea [62-56-6] M 76.1, m 179°,  $pK^{20}$  -1.19 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from absolute EtOH, MeOH, acetonitrile or water. Dried under vacuum over H<sub>2</sub>SO<sub>4</sub> at room temperature.

**9H-Thioxanthene-9-one** (thioxanthone) [492-22-8] M 212.3, m 200-202°, 209°, 212-214°, b 371-373°/712mm. Yellow needles from CHCl<sub>3</sub> or EtOH and sublimes *in vacuo*. Sol in CS<sub>2</sub>, hot AcOH and soln in concn  $H_2SO_4$  to give a yellow color with green fluorescence in VIS light. The sulfone has m 187° (from EtOH), and the hydrazone has m 115° (yellow leaflets from EtOH/\*C<sub>6</sub>H<sub>6</sub>). [Szmant et al. J Org Chem 18 745 1953; Ullmann et al. Chem Ber 49 2509 1916; NMR: Sharpless et al. Org Magn Res 6 115 1974.]

L-Threonine [72-19-5] M 119.1, m 251-253°,  $[\alpha]_D^{26}$ -28.4° (H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup> 2.17, pK<sub>2</sub><sup>25</sup> 9.00. Likely impurities are *allo*-threonine and glycine. Crystd from water by adding 4 volumes of EtOH. Dried and stored in a desiccator.

Thymidine [50-89-5] M 242.2, m 185°, pK<sub>2</sub><sup>25</sup>9.65. Crystd from ethyl acetate.

**Thymine** [65-71-4] **M 126.1, m 326°, pK^{25} 9.82.** Crystd from ethyl acetate or water. Purified by preparative (2mm thick) TLC plates of silica gel, eluting with ethyl acetate/isopropanol/water (75:16:9, v/v;  $R_F$  0.75). Spot localised by uv lamp, cut from plate, placed in MeOH, shaken and filtered through a millipore filter, then rotary evapd. [Infante et al. J Chem Soc, Faraday Trans 1 68 1586 1973.]

Thymolphthalein complexone [1913-93-5] M 720.8, m 190°(dec),  $pK_1^{18.2}$  7.35,  $pK_2^{18.2}$  12.25. Purification as for phthalein complexone except that it was synthesised from thymolphthalein instead of cresolphthalein.

Tiglic acid [80-59-1] M 100.1, m 63.5-64°, b 198.5°, pK<sup>18</sup> 4.96. Crystd from water.

Tinuvin P (2-[2H-benzotriazol-2-yl]-p-cresol) [50936-05-5] M 225.3, m 131-133°,  $pK_{Est(1)}\sim 1.6$  (N protonation),  $pK_{Est(2)}\sim 8$  (phenolic OH). Recrystd from *n*-heptane or Me<sub>2</sub>CO/pentane. [Woessner et al. J Phys Chem 81 3629 1985.]

*o*-Tolidine (3,3'-dimethylbenzidine) [119-93-7] M 212.3, m 131-132°, pK<sup>25</sup> 4.45. Dissolved in \*benzene, percolated through a column of activated alumina and crystd from \*benzene/pet ether.

*p*-Tolualdehyde [104-87-0] M 120.2, b 83-85°/0.1mm, 199-200°/760mm, d 1.018, n 1.548. Steam distd, dried with CaSO<sub>4</sub> and fractionally distd.

o-Toluamide [527-85-5] M 135.2, m 141°. Crystd from hot water (10mL/g) and dried in air.

Toluene [108-88-3] M 92.1, b 110.6°, d<sup>10</sup> 0.87615, d<sup>25</sup> 0.86231, n 1.49693, n<sup>25</sup> 1.49413. Dried with CaCl<sub>2</sub>, CaH<sub>2</sub> or CaSO<sub>4</sub>, and dried further by standing with sodium, P<sub>2</sub>O<sub>5</sub> or CaH<sub>2</sub>. It can be fractionally distd from sodium or P2O5. Unless specially purified, toluene is likely to be contaminated with methylthiophenes and other sulfur containing impurities. These can be removed by shaking with conc  $H_2SO_4$ , but the temperature must be kept below 30° if sulfonation of toluene is to be avoided. A typical procedure consists of shaking toluene twice with cold conc  $H_2SO_4$  (100mL of acid per L), once with water, once with aqueous 5% NaHCO3 or NaOH, again with H2O, then drying successively with CaSO4 and P2O5, with final distn from P2O5 or over LiAlH4 after refluxing for 30min. Alternatively, the treatment with NaHCO3 can be replaced by boiling under reflux with 1% sodium amalgam. Sulfur compounds can also be removed by prolonged shaking of the toluene with mercury, or by two distns from AlCl<sub>3</sub>, the distillate then being washed with water, dried with K<sub>2</sub>CO<sub>3</sub> and stored with sodium wire. Other purification procedures include refluxing and distn of sodium dried toluene from diphenylpicrylhydrazyl, and from SnCl<sub>2</sub> (to ensure freedom from peroxides). It has also been co-distd with 10% by volume of ethyl methyl ketone, and again fractionally distd. [Brown and Pearsall J Am Chem Soc 74 191 1952.] For removal of carbonyl impurities see \*benzene. Toluene has been purified by distn under nitrogen in the presence of sodium benzophenone ketyl. Toluene has also been dried with MgSO<sub>4</sub>, after the sulfur impurities have been removed, and then fractionally distd from  $P_2O_5$  and stored in the dark [Tabushi et al. J Am Chem Soc 107 4465 1985]. Toluene can be purified by passage through a tightly packed column of Fuller's earth.

**Rapid purification:** Alumina,  $CaH_2$  and 4A molecular sieves (3% w/v) may be used to dry toluene (6h stirring and standing). Then the toluene is distd, discarding the first 5% of distillate, and is stored over molecular sieves (3A, 4A) or Na wire.

Toluene-2,4-diamine [95-80-7] M 122.2, m 99°, b 148-150°/8mm, 292°/760 mm,  $pK_{Est(1)}\sim 2.5$ ,  $pK_{Est(2)}\sim 4.4$ . Recrystd from water containing a very small amount of sodium dithionite (to prevent air oxidation), and dried under vacuum. Also cryst from \*benzene.

o-Toluenesulfonamide [88-19-7] M 171.2, m 155.5°. Crystd from hot water, then from EtOH or Et<sub>2</sub>O-pet ether.

*p*-Toluenesulfonamide [70-55-3] M 171.2, m 137-137.5°, 138°. Crystd from hot water, then from EtOH or Et<sub>2</sub>O-pet ether.

*p*-Toluenesulfonic acid [6192-52-5] M 190.2, m 38° (anhydrous), m 105-107° (monohydrate), pK 1.55. Purified by pptn from a satd soln at 0° by introducing HCl gas. Also crystd from conc HCl, then crystd from dilute HCl (charcoal) to remove benzenesulfonic acid. It has been crystd from EtOH/water. Dried in a vacuum desiccator over solid KOH and CaCl<sub>2</sub>. *p*-Toluenesulfonic acid can be dehydrated by azeotropic distn with \*benzene or by heating at 100° for 4h under water-pump vacuum. The anhydrous acid can be crystd from \*benzene, CHCl<sub>3</sub>, ethyl acetate, anhydrous MeOH, or from acetone by adding a large excess of \*benzene. It can be dried under vacuum at 50°.

**Toluenesulfonic acid hydrazide** (tosylhydrazide) [1576-35-8] M 186.2, m 108-110°, 109-110°. Dissolve in hot MeOH (~1g/4mL), filter through Celite and ppte material by adding 2-2.5 vols of distd H<sub>2</sub>O. Air or vac dry. [Fiedman et al. Org Synth Coll Vol V 1055 1973.]

*p*-Toluenesulfonyl chloride (tosyl chloride) [98-59-9] M 190.7, m 66-69°, 67.5-68.5°, 69°, b 138-139°/9mm, 146°/15mm, 167°/36mm. Material that has been standing for a long time contains tosic acid and HCl and has m ca 65-68°. It is purified by dissolving (10g) in the minimum volume of CHCl<sub>3</sub> (ca 25mL) filtered, and diluted with five volumes (i.e. 125mL) of pet ether (b 30-60°) to precipitate impurities. The soln is filtered, clarified with charcoal and concentrated to 40mL by evaporation. Further evaporation to a very small volume gave 7g of white crystals which were analytically pure, m 67.5-68.5°. (The insoluble material was largely tosic acid and had m 101-104°). [Pelletier Chem Ind (London) 1034 1953.]

Also crystd from toluene/pet ether in the cold, from pet ether (b  $40-60^{\circ}$ ) or \*benzene. Its soln in diethyl ether has been washed with aqueous 10% NaOH until colourless, then dried (Na<sub>2</sub>SO<sub>4</sub>) and crystd by cooling in

p-Toluenethiol [106-45-6] M 124.2, m 43.5-44°, pK<sup>25</sup> 6.82. Crystd from pet ether (b 40-70°).

Toluhydroquinone (2-methylbenzene-1,4-diol) [95-71-6] M 124.1, m 128-129°,  $pK_1^{20} 10.15$ ,  $pK_2^{20} 11.75$ . Crystd from EtOH.

o-Toluic acid [118-90-1] M 136.2, m 102-103°, pK<sup>25</sup> 3.91. Crystd from \*benzene (2.5mL/g) and dried in air.

*m*-Toluic acid [99-04-7] M 136.2, m 111-113°, pK<sup>25</sup> 4.27. Crystd from water.

*p*-Toluic acid [99-94-5] M 136.2, m 178.5-179.5°, pK<sup>25</sup> 4.37. Crystd from water, water/EtOH (1:1), MeOH/water or \*benzene.

o-Toluidine (2-methylaniline) [95-53-4] M 107.2, f -16.3°, b 80.1°/10mm, 200.3°/760mm, d 0.999, n 1.57246,  $n^{25}$  1.56987,  $pK^{25}$  4.45. In general, methods similar to those for purifying aniline can be used, e.g. distn from zinc dust, at reduced pressure, under nitrogen. Berliner and May [J Am Chem Soc 49 1007 1927] purified via the oxalate. Twice-distd o-toluidine was dissolved in four times its volume of diethyl ether and the equivalent amount of oxalic acid needed to form the dioxalate was added as its soln in diethyl ether. (If p-toluidine is present, its oxalate pptes and can be removed by filtration.) Evapn of the ether soln gave crystals of o-toluidine dioxalate. They were filtered off, recryst five times from water containing a small amount of oxalic acid (to prevent hydrolysis), then treated with dilute aqueous Na<sub>2</sub>CO<sub>3</sub> to liberate the amine which was separated, dried (CaCl<sub>2</sub>) and distd under reduced pressure.

*m*-Toluidine (3-methylaniline) [108-44-1] M 107.2, f -30.4°, b 82.3°/10mm, 203.4°/ 760mm, d 0.989, n 1.56811, n<sup>25</sup> 1.56570, pK<sup>25</sup> 4.71. It can be purified as for aniline. Twice-distd, *m*-toluidine was converted to the hydrochloride using a slight excess of HCl, and the salt was fractionally crystd from 25% EtOH (five times), and from distd water (twice), rejecting, in each case, the first material that crystd. The amine was regenerated and distd as for *o*-toluidine. [Berliner and May J Am Chem Soc 49 1007 1927.]

*p*-Toluidine (4-methylaniline) [106-49-0] M 107.2, m 44.8°, b 79.6°/10mm, 200.5°/ 760mm, d 0.962, n 1.5636, n <sup>59.1</sup> 1.5534,  $pK^{25}$  5.08. In general, methods similar to those for purifying aniline can be used. It can be separated from the *o*- and *m*-isomers by fractional crystn from its melt. *p*-Toluidine has been crystd from hot water (charcoal), EtOH, \*benzene, pet ether or EtOH/water (1:4), and dried in a vacuum desiccator. It can also be sublimed at 30° under vacuum. For further purification, use has been made of the oxalate, the sulfate and acetylation. The oxalate, formed as described for *o*-toluidine, was filtered, washed and recrystd three times from hot distd water. The base was regenerated with aq Na<sub>2</sub>CO<sub>3</sub> and recrystd three times from distd water. [Berliner and May *J Am Chem Soc* 49 1007 1927.] Alternatively, *p*-toluidine was converted to its acetyl derivative which, after repeated crystn from EtOH, was hydrolysed by refluxing (50g) in a mixture of 500mL of water and 115mL of conc H<sub>2</sub>SO<sub>4</sub> until a clear soln was obtained. The amine sulfate was isolated, suspended in water, and NaOH was added. The free base was distd twice from zinc dust under vacuum. The *p*-toluidine was then recrystd from pet ether and dried in a vacuum desiccator or in a vacuum for 6h at 40°. [Berliner and Berliner *J Am Chem Soc* 76 6179 1954; Moore et al. *J Am Chem Soc* 108 2257 1986.]

Toluidine Blue O [93-31-9] M 305.8, CI 52040,  $\lambda$ max 626nm, pK<sup>25</sup> 7.5. Crystd from hot water (18mL/g) by adding one and a half volumes of alcohol and chilling on ice. Dried at 100° in an oven for 8-10h.

*p*-Toluidine hydrochloride [540-23-8] M 143.6, m 245.9-246.1°. Crystd from MeOH containing a few drops of conc HCl. Dried under vacuum over paraffin chips.

2-p-Toluidinylnaphthalene-6-sulfonic acid [7724-15-4] M 313.9,  $pK_{Est} \sim 0$ . Crystd twice from 2% aqueous KOH and dried under high vacuum for 4h at room temperature. Crystd from water. Tested for purity by TLC on silica gel with isopropanol as solvent. The free acid was obtained by acidifying a satd aqueous soln.

o-Tolunitrile [529-19-1] M 117.2, b 205.2°, d 0.992, n 1.5279. Fractionally distd, washed with conc HCl or 50%  $H_2SO_4$  at 60° until the smell of isonitrile had gone (this also removed any amines), then washed with saturated NaHCO<sub>3</sub> and dilute NaCl solns, then dried with K<sub>2</sub>CO<sub>3</sub> and redistd.

*m*-Tolunitrile [620-22-4] M 117.2, b 209.5-210°/773mm, d 0.986, n 1.5250. Dried with MgSO<sub>4</sub>, fractionally distd, then washed with aqueous acid to remove possible traces of amines, dried and redistd.

*p*-Tolunitrile [104-85-8] M 117.2, m 29.5°, b 104-106°/20mm. Melted, dried with MgSO<sub>4</sub>, fractionally crystd from its melt, then fractionally distd under reduced pressure in a 6-in spinning band column. [Brown J Am Chem Soc 81 3232 1959.] It can also be crystd from \*benzene/pet ether (b 40-60°).

4-Tolyl-2-benzoic acid (4'-methylbiphenyl-2-carboxylic acid) [7148-03-0] M 196.2, m 138-139°, pK<sup>25</sup> 3.64. Crystd from toluene.

p-Tolylacetic acid [622-47-9] M 150.2, m 94°. See 4-methylphenylacetic acid on p. 297.

p-Tolyl carbinol (4-methylbenzyl alcohol) [589-18-4] M 122.2, m 61°, b 116-118°/20mm, 217°/760mm. Crystd from pet ether (b 80-100°, 1g/mL). It can also be distd under reduced pressure.

*p*-Tolyl disulfide [103-19-5] M 246.4, m 45-46°. Purified by chromatography on alumina using hexane as eluent, then crystd from MeOH. [Kice and Bowers J Am Chem Soc 84 2384 1962.]

**p**-Tolylsulfonylmethyl isocyanide (tosylmethyl isocyanide, TOSMIC) [36635-61-7] M 195.2, m 114-115°(dec), 116-117°(dec). Use an efficient fume cupboard. Purify by dissolving TOSMIC (50g) in CH<sub>2</sub>Cl<sub>2</sub> (150mL) and pass through a column (40x3cm) containing neutral alumina (100g) in CH<sub>2</sub>Cl<sub>2</sub> and eluting with CH<sub>2</sub>Cl<sub>2</sub>. A nearly colorless soln (700mL) is collected, evaporated *in vacuo* and the residue (42-47g) of TOSMIC (m 113-114° dec) is recrystd once from MeOH (m 116-117° dec). [Hoogenboom et al. Org Synth 57 102 1977; Lensen Tetrahedron Lett 2367 1972..] Also recrystd from EtOH (charcoal) [Saito and Itano, J Chem Soc, Perkin Trans 1 1 1986].

p-Tolyl urea [622-51-5] M 150.2, m 181°. Crystd from EtOH/water (1:1).

*trans*-Traumatic acid (2-dodecene-1,12-dioic acid) [6402-36-4] M 228.3, m 165-166°, 150-160°/0.001mm, pK<sub>Est(1)</sub>~4.2, pK<sub>Est(2)</sub>~4.6. Crystd from EtOH, acetone or glyme.

 $\alpha, \alpha$ '-Trehalose (2H<sub>2</sub>O) [6138-23-4] M 378.3, m 96.5-97.5°, 203° (anhydrous). Crystd (as the dihydrate) from aqueous EtOH. Dried at 13°.

**1,2,3-Triaminopropane trihydrochloride** [free base 2/29/-99-6] M 198.7, m 250°,  $pK_1^{20}$  3.72,  $pK_2^{20}$  7.95,  $pK_3^{20}$  9.59. Cryst from EtOH.

**1,5,7-Triazabicyclo[4.4.0]dec-5-ene** (TBD, **1,3,4,6,7,8-hexahydro-2h-pyrimido[1,2-a]-pyrimidine**) [5807-14-7] **M 139.2, m 125-130°, pK ~ 16** Cryst from Et<sub>2</sub>O but readily forms white crystals of the carbonate. It is a strong base (see pK, i.e. about 100 times more basic than tetramethylguanidine. The picrate has m 220.5-222° (from EtOH). Forms the 5-nitro deivative m 14.5-160° that gives a 5-nitro nitrate salt m 100-101° (from EtOH-Et<sub>2</sub>O) and a 5-nitro picrate m 144-145° (from H<sub>2</sub>O). [McKay and Kreling Can J Chem **35** 1438 1957; Schwesinger Chimia **39** 369 1985; Hilpert et al. J Chem Soc, Chem Commun 1401 1983; Kamfen and Eschenmoser Helv Chim Acta **72** 185 1989].

**1,2,4-Triazole** [288-88-0] **M 69.1, m 121°, 260°, pK\_1^{25} 2.27** (basic),  $pK_2^{25}$  **10.26** (acidic). Crystd from EtOH or water [Barszcz et al. J Chem Soc, Dalton Trans 2025 1986].

**Tribenzylamine** [620-40-6] **M 287.4, m 93-94°, 230°/13mm, pK**<sub>Est</sub> <0. Crystd from abs EtOH or pet ether. Dried in a vacuum over  $P_2O_5$  at room temperature. *HCl* has m 226-228° (from EtOH) and *picrate* has m 191° (from H<sub>2</sub>O or aq EtOH).

2,4,6-Tribromoacetanilide [607-93-2] M 451.8, m 232°. Crystd from EtOH.

**2,4,6-Tribromoaniline** [147-82-0] **M 329.8, m 120°, pK\_{Est} \sim -0.5 (aq H<sub>2</sub>SO<sub>4</sub>).** Crystd from MeOH.

sym-Tribromobenzene [626-39-1] M 314.8, m 122°. Crystd from glacial acetic acid/water (4:1), then washed with chilled EtOH and dried in air.

**Tribromochloromethane** [594-15-0] **M 287.2, m 55°.** Melted, washed with aqueous  $Na_2S_2O_3$ , dried with BaO and fractionally crystd from its melt.

**2,4,6-Tribromophenol** [118-79-6] **M 330.8, m 94°, pK^{25} 6.00.** Crystd from EtOH or pet ether. Dried under vacuum over P<sub>2</sub>O<sub>5</sub> at room temperature.

**Tri-***n***-butylamine** [102-82-9] **M** 185.4, **b** 68°/3mm, 120°/44mm, **d** 0.7788, **n** 1.4294,  $pK^{25}$ 9.93. Purified by fractional distn from sodium under reduced pressure. Pegolotti and Young [J Am Chem Soc 83 3251 1961] heated the amine overnight with an equal volume of acetic anhydride, in a steam bath. The amine layer was separated and heated with water for 2h on the steam bath (to hydrolyse any remaining acetic anhydride). The soln was cooled, solid K<sub>2</sub>CO<sub>3</sub> was added to neutralize any acetic acid that had been formed, and the amine was separated, dried (K<sub>2</sub>CO<sub>3</sub>) and distd at 44mm pressure. Davis and Nakshbendi [J Am Chem Soc 84 2085 1926] treated the amine with one-eighth of its weight of benzenesulfonyl chloride in aqueous 15% NaOH at 0-5°. The mixture was shaken intermittently and allowed to warm to room temperature. After a day, the amine layer was washed with aq NaOH, then water and dried with KOH. (This treatment removes primary and secondary amines.) It was further dried with CaH<sub>2</sub> and distd under vacuum.

Tri-n-butylammonium hydrobromide [37026-85-0] M 308.3, m 75.2-75.9°. Crystd from ethyl acetate.

**Tri-***n***-butylammonium nitrate** [33850-87-2] **M 304.5.** Crystd from mixtures of *n*-hexane and acetone (95:5). Dried over  $P_2O_5$ .

Tri-n-butylammonium perchlorate [14999-66-7] M 285.5. Recrystd from n-hexane.

sym-Tri-tert-butylbenzene [1460-02-2] M 246.4, m 73.4-73.9°. Crystd from EtOH.

2,4,6-Tri-tert-butylphenol [732-26-3] M 262.4, m 129-132°, 131°/1mm, 147°/10 mm, 278°/760mm, pK<sup>25</sup> 12.19. Crystd from *n*-hexane or several times from 95% EtOH until the EtOH soln was colourless [Balasubramanian and Bruice J Am Chem Soc 108 5495 1986]. It has also been purified by sublimation [Yuan and Bruice J Am Chem Soc 108 1643 1986; Wong et al. J Am Chem Soc 109 3428 1987]. Purification has been achieved by passage through a silica gel column followed by recrystn from *n*-hexane [Kajii et al. J Phys Chem 91 2791 1987].

Tricarballylic acid (propane-1,2,3-tricarboxylic acid) [99-14-9] M 176.1, m 166°,  $pK_1^{25}$ 3.47,  $pK_2^{25}$  4.54,  $pK_3^{20}$  5.89. Crystd from diethyl ether.

**Trichloroacetamide** [594-65-0] **M 162.4, m 139-141°, b 238-240°.** Its xylene soln was dried with  $P_2O_5$ , then fractionally distd.

Trichloroacetanilide [2563-97-5] M 238.5, m 95°. Crystd from \*benzene.

**Trichloroacetic acid** [76-03-9] **M 163.4, m 59.4-59.8°, pK^{25} 0.51.** Purified by fractional crystn from its melt, then crystd repeatedly from dry \*benzene and stored over conc H<sub>2</sub>SO<sub>4</sub> in a vac desiccator. It can also be crystd from CHCl<sub>3</sub> or cyclohexane, and dried over P<sub>2</sub>O<sub>5</sub> or Mg(ClO<sub>4</sub>)<sub>2</sub> in a vac desiccator. Trichloroacetic acid can be fractionally distd under reduced pressure from MgSO<sub>4</sub>. Layne, Jaffé and Zimmer [*J Am Chem Soc* **85** 435 1963] dried trichloroacetic acid in \*benzene by distilling off the \*benzene-water azeotrope, then crystd the acid from the remaining \*benzene soln. Manipulations were carried out under nitrogen. [Use a well ventilated fume cupboard].

2,3,4-Trichloroaniline [634-67-3] M 196.5, m 67.5°, b 292°/774mm, pK<sub>Est</sub> ~1.3. Crystd from ligroin.

2,4,5-Trichloroaniline [636-30-6] M 196.5, m 96.5°, b 270°/760mm, pK 1.09. Crystd from ligroin.

**2,4,6-Trichloroaniline** [634-93-5] **M 196.5, m 78.5°, b 127°/14mm, 262°/746mm, pK 0.03.** Crystd from ligroin.

1,2,3-Trichlorobenzene [87-61-6] M 181.5, m 52.6°. Crystd from EtOH.

**1,2,4-Trichlorobenzene** [120-82-1] M **181.5, m 17°, b 210°.** Separated from a mixture of isomers by washing with fuming  $H_2SO_4$ , then water, drying with CaSO<sub>4</sub> and slowly fractionally distilling. [Jensen, Marino and Brown J Am Chem Soc **81** 3303 1959.]

1,3,5-Trichlorobenzene [108-70-3] M 181.5, m 64-65°. Recrystd from dry \*benzene or toluene.

**3,4,5-Trichloro**-*o*-cresol (**3,4,5-trichloro-2-methylphenol**) [608-92-4] M 211.5, m 77°, pK<sub>Est</sub> ~7.6. Crystd from pet ether.

2,3,5-Trichloro-p-cresol [608-91-3] M 211.5, m 66-67°, pK<sub>Est</sub> ~6.9. Crystd from pet ether.

**1,1,1-Trichloroethane** [71-55-6] M **133.4, f -32.7°, b 74.0°, d 1.337, n 1.4385.** Washed successively with conc HCl (or conc H<sub>2</sub>SO<sub>4</sub>), aq 10% K<sub>2</sub>CO<sub>3</sub> (Na<sub>2</sub>CO<sub>3</sub>), aq 10% NaCl, dried with CaCl<sub>2</sub> or Na<sub>2</sub>SO<sub>4</sub>, and fractionally distd. It can contain up to 3% dioxane as preservative. This is removed by washing successively with 10% aq HCl, 10% aq NaHCO<sub>3</sub> and 10% aq NaCl; and distd over CaCl<sub>2</sub> before use.

1,1,2-Trichloroethane [79-00-5] M 133.4, f -36.3°, b 113.6°, d 1.435, n 1.472. Purification as for 1,1,1-trichloroethane above.

**Trichloroethylene** [79-01-6] M 131.4, f -88°, b 87.2°, d 1.463,  $n^{21}$  1.4767. Undergoes decomposition in a similar way to CHCl<sub>3</sub>, giving HCl, CO, COCl<sub>2</sub> and organic products. It reacts with KOH, NaOH and 90% H<sub>2</sub>SO<sub>4</sub>, and forms azeotropes with water, MeOH, EtOH, and acetic acid. It is purified by washing successively with 2M HCl, water and 2M K<sub>2</sub>CO<sub>3</sub>, then dried with K<sub>2</sub>CO<sub>3</sub> and CaCl<sub>2</sub>, and fractionally distd immediately before use. It has also been steam distd from 10% Ca(OH)<sub>2</sub> slurry, most of the water being removed from the distillate by cooling to -30° to -50° and filtering off the ice through chamois skin: the trichloroethylene was then fractionally distd at 250mm pressure and collected in a blackened container. [Carlisle and Levine *Ind Eng Chem (Anal Ed)* 24 1164 1932.]

2,4,5-Trichloro-1-nitrobenzene [89-69-0] M 226.5, m 57°. Crystd from EtOH.

3,4,6-Trichloro-2-nitrophenol [82-62-2] M 242.4, m 92-93°,  $pK_{Est} \sim 4.1$ . Crystd from pet ether or EtOH.

2,4,5-Trichlorophenol [95-95-4] M 197.5, m 67°, b 72°/1mm, pK<sup>25</sup> 7.0. Crystd from EtOH or pet ether.

2,4,6-Trichlorophenol [88-06-2] M 197.5, m 67-68°, pK<sup>25</sup> 6.23. Crystd from \*benzene, EtOH or EtOH/water.

**3,4,5-Trichlorophenol** [609-19-8] **M 197.5, m 100°, pK<sup>25</sup> 7.84.** Crystd from pet ether/\*benzene mixture.

2,4,5-Trichlorophenoxyacetic acid (2,4,5-T) [93-76-5] M 255.5, m 153°, 155-158°, pK<sup>25</sup> 2.83. Crystd from \*benzene. (CANCER SUSPECT)

**1,1,2-Trichlorotrifluoroethane** [76-13-1] **M 187.4, b 47.6°/760mm, d 1.576, n 1.360.** Washed with water, then with weak alkali. Dried with  $CaCl_2$  or  $H_2SO_4$  and distd. [Locke et al. J Am Chem Soc 56 1726 1934.]

Tricycloquinazoline [195-84-6] M 230.3, m 322-323°. Crystd repeatedly from toluene, followed by vac sublimation at 210° at a pressure of 0.15-0.3 Torr in subdued light.

Tridecanoic acid [638-53-9] M 214.4, m 41.8°, 44.5-45.5° (several forms), b 199-200°/24mm, pK<sub>Est</sub> ~5.0. Crystd from acetone.

7-Tridecanone [462-18-0] M 198.4, m 33°, b 255°/766mm. Crystd from EtOH.

**Tri-***n***-dodecylammonium nitrate** [2305-34-2] **M 585.0.** Crystd from *n*-hexane/acetone (95:5) and kept in a desiccator over  $P_2O_5$ .

**Tri**-*n*-dodecylammonium perchlorate [5838-82-4] M 622.4. Recrystd from *n*-hexane or acetone and kept in a desiccator over  $P_2O_5$ .

Triethanolamine hydrochloride [637-39-8] M 185.7, m 177°, pK<sup>25</sup> 7.92 (free base). Crystd from EtOH. Dried at 80°.

1,1,2-Triethoxyethane [4819-77-6] M 162.2, b 164°, d 0.897, n 1.401. Dried with Na<sub>2</sub>SO<sub>4</sub>, and distd.

**Triethylamine** [121-44-8] **M 101.2, b 89.4°, d 0.7280, n 1.4005, pK^{25} 10.82.** Dried with CaSO<sub>4</sub>, LiAlH<sub>4</sub>, Linde type 4A molecular sieves, CaH<sub>2</sub>, KOH, or K<sub>2</sub>CO<sub>3</sub>, then distd, either alone or from BaO, sodium, P<sub>2</sub>O<sub>5</sub> or CaH<sub>2</sub>. It has also been distd from zinc dust, under nitrogen. To remove traces of primary and secondary amines, triethylamine has been refluxed with acetic anhydride, benzoic anhydride, phthalic anhydride, then distd, refluxed with CaH<sub>2</sub> (ammonia-free) or KOH (or dried with activated alumina), and again distd. Another purification involved refluxing for 2h with *p*-toluenesulfonyl chloride, then distd. Grovenstein and Williams [*J Am Chem Soc* 83 412 1961] treated triethylamine (500mL) with benzoyl chloride (30mL), filtered off the ppte, and refluxed the liquid for 1h with a further 30mL of benzoyl chloride. After cooling, the liquid was filtered, distd, and allowed to stand for several hours with KOH pellets. It was then refluxed with, and distd from, stirred molten potassium. Triethylamine has been converted to its hydrochloride, crystd from EtOH (to m 254°), then liberated with aq NaOH, dried with solid KOH and distd from sodium under nitrogen.

**Triethylammonium hydrobromide** [636-70-4] **M 229.1, m 248°.** Equimolar portions of triethylamine and aqueous solutions of HBr in acetone were mixed. The ppted salt was washed with anhydrous acetone and dried in vacuum for 1-2h. [Odinekov et al. J Chem Soc, Faraday Trans 2 80 899 1984.] Recrystd from CHCl<sub>3</sub> or EtOH.

Triethylammonium hydrochloride [554-68-7] M 137.7, m 257-260°(dec). Purified like the bromide above.

**Triethylammonium hydroiodide** [4636-73-1] **M 229.1, m 181°.** Purified as for triethylammonium bromide, except the soln for pptn was precooled acetone at -10° and the ppte was twice recrystd from a cooled acetone/hexane mixture at -10°.

**Triethylammonium trichloroacetate** [4113-06-8] **M 263.6.** Equimolar solns of triethylamine and trichloroacetic acid in *n*-hexane were mixed at  $10^{\circ}$ . The solid so obtained was recrystd from CHCl<sub>3</sub>/\*benzene.

**Triethylammonium trifluoroacetate** [454-49-9] **M 196.2.** Purified as for the corresponding trichloroacetate. The salt was a colourless liquid at ambient temperature.

**1,2,4-Triethylbenzene** [877-44-1] **M 162.3, b 96.8-97.1°/12.8mm, d 0.8738, n 1.5015.** For separation from a commercial mixture see Dillingham and Reid [*J Am Chem Soc* **60** 2606 1938].

**1,3,5-Triethylbenzene** [102-25-0] **M 162.3, b 102-102.5°, d 0.8631, n 1.4951.** For separation from a commercial mixture see Dillingham and Reid [J Am Chem Soc 60 2606 1938].

Triethylene glycol [112-27-6] M 150.2, b 115-117°/0.1mm, 278°/760mm,  $n^{15}$  1.4578,  $d^{15}$  1.1274. Dried with CaSO<sub>4</sub> for 1 week, then repeatedly and very slowly fractionally distd under vacuum. Stored in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. It is very hygroscopic.

Triethylene glycol dimethyl ether (triglyme) [112-49-2] M 178.2, b 225°, d 0.987, n 1.425. Refluxed with, and distd from sodium hydride or LiAlH<sub>4</sub>.

Triethylenetetramine (TRIEN, TETA, trientine) [112-24-3] M 146.2, m 12°, b 157°/20mm, d 0.971, n 1.497,  $pK_1^{25}$  3.32,  $pK_2^{25}$  6.67,  $pK_3^{25}$  9.20,  $pK_4^{25}$  9.92. Dried with sodium, then distd under vac. Further purification has been via the nitrate or the chloride. For example, Jonassen and Strickland [J Am Chem Soc 80 312 1958] separated TRIEN from admixture with TREN (38%) by soln in EtOH, cooling to approximately 5° in an ice-bath and adding conc HCl dropwise from a burette, keeping the temperature below 10°, until all of the white crystalline ppte of TREN.HCl had formed and been removed. Further addition of HCl then ppted thick creamy white TRIEN.HCl which was crystd several times from hot water by adding an excess of cold EtOH. The crystals were finally washed with Me<sub>2</sub>CO, then Et<sub>2</sub>O and dried in a vacuum desiccator.

**Triethylenetetramine tetrahydrochloride (TRIEN.HCl)** [4961-10-4] **M 292.1, m 266-270°.** Crystd repeatedly from hot water by pptn with cold EtOH or EtOH/HCl. Washed with acetone and abs EtOH and dried in a vacuum oven at 80° (see TRIEN above).

**Triethyl orthoformate** (1,1,1-triethoxymethane) [122-51-0] M 148.2, m 30°, b 60°/30mm, 144-146°, d 0.891, n 1.392. Fractionate first at atm press, then in a vac. If impure, then wash with H<sub>2</sub>O, dry over anhyd K<sub>2</sub>CO<sub>3</sub>, filter and fractionate through a Widmer column. [Sah and Ma J Am Chem Soc 54 2964 1932; Ohme and Schmitz Justus Liebigs Ann Chem 716 207 1968.] IRRITANT and FLAMMABLE.

**Triethyloxonium fluoroborate** [368-39-8] **M 190.0, m 92-93°(dec).** Crystd from diethyl ether. Very hygroscopic, and should be handled in a dry box and stored at 0°. [Org Synth 46 113 1966.] Pure material should give a clear and colourless soln in dichloromethane (1 in 50, w/v).

**Trifluoroacetic acid** [76-05-1] M **114.0, f** -15.5°, b 72.4°, d 1.494, n 1.2850,  $pK^{25}$  0.52. The purification of trifluoroacetic acid, reported in earlier editions of this work, by refluxing over KMnO<sub>4</sub> for 24h and slowly distilling has resulted in very **SERIOUS EXPLOSIONS** on various occasions, but not always. This apparently depends on the source and/or age of the acid. The method is NOT RECOMMENDED. Water can be removed by adding trifluoroacetic anhydride (0.05%, to diminish water content) and distd. [Conway and Novak J Phys Chem 81 1459 1977]. It can be refluxed and distd from P<sub>2</sub>O<sub>5</sub>. It is further purified by fractional crystn by partial freezing and again distd. Highly TOXIC vapour.

**Trifluoroacetic anhydride** [407-25-0] **M 210.0, b 38-40°/760mm, d 1.508.** Purification by distilling over KMnO<sub>4</sub>, as for the acid above is **EXTREMELY DANGEROUS** due to the possibility of **EXPLOSION**. It is best purified by distilling from  $P_2O_5$  slowly, and collecting the fraction boiling at 39.5°. Store in a dry atmosphere. **Highly TOXIC vapour.** 

1,1,1-Trifluoro-2-bromoethane [421-06-7] M 163.0. See 1-bromo-3,3,3-trifluoroethane on p. 142.

2,2,2-Trifluoroethanol [75-89-8] M 100.0, b 72.4°/738mm, d 1.400, pK<sup>25</sup> 12.8. Dried with CaSO<sub>4</sub> and a little NaHCO<sub>3</sub> (to remove traces of acid). Highly TOXIC vapour.

**Trifluoromethanesulfonic anhydride (triflic anhydride)** [358-23-6] M 282.1, b 82-85°, 84°, d 1.71, n 1.322. Distil through a short Vigreux column. Could be freshly prepd from the anhydrous acid (11.5g) and  $P_2O_5$  (11.5g, or half this weight) by setting aside at room temp for 1h, distilling off volatile products then through a short Vigreux column. Readily hydrolysed by  $H_2O$  and decomposes appreciably after a few days to liberate  $SO_2$  and produce a viscous liquid. Store dry at low low temp. [Burdon et al. J Chem Soc 2574 1957; Beard et al. J Org Chem 38 373 1973.] Highly TOXIC vapour.

4-(Trifluoromethyl)acetophenone [709-63-7] M 188.2, m 31-33°, b 79-81°/9mm. Purified by distillation or sublimation *in vacuo*.

**3-Trifluoromethyl-4-nitrophenol** [88-30-2] **M 162.1, m 81°, pK**<sub>Est</sub> ~6.1. Crystd from \*benzene or from pet ether/\*benzene mixture.

 $\alpha, \alpha, \alpha$ -Trifluorotoluene (benzotrifluoride) [98-08-8] M 144.1, b 102.5°, d 1.190, n<sup>30</sup> 1.4100. Purified by repeated treatment with boiling aqueous Na<sub>2</sub>CO<sub>3</sub> (until no test for chloride ion was obtained), dried with K<sub>2</sub>CO<sub>3</sub>, then with P<sub>2</sub>O<sub>5</sub>, and fractionally distd.

Triglycyl glycine (tetraglycine) [637-84-3] M 246.2, m 270-275°(dec). Crystd from distilled water (optionally, by the addition of EtOH).

Trigonelline (1-methylnicotinic acid zwitterion) [535-83-1] M 137.1, m 218°(dec). Crystd (as monohydrate) from aqueous EtOH, then dried at 100°.

2,3,4-Trihydroxybenzoic acid [610-02-6] M 170.1, m 207-208°, pK<sub>Est(1)</sub>~3.4, pK<sub>Est(2)</sub>~7.8, pK<sub>Est(3)</sub>>12. Crystd from water.

2,4,6-Trihydroxybenzoic acid [83-30-7] M 170.1, m 205-212°(dec), pK<sub>Est(1)</sub>~1.5, pK<sub>Est(2)</sub>~8.0, pK<sub>Est(3)</sub>>12. Crystd from water.

4',5,7-Trihydroxyflavone (apigenin) [520-36-5] M 270.2, m 296-298°, 300-305°, 345-350° (pK's 7-10, for phenolic OH). Crystd from aq pyridine or aq EtOH. Dyes wool yellow when with added Cr.

**3,4,5-Triiodobenzoic acid** [2338-20-7] **M 499.8, m 289-290°, 293°, pK<sup>25</sup> 0.65.** Crystd from aqueous EtOH or water.

**3,4,5-Triiodobenzyl chloride** [52273-54-8] **M 504.3, m 138°.** Crystd from CCl<sub>4</sub>/pet ether (charcoal).

3,3',5-Triiodo-S-thyronine [6893-02-3] M 651.0, m 236-237°(dec),  $[\alpha]_D^{29.5} + 21.5°$ (EtOH/1M aq HCl, 2:1),  $pK_1^{25}$  6.48,  $pK_2^{25}$  7.62,  $pK_3^{25}$  7.82. Likely impurities are as in *thyroxine*. Purified by dissolving in dilute NH<sub>3</sub> at room temperature, then crystd by addition of dilute acetic acid to pH 6.

Trimellitic (benzene-1,2,4-tricarboxylic) acid [528-44-9] M 210.1, m 218-220°,  $pK_1^{25}$  2.42,  $pK_2^{25}$  3.71,  $pK_3^{25}$  5.01. Crystd from acetic acid or aqueous EtOH.

1,2,3-Trimethoxybenzene [634-36-6] M 168.2, m 45-46°. Sublimed under vacuum.

1,3,5-Trimethoxybenzene [621-23-8] M 168.2, m 53°. Sublimed under vacuum.

**Trimethylamine** [75-50-3] **M 59.1, b 3.5°, pK^{25} 9.80.** Dried by passage of the gas through a tower filled with solid KOH. Water and impurities containing labile hydrogen were removed by treatment with freshly sublimed, ground, P<sub>2</sub>O<sub>5</sub>. Has been refluxed with acetic anhydride, and then distd through a tube packed with HgO and BaO. [Comyns *J Chem Soc* 1557 1955.] For more extensive purification, trimethylamine has been converted to the hydrochloride, crystd (see below), and regenerated by treating the hydrochloride with excess aq 50% KOH, the gas passing through a CaSO<sub>4</sub> column into a steel cylinder containing sodium ribbon. After 1-2 days, the cylinder was cooled at -78° and hydrogen and air were removed by pumping. [Day and Felsing *J Am Chem Soc* **72** 1698 1950.] Trimethylamine has also been trap-to-trap distd and then freeze-pump-thaw degassed [Halpern et al. *J Am Chem Soc* **108** 3907 1986].

**Trimethylamine hydrochloride** [593-81-7] **M 95.7, m >280°(dec).** Crystd from CHCl<sub>3</sub>, EtOH or *n*-propanol, and dried under vacuum. It has also been crystd from \*benzene/MeOH, MeOH/diethyl ether and dried under vacuum over paraffin wax and H<sub>2</sub>SO<sub>4</sub>. Stood over P<sub>2</sub>O<sub>5</sub>. It is *hygroscopic*.

Trimethylamine hydroiodide [20230-89-1] M 186.0, m 263°. Crystd from MeOH.

1,2,4-Trimethylbenzene (pseudocumene) [95-63-6] M 120.2, m -43.8°, b 51.6°/10mm, 167-168°/760mm, d 0.889, n 1.5048. Refluxed over sodium and distd under reduced pressure.

2,4,6-Trimethylbenzoic acid (mesitoic acid) [480-63-7] M 164.2, m 155°, pK<sup>25</sup> 3.45. Crystd from water, ligroin or carbon tetrachloride [Ohwada et al. J Am Chem Soc 108 3029 1986].

Trimethyl-1,4-benzoquinone [935-92-2] M 150.1, m 29-30°, 36°, b 98°/10mm, 108°/18mm. Distd in a vac or sublimed *in vacuo* before use. [Smith et al. J Am Chem Soc 60 318 1939.]

**R**-(-)-2,2,6-Trimethyl-1,4-cyclohexanedione [60046-49-3] M 154.2, m 88-90°, 91-92°,  $[\alpha]_D^{20}$ -270° (c 0.4%, MeOH),  $[\alpha]_D^{20}$ -275° (c 1, CHCl<sub>3</sub>). Obtained from fermentation and purified by recrystn from diisopropyl ether. [ORD: Leuenberger et al. *Helv Chim Acta* 59 1832 1976.] The racemate has m 65-67° and the 4-(4-phenyl)semicarbazone has m 218-220° (from CH<sub>2</sub>Cl<sub>2</sub>-MeOH) [Isler et al. *Helv Chim Acta* 39 2041 1956.]

2,2,5-Trimethylhexane [3522-94-9] M 128.3, m -105.8°, b 124.1°, d 0.716, n 1.39971,  $n^{25}$  1.39727. Extracted with conc H<sub>2</sub>SO<sub>4</sub>, washed with H<sub>2</sub>O, dried (type 4A molecular sieves), and fractionally distd.

Trimethyl-1,4-hydroquinone (2,3,5-trimethylbenzene-1,4-diol) [700-13-0] M 152.2, m 173-174°,  $pK_{Est(1)}$ ~ 11.1,  $pK_{Est(2)}$ ~ 12.7. Recrystd from water, under anaerobic conditions.

1',3',3'-Trimethyl-6-nitrospiro[2H-benzopyran-2,2'-indoline] [1498-88-0] M 322.4, m 180°. Recrystd from absolute EtOH [Hinnen et al. Bull Soc Chim Fr 2066 1968; Ramesh and Labes J Am Chem Soc 109 3228 1987].

Trimethylolpropane [77-99-6] M 134.2, m 57-59°. Crystd from acetone and ether.

**2,2,3-Trimethylpentane** [564-02-3] **M 114.2, b 109.8°, d 0.7161, n 1.40295, n<sup>25</sup> 1.40064.** Purified by azeotropic distn with 2-methoxyethanol, which was subsequently washed out with water. The trimethylpentane was then dried and fractionally distd. [Forziati et al. J Res Nat Bur Stand 36 129 1946.]

2,2,4-Trimethylpentane (isooctane) [540-84-1] M 114.2, b 99.2°, d 0.693, n 1.39145, n<sup>25</sup> 1.38898. Distd from sodium, passed through a column of silica gel or activated alumina (to remove traces of olefins), and again distd from sodium. Extracted repeatedly with conc  $H_2SO_4$ , then agitated with aqueous KMnO<sub>4</sub>, washed with water, dried (CaSO<sub>4</sub>) and distd. Purified by azeotropic distn with EtOH, which was subsequently washed out with water, and the trimethylpentane was dried and fractionally distd. [Forziati et al. J Res Nat Bur Stand **36** 126 1946.] Also purified by fractional crystn.

**2,3,5-Trimethylphenol** [697-82-5] **M 136.2, m 95-96°, b 233°/760mm, pK<sup>25</sup> 10.67.** Crystd from water or pet ether.

2,4,5-Trimethylphenol [496-78-6] M 136.2, m 70.5-71.5°, pK<sup>25</sup> 10.57. Crystd from water.

2,4,6-Trimethylphenol [527-60-6] M 136.2, m 69°, b 220°/760mm, pK<sup>25</sup> 10.86. Crystd from water and sublimed *in vacuo*.

**3,4,5-Trimethylphenol** [527-54-8] **M 136.2, m 107°, b 248-249°/760mm, pK<sup>25</sup> 10.25.** Crystd from pet ether.

Trimethylphenylammonium benzenesulfonate [16093-66-6] M 293.3. Crystd repeatedly from MeOH (charcoal).

2,2,4-Trimethyl-6-phenyl-1,2-dihydroquinoline [3562-69-4] M 249.3, m 102°. Vacuum distd, then crystd from absolute EtOH.

2,4,6-Trimethylpyridine (sym-collidine) [108-75-8] M 121.2, m -46°, b 10°/2.7mm, 36-37°/2mm, 60.7°/13mm, 65°/31mm, 170.4°/760mm, 175-178°/atm, d<sup>25</sup> 0.9100,  $n_D^{20}$  1.4939, 1.4981,  $n^{25}$  1.4959, pK<sup>25</sup> 6.69. Commercial samples may be grossly impure. Likely contaminants include 3,5-dimethylpyridine, 2,3,6-trimethylpyridine and water. Brown, Johnson and Podall [*J Am Chem Soc* 76 5556 1954] fractionally distd 2,4,6-trimethylpyridine under reduced pressure through a 40-cm Vigreux column and added to 430mL of the distillate slowly, with cooling to 0°, 45g of BF<sub>3</sub>-diethyl etherate. The mixture was again distd, and an equal volume of dry \*benzene was added to the distillate. Dry HCl was passed into the soln, which was kept cold in an ice-bath, and the hydrochloride was filtered off. It was recrystd from abs EtOH (1.5mL/g) to m 286-287°(sealed tube). The free base was regenerated by treatment with aq NaOH, then extracted with \*benzene, dried (MgSO<sub>4</sub>) and distd under reduced pressure. Sisler et al. [*J Am Chem Soc* 75 446 1953] ppted trimethylpyridine as its phosphate from a soln of the base in MeOH by adding 85% H<sub>3</sub>PO<sub>4</sub>, shaking and cooling. The free base was regenerated as above. Garrett and Smythe [*J Chem Soc* 763 1903] purified the trimethylpyridine via the HgCl<sub>2</sub> complex. It is more soluble in cold than hot H<sub>2</sub>O [sol 20.8% at 6°, 3.5% at 20°, 1.8% at 100°].

Also purified by dissolving in CHCl<sub>3</sub>, adding solid K<sub>2</sub>CO<sub>3</sub> and Drierite, filtering and fractionally distilling through an 8in helix packed column. The *sulfate* has **m** 205°, and the *picrate* (from hot H<sub>2</sub>O) has **m** 155-156°. [Frank and Meikle J Am Chem Soc 72 4184 1950.]

Trimethylsulfonium iodide [2181-42-2] M 204.1, m 215-220°(dec). Crystd from EtOH.

1,3,7-Trimethyluric acid [5415-44-1] M 210.2, m 345°(dec), pK 6.0. Crystd from water.

1,3,9-Trimethyluric acid [7464-93-9] M 210.2, m 340°, 347°, pK<sup>20</sup> 9.39. Crystd from water.

**1,7,9-Trimethyluric acid** [55441-82-2] **M 210.2, m 316-318 (dec)<sup>o</sup>, 345<sup>o</sup>, pK<sub>Est</sub> ~9.0.** Crystd from water or EtOH, and sublimed *in vacuo*.

Trimyristin [555-45-3] M 723.2, m 56.5°. Crystd from diethyl ether.

2,4,6-Trinitroanisole [606-35-9] M 243.1, m 68°. Crystd from EtOH or MeOH. Dried under vac.

**1,3,6-Trinitrobenzene** [99-35-4] **M 213.1, m 122-123°.** Crystd from glacial acetic acid, CHCl<sub>3</sub>, CCl<sub>4</sub>, EtOH aq EtOH or EtOH/\*benzene, after (optionally) heating with dil HNO<sub>3</sub>. Air dried. Fused, and crystd under vacuum.

2,4,6-Trinitrobenzenesulfonic acid hydrate (TNBS, picrylsulfonic acid) [2508-19-2] M 293.2, m 180°,  $\lambda$ max 240nm ( $\epsilon$  650 M<sup>-1</sup>cm<sup>-1</sup>), pK<sub>Est</sub>~ <0. It is also available as 0.1M and 5% w/v solns in H<sub>2</sub>O. Recrystd from 1M HCl and dried at 100° or a mixt of EtOH (50mL), H<sub>2</sub>O (30mL) and conc HCl (70mL) for 65g of acid. The diethanolamine salt had m 182-183° [Golumbic J Org Chem 11 518 1946].

2,4,6-Trinitrobenzoic acid [129-66-8] M 225.1, m 227-228°, pK<sup>25</sup> 0.65. Crystd from distilled water. Dried in a vacuum desiccator.

**2,4,6-Trinitro**-*m*-**cresol** [602-99-3] **M 243.1, m 107.0-107.5°, pK 2,8.** Crystd successively from H<sub>2</sub>O, aq EtOH and \*benzene/cyclohexane, then dried at 80° for 2h. [Davis and Paabo J Res Nat Bur Stand 64A 533 1960.]

2,4,7-Trinitro-9-fluorenone [129-79-3] M 315.2, m 176°. Crystd from nitric acid/water (3:1), washed with water and dried under vacuum over P<sub>2</sub>O<sub>5</sub>, or recrystd from dry \*benzene.

**2,4,6-Trinitrotoluene** (TNT) [118-96-7] M 227.1, m 81.0-81.5°. Crystd from \*benzene and EtOH. Then fused and allowed to cryst under vacuum. Gey, Dalbey and Van Dolah [*J Am Chem Soc* 78 1803 1956] dissolved TNT in acetone and added cold water (1:2:15), the ppte was filtered, washed free from solvent and stirred with five parts of aq 8% Na<sub>2</sub>SO<sub>3</sub> at 50-60° for 10min. It was filtered, washed with cold water until the effluent was colourless, and air dried. The product was dissolved in five parts of hot CCl<sub>4</sub>, washed with warm water until the washings were colourless and TNT was recoverd by cooling and filtering. It was recrystd from 95% EtOH and carefully dried over H<sub>2</sub>SO<sub>4</sub>. The dry solid should not be heated without taking precautions for a possible **EXPLOSION**.

2,4,6-Trinitro-m-xylene [632-92-8] M 241.2, m 182.2°. Crystd from ethyl methyl ketone.

**Tri-n-octylamine** [1116-76-3] **M 353.7, b 164-168°/0.7mm, 365-367°/760mm, d 0.813, n 1.450, pK<sup>25</sup> 10.65.** It was converted to the amine hydrochloride etherate which was recrystd four times from diethyl ether at -30° (see below). Neutralisation of this salt regenerated the free amine. [Wilson and Wogman J Phys Chem 66 1552 1962.] Distd at 1-2mm pressure.

**Tri-n-octylammonium chloride** [1188-95-0] **M 384.2, m 78-79°, pK 8.35 (in 70% aq EtOH).** Crystd from Et<sub>2</sub>O, then *n*-hexane (see above). [Burrows et al. J Chem Soc 200 1947.]

Tri-n-octylammonium perchlorate [2861-99-6] M 454.2, m >300°(dec). Crystd from n-hexane.

1,3,5-Trioxane [110-88-3] M 90.1, m 64°, b 114.5°/759mm. Crystd from sodium-dried diethyl ether or water, and dried over CaCl<sub>2</sub>. Purified by zone refining.

**Trioxsalen** (2,5,9-trimethyl-7*H*-furo[3,2-g]benzopyran-7-one) [3902-71-4] M 228.3, m 233-235°, 234.5-235°. Purified by recrystn from CHCl<sub>3</sub>. If too impure it is fractionally crystd from CHCl<sub>3</sub>-pet ether (b 30-60°) using Norit and finally crystd from CHCl<sub>3</sub> alone to give colourless prisms, m 234.5-235°. It is a photosensitiser so it should be stored in the dark. [UV: Kaufmann J Org Chem 26 117 1961; Baeme et al. J Chem Soc 2976 1949.]

Tripalmitin [555-44-2] M 807.4, m 66.4°. Crystd from acetone, diethyl ether or EtOH.

**Triphenylamine** [603-34-9] M 245.3, m 127.3-127.9°, pK -5.0 (in fluorosulfuric acid). Crystd from EtOH or from \*benzene/abs EtOH, diethyl ether and pet ether. It was sublimed under vacuum and carefully dried in a vacuum line. Stored in the dark under nitrogen. 1,3,5-Triphenylbenzene [612-71-5] M 306.4, m 173-175°. Purified by chromatography on alumina using \*benzene or pet ether as eluents.

Triphenylene [217-59-4] M 228.3, m 198°, b 425°. Purified by zone refining or crystn from EtOH or CHCl<sub>3</sub>, and sublimed.

**1,2,3-Triphenylguanidine** [101-01-9] **M 287.3, m 144°, pK 9.10.** Crystd from EtOH or EtOH/water, and dried under vacuum.

**Triphenylmethane** [519-73-3] **M 244.3, m 92-93°.** Crystd from EtOH or \*benzene (with one molecule of \*benzene of crystallisation which is lost on exposure to air or by heating on a water bath). It can also be sublimed under vacuum. It can also be given a preliminary purification by refluxing with tin and glacial acetic acid, then filtered hot through a glass sinter disc, and ppted by addition of cold water.

Triphenylmethanol (triphenylcarbinol) [76-84-6] M 260.3, m 164°, b 360-380° (without dec),  $pK^{25}$  -6.63 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from EtOH,MeOH, CCl<sub>4</sub> (4mL/g), \*benzene, hexane or pet ether (b 60-70°). Dried at 90°. [Ohwada et al. J Am Chem Soc 108 3029 1986.]

Triphenylmethyl chloride (trityl chloride) [76-83-5] M 278.9, m 111-112°. Crystd from isooctane. Also crystd from 5 parts of pet ether (b 90-100°) and 1 part of acetyl chloride using 1.8g of solvent per g of chloride. Dried in a desiccator over soda lime and paraffin wax. [Org Synth Coll Vol III 841 1955; Thomas and Rochow J Am Chem Soc 79 1843 1957; Moisel et al. J Am Chem Soc 108 4706 1986.]

2,3,5-Triphenyltetrazolium chloride (TTC) [298-96-4] M 334.8, m 243°(dec). Crystd from EtOH or CHCl<sub>3</sub>, and dried at 105°.

**Tri-***n***-propylamine** [102-69-2] **M 143.3, b 156.5°, d 0.757, n 1.419, pK<sup>25</sup> 10.66.** Dried with KOH and fractionally distd. Also refluxed with toluene-*p*-sulfonyl chloride and with KOH, then fractionally distd. The distillate, after addn of 2% phenyl isocyanate, was redistd and the residue fractionally distd from sodium. [Takahashi et al. J Org Chem 52 2666 1987.]

Tripyridyl triazine [3682-35-7] M 312.3, m 245-248°. Purified by repeated crystn from aq EtOH.

Tris-(2-aminoethyl)amine (TREN) [4097-89-6] M 146.2, b 114°/15mm, 263°/744mm, d 0.977, n 1.498,  $pK_1^{25}$  8.42,  $pK_2^{25}$  9.44,  $pK_3^{25}$  10.13. For a separation from a mixture containing 62% TRIEN, see entry under triethylenetetramine. Also purified by conversion to the hydrochloride (see below), recrystn and regeneration of the free base [Xie and Hendrickson J Am Chem Soc 109 6981 1987].

Tris-(2-aminoethyl)amine trihydrochloride [14350-52-8] M 255.7, m 300°(dec). Crystd several times by dissolving in a minimum of hot water and precipitating with excess cold EtOH. The ppte was washed with acetone, then diethyl ether and dried in a vacuum desiccator.

Tris(d,d-dicamopholylmethanato)europium (III) [52351-64-1] M 108.5, m 220-227.5°, 229-232°,  $[\alpha]_D^{25} + 28.6°$  (c 5.4, CCl<sub>4</sub>; and varies markedly with concentration). Dissolve in pentane, filter from any insol material, evaporate to dryness and dry the residue (white powder) at 100°/0.1mm for 36h. The IR has v 1540cm<sup>-1</sup>. [McCreary et al. J Am Chem Soc 96 1038 1974.]

Tris-(dimethylamino)methane (N, N, N', N'', N'', N'') hexamethylmethanetriamine) [5762-56-1] M 145.3, b 42-43°/12mm, n 1.4349, pK<sub>Est</sub> ~ 10. Dry over KOH and dist through a Vigreux column at waterpump vacuum. Store in absence of CO<sub>2</sub>. [Bredereck et al. *Chem Ber* 101 1885 1968 and Angew Chem, Int Ed Engl 5 132 1966.]

**Tris-(hydroxymethyl)methylamine (TRIS)** [77-86-1] **M 121.1, m 172°, pK^{25} 8.07.** Tris can ordinarily be obtained in highly pure form suitable for use as an acidimetric standard. If only impure material is available, it should be crystd from 20% EtOH. Dry in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> or CaCl<sub>2</sub>.

Alternatively, it is dissolved in twice its weight of water at 55-60°, filtered, concd to half its volume and poured slowly, with stirring, into about twice the volume of EtOH. The crystals which separate on cooling to  $3-4^{\circ}$  are filtered off, washed with a little MeOH, air dried by suction, then finally ground and dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. It has also been crystd from water, MeOH or aq MeOH, and vacuum dried at 80° for 2 days.

Tris-(hydroxymethyl)methylamonium hydrochloride (TRIS-HCl) [1185-53-1] M 157.6, m 149-150°(dec). Crystd from 50% EtOH, then from 70% EtOH. Tris-hydrochloride is also available commercially in a highly pure state. Otherwise, crystd from 50% EtOH, then 70% EtOH, and dried below 40° to avoid risk of decomposition.

1,1,1-Tris-(hydroxymethyl)ethane (2-hydroxymethyl-2-methyl-1,3-propanediol) [77-85-0] M 120.2, m 200°. Dissolved in hot tetrahydrofuran, filtered and ppted with hexane. It has also been crystd from acetone/water (1:1). Dried in vacuum.

*N*-Tris-(hydroxymethyl)methyl-2-aminomethanesulfonic acid (TES) [7365-44-8] M 229.3, m 224-226°(dec), pK<sup>20</sup> 7.50. Crystd from hot EtOH containing a little water.

*N*-Tris-(hydroxymethyl)methylglycine (TRICINE) [5704-04-1] M 179.2, m 186-188°(dec),  $pK_1^{20} \sim 2.3$ ,  $pK_2^{20} \approx 8.15$ . Crystd from EtOH and water.

Tris-(hydroxymethyl)nitromethane [2-(hydroxymethyl)-2-nitro-1,3-propanediol] [126-11-4] M 151.1, m 174-175°(dec, tech grade), 214°(pure). Crystd from CHCl<sub>3</sub>/ethyl acetate or ethyl acetate/\*benzene. It is an acid and a 0.1M sol in H<sub>2</sub>O has pH 4.5. IRRITANT.

Tris-[(3-trifluoromethylhydroxymethylene)-d-camphorato] europium (III) [Eu(tfc)<sub>3</sub>] [34830-11-0] M 893.6, m 195-299° (dec), ~220°,  $[\alpha]_D^{24}$ +152° (c 2, CCl<sub>4</sub>; and varies markedly with concentration). Purified by extraction with pentane, filtered and filtrate evapd and the residual bright yellow amorphous powder is dried at 100°/0.1mm for 36h. A sample purified by fractional molecular distn at 180-200°/0.004mm gave a liquid which solidified and softened at ~130° and melted at ~180° and was analytically pure. IR (CCl<sub>4</sub>) v: 1630-1680cm<sup>-1</sup> and NMR (CCl<sub>4</sub>)  $\delta$  broad: -1.3 to 0.5, -0.08 (s), 0.41 (s), 1.6-2.3 and 3.39 (s). [McCreary et al. J Am Chem Soc 96 1038 1974; ; Goering et al. J Am Chem Soc 93 5913 1971.]

1,3,5-Trithiane [291-21-4] M 138.3, m 220°(dec). Crystd from acetic acid.

Triuret (1,3-dicarbamoylurea) [556-99-0] M 146.1, m 233<sup>o</sup>(dec). Crystd from aq ammonia. Gives mono and dipotassium salts.

**Tropaeolin 00**, [554-73-4] **M 316.3**,  $pK_{Est(2)} \sim 5.8$ ,  $pK_{Est(3)} \sim 10.3$ . Recrystd twice from water [Kolthoff and Gus J Am Chem Soc 60 2516 1938].

**Tropaeolin 000** (see Orange II p. 477 in Chapter 5). Purified by salting out from hot distilled water using sodium acetate, then three times from distilled water and twice from EtOH.

3-Tropanol (Tropine) [120-29-6] M 141.2, m 63°, b 229°/760mm, pK<sup>15</sup> 3.80. Distd in steam and crystd from diethyl ether. Hygroscopic.

*dl*-Tropic (3-hydroxy-2-phenylpropionic) acid [529-64-6] M 166.2, m 118°, pK<sup>25</sup> 4.12. Crystd from water or \*benzene.

Tropolone [533-75-5] M 122.1, m 49-50°, b 81-84°/0.1mm,  $pK_1$  -0.53 (protonation of CO, aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2$  6.67 (acidic OH). Crystd from hexane or pet ether and sublimed at 40°/4mm.

Tryptamine [(3-2-aminoethyl)indole)] [61-54-1] M 160.1, m 116°,  $pK_1^{25}$ -6.31 (aq H<sub>2</sub>SO<sub>4</sub>, diprotonation),  $pK_{Est(2)}$ ~4.9,  $pK_3^{25}$  16.60 (acidic indole NH). Crystd from \*benzene.

Tryptamine hydrochloride [343-94-2] M 196.7, m 252-253°. Crystd from EtOH/water.

L-Tryptophan [73-22-3] M 204.3, m 278°,  $[\alpha]_D^{20}$  -33.4° (EtOH),  $[\alpha]_{546}^{20}$  -36° (c 1, H<sub>2</sub>O), pK<sub>1</sub><sup>25</sup> -6.23 (aq H<sub>2</sub>SO<sub>4</sub>), pK<sub>2</sub><sup>25</sup> 2.46, pK<sub>3</sub><sup>25</sup> 9.41, pK<sub>4</sub><sup>25</sup> 14.82 (acidic NH, in aq NaOH). Crystd from water/EtOH, washed with anhydrous diethyl ether and dried at room temperature under vac over P<sub>2</sub>O<sub>5</sub>.

**Tryptophol** [3-(2-hydroxyethyl)indole] [526-55-6] M 161.2, m 59°, b 174°/2mm. Crystd from diethyl ether/pet ether,  $*C_6H_6$ ,  $*C_6H_6$ /pet ether. The *picrate* has m 98-100° (from  $*C_6H_6$ ).

(+)-Tubocurarine chloride (5H<sub>2</sub>O) [57-94-3] M 771.7, m 274-275°(dec) (anhydrous),  $[\alpha]_{546}^{20}$ +235° (c 0.5, H<sub>2</sub>O), pK<sub>Est(1)</sub>~8.5, pK<sub>Est(2)</sub>~8.8. Crystd from water and forms various hydrates.

D(+)-Turanose [547-25-1] M 342.3, m 168-170°,  $[\alpha]_D^{20}$  +88° (c 4, H<sub>2</sub>O). Crystd from water by addition of EtOH.

Tyramine (4-hydroxybenzylamine) [51-67-2] M 137.2, m 164-165°,  $pK_1^{25}$  9.74 (OH),  $pK_2^{25}$  10.52 (NH<sub>2</sub>). Crystd from \*benzene or EtOH.

Tyramine hydrochloride [60-19-5] M 173.6, m 274-276°. Crystd from EtOH by addition of diethyl ether, or from conc HCl.

Tyrocidine A (cyclic decapeptide antibiotic with two D-Phe amino acids) [1481-70-5] M 1268.8, m 240°(dec),  $[\alpha]_D^{25}$ -115° (c 0.91, MeOH). Crystd as hydrochloride from MeOH or EtOH and HCl. [Paladin and Craig J Am Chem Soc 76 688 1954; King and Craig J Am Chem Soc 77 6624 1955; Okamoto et al. Bull Chem Soc Jpn 50 231 1977.]

L-Tyrosine [60-18-4] M 181.2, m 290-295°(dec),  $[\alpha]_D^{25}$ -10.0° (5M HCl),  $pK_1^{25}$ 2.18 (CO<sub>2</sub>H),  $pK_2^{25}$ 9.21 (OH),  $pK_3^{20}$  10.47 (NH<sub>2</sub>). Likely impurities are L-cysteine and the ammonium salt. Dissolved in dilute ammonia, then crystd by adding dilute acetic acid to pH 5. Also crystd from water or EtOH/water, and dried at room temperature under vacuum over P<sub>2</sub>O<sub>5</sub>.

**Umbelliferone** (7-hydroxycoumarin) [93-35-6] M 162.2, m 225-228°, pK<sub>Est</sub> ~8.0. Crystd from water.

Undecan-1-ol [112-42-5] M 172.3, m 16.5°. Purified by repeated fractional crystn from its melt or by distn in a vacuum.

Undec-10-enoic acid [112-38-9] M 184.3, m 25-25.5°, b 131°/1mm, 168°/15mm, pK<sub>Est</sub> ~5.0. Purified by repeated fractional crystn from its melt or by distn in a vacuum.

Uracil [66-22-8] M 122.1, m 335°(dec), pK<sub>1</sub><sup>25</sup> 9.43, pK<sub>2</sub><sup>25</sup> 13.3-14.2. Crystd from water.

Uramil (5-aminobarbituric acid) [118-78-5] M 143.1, m 310-312°, 320°, >400°(dec),  $pK_{Est(1)}$ ~3.9,  $pK_{Est(2)}$ ~8.0,  $pK_{Est(3)}$ ~12.5. Crystd from water.

Urea [57-13-6] M 60.1, m 132.7-132.9°,  $pK^{25}$  0.12. Crystd twice from conductivity water using centrifugal drainage and keeping the temperature below 60°. The crystals were dried under vacuum at 55° for 6h. Levy and Margouls [J Am Chem Soc 84 1345 1962] prepared a 9M soln in conductivity water (keeping the temperature below 25°) and, after filtering through a medium-porosity glass sinter, added an equal volume of absolute EtOH. The mixture was set aside at -27° for 2-3 days and filtered cold. The ppte was washed with a small amount of EtOH and dried in air. Crystn from 70% EtOH between 40° and -9° has also been used. Ionic impurities such as ammonium isocyanate have been removed by treating the conc aqueous soln at 50° with

Amberlite MB-1 cation- and anion-exchange resin, and allowing to crystallise. [Benesch, Lardy and Benesch J Biol Chem 216 663 1955.] Also crystd from MeOH or EtOH, and dried under vacuum at room temperature.

Urea nitrate [124-47-0] M 123.1, m 152°(dec). Crystd from dilute HNO<sub>3</sub>.

Uric acid [69-93-2] M 168.1, m >300°, pK<sub>1</sub> 5.75, pK<sub>2</sub> 10.3. Crystd from hot distilled water.

Uridine [58-96-8] M 244.2, m 165°,  $[\alpha]_D^{20}$  +4.0° (H<sub>2</sub>O), pK<sup>25</sup> 9.51 (9.25). Crystd from aqueous 75% MeOH.

Urocanic acid (4-imidazolylacrylic acid) [104-98-3] M 138.1, m 225°, 226-228°,  $pK_{Est(1)}\sim 2.5$ ,  $pK_{Est(2)}\sim 6$ ,  $pK_{Est(3)}\sim 11$ . Crystd from water and dried at 100°.

Ursodeoxycholic acid [128-13-2] M 392.5, m 203°,  $[\alpha]_D^{20}$  +60° (c 0.2, EtOH), pK<sub>Est</sub> ~4.8. Crystd from EtOH.

(+)-Usnic acid [2,6-diacetyl-3,7,9-trihydroxy-8,9b-dimethyldibenzofuran-1(2H)-one] [7562-61-0] M 344.3, m 204°. See (+)-usnic acid on p. 573 in Chapter 6.

trans-Vaccenic acid (octadec-11-enoic acid) [693-72-1] M 282.5, m 43-44°, pK<sub>Est</sub> ~ 4.9. Crystd from acetone. The methyl ester has b 174-175°/5mm.

*n*-Valeraldehyde [110-62-3] M 86.1, b 103°, d 0.811, n<sup>25</sup> 1.40233. Purified via the bisulfite derivative. [Birrell and Trotman-Dickinson J Chem Soc 2059 1960.]

n-Valeramide (pentanamide) [626-97-1] M 101.1, m 115-116°. Crystd from EtOH.

Valeric acid (*n*-pentanoic acid) [109-52-4] M 102.1, b 95°/22mm, 186.4°/atm, d 0.938, n 1.4080,  $pK^{25}$  4.81. Water was removed from the acid by distn using a Vigreux column, until the boiling point reached 183°. A few crystals of KMnO<sub>4</sub> were added, and after refluxing, the distn was continued, [Andrews and Keefer J Am Chem Soc 83 3708 1961.]

δ-Valerolactam (2-piperidone) [675-20-7] M 99.1, m 38.5-39.5°, 39-40°, 40°, b 81-82°/0.1mm, 136-137°/15mm, pK 0.75 (in AcOH). Purified by repeated fractional distn. [Cowley J Org Chem 23 1330 1958; Reppe et al. Justus Liebigs Ann Chem 596 198 1955; IR: Huisgen et al. Chem Ber 90 1437 1957.] The hydrochloride has m 183-184° (from isoPrOH or EtOH-Et<sub>2</sub>O) [Hurd et al. J Org Chem 17 865 1952], and the oxime has m 122.5° (from pet ether) [Behringer and Meier Justus Liebigs Ann Chem 607 67 1957]. Picrate has m 92-93°.

 $\gamma$ -Valerolactone (± 4,5-dihydro-5-methyl-2(3*H*)-furanone) [108-29-2] M 100.1, m -37°, 36°, b 82-85°/10mm, 102-103°/28mm, 125.3°/68mm, 136°/100mm, 205.75-206.25°/754mm,  $d_4^{20}$  1.072,  $n_D^{20}$  1.4322. Purified by repeated fractional distillation [Boorman and Linstead J Chem Soc 577, 580 1933]. IR v: 1790 (CS<sub>2</sub>), 1775 (CHCl<sub>3</sub>) cm<sup>-1</sup> [Jones et al. Can J Chem 37 2007 1959]. The BF<sub>3</sub>-complex distils at 110-111°/20mm [Reppe et al. Justus Liebigs Ann Chem 596 179 1955]. It is characterised by conversion to  $\gamma$ -hydroxy-n-valeramide by treatment with NH<sub>3</sub>, m 51.5-52° (by slow evapn of a CHCl<sub>3</sub> soln).

δ-Valerolactone (tetrahydro-2*H*-pyran-2-one) [542-28-9] M 100.1, m -13°, -12°, b 88°/4mm, 97°/10mm, 124°/24mm, 145-146°/40mm, 229-229.5°/atm,  $d_4^{20}$  1.1081,  $n_D^{20}$ 1.4568. Purified by repeated fractional distn. IR v: 1750 (in CS<sub>2</sub>), 1732 (in CHCl<sub>3</sub>), 1748 (in CCl<sub>4</sub>) and 1733 (in MeOH) cm<sup>-1</sup>. [Huisgen and Ott *Tetrahedron* 6 253 1959; Linstead and Rydon *J Chem Soc* 580 1933; Jones et al. Can J Chem 37 2007 1959.] Valeronitrile [110-59-8] M 83.1, b 142.3°, d 0.799,  $n^{15}$  1.39913,  $n^{30}$  1.39037. Washed with half its volume of conc HCl (twice), then with saturated aqueous NaHCO<sub>3</sub>, dried with MgSO<sub>4</sub> and fractionally distd from P<sub>2</sub>O<sub>5</sub>.

L-Valine [72-18-4] M 117.2, m 315°,  $[\alpha]_D^{20}$  +266.7° (6M HCl), pK<sub>1</sub> 2.26, pK<sub>2</sub> 9.68. Crystd from water by addition of EtOH.

Vanillin (4-hydroxy-3-methoxybenzaldehyde) [121-33-5] M 152.2, m 83°, b 170°/15 mm, pK<sup>25</sup> 7.40. Crystd from water or aqueous EtOH, or by distn *in vacuo*.

Veratraldehyde [120-14-9] M 166.2, m 42-43°. Crystd from diethyl ether, pet ether, CCl<sub>4</sub> or toluene.

Variamine Blue RT [4-(phenylamino)benzenediazonium sulfate (1:1)] [4477-28-5] M 293.3, CI 37240,  $\lambda_{max}$  377 nm. Dissolved 10g in 100mL of hot water. Sodium dithionite (0.4g) was added, followed by active carbon (1.5g) and filtered hot. To the colourless or slightly yellow filtrate a soln of saturated NaCl was added and the mixture cooled. The needles were filtered off, washed with cold water, dried at room temperature, and stored in a dark bottle (light sensitive). [Erdey Chem Analyst 48 106 1959.]

Vicine (2,4-diamino-5- $\beta$ -D-glucopyranosidoxy-6-hydroxypyrimidine) [152-93-2] M 304.3, m 243-244°,  $[\alpha]_D^{20}$ -12° (c 4, 0.2N NaOH). Crystd from water or aqueous 85% EtOH, and dried at 135°.

Vinyl acetate [108-05-4] M 86.1, b 72.3°, d 0.938, n 1.396. Inhibitors such as hydroquinone, and other impurities are removed by drying with CaCl<sub>2</sub> and fractionally distilling under nitrogen, then refluxing briefly with a small amount of benzoyl peroxide and redistilling under nitrogen. Stored in the dark at  $0^{\circ}$ .

9-Vinylanthracene [2444-68-0] M 204.3, m 65-67°, b 61-66°/10mm. Purified by vacuum sublimation. Also by chromatography on silica gel with cyclohexane as eluent, and recrystd from EtOH [Werst et al. J Am Chem Soc 109 32 1987].

Vinyl butoxyethyl ether [4223-11-4] M 144.2. Washed with aqueous 1% NaOH, dried with CaH<sub>2</sub>, then refluxed with and distd from, sodium.

*N*-Vinylcarbazole [1484-13-5] M 193.3, m 66°. Crystd repeatedly from MeOH in amber glassware. Vacuum sublimed.

Vinylene carbonate [872-36-6] M 86.1, m 22°. Purified by zone melting.

Vinyl chloroformate [5130-24-5] M 106.5, b 46.5°/80mm, 67-69°/atm, 109-110°/760mm,  $d_4^{20}$  1.136,  $n_D^{23}$  1.420. It has been fractionated through a Todd column (Model A with ~60 plates, see p. 174) under atmospheric pressure and purity can be checked by gas chromatography. It has IR with v at 3100 + 2870 (CH<sub>2</sub>), 1780 (C=O), 1640 (C=C) and 940 (CH<sub>2</sub> out-of-plane) and 910 (CH<sub>2</sub> wagging) cm<sup>-1</sup>. [IR: Lee J Org Chem 30 3943 1965; Levaillant Ann Chim (Paris) 6 504 1936.] Used for protecting NH<sub>2</sub> groups in peptide synthesis [Olofson et al. Tetrahedron Lett 1563 1977].

1-Vinylnaphthalene [826-74-4] M 154.2, b 124-125% Fractionally distd under reduced pressure on a spinning-band column, dried with CaH<sub>2</sub> and again distd under vacuum. Stored in sealed ampoules in a freezer.

2-Vinylpyridine monomer [100-69-6] M 105.1, b 79-82°/29mm, d 0.974, n 1.550,  $pK^{25}$  4.92. Steam distd, then dried with MgSO<sub>4</sub> and distd under vacuum.

4-Vinylpyridine monomer [100-43-6] M 105.1, b 40-41°/1.4mm, 54°/5mm, 58-61°/12mm, 68°/18mm, 79°/33mm,  $d_4^{20}$  0.9836,  $n_D^{20}$  1.5486, pK<sup>25</sup> 5.62. Purified by fractional distillation under a good vacuum and in a N<sub>2</sub> atmosphere and stored in sealed ampoules under N<sub>2</sub>, and kept in the dark at -20°.

The picrate has m 175-176°. [UV: Coleman and Fuoss J Am Chem Soc 77 5472 1955; Overberger et al. J Polymer Sci 27 381 1958; Petro and Smyth J Am Chem Soc 79 6142 1957.] Used for alkylating SH groups in peptides [Anderson and Friedman Can J Biochem 49 1042 1971; Cawins and Friedman Anal Biochem 35 489 1970].

Vinyl stearate [111-63-7] M 310.5, m 35°, b 166°/1.5mm. Vacuum distd under nitrogen, then crystd from acetone (3mL/g) or ethyl acetate at 0°.

Violanthrene (dibenzanthrene, 5,10-dihydroviolanthrene A) [81-31-2] M 428.5. Purified by vacuum sublimation over Cu in a muffle furnace at 450°/25mm in a CO<sub>2</sub> atmosphere [Scholl and Meyer Chem Ber 67 1229 1934]. Violanthrene A (anthro[9,1,2-cde]benzo[rst]pentaphene [188-87-4] M 426.5 has m 506°. [Clar Chem Ber 76 458 1943.]

Viologen (4,4'-dipyridyl dihydrochloride) [27926-72-3] M 229.1, m >300°. Purified by pptn on adding excess of acetone to a concentrated solution in aqueous MeOH. It has also been recrystd several times from MeOH and dried at 70° under vacuum for 24h [Prasad et al. J Am Chem Soc 108 5135 1986], and recrystd three times from MeOH/isopropanol [Stramel and Thomas J Chem Soc, Faraday Trans 82 799 1986].

Visnagin (4-methoxy-7-methyl-5*H*-furo[3,2-g][1]benzopyran-5-one) [82-57-5] M 230.2, m 142-145°. Crystd from water.

*dl*-Warfarin (4-hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one) [81-81-2] M 308.3, m 161°. Crystd from MeOH. The *acetate* has m 182-183° and 2,4-dinitrophenylhydrazone has m 215-216°. Effective anticoagulant and rodenticide.

**Xanthatin** (3-methylene-7-methyl-6-[3-oxo-1-buten-1-yl]cyclohept-5-ene-[10,11b]furan-2-one) [26791-73-1] M 246.3, m 114.5-115°,  $[\alpha]_D$  -20° (EtOH). Crystd from MeOH or EtOH. UV:  $\lambda_{max}$  213 and 275nm ( $\epsilon$  22800 and 7300).

Xanthene [92-83-1] M 182.2, m 100.5°, b 310-312°/760mm. Crystd from \*benzene or EtOH.

**9-Xanthenone (xanthone)** [90-47-1] **M 196.2, m 175.6-175.4°.** Crystd from EtOH (25mL/g) and dried at 100°. It has also been recrystd from *n*-hexane three times and sublimed *in vacuo*. [Saltiel J Am Chem Soc 108 2674 1986].

Xanthopterin (H<sub>2</sub>O) see entry on p. 576 in Chapter 6.

**Xanthorhamnin** [1324-63-6] **M 770.7, m 195°,**  $[\alpha]_D^{20}$  +3.75° (EtOH). Crystd from a mixture of ethyl and isopropyl alcohols, air dried, then dried for several hours at 110°.

Xanthosine  $(2H_2O)$  [9-( $\beta$ -D-ribosyl)purin-2,6(1H,3H)-dione] [5968-90-1] M 320.3,  $[\alpha]_D^{20}$ -53° (c 8, 0.3M NaOH),  $pK_1^{25}$  <2.5,  $pK_2^{25}$  5.67,  $pK_3^{25}$  12.85. Crystd from EtOH or water (as dihydrate).

Xanthurenic acid (5,8-dihydroxyquiniline-2-carboxylic acid) [59-00-7] M 205.2, m 286°, 290-295°(dec),  $pK_{Est(1)} \sim 1.5$ ,  $pK_{Est(2)} \sim 4.9$ ,  $pK_{Est(3)} \sim 9.8$ . Ppted by the addition of 2N formic acid to its soln in hot 2M ammonia (charcoal). Filter solid off, dry in a vac at ~80° in the dark. UV (H<sub>2</sub>O) has  $\lambda$ max nm ( $\epsilon$  M<sup>-1</sup>cm<sup>-1</sup>): 243 (30,000) and 342 (6,500). The methyl ester has m 262° (from MeOH).

Xanthydrol [90-46-0] M 198.2, m 123-124°. Crystd from EtOH and dried at 40-50°.

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**Xylene** [1330-20-7] **M 106.1 (mixed isomers).** Usual impurites are ethylbenzene, paraffins, traces of sulfur compounds and water. It is not practicable to separate the m-, and p-isomers of xylene by fractional distn, although, with a sufficiently efficient still, o-xylene can be fractionally distd from a mixture of isomers. Purified (and dried) by fractional distn from LiAlH<sub>4</sub>, P<sub>2</sub>O<sub>5</sub>, CaH<sub>2</sub> or sodium. This treatment can be preceded by shaking successively with conc H<sub>2</sub>SO<sub>4</sub>, water, aqueous 10% NaOH, water and mercury, and drying with CaCl<sub>2</sub> for several days. Xylene can be purified by azeotropic distn with 2-ethoxyethanol or 2-methoxyethanol, the distillate being washed with water to remove the alcohol, then dried and fractionally distilled.

o-Xylene [95-47-6] M 106.2, f -25.2°, b 84°/14mm, 144.4°/760mm, d 0.88020, d<sup>25</sup> 0.87596, n 1.50543, n<sup>25</sup> 1.50292. The general purification methods listed under xylene are applicable [Clarke and Taylor J Am Chem Soc 45 831 1923]. o-Xylene (4.4Kg) is sulfonated by stirring for 4h with 2.5L of conc H<sub>2</sub>SO<sub>4</sub> at 95°. After cooling, and separating the unsulfonated material, the product was diluted with 3L of water and neutralised with 40% NaOH. On cooling, sodium o-xylene sulfonate separated and was recrystd from half its weight of water. [A further crop of crystals was obtained by concentrating the mother liquor to one-third of its volume]. The salt was dissolved in the minimum amount of cold water, then mixed with the same amount of cold water, and with the same volume of conc H<sub>2</sub>SO<sub>4</sub> and heated to 110°. o-Xylene was regenerated and steam distd. It was then dried and redistd.

*m*-Xylene [108-38-3] M 106, f -47.9°, b 139.1°, d 0.86417,  $d^{25}$  0.85990, n 1.49721,  $n^{25}$  1.49464. The general purification methods listed under *xylene* are applicable. The *o*- and *p*-isomers can be removed by their selective oxidation when a *m*-xylene sample containing them is boiled with dilute HNO<sub>3</sub> (one part conc acid to three parts water). After washing with water and alkali, the product can be steam distd, then distd and purified by sulfonation. [Clarke and Taylor J Am Chem Soc 45 831 1923.] *m*-Xylene is selectively sulfonated when a mixture of xylenes is refluxed with the theoretical amount of 50-70% H<sub>2</sub>SO<sub>4</sub> at 85-95° under reduced pressure. By using a still resembling a Dean and Stark apparatus, water in the condensate can be progressively withdrawn while the xylene is returned to the reaction vessel. Subsequently, after cooling, then adding water, unreacted xylenes are distd off under reduced pressure. The *m*-xylene sulfonic acid is subsequently hydrolysed by steam distn up to 140°, the free *m*-xylene being washed, dried with silica gel and again distd. Stored over molecular sieves Linde type 4A.

*p*-Xylene [106-42-3] M 106.2, f 13.3, b 138.3°, d 0.86105,  $d^{25}$  0.85669, n 1.49581,  $n^{25}$  1.49325. The general purification methods listed for *xylene* are applicable. *p*-Xylene can readily be separated from its isomers by crystn from such solvents as MeOH, EtOH, isopropanol, acetone, butanone, toluene, pentane or pentene. It can be further purified by fractional crystn by partial freezing, and stored over sodium wire or molecular sieves Linde type 4A. [Stokes and French J Chem Soc, Faraday Trans 1 76 537 1980.]

Xylenol Orange  $\{3H-2,1\text{-}benzoxathiol-3\text{-}ylidene-bis-[(6-hydroxy-5-methyl-m-phenylene)-methylnitrilo]tetraacetic acid, S,S-dioxide} [1611-35-4] M 672.6, m 210°(dec), <math>\varepsilon_{578}$  6.09 x 10<sup>4</sup> (pH 14),  $\varepsilon_{435}$  2.62 x 10<sup>4</sup> (pH 3.1), pK<sub>1</sub> -1.74, pK<sub>2</sub> -1.09 (aq H<sub>2</sub>SO<sub>4</sub>-HNO<sub>3</sub>), pK<sub>3</sub> 2.58, pK<sub>4</sub> 3.23, pK<sub>5</sub> 6.46, pK<sub>6</sub> 10.46, pK<sub>7</sub> 12.28. Generally contaminated with starting material (cresol red) and semixylenol orange. Purified by ion-exchange chromatography using DEAE-cellulose, eluting with 0.1M NaCl soln which will give the sodium salt. Cresol Red, semixylenol orange and iminodiacetic acid bands elute first. This procedure will give the sodium salt of the dye. To obtain the free acid dissolve the salt in H<sub>2</sub>O and acidify with AcOH. Filter off, wash with H<sub>2</sub>O and dry first in air and then in a vac deisiccator over P<sub>2</sub>O<sub>5</sub> in the dark [Sato, Yokoyama and Momoki Anal Chim Acta 94 317 1977].

 $\alpha$ -D-Xylose [58-86-6] M 150.1, m 146-147°,  $[\alpha]_D^{20}$  -18.8° (c 4, H<sub>2</sub>O). Purified by slow crystn from aq 80% EtOH or EtOH, then dried at 60° under vac over P<sub>2</sub>O<sub>5</sub>. Stored in a vacuum desiccator over CaSO<sub>4</sub>.

*m*-Xylylene diisocyanate [3634-83-1] M 188.2, b 88-89°/0.02mm, 130°/2mm, d<sub>4</sub><sup>20</sup> 1.204, n<sub>D</sub><sup>20</sup> 1.4531. Purified by repeated distn through a 2 plate column. [Ferstundig and Scherrer J Am Chem Soc 81 4838 1959.]

 $\alpha$ -Yohimbine [146-48-5] M 354.5, m 278°(dec),  $[\alpha]_D^{20}$  +55.6° (c 2, EtOH),  $pK_1^{22}$  3.0,  $pK_2^{22}$  7.45. Crystd from EtOH, and dried to remove EtOH of crystn. For  $\gamma$ -Yohimbine see ajmalicine on p. 98.

Zeaxanthin [all trans- $\beta$ -carotene-3,3'(R,R')-diol] [144-68-3] M 568.9, m 207°, 215.5°,  $\lambda_{max}$  275 (log  $\epsilon$  4.34), 453 (log  $\epsilon$  5.12), 480 (log  $\epsilon$  5.07) in EtOH. Yellow plates (with a blue lustre) from MeOH or EtOH.

### **CHAPTER 5**

## PURIFICATION OF INORGANIC AND METAL ORGANIC CHEMICALS

# (Including Organic compounds of B, Bi, P, Se, Si, and ammonium and metal salts of organic acids)

The most common method of purification of inorganic species is by recrystallisation, usually from water. However, especially with salts of weak acids or of cations other than the alkaline and alkaline earth metals, care must be taken to minimise the effect of hydrolysis. This can be achieved, for example, by recrystallising acetates in the presence of dilute acetic acid. Nevertheless, there are many inorganic chemicals that are too insoluble or are hydrolysed by water so that no general purification method can be given. It is convenient that many inorganic substances have large temperature coefficients for their solubility in water, but in other cases recrystallisation is still possible by partial solvent evaporation.

Organo-metallic compounds, on the other hand, behave very much like organic compounds, e.g. they can be redistilled and may be soluble in organic solvents. A note of **caution** should be made about handling organo-metallic compounds, e.g. arsines, because of their **potential toxicities**, particularly when they are volatile. Generally the suppliers of such compounds provide details about their safe manipulation. These should be read carefully and adhered to closely. If in any doubt always assume that the materials are lethal and treat them with utmost care. The same **safety precautions** about the handling of substances as stated in Chapter 4 should be followed here (see Chapter 1).

For information on **ionization (pK)** see Chapter 1, p. 7, and Chapter 4, p. 80. In order to avoid repetition, the literature (or predicted) pK values of anionic and/or cationic species are usually reported at least once, and in several cases is entered for the free acid or free base, e.g.  $Na_2SO_4$  will have a pK value for  $Na^+$  at the entry for NaOH and the pK values for  $SO_4^{2^-}$  at the entries for  $H_2SO_4$ . When the pK values of the organic counter-ions are not given in this Chapter, as in case of sodium benzoate, the reader is referred to the value(s) in Chapter 4, e.g. of benzoic acid.

Abbreviations of titles of periodical are defined as in the Chemical Abstracts Service Source Index (CASSI). A note on other abbreviations is in Chapter 1, p. 30.

**Benzene**, which has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallisation is now considered a **very dangerous substance** so it has to be used with extreme care. We emphasised that an alternative solvent to benzene (e.g. toluene, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if benzene has to be used then all operations have to be performed in a well ventilated fumehood and precautions taken to avoid inhalation and contact with skin and eyes. Whenever benzene is mentioned in the text and asterisk e.g.  ${}^{*}C_{6}H_{6}$  or  ${}^{*}$  benzene, is inserted to remind the user that special precaution should be adopted.

**Organic dyes** which are *not* complexed or are salts of metals are included in Chapter 4 (use the CAS Registry Numbers to find them). Commercially available polymer supported reagents are indicated with § under the appropriate reagent.

Acetarsol see N-Acetyl-4-hydroxy-m-arsanilic acid.

Acetonyltriphenylphosphonium chloride [1235-21-8] M 354.8, m 237-238°, 244-246° (dec). Recrystd from CHCl<sub>3</sub> + \*C<sub>6</sub>H<sub>6</sub> + pet ether (b 60-80°) and by dissolving in CHCl<sub>3</sub> and pouring it into dry Et<sub>2</sub>O.  $\lambda_{max}^{EtOH}$  nm( $\varepsilon$ ) 255(3,600), 262(3,700), 268(4,000) and 275(3,100). The *iodide salt* crystallises from H<sub>2</sub>O and has m 207-209°. [J Org Chem 22 41 1957.] IRRITANT and hygroscopic. When shaken with a 10% aqueous soln of Na<sub>2</sub>CO<sub>3</sub> (8h) it gives acetylmethylene triphenyl phosphorane which is recrystd from MeOH-H<sub>2</sub>O and after drying at 70°/0.1mm has m 205-206°. UV:  $\lambda$ max nm( $\varepsilon$ ) 268 (6600), 275 (6500) and 288 (5700); IR:v (cm<sup>-1</sup>) 1529 (s), 1470 (m), 1425 (s), 1374 (m), 1105 (s) and 978 (s). [J Org Chem 22 41, 44 1957.]

3*R*,4*R*,1'*R*-4-Acetoxy-3-[1-(*tert*-butylmethylsilyloxy)ethyl]-2-azetinone [76855-69-1] M 287.4, m 107-108°,  $[\alpha]_D^{20} + 55°$  (c 0.5, toluene),  $[\alpha]_D^{20} + 53.7°$  (c 1.04, CHCl<sub>3</sub>). Purified by chromatography on silica gel (3 x 14cm) for 50g of ester using 20% EtOAc in *n*-hexane. The eluate is evaporated and the residue recryst from hexane as white fluffy crystals. [*Tetrahedron* 39 2505 1983.]

Acetylenedicarboxylic acid monopotassium salt [928-04-1] M 152.2. Very soluble in  $H_2O$ , but can be crystd from small volume of  $H_2O$  in small crystals. These are washed with EtOH and dried over  $H_2SO_4$  at 125°. [Chem Ber 10 841 1877; Justus Liebigs Ann Chem 272 133 1893.]

Acetylferrocene (ferrocenyl methylketone) [1271-55-2] M 228.1, m 86°, 86-87°. Orange-red crystals, recrystd from isooctane and sublimed at 100°/1mm. The oxime has m 167-170° (from Et<sub>2</sub>O or aq EtOH). The semicarbazone has m 198-201° (from EtOH). [J Am Chem Soc 77 2022 3009 1955; J Chem Soc 650 1958.]

**N-Acetyl-4-hydroxy-***m***-arsanilic acid** [97-44-9] **M 275.1, pK<sub>1</sub> 3.73, pK<sub>2</sub> 7.9, pK<sub>3</sub> 9.3.** Crystd from water.

Allyl trimethylsilane (2-propenyltrimethylsilane) [762-72-1] M 114.3, b 83.0-84.5°, 84-88°, 85.5-86.0°, d 0.713, n 1.405. Fractionate through an efficient column at atm pressure. If impure dissolve in THF, shake with  $H_2O(2x)$ , dry ( $Na_2SO_4$ ) and fractionate. [Cudlin and Chvalovský Collect Czech Chem Commun 27 1658 1962.]

Allyl tri-*n*-butylstannane (allyl tributyl tin) [24850-33-7] M 331.1, b 88-92°/0.2 mm, 115°/17mm, d 1.068, n 1.487. A possible impurity is tributylchlorostannane — test for Cl as Cl ion after hydrolysing. Dissolve in \*C<sub>6</sub>H<sub>6</sub> (or toluene), shake with dil aq NaOH, dry (CaCl<sub>2</sub>), and dist in a vac [Jones et al. J Chem Soc 1446 1947; Aldrichimica Acta 17 75 1984 and 20 45 1987].

Alizarin Red S (3,4-dihydroxy-9,10-dioxo-2-anthracene sulfonic acid, Na salt.  $H_2O$ ) [130-22-3] M 360.4,  $pK_1^{25} < 1$ ,  $pK_2^{25} 5.49$ ,  $pK_3^{25}$  10.85 (11.01). Commercial samples contain large amounts of sodium and potassium chlorides and sulfates. It is purified by passing through a Sephadex G-10 column, followed by elution with water, then 50% aq EtOH [King and Pruden Analyst (London) 93 601 1968]. Finally dissolve in EtOH and ppte with Et<sub>2</sub>O several times [J Phys Chem 54 829 1950; polarography J Am Chem Soc 70 3055 1948].

Alumina (neutral) [1344-28-1] M 102.0 (anhyd.). Stirred with hot 2M HNO<sub>3</sub>, either on a steam bath for 12h (changing the acid every hour) or three times for 30min, then washed with hot distilled water until the washings had pH 4, followed by three washings with hot MeOH. The product was dried at 270° [Angyal and Young JAm Chem Soc 81 5251 1959]. For the preparation of alumina for chromatography see Chapter 1.

Aluminum acetylacetonate [13963-57-0] M 324.3, m 192-194°, 195°. Crystd several times from \*benzene or aqueous MeOH,  $\lambda_{max}$  216 and 286mn. [J Phys Chem 62 440 1958.] It can be purified by sublimation and has the following solubilities in g per cent: \*C<sub>6</sub>H<sub>6</sub> 35.9 (20°), 47.6 (40°), toluene 15.9 (20°), 22.0 (40°) and acetylacetone 6.6 (20°), 10.4 (40°). [Inorg Synth 5 105 1957.]

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Aluminium ammonium sulfate  $(10H_2O)$  [7784-26-1] M 453.3, m 93°,  $pK_1^{25}$  4.89,  $pK_2^{25}$  5.43,  $pK_3^{25}$  5.86 (fAl<sup>3+</sup> aquo),  $pK_4^{25}$  11.22 [aluminate Al(OH)<sub>4</sub><sup>-</sup>]. Crystd from hot H<sub>2</sub>O and cool in ice.

Aluminium bromide [7727-15-3] M 266.7, m 97°, b 114°/10mm. Refluxed and then distilled from pure aluminium chips in a stream of nitrogen into a flask containing more of the chips. It was then distd under vacuum into ampoules [Tipper and Walker J Chem Soc 1352 1959]. Anhydrous conditions are essential, and the white to very light brown solid distillate can be broken into lumps in a dry-box (under nitrogen). Fumes in moist air.

Aluminium caesium sulfate  $(12H_2O)$  [7784-17-0 (12H<sub>2</sub>O); 14284-36-7] M 568.2. Crystd from hot water (3mL/g).

Aluminium chloride (anhydrous) [7446-70-0] M 133.3, m 192.6°. Sublimed several times in an all glass system under nitrogen at 30-50mm pressure. Has also been sublimed in a stream of dry HCl and has been subjected to a preliminary sublimation through a section of granular aluminium metal [for manipulative details see Jensen J Am Chem Soc 79 1226 1957]. Fumes in moist air.

Aluminum ethoxide [555-75-9] M 162.2, m 154-159°, 146-151°, b 187-190°/7mm, 210-214°/13mm. Crystd from  $CS_2$  [m 139°,  $CS_2$  complex] and distd in a vacuum. Molecular weight corresponds to [Al(OEt)<sub>3</sub>]<sub>4</sub> [J Phys Chem 39 1127 1935; J Am Chem Soc 69 2605 1947].

Aluminium fluoride (anhydrous) [7784-18-4] M 84.0, m 250°. Technical material may contain up to 15% alumina, with minor impurities such as aluminium sulfate, cryolite, silica and iron oxide. Reagent grade  $AlF_3$  (hydrated) contains only traces of impurities but its water content is very variable (may be up to 40%). It can be dried by calcining at 600-800° in a stream of dry air (some hydrolysis occurs), followed by vacuum distn at low pressure in a graphite system, heated to approximately 925° (condenser at 900°) [Henry and Dreisbach J Am Chem Soc 81 5274 1959].

Aluminium isopropoxide [555-31-7] M 204.3, m 119°, b 94°/0.5mm, 135°/10mm. Distd under vacuum. Hygroscopic.

Aluminium nitrate (9H<sub>2</sub>O) [7784-27-2 (9H<sub>2</sub>O); 13473-90-0] M 375.1. Crystd from dilute HNO<sub>3</sub>, and dried by passing dry nitrogen through the crystals for several hours at 40°. After 2 recrystns of ACS grade it had S, Na and Fe at 2.2, 0.01 and 0.02 ppm resp.

Aluminium potassium sulfate (12H<sub>2</sub>O, alum) [7784-24-9] M 474.4, m 92°. Crystd from weak aqueous H<sub>2</sub>SO<sub>4</sub> (*ca* 0.5mL/g).

Aluminium rubidium sulfate (12H<sub>2</sub>O) [7784-29-4] M 496.2. Crystd from aq H<sub>2</sub>SO<sub>4</sub> (ca 2.5mL/g).

Aluminium sulfate (anhydrous) [ $10043 \cdot 01 \cdot 3$ ] M 342.2, m 765°(dec); Al<sub>2</sub>O<sub>3</sub> 14-18 H<sub>2</sub>O [ $17927 \cdot 65 \cdot 0$ ]; Al<sub>2</sub>O<sub>3</sub> 18 H<sub>2</sub>O [ $7784 \cdot 31 \cdot 8$ ]. Crystd from hot dilute H<sub>2</sub>SO<sub>4</sub> (1 mL/g) by cooling in ice. When a soln of alumina (Al<sub>2</sub>O<sub>3</sub>) in conc H<sub>2</sub>SO<sub>4</sub> is slowly cooled, Al<sub>2</sub>SO<sub>4</sub> 17 or 18H<sub>2</sub>O deposits as a crystalline mass . Al<sub>2</sub>SO<sub>4</sub> 17H<sub>2</sub>O is the stable form in equilibrium with its saturated aqueous soln at 25° [Smith J Am Chem Soc 64 41 1942]. This is purified by dissolving in a small vol of H<sub>2</sub>O and adding EtOH until the sulfate readily crystallises from the oily supersaturated soln. It forms Al<sub>2</sub>O<sub>3</sub> 16H<sub>2</sub>O between 0-112°. On gradual heating the hydrate melts giving the anhydrous salt at *ca* 250°. Several hydrates up to 27H<sub>2</sub>O have been described. Further heating to red heat (~ 600-800) causes decomposition to Al<sub>2</sub>O<sub>3</sub> + SO<sub>3</sub> + SO<sub>2</sub> and O<sub>2</sub> [Cobb J Soc Chem Ind 29 250 1910]. ACS reagent is Al<sub>2</sub>O<sub>3</sub> 18H<sub>2</sub>O (98+%).

Aluminum triethyl (triethyl aluminum) [97-93-8] M 114.2, b 69°/1.5mm, 76°/2.5mm, 129-131°/55mm,  $d_4^{20}$  0.695,  $n_D^{20}$  1.394. Purified by fractionation in an inert atmosphere under vacuum in a 50cm column containing a heated nichrome spiral, taking the fraction 112-114°/27mm. It is very sensitive to H<sub>2</sub>O and should be stored under N<sub>2</sub>. It should not contain chloride which can be shown by hydrolysis and testing with AgNO<sub>3</sub>. [J Am Chem Soc 75 4828 51931953; NMR: J Am Chem Soc 81 3826 1959.]

Aluminium tri-tert-butoxide [556-91-2] M 246.3, m 208-210°(dec). Crystd from \*benzene and sublimed at 180°.

Aluminium trimethanide (trimethyl aluminium) [75-24-1] M 72.1, m 15.2°, b 111.5°/488.2mm, 124.5°/atm,  $d_4^{20}$  0.725. Distd through a 10-20 theoretical plates column under 1 atm of N<sub>2</sub> (better with very slow take-off). Attacks grease (use glass joints). Also vac distd over Al in absence of grease, into small glass vials and sealed under N<sub>2</sub>. Purity is measured by freezing point. Reacts with H<sub>2</sub>O, is non-conducting in \*C<sub>6</sub>H<sub>6</sub> and is HIGHLY FLAMMABLE. [J Chem Soc 4681946; J Am Chem Soc 68 2204 1946.]

4-Aminophenylmercuric acetate [6283-24-5] M 371.8, m 168°, 175°(dec), 180°(dec). Recrystd from hot dilute AcOH and dried in air. [J Indian Chem Soc 32 613 1955; Justus Liebigs Ann Chem 465 269 1928.]

Ammonia (gas) [7664-41-7] M 17.0,  $pK^{25}$  9.25. Major contaminants are water, oil and noncondensible gases. Most of these impurities are removed by passing the ammonia through a trap at -22° and condensing it at -176° under vacuum. Water is removed by distilling the ammonia into a tube containing a small lump of sodium. Also dried by passage through porous BaO, or over alumina followed by glass wool impregnated with sodium (prepared by soaking the glass wool in a solution of sodium in liquid ammonia, and evaporating off the ammonia). It can be rendered oxygen-free by passage through a soln of potassium in liquid ammonia.

Ammonia (liquid) [7664-41-7] M 17.0, m -77.7°, b -33.4°,  $n_D$  1.325, d 0.597, d<sup>-79</sup> 0.817g/mL. Dried, and stored, with sodium in a steel cylinder, then distd and condensed by means of liquid air, the non-condensable gases being pumped off. In order to obtain liquid NH<sub>3</sub> from a cylinder turn the cylinder up-side-down (i.e. with the valve at the bottom, use a metal stand to secure it in this position) and lead a plastic tube from the tap to a measuring cylinder placed in an efficient fume cupboard which is kept running. Turn the tap on and allow the ammonia to be released. At first, gas and liquid will splatter out (make sure that the plastic tube is secure) but soon the liquid will drip into the measuring cylinder. The high latent heat of evaporation will cool the ammonia so that the liquid will remain cool and not boil vigorously. If the ammonia is required dry the necessary precautions should be taken, i.e. the gas is allowed to flow through tubes packed with coarse CaO pellets.

Ammonia (aqueous) [7664-41-7] M 17.0 +  $H_2O$ , d 0.90 (satd, 27% w/v, 14.3 N),  $pK^{25}$  9.25. Obtained metal-free by saturating distilled water, in a cooling bath, with ammonia (from tank) gas. Alternatively, can use isothermal distn by placing a dish of conc aq ammonia and a dish of pure water in an empty desiccator and leaving for several days. AMMONIA (gas, liquid or aq soln) is very irritating and should not be inhaled in large volumes as it can lead to olfactory paralysis (temporary and partially permanent).

Ammonium acetate [631-61-8] M 77.1, m 112-114°, d 1.04. Crystd twice from anhydrous acetic acid, dried under vacuum for 24h at 100° [Proll and Sutcliff *Trans Faraday Soc* 57 1078 1961].

Ammonium benzoate [1863-63-4] M 139.2, m 198°, 200°(dec), d 1.26. Crystd from EtOH.

Ammonium bisulfate (ammonium hydrogen sulfate) [7803-63-6] M 115.1°, m ~147°, d 1.79, pK<sup>25</sup> 1.96 (HSO<sub>4</sub>°). Crystd from water at room temperature (1mL/g) by adding EtOH and cooling.

Ammonium bromide [12124-97-9] M 98.0, m 450°(sublimes), d 2.43. Crystd from 95% EtOH.

Ammonium chloride [12125-02-9] M 53.5, m 338°(sublime point, without melting), d 1.53. Crystd several times from conductivity water (1.5mL/g) between 90° and 0°. Sublimes. After one crystn, ACS grade had: metal(ppm) As (1.2), K (1), Sb (7.2), V (10.2).

Ammonium chromate [7788-98-9] M 152.1, m 185°(dec), d 1.81,  $pK_1^{25}0.74$ ,  $pK_2^{25}6.49$  (for H<sub>2</sub>CrO<sub>4</sub>). Crystd from weak aqueous ammonia (*ca* 2.5mL/g) by cooling from room temperature.

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Ammonium dichromate [7789-09-5] M 252.1, m 170°(dec), d 1.26. Crystd from weak aq HCl (ca lmL/g). (Possible carcinogen)

Ammonium dihydrogen arsenate [13462-93-6] M 159.0, m 300°(dec). Crystd from water (1mL/g).

Ammonium dihydrogen orthophosphate [7722-76-1] M 115.0, m 190°, d 1.80. Crystd from water (0.7mL/g) between 100° and 0°.

Ammonium dodecylsulfate [2235-54-3] M 283.4. Recrystd first from 90% EtOH and then twice from abs EtOH, finally dried in a vacuum.

Ammonium ferric oxalate  $(3H_2O)$  [13268-42-3] M 428.1, m ~160°(dec), d 1.77. Crystd from hot water (0.5mL/g).

Ammonium ferric sulfate  $(12H_2O)$  [7783-83-7 (12H<sub>2</sub>O); 10138-04-2 (anhydr)] M 482.2, m ~37°, d 1.71. Crystd from aqueous ethanol.

Ammonium ferrous sulfate  $(6H_2O)$  [7783-85-9  $(6H_2O)$ ; 10045-89-3 (anhydr)] M 392.1, m 100°(dec), d 1.86. A soln in warm water (1.5mL/g) was cooled rapidly to 0°, and the resulting fine crystals wcrc filtered at the pump, washed with cold distilled water and pressed between sheets of filter paper to dry.

Ammonium formate [540-69-2] M 63.1, m 116°, 117.3°,  $d_4^{45}$  1.280. Heat solid in NH<sub>3</sub> vapour and dry in vacuum till NH<sub>3</sub> odour is faint. Recryst from abs EtOH and then keep in a desiccator over 99% H<sub>2</sub>SO<sub>4</sub> in vacuo. It is very hygroscopic. Exists in two forms, stable needles and less stable plates. Also forms acid salts, i.e. HCO<sub>2</sub>NH<sub>4</sub>.3HCO<sub>2</sub>H and HCO<sub>2</sub>NH<sub>4</sub>.HCO<sub>2</sub>H. [J Am Chem Soc 43 1473 1921; 63 3124 1941.]

Ammonium hexachloroiridate (IV) [16940-92-4] M 441.0. Ppted several times from aqueous soln by saturation with ammonium chloride. This removes any palladium and rhodium. Then washed with ice-cold water and dried over cone  $H_2SO_4$  in a vacuum desiccator. If osmium or ruthenium is present, it can be removed as the tetroxide by heating with cone HNO<sub>3</sub>, followed by cone HClO<sub>4</sub>, until most of the acid has been driven off. (This treatment is repeated). The near-dry residue is dissolved in a small amount of water and added to excess NaHCO<sub>3</sub> soln and bromine water. On boiling, iridic (but not platinic) hydroxide is ppted. It is dissolved in HCl and ppted several times, then dissolved in HBr and treated with HNO<sub>3</sub> and HCl to convert the bromides to chlorides. Saturation with ammonium chloride and cooling precipitates ammonium hexachloroiridate which is filtered off and purified as above [Woo and Yost J Am Chem Soc 53 884 1931].

Ammonium hexacyanoferrate II hydrate [14481-29-9] M 284.1, m dec on heating. The pale yellow trihydrate powder can be washed with 10% aq NH<sub>3</sub>, filtd, then washed several times with EtOH and Et<sub>2</sub>O, and dried at room temp. Decomposes in vacuum above 100° and should be stored away from light and under N<sub>2</sub>. In light and air it decomposes by losing NH<sub>3</sub>. [Handbook of Preparative Inorganic Chem (Ed. Brauer) Vol II 1509 1965.]

Ammonium hexafluorophosphate [16941-11-0] M 163.0,  $d_4^{18}$  2.181,  $pK_1^{25} \sim 0.5$ ,  $pK_2^{25} 5.12$  (for fluorophosphoric acid H<sub>2</sub>PO<sub>3</sub>F). Crystallises from H<sub>2</sub>O in square plates. Decomposes on heating before melting. Soluble in H<sub>2</sub>O at 20° (74.8% w/v), also very soluble in Me<sub>2</sub>CO, MeOH, EtOH and MeOAc and is decomposed by boiling acids. [*Chem Ber* 63 1063 1930.]

Ammonium hexafluorosilicate [16919-19-0] M 178.1,  $pK_2$  1.92 (for  $H_2SiF_6$ ). Crystd from water (2mL/g). After 3 recrystns of Tech grade it had Li, Na, K and Fe at 0.3, 0.2, 0.1 and 1.0 ppm resp.

Ammonium hypophosphite [7803-65-8] M 83.0. Crystd from hot EtOH.

Ammonium iodate [13446-09-8] M 192.9, pK<sup>25</sup> 0.79 (IO<sup>3+</sup>). Crystd from water (8mL/g) between 100° and 0°.

Ammonium iodide [12027-06-4] M 144.9, sublimes with dec ~405°, d 2.51. Crystd from EtOH by addition of ethyl iodide. Very hygroscopic. Stored in the dark.

Ammonium ionophore I (Nonactin) [6833-86-7] M 736.9, m 147-148°,  $[\alpha]_D^{20}$  0° (c 1.2, CHCl<sub>3</sub>). Crystd from MeOH in colourless needles and is dried at 20° in high vac. A selectophore with high sensitivity for NH<sub>4</sub><sup>+</sup> ions. [Helv Chim Acta 38 1445 1955, 45 129 1962, 55 1371 1972; Acta Cryst 27B 1680 1971.]

Ammonium magnesium chloride (6H<sub>2</sub>O) [60314-43-4] M 256.8. Crystd from water (6mL/g) by partial evapn in a desiccator over KOH (deliquescent).

Ammonium magnesium sulfate (6H<sub>2</sub>O) [20861-69-2] M 360.6. Crystd from water (1mL/g) between 100° and 0°.

Ammonium manganous sulfate (6H<sub>2</sub>O) [13566-22-8] M 391.3. Crystd from water (2mL/g) by partial evapn in a desiccator.

Ammonium metavanadate [7803-55-6] M 117.0, m 200°(dec). See ammonium (meta) vanadate on p. 395.

Ammonium molybdate [13106-76-8] M 196.0,  $pK_1^{25}$  0.9 (proton addition),  $pK_2^{25}$  3.57,  $pK_3^{25}$  4.08 (for H<sub>2</sub>MoO<sub>4</sub>). Crystd from water (2.5mL/g) by partial evapn in a desiccator.

Ammonium nickel sulfate (6H<sub>2</sub>O) [7785-20-8 (6H<sub>2</sub>O); 15699-18-0 (anhydr)] M 395.0, d 1.923. Crystd from water (3mL/g) between 90° and 0°.

Ammonium nitrate [6484-52-2] M 80.0, m 210°(dec explosively), d 1.72. Crystd twice from distilled water (1mL/g) by adding EtOH, or from warm water (0.5mL/g) by cooling in an ice-salt bath. Dried in air, then under vacuum. After 3 recrystns of ACS grade it contained Li and B at 0.03 and 0.74 ppm resp.

Ammonium oxalate (H<sub>2</sub>O) [6009-70-7] M 142.1, d 1.50. Crystd from water (10mL/g) between 50° and 0°.

Ammonium perchlorate [7790-98-9] M 117.5, d 1.95,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd twice from distilled water (2.5mL/g) between 80° and 0°, and dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. Drying at 110° might lead to slow decomposition to chloride. POTENTIALLY EXPLOSIVE.

Ammonium peroxydisulfate [7727-54-0] M 228.2, m dec when heated wet liberating oxygen, d 1.98. Recrystd at room temperature from EtOH/water.

Ammonium picrate [131-74-8] M 246.1, m EXPLODES above 200°. Crystd from EtOH and acetone.

Ammonium reineckate (Reineckate salt) [13573-16-5] M 345.5, m 270-273°(dec). Crystd from water, between 30° and 0°, working by artificial light. Solns of reineckate decompose slowly at room temperature in the dark and more rapidly at higher temperatures or in diffuse sunlight.

Ammonium selenate [7783-21-3] M 179.0, d 2.19, m dec on heating. Crystd from water at room temperature by adding EtOH and cooling.

Ammonium sulfamate [7773-06-0] M 114.1, m 132-135°, dec at 160°. Crystd from water at room temperature (1mL/g) by adding EtOH and cooling.

Ammonium sulfate [7783-20-2] M 132.1, m 230°(dec), 280°(dec), d 1.77. Crystd twice from hot water containing 0.2% EDTA to remove metal ions, then finally from distilled water. Dried in a desiccator for 2 weeks over Mg(ClO<sub>4</sub>)<sub>2</sub>. After 3 recrystns ACS grade had Ti, K, Fe, Na at 11, 4.4, 4.4, 3.2 ppm resp.

Ammonium tetrafluoroborate [13826-83-0] M 104.8, pK<sup>25</sup> 2.77 (for HBF<sub>4</sub>). Crystd from conductivity water (1mL/g) between 100° and 0°.

Ammonium tetraphenylborate [14637-34-4] M 337.3, m ca 220°(dec). Dissolve in aqueous Me<sub>2</sub>CO and allow crystn to proceed slowly otherwise very small crystals are formed. No trace of Me<sub>2</sub>CO was left after drying at 120° [*Trans Faraday Soc* 53 19 1957]. The salt was ppted from dilute AcOH soln of sodium tetraphenylborane in the presence of NH<sub>4</sub><sup>+</sup> ions. After standing for 5min, the ppte was filtered off onto a sintered porcelain crucible, washed with very dilute AcOH and dried at room temp for at least 24h [*Anal Chem* 28 1001 1956]. Alternatively a soln of sodium tetraphenylborane (5% excess) in H<sub>2</sub>O is added to NH<sub>4</sub>Cl soln. After 5min the ppte is collected, washed several times with H<sub>2</sub>O and recryst from aqueous Me<sub>2</sub>CO. [*Analyt Chim Acta* 19 342 1958.]

Ammonium thiocyanate [1762-95-4] M 76.1, m  $138^{\circ}(dec)$ ,  $149^{\circ}(dec)$ ,  $pK^{25}$  -1.85 (for HSCN), 149. Crystd three times from dilute HClO<sub>4</sub>, to give material optically transparent at wavelengths longer than 270nm. Has also been crystd from absolute MeOH and from acetonitrile.

Ammonium tungstate (VI) [11120-25-5] M 283.9,  $pK_1^{25}$  2.20,  $pK_2^{25}$  3.70 (for tungstic acid, H<sub>2</sub>WO<sub>4</sub>). Crystd from warm water by adding EtOH and cooling.

Ammonium (meta) vanadate [7803-55-6] M 117.0,  $d_{10}^{20}$  2.326. Wash with H<sub>2</sub>O until free from Cl<sup>-</sup> and dry in air. It is soluble in H<sub>2</sub>O (5.18g/100mL at 15°, 10.4g/100mL at 32°) but is more soluble in dilute NH<sub>3</sub>. Crystd from conductivity water (20mL/g). When heated at relatively low temperatures it loses H<sub>2</sub>O and NH<sub>3</sub> to give vanadium oxide (V<sub>2</sub>O<sub>5</sub>) and at 210° it forms lower oxides. [*Inorg Synth* 3 117 1950.] After washing Tech grade with H<sub>2</sub>O it had Na, Mn and U at 0.06, 0.2 and 0.1 ppm resp.

n-Amylmercuric chloride [544-15-0] M 307.2, m 110°. Crystd from EtOH.

Anthraquinone Blue B (Acid Blue 45, 1,5-diamino-4,8-dihydroxy-9,10-anthraquinone-3,7disulfonic acid di-Na salt) [286]-02-1] M 474.3, m >300°, CI 63010,  $\lambda$ max 595nm, pK<sub>Est(1)</sub>~<0, pK<sub>Est(2)</sub>~2, pK<sub>Est(3)</sub>~9. Purified by salting out three times with sodium acetate, followed by repeated extraction with EtOH [McGrew and Schneider J Am Chem Soc 72 2547 1950].

Anthraquinone Blue RXO [4403-89-8] M 445.5. Purified by salting out three times with sodium acetate, followed by repeated extraction with EtOH [McGrew and Schneider J Am Chem Soc 72 2547 1950].

Anthraquinone Green G [Acid Green 25, Alizarin Cyanine Green F, 1,4-bis-(4-methyl-2sulfophenyl-1-amino)-9,10-anthraquinone di-Na salt] [4403-90-1] M 624.6, m 235-238°, CI 61570,  $\lambda$ max 642nm, pK >0. Purified by salting out three times with sodium acetate, followed by repeated extraction with EtOH [McGrew and Schneider J Am Chem Soc 72 2547 1950]. It is a green powder that slightly sol in Me<sub>2</sub>CO, EtOH and pyridine. Sol in conc H<sub>2</sub>SO<sub>4</sub> to give a blue soln which becomes turquoise on dilution. [Allen et al. J Org Chem 7 63 1942.]

9,10-Anthraquinone-2,6-disulfonic acid (disodium salt) [853-68-9] M 412.3, m >325°, pK<sub>Est</sub> ~<0 (for SO<sub>3</sub>H). Crystd three times from water, in the dark [Moore et al. J Chem Soc. Faraday Trans1 82 745 1986].

**9,10-Anthraquinone-2-sulfonic acid (Na salt, H<sub>2</sub>O)** [131-08-8] M **328.3, pK**<sub>Est</sub> ~<**0** (SO<sub>3</sub>H). Crystd from H<sub>2</sub>O or MeOH (charcoal). [Costa and Bookfield J Chem Soc, Faraday Trans 1 **82** 991 1986].

Antimony (V) pentafluoride [7783-70-2] M 216.7, m 7.0°, 8.3°, b 141°, 150°, 148-150°, d 2.99,  $pK^{25}$  2.55 [for HSb(OH)<sub>6</sub> = Sb(OH)<sub>6</sub><sup>-</sup> + H<sup>+</sup>]. Purified by vacuum distillation preferably in a

#### Purification of Inorganic and Metal-Organic Chemicals

quartz apparatus, and stored in quartz or aluminum bottles. It is a hygroscopic viscous liquid which reacts violently with H<sub>2</sub>O and is hydrolysed by alkalis. It is **POISONOUS** and attacks the skin. [J Chem Soc 2200 1950; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 200 1965.]

Antimony trichloride [10025-91-9] M 228.1, m 73°, b 283°,  $pK_1^{25}$  1.4,  $pK_2^{25}$  11.0 (11.8),  $pK_3^{25}$  12.95 (for Sb<sup>3+</sup> aquo). Dried over P<sub>2</sub>O<sub>5</sub> or by mixing with toluene or xylene and distilling (water is carried off with the organic solvent), then distd twice under dry nitrogen at 50mm, degassed and sublimed twice in a vacuum into ampoules. Can be crystd from CS<sub>2</sub>. Deliquescent. Fumes in moist air.

Antimony trifluoride [7783-56-4] M 178.8, m 292°. Crystd from MeOH to remove oxide and oxyfluoride, then sublimed under vacuum in an aluminium cup on to a water-cooled copper condenser [Woolf J Chem Soc 279 1955].

Antimony triiodide [7790-44-5] M 502.5, m 167°. Sublimed under vacuum.

Antimony trioxide [1309-64-4] M 291.5, m 656°. Dissolved in minimum volume of dilute HCl, filtered, and six volumes of water were added to ppte a basic antimonous chloride (free from Fe and Sb<sub>2</sub>O<sub>5</sub>). The ppte was redissolved in dilute HCl, and added slowly, with stirring, to a boiling soln (containing a slight excess) of Na<sub>2</sub>CO<sub>3</sub>. The oxide was filtered off, washed with hot water, then boiled and filtered, the process being repeated until the filtrate gave no test for chloride ions. The product was dried in a vacuum desiccator [Schuhmann J Am Chem Soc 46 52 1924]. After on cryst(pptn?), the oxide from a Chinese source had: metal (ppm) Al (8), Ag (0.2), As (56), Cr (6), Ge (0.4), Mn (0.2), Na (16), Ni (2.2) Pb (2.4), Sn (0.4) and V (32).

Aqua regia. This is prepared by adding slowly concentrated HNO<sub>3</sub> (1 vol) to concentrated hydrochloric acid (3 vols) in a glass container. This mixture is used to dissolve metals, including noble metals and alloys, as well as minerals and refractory substances. It is done by suspending the material and boiling (EFFICIENT FUME CUPBOARD — EYE PROTECTION] to dryness and repeating the process until the residue dissolves in  $H_2O$ . If the aqua regia is to be stored for long periods it is advisable to dilute it with one volume of  $H_2O$  which will prevent it from releasing chlorine and other chloro and nitrous compounds which are objectionable. Store cool in a fume cupboard. However, it is good laboratory practice to prepare it freshly and dispose of it down the fume cupboard sink with copious amounts of water.

**Argon** [7440-37-1] **M 39.95, b -185.6°.** Rendered oxygen-free by passage over reduced copper at 450°, or by bubbling through alkaline pyrogallol and  $H_2SO_4$ , then dried with CaSO<sub>4</sub>, Mg(ClO<sub>4</sub>)<sub>2</sub>, or Linde 5A molecular sieves. Other purification steps include passage through Ascarite (asbestos impregnated with sodium hydroxide), through finely divided uranium at about 800° and through a -78° cold trap.

Alternatively the gas is passed over CuO pellets at 300° to remove hydrogen and hydrocarbons, over Ca chips at 600° to remove oxygen and, finally, over titanium chips at 700° to remove nitrogen. Also purified by freezepump-thaw cycles and by passage over sputtered sodium [Arnold and Smith J Chem Soc, Faraday Trans 2 77 861 1981].

o-Arsanilic acid [2045-00-3] M 216.1, m 153°,  $pK_1^{22} 3.77$  (AsO<sub>3</sub>H<sub>2</sub>),  $pK_2^{22} 8.66$  (AsO<sub>3</sub>H<sup>-</sup>). Crystd from water or ethanol/ether. POISONOUS.

*p*-Arsanilic acid [98-50-0] M 216.1, m 232°,  $pK_1^{22}$  4.05 (AsO<sub>3</sub>H<sub>2</sub>),  $pK_2^{22}$  8.66 (AsO<sub>3</sub>H<sup>-</sup>). Crystd from water or ethanol/ether. POISONOUS.

Arsenazo I [3(2-arsonophenylazo)-4,5-dihydroxy-2,7-naphthalenedisulfonic acid di Na salt] [66019-20-3] M 614.3,  $\varepsilon$  2.6 x 10<sup>4</sup> at 500nm, pH 8.0; pK<sub>1</sub> 0.6(0.8), pK<sub>2</sub> 3.52, pK<sub>3</sub> 2.97(AsO<sub>3</sub>H<sub>2</sub>), pK<sub>4</sub> 8.20(AsO<sub>3</sub>H<sup>-</sup>), pK<sub>5</sub> 9.98(OH), pK<sub>6</sub> 15.0. A saturated aqueous soln of the free acid was slowly added to an equal volume of conc HCl. The orange ppte was filtered, washed with acetonitrile and dried for 1-2h at 110° [Fritz and Bradford Anal Chem 30 1021 1958].

Arsenazo III [3,6-bis(2-arsonophenylazo)-4,5-dihydroxy-2,7-naphthalenedisulfonic acid di Na salt] [62337-00-2] M 776.4, pK<sub>1</sub> -2.7, pK<sub>2</sub> -2.7, pK<sub>3</sub> 0.6, pK<sub>4</sub> 0.8, pK<sub>5</sub> 1.6, pK<sub>6</sub> 3.4,

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 $pK_7$  6.27,  $pK_8$  9.05,  $pK_9$  11.98,  $pK_{10}$  15.1. Contaminants include monoazo derivatives, starting materials for synthesis and by-products. Partially purified by pptn of the dye from aqueous alkali by addition of HCl. More thorough purification by taking a 2g sample in 15-25mL of 5% aq NH<sub>3</sub> and filter. Add 10mL HCl (1:1) to the filtrate to ppte the dye. Repeat procedure and dissolve solid dye (0.5g) in 7mL of a 1:1:1 mixture of *n*-propanol:conc NH<sub>3</sub>:water at 50°. After cooling, filter soln and treat the filtrate on a cellulose column using 3:1:1 mixture of *n*-propanol:conc NH<sub>3</sub>:water as eluent. Collect the blue band and evaporate to 10-15mL below 80°, then add 10mL conc HCl to ppte pure Arsenazo III. Wash with EtOH and air-dry [Borak et al. *Talanta* 17 215 1970]. The purity of the dye can be checked by paper chromatography using M HCl as eluent.

Arsenic [7440-38-2] M 74.9, m 816°. Heated under vacuum at 350° to sublime oxides, then sealed in a Pyrex tube under vacuum and sublimed at 600°, the arsenic condensing in the cooler parts of the tube. Stored under vacuum [Shih and Peretti J Am Chem Soc 75 608 1953]. POISONOUS.

Arsenic acid (arsenic pentoxide hydrate, arsenic V oxide hydrate, orthoarsenic acid) [12044-50-7] M 229.8 +  $xH_2O$ ,  $pK_1^{25}2.26$ ,  $pK_2^{25}6.76$ ,  $pK_3^{25}11.29$  ( $H_3AsO_4$ ). Cryst from conc solns of boiling conc HNO<sub>3</sub> as rhombic crystls. Dried in vac to give hemihydrate (hygroscopic). Heating above 300° yields  $As_2O_5$ . [Thaler Z Anorg Allg Chem 246 19 1941.] POISONOUS.

Arsenic tribromide [7784-33-0] M 314.6, m 31.1°, b 89°/11mm, 221°/760mm. Distd under vacuum. POISONOUS.

Arsenic trichloride (butter of arsenic) [7784-34-1] M 181.3, b 25°/11mm, 130.0°. Refluxed with arsenic for 4h, then fractionally distd. The middle fraction was stored with sodium wire for two days, then again distd [Lewis and Sowerby J Chem Soc 336 1957]. Fumes in moist air and readily hydrolysed by H<sub>2</sub>O. **POISONOUS.** 

Arsenic triiodide [7784-45-4] M 455.6, m 146°, b 400°/atm. Crystd from acetone, sublimes below 100°. POISONOUS

Arsenic III oxide (arsenic trioxide, arsenious oxide) [1327-53-3] M 197.8, three forms: m ~200°(amorphous glass), m 275°(sealed tube, octahedral, common form, sublimes > 125° without fusion but melts under pressure), m ~312°,  $pK_1^{20}9.27$ ,  $pK_2^{20}13.54$ ,  $pK_3^{20}13.99$  (for H<sub>3</sub>AsO<sub>3</sub>). Crystd in octahedral form from H<sub>2</sub>O or from dil HCl (1:2), washed, dried and sublimed (193°/760mm). Analytical reagent grade material is suitable for use as an analytical standard after it has been dried by heating at 105° for 1-2h or has been left in a desiccator for several hours over conc H<sub>2</sub>SO<sub>4</sub>. **POISONOUS (particulary the vapour, handle in a ventilated fume cupboard)**.

Aurothioglucose (gold thioglucose) [12192-57-3] M 392.2. Purified by dissolving in  $H_2O$  (0.05g in 1mL) and ppting by adding EtOH. Yellow cryst with slight mercaptan odour. Decomposes slowly in  $H_2O$ , sol in propylene glycol but insol in EtOH and other common organic solvents. [FEBS Lett 98 351 1970.]

**Barium (metal)** [7440-39-3] M 137.3, m 727°. Cleaned by washing with diethyl ether to remove adhering paraffin, then filed in an argon-filled glove box, washed first with ethanol containing 2% conc HCl, then with dry ethanol. Dried under vacuum and stored under argon [Addison, Coldrey and Halstead J Chem Soc 3868 1962]. Has also been purified by double distn under 10mm argon pressure.

**Barium acetate** [543-80-6] M 255.4. Crystd twice from anhydrous acetic acid and dried under vacuum for 24h at 100°.

**Barium bromate** [13967-90-3] M 265.3. Crystd from hot water (20mL/g). The monohydrate melts at 260°(dec).

Barium bromide  $(2H_2O)$  [7791-28-8] M 333.2, m at 75° loses first  $H_2O$  and at 120° loses the second  $H_2O$ . Crystd from water (1mL/g) by partial evaporation in a desiccator.

**Barium chlorate** ( $H_2O$ ) [10294-38-9 (hydrate); 13477-00-4 (anhydr)] M 322.3, m 414°. Crystd from water (1mL/g) between 100° and 0°.

**Barium chloride (2H<sub>2</sub>O)** [10326-27-9] M 244.3, m ~120°(dec, hydrate), 963° (anhyd). Twice crystd from water (2mL/g) and oven dried to constant weight.

Barium dithionate  $(2H_2O)$  [13845-17-5] M 333.5, m >150° loses SO<sub>2</sub>, pK<sup>25</sup> 0.49 (for H<sub>2</sub>S<sub>2</sub>O<sub>6</sub>, theory pK<sub>1</sub> -3.4, pK<sub>2</sub> -0.2). Crystd from water.

Barium ferrocyanide (6H<sub>2</sub>O) [13821-06-2] M 594.8, m 80°(dec),  $pK_3^{25}$  2.57,  $pK_4^{25}$  4.35 (for ferrocyanide). Crystd from hot water (100mL/g).

**Barium fluoride** [7787-32-8] **M 175.3, m 1353°, 1368°, b 2260°, d 4.83.** Washed well with distd H<sub>2</sub>O and dried in vacuum Sol in H<sub>2</sub>O [1.6g (10°), 1.6g (20°) and 1.62g (30°) per L), mineral acids and aq NH<sub>4</sub>Cl. May be stored in glass bottles. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 234 1963.]

**Barium formate** [541-43-5] M 277.4, pK<sup>25</sup> 3.74 (for HCO<sub>2</sub>H). Crystd from warm water (4mL/g) by adding EtOH and cooling.

Barium hydroxide (8H<sub>2</sub>O) [12230-71-6] M 315.5, m 78°, pK<sub>1</sub><sup>25</sup>13.13, pK<sub>2</sub><sup>25</sup>13.36. Crystd from water (1mL/g).

Barium hypophosphite (H<sub>2</sub>O) [14871-79-5] M 285.4. Ppted from aq soln (3mL/g) by adding EtOH.

Barium iodate ( $H_2O$ ) [7787-34-0] M 487.1, m 130°(loses  $H_2O$ ), 476°(dec). Crystd from a large volume of hot water by cooling.

**Barium iodide**  $(2H_2O)$  [7787-33-9  $(2H_2O)$ ; 13718-50-8 (anhydr)] M 427.2, m 740°(dec). Crystd from water (0.5mL/g) by partial evapn in a desiccator. POISONOUS.

**Barium ionophore I** [N, N, N', N'-tetracyclohexyloxy-bis-(o-phenyleneoxy)diacetamide] [96476-01-6] M 644.9, m 156-158°. Purified by chromatography on a Kieselgel column and eluted with CH<sub>2</sub>Cl<sub>2</sub>-EtOAc (5:1), and recryst from EtOH-Me<sub>2</sub>CO as colourless crystals. It is an electrically neutral ionophore with high selectivity for Ba<sup>2+</sup> ions and with high lipophilicity. [*Chem Ber* 118 1071 1985.]

**Barium manganate (barium permanganate)** [7787-35-1] M 256.3, d 3.77. Wash with conductivity H<sub>2</sub>O by decantation until the supernatant gives a faint test for Ba<sup>2+</sup>. Remove excess H<sub>2</sub>O in vac (IMPORTANT), then heat at 100° and the last traces of H<sub>2</sub>O are removed in a vac desiccator over P<sub>2</sub>O<sub>5</sub>. Store over KOH. It disproportionates in hot H<sub>2</sub>O or dil acid to Ba(MnO<sub>2</sub>)<sub>2</sub> and MnO<sub>2</sub>, and is a mild oxidant. [*J Am Chem Soc* 44 1965 1924; Inorg Synth 11 56 1960.]

**Barium nitrate** [10022-31-8] M 261.4, m 593°(dec). Crystd twice from water (4mL/g) and dried overnight at 110°. POISONOUS.

Barium nitrite (H<sub>2</sub>O) [7787-38-4] M 247.4, m 217<sup>o</sup>(dec). Crystd from water (1mL/g) by cooling in an ice-salt bath. POISONOUS.

Barium perchlorate [13465-95-7] M 336.2, m 505°, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd twice from water.

Barium propionate  $(H_2O)$  [5908-77-0] M 301.5, pK<sup>24</sup> 4.88 (for propionic acid). Crystd from warm water (50mL/g) by adding EtOH and cooling.

**Barium sulfate** [7722-43-7] M 233.4, m >1580°. Washed five times by decantation with hot distilled water, dialysed against distd water for one week, then freeze-dried and oven dried at 105° for 12h.

**Barium tetrathionate** [82203-66-5] M **361.6.** Purified by dissolution in a small volume of water and ppted with EtOH below 5°. After drying the salt was stored in the dark at  $0^{\circ}$ .

**Barium thiocyanate** (2  $H_2O$ ) [2092-17-3] M 289.6, pK<sup>25</sup> -1.85 (for HSCN). Crystd from water (2.5mL/g) by partial evaporation in a desiccator.

**Barium thiosulfate** [35112-53-9] M 249.5, m 220°(dec),  $pK_1^{25}0.6$ ,  $pK_2^{25}1.74$  (for  $H_2S_2O_3$ ). Very slightly soluble in water. Washed repeatedly with chilled water and dried in air at 40°.

**Benzaldehyde-2-sulfonic acid sodium salt** [1008-72-6] **M 208.2, m dec on heating.** Forms prisms or plates by extracting with boiling EtOH, filtering, evaporate to dryness and recrystallise the Na salt from a small volume of H<sub>2</sub>O. The *N*-phenylhydrazone sodium salt recrysts from H<sub>2</sub>O, **m** 174.5°. [Gnehm and Schüle Justus Liebigs Ann Chem **299** 363 1898.]

Benzenechromium tricarbonyl [12082-08-5] M 214.1, m 163-166°. Purified by sublimation in vacuo.

**Benzeneselenenyl bromide** (phenylselenenyl bromide) [34837-55-3] M 236.0, m 58-62°, 60°, 62°, b 107-108°/15mm, 134°/35mm. Dist in a vac, recryst from pet ether, CHCl<sub>3</sub> (EtOH free), or Et<sub>2</sub>O (cooling mixture) as dark red or orange crysts, sublimes at 25°/0.001mm [Behaghel et al. Chem Ber 65 815 1932; Pitteloud and Petrzilka Helv Chim Acta 62 1319 1979]. HIGHLY TOXIC

Benzeneselenenyl chloride (benzeneselenyl chloride, phenylselenenyl chloride) [5707-04-0] M 191.5, m 59-60°, 64-65°, b 92°/5mm, 120°/20mm. Purified by distn in vac and recrystn (orange needles) from hexane [Foster J Am Chem Soc 55 822 1933, Foster et al. Recl Trav Chim, Pays-Bas 53 405, 408 1934; Behaghel and Seibert Chem Ber 66 714 1933.] HIGHLY TOXIC.

**Benzeneseleninic acid** [6996-92-5] **M 189.1, m 122-124°, pK<sup>25</sup> 4.70.** Add 10% excess of 15M NH<sub>3</sub> to the solid acid and stir until the solid dissolves, filter, decolorise with charcoal (2x, Norite) and acidify by slow addn of 6M HCl, filter solid and wash with H<sub>2</sub>O. Dissolve the acid in the minimum vol of MeOH and this soln is added dropwise to boiling H<sub>2</sub>O until cloudiness appears. At this point add 25% more boiling H<sub>2</sub>O, filter hot (decolorise if necessary) and cool rapidly with scratching to 0°. After 30min the solid is filtd off and recryst as before but with very slow cooling. The colorless needles are filtered off and dried in a vac desiccator (CaCl<sub>2</sub>) before the melting point is measured [McCullough and Gould J Am Chem Soc 71 674 1949].

**Benzeneseleninic anhydride** [17697-12-0] **M 360.1, m 124-126°, 164-165°, 170-173°**. When the anhydride is recrystd from  $*C_6H_6$  it has **m** 124-126° but when this is heated at 140°/1h in a vac or at 90°/2h it had **m** 164-165° and gives a solid **m** 124-126° when recrystd from  $*C_6H_6$ . Both depress the melting point of the acid PhSeO<sub>2</sub>H. If the high melting anhydride is dissolved in  $*C_6H_6$  and seeded with the high melting anhydride, the high melting anhydride crystallises out. It readily absorbs H<sub>2</sub>O to form the acid (PhSeO<sub>2</sub>H, **m** 122-124°). Because of this the commercial anhydride could contain up to 30% of the acid. Best purified by converting to the HNO<sub>3</sub> complex (**m** 112°) and heating this *in vacuo* at 120°/72h to give the anhydride as a white powder **m** 164-165°. Alternatively heat the anhydride *in vacuo* at 120°/72 h until IR shows no OH band. [Ayvrey et al. J Chem Soc 2089 1962; Barton et al. J Chem Soc, Perkin Trans 1 567 1977.] **TOXIC** solid.

**Benzeneselenol** (phenylselenol, selenophenol) [645-96-5] M 157.1, b 57-59°/8mm, 71-72°/18mm, 84-86°/25mm, d 1.480, n 1.616. Dissolve in aq N NaOH, acidify with conc HCl and extract with Et<sub>2</sub>O, dry over CaCl<sub>2</sub>, filter, evap on a steam bath and distil from a Claisen flask or through a short

column collecting the middle fraction and seal immediately in a glass vial, otherwise the colourless liquid becomes yellow. The alkali insol materials consist of diphenylselenide (b  $167^{\circ}/16$ mm) and diphenyldiselenide, m  $63^{\circ}$  (from EtOH). TOXIC, use rubber gloves. It has a foul odour. [Foster *Org Synth* Coll Vol III 771 1955.]

**Benzeneselenonic acid (benzeneselenoic acid)** [39254-48-3] M 205.1, m 64°,  $pK^{25}$  4.79. Purified by dissolving in H<sub>2</sub>O and passing through a strong cation exchange resin (H<sup>+</sup> form). Evap under reduced pressure and dry in a high vac to give colourless hygroscopic crysts [Dostal et al. Z Chem 6 153 1966 and IR: Chem Ber 104 2044 1971].

Benzenestibonic acid [535-46-6] M 248.9, m >250°(dec). Crystd from acetic acid, or from EtOH-CHCl<sub>3</sub> mixture by addition of water.

**Benzenesulfinic acid Na salt** [873-55-2] **M 164.2, m >300°, pK<sup>25</sup> 2.16 (2.74; for PhSO<sub>2</sub>H).** Dissolve in the minimum vol of O<sub>2</sub> free H<sub>2</sub>O (prepared by bubbling N<sub>2</sub> through for 2 h) and adding O<sub>2</sub> free EtOH (prepared as for H<sub>2</sub>O), set aside at 4° overnight under N<sub>2</sub>, filtd, washed with abs EtOH, then Et<sub>2</sub>O and dried in a vac. The Na salt is relatively stable to air oxidation, but is best kept under N<sub>2</sub> in the dark. Also recrystd from EtOH and dried at 120° for 4h in a vacuum [Kornblum and Wade J Org Chem **52** 5301 1987].

Benzopurpurin 4B  $\{3,3'-[(3,3'-dimethyl[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[4-amino-1$  $naphthalenesulfonic acid di-Na salt, Direct red 2\} [992-59-6] M 724.7, <math>\lambda max$  500nm, CI 23500, pK<0. Crystd from H<sub>2</sub>O. It is a biological stain that is violet at pH 1.2 and red at pH 4.0 and is used for detecting Al, Mg, Hg, Au and U.

**Benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP reagent)** [56602-33-6] M 442.29, m > 130° (dec), 147-149° (dec). Dissolve in  $CH_2Cl_2$ , dry (MgSO<sub>4</sub>), filter, conc under vac then add dry  $Et_2O$  and filter off first crop. Add  $CH_2Cl_2$  to the filtrate and concentrate again to give a second crop. Solid is washed with dry  $Et_2O$  and dried in vac. Also recryst from dry  $Me_2CO/Et_2O$  and check purity by NMR. Store in the dark. [Castro et al. Synthesis 751 1976.]

**Benzylidene-bis-(tricyclohexylphosphine) dichlororuthenium (Grubbs catalyst)** [172222-30-9] **M 823.0.** Repeatedly wash with Me<sub>2</sub>CO and MeOH and dry in vac. Alternatively dissolve in  $CH_2Cl_2$  concentrate to half vol, filter, add MeOH to ppte it as purple microcrystals. Filter off, wash several times with Me<sub>2</sub>CO and MeOH and dry in a vac for several hours. [Scwab, Grubbs and Ziller J Am Chem Soc 118 100 1996; Miller, Blackwell and Grubbs J Am Chem Soc 118 9606 1966.] **§** A polymer supported version is available.

Benzyl Orange [4-(4-benzylaminophenylazo)benzenesulfonic acid potassium salt] [589-02-6] M 405.5, pK<sub>Est(1)</sub>~<0, pK<sub>Est(2)</sub>~3.8. Crystd from H<sub>2</sub>O.

**Benzyltriphenylphosphonium chloride** [1100-88-5] M 388.9, m 280° (sintering), 287-288°. Wash with  $Et_2O$  and crystallise from EtOH (six sided plates). Hygroscopic and forms crystals with one mol H<sub>2</sub>O. [Justus Liebigs Ann Chem 229 320 1885; Chem Ber 83 291 1950.]

Beryllium acetate (basic)  $[Be_4O(OAc)_6]$  [1332-52-1] M 406.3, m 285-286°. Crystd from chloroform.

Beryllium potassium fluoride [7787-50-0] M 105.1. Crystd from hot water (25mL/g).

**Beryllium sulfate** (4H<sub>2</sub>O) [7787-56-6] M 177.1, m ~100°(dec),  $pK_1^{25}3.2$ ,  $pK_2^{25}$ ~6.5 (Be<sup>2+</sup>). Crystd from weak aqueous H<sub>2</sub>SO<sub>4</sub>.

**Bicyclo[2.2.1]hepta-2,5-diene rhodium (I) chloride dimer (norbornadiene rhodium chloride complex dimer)** [12257-42-0] **M 462, m 240°(dec).** Recrystd from hot CHCl<sub>3</sub>-pet ether as fine crystals soluble in CHCl<sub>3</sub> and  ${}^{*}C_{6}H_{6}$  but almost insoluble in Et<sub>2</sub>O or pet ether. [J Chem Soc 3178 1959.]

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**R**-(-)-1,1'-Binaphthyl-2,2'-diylhydrogen phosphate [39648-67-4] M 348.3, m 217°,  $[\alpha]_D^{20}$ -608° (c 1, MeOH), pK<sup>20</sup> 0.74. Recrystallise from EtOH. Reflux for 3h in N NaOH is required to hydrolyse the cyclic phosphate. [Tetrahedron Lett 4617 1971; Tetrahedron Lett 24, 343 1983.]

S-(+)-1,1'-Binaphthyl-2,2'-diylhydrogen phosphate [35193-64-7] M 348.3,  $[\alpha]_D^{20}$ +608° (c 1, MeOH), pK<sup>20</sup>0.74. Recrystallise from EtOH. Reflux for 3h in N NaOH is required to hydrolyse the cyclic phosphate. [Tetrahedron Lett 4617 1971; Tetrahedron Lett 24, 343 1983.]

**2-Biphenylyl diphenyl phosphate** [132-29-6] **M 302.4, n<sup>25</sup>1.5925.** Vacuum distd, then percolated through an alumina column. Passed through a packed column maintained at 150° to remove residual traces of volatile materials by a counter-current stream of nitrogen at reduced pressure. [Dobry and Keller J Phys Chem **61** 1448 1957.]

**2,2'-Bipyridinium chlorochromate** [76899-34-8] **M 292.6.** Washed with cold conc HCl then  $H_2O$  (sintered glass funnel) and dried in vacuum (CaCl<sub>2</sub>) to a free flowing yellow-brown powder. Stored in the dark. [Synthesis 691 1980; Synth Commun 10 951 1980.] SUSPECTED CARCINOGEN.

**2,2'-Biquinolin-4,4'-dicarboxylic acid dipotassium salt** [63451-34-3] **M 420.51.** Recryst from H<sub>2</sub>O. The Cu salt has  $\lambda_{max}$  at 562nm. [Anal Biochem 56 4409 1973.]

**Bis**-(*p*-tert-butylphenyl)phenyl phosphate [115-87-7] M 438.5, b 281°/5mm, n<sup>25</sup> 1.5412. Same as for 2-biphenylyl diphenyl phosphate (above).

Bis-(2-chlorophenyl) phenyl phosphate [597-80-8] M 395, b 254°/4mm, n<sup>25</sup> 1.5767. Same as for 2-biphenylyl diphenyl phosphate above.

**Bis-(1,5-cyclooctadiene)nickel (0)** [1295-35-8] M 275.0, m 142° (dec). Available in sealed ampoules under N<sub>2</sub>. All procedures should be carried out in a dry box and in an atmosphere of N<sub>2</sub> or Argon in subdued light because the complex is light and oxygen sensitive and flammable. The solid is washed with dry  $Et_2O$  (under Ar) and separates from toluene as yellow crysts. Filter under Ar gas pressure, place the crysts in a container and dry under a vac of 0.01 mm to remove adhered toluene, flush with Ar and seal under Ar or N<sub>2</sub> in glass ampoules. [Semmelhack Org Reactions 19 115 and 1781972; Wilke et al. Justus Liebigs Ann Chem 699 1 1966.] SUSPECTED CARCINOGEN.

Bis(2,9-dimethyl-1,10-phenanthroline) copper(I) perchlorate [54816-44-5] M 579.6, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from acetone.

2,2'-Bis-(diphenylphosphino)-1,1'-binaphthyl (BINAP) [RS 98327-87-8] M 622.7, m 283-286°, [R-(+)-76189-55-4] m 241-242°, [S-(-)-76189-56-5] m 241-242°, [ $\alpha$ ]  $_{\rm D}^{20}$  (+) and (-) 233° (c 0.3 toluene). Dissolve the individual enantiomers in toluene, wash with 30% aq NaOH, three times with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evap to ~15% of its vol and add an equal vol of degassed MeOH. Collect the solid, wash with MeOH and dry at 80°/0.005mm for 6h. Recryst from 1:1 mixt of toluene-EtOH to optical purity (m 241-242°)[Takaya et al. Org Synth 67 20 1989].

§ A polymer supported version is available.

**1,4-Bis-(diphenylphosphino)butane** [7688-25-7] **M 426.5, m 135-136°.** Recrystd from EtOH [Trippett J Chem Soc 4263 1961].

**2***R*,**3***R*-(+)-**2**,**3**-Bis(diphenylphosphino)butane (*R*,*R*-CHIRAPHOS) [74839-84-2], **2***S*,**3***S*-(-)-**2**,**3**-bis(di-phenylphosphino)butane (*S*,*S*-CHIRAPHOS) [64896-28-2] M 426.5, m 108-109°,  $[\alpha]_{D}^{20}$  (+) and (-) 200° (c 1.5 CHCl<sub>3</sub>). Recryst d from abs EtOH (~6g in 60mL) as colorless plates [Fryzuk and Bosnich J Am Chem Soc 99 6262 1977 and 101 3043 1979].

#### Purification of Inorganic and Metal-Organic Chemicals

**1,2-Bis-(diphenylphosphino)ethane (DIPHOS)** [1663-45-2] **M 398.4, m 139-140°,140-142°, 143-144°, pK**<sub>Est</sub> ~4.5. Recrystd from aq EtOH or  $*C_6H_6$ . The dimethiodide recrystd from MeOH has **m** 305-307° and the dioxide recrystd from toluene or DMF (needles), or  $*C_6H_6$  (plates) has **m** 252-254° (276-278°) [Isslieb et al. Chem Ber 92 3175 1959; NMR: Aquiar et al. J Org Chem 29 1660 1964; Bäckvall et al. J Org Chem 52 5430 1987].

1,1'-Bis-(diphenylphosphino)ferrocene [12150-46-8] M 554.4, m 181-183°, 184-194°. Wash with distilled H<sub>2</sub>O and dry in a vacuum. Dissolve in *ca* 5 parts of hot dioxane and cool to give orange crystals m 181-183°. Recrystn from  ${}^{*}C_{6}H_{6}$ -heptane (1:2) gives product with m 183-184°. [J Organomet Chem 27 241 1971.]

**Bis-(2-ethylhexyl) 2-ethylhexyl phosphonate** [25103-23-5] **M 434.6, n<sup>25</sup> 1.4473.** Purified by stirring an 0.4M soln in \*benzene with an equal volume of 6M HCl at ca 60° for 8h. The \*benzene layer was then shaken successively with equal volumes of water (twice), aqueous 5% Na<sub>2</sub>CO<sub>3</sub> (three times), and water (eight times), followed by evaporation of the \*benzene and distilled under reduced pressure at room temperature (using a rotating evacuated flask). Stored in dry, dark conditions [Peppard et al. *J Inorg Nucl Chem* **24** 1387 *1962*]. Vacuum distilled, then percolated through an alumina column before finally passed through a packed column maintained at 150° where residual traces of volatile materials were removed by a counter-current stream of N<sub>2</sub> at reduced pressure [Dobry and Keller *J Phys Chem* **61** 1448 *1957*].

**Bis-(2-ethylhexyl) phosphoric acid** [298-07-7] **M 322.4.** See di-(2-ethylhexyl) phosphoric acid on p. 418.

Bis(ethyl)titanium(IV) chloride [2247-00-9] M 177.0. Crystd from boiling toluene.

Bis(ethyl)zirconium(IV) chloride [92212-70-9] M 220.3. Crystd from boiling toluene.

2,4-Bis-(methylthio)-1,3,2 $\lambda^5$ ,4 $\lambda^5$ -dithiadiphosphetane-2,4-dithione (Davy's reagent) [82737-61-9] M 284.4, m 160°. Recrystd from \*C<sub>6</sub>H<sub>6</sub> in yellow plates or from hot trichlorobenzene. The low m observed in the literature (112° with gradual softening at 68-102°) has been attributed to the presence of elemental sulfur in the crystals. [*Tetrahedron* 40 2663 1984; J Org Chem 22 789 1957.]

**Bismuth** [7440-69-9] M 209.0, m 271-273°. Melted in an atmosphere of dry helium and filtered through dry Pyrex wool to remove any bismuth oxide present [Mayer, Yosim and Topol J Phys Chem 64 238 1960].

**Bismuthiol I** (2,5-dimercapto-1,3,4-thiadiazole) potassium salt [4628-94-8] M 226.4, m 275-276°(dec),  $pK_{Est(1)}$ ~4.1. Usually contaminated with disulfide. Purified by crystn from EtOH. Reagent for detection of Bi,Cu, Pb and Sb.

**Bismuth trichloride** [7787-60-2] **M 315.3, m 233.6°, pK<sup>25</sup> 1.58** ( $Bi_3^+ = BiOH_2^+ + H^+$ ). Sublimed under high vacuum, or dried under a current of HCl gas, followed by fractional distn, once under HCl and once under argon.

*N*, *N'*-Bis-(salicylidene)ethylenediamine cobalt (II) [Co(SALEN)<sub>2</sub>, salcomine] [14167-18-1] M 325.2. The powder should have an oxygen capacity of 4.7-4.8% as measured by the increase in wt under  $O_2$  at 100 pounds pressure at *ca* 20°. The  $O_2$  is expelled on heating the material to 65°. Recryst from pyridine, CHCl<sub>3</sub> or \*C<sub>6</sub>H<sub>6</sub>, and the solvent may be removed by heating at 120° in a vac. However this heating may mean reduced  $O_2$  capacity. In the dry state it absorbs  $O_2$  turning from maroon colour to black. [Diehl and Hack *Inorg Synth* 3 196 1950.]

**Bis-(tetrabutylammonium) dichromate** [56660-19-6] **M 700.9, m 139-142°.** Wash with water and dry in a vacuum. Crystallises from hexane (m 79-80°). [Synth Commun 10 75 1980.] (Possible CARCINOGEN).

**Bis-[4-(1,1,3,3-tetramethylbutyl)phenyl]phosphate calcium salt (Selectophore)** [40835-97-0] **M 987.3.** The Ca diester salt is washed with  $H_2O(x3)$  and MeOH (x3) alternately and dried in a vacuum oven at 50°. If the Ca salt is contaminated with much Ca salt of the monoester then it (10g) is converted to the free acid by adding 6N HCl (*ca* 10vols) and Et<sub>2</sub>O (> 50vols) to it and stirred vigorously to form the free acids. When no white ppte remained (*ca* 5min), the Et<sub>2</sub>O is separated, washed with  $H_2O(2x > 50 \text{ mL})$  and dried by filtering through a bed of anhydrous Na<sub>2</sub>SO<sub>4</sub> (11 x 5 cm) which is then washed with Et<sub>2</sub>O (2 x >50 mL). Evapn gives an oil (TLC R<sub>F</sub> 0.81 for diester and 0.50 for monoester). The oil is dissolved in \*benzene (*ca* 25mL) and extracted with ethane-1,2-diol (25mL, 10x). After ten washings, a small sample of the \*benzene layer is washed twice with H<sub>2</sub>O to remove the diol and showed that it is pure bis-[4-(1,1,3,3-tetramethylbutyl)-phenyl)phosphoric acid by TLC, i.e. no monophosphate. To form the Ca salt the oil is dissolved in MeOH and to it is added the equivalent amount of CaCl<sub>2</sub> together with aq NaOH to keep the pH >10. The resulting white ppte is collected washed alternately with 3 batches of H<sub>2</sub>O and MeOH and dried in a vacuum oven at 50°. [*J* Inorg Nucl Chem **40** 1483 1978.]

2,4-Bis-(p-tolylthio)-1,3, $2\lambda^5$ , $4\lambda^5$ -dithiadiphosphetane-2,4-dithione (Heimgartner's reagent) [114234-09-2] M 436.6, m 175-176°. Recrystallise from toluene (light yellow solid), wash with Et<sub>2</sub>O and dry in a vacuum. [Helv Chim Acta 70 1001 1987.]

*N*, *O*-Bis-(trimethylsilyl)acetamide (BSA) [10416-59-8] M 203.4, b 71-73°/35mm, d 0.836, 1.4150. Fractionate through a spinning band column and collect liquid b 71-73°/35mm, and not higher because the main impurity MeCONHSiMe<sub>3</sub> distills at b 105-107°/35mm. Used for derivatising alcohols and sugars [Klebe et al. J Am Chem Soc 88 3390 1966, see Carbohydr Res 241 209 1993 and 237 313 1992]. It is FLAMMABLE and TOXIC.

**Bis-(trimethylsilyl)acetylene** [14630-40-1] **M 170.4, m 26°, b 134-136°/atm.** Dissolve in pet ether, wash with ice-cold dilute HCl. The pet ether extract is dried (MgSO<sub>4</sub>), evaporated and fractionated at atmospheric pressure. [J Organomet Chem 37 45 1972.]

**Bis-(trimethylsilyl) sulfide (hexamethyldisilathiane)** [3385-94-2] **M 178.5, b 65-67°/16mm, 162.5-163.5°/750mm corr, 164°/760mm, d 0.85, n 1.4598.** Dissolve in pet ether (b ca 40°), remove solvent and distilled. Redistilled under atmospheric pressure of dry N<sub>2</sub>. It is collected as a colourless liquid which solidifies to a white solid in Dry-ice. On standing for several days it turns yellow possibly due to liberation of sulfur. Store below 4° under dry N<sub>2</sub>. [J Chem Soc 3077 1950.]

**Bis-(triphenylphosphine)nickel(II)** chloride [14264-16-5] M 654.2, m 225°(dec). Wash with glacial AcOH and dry in vac over  $H_2SO_4$  and KOH until AcOH is removed. [J Chem Soc 719 1958.]

**Boric acid** (boracic acid) [10043-35-3] M 61.8, m 171°,  $pK^{25}$  9.23. Crystd three times from H<sub>2</sub>O (3mL/g) between 100° and 0°, after filtering through sintered glass. Dried to constant weight over metaboric acid in a desiccator. It is steam volatile. After 2 recrystns of ACS grade it had Ag at 0.2 ppm.

**9-Borabicyclo[3.3.1]nonane** (**9BBN**) [monomer 280-64-8] [dimer 21205-91-4 or 70658-61-6] [1:1 coordination compound with tetrahydrofuran 76422-63-4] M 122.0 (monomer), 244.0 (dimer), m 141-143° (monomer), 150-152°, 154-155° (dimer), b 195°/12mm. Available as the solid dimer or in tetrahydrofuran soln. The solid is relatively stable and can be purified by distn in a vacuum (as dimer) and by recrystn from tetrahydrofuran (solubility at room temp is 9.5%, 0.78M), filter solid under N<sub>2</sub> wash with dry pentane and dry *in vacuo* at *ca* 100°. The solid is a dimer (IR 1567cm<sup>-1</sup>), stable in air (for *ca* 2 months), and can be heated for 24h at 200° in an inert atmosphere without loss of hydride activity. It is a dimer in tetrahydrofuran soln also (IR 1567cm<sup>-1</sup>). It is sensitive to H<sub>2</sub>O and air (O<sub>2</sub>) in soln. Concentration in soln can be determined by reaction with MeOH and measuring the vol of H<sub>2</sub> liberated, or it can be oxidised to *cis*-cyclooctane-1,5-diol (m 73.5-74.5°). [IR: J Am Chem Soc **90** 5280 1968, **96** 7765 1974; J Org Chem **41** 1778 1976, **46** 3978 1981.]

Borane pyridine complex [110-51-0] M 92.9, m 8-10°, 10-11°, b 86°/7mm, 100-101°/12mm,  $d_4^{20}$  0.785. Dissolve in Et<sub>2</sub>O and wash with H<sub>2</sub>O in which it is insol. Evap Et<sub>2</sub>O and distil

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(gives better than 99.8% purity). Its vap pressure is less than 0.1mm at room temp. [J Am Chem Soc 77 1506 1955.]

Borane triethylamine complex [1722-26-5] M 115.0, b 76°/4mm, 97.0°/12mm,  $d_4^{20}$  0.78. Distil in a vacuum using a 60cm glass helices packed column. [J Am Chem Soc 64 325 1942, 84 3407 1962; Tetrahedron Lett 4703 1968.]

Borane trimethylamine complex [75-22-9] M 73.0, m 94-94.5°, b 171°/atm. Sublimed using equipment described in J Am Chem Soc 59 780 1937. Its vapour pressure is 86mm at 100°. Colourless hexagonal crystals varying from needles to short lumps, slightly soluble in H<sub>2</sub>O (1.48% at 30°), EtOH (1%), hexane (0.74%) but very soluble in Et<sub>2</sub>O,  ${}^{*}C_{6}H_{6}$  and AcOH. Stable at 125°. [J Am Chem Soc 59 780 1939, 104 325 1942.]

**Boron trichloride (trichloroborane)** [10294-34-5] M 117.2, b 0°/476mm. Purified (from chlorine) by passage through two mercury-filled bubblers, then fractionally distd under vacuum. In a more extensive purification the nitrobenzene addition compound is formed by passage of the gas over nitrobenzene in a vacuum system at 10°. Volatile impurities are removed from the crystalline yellow solid by pumping at -20°, and the BCl<sub>3</sub> is recovered by warming the addition compound at 50°. Passage through a trap at -78° removes entrained nitrobenzene; the BCl<sub>3</sub> finally condensing in a trap at -112° [Brown and Holmes J Am Chem Soc 78 2173 1956]. Also purified by condensing into a trap cooled in acetone/Dry-ice, where it was pumped for 15min to remove volatile impurities. It was then warmed, recondensed and again pumped.

**Boron trifluoride** [7637-07-2] **M 67.8, b -101°/760mm.** The usual impurities - bromine, BF<sub>5</sub>, HF and non-volatile fluorides - are readily separated by distn. Brown and Johannesen [J Am Chem Soc 72 2934 1950] passed BF<sub>3</sub> into benzonitrile at 0° until the latter was satd. Evacuation to 10<sup>-5</sup>mm then removed all traces of SiF<sub>4</sub> and other gaseous impurities. [A small amount of the BF<sub>3</sub>-benzonitrile addition compound sublimed and was collected in a U-tube cooled to -80°]. Pressure was raised to 20mm by admitting dry air, and the flask containing the BF<sub>3</sub> addition compound was warmed with hot water. The BF<sub>3</sub> evolved was passed through a -80° trap (to condense any benzonitrile) into a tube cooled in liquid air. The addition compound with anisole can also be used. For drying, BF<sub>3</sub> can be passed through H<sub>2</sub>SO<sub>4</sub> saturated with boric oxide. Fumes in moist air. [Commercially available as a 1.3M soln in MeOH or PrOH.]

**Boron trifluoride diethyl etherate** [109-63-7] M 141.9, b 67°/43mm, b 126°/760mm, d 1.154, n 1.340. Treated with a small quantity of diethyl ether (to remove an excess of this component), and then distd under reduced pressure, from CaH<sub>2</sub>. Fumes in moist air. TOXIC.

**Bromine** [7726-95-6] M 159.8, b 59°, d 3.102, n 1.661. Refluxed with solid KBr and distd, dried by shaking with an equal volume of conc H<sub>2</sub>SO<sub>4</sub>, then distd. The H<sub>2</sub>SO<sub>4</sub> treatment can be replaced by direct distn from BaO or P<sub>2</sub>O<sub>5</sub> A more extensive purification [Hildenbrand et al. *J Am Chem Soc* 80 4129 1958] is to reflux about 1L of bromine for 1h with a mixture of 16g of CrO<sub>3</sub> in 200mL of conc H<sub>2</sub>SO<sub>4</sub> (to remove organic material). The bromine is distd into a clean, dry, glass-stoppered bottle, and chlorine is removed by dissolving *ca* 25g of freshly fused CsBr in 500mL of the bromine and standing overnight. To remove HBr and water, the bromine was then distd back and forth through a train containing alternate tubes of MgO and P<sub>2</sub>O<sub>5</sub>. HIGHLY TOXIC.

Bromine pentafluoride [7789-30-2] M 174.9, m -60.5°, b 41.3°, d<sup>25</sup> 2.466. Purified via its KF complex, as described for chlorine trifluoride. HIGHLY TOXIC.

**2-Bromoallyltrimethylsilane** [81790-10-5] **M 193.2, b 64-66°/10mm, 82-85°/58-60mm, d\_4^{20} <b>1.13.** Fractionally distd through an efficient column. It is **flammable.** [J Am Chem Soc **104** 3733 6879 1982.]

**2-Bromo-1,3,2-benzodioxaborole** [51901-85-0] **M 198.8, m 47°, 51-53°, b 76°/9mm.** Keep at 20°/15mm for some time and then fractionally distil. [J Chem Soc 1529 1959.]

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*IR(endo,anti)*-3-Bromocamphor-8-sulfonic acid ammonium salt [55870-50-3] M 328.2, m 284-285°(dec),  $[\alpha]_D^{25}$ +84.8° (c 4, H<sub>2</sub>O). Passage of a hot aqueous soln through an alumina column removed water-soluble coloured impurities which remained on the column when the ammonium salt was eluted with hot water. The salt was crystd from water and dried over CaCl<sub>2</sub> [Craddock and Jones *J Am Chem Soc* 84 1098 1962; Kauffmann *J Prakt Chem* 33 295 1966].

**Bromopyrogallol Red** [16574-43-9] M 576.2, ε 5.45 x 10<sup>4</sup> at 538nm (water pH 5.6-7.5). See Bromopyrogallol Red (5,5'-dibromopyrogallolsulfonephthalein) on p. 141 in Chapter 4.

**Bromosulfalein** (phenoltetrabromophthalein 3',3'-disulfonic acid disodium salt) [71-67-0]M 838.0. Purified by TLC on silica Gel G (Merck 250µ particle size) in two solvent systems (BuOH-AcOH-H<sub>2</sub>O 30:7.5:12.5 v/v; and BuOH-propionic acid-H<sub>2</sub>O 30:20:7.5 v/v). When the solvent reached a height of 10cm the plate was removed, dried in air and developed with NH<sub>3</sub> vapour giving blue coloured spots. Also the dye was chromatographed on MN Silica Gel with *t*-BuOH-H<sub>2</sub>O-*n*-BuOH (32:10:5 v/v and visualised with a dilute KOH (or NaOH if the Na salt is required) spray. The product corresponding to bromosulfalein was scraped off and eluted with H<sub>2</sub>O, filtered and evap to dryness in a vacuum. It was dissolved in H<sub>2</sub>O and filtered through Sephadex G-25 and evaporated to dryness. [UV and IR identification: *J Pharm Sci* 57 819 1968; NMR: Chem Pharm Bull Jpn 20 581 1972; Anal Biochem 83 75 1977.]

Bromtrimethylsilane (trimethylbromosilane, trimethylsilyl bromide) [2857-97-8] M 153.1, m -43.5° to -43.2°; b 40.5°/200mm, 77.3°/735mm, 79°/744mm, 79.8-79.9°/754mm,  $d_4^{20}$ 1.1805,  $d_4^{20}$  1.190,  $n_D^{20}$  1.422. Purified by repeated fractional distillation and stored in sealed ampoules in the dark. [*J Am Chem Soc* 75 1583 1953.] Also fractionally distd through a 15 plate column (0.8 x 32cm packed with 1/16in single turn helices from Pt-Ir wire). [*J Am Chem Soc* 68 1161 1946; 70 433 1948.]

tert-Butyldiphenylchlorosilane (TBDPSCl, tert-butylchlorodiphenylsilane) [58479-61-1] M 274.9, b 90%/0.015mm, d 1.057, n 1.568. Purified by repeated fractional distn. It is soluble in DMF and pentane [Hanessian and Lavalee Can J Chem 53 2975 1975; Robl et al. J Med Chem 34 2804 1991].

n-Butylmercuric chloride [543-63-5] M 293.1, m 130°. Crystd from EtOH.

**n-Butylphenyl n-butylphosphonate** [36411-99-1] **M 270.3.** Crystd three times from hexane as its compound with uranyl nitrate. See *tri-n-butyl phosphate* below.

*tert*-Butyldimethylsilyl chloride (TBDMSCl) [18162-48-6] M 150.7, m 87-89°, 92.5°, b 125°/760mm. Fractionally distd at atmospheric pressure. [J Am Chem Soc 76 1030 1954; 94 6190 1972.]

*p-tert*-Butylphenyl diphenyl phosphate [981-40-8] M 382.4, b 261°/6mm,  $n^{25}$  1.5522. Purified by vacuum distn, and percolation through an alumina column, followed by passage through a packed column maintained at 150° to remove residual traces of volatile materials in a counter-current stream of N<sub>2</sub> at reduced pressure [Dobry and Keller J Phys Chem 61 1448 1957].

*n*-Butylstannoic acid [PhSn(OH)<sub>3</sub>, trihydroxy-*n*-butylstannane] [22719-01-3] M 208.8. Purified by adding excess KOH in CHCl<sub>3</sub> to remove *n*-BuSn(OH)Cl<sub>2</sub> and *n*-BuSn(OH)<sub>2</sub>Cl, and isolated by acidification [Holmes et al. J Am Chem Soc 109 1408 1987].

**Cacodylic acid** (dimethylarsinic acid) [75-60-5] M 138.0, m 195-196°, pK<sup>25</sup> 6.15 [Me<sub>2</sub>As(O)OH]. Crystd from warm EtOH (3mL/g) by cooling and filtering. Dried in vacuum desiccator over CaCl<sub>2</sub>. Has also been twice recrystd from propan-2-ol. [Koller and Hawkridge J Am Chem Soc 107 7412 1985.]

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Cadion [1-(4-nitrophenyl)-3-(4-phenylazophenyl)-triazene] [5392-67-6] M 346, m 198°. Commercial cadion is purified by recrystn from 95% EtOH and dried. It is stable in 0.2 N KOH (in 20% aqueous EtOH) at 25°. It is a sensitive reagent for Cd, and the Cd complex has  $\lambda$ max (EtOH) 475nm. [Aust Chem Inst J Proc 4 26 1937; Anal Chim Acta 19 377 1958.]

Cadmium [7440-43-9] M 112.4, m 321.1°, b 767°. Oxide has been removed by filtering the molten metal, under vacuum through quartz wool.

Cadmium acetate  $(2H_2O)$  [5743-04-4] M 230.5, m 255°(anhydr), d 2.01 (hydr), 2.34 (anhydr),  $pK_1^{25}9.7$ ,  $pK_2^{25}\sim11.0$  (for Cd<sup>2+</sup>). Crystd twice from anhydrous acetic acid and dried under vacuum for 24h at 100°.

**Cadmium bromide** (4H<sub>2</sub>O) [13464-92-1 (4H<sub>2</sub>O); 7789-42-6 (anhydr)] M 344.2, m 566°, b 963, d 5.19°. Crystd from water (0.6mL/g) between 100° and 0°, and dried at 110°. Forms monohydrate below 36° and the 4H<sub>2</sub>O above 36°.

Cadmium chloride [10108-64-2] M 183.3, m 568°, b 960°, d 4.06. Crystd from water (1mL/g) by addition of EtOH and cooling.

Cadmium fluoride [7790-79-6] M 150.4, m >1000°, b 1748°, d 6.35. Crystd by dissolving in water at room temperature (25mL/g) and heating to 60°.

Cadmium iodide [7790-80-9] M 366.2, m 388°, b 787°, d 5.66. Crystd from ethanol (2mL/g) by partial evaporation.

**Cadmium ionophore I** [N,N,N',N'-tetramethyl-3,6-dioxooctanedi-(thioamide)] [73487-00-0]M 432.7, m 35-36°. Wash well with pet ether, then several times with 2N HCl (if it has a slight odour of pyridine) then H<sub>2</sub>O and dry in a vacuum over H<sub>2</sub>SO<sub>4</sub>. It is a polar selectrophore for Cd. [Helv Chim Acta 63 217 1980.]

Cadmium lactate [16039-55-7] M 290.6. Crystd from water (10mL/g) by partial evapn in a desiccator.

Cadmium nitrate  $(4H_2O)$  [10022-68-1] M 308.5, m 59.5°. Crystd from water (0.5mL/g) by cooling in ice-salt.

Cadmium potassium iodide [13601-63-3] M 532.2. Crystd from ethanol by partial evapn.

Cadmium salicylate [19010-79-8] M 248.5, 242°(dec). Crystd from distd H<sub>2</sub>O by evapn in a desiccator.

**Cadmium sulfate** [7790-84-3 (for  $3CdSO_4 8H_2O$ ); 10124-36-4 (anhydr)] **M 208.4** (anhydr), 769.5 (hydr). Crystd from distd water by partial evapn in a desiccator. On heating gives monohydrate at 80°.

Calcein sodium salt [2',7'-bis-{N, N-di(carboxymethyl)aminomethyl}fluorescein Na salt, Fluorexon, Fluorescein Complexon] [1461-15-0] M 666.5,  $pK_{Est(1)} \sim 1.9$ ,  $pK_{Est(2)} \sim 2.5$ ,  $pK_{Est(3)} \sim 8.0$ ,  $pK_{Est(4)} \sim 10.5$  (all for N-CH<sub>2</sub>COOH), and  $pK_{Est(5)} \sim 3.5$  (for benzoic COOH). Dissolve in distilled H<sub>2</sub>O and acidify with dilute HCl to pH 3.5. Filter off the solid acid and wash well with H<sub>2</sub>O. Redissolve *ca* 10g in 300mL H<sub>2</sub>O containing 12g of NaOAc. Ppte again by adding HCl, filter and wash with H<sub>2</sub>O. Add the solid to 200mL of EtOH stir for 1h and filter. Repeat the EtOH wash and dry the bright yellow solid in a vacuum. This acid decomposes on heating at *ca* 180°. See below for the prepn of the Na salt. [Anal Chem 28 882 1956].

Dissolve in H<sub>2</sub>O and acidify with 3N HCl to pH 3.5. Collect the solid and wash with H<sub>2</sub>O. The air-dried ppte is extracted with 70% aqueous EtOH, filtered hot and cooled slowly. Fine yellow needles of the acid crystallise out, are filtered and dissolved in the minimum quantity of 0.01N NaOH and reppted with N HCl to pH 3.5. It is then recrystd from 70% aqueous EtOH (3x). The final product (acid) is dried at 80° in a vacuum for 24h, m >300°dec. It contains one mol of water per mol of acid ( $C_{30}H_{36}N_4O_{13}.H_2O$ ). The product is pure as revealed

by electrophoresis at pH 5.6 and 8.6, and by TLC in *i*-BuOH-*i*-PrOH-AcOH-H<sub>2</sub>O (60:60:5:5 by vol) or *i*-PrOH or pH 8.0 borate buffer. [Wallach et al. Anal Chem 31 456 1959.]

The Na salt is prepared by dissolving the in  $H_2O$  containing 2 mols of NaOH per mol of acid reagent and lyophilising. It complexes with Ca and Mg ions.

**Calcium** [7440-70-2] **M 40.1, m 845°.** Cleaned by washing with ether to remove adhering paraffin, filed in an argon-filled glove box, and washed with ethanol containing 2% of conc HCl. Then washed with dry ethanol, dried in a vac and stored under pure argon [Addison, Coldrey and Halstead, *J Chem Soc* 3868 1962].

Calcium acetate monohydrate [5743-26-0 ( $H_2O$ ), 62-54-4 ( $xH_2O$ )] M 176.2 ( $H_2O$ ), m 150° (loses  $H_2O$ ),  $pK^{25}$  12.7 (for Ca<sub>2</sub><sup>+</sup>). Crystd from water (3mL/g) by partial evapn in a desiccator.

Calcium benzoate (3H<sub>2</sub>O) [2090-05-3] M 336.4. Crystd from water (10m/g) between 90° and 0°.

**Calcium bromide** (H<sub>2</sub>O) [62648-72-0; 71626-99-8  $(xH_2O)$ ; 7789-41-5 (anhydr)] M 217.9, d 3.35. Crystd from EtOH or Me<sub>2</sub>CO. It loses H2O on heating and is anhydrous at 750° then it loses Br. Deliquescent.

Calcium butyrate [5743-36-2] M 248.2. Crystd from water (5mL/g) by partial evapn in a desiccator.

Calcium carbamate [543-88-4] M 160.1. Crystd from aqueous ethanol.

**Calcium chloride (anhydrous)** [10043-52-4] **M 111.0, m 772°, b >1600°, d\_4^{15} 2.15.** Available as fused granules or cubic crystals. It is very hygroscopic. Very soluble in H<sub>2</sub>O (exothermic), and EtOH. Store in a tightly closed container.

**Calcium chloride**  $(2H_2O)$  [10035-04-8] M 147.0, m 175°(dehydr), 772°(dec). Crystd from ethanol, and is hygroscopic. Loses H<sub>2</sub>O at 200° so it can be dried at high temperatures to dehydrate. *Hexahydrate* [7774-34-7] has m 30° and d 1.67.

Calcium dithionite [13812-88-9] M 168.2, m dec on heating. Crystd from water, or water followed by acetone and dried in air at room temperature.

Calcium D-gluconate monohydrate [299-28-5] M 448.4, m dec on heating,  $\{\alpha\}_{546}^{20} + 11.0^{\circ}$ ,  $[\alpha]_D^{20} + 9.0^{\circ}$  (c 1.2, H<sub>2</sub>O). It is sol in H<sub>2</sub>O (3.5g in 100g at 25°). Dissolve in H<sub>2</sub>O, filter and ppte by adding MeOH. Filter off solid and dry in a vacuum at 85°. Alternatively, dissolve in H<sub>2</sub>O, filter (from insol inorganic Ca) and evaporate to dryness under vacuum at 85°. [J Am Pharm Assoc 41 366 1952.]

Calcium D-heptagluconate dihydrate [17140-60-2] M 526.4,  $[\alpha]_{546}^{20}$  +5.2°,  $[\alpha]_D^{20}$  +4.4° (c 5, H<sub>2</sub>O). Purified same as calcium D-gluconate.

**Calcium formate** [544-17-2] **M 130.1, m dec on heating, d 2.01.** Crystd from water (5mL/g) by partial evaporation in a desiccator.

**Calcium hexacyanoferrate** (II)  $(11H_2O)$  [13821-08-4] M 490.3. Recryst three times from conductivity H<sub>2</sub>O and air dried to constant weight over partially dehydrated salt. [*Trans Faraday Soc* 45 855 1949.] Alternatively the Ca salt can be purified by pptn with absolute EtOH in the cold (to avoid oxidation) from an air-free saturated aqueous soln. The pure lemon yellow crystals are centrifuged, dried in a vacuum desiccator first over dry charcoal for 24h, then over partly dehydrated salt and stored in a dark glass stoppered bottle. No deterioration occurred after 18 months. No trace of Na, K or NH<sub>4</sub> ions could be detected in the salt from the residue after decomposition of the salt with conc H<sub>2</sub>SO<sub>4</sub>. Analyses indicate 11mols of H<sub>2</sub>O per mol of salt. The solubility in H<sub>2</sub>O is 36.45g (24.9°) and 64.7g (44.7°) per 100g of solution. [J Chem Soc 50 1926.]

Calcium hydroxide [1305-62-0] M 74.1, m loses  $H_2O$  on heating,  $pK^{25}$  12.7 (for Ca<sup>2+</sup>). Heat analytical grade calcium carbonate at 1000° during 1h. Allow the resulting oxide to cool and add slowly to

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water. Heat the suspension to boiling, cool and filter through a sintered glass funnel of medium porosity (to remove soluble alkaline impurities). Dry the solid at 110° and crush to a uniformly fine powder.

Calcium iodate [7789-80-2  $(H_2O)$ ] M 389.9, m >540°, pK<sup>25</sup> 0.79 (for HIO<sub>3</sub>). Crystd from water (100mL/g).

**Calcium iodide**  $(xH_2O)$  [71626-98-7  $(xH_2O)$ ; 10102-68-8 (anhydr)] M 293.9 (for 4H<sub>2</sub>O), m 740°, b 1100°. Dissolved in acetone, which was then diluted and evaporated. This drying process was repeated twice, then the CaI<sub>2</sub> was crystd from acetone-diethyl ether and stored over P<sub>2</sub>O<sub>5</sub>. Very hygroscopic when anhydrous and is light sensitive [Cremlyn et al. J Chem Soc 528 1958]. Hexahydrate has m 42°.

**Calcium ionophore I (ETH 1001)** [58801-34-6] **M 685.0.** This is a neutral Ca selectophore. It can be purified by thick layer (2mm) chromatography (Kieselgel  $F_{245}$ ) and eluted with Me<sub>2</sub>CO-CHCl<sub>3</sub> (2:1). [Helv Chim Acta 56 1780 1973.]

**Calcium ionophore II (ETH 129)** [74267-27-9] **M 460.7, m 153-154°.** Recrystd from Me<sub>2</sub>CO. It forms 1:2 and 1:3 metal/ligand complexes with Mg<sup>2+</sup> and Ca<sup>2+</sup> ions respectively, and induces selectivity in membranes for Ca<sup>2+</sup> over Mg<sup>2+</sup> by a factor of  $ca \ 10^4$ . [Helv Chim Acta 63 191 1980.]

**Calcium ionophore III** [A23187 calcimycin] [52665-69-7] M 523.6, m 181-182°,  $[\alpha]_D^{25}$ -56.0° (c 1, CHCl<sub>3</sub>). Recrystallises from Me<sub>2</sub>CO as colourless needles. Protect from light and moisture, store in a refrigerator. Soluble in Me<sub>2</sub>SO or EtOH and can be stored for 3 months without loss of activity. Mg and Ca salts are soluble in organic solvents and cross biological membranes. It has a pKa of 6.9 in 90% Me<sub>2</sub>SO. The Ca complex cryst from 50% EtOH as colourless prisms. *Highly* **TOXIC** [Ann Rev Biochem 45 501 1976; J Am Chem Soc 96 1932 1974, J Antibiotics 29 424 1976.]

Calcium isobutyrate [533-90-4] M 248.2. Crystd from water (3mL/g) by partial evapn in a desiccator.

Calcium lactate (5H<sub>2</sub>O) [814-80-2] M 308.3, m anhydr at 120°. Crystd from warm water (10mL/g) by cooling to 0°.

**Calcium nitrate (4H<sub>2</sub>O)** [13477-34-4] M 236.1, m 45°(dehydr), 560°(anhydr). Crystd four times from water (0.4mL/g) by cooling in a CaCl<sub>2</sub>-ice freezing mixture. The tetrahydrate was dried over conc H<sub>2</sub>SO<sub>4</sub> and stored over P<sub>2</sub>O<sub>5</sub>, to give the anhydrous salt. It is deliquescent. After 3 recrystns of ACS grade it had Co, Fe, Mg, Sr and Zn at 0.2, 1. 0, 0.02, 10 and 0.02 ppm resp.

**Calcium nitrite** (2H<sub>2</sub>O) [13780-06-8 (30% w/w aq soln)] M 150.1(hydr), m dec on heating, d 2.22. Crystd from hot water (1.4mL/g) by adding ethanol and cooling to give the hydrate. It is deliquescent.

(+)-Calcium pantothenate (H<sub>2</sub>O) (D(+)- 137-08-6; 63409-48-3] M 476.5. See R(+)-pantothenic acid calcium salt on p. 555 in Chapter 6.

**Calcium permanganate**  $(4H_2O)$  [10118-76-0 (anhydr)] M 350.0 (for  $4H_2O$ ). Crystd from water (3.3mL/g) by partial evapn in a desiccator. It is deliquescent.

Calcium propionate [4075-81-4] M 186.2, m dec on heating. Crystd from water (2mL/g) by partial evapn in a desiccator.

Calcium salicylate (2H<sub>2</sub>O) [824-35-1] M 350.4. Crystd from water (3mL/g) between 90° and 0°.

**Calcium sulfate dihydrate** [10101-41-4] **M 172.1, m 150(dec), d 2.32.** Loses only part of its  $H_2O$  at 100-150° (see below). Soluble in  $H_2O$  and very slowly soluble in glycerol. Insoluble in most organic solvents.

**Calcium sulfate hemihydrate** [10034-76-1] **M 145.2.** Sol in H<sub>2</sub>O (0.2 parts/100 at 18.75°). Completely dehydrated >650°. Dry below 300° to give a solid with estimated pore size ca 38% of vol. Anhydrous CaSO<sub>4</sub> has high affinity for H<sub>2</sub>O and will absorb 6.6% of its weight of H<sub>2</sub>O to form the hemihydrate (gypsum). It sets to a hard mass with H<sub>2</sub>O, hence should be kept in a tightly sealed container.

Calcium thiosulfate [10124-41-1] M 152.2, m 43-49°,  $pK_1^{25}$  0.6,  $pK_2^{25}$  1.74 (for  $H_2S_2O_3$ ). Recrystd from water below 60° in a N<sub>2</sub> atmosphere, followed by drying with EtOH and Et<sub>2</sub>O. Stored in a refrigerator. [Pethybridge and Taba J Chem Soc, Faraday Trans 1 78 1331 1982.]

(4-Carbamylphenylarsylenedithio)diacetic acid [531-72-6] M 345.1, pK<sub>Est</sub>~3.5. Crystd from MeOH or EtOH.

**Carbonate ionophore I [ETH 6010] (heptyl 4-trifluoroacetylbenzoate)** [129476-47-7] M **316.3, b 170°/0.02 Torr, d 0.909.** Purified by flash chromatography (2g of reagent with 30g of Silica Gel 60) and eluted with EtOAc/hexane (1:19). The fractions that absorbed at 260nm were pooled, evapd and dried at room temp (10.3 Torr). The oily residue was distd in a bubbled-tube apparatus (170°/0.02 Torr). Its IR (CHCl<sub>3</sub>) had peaks at 1720, 1280, 940cm<sup>-1</sup> and its sol in tetrahydrofuran is 50mg/0.5mL. It is a lipophilic neutral ionophore selective for carbonate as well as being an optical humidity sensor. [Anal Chim Acta 233 41 1990.]

**Carbon dioxide** [124-38-9] M 44.0, sublimes at -78.5°,  $pK_1^{25}6.35$ ,  $pK_2^{25}10.33$  (for H<sub>2</sub>CO<sub>3</sub>). Passed over CuO wire at 800° to oxidise CO and other reducing impurities (such as H<sub>2</sub>), then over copper dispersed on Kieselguhr at 180° to remove oxygen. Drying at -78° removed water vapour. Final purification was by vacuum distn at liquid nitrogen temperature to remove non-condensable gases [Anderson, Best and Dominey J Chem Soc 3498 1962]. Sulfur dioxide can be removed at 450° using silver wool combined with a plug of platinised quartz wool. Halogens are removed by using Mg, Zn or Cu, heated to 450°.

Carbon disulfide, see entry on p. 156 in Chapter 4.

**Carbon monoxide** [630-08-0] **M 28.0, b -191.5°.** Iron carbonyl is a likely impurity in CO stored under pressure in steel tanks. It can be decomposed by passage of the gas through a hot porcelain tube at 350-400°. Passage through alkaline pyrogallol soln removes oxygen (and CO<sub>2</sub>). Removal of CO<sub>2</sub> and water are effected by passage through soda-lime followed by Mg(ClO<sub>4</sub>)<sub>2</sub>. Carbon monoxide can be condensed and distd at -195°. **HIGHLY POISONOUS gas.** 

**Carbonyl bromide** [593-95-3] **M 187.8, b 64.5°/760mm.** Purified by distn from Hg and from powdered Sb to remove free bromine, then vacuum distd to remove volatile SO<sub>2</sub> (the major impurity) [Carpenter et al. J Chem Soc, Faraday Trans 2 384 1977]. **TOXIC** 

**Carbonyl sulfide** [463-58-1] M 60.1, m -138°, b -47.5°, -50°. Purified by scrubbing through three consecutive fritted washing flasks containing conc NaOH at 0° (to remove HCN), and then through conc H<sub>2</sub>SO<sub>4</sub> (to remove CS<sub>2</sub>) followed by a mixture of NaN<sub>3</sub> and NaOH solution; or passed through traps containing satd aq lead acetate, then through a column of anhydrous CaSO<sub>4</sub>. Then freeze-pumped repeatedly and distd through a trap packed with glass wool and cooled to -130° (using an *n*-pentane slurry). It liquefies at 0°/12.5mm. The gas is stored over conc H<sub>2</sub>SO<sub>4</sub>. TOXIC

Catecholborane (1,3,2-Benzodioxaborole) [274-07-7] M 119.2, b 50°/50mm, 66°/80mm, 76-77°/100mm, 88°/165mm, d 1.125, n 1.507 (also available as a 1.0M soln in THF). A moisture sensitive flammable liquid which is purified by distn in a vacuum under a N<sub>2</sub> atmosphere and stored under N<sub>2</sub> at 0-4°. It liberates H<sub>2</sub> when added to H<sub>2</sub>O or MeOH. A soln in THF after 25h at 25° has residual hydride of 95% (under N<sub>2</sub>) and 80% (under air) [Brown and Gupta J Am Chem Soc 97 5249 1975].

Celite 545 (diatomaceous earth) [12003-10-0]. Stood overnight in conc HCl after stirring well, then washed with distilled water until neutral and free of chloride ions. Washed with methanol and dried at 50°.

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**Ceric ammonium nitrate** [16774-21-3] M 548.2,  $pK_1^{25}$ -1.15,  $pK_2^{25}$ -0.72,  $pK_3^{25}$  1.68,  $pK_4^{25}$ 2.29 (for aquo Ce<sup>4+</sup>). Ceric ammonium nitrate (125g) is warmed with 100mL of dilute HNO<sub>3</sub> (1:3 v/v) and 40g of NH<sub>4</sub>NO<sub>3</sub> until dissolved, and filtered off on a sintered-glass funnel. The solid which separates on cooling in ice is filtered off on a sintered funnel (at the pump) and air is sucked through the solid for 1-2 h to remove most of the nitric acid. Finally, the solid is dried at 80-85°.

**Cerous acetate** [537-00-8] **M 317.3, pK\_1^{25} 8.1 (9.29), pK\_2^{25} 16.3, pK\_3^{25} 26.0 (for Ce<sup>3+</sup>). Crystd twice from anhydrous acetic acid, then pumped dry under vacuum at 100° for 8h.** 

**Cesium bromide** [7787-69-1] **M 212.8, m 636°, b** ca 1300°, d 4.44. Very soluble in H<sub>2</sub>O, soluble in EtOH but insoluble in Me<sub>2</sub>CO. Dissolve in the minimum volume of H<sub>2</sub>O, filter and ppte by adding Me<sub>2</sub>CO. Filter solid and dry at 100°. Also recrystd from water (0.8mL/g) by partial evaporation in a desiccator.

Cesium carbonate [534-17-8] M 325.8, m 792°(at red heat). Crystd from ethanol (10mL/g) by partial evaporation.

Cesium chloride [7647-17-8] M 168.4, m 645°, b 1303°, d 3.99. Soluble in  $H_2O$  but can be purified by crystn from  $H_2O$  [sol in g per cent: 162.3(0.7°), 182.2(16.2°) and 290(at bp 119.4°)] and dried in high vac. Sol in EtOH and is deliquescent, keep in a tightly closed container. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 951 1963.] For further purification of CsCl, a conc aqueous soln of the practically pure reagent is treated with an equivalent weight if  $I_2$  and  $Cl_2$  bubbled into the soln until pptn of CsCl<sub>2</sub>I ceased. Recrystn yields a salt which is free from other alkali metals. It is then decomposed to pure CsCl on heating. [J Am Chem Soc 52 3886 1930.] Also rerystd from acetone-water, or from water (0.5mL/g) by cooling in CaCl<sub>2</sub>/ice. Dried at 78° under vacuum.

Cesium chromate [56320-90-2] M 381.8,  $pK_1^{25}$  0.74,  $pK_2^{25}$  6.49 (for  $H_2CrO_4$ ). Crystd from water (1.4mL/g) by partial evapn in a desiccator.

Cesium fluoride [13400-13-0] M 151.9, m 703°. Crystd from aqueous soln by adding ethanol.

Cesium iodide [7789-17-5] M 259.8, m 621°, b~1280°, d 4.5. Crystd from warm water (1mL/g) by cooling to -5°.

Cesium nitrate [7789-18-6] M 194.9, m 414°(dec), d 3.65. Crystd from water (0.6mL/g) between 100° and 0°. After 1 crystn of 99.9% grade it had K, Na and Se at 0.8, 0.4 and 0.2 ppm resp.

Cesium oleate [31642-12-3] M 414.4. Crystd from EtOAc, dried in an oven at  $40^{\circ}$  and stored over  $P_2O_5$ .

Cesium perchlorate [13454-84-7] M 232.4,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from water (4mL/g) between 100° and 0°.

**Cesium perfluoro-octanoate** [17125-60-9] **M 546.0.** Recrystd from a butanol-petroleum ether mixture, dried in an oven at  $40^{\circ}$  and stored over  $P_2O_5$  under vacuum.

Cesium sulfate [10294-54-9] M 361.9, m 1005°, d 4.24. Crystd from water (0.5mL/g) by adding ethanol and cooling.

Chloramine-T (*N*-chloro-*p*-toluenesulfonamide sodium salt)  $3H_2O$  [7080-50-4] M 281.7, m 168-170°(dec). Crystd from hot water (2mL/g). Dried in a desiccator over CaCl<sub>2</sub> where it loses water. Protect from sunlight. Used for detection of bromate and halogens, and Co, Cr, Fe, Hg, Mn, Ni and Sb ions.

Chlorazol Sky Blue FF {6,6'-[(3,3'-dimethoxy[1,1'-biphenyl]-4,4'-diyl)bis(azo)bis(4amino-5-hydroxy-1,3-naphthylenedisulfonic acid) tetra-Na salt [2610-05-1] M 996.9, m

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>300°(dec). Freed from other electrolytes by adding aqueous sodium acetate to a boiling soln of the dye in distd water. After standing, the salted-out dye was filtered on a Büchner funnel, the process being repeated several times. Finally, the ppted dye was boiled several times with absolute EtOH to wash out any sodium acetate, then dried (as the sodium salt) at 105°. [McGregor, Peters and Petropolous *Trans Faraday Soc* 58 1045 1962.]

**Chlorine** [7782-50-5] **M 70.9, m -101.5°, b -34.0°, d 2.898.** Passed in succession through aqueous KMnO<sub>4</sub>, dilute H<sub>2</sub>SO<sub>4</sub>, conc H<sub>2</sub>SO<sub>4</sub>, and a drying tower containing Mg(ClO<sub>4</sub>)<sub>2</sub>. Or, bubbled through with water, dried over P<sub>2</sub>O<sub>5</sub> and distd from bulb to bulb in a vac line. **HIGHLY TOXIC.** 

**Chlorine trifluoride** [7790-91-2] **M 92.5, b 12.1°.** Impurities include chloryl fluoride, chlorine dioxide and hydrogen fluoride. Passed first through two U-tubes containing NaF to remove HF, then through a series of traps in which the liquid is fractionally distd. Can be purified *via* the KF complex, KClF<sub>4</sub>, formed by adding excess ClF<sub>3</sub> to solid KF in a stainless steel cylinder in a dry-box and shaking overnight. After pumping out the volatile materials, pure ClF<sub>3</sub> is obtained by heating the bomb to 100-150° and condensing the evolved gas in a -196° trap [Schack, Dubb and Quaglino *Chem Ind (London)* 545 1967]. **HIGHLY TOXIC.** 

Chlorodiphenylphosphine (diphenylphosphinous chloride) [1079-66-9] M 220.6, m 15-16°, b 124-126°/0.6mm, 174°/5mm, 320°/atm, d 1.229, n 1.636. Air sensitive, pale yellow lachrymatory liquid which is purified by careful fractional distn and discarding the lower boiling fraction which contains the main impurity PhPCl<sub>2</sub> (b 48-51°/0.7mm); and checking for tmpurities by NMR. [Weinberg J Org Chem 40 3586 1975; Honer et al. Chem Ber 94 2122 1961.]

4-(Chloromercuri)benzenesulfonic acid monosodium salt [14110-97-5] M 415.2, dec on heating. The free acid is obtained by acidifying an aq soln, filtering off the acid, washing it with H<sub>2</sub>O and recrystallising from hot H<sub>2</sub>O to give a colourless solid which is dried in a vacuum over P<sub>2</sub>O<sub>5</sub> and should give negative Cl<sup>-</sup> ions. The Na salt is made by dissolving in one equivalent of aqueous NaOH and evaporate to dryness. [*Chem Ber* 67 130 1934; *J Am Chem Soc* 76 4331 1954.] HIGHLY TOXIC.

**4-Chloromercuribenzoic acid** [59-85-8] M **357.2, m** >**300°.** Its suspension in water is stirred with enough 1M NaOH to dissolve most of it: a small amount of insoluble matter is removed by centrifugation. The chloromercuribenzoic acid is then ppted by adding 1M HCl and centrifuged off. The pptn is repeated twice. Finally, the ppte is washed three times with distilled water (by centrifuging), then dried in a thin layer under vacuum over  $P_2O_5$  [Boyer J Am Chem Soc **76** 4331 1954].

**Chloromethylphosphonic acid dichloride** [1983-26-2] M 167.4, b 50°/0.5mm, 52-53(59)°/2mm, 63-65°/3mm, 78-79°/10mm, 87-88°/15mm, 102-103°/30mm,  $d_4^{20}$  1.638,  $n_D^{20}$  1.4971. Fractionally distd using a short Claisen column and redistd. The *aniline salt* has m 199-201°. The <sup>31</sup>P NMR has a line at -38±2 ppm from 85% H<sub>3</sub>PO<sub>4</sub>. [Kinnear and Perren J Chem Soc 3437 1952; NMR: J Am Chem Soc 78 5715 1956; J Org Chem 22 462 1957.]

**2-Chloro-2-oxo-1,3,2-dioxaphospholane** [6609-64-9] **M 142.5, m 12-14°, b 89-91°/0.8 mm,**  $d_4^{20}$ **1.549,**  $n_D^{20}$ **1.448.** Should be distd at high vacuum as some polymerisation occurs on distn. It has IR bands at 3012, 2933, 1477, 1366, 1325, 1040, 924 and 858 cm<sup>-1</sup>. In H<sub>2</sub>O at 100° it is hydrolysed to HOCH<sub>2</sub>CH<sub>2</sub>OPO<sub>3</sub>H<sub>2</sub> in 30min [IR: Cox and Westheimer J Am Chem Soc **80** 5441 1958].

**2-Chlorophenyl diphenyl phosphate** [115-85-5] **M 360.7, b 236°/4mm, n<sup>25</sup> 1.5707.** Purified by vacuum distn, percolated through a column of alumina, then passed through a packed column maintained by a countercurrent stream of nitrogen at reduced pressure [Dobry and Keller J Phys Chem **61** 1448 1957].

Chlorosulfonic (chlorosulfuric) acid [7790-94-5] M 116.5, b 151-152°/750mm, d<sub>4</sub> 1.753, n 1.4929, pK -5.9 (aq H<sub>2</sub>SO<sub>4</sub>). Distd in an all-glass apparatus, taking the fraction boiling at 156-158°. Reacts EXPLOSIVELY with water [Cremlyn *Chlorosulfonic acid: A Versatile Reagent*, Royal Society of Chemistry UK, 2002, 308 pp, ISBN 0854044981].

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**Chloro-(2,2':6',2'-terpyridine)platinum (II) chloride (2H<sub>2</sub>O)** [60819-00-3] M 535.3. Recrystd from hot dilute HCl and cooling to give the red dihydrate. The trihydrate crysts slowly from a cold aq soln and is air dried. The red dihydrate can be obtained from the trihydrate by desiccation over conc H<sub>2</sub>SO<sub>4</sub>, by washing with EtOH or by precipitating from a warm aq soln with HCl. The dihydrate is also formed by decomposing the black trihydrate form by heating in water (slowly), or more rapidly with hot 2N HCl. [J Chem Soc 1498 1934.]

**Chloro-tri-isopropyl titanium** [20717-86-6] **M 260.6, m 45-50°, b 61-65°/0.1mm.** Distd under vacuum and sets slowly to a solid on standing. Stock reagents are made by dissolving the warm liquid in pentane, toluene,  $Et_2O$ , THF,  $CH_2Cl_2$ , and can be stored in pure state or in soln under dry N<sub>2</sub> for several months. The reagent is *hygroscopic* and is hydrolysed by H<sub>2</sub>O. [*Chem Ber* **118** 1421 1985.]

Chlorotriphenylsilane (triphenylchlorosilane) [76-86-8] M 294.9, m 90-92°, 91-93°, 94-95°, 97-99°, b 156°/1mm, 161°/0.6mm. Likely impurities are tetraphenylsilane, small amounts of hexaphenyldisiloxane and traces of triphenylsilanol. Purified by distn at 2mm, then crystd from EtOH-free CHCl<sub>3</sub>, and from pet ether (b 30-60°) or hexane by cooling in a Dry-ice/acetone bath. [J Chem Soc 3671 1957; J Am Chem Soc 72 4471 1958, 77 6395 1955, 79 1843 1957.]

Chlorotris(triphenylphosphine) rhodium I (Wilkinson's catalyst) [14694-95-2] M 925.2, m 138°(dec), 140°(dec), 157-158°(dec). Forms dark burgundy crysts from hot EtOH after refluxing for 30min. When the soln is heated for only 5min orange crystals are formed, Heating the orange crystals in EtOH yields red crystals. Crystn from Me<sub>2</sub>CO gives the orange crystals. The two forms have similar IR spectra but X-rays are slighly different. [Osborne et al. J Chem Soc (A) 1711 1966; Osborne and Wilkinson Inorg Synth 10 67 1967; Bennett and Donaldson Inorg Chem 16 655 1977.] Sol in CH<sub>2</sub>Cl<sub>2</sub> ~2% (25°), in toluene 0.2% (25°), and less sol in Me<sub>2</sub>CO, MeOH, BuOH and AcOH, but insol in pet ethers and cyclohexane. It reacts with donor solvents such as pyridine, DMSO and MeCN.

**Chromeazurol S** [1667-99-8] M 539.3,  $\lambda_{max}$  540nm,  $\varepsilon$  7.80 x 10<sup>4</sup> (10M HCl), CI 43825,  $pK_1^{25} < 0$ ,  $pK_2^{25} 2.25$ ,  $pK_3^{25}$  4.88,  $pK_4^{25}$  11.75. Crude phenolic triphenylmethanecarboxysulfonic acid triNa salt (40g) is dissolved in water (250mL) and filtered. Then added conc HCl (50mL) to filtrate, with stirring. Ppte is filtered off, washed with HCl (2M) and dried. Redissolved in water (250mL) and pptn repeated twice more in water bath at 70°. Then dried under vacuum over solid KOH (first) then P<sub>2</sub>O<sub>5</sub> [Martynov et al. *Zh Analyt Khim* 32 519 1977]. It has also been purified by paper chromatography using *n*-butanol, acetic acid and water (7:3:1). First and second spots were extracted. It chelates Al and Be. Used for estimating fluoride.

**Chromic chloride (anhydrous)** [10025-73-7] M 158.4, m 1152°,  $pK_1^{25}$  3.95,  $pK_2^{25}$  5.55,  $pK_3^{25}$  10.5 (for Cr<sup>3+</sup>). Sublimed in a stream of dry HCl. Alternatively, the impure chromic chloride (100g) was added to 1L of 10% aq K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and several millilitres of conc HCl, and the mixture was brought to a gentle boil with constant stirring for 10 min. (This removed a reducing impurity.) The solid was separated, and washed by boiling with successive 1L lots of distilled water until the wash water no longer gave a test for chloride ion, then dried at 110° [Poulsen and Garner J Am Chem Soc 81 2615 1959].

**Chromium (III) acetylacetonate** [21679-31-2] M 349.3, m 212-216°, 216°,  $pK^{25}$  4.0 (see **chromic chloride**). Purified by dissolving 6g in hot  ${}^{*}C_{6}H_{6}$  (20mL) and adding 75mL of pet ether slowly. Cool to room temp then chill on ice, filter off and dry in air to give 2.9g. Also crystallises from EtOH. Sol in heptane,  ${}^{*}C_{6}H_{6}$ , toluene and pentane-2,4-dione at 20-40°. It forms a 1:2 complex with CHCl<sub>3</sub>. [Inorg Synth 5 130 1957; J Am Chem Soc 80 1839 1958.]

**Chromium ammonium sulfate** (12H<sub>2</sub>O) [34275-72-4 (hydr); 13548-43-1 (anhydr)] M 478.4, m 94° loses 9H<sub>2</sub>O then dehydr at 300°, d 1.72. Crystd from a saturated aqueous soln at 55° by cooling slowly with rapid mechanical stirring. The resulting fine crystals were filtered on a Büchner funnel, partly dried on a porous plate, then equilibrated for several months in a vacuum desiccator over crude chromium ammonium sulfate (partially dehydrated by heating at 100° for several hours before use) [Johnson, Hu and Horton J Am Chem Soc 75 3922 1953].

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**Chromium (II) chloride (anhydrous)** [10049-05-5] **M 122.9, m 824°**,  $d_4^{14}$  2.75. Obtained from the dihydrate by heating *in vacuo* at 180°. It is a very *hygroscopic* white powder which dissolves in H<sub>2</sub>O to give a sky blue solution. Stable in dry air but oxidises rapidly in moist air and should be stored in air tight containers. It sublimes at 800° in a current of HCl gas and cooled in the presence of HCl gas. Alternatively it can be washed with air-free Et<sub>2</sub>O and dried at 110-120°. [Inorg Synth 3 150 1950.]

**Chromium hexacarbonyl** [13007-92-6] **M 220.1, m 130°(dec), d 1.77.** Wash with cold EtOH then  $Et_2O$  and allow to dry in air. Alternatively recrystallise from dry  $Et_2O$ . This is best accomplished by placing the hexacarbonyl in a Soxhlet extractor and extracting exhaustively with dry  $Et_2O$ . Pure  $Cr(CO)_6$  is filtered off and dried in air. Completely colourless refracting crystals are obtained by sublimation at 40-50°/<0.5mm in an apparatus where the collecting finger is cooled by Dry Ice and in which there is a wide short bore between the hot and cold sections to prevent clogging by the crystals. Loss of product in the crystn and sublimation is slight. It is important not to overdo the drying as the solid is appreciably volatile and **TOXIC** [vapour pressure is 0.04(8°), 1.0(48°) and 66.5(100°) mm]. Also do not allow the  $Et_2O$  solns to stand too long as a brown deposit is formed which is sensitive to light, and to avoid the possibility of violent decomposition. It sinters at 90°, dec at 130°, and **EXPLODES** at 210°. [Inorg Synth 3 156 1950; J Am Chem Soc 83 2057 1961.]

Chromium potassium sulfate  $(12H_2O)$  [7788-99-0] M 499.4,  $pK_1^{25}0.74$ ,  $pK_2^{25}6.49$  (for  $H_2CrO_4$ , chromic acid). Crystd from hot water (2mL/g) by cooling.

Chromium trioxide (chromic anhydride) [1333-82-0] M 100.0, m 197°, dec at 250° to Cr<sub>2</sub>O<sub>3</sub>, d 2.70 (pK<sub>1</sub><sup>25</sup> 0.74, pK<sub>2</sub><sup>25</sup> 6.49, for H<sub>2</sub>CrO<sub>4</sub>, chromic acid). Red crystals from water (0.5mL/g) between 100° and -5°, or from water/conc HNO<sub>3</sub> (1:5). It separates when potassium or sodium dichromate are dissolved in conc H<sub>2</sub>SO<sub>4</sub>. Dried in a vacuum desiccator over NaOH pellets; hygroscopic, powerful oxidant, can ignite with organic compounds. It is a skin and pulmonary **IRRITANT**. § Commercially available on polymer support. CANCER SUSPECT.

Chromium (III) tris-2,4-pentanedionate [21679-31-2] M 349.3, m 216°, pK<sup>25</sup> 4.0 (see chromic chloride). See chromium (III) acetylacetonate on p. 412.

Chromoionophore I [ETH 5294] [9-diethylamino-5-octadecanoyl-imino-5-H-benzo[a]phenoxazine] [125829-24-5] M 583.9. Purified by flash chromatography (Silica Gel) and eluted with EtOAc. The coloured fractions are pooled, evaporated and recrystd from EtOAc. It is a lipophilic chromoionophore and is a selectophore for K and Ca ions. [Anal Chem 62 738 1990.]

Chromotropic acid (4,5-dihydroxynaphthalene-2,7-disulfonic acid di-Na salt) [5808-22-0 ( $2H_2O$ )] M 400.3, m >300°, pK<sub>1</sub> 0.61(SO<sub>3</sub><sup>-</sup>), pK<sub>2</sub> 0.7(SO<sub>3</sub><sup>-</sup>), pK<sub>3</sub> 5.45(OH), pK<sub>4</sub> 15.5(OH). See disodium 4,5(1,8)-dihydroxynaphthalene-2,7(3,6)-disulfonate ( $2H_2O$ ) on p. 421.

Chromyl chloride [14977-61-8] M 154.9, b 115.7°, d 1.911. Purified by distn under reduced pressure. TOXIC.

Claisen alkali (alkali Claisen). Prepared from KOH (35g) in H<sub>2</sub>O (25mL) and diluted to 100mL with MeOH. STRONGLY CAUSTIC.

Cobalt (II) meso-5.10,15,20-tetraphenylporphine complex [14172-90-8] M 671.7. Brown crystals from Et<sub>2</sub>O or CHCl<sub>3</sub>-MeOH (cf iron chloride complex). Recrystd by extraction (Soxhlet) with  $*C_6H_6$ . Sol in most organic solvents except MeOH and pet ether. [UV, IR: J Am Chem Soc 70 1808 1948; 81 5111 1959.]

Cobaltous acetate  $(4H_2O)$  [6147-53-1] M 249.1,  $pK_1^{25}9.85$  (for Co<sup>2+</sup>). Crystd several times as the tetrahydrate from 50% aqueous acetic acid. Converted to the anhydrous salt by drying at 80%/1mm for 60h.

Cobaltous acetylacetonate [14024-48-7] M 257.2, m 172°. Crystd from acetone.

**Cobaltous ammonium sulfate (6H<sub>2</sub>O)** [13596-46-8] **M 395.5, d 1.90.** Crystd from boiling water (2mL/g) by cooling. Washed with ethanol.

Cobaltous bromide  $(6H_2O)$  [85017-77-2  $(xH_2O)$ ; 7789-43-7 (anhydr)] M 326.9  $(6H_2O)$ , m 47°(dec), b 100°(dec), d 4.9. Crystd from water (1mL/g) by partial evaporation in a desiccator.

**Cobaltous chloride** ( $6H_2O$ ) [7791-13-1 ( $6H_2O$ ); 7646-79-9 (anhydr)] M 237.9, m 87°(dec), d 1.92. A saturated aqueous soln at room temperature was fractionally crystd by standing overnight. The first half of the material that crystd in this way was used in the next crystn. The process was repeated several times, water being removed in a dry-box using air filtered through glass wool and dried over CaCl<sub>2</sub> [Hutchinson J Am Chem Soc 76 1022 1954]. Has also been crystd from dilute aq HCl.

**Cobaltous nitrate** (6H<sub>2</sub>O) [10026-22-9] M 291.0, m ~55(6H<sub>2</sub>O), 100-105°(dec), d 1.88. Crystd from water (1mL/g), or ethanol (1mL/g), by partial evapn. After 3 crystns (H<sub>2</sub>O) it contains: metal(ppm) As (8), Fe (1.2), K (1), Mg (4), Mn (4), Mo (4), Na (0.6), Ni (18), Zn (1.6).

Cobaltous perchlorate ( $6H_2O$ ) [13478-33-6] M 365.9, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from warm water (0.7mL/g) by cooling.

Cobaltous potassium sulfate [13596-22-0] M 329.4. Crystd from water (1mL/g) between 50° and 0°, and dried in a vacuum desiccator over conc H<sub>2</sub>SO<sub>4</sub>.

Cobaltous sulfate  $(7H_2O)$  [10026-24-1 (7H<sub>2</sub>O); 60459-08-7 (xH<sub>2</sub>O); 10124-43-3 (anhydr)] M 281.1, m 41°(dec), d 2.03. Crystd three times from conductivity water (1.3mL/g) between 100° and 0°.

Copper (I) thiophenolate [1192-40-1] M 172.7, m ca 280°,  $pK_1^{25}6.62$  (for PhS<sup>-</sup>). The Cu salt can be extracted from a thimble (Soxhlet) with boiling MeOH. It is a green-brown powder which gives a yellow-green soln in pyridine. Wash with EtOH and dry in a vacuum. It can be ppted from a pyridine soln by addition of H<sub>2</sub>O, collect ppte, wash with EtOH and dry in a vacuum. [Synthesis 662 1974; J Am Chem Soc 79 170 1957; Chem Ber 90 425 1957.]

12-Crown-4 (lithium ionophore V, 1,4,7,10-tetraoxacyclododecane) [294-93-9] M 176.2, m 17°. The distilled crude product had to be crystd from pentane at -20° to remove acyclic material. It is then dried over P<sub>2</sub>O<sub>5</sub>. [Acta Chem Scand 27 3395 1973.]

Cupferon ammonium salt (N-nitroso-N-phenylhydroxylamine ammonium salt) [135-20-6] M 155.2, m 150-155°(dec), 162.5-163.5°, 163-164°,  $pK^{25}$  4.16 (free base). Recrystd twice from EtOH after treatment with Norite and finally once with EtOH. The crystals are washed with diethyl ether and air dried then stored in the dark over solid ammonium carbonate. A standard soln (*ca* 0.05M prepared in airfree H<sub>2</sub>O) is prepared daily from this material for analytical work and is essentially 100% pure. [Anal Chem 26 1747 1954.] It can also be washed with Et<sub>2</sub>O, dried and stored as stated. In a sealed, dark container it can be stored for at least 12 months without deterioration.  $\lambda max 260nm$  (CHCl<sub>3</sub>). [Org Synth Coll Vol I 177 1948; J Am Chem Soc 78 4206 1956.] Possible CARCINOGEN.

Cupric acetate (H<sub>2</sub>O) [6046-93-1 (H<sub>2</sub>O); 142-71-2 (anhydr)] M 199.7, m 115°, 240°(dec), d 1.88,  $pK_1^{25}$  8.0,  $pK_2^{25}$  13.1 (for Cu<sup>2+</sup>). Crystd twice from warm dilute acetic acid solns (5mL/g) by cooling.

Cupric ammonium chloride (2H<sub>2</sub>O) [10534-87-9 (hydr); 15610-76-1 (anhydr)] M 277.5, m 110-120<sup>o</sup>(anhydr) then dec at higher temp, d 2.0. Crystd from weak aqueous HCl (1mL/g).

Cupric benzoate [533-01-7] M 305.8. Crystd from hot water.

**Cupric bromide** [7789-45-9] **M 223.4, m 498°, b 900°, d 4.7.** Crystd twice by dissolving in water (140mL/g), filtering to remove any Cu<sub>2</sub>Br<sub>2</sub>, and concentrating under vac at 30° until crystals appeared. The cupric bromide was then allowed to crystallise by leaving the soln in a vac desiccator containing  $P_2O_5$  [Hope, Otter and Prue J Chem Soc 5226 1960].

**Cupric chloride** [7447-39-4] M 134.4, m 498°, 630°(dec). Crystd from hot dilute aq HCl (0.6mL/g) by cooling in a CaCl<sub>2</sub>-ice bath. Dehydrated by heating on a steam-bath under vacuum. It is deliquescent in moist air but efflorescent in dry air.

Cupric lactate (H<sub>2</sub>O) [814-81-3] M 295.7. The monohydrate crysts from hot H<sub>2</sub>O (3mL/g) on cooling.

**Cupric nitrate** ( $3H_2O$ ) [10031-43-3 ( $3H_2O$ ); 3251-23-8 (anhydr)] M 241.6, m 114°, b 170°(dec), d 2.0. Crystd from weak aqueous HNO<sub>3</sub> (0.5mL/g) by cooling from room temperature. The anhydrous salt can be prepared by dissolving copper metal in a 1:1 mixture of liquid NO<sub>2</sub> and ethyl acetate and purified by sublimation [Evans et al. J Chem Soc, Faraday Trans 1 75 1023 1979]. The hexahydrate dehydr to trihydrate at 26°, and the anhydrous salt sublimes between 150 and 225°, but melts at 255-256° and is deliquescent.

Cupric oleate [1/20-44-1] M 626.5. Crystd from diethyl ether.

Cupric perchlorate (6H<sub>2</sub>O) [10294-46-9 (hydr); 13770-18-8] M 370.5, m 230-240°,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from distilled water. The anhydrous salt is hygroscopic.

Cupric phthalocyanine [147-14-8] M 576.1. Precipitated twice from conc  $H_2SO_4$  by slow dilution with water. Also purified by two or three sublimations at 580° in an argon flow at 300-400Pa.

**Cupric sulfate** [7758-98-7] **M 159.6, m >560°.** After adding 0.02g of KOH to a litre of nearly saturated aq soln, it was left for two weeks, then the ppte was filtered on to a fibreglass filter with pore diameter of 5-15 microns. The filtrate was heated to 90° and allowed to evaporate until some  $CuSO_4.5H_2O$  had crystd. The soln was then filtered hot and cooled rapidly to give crystals which were freed from mother liquor by filtering under suction [Geballe and Giauque *J Am Chem Soc* 74 3513 1952]. Alternatively crystd from water (0.6mL/g) between 100° and 0°.

Cupric trifluoromethylsulfonate (copper II triflate) [34946-82-2] M 361.7,  $pK^{25}$  <-3.0 (for triflic acid). Dissolve in MeCN, add dry Et<sub>2</sub>O until cloudy and cool at -20° in a freezer. The light blue ppte is collected and dried in a vacuum oven at 130°/20mm for 8h. It has  $\lambda$ max 737nm ( $\varepsilon$  22.4M<sup>-1</sup>cm<sup>-1</sup>) in AcOH. [*J Am Chem Soc* 95 330 1973]. It has also been dried in a vessel at 0.1Torr by heating with a Fischer burner [*J Org Chem* 43 3422 1978]. It has been dried at 110-120°/5mm for 1h before use and forms a \*benzene complex which should be handled in a dry box because it is air sensitive [*Chem Pharm Bull Jpn* 28 262 1980; *J Am Chem Soc* 95 330 1973].

Cuprous bromide [7787-70-4] M 143.4, m 497°, b 1345°, d 4.72. Purified as for cuprous iodide but using aqueous NaBr.

**Cuprous bromide dimethylsulfide complex** [54678-23-8] **M 205.6, m** ca 135°(dec). Purified by recrystn in the presence of Me<sub>2</sub>S. A soln of the complex (1.02g) in Me<sub>2</sub>S (5mL) is slowly diluted with hexane (20mL) and the pure colourless prisms of the complex (0.96g) separate and are collected and dried, **m** 124-129°dec. The complex is insoluble in hexane, Et<sub>2</sub>O, Me<sub>2</sub>CO, CHCl<sub>3</sub> and CCl<sub>4</sub>. It dissolves in DMF and DMSO but the soln becomes hot and green indicating dec. It dissolves in \*C<sub>6</sub>H<sub>6</sub>, Et<sub>2</sub>O, MeOH and CHCl<sub>3</sub> if excess of Me<sub>2</sub>S is added a colourless soln is obtained. [*J Org Chem* 40 1460 1975.] Prior to use, the complex was dissolved in Me<sub>2</sub>S and evaporated to dryness in the weighed reaction flask [*J Organomet Chem* 228 321 1983].

**Cuprous chloride** [7758-89-6] **M 99.0, m 430°, b~1400°.** Dissolved in strong HCl, ppted by dilution with water and filtered off. Washed with ethanol and diethyl ether, then dried and stored in a vacuum desiccator [Österlöf Acta Chem Scand 4 375 1950]. Alternatively, to an aq. soln of CuCl<sub>2</sub>.2H<sub>2</sub>O was added, with stirring,

an aqueous soln of anhydrous sodium sulfite. The colourless product was dried at  $80^{\circ}$  for 30min and stored under N<sub>2</sub>. CuCl<sub>2</sub> can be purified by zone-refining [Hall et al. *J Chem Soc, Faraday Trans 1* **79** 243 1983].

**Cuprous cyanide** [544-92-3] **M 89.6, m 474°.** Wash thoroughly with boiling  $H_2O$ , then with EtOH. Dry at 100° to a fine soft powder. [J Chem Soc 79 1943.]

**Cuprous iodide** [7681-65-4] **M 190.5, m 605°, b 1336°, d\_4^{25} 5.63.** It can be freshly prepared by dissolving an appropriate quantity of CuI in boiling saturated aqueous NaI over 30min. Pure CuI is obtained by cooling and diluting the soln with water, followed by filtering and washing sequentially with H<sub>2</sub>O, EtOH, EtOAc and Et<sub>2</sub>O, pentane, then drying *in vacuo* for 24h [Dieter, *J Am Chem Soc* **107** 4679 *1985*]. Alternatively wash with H<sub>2</sub>O then EtOH and finally with Et<sub>2</sub>O containing a little iodine. Traces of H<sub>2</sub>O are best removed first by heating at 110° and then at 400°. Exess of I<sub>2</sub> is removed completely at 400°. It dissolves in Et<sub>2</sub>O if an amine is present to form the amine complex. [*Chem Ind (London)* 1180 *1957*.]

**Cuprous iodide trimethylphosphite** [34836-53-8] M 314.5, m 175-177°, 192-193°. Cuprous iodide dissolves in a  $C_6H_6$  soln containing trimethylphosphite to form the complex. The complex crystallises from  $C_6H_6$  or pet ether. [Chem Ber 38 1171 1905; Bull Chem Soc Jpn 34 1177 1961.]

Cuprous thiocyanate [18223-42-2] M 121.6, pK<sup>25</sup> -1.85 (for HSCN). Purified as for cuprous iodide but using aq NaSCN.

Cyanamide [420-04-2] M 42.0, m 43°, 45°, 46°, b 85-87°/0.5mm,  $pK_1^{20}$  -0.36 (1.1 at 29°),  $pK_2^{20}$  10.27. Purified by placing *ca* 15g in a Soxhlet thimble and extracting exhaustively (2-3h) with two successive portions of Et<sub>2</sub>O (400mL, saturated with H<sub>2</sub>O by shaking before use) containing two drops of 1N acetic acid. Two successive portions of Et<sub>2</sub>O are used so that the NH<sub>2</sub>CN is not heated for too long. Each extract is dried over Na<sub>2</sub>SO<sub>4</sub>(30g), then combined and evaporated under reduced pressure. The NH<sub>2</sub>CN may be stored unchanged at 0° in Et<sub>2</sub>O soln in the presence of a trace of AcOH. Extracts from several runs may be combined and evaporated together. The residue from evaporation of an Et<sub>2</sub>O soln is a colourless viscous oil which sets to a solid, and can be recrystd from a mixture of 2 parts of \*C<sub>6</sub>H<sub>6</sub> and 1 part of Et<sub>2</sub>O. Concentrating an aqueous soln of NH<sub>2</sub>CN at high temps causes **EXPLOSIVE** polymerisation. [Org Synth Coll Vol IV 645 1963; Inorg Synth 3 39 1950; J Org Chem 23 613 1958.] Hygroscopic.

**Cyanogen bromide** [506-68-3] **M 105.9, m 49-51°, b 60-62°/atm.** All operations with this substance should be performed in a very efficient fume cupboard - it is very **POISONOUS** and should be handled in small amounts. Fresh commercial material is satisfactory for nearly all purposes and does not need to be purified. It is a white crystalline solid with a strong cyanide odour. If it is reddish in colour and partly liquid or paste-like then it is too far gone to be purified, and fresh material should be sought. It can be purified by distn using small amounts at a time, and using a short wide-bore condenser because it readily solidifies to a crystalline white solid and may clog the condenser. An appropriate gas mask should be used when transferring the molten solid from one container to another and the operation should be done in an efficient fume cupboard. The melting point (**m** 49-51°) should be measured in a sealed tube. [Org Synth Coll Vol II 150 1948.]

**Cyanogen iodide** [506-78-5] **M 152.9, m 146-147°.** This compound is **POISONOUS** and the precautions for cyanogen bromide (above) apply here. The reagent (ca 5.9g) is dissolved in boiling CHCl<sub>3</sub> (15mL), filtered through a plug of glass wool into a 25mL Erlenmeyer flask. Cool to room temperature for 15min, then place in an ice-salt bath and cool to  $-10^\circ$ . This cooling causes a small aqueous layer to separate as ice. The ice is filtered with the CNI, but melts on the filter and is also removed with the CHCl<sub>3</sub> used as washing liquid. The CNI which is collected on a sintered glass funnel is washed 3x with CHCl<sub>3</sub> (1.5mL at 0°) and freed from last traces of solvent by being placed on a watch glass and exposed to the atmosphere in a good fume cupboard at room temp for 1h to give colourless needles (ca 4.5g), **m** 146-147° (sealed capillary totally immersed in the oil bath). The yield depends slightly on the rapidity of the operation, in this way loss by sublimation can be minimised. If desired, it can be sublimed under reduced pressure at temps at which CNI is only slowly decomposed into I<sub>2</sub> and (CN)<sub>2</sub>. The vacuum will need to be renewed constantly due to the volatility of CNI. [Org Synth 32 29 1952.]

**Decaborane** [17702-41-9] M 122.2, m 99.7-100°. Purified by vacuum sublimation at 80°/0.1mm, followed by crystn from methylcyclohexane, CH<sub>2</sub>Cl<sub>2</sub>, or dry olefin-free-*n*-pentane, the solvent being subsequently removed by storing the crystals in a vacuum desiccator containing CaCl<sub>2</sub>.

**Deuterium** [7782-39-0] **M 4.** Passed over activated charcoal at -195° [MacIver and Tobin J Phys Chem 64 451 1960]. Purified by diffusion through nickel [Pratt and Rogers, J Chem Soc, Faraday Trans 192 1589 1976]. Always check deuterium for radioactivity to find out the amount of tritium in it (see D<sub>2</sub>O below).

**Deuterium oxide** [7789-20-0] **M 20, f 3.8°/760mm, b 101.4°/760mm, d 1.105.** Distd from alkaline KMnO<sub>4</sub> [de Giovanni and Zamenhof *Biochem J* 92 79 1963]. **NOTE that D<sub>2</sub>O invariably contains tritiated water and will therefore be RADIOACTIVE; always check the radioactivity of D<sub>2</sub>O in a scintillation counter before using.** 

cis-Diamminedichloroplatinum(II) (Cisplatin) [15663-27-1] M 300.1, m 270°(dec). Recrystd from dimethylformamide and the purity checked by IR and UV-VIS spectroscopy. [Raudaschl et al. *Inorg Chim Acta* 78 143 1983.] HIGHLY TOXIC, SUSPECTED CARCINOGEN.

**Diammonium hydrogen orthophosphate** [7783-28-0] **M 132.1.** Crystd from water (1mL/g) between 70° and 0°. After one crystn of ACS grade had Fe, Mo, Na, Se and Ti at 1, 0.2, 1.4, 0.2 and 0.8ppm resp.

**Di-n-amyl n-amylphosphonate** [6418-56-0] **M 292.4, b 150-151<sup>o</sup>/2mm, n 1.4378.** Purified by three crystns of its uranyl nitrate complex from hexane (see *tributyl phosphate*). Extracts Zr<sup>2+</sup> from NaCl solns.

**6,6-Dibenzyl-14-crown-4** (lithium ionophore VI; **6,6-dibenzyl-1,4,8,11-tetra-oxa-cyclo-tetradecane**) [106868-21-7] M **384.5**, m **102-103**°. Dissolve in CHCl<sub>3</sub>, wash with saturated aqueous NaCl, dry with MgSO<sub>4</sub>, evaporate and purify by chromatography on silica gel and gradient elution with  $C_6H_6$ -MeOH followed by preparative reverse phase HPLC on an octadecyl silanised silica (ODS) column and eluting with MeOH. It can be crystd from MeOH ( $v_{KBr}$  1120 cm<sup>-1</sup>, C-O-C). [J Chem Soc Perkin Trans 1 1945 1986.]

**Di-n-butyl boron triflate (di-n-butylboryl trifluoromethanesulfonate)** [60669-69-4] M **274.1, b 37°/0.12mm, 60°/2mm, pK<sup>25</sup> <-3.0 (for triflic acid).** Distil in vacuum under argon and store under argon. Should be used within 2 weeks of purchase or after redistn. Use a short path distn system. It has IR bands in CCl<sub>4</sub> at v 1405, 1380, 1320, 1200 and 1550cm<sup>-1</sup>; and <sup>13</sup>C NMR (CDCl<sub>3</sub>) with  $\delta$  at 118.1, 25.1, 21.5 and 13.6. [Org Synth 68 83 1990; J Am Chem Soc 103, 3099 1981.] TOXIC

**Di-n-butyl cyclohexylphosphonate** [1085-92-3] **M 245.4.** The compound with uranyl nitrate was crystd three times from hexane. For method see *tributyl phosphate*.

Di-tert-butyl dichlorosilane (DTBCl<sub>2</sub>) [18395-90-9] M 213.2, m -15°, b 190°/729mm, 195-197°/atm, d 1.01. Purified by fractional distn. It is a colourless liquid with a pleasant odour and does not fume in moist air, but does not titrate quantitatively with excess of dil alkali. [J Am Chem Soc 70 2877 1948.]

**Di-n-butyl n-butylphosphonate** [78-46-6] **M 250.3, b 150-151°/10mm, 160-162°/20mm, n<sup>25</sup> 1.4302.** Purified by three recrystallisations of its compound with uranyl nitrate, from hexane. For method, see *tributyl phosphate*.

**Di**-tert-butyl silyl bis(trifluoromethanesulfonate) [85272-31-7] M 440.5, b 73.5-74.5°/0.35mm, d1.36 (see pK for triflic acid). Purified by fractional distillation. It is a pale yellow liquid which should be stored under argon. It is less reactive than the diisopropyl analogue. The presence of the intermediate monochloro compound can be detected by <sup>1</sup>H NMR, (CHCl<sub>3</sub>): tert-Bu<sub>2</sub>Si(OTf)<sub>2</sub> [ $\delta$  1.25s]; but

impurities have  $\delta$  1.12s for tert-Bu<sub>2</sub>Si(H)OTf and  $\delta$  1.19s for tert-Bu<sub>2</sub>HSi(Cl)OTf. [Tetrahedron Lett 23 487 1982.] TOXIC.

**Di-n-butyltin oxide** [818-08-6] **M 248.9, m >300°.** It is prepd by hydrolysis of di-n-butyltin dichloride with KOH. Hence wash with a little aq M KOH then  $H_2O$  and dry at ~80°/10mm until the IR is free from OH bands. [Cummings Aust J Chem 18 98 1965.]

**Dicarbonyl(cyclopentadienyl)Co** (I) [1207-25-0] M 180.1, b 75°/22mm, b 139-140°(dec)/710mm. Best distd in an atmosphere of CO in a vac. The red brown liquid decomposes slightly on distn even in a vac to liberate some CO. Operations should be performed in an efficient fume cupboard. It is sol in organic solvents and stable in air but decomposes slowly in sunlight and rapidly under UV. [Piper et al. J Inorg Nucl Chem 1 165 1955.] TOXIC.

Dichlorodimethylsilane see dimethylchlorosilane p. 419.

2,6-Dichlorophenol-indophenol sodium salt  $(2H_2O)$  [620-45-1] M 326.1,  $\varepsilon$  2.1 x 10<sup>4</sup> at 600nm and pH 8, pK<sup>30</sup> 5.7 (oxidised form), pK<sub>1</sub><sup>30</sup> 7.0, pK<sub>2</sub><sup>30</sup> 10.1 (reduced form). Dissolved in 0.001M phosphate buffer, pH 7.5 (alternatively, about 2g of the dye was dissolved in 80mL of M HCl), and extracted into diethyl ether. The extract was washed with water, extracted with aqueous 2% NaHCO<sub>3</sub>, and the sodium salt of the dye was ppted by adding NaCl (30g/100mL of NaHCO<sub>3</sub> soln), then filtered off, washed with dilute NaCl soln and dried.

**Dicobalt octacarbonyl** [10210-68-1] **M 341.9, m 51°.** Orange-brown crystals by recrystn from *n*-hexane under a carbon monoxide atmosphere [Ojima et al. J Am Chem Soc **109** 7714 1987; see also Hileman in *Preparative Inorganic Reactions*, Jolly Ed. Vol 1 101 1987].

Diethyl aluminium chloride [96-10-6] M 120.6, m -75.5°, b 106.5-108°/24.5mm, d 0.96. Distd from excess dry NaCl (to remove ethyl aluminium dichloride) in a 50-cm column containing a heated nichrome spiral.

**O,O-Diethyl-S-2-diethylaminoethyl phosphorothiolate** [78-53-5] M 269.3, m 98-99°. Crystd from isopropanol/diethyl ether.

Di-(2-ethylhexyl)phosphoric acid ('diisooctyl' phosphate) [27215-10-7; 298-07-7] M 322.4, b 209°/10mm, d 0.965, pK<sub>Est</sub> ~1.7. Contaminants of commercial samples include the monoester, polyphosphates, pyrophosphate, 2-ethylhexanol and metal impurities. Dissolved in *n*-hexane to give an 0.8M soln. Washed with an equal volume of M HNO<sub>3</sub>, then with saturated (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> soln, with 3M HNO<sub>3</sub>, and twice with water [Petrow and Allen Anal Chem 33 1303 1961]. Similarly, the impure sodium salt, after scrubbing with pet ether, was acidified with HCl and the free organic acid was extracted into pet ether and purified as above. [Peppard et al. J Inorg Nucl Chem 7 231 1958] or Stewart and Crandall [J Am Chem Soc 73 1377 1951]. Purified also via the copper salt [McDowell et al. J Inorg Nucl Chem 38 2127 1976].

**Diethylmethylsilane** [760-32-7] M 102.3, b 78.4°/760mm, 77.2-77.6°/atm, d 0.71. Fractionally distilled through a *ca* 20 plate column and the fraction boiling within a range of less than 0.5° is collected. [*Izv Akad Nauk SSSR Otd Khim* 1416 1957; J Am Chem Soc 69 2600 1947.]

Diethyl trimethylsilyl phosphite [13716-45-5] M 210.3, b 61°/10mm, 66°/15mm, d 0.9476, n 1.4113. Fractionated under reduced pressure and has  $\delta_P$  -128 ±0.5 relative to H<sub>3</sub>PO<sub>4</sub>. [J Org Chem 46 2097 1981; J Gen Chem USSR (Engl Transl) 45 231 1975.]

N,N-Diethyltrimethylsilylamine [996-50-9] M 145.3, b 33°/26mm, 126.8-127.1°/738mm, 126.1-126.4°, d 0.763, n 1.411. Fractionated through a 2ft vac-jacketed column containing Helipak packing with a reflux ratio of 10:1. [J Am Chem Soc 68 241 1946; J Org Chem 23 50 1958; J Prakt Chem 9 315 1959.]

*N*, *N'*-Diheptyl-*N*, *N'*-5,5-tetramethyl-3,7-dioxanonanediamide [lithium ionophore I (ETH 149)] [58821-96-8] M 442.7. Purified by chromatography on Kieselgel using CHCl<sub>3</sub> as eluent (IR v 1640cm<sup>-1</sup>). [Helv Chim Acta 60 2326 1977.]

Dihexadecyl phosphate [2197-63-9] M 546.9, m 75°, pK<sub>Est</sub> ~1.2. Crystd from MeOH [Lukac J Am Chem Soc 106 4387 1984].

1,2-Dihydroxybenzene-3,5-disulfonic acid, di-Na salt (TIRON) [149-45-1] M 332.2,  $\varepsilon$  6.9 x 10<sup>4</sup> at 260nm, pH 10.8, pK<sub>1</sub> and pK<sub>2</sub> <2 (for SO<sub>3</sub><sup>-</sup>), pK<sub>3</sub> 7.7, pK<sub>4</sub> 12.6 (for OHs of disulfonate dianion). Recrystd from water [Hamaguchi et al. Anal Chim Acta 9 563 1962]. Indicator color reagent for Fe, Mn, Ti and Mo ions and complexes with Al, Cd, Co, Co, Fe (III), Mn, Pd, UO<sub>2</sub><sup>2+</sup>, VO<sup>2+</sup> and Zn.

**Diisooctyl phenylphosphonate** [49637-59-4] **M 378.5, n^{25} 1.4780.** Vacuum distilled, percolated through a column of alumina, then passed through a packed column maintained at 150° to remove residual traces of volatile materials in a countercurrent stream of N<sub>2</sub> at reduced pressure [Dobry and Keller J Phys Chem **61** 1448 1957].

Diisopropyl chlorosilane (chlorodiisopropylsilane) [2227-29-4] M 150.7, b 59°/8mm, 80°/10mm, 200°/738mm, d 0.9008, n, 1.4518. Impurities can be readily detected by <sup>1</sup>H NMR. Purified by fractional distn [J Am Chem Soc 69 1499 1947; J Chem Soc 3668 1957; J Organometal Chem 282 175 1985].

**Dilongifolyl borane** [77882-24-7] **M 422.6, m 169-172°**. Wash with dry  $Et_2O$  and dry in a vacuum under N<sub>2</sub>. It has **m** 160-161° in a sealed evacuated capillary. It is sparingly soluble in pentane, tetrahydrofuran, carbon tetrachloride, dichloromethane, and chloroform, but the suspended material is capable of causing asymmetric hydroboration. Disappearance of solid indicates that the reaction has proceeded. [J Org Chem 46 2988 1981.]

**Dimethyl carbonate** [616-38-6] **M 90.1, b 89.5°/755mm, 90.2°/atm, d 1.0446, n 1.3687.** If the reagent has broad intense bands at 3300cm<sup>-1</sup> and above (i.e. OH streching) then it should be purified further. Wash successively with 10% Na<sub>2</sub>CO<sub>3</sub> soln, saturated CaCl<sub>2</sub>, H<sub>2</sub>O and dried by shaking mechanically for 1h with anhydrous CaCl<sub>2</sub>, and fractionated. [*J Chem Soc* 78 1939, 1847 1948.]

**Dimethyl dicarbonate (dimethyl pyrocarbonate)** [4525-33-1] M 134.1, m 15.2°, b 45-46°/5mm, d 1.2585, n 1.3950. Dissolve in Et<sub>2</sub>O, shake with a small vol of 0.1N HCl, dry Et<sub>2</sub>O with Na<sub>2</sub>SO<sub>4</sub> and distil in vac below 100° to give a clear liquid. It dec to CO<sub>2</sub> and dimethyl carbonate on heating at 123-149°. It is readily hydrolysed by H<sub>2</sub>O and is an **IRRITANT**. [*J Gen Chem USSR* 22 1546 1952; see also *Chem Ber* 71 1797 1938.]

Dimethyldichlorosilane [75-78-5] M 129.1, m -75.5°, b 68.5-68.7°/750mm, 70.5°/760mm, d 1.0885, n 1.4108. Other impurities are chlorinated silanes and methylsilanes. Fractionated through a 3/8in diameter 7ft Stedman column rated at 100 theoretical plates at almost total reflux (see p. 441). See purification of MeSiCl<sub>2</sub>. [J Am Chem Soc 70 3590 1948.]

2,6-Dimethyl-1,10-phenanthrolinedisulfonic acid, di-Na salt ( $H_2O$ ) (bathocuproinedisulfonic acid di-Na salt) [52698-84-7] M 564.5, pK<sub>Est</sub>~0 (for free acid). Inorganic salts and some coloured species can be removed by dissolving the crude material in the minimum volume of water and precipitating by adding EtOH. Purified reagent can be obtained by careful evapn of the filtrate.

Dimethylphenylsilyl chloride (chlorodimethylphenylsilane) [768-33-2] M 170.7, b 85-87°/32mm, 196°/atm, d 1.017, n 1.509. See phenyl methyl chlorosilane on p. 449.

Dinitrogen tetroxide (nitrogen dioxide,  $N_2O_4$ ) [10544-72-6] M 92.0 m -11.2°, b 21.1°. Purified by oxidation at 0° in a stream of oxygen until the blue colour changed to red-brown. Distd from  $P_2O_5$ , then solidified on cooling in a deep-freeze (giving nearly colourless crystals). Oxygen can be removed by alternate freezing and melting. TOXIC VAPOUR.

Dioctyl phenylphosphonate [1754-47-8] M 378.8, d 1.485, n<sup>25</sup> 1.4780. Purified as described under diisooctyl phenylphosphonate.

(1,3-Dioxalan-2-ylmethyl)triphenylphosphonium bromide [52509-14-5] M 429.3, m 191.5-193°, 193-195°. Wash the crysts with Et<sub>2</sub>O, dry in a vac and recryst from CH<sub>2</sub>Cl<sub>2</sub>-dry Et<sub>2</sub>O to give prisms m 172-174°, which is raised to 191.5-193°, on drying at 56°/0.5mm. [Cresp et al. J Chem Soc, Perkin Trans 1 37 1974.]

Diphenyldiselenide [1666-13-3] M 312.1, m 62-64. Crystd twice from hexane [Kice and Purkiss J Org Chem 52 3448 1987].

Diphenyl hydrogen phosphate [838-85-7] M 250.2, m 99.5°, pK<sup>20</sup> 0.26. Crystd from CHCl<sub>3</sub>/pet ether.

**Diphenylmercury** [587-85-9] M **354.8**, m **125.5-126°**. Sublimed, then crystd from nitromethane or ethanol. If phenylmercuric halides are present they can be converted to phenylmercuric hydroxide which, being much more soluble, remains in the alcohol or \*benzene used for crystn. Thus, crude material (10g) is dissolved in warm ethanol (*ca* 150mL) and shaken with moist  $Ag_2O$  (*ca* 10g) for 30min, then heated under reflux for 30min and filtered hot. Concentration of the filtrate by evaporation gives diphenylmercury, which is recrystd from \*benzene [Blair, Bryce-Smith and Pengilly J Chem Soc 3174 1959]. TOXIC.

4,7-Diphenyl-1,10-phenanthrolinedisulfonic acid, di-Na salt  $3H_2O$  (bathophenanthrolinedisulfonic acid di-Na salt) [52746-49-3] M 590.6, m 300°, pK<sub>Est</sub>~0 (for free acid). Dissolve crude sample in the minimum volume of water and add EtOH to ppte the contaminants. Carefully evaporate the filtrate to obtain pure material.

It forms a dark red complex with Fe<sup>2+</sup> with  $\lambda_{max}$  535nm ( $\varepsilon 2.23 \times 10^4$ mol<sup>-1</sup> cm<sup>-1</sup>) [Anal Chim Acta 115 407 1980]. Prepared by sulfonating bathophenanthroline with ClSO<sub>3</sub>H: to 100g of bathophenanthroline was added 0.5mL of Fe free ClSO<sub>3</sub>H and heated over a flame for 30sec. Cool and carefully add 10mL of pure distd H<sub>2</sub>O and warm on a water bath with stirring till all solid dissolved. A stock soln is made by diluting 3mL of this reagent to 100mL with 45% aq NaOAc, filter off the solid and store in a dark bottle. In this way it is stable for several months. [Am J Clinical Pathology **29** 590 1958.]

**Diphenylphosphinic acid** [1707-03-5] **M 218.2, m 194-195°, pK<sup>20</sup> 1.72.** Recrystd from 95% EtOH and dried under vacuum at room temperature. [see Kosolapoff Organophosphorus Compounds J Wiley, NY, 1950; Kosolapoff and Maier Organic Phosphorus Compounds Wiley-Interscience, NY, 1972-1976.]

**Diphenylsilane** [775-12-2] M 184.3, b 75-76°/0.5mm, 113-114°/9mm, 124-126°/11mm, 134-135°/16mm, d 1.0027, n 1.5802, 1.5756. Dissolve in  $Et_2O$ , mix slowly with ice-cold 10% AcOH. The  $Et_2O$  layer is then shaken with  $H_2O$  until the washings are neutral to litmus. Dry over  $Na_2SO_4$ , evaporate the  $Et_2O$  and distil the residual oil under reduced pressure using a Claisen flask with the take-off head modified into a short column.  $Ph_2SiH_2$  boils at 257°/760mm but it cannot be distd at this temp because exposure to air leads to flashing, decomposition and formation of silica. It is a colourless, odourless oil, miscible with organic solvents but not  $H_2O$ . A possible impurity is  $Ph_3SiH$  which has m 43-45° and would be found in the residue. [J Org Chem 18 303 1953; J Am Chem Soc 74 6481952, 81 5925 1959.]

Diphenylsilanediol [947-42-2] M 216.3, m 148°(dec). Crystd from CHCl<sub>3</sub>-methyl ethyl ketone.

**Diphenyl tolyl phosphate** [26444-49-5] **M 340.3, n<sup>25</sup> 1.5758.** Vac distd, then percolated through a column of alumina. Finally, passed through a packed column maintained at 150° to remove traces of volatile

impurities in a countercurrent stream of nitrogen at reduced pressure. [Dobry and Keller J Phys Chem 61 1448 1947.]

**Disodium calcium ethylenediaminetetraacetate** [39208-14-5] M 374.3, (see pKs for EDTA in entry below). Dissolved in a small amount of water, filtered and ppted with excess EtOH. Dried at 80°.

**Disodium dihydrogen ethylenediaminetetraacetic acid**  $(2H_2O)$  [6381-92-6] M 372.2, m 248°(dec),  $pK_1^{25}0.26 \ pK_2^{25}0.96$ ,  $pK_3^{25}2.60$ ,  $pK_4^{25}2.67$ ,  $pK_5^{25}6.16$ ,  $pK_6^{25}10.26$  (see EDTA Cha 4). Analytical reagent grade material can be used as primary standard after drying at 80°. Commercial grade material can be purified by crystn from water or by preparing a 10% aqueous soln at room temperature, then adding ethanol slowly until a slight permanent ppte is formed, filtering, and adding an equal volume of ethanol. The ppte is filtered off on a sintered-glass funnel, is washed with acetone, followed by diethyl ether, and dried in air overnight to give the dihydrate. Drying at 80° for at least 24h converts it to the anhydrous form.

Disodium 4,5(1,8)-dihydroxynaphthalene-2,7(3,6)-disulfonate (2H<sub>2</sub>O) [5808-22-0] M 400.3, m >300°, pK<sub>1</sub> 0.61(SO<sub>3</sub><sup>-</sup>), pK<sub>2</sub> 0.7(SO<sub>3</sub><sup>-</sup>), pK<sub>3</sub> 5.45(OH), pK<sub>4</sub> 15.5(OH). Crystd from H<sub>2</sub>O or H<sub>2</sub>O by addition of EtOH. Complexes with Ag, ClO<sub>3</sub><sup>-</sup>, Cr, Hg, NO<sub>2</sub><sup>-</sup>, NO<sub>3</sub><sup>-</sup> and Ti. [cf Chromotropic acid p. 413.]

**Disodium** ethylenebis[dithiocarbamate] [142-59-6] M 436.5,  $pK_{Est} \sim 3.0$ . Crystd (as hexahydrate) from aqueous ethanol.

**Disodium-B-glycerophosphate** [819-83-0  $(4H_2O)$ ] M 216.0, m 102-104°,  $pK_2^{25}6.66$  (free acid). Crystd from water.

**Disodium hydrogen orthophosphate (anhydrous)** [7558-79-4] M 142.0, (see pK of  $H_3PO_4$ ). Crystd twice from warm water, by cooling. Air dried, then oven dried overnight at 130°. *Hygroscopic*: should be dried before use.

Disodium magnesium ethylenediaminetetraacetate [14402-88-1] M 358.5,  $pK_1^{25}$  0.26  $pK_2^{25}$  0.96,  $pK_3^{25}$  2.60,  $pK_4^{25}$  2.67,  $pK_5^{25}$  6.16,  $pK_6^{25}$  10.26 (see EDTA on p. 237 in Chapter 4). Dissolved in a small amount of water, filtered and ppted with an excess of MeOH. Dried at 80°.

Disodium naphthalene-1,5-disulfonate [1655-29-4] M 332.3, pK<sub>Est</sub> ~0. Recrystd from aqueous acetone [Okahata et al. J Am Chem Soc 108 2863 1986].

**Disodium 4-nitrophenylphosphate (6H<sub>2</sub>O)** [4264-83-9] **M 371.1** Dissolve in hot aqueous MeOH, filter and ppte by adding Me<sub>2</sub>CO. Wash the solid with Me<sub>2</sub>CO and repeat the purification. Aq MeOH and Et<sub>2</sub>O can also be used as solvents. The white fibrous crystals contain less than 1% of free 4-nitrophenol [assay: J Biol Chem 167 57 1947].

**Disodium phenylphosphate**  $(2H_2O)$  [3279-54-7] M 254.1,  $pK_1^{25}$  1.46,  $pK_2^{25}$  6.29 [for **PhPO(OH)**<sub>2</sub>]. Dissolved in a minimum amount of methanol, filtering off an insoluble residue of inorganic phosphate, then ppted by adding an equal volume of diethyl ether. Washed with diethyl ether and dried [Tsuboi *Biochim Biophys Acta* 8 173 1952].

**Disodium succinate** [150-90-3] **M 162.1.** Crystd twice from water (1.2mL/g) and dried at 125°. Freed from other metal ions by passage of a 0.1M soln through a column of Dowex resin A-1 (Na form).

Di-p-tolylmercury [50696-65-6] M 382.8, m 244-246°. Crystd from xylene.

Di-p-tolyl phenylphosphonate [94548-75-1] M 388.3, n<sup>25</sup> 1.5758. Purified as described under diisooctyl phenylphosphonate.

**1,3-Divinyl-1,1,3,3-tetramethyldisiloxane** [2627-95-4] M **186.4, m -99.7°; b 128-129°/atm, 139°/760mm, d 0.811, n 1.4122.** Dissolve in  $Et_2O$ , wash with  $H_2O$ , dry over  $CaCl_2$  and distil. [J Am Chem Soc 77 1685 1955; Collect Czech Chem Comm **24** 3758 1959.]

**Eosin B** (Bluish, Eosin Scarlet, 4',5'-dibromo-2',7'-dinitrofluorescein disodium salt) [548-24-3] M 624.1,  $\lambda_{max}$  514nm, CI 45400. Freed from inorganic halides by repeated crystn from butan-1-ol.

**Eosin Y (as di-Na salt)** [17372-87-1] **M 691.9.** Dissolved in water and ppted by addition of dilute HCl. The ppte was washed with water, crystd from ethanol, then dissolved in the minimum amount of dilute NaOH soln and evaporated to dryness on a water-bath. The purified disodium salt was then crystd twice from ethanol [Parker and Hatchard Trans Faraday Soc 57 1894 1961].

Eosin YS (Eosin Yellowish, 2',4',5'7'-tetrabromofluorescein di-Na salt) [17372-87-1] M 691.9, CI 45380. Dissolve in the minimum vol of H<sub>2</sub>O (1g/mL), filter and add EtOH until separation of salt is complete. Filter off, wash with abs EtOH, then Et<sub>2</sub>O and dry first in air, then at 100°. Used for staining blood cells and for estimating traces of Ag. [Selsted and Becker Anal Biochem 155 270 1986; El-Ghamry and Frei Anal Chem 40 1986 1968.]

Eriochrome Black T [1787-61-7] M 416.4,  $A_{1cm}^{\%}(\lambda max)$  656(620nm) at pH 10, using the dimethylammonium salt,  $pK_2^{25}$  5.81,  $pK_3^{25}$  11.55. The sodium salt (200g) was converted to the free acid by stirring with 500mL of 1.5M HCl, and, after several minutes, the slurry was filtered on a sintered-glass funnel. The process was repeated and the material was air dried after washing with acid. It was extracted with \*benzene for 12h in a Soxhlet extractor, then the \*benzene was evaptd and the residue was air dried. A further desalting with 1.5M HCl (1L) was followed by crystn from dimethylformamide (in which it is very soluble) by forming a saturated soln at the boiling point, and allowing to cool slowly. The crystalline dimethylammonium salt so obtained was washed with \*benzene and treated repeatedly with dilute HCl to give the insoluble free acid which, after air drying, was dissolved in alcohol, filtered and evaporated. The final material was air dried, then dried in a vacuum desiccator over Mg(ClO<sub>4</sub>)<sub>2</sub> [Diehl and Lindstrom, Anal Chem **31** 414 1959]. Indicator for complexometry of alkaline earth metals.

Eriochrome Blue Black R (Palatine Chrome Black 6BN, Calcon, 3-hydroxy-4-(2-hydroxy-1-naphthylazo)naphthalene-1-sulfonic acid Na salt] [2538-85-4] M 416.4,  $pK_2^{25}7.0$ ,  $pK_3^{25}$  13,5. Freed from metallic impurities by three pptns from aqueous soln by addn of HCl. The ppted dye was dried at 60° under vacuum. Indicator for complexometry of Al, Fe and Zr.

Ethoxycarbonylmethylene triphenylphosphonium bromide [1530-45-6] M 429.3, m 155-155.5°, 158°(dec). Wash with pet ether (b 40-50°) and recryst from CHCl<sub>3</sub>/Et<sub>2</sub>O and dry in high vac at 65°. [Isler et al. *Helv Chim Acta* 40 1242 1957; Wittig and Haag Chem Ber 88 1654, 1664 1955.]

(Ethoxycarbonylmethylene)triphenylphosphorane [ethyl (triphenylphosphoranylidene)acetate] [1099-45-2] M 348.4, m 116-117°, 128-130°. Cryst by dissolving in AcOH and adding pet ether (b 40-50°) to give colorless plates. UV  $\lambda \max(A_{1mm}^{1\%})$ : 222nm (865) and 268nm (116) [Isler et al. Helv Chim Acta 40 1242 1957].

Ethylarsonic acid [507-32-4] M 154.0, m 99.5°,  $pK_1$  4.72 (As(OH)O<sup>-</sup>),  $pK_2$  8.00 [AsO<sub>2</sub><sup>2-</sup>]. Crystd from ethanol.

**2-Ethyl-1,2-benzisoxazolium tetrafluoroborate** [4611-62-5] **M 235.0, m 107-109°, 109.5-110.2°.** Recrystd from MeCN-EtOAc to give magnificent crystals. It is not hygroscopic but on long exposure to moisture it etches glass. It is light-sensitive and should be stored in brown glass bottles. UV (H<sub>2</sub>O),  $\lambda$ max 258nm ( $\varepsilon$  13 100) and  $\lambda$ max 297nm ( $\varepsilon$  2 900); IR (CH<sub>2</sub>Cl<sub>2</sub>): 1613 (C=N) and 1111-1000 (BF<sub>4</sub><sup>+</sup>) [UV, IR, NMR: Kemp and Woodward *Tetrahedron* **21** 3019 1965].

Ethylene bis(diphenylphosphine) [1,2-bis(diphenylphosphino)ethane] [1663-45-2] M 398.4, m 139-140°. See 1,2-bis-(diphenylphosphino)ethane (DIPHOS) on p. 402.

Ethylmercuric chloride [107-27-7] M 265.1, m 193-194°. Mercuric chloride can be removed by suspending ethylmercuric chloride in hot distilled water, filtering with suction in a sintered-glass crucible and drying. Then crystd from ethanol and sublimed under reduced pressure. It can also be crystd from water.

Ethylmercuric iodide [2440-42-8] M 356.6, m 186°. Crystd once from water (50mL/g).

Ethyl Orange (sodium 4,4'-diethylaminophenylazobenzenesulfonate) [62758-12-7] M 355.4, pK<sub>Est</sub> ~ 3.8. Recrystd twice from water.

Ethyl trimethylsilylacetate [4071-88-9] M 160.3, b 74.5°/41mm, 75.5°/42mm, 157°/730mm, d 0.8762, n 1.4149. Purified by distilling *ca* 10g of reagent through a 15cm, Vigreux column and then redistilling through a 21cm glass helices-packed column [*J Am Chem Soc* 75 994 1953]. Alternatively, dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dilute Na<sub>2</sub>CO<sub>3</sub>, dry over Na<sub>2</sub>CO<sub>3</sub>, evaporate Et<sub>2</sub>O, and distil through a column of 15 theoretical plates [*J Am Chem Soc* 70 2874 1948].

Ethyl 3-(trimethylsilyl)propionate [17728-88-0] M 174.3, b 93°/40mm, 178°-180°/atm, d 0.8763, n 1.4198. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dilute Na<sub>2</sub>CO<sub>3</sub>, dry over Na<sub>2</sub>SO<sub>4</sub>, evaporate Et<sub>2</sub>O and fractionally distil. [J Am Chem Soc 72 1935 1950.]

Ethynyl tributylstannane [994-89-8] M 315.1, b 76°/0.2mm, 130-135°/0.7mm, 200°/2mm, d 1.1113, n 1.4770. Purified by dissolving the reagent (*ca* 50g) in heptane (250mL), washing with H<sub>2</sub>O (100mL), drying (MgSO<sub>4</sub>), evaporating and distilling in a vacuum. It has IR v 3280 ( $\equiv$ C-H), 2950, 2850, 2005 (C $\equiv$ C), 1455, 1065 and 865cm<sup>-1</sup>. [J Org Chem 46 5221 1981; J Am Chem Soc 109 2138 1987; J Gen Chem USSR (Engl Edn) 37 1469 1967.]

Ethynyl trimethylsilane [1066-54-2] M 98.2, b 53°/atm, 52.5°/atm, d 0.71, n 1.3871. Distil through an efficient column. The IR has bands at 2041 (C=C) and 3289 (=C-H) cm<sup>-1</sup>. [Chem Ber 92 30 1959.]

Ethyl triphenylphosphonium bromide [1530-32-1] M 371.3, m 203-205°. Recrystd from H<sub>2</sub>O and dried in high vacuum at 100°. IR has bands at 1449, 1431 and 997cm<sup>-1</sup>. [Justus Liebigs Ann Chem 606 1 1957; J Org Chem 23 1245 1958.]

**Europium (III) acetate (2H<sub>2</sub>O)** [62667-64-5] M 383.1,  $pK_1^{25}$ 8.31 (for aquo Eu<sup>3+</sup>). Recrystd several times from water [Ganapathy et al. J Am Chem Soc 108 3159 1986]. For europium shift reagents see lanthanide shift reagents in Chapter 4.

**Ferric acetylacetonate** [14024-18-1] M 353.2, m 181.3-182.3°. Recrystd twice from \*benzene-pet ether m 181.3-182.3° corr [*J Chem Soc* 1256 1938]. Recrystd from EtOH or Et<sub>2</sub>O, m 179° [*Justus Liebigs Ann Chem* 323 13 1902]. Recrystd from absolute EtOH, m 159.5° [*Chem Ber* 67 286 1934]. Dry for 1hr at 120°.

Ferric Bromide [10031-26-2] M 395.6, m >130°(dec). Subimed in a sealed tube with  $Br_2$  at 120°-200°. [Lux in Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II, p 1494 1963.]

Ferric chloride (anhydrous) [7705-08-0] M 162.2, m >300°(dec). Sublimed at 200° in an atmosphere of chlorine. Stored in a weighing bottle inside a desiccator.

Ferric chloride  $(6H_2O)$  [10025-77-1] M 270.3, m 37°(dec),  $pK_1^{25}2.83$ ,  $pK_2^{25}4.59$  (for hydrolysis of Fe<sup>3+</sup>). An aqueous soln, saturated at room temperature, was cooled to -20° for several hours. Pptn was slow, even with scratching and seeding, and it was generally necessary to stir overnight. The presence of free HCl retards the pptn [Linke J Phys Chem 60 91 1956].

Ferric nitrate  $(9H_2O)$  [7782-61-8] M 404.0, m 47°(dec). Cryst from aqueous solutions of moderately strong HNO<sub>3</sub> as the violet nonahydrate. With more concentrated aqueous solns (containing some HNO<sub>3</sub>), the hexahydrate crysts out. The anhydrous salt is slightly deliquescent and decomposes at 47°.

Ferric perchlorate (9H<sub>2</sub>O) [13537-24-1] M 516.3,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd twice from conc HClO<sub>4</sub>, the first time in the presence of a small amount of H<sub>2</sub>O<sub>2</sub> to ensure that the iron is fully oxidised [Sullivan J Am Chem Soc 84 4256 1962]. Extreme care should be taken with this preparation because it is potentially DANGEROUS.

**Ferric sulfate**  $(xH_2O)$  [10028-22-5] M 399.9 +  $xH_2O$ . Dissolve in the minimum volume of dilute aqueous H<sub>2</sub>SO<sub>4</sub> and allow to evaporate at room temp until crystals start to form. Do not concentrate by boiling off the H<sub>2</sub>O as basic salts will be formed. Various hydrates are formed the—common ones are the dodeca and nona hydrates which are violet in colour. The anhydrous salt is colourless and very hygroscopic but dissolves in H<sub>2</sub>O slowly unless ferrous sulfate is added.

**Ferrocene** [102-54-5] **M 186.0, m 173-174°.** Purified by crystn from pentane or cyclohexane (also  ${}^{*}C_{6}H_{6}$  or MeOH can be used). Moderately soluble in Et<sub>2</sub>O. Sublimes readily above 100°. Crystallisation from EtOH gave **m** 172.5-173°. [Org Synth Coll Vol IV 473 1963; J Chem Soc 632 1952.] Also crystd from methanol and sublimed *in vacuo*. [Saltiel et al. J Am Chem Soc 109 1209 1987.]

Ferrocene carboxaldehyde [12093-10-6] M 214.1, m 117-120°, 118-120°, 121°, 124.5°. Red crystals from EtOH or pet ether and sublimed at 70°/1mm. Semicarbazone m 217-219°(dec) cryst from aqueous EtOH. O-Acetyloxime m 80-81° cryst from hexane [J Org Chem 22 355 1957]. 2,4-Dinitrophenylhydrazone m 248°(dec). [Beilstein 16 4th Suppl 1798; J Am Chem Soc 79 3416 1957; J Chem Soc 650 1958.]

Ferrocene carboxylic acid [1271-42-7] M 230.1, m 210°(dec), 225-230°(dec). Yellow crystals from pet ether. Also crystd from aqueous ethanol. [Matsue et al. J Am Chem Soc 107 3411 1985.] Acid chloride m 49° crystallises from pentane,  $\lambda max 458nm$  [J Org Chem 24 280 1959]. Methyl ester crystallises from aq MeOH m 70-71°. Anhydride m 143-145° from pet ether [J Org Chem 24 1487 1959]. Amide m 168-170° from CHCl<sub>3</sub>-Et<sub>2</sub>O or m 167-169° from \*C<sub>6</sub>H<sub>6</sub>-MeOH. [J Am Chem Soc 77 6295 1955; 76 4025 1954.]

**Ferrocene-1,1'-dicarboxylic acid** [1293-87-4] **M 274.1, m >250°(dec), >300°.** Orange-yellow crystals from AcOH. Sublimes above 230°. *Monomethyl ester* **m** 147-149° [Dokl Acad Nauk USSSR 115, 518 1957]. Dimethyl ester **m** 114-115° [J Am Chem Soc 74, 3458 1958]. Diacid chloride **m** 92-93° from pet ether. [Dokl Acad Nauk SSSR 120 1267 1958; 127 333 1959.]

Ferrocene-1,1,-dimethanol [1291-48-1] M 246.1, m 107-108°. Obtained from the diacid with LiAlH<sub>4</sub> reduction and recrystd from Et<sub>2</sub>O-pet ether. [J Am Chem Soc 82 4111 1960.]

**Ferrous bromide** [20049-65-4] M **215.7** +  $xH_2O$ , m 684°, d<sup>25</sup> 4.63. Crystn from air-free H<sub>2</sub>O provides the *hexahydrate* as pale green to bluish-green rhombic prisms. On heating at 49° H<sub>2</sub>O is lost and the *tetrahydrate* is formed. Further heating at 83° more H<sub>2</sub>O is lost and the *dihydrate* is formed as a light yellow to dark brown *hygroscopic* powder. The ferrous iron in the aqueous solns of these salts readily oxidises to ferric iron. The salts should be stored over H<sub>2</sub>SO<sub>4</sub> under N<sub>2</sub> in tightly closed containiners. They have some solubility in EtOH. [*Chem Ber* 38 236 1904.]

Ferrous chloride  $(4H_2O)$  [13478-10-9] M 198.8, m 105°(dec),  $pK_1^{25}$  6.7,  $pK_2^{25}$  9.3 (for aquo Fe<sup>2+</sup>). A 550mL round-bottomed Pyrex flask was connected, *via* a glass tube fitted with a medium porosity

sintered-glass disc, to a similar flask. To 240g of FeCl<sub>2</sub>.4H<sub>2</sub>O in the first flask was added conductivity water (200mL), 38% HCl (10mL), and pure electrolytic iron (8-10g). A stream of purified N<sub>2</sub> was passed through the assembly, escaping through a mercury trap. The salt was dissolved by heating which was continued until complete reduction had occurred. By inverting the apparatus and filtering (under N<sub>2</sub> pressure) through the sintered glass disc, unreacted iron was removed. After cooling and crystn, the unit was again inverted and the crystals of ferrous chloride were filtered free from mother liquor by applied N<sub>2</sub> pressure. Partial drying by overnight evacuation at room temperature gave a mixed hydrate which, on further evacuation on a water bath at 80°, lost water of hydration and its absorbed HCl (with vigorous effervescence) to give a white powder, FeCl<sub>2</sub>.2H<sub>2</sub>O [Gayer and Wootner J Am Chem Soc **78** 3944 1956].

**Ferrous chloride** [7758-94-3] **M 126.8, m 674°, b 1023°, d<sup>25</sup> 3.16.** Sublimes in a stream of HCl at *ca* 700°, or in H<sub>2</sub> below 300°. Its vapour pressure at 700° is 12mm. Anhydrous FeBr<sub>2</sub> can be obtained by carefully dehydrating the *tetrahydrate* in a stream of HBr and N<sub>2</sub>, and it can be sublimed under N<sub>2</sub>. White *hygroscopic* rhombohedral crystals with a green tint. They oxidise in air to FeCl<sub>3</sub> + Fe<sub>2</sub>O<sub>3</sub>. Sol in H<sub>2</sub>O, EtOH Me<sub>2</sub>CO but insol in Et<sub>2</sub>O. The *tetrahydrate* is pale green to pale blue in colour and loses 2H<sub>2</sub>O at 105-115°. The *dihydrate* loses H<sub>2</sub>O at 120°. The ferrous iron in the aqueous solns of these salts readily oxidises to ferric iron. [*Inorg Synth* **6** 172 1960; Handbook of Preparative Inorganic Chemistry (Ed Brauer) Vol II 1491 1965.]

Ferrous perchlorate (6H<sub>2</sub>O) [13933-23-8] M 362.9,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from HClO<sub>4</sub>.

Ferrous sulfate (7H<sub>2</sub>O) [7782-63-0] M 278.0, m ~60°(dec). Crystd from 0.4M H<sub>2</sub>SO<sub>4</sub>.

**Fluorine** [7782-41-4] **M 38.0, b -129.2°.** Passed through a bed of NaF at 100° to remove HF and SiF<sub>4</sub>. [For description of stills used in fractional distn, see Greenberg et al. J Phys Chem 65 1168 1961; Stein, Rudzitis and Settle Purification of Fluorine by Distillation, Argonne National Laboratory, ANL-6364 1961 (from Office of Technical Services, US Dept of Commerce, Washington 25).] **HIGHLY TOXIC.** 

Fluoroboric acid [16872-11-0] M 87.8, pK -4.9. Crystd several times from conductivity water.

Fluorotrimethylsilane (trimethylsilyl fluoride, TMSF) [420-56-4] M 92.2, m -74°, b 16°/760mm, 19°/730mm, d<sup>o</sup> 0.793. It is a FLAMMABLE gas which is purified by fractional distn through a column at low temperature and with the exclusion of air [Booth and Suttle J Am Chem Soc 68 2658 1946; Reid and Wilkins J Chem Soc 4029 1955].

**Gallium** [7440-55-3] M 69.7, m 29.8°. Dissolved in dilute HCl and extracted into Et<sub>2</sub>O. Pptn with H<sub>2</sub>S removed many metals, and a second extraction with Et<sub>2</sub>O freed Ga more completely, except for Mo, Th(III) and Fe which were largely removed by pptn with NaOH. The soln was then electrolysed in 10% NaOH with a Pt anode and cathode (2-5A at 4-5V) to deposit Ga, In, Zn and Pb, from which Ga was obtained by fractional crystn of the melt [Hoffman *J Res Nat Bur Stand* 13 665 1934]. Also purified by heating to boiling in 0.5-1M HCl, then heating to 40° in water and pouring the molten Ga with water under vacuum onto a glass filter (30-50  $\mu$  pore size), to remove any unmelted metals or oxide film. The Ga was then fractionally crystd from the melt under water.

Gallium (III) Chloride [13450-90-3] M 176.1, m 77.8°, b 133°/100mm, 197.7°/700mm, d 2.47,  $pK_1^{25} 2.91$ ,  $pK_2^{25} 3.70$ ,  $pK_3^{20} 4.42$  (for Ga<sup>3+</sup>). Pure compound can be obtained by redistn in a stream of Cl<sub>2</sub> or Cl<sub>2</sub>/N<sub>2</sub> followed by vacuum sublimation or zone refining. Colourless needles which give gallium dichloride [Ga(GaCl<sub>4</sub>), m 172.4°] on heating. Dissolves in H<sub>2</sub>O with liberation of heat. Soluble in Et<sub>2</sub>O. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 846 1963.]

Gallium (III) nitrate  $(9H_2O)$  [63462-65-7] M 417.9, m ca 65°. Recrystd from H<sub>2</sub>O (sol: 295g/100mL at 20°). White deliquescent colourless powder soluble in H<sub>2</sub>O, absolute EtOH and Et<sub>2</sub>O. Loses

HNO<sub>3</sub> upon heating at 40°. Addition of Et<sub>2</sub>O to a warm ethanolic soln (40-50°) of Ga(NO<sub>3</sub>)<sub>3</sub> 9H<sub>2</sub>O precipitates Ga(OH)<sub>2</sub>NO<sub>3</sub>.Ga(OH)<sub>3</sub>.2H<sub>2</sub>O. If the salt has partly hydrolysed, dissolve in conc HNO<sub>3</sub>, reflux, dilute with H<sub>2</sub>O and concentrate on a sand bath. Wash several times by adding H<sub>2</sub>O and evaporate until there is no odour of acid. Dilute the residue to a Ga concentration of 26g/100mL. At this concentration, spongy Ga(NO<sub>3</sub>)<sub>3</sub>.xH<sub>2</sub>O separates from the viscous soln. After standing for several days the crystals are collected and dried in a stream of dry air first at room temp then at 40°. Dehydration is complete after 2 days. Recrystallise from H<sub>2</sub>O and dry on a water pump at room temperature. [*Z Naturforsch* **20B** 71 *1965*; *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Vol I 856*1963*.]

**Gallium (III) sulfate** [13494-91-2 (anhydr); 13780-42-2 (hydr)] **M 427.6.** Recrystn from H<sub>2</sub>O gives the 16-18H<sub>2</sub>O hydrate (sol at 20° is 170g/100mL). Alternatively dissolve in 50% H<sub>2</sub>SO<sub>4</sub> and evaporate (60-70°), cool and ppte by adding EtOH/Et<sub>2</sub>O. On heating at 165° it provides the anhydrous salt which is a white hygroscopic solid. [Z Naturforsch 20B 71 1965.]

**Germanium** [7440-56-4] **M 72.6, m 937°, 925-975°, b 2700°, d 5.3.** Copper contamination on the surface and in the bulk of single crystals of Ge can be removed by immersion in molten alkali cyanide under N<sub>2</sub>. The Ge was placed in dry cyanide powder in a graphite holder in a quartz or porcelain boat. The boat was then inserted into a heated furnace which, after a suitable time, was left to cool to room temperature. At 750°, a 1mm thickness requires about 1min, whereas 0.5cm needs about half hour. The boat was removed and the samples were taken out with plastic-coated tweezers, carefully rinsed in hot water and dried in air [Wang J Phys Chem 60 45 1956].

Germanium (IV) oxide [1310-53-8] M 104.6, m 1080°(soluble form),  $d^{25}$  6.239; m 1116°(insoluble form)  $d^{25}$  4.228,  $pK_1^{25}$ 9.02,  $pK_2^{25}$ 12.82 (for germanic acid  $H_2$ GeO<sub>3</sub>). The oxide (GeO<sub>2</sub>) is usually prepared by hydrolysing redistd GeCl<sub>4</sub> and igniting in order to remove H<sub>2</sub>O and chloride. It can be further purified by dissolving in hot H<sub>2</sub>O (sol: 4g/L cold) evaporating and drying the residual crystalline solid. When the *soluble* form (which is produced in H<sub>2</sub>O at 355°) is heated for 100h it is converted to the *insoluble* form. This form is stable at temperatures up to 1033°, and fusion at 1080° for 4h causes complete devitrification and it reverts to the *soluble* form. [J Am Chem Soc 46 2358 1924, 47 1945 1925, 54 2303 1032.]

Germanium tetrachloride [10038-98-9] M 214.4, m -49.5° ( $\alpha$ ), -52.0° ( $\beta$ ), b 83.1°/760mm, 86.5°/760mm corr, d<sup>20</sup><sub>4</sub>1.84. Traces of Cl<sub>2</sub> and HCl can be removed from the liquid by blowing dry air through it for a few hours at room temperature or shake it with Hg or Hg<sub>2</sub>Cl<sub>2</sub> and then fractionally distil in a vacuum. It decomposes on heating at 950°. It has a sharp penetrating odour and fumes in moist air to give a chalky coat of GeO<sub>2</sub>. It is slowly hydrolysed by H<sub>2</sub>O to give GeO<sub>2</sub>. [*J Am Chem Soc* 44 306 1922.]

Germanium tetraethoxide [14165-55-0] M 252.8, m -72°; b 54.5°/5mm, 71-72°/11mm, 188-190°/722mm, d<sup>25</sup> 1.1288. Distil through a 10cm Vigreux column under reduced pressure. Alternatively distil through a Fensche glass helices column fitted with a total condensation variable take-off stillhead. Fractionate under reduced pressure using a reflux ratio of 10:1. [J Am Chem Soc 75 718 1953; J Chem Soc 4916 1956.]

Glass powder (100-300 mesh). Washed with 10% HNO<sub>3</sub>, water and dried.

Gold (III) bromide (gold tribromide) [10294-28-7] M 436.7, m 150°(dec). Purified by adding pure Br<sub>2</sub> to the dark powder, securely stopper the container, warm a little and shake while keeping away from light for *ca* 48h. Remove the stopper and place over NaOH until free Br<sub>2</sub> is no longer in the apparatus (48-60h). The bright yellow needles of the tribromide are stable over NaOH in the dark. It is sol in H<sub>2</sub>O and in EtOH where it is slowly reduced. Keep in a cooled closed container and protect from light as decomposition causes gold to be formed. Aurobromic acid can be obtained by adding the calculated amount of conc HBr to AuBr<sub>3</sub> (actually Au<sub>2</sub>Br<sub>6</sub>) until all dissolves, whereby the acid crystallises out as HAuBr<sub>4</sub>.5H<sub>2</sub>O, deliquescent solid soluble in EtOH with m *ca* 27°, and store as above. [J Chem Soc 2410 1931, 217, 219 1935.]

Gold (III) chloride (hydrate) [16903-35-8] M 339.8 + xH<sub>2</sub>O, m 229°, b 354°(dec), d 3.9. Obtained as a dark red crystalline mass by dissolving Au in aqua regia and evaporating. When sublimed at  $180^{\circ}$  the crystals are ruby red. The anhydrous salt is *hygroscopic* sol in H<sub>2</sub>O but sparingly soluble in EtOH and Et<sub>2</sub>O. Aurochloric acid is formed when AuCl<sub>3</sub> is dissolved in HC!. [J Am Chem Soc 35 553 1913; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1056 1965.]

Gold (I) cyanide [506-65-0] M 223.0, m dec on heating. The lemon yellow powder is sparingly soluble in H<sub>2</sub>O and EtOH but soluble in aqueous NH<sub>3</sub>. It is obtained by heating H[Au(CN)<sub>2</sub>] at 110°. Wash well with H<sub>2</sub>O and EtOH and dry at 110°. It has an IR band at v 2239cm<sup>-1</sup> typical fo C=N stretching vibration. [Handbook of Preparative Inorg anic Chemistry (Ed. Brauer) Vol II 1064 1965.] CARE: may evolve HCN.

Gold (I) iodide [10294-31-2] M 323.9, m 120°(dec), d 8.25. It has been prepared by heating gold and iodine in a tube at 120° for 4 months. Since it decomposes to Au and I<sub>2</sub> in the presence of UV light and heat then the main impurity is Au. The salt is therefore purified by heating at 120° with I<sub>2</sub> for several weeks. The crystals should be kept dry and in a cool place in the dark. [Z Naturforsch 11B 604 1956.]

Gold (III) oxide hydrate [1303-58-8] M 441.9 + xH<sub>2</sub>O, evolves O<sub>2</sub> at 110°, pK<sub>1</sub><sup>25</sup> < 11.7, pK<sub>2</sub><sup>25</sup> 13.36, pK<sub>3</sub><sup>25</sup> >15.3 [for Au(OH)<sub>3</sub>]. Most probable impurities are Cl<sup>-</sup> ions. Dissolve in strong boiling KOH soln (*ca* 5M) and precipitate (care) with excess of 3N H<sub>2</sub>SO<sub>4</sub>. Then shake and centrifuge, resuspend in H<sub>2</sub>O and repeat wash several times until free from SO<sub>4</sub> and Cl ions. This gives a *wet* oxide which is dried in air, and dec to Au in sunlight. It is best to keep it wet as it decomposes on drying (analyse wet sample). Store away from light in the presence of H<sub>2</sub>O vapour. It evolves O<sub>2</sub> at 110°. It is insoluble in H<sub>2</sub>O but soluble in HCl and conc HNO<sub>3</sub>. [J Am Chem Soc 49 1221 1927.]

**Graphite** [7782-42-5]. Treated with hot 1:1 HCl. Filtered, washed, dried, powdered and heated in an evacuated quartz tube at 1000° until a high vacuum was obtained. Cooled and stored in an atmosphere of helium [Craig, Van Voorhis and Bartell J Phys Chem 60 1225 1956].

**Haematoporphyrin IX** [8,13-bis(1-hydroxyethyl)-3,7,12,17-tetramethyl-21*H*-23*H*-porphin-2,18-dipropionic acid [14459-29-1] M 598.7,  $pK_{Est} \sim 4.8$  (-CH<sub>2</sub>CH<sub>2</sub>COOH). See hematoporphyrin on p. 541 in Chapter 6.

Helium [7440-59-7] M 4.0. Dried by passage through a column of Linde 5A molecular sieves and CaSO<sub>4</sub>, then passed through an activated-charcoal trap cooled in liquid N<sub>2</sub>, to adsorb N<sub>2</sub>, argon, xenon and krypton. Passed over CuO pellets at 300° to remove hydrogen and hydrocarbons, over Ca chips at 600° to remove oxygen, and then over titanium chips at 700° to remove N<sub>2</sub> [Arnold and Smith J Chem Soc, Faraday Trans 2 77 861 1981].

Hexabutyldistannane [hexabutylditin, bis(tributyl)tin] [813-19-4] M 580.4, b 160-162°/0.3mm, d 1.148, n 1.512. Purified by distn in a vacuum and stored in the dark. [Shirai et al. Yakugaku Zasshi 90 59 1970, Chem Abstr 72 90593 1970.]

Hexachlorocyclotriphosphazene [940-71-6] M 347.7, m 113-114°, 113-115°. See phosphonitrilic chloride trimer on p. 450.

Hexachloroplatinic acid hydrate  $(H_2PtCl_6, chloroplatinic acid, platinum IV chloride soution) [16941-12-1] M 409.8 + H<sub>2</sub>O, m 60° (deliquescent solid). If it is to be purified, or regenerated from Pt recovered from catalytic hydrogenations, it was dissolved in aqua regia followed by evaporation to dryness and dissolution in the minimum vol of H<sub>2</sub>O. Then the aqueous solution was treated with saturated ammonium chloride until all the ammonium hexachloroplatinate separated. The (NH<sub>4</sub>)<sub>2</sub>PtCl<sub>6</sub> was filtered off and dried at 100°. Ignite the salt to give Pt sponge, dissolve the Pt sponge in aqua regia, boil to$ 

dryness, dissolve in concentrated HCl, boil to dryness again and repeat the process. Protect from light. [Hickers J Am Chem Soc 43 1268 1921; Org Synth Coll Vol I 463, 466 1941; Bruce J Am Chem Soc 58 687 1936.]

Hexaethyldisiloxane [924-49-0] M 246.5, b 114-115°/16mm, 235.5°/760mm, d 0.8443, n 1.4330. Distil in a vacuum, but can be distilled at atmospheric pressure without decomposition. It is characterised by completely dissolving in conc H<sub>2</sub>SO<sub>4</sub>. [J Chem Soc 3077 1950.]

2,2,4,4,6,6-Hexamethylcyclotrisiloxane [1009-93-4] M 219.5, m -10°, b 81-82°/19 mm, 111-112°/85mm, 188°/756mm, d 0.9196, n 1.448. Purified by fractional distillation at atmospheric pressure until the temperature reaches 200°. The residue in the flask is mostly octamethylcyclotetrasilazane. [J Am Chem Soc 70 3888 1948.]

**Hexamethyldisilane** [1450-14-2] **M 164.4, m 9-12°, b 113.1°/750mm, d 0.7272, n 1.4229.** Most likely impurity is trimethylchlorosilane (*cf* boiling point). Wash with H<sub>2</sub>O, cold conc H<sub>2</sub>SO<sub>4</sub>, H<sub>2</sub>O again then aqueous NaHCO<sub>3</sub>, dry over CaSO<sub>4</sub> and fractionate at atmospheric pressure. [*J Chem Soc* 2811 1958.] Grossly impure sample (25% impurities) was purified by repeated spinning band distn. This lowered the impurity level to 500 ppm. The main impurity was identified as 1-hydroxypentamethyldisilane.

Hexamethyldisilazane (HMDS) [999-97-3] M 161.4, b 125-125.6°/atm, 126°/760mm, d 0.7747, n 1.407. Possible impurity is Me<sub>3</sub>SiCl. Wash well with pet ether and fractionate through a vacuum jacketed column packed with Helipac using a reflux ratio of 10:1. [J Org Chem 23 50 1958.]

Hexamethyldisiloxane [107-46-0] M 162.4, b 99.4°/760mm, 100.4°/764mm, d 0.7633, n 1.3777. Fractionally distilled through a column packed with glass helices with *ca* 15 theoretical plates. [*J Am Chem Soc* 76 2672 1954; *J Gen Chem USSR (Engl ed)* 25 469 1955.]

**Hexamethylditin** (hexamethyldistannane) [661-69-8] M 327.6, m 23.5°, b 85-88°/45 mm, 182°/756mm,  $d^{25}$  1.57. Wash with H<sub>2</sub>O and extract with <sup>\*</sup>C<sub>6</sub>H<sub>6</sub>, dry by filtering through powdered Na<sub>2</sub>SO<sub>4</sub>, remove <sup>\*</sup>C<sub>6</sub>H<sub>6</sub> on a rotary evaporator and fractionally dist the oily residue under vacuum (b 85-88°/45mm). It boils at ca 182° at atmospheric press but it cannot be distilled in air because the hot vapours flash in the condenser. [J Am Chem Soc 47 2361 1925, 63 2509 1941; Trans Faraday Soc 53 1612 1957.]

Hexamethylphosphoric triamide (HMPA) [680-31-9] M 179.2, f 7.2°, b 68-70°/1 mm, 235°/760mm, d 1.024, n 1.460. The industrial synthesis is usually by treatment of POCl<sub>3</sub> with excess of dimethylamine in isopropyl ether. Impurities are water, dimethylamine and its hydrochloride. It is purified by refluxing over BaO or CaO at about 4mm pressure in an atmosphere of nitrogen for several hours, then distd from sodium at the same pressure. The middle fraction (b ca 90°) is collected, refluxed over sodium under reduced pressure under nitrogen and distd. It is kept in the dark under nitrogen, and stored in solid CO<sub>2</sub>. Can also be stored over 4A molecular sieves.

Alternatively, it is distd under vacuum from  $CaH_2$  at 60° and crystd twice in a cold room at 0°, seeding the liquid with crystals obtained by cooling in liquid nitrogen. After about two-thirds frozen, the remaining liquid is drained off [Fujinaga, Izutsu and Sakara *Pure Appl Chem* 44 117 1975]. For tests of purity see Fujinaga et al. in *Purification of Solvents*, Coetzee Ed., Pergamon Press, Oxford, 1982. For efficiency of desiccants in drying HMPT see Burfield and Smithers [J Org Chem 43 3966 1978; Sammes et al. J Chem Soc, Faraday Trans 1 281 1986]. CARCINOGEN.

Hexamethylphosphorous triamide (HMPT) [1608-26-0] M 163.2, m 7.2°, b 49-51°/12mm, 162-164°/12mm, d 0.989, n 1.466. It may contain more than 1% of phosphoric triamide. The yellow oil is first distd at atm press then under reduced press and stored under  $N_2$ . It is air sensitive, TOXIC, should not be inhaled and is absorbed through the skin. [Mark Org Synth Coll Vol V 602 1973.]

Hexamminecobalt(III) chloride [10534-89-1] M 267.5. Crystd from warm water (8mL/g) by cooling. [Bjerrum and McReynolds *Inorg Synth* 2 217 1946.]

Hexammineruthenium(III) chloride [14282-91-8] M 309.6. Crystd twice from 1M HCl.

Hexarhodium hexadecacarbonyl [28407-51-4] M 1065.6, m 220°(dec, in air), d 2.87. Slowly loses CO when heated in air; may be regenerated by heating at 80-200° in the presence of CO at 200atm pressure for 15h, preferably in the presence of Cu. Forms black crystals which are insoluble in hexane. It has bands at 2073, 2026 and 1800cm<sup>-1</sup> in the IR. [Z Anorg Allg Chem 251 96 1963; J Am Chem Soc 85 1202 1963; Tetrahedron Lett 22 1783 1981.]

Hydrazine (anhydrous) [302-01-2] M 32.1, f 1.5-2.0°, b 47°/26mm, 56°/71mm, 113-113.5°/atm, n 1.470, d 1.91,  $pK_1^{25}$  -0.88,  $pK_2^{25}$ 8.11. Hydrazine hydrate is dried by refluxing with an equal weight of KOH pellets for 3h, then distilled from fresh NaOH or BaO in a current of dry N<sub>2</sub>.

Hydrazine dihydrochloride [5341-61-7] M 105.0, m 198°, d 1.42. Crystd from aqueous EtOH and dried under vacuum over CaSO<sub>4</sub>.

Hydrazine monohydrochloride [2644-70-4] M 68.5, m 89°. Prepared by dropwise addition of cold conc HCl to cold liquid hydrazine in equimolar amounts. The crystals were harvested from water and were twice recrystd from absolute MeOH and dried under vacuum. [Kovack et al. J Am Chem Soc 107 7360 1985.]

Hydriodic acid [10034-85-2] M 127.9, b 127°(aq azeotrope), d 1.701,  $pK^{25}$  -8.56. Iodine can be removed from aqueous HI, probably as the amine hydrogen triiodide, by three successive extractions using a 4% soln of Amberlite LA-2 (a long-chain aliphatic amine) in CCl<sub>4</sub>, toluene or pet ether (10mL per 100mL of acid). [Davidson and Jameson Chem Ind (London) 1686 1963.] Extraction with tributyl phosphate in CHCl<sub>3</sub> or other organic solvents is also suitable. Alternatively, a De-acidite FF anion-exchange resin column in the OH<sup>-</sup>-form using 2M NaOH, then into its 1<sup>-</sup>-form by passing dilute KI soln, can be used. Passage of an HI solution under CO<sub>2</sub> through such a column removes polyiodide. The column can be regenerated with NaOH. [Irving and Wilson Chem Ind (London) 653 1964]. The earlier method was to reflux with red phosphorus and distil in a stream of N<sub>2</sub>. The colourless product was stored in ampoules in the dark [Bradbury J Am Chem Soc 74 2709 1952; Inorg Synth 1 157 1939]. Fumes in moist air. HARMFUL VAPOURS.

Hydrobromic acid [10035-10-6] M 80.9, b 125°(aq azeotrope, 47.5% HBr), d 1.38 (34% HBr), pK<sup>25</sup> -8.69. A soln of aqueous HBr ca 48% (w/w, constant boiling) was distilled twice with a little red phosphorus, and the middle half of the distillate was taken. (The azeotrope at 760mm contains 47.8% (w/w) HBr.) [Hetzer, Robinson and Bates J Phys Chem 66 1423 1962]. Free bromine can be removed by Irvine and Wilson's method for HI (see above), except that the column is regenerated by washing with an ethanolic solution of aniline or styrene. Hydrobromic acid can also be purified by aerating with H<sub>2</sub>S, distilling and collecting the fraction boiling at 125-127°. [Inorg Synth 1 155 1939.] HARMFUL VAPOURS.

Hydrochloric acid [7647-01-0] M 36.5, b 108.6° (aq azeotrope, 20.2% HCl), d 1.09(20%),  $pK^{25}$ -6.1. Readily purified by fractional distillation as constant boiling point acid, following dilution with H<sub>2</sub>O. The constant-boiling fraction contains 1 mole of HCl in the following weights of distillate at the stated pressures: 179.555g (730mm), 179.766g (740mm), 179.979 (750mm), 180.193 (760mm), 180.407 (770mm) [Foulk and Hollingsworth J Am Chem Soc 45 1220 1923..] HARMFUL VAPOURS.

Hydrofluoric acid [7664-39-3] M 20.0, b 112.2°(aq azeotrope, 38.2% HF), d 1.15 (47-53% HF), pK<sup>25</sup> 3.21. Freed from lead (Pb ca 0.002ppm) by co-precipitation with  $SrF_2$ , by addition of 10mL of 10%  $SrCl_2$  soln per kilogram of the conc acid. After the ppte has settled, the supernatant is decanted through a filter in a hard-rubber or paraffin lined-glass vessel [Rosenqvist Am J Sci 240 358 1942. Pure aqueous HF solutions (up to 25M) can be prepared by isothermal distn in polyethylene, polypropylene or platinum apparatus [Kwestroo and Visser Analyst 90 297 1965]. HIGHLY TOXIC.

**Hydrogen** [1333-74-0] **M 2.0, m -259.1°, -252.9°.** Usually purified by passage through suitable absorption train. Carbon dioxide is removed with KOH pellets, soda-lime or NaOH pellets. Oxygen is removed with a "De-oxo" unit or by passage over Cu heated to 450-500°, Cu on Kieselguhr at 250°. Passage over a mixture of  $MnO_2$  and CuO (Hopcalite) oxidises any CO to CO<sub>2</sub> (which is removed as above). Hydrogen can be dried by passage through dried silica-alumina at -195°, through a dry-ice trap followed by a liquid-N<sub>2</sub> trap

packed with glass wool, through  $CaCl_2$  tubes, or through  $Mg(ClO_4)_2$  or  $P_2O_5$ . Other purification steps include passage through a hot palladium thimble [Masson J Am Chem Soc 74 4731 1952], through an activatedcharcoal trap at -195°, and through non-absorbent cotton-wool filter or small glass spheres coated with a thin layer of silicone grease. Potentially VERY EXPLOSIVE in air.

Hydrogen bromide (anhydrous) [10035-10-6] M 80.9. Dried by passage through  $Mg(ClO_4)_2$  towers. This procedure is hazardous, see Stoss and Zimmermann [Ind Eng Chem 17 70 1939]. Shaken with mercury, distd through a -78° trap and condensed at -195°/10<sup>-5</sup>mm. Fumes in moist air. HARMFUL VAPOURS.

**Hydrogen chloride** [7647-01-0] **M 36.5.** Passed through conc  $H_2SO_4$ , then over activated charcoal and silica gel. Fumes in moist air. Hydrogen chloride in gas cylinder include ethylene, 1,1-dichloroethane and ethyl chloride. The latter two may be removed by fractionating the HCl through a trap cooled to -112°. Ethylene is difficult to remove. Fumes in moist air. **HARMFUL VAPOURS.** 

**Hydrogen cyanide (anhydrous)** [74-90-8] M 27.0, b 25.7°,  $pK^{25}$  9.21 (aq acid). Prepared from NaCN and H<sub>2</sub>SO<sub>4</sub>, and dried by passage through H<sub>2</sub>SO<sub>4</sub> and over CaCl<sub>2</sub>, then distilled in a vacuum system and degassed at 77°K before use [Arnold and Smith J Chem Soc, Faraday Trans 2 77 861 1981]. Cylinder HCN may contain stabilisers against explosive polymerisation, together with small amounts of H<sub>3</sub>PO<sub>4</sub>, H<sub>2</sub>SO<sub>4</sub>, SO<sub>2</sub>, and water. It can be purified by distn over P<sub>2</sub>O<sub>5</sub>, then frozen in Pyrex bottles at Dry-ice temperature for storage. **EXTREMELY POISONOUS.** 

**Hydrogen fluoride (anhydrous)** [7664-39-3] **M 20.0, b 19.4°.** Can be purified by trap-to-trap distn, followed by drying over  $CoF_2$  at room temperature and further distn. Alternatively, it can be absorbed on NaF to form NaHF<sub>2</sub> which is then heated under vacuum at 150° to remove volatile impurities. The HF is regenerated by heating at 300° and stored with  $CoF_3$  in a nickel vessel, being distilled as required. (Water content *ca* 0.01%.) To avoid contact with base metal, use can be made of nickel, polychlorotrifluoroethylene and gold-lined fittings [Hyman, Kilpatrick and Katz J Am Chem Soc 79 3668 1957]. HIGHLY TOXIC.

**Hydrogen iodide (anhydrous)** [10034-85-2] **M 127.9, b -35.5°.** After removal of free iodine from aqueous HI, the solution is frozen, then covered with  $P_2O_5$  and allowed to melt under vacuum. The gas evolved is dried by passage through  $P_2O_5$  on glass wool. It can be freed from iodine contamination by repeated fractional distillation at low temperatures. Fumes in moist air. **HARMFUL VAPOURS.** 

Hydrogen ionophore II (ETH 1907) (4-nonadecylpyridine - Proton ionophore) [70268-36-9] M 345.6, b 180°/0.07mm, pK<sub>Est</sub>~ 6.0. Dissolve the waxy solid (*ca* 60g) in CHCl<sub>3</sub> (200mL), wash with H<sub>2</sub>O (3 x 200mL), dry and evaporate to dryness then distil in vacuum. A waxy solid is formed on cooling the distillate. UV: 257nm ( $\epsilon$  1.86 x 10<sup>3</sup> M<sup>-1</sup>cm<sup>-1</sup>), 308nm ( $\epsilon$  1.7 x 10<sup>2</sup> M<sup>-1</sup>cm<sup>-1</sup>). [IR, NMR UV: *Inorg Chem* 18 2160 1979.]

Hydrogen ionophore III (N, N-dioctadecyl methylamine) [4088-22-6] M 536.0, m 40°, 44-46°, 48-49°, b 252-259°, pK<sub>Est</sub>~ 10. It can be distd at high vacuum; but dissolving in \*C<sub>6</sub>H<sub>6</sub>, filtering and evaporating gives a waxy solid suitable for electrode use. It recrystallises from Me<sub>2</sub>CO. [*Chem Ber* 69 60 1936; *Talanta* 34 435 1987.]

Hydrogen ionophore IV ETH 1778 (octadecyl isonicotinate) [103225-02-1] M 375.6, m 57.5°, pK<sub>Est</sub>~ 3.5 . Dissolve in Et<sub>2</sub>O and wash 3 times with H<sub>2</sub>O. Dry, evaporate, and recrystallise the residue from EtOAc/hexane (4:1). [*Anal Chem* 58 2285 1986.]

Hydrogen peroxide [7722-84-1] M 34.0, d 1.110, pK<sup>25</sup> 11.65. The 30% material has been steam distilled using distilled water. Gross and Taylor  $[J \ Am \ Chem \ Soc 72 \ 2075 \ 1950]$  made 90% H<sub>2</sub>O<sub>2</sub> approximately 0.001M in NaOH and then distilled under its own vapour pressure, keeping the temperature below 40°, the receiver being cooled with a Dry-ice/isopropyl alcohol mush. The 98% material has been rendered anhydrous by repeated fractional crystn in all-quartz vessels. EXPLOSIVE IN CONTACT WITH ORGANIC MATERIAL.

Hydrogen sulfide [7783-06-4] M 34.1, b -59.6°,  $pK_1^{25}$  7.05,  $pK_2^{25}$  12.89. Washed, then passed through a train of flasks containing saturated Ba(OH)<sub>2</sub> (2x), water (2x), and dilute HCl [Goates et al. J Am Chem Soc 73 707 1951]. HIGHLY POISONOUS.

Hydroquinone-2-sulfonic acid K salt [21799-87-1] M 228.3, m 250°(dec),  $pK_{Est(1)} \sim 1$ ,  $pK_{Est(2)} \sim 8.5$ ,  $pK_{Est(3)} \sim 11$ . Recrystd from water.

Hydroxylamine [7803-49-8] M 33.0, m 33.1°, b 56.5°/22mm, d 1.226, pK<sup>20</sup> 5.96. Crystd from *n*-butanol at -10°, collected by vacuum filtration and washed with cold diethyl ether. Harmful vapours.

Hydroxylamine hydrochloride [5470-11-1] M 69.5, m 151°. Crystallised from aqueous 75% ethanol or boiling methanol, and dried under vacuum over CaSO<sub>4</sub> or  $P_2O_5$ . Has also been dissolved in a minimum of water and saturated with HCl; after three such crystns it was dried under vacuum over CaCl<sub>2</sub> and NaOH.

Hydroxylamine sulfate [10039-54-0] M 164.1, m 170°(dec). Crystallised from boiling water (1.6mL/g) by cooling to 0°.

**Hydroxylamine-O-sulfonic acid** [2950-43-8] **M** 113.1, **m** 210-211°, 215°(dec),  $pK^{45}$  1.48. Stir the solid vigorously with anhydrous Et<sub>2</sub>O and filter off using large volumes of dry Et<sub>2</sub>O. Drain dry at the pump for 5min and then for 12-14h in a vacuum. Store in a vacuum desiccator/conc H<sub>2</sub>SO<sub>4</sub>. Determine the purity by oxidation of iodide to I<sub>2</sub>. Must be stored in a dry atmosphere at 0-4°. It decompose slowly in H<sub>2</sub>O at 25° and more rapidly above this temperature. [*Inorg Synth* 5 122 1957.]

Hydroxynaphthol Blue tri-Na salt [63451-35-4] M 620.5, m dec on heating,  $pK_{Est} < 0$ . Crude material was treated with hot EtOH to remove soluble impurities, then dissolved in 20% aqueous MeOH and chromatographed on a cellulose powder column with propanol:EtOH:water (5:5:4) as eluent. The upper of three zones was eluted to give the pure dye which was ppted as the monosodium salt trihydrate by adding conc HCl to the concentrated eluate [Ito and Ueno Analyst 95 583 1970].

**4-Hydroxy-3-nitrobenzenearsonic acid** [121-19-7] **M 263.0.** See 2-nitrophenol-4-arsonic acid on p. 446.

Hydroxyurea [127-07-1] M 76.1, m 70-72° (unstable form), m 133-136°, 141° (stable form), pK 10.6. Recrystallise from absolute EtOH (10g in 150mL). Note that the rate of solution in boiling EtOH is slow (15-30 min). It should be stored in a cool dry place but some decomposition could occur after several weeks. [Org Synth Coll Vol V 645 1973.] It is very soluble in H<sub>2</sub>O and can be crystd from Et<sub>2</sub>O. [Acta Chem Scand 10 256 1956.]

Hypophosphorous acid (Phosphinic acid) [6303-21-5] M 66.0, m 26.5°,  $d_4^{30}$  1.217, 1.13 and 1.04 for 50, 30-32, and 10% aq solns resp, pK<sup>25</sup> 1.31 (H<sub>3</sub>PO<sub>2</sub>). Phosphorous acid is a common contaminant of commercial 50% hypophosphorous acid. Jenkins and Jones [*J Am Chem Soc* 74 1353 *1952*] purified this material by evaporating about 600mL in a 1L flask at 40°, under reduced pressure (in N<sub>2</sub>), to a volume of about 300mL. After the soln was cooled, it was transferred to a wide-mouthed Erlenmeyer flask which was stoppered and left in a Dry-ice/acetone bath for several hours to freeze (if necessary, with scratching of the wall). When the flask was then left at *ca* 5° for 12h, about 30-40% of it liquefied, and again filtered. This process was repeated, then the solid was stored over Mg(ClO<sub>4</sub>)<sub>2</sub> in a vacuum desiccator in the cold. Subsequent crystns from *n*-butanol by dissolving it at room temperature and then cooling in an ice-salt bath at -20° did not appear to purify it further. The free acid forms deliquescent crystals **m** 26.5°, and is soluble in H<sub>2</sub>O and EtOH. The NaH<sub>2</sub>PO<sub>2</sub> salt can be purified through an anion exchange resin [*Z Anorg Allg Chem* 260 267 *1949*.]

**Indigocarmine** (2[1,3-dihydro-3-oxo-5-sulfo-2*H*-indol-2-ylidene]-2,3-dihydro-3oxo-1*H*-indole-5-sulfonic acid di-Na salt) [860-22-0] M 466.4, pK<sub>1</sub><sup>20</sup> 2.8, p K<sub>2</sub><sup>20</sup> 12.3. Its

solubility in  $H_2O$  is 1g/100mL at 25°. Could be purified by dissolving in  $H_2O$ , filtering and adding EtOH to cause the salt to separate. Wash the solid with EtOH,  $Et_2O$  and dry *in vacuo*. [Vörlander and Schubert Chem Ber 34 1860 1901; UV: Smit et al. Anal Chem 27 1159 1955; Preisler et al. J Am Chem Soc 81 1991 1959.]

Indium [7440-74-6] M 114.8, m 156.6°, b 2000°, d 7.31. Before use, the metal surface can be cleaned with dilute HNO<sub>3</sub>, followed by a thorough washing with water and an alcohol rinse.

Indium (III) chloride [10025-82-8] M 211.2, m 586°, d 4.0,  $pK_1^{25}$  3.54,  $pK_2^{25}$  4.28,  $pK_3^{25}$  5.16 (for aquo In<sup>3+</sup>). The anhydrous salt forms yellow deliquescent crystals which can be sublimed at 600° in the presence of Cl<sub>2</sub>/N<sub>2</sub> (1:1) {does not melt}. It is resublimed in the presence of Cl<sub>2</sub>/N<sub>2</sub> (1:10) and finally heated to 150° to expel excess Cl<sub>2</sub>. It is soluble in H<sub>2</sub>O and should be stored in a tightly closed container. [*J Am Chem Soc* 55 1943 1933.]

Indium (III) oxide [1312-43-2] M 277.6, d 7.18, m sublimes at 850°. Wash with  $H_2O$  and dry below 850°. Volatilises at 850° and dissolves in hot mineral acids to form salts. Store away from light because it darkens due to formation of In.

Indium sulfate [13464-82-9] M 517.8. Crystd from dilute aqueous H<sub>2</sub>SO<sub>4</sub>.

Indium (III) sulfate  $(5H_2O)$  [17069-79-3] M 607.9, d 3.44. Dissolve in strong H<sub>2</sub>SO<sub>4</sub> and slowly evaporate at *ca* 50°. Wash crystals with glacial AcOH and then heat in a furnace at a temperature of 450-500° for 6h. Sol in H<sub>2</sub>O is 5%. The pentahydrate is converted to an anhydrous *hygroscopic* powder on heating at 500° for 6h; but heating above this temperature over N<sub>2</sub> yields the oxide sulfate. Evaporation of neutral aqueous solutions provides basic sulfates. [*J Am Chem Soc* 55 1943 1933, 58 2126 1936.]

**Iodic acid** [7782-68-5] **M 175.9, m 118°(dec), d 4.628, pK<sup>25</sup> 0.79.** Dissolve in the minimum volume of hot dilute HNO<sub>3</sub>, filter and evaporate in a vacuum desiccator until crystals are formed. Collect crystals and wash with a little cold H<sub>2</sub>O and dry in air in the dark. Soluble in H<sub>2</sub>O: 269g/100mL at 20° and 295g/100mL at 40°. Soluble in dilute EtOH and darkens on exposure to light. It is converted to HIO<sub>3</sub>.I<sub>2</sub>O<sub>5</sub> on heating at 70°, but at 220° complete conversion to HIO<sub>3</sub> occurs. [*J Am Chem Soc* 42 1636 1920, 53 44 1931.]

**Iodine** [7553-56-2] M 253.8, m 113.6°. Usually purified by vacuum sublimation. Preliminary purifications include grinding with 25% by weight of KI, blending with 10% BaO and subliming; subliming with CaO; grinding to a powder and treating with successive portions of H<sub>2</sub>O to remove dissolved salts, then drying; and crystn from \*benzene. Barrer and Wasilewski [*Trans Faraday Soc* 57 1140 1961] dissolved I<sub>2</sub> in conc KI and distilled it, then steam distilled three times, washing with distilled H<sub>2</sub>O. Organic material was removed by sublimation in a current of O<sub>2</sub> over platinum at about 700°, the iodine being finally sublimed under vacuum. HARMFUL VAPOURS.

Iodine monobromide [7789-33-5] M 206.8, m 42°. Purified by repeated fractional crystallisation from its melt.

Iodine monochloride [7790-99-0] M 162.4, m 27.2°. Purified by repeated fractional crystallisation from its melt.

**Iodine pentafluoride** [7783-66-6] M 221.9, m -8.0°, b 97°. Rogers et al. [J Am Chem Soc 76 4843 1954] removed dissolved iodine from IF<sub>5</sub> by agitating with a mixture of dry air and ClF<sub>3</sub> in a Fluorothene beaker using a magnetic stirrer. The mixture was transferred to a still and the more volatile impurities were pumped off as the pressure was reduced below 40mm. The still was gradually heated (kept at 40mm) to remove the ClF<sub>3</sub> before IF<sub>5</sub> distilled. Stevens [J Org Chem 26 3451 1961] pumped IF<sub>5</sub> under vacuum from its cylinder, trapping it at -78°, then allowing it to melt in a stream of dry N<sub>2</sub>. HARMFUL VAPOURS.

Iodine trichloride [865-44-1] M 233.3, m 33°, b 77°(dec). Purified by sublimation at room temperature.

**Iodomethyl trimethylsilane** [4206-67-1] M 214.1, b 139.5°/744mm, d 1.44,  $n_D^{25}$  1.4917. If slightly violet in colour wash with aqueous 1% sodium metabisulfite, H<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub> and fractionally distil at atmospheric pressure. [J Am Chem Soc 68 481 1946.]

Iodotrimethylsilane (trimethylsilyl iodide, TMSI) [16029-98-4] M 200.1, b 106.8°/742mm, 107.5°/760mm, d 1.470. Add a little antimony powder and fractionate with this powder in the still. Stabilise with 1% wt of Cu powder. [J Chem Soc 3077 1950.]

Iridium [7439-88-5] M 192.2, m 2450°, b ~4500°, d 22.65. It is a silver white hard solid which oxidises on the surface in air. Scrape the outer tarnished layer until silver clear and store under paraffin. Stable to acids but dissolves in aqua regia. [Chem Rev 32 277 1943.]

**Iridium (IV) chloride hydrate (hexachloroiridic acid)**  $[16941-92-7 (6H_2O); 207399-11-9 (xH_2O)]$ **M 334.0+H<sub>2</sub>O.** If it contains nitrogen then repeatedly concentrate a conc HCl solution until free from nitrogen, and dry free from HCl in a vac over CaO until crystals are formed. The solid is very hygroscopic. [J Am Chem Soc 53 884 1931; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1592 1965.]

Iron (wire) [7439-89-6] M 55.9, m 1535°. Cleaned in conc HCl, rinsed in de-ionised water, then reagent grade acetone and dried under vacuum.

**Iron ennecarbonyl** (di-iron nonacarbonyl) [15321-51-4] M 363.7, m 100°(dec). Wash with EtOH and Et<sub>2</sub>O and dry in air. Sublimes at 35° at high vacuum. Dark yellow plates stable for several days when kept in small amounts. Large amounts, especially when placed in a desiccator spontaneously *ignite* in a period of one day. It decomposes in moist air. It is insoluble in hydrocarbon solvents but forms complexes with several organic compounds. [*J Am Chem Soc* 72 1107 1950; *Chem Ber* 60 1424 1927.]

Iron (III) meso-5,10,15,20-tetraphenylporphine chloride complex [16456-81-8] M 704.0. Crystallise by extraction from a thimble (Soxhlet) with CHCl<sub>3</sub>. Concentrate the extract to ca 10mL and add ca 80mL of hot MeOH. Dark blue crystals separate on cooling. It can be recrystallised several times from CHCl<sub>3</sub>-MeOH. Avoid prolonged heating. It is quite soluble in organic solvents but insoluble in pet ether. [J Am Chem Soc 70 1808 1948; UV: 73 4315 1951.]

**Iron pentacarbonyl (pentacarbonyl iron)** [13463-40-6] M 195.9, m -20°, b 102.8°/749 mm, 103°/760 mm, n 1.520, d 1.490. It is a pale yellow viscous liq which is PYROPHORIC and readily absorbed by the skin. HIGHLY TOXIC (protect from light and air). It should be purified in a vacuum line by distilling and collecting in a trap at -96° (toluene-Dry ice slush). It has been distd at atm pressure (use a very efficient fume cupboard). At 180°/atm it decomps to give Fe and CO. In UV light in pet ether it forms Fe<sub>2</sub>(CO)<sub>9</sub>. [Hagen et al. *Inorg Chem* 17 1369 1978; Ewens et al. *Trans Faraday Soc* 35 6811 1939.]

Isopropyldimethyl chlorosilane [3634-56-8] M 140.7, b 109.8-110.0°/738mm, d 0.88, n 1.4158. Probable impurity is Me<sub>3</sub>SiCl (b 56.9°/783mm) which can be removed by efficient fractional distillation. [J Am Chem Soc 76 801 1954.]

(2,3-O-Isopropylidene)-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane (DIOP) [4R,5S-(-)-32305-98-9; 4S,5R-(+)- 37002-48-5] M 498.5, m 88-90°,  $[\alpha]_D^{19}$  (-) and (+) 26° (c 2.3, CHCl<sub>3</sub>), pK<sub>Est</sub> ~ 4.5. It has been recrystd from \*C<sub>6</sub>H<sub>6</sub>-pet ether. After 2 recrystns from EtOH it was pure by TLC on silica gel using Me<sub>2</sub>CO-hexane as solvent. [Kagan and Dang J Am Chem Soc 94 6429 1972.]

## Lanthanide shift reagents see p. 277 in Chapter 4.

Lanthanum [7439-91-0] M 138.9, m 920°, b 3470°, d 6.16. White metal that slowly tarnishes in air due to oxidation. Slowly decomposed by  $H_2O$  in the cold and more rapidly on heating to form the

hydroxide. The metal is cleaned by scraping off the tarnished areas until the shiny metal is revealed and stored under oil or paraffin. It burns in air at 450°.

Lanthanum triacetate [917-70-4] M 316.0,  $pK_1^{25}$  9.06 (for aquo La<sup>3+</sup>). Boil with redistilled Ac<sub>2</sub>O for 10min (does not dissolve and is a white solid). Cool, filter, wash with Ac<sub>2</sub>O and keep in a vacuum desiccator (NaOH) till free from solvent. [J Indian Chem Soc 33 877 1956.]

*N*-Lauroyl-*N*-methyltaurine sodium salt (sodium *N*-decanoyl-*N*-methy-2-aminoethane sulfonate) [4337-75-1] M 343.5,  $pK_{Est} \sim 1.5$ . Prepared from methyldecanoate (at 180° under N<sub>2</sub>) or decanoyl chloride and sodium *N*-methylcthane sulfonate and purified by dissolving in H<sub>2</sub>O and precipitating by addition of Et<sub>2</sub>O. Decomposes on heating. [Desseigne and Mathian *Mém Services Chim Etat Paris* 31 359 1944, Chem Abstr 41 705 1947.]

Lead II acetate [301-04-2 (anhydr); 6080-56-4 (3H<sub>2</sub>O)] M 325.3, m 280°,  $pK_1^{25}$  7.1 (for Pb<sup>2+</sup>),  $pK_2^{25}$  10.1 (HPbO<sub>2</sub><sup>-</sup>),  $pK_3^{25}$  10.8 (PbO<sub>2</sub><sup>2-</sup>). Crystallised twice from anhydrous acetic acid and dried under vacuum for 24h at 100°.

Lead (bis-cyclopentadienyl) [1294-74-2] M 337.4. Purified by vacuum sublimation. Handled and stored under  $N_2$ .

Lead (II) bromide [10031-22-8] M 367.0, m 373°. Crystallised from water containing a few drops of HBr (25mL of water per gram PbBr<sub>2</sub>) between 100° and 0°. A neutral solution was evaporated at 110° and the crystals that separated were collected by rapid filtration at 70°, and dried at 105° (to give the *monohydrate*). To prepare the anhydrous bromide, the hydrate is heated for several hours at 170° and then in a Pt boat at 200° in a stream of HBr and H<sub>2</sub>. Finally fused [Clayton et al. J Chem Soc, Faraday Trans 1 76 2362 1980].

Lead (II) chloride [7758-95-4] M 278.1, m 501°. Crystallised from distilled water at 100° (33mL/g) after filtering through sintered-glass and adding a few drops of HCl, by cooling. After three crystns the solid was dried under vacuum or under anhydrous HCl vapour by heating slowly to 400°.

Lead diethyldithiocarbamate [17549-30-3] M 503.7,  $pK_1^{25}$  3.36 (for N, N-diethyldithiocarbamate). Wash with H<sub>2</sub>O and dry at 60-70°, or dissolve in the min vol of CHCl<sub>3</sub> and add the same vol of EtOH. Collect the solid that separates and dry as before. Alternatively, recryst by slow evaporation of a CHCl<sub>3</sub> soln at 70-80°. Filter the crystals, wash with H<sub>2</sub>O until all Pb<sup>2+</sup> ions are eluted (check by adding chromate) and then dry at 60-70° for at least 10h. [Justus Liebigs Ann Chem 49 1146 1977.]

Lead (II) formate [811-54-4] M 297.3, m 190°. Crystd from aqueous formic acid.

Lead (II) iodide [10101-63-0] M 461.0, m 402°. Crystd from a large volume of water.

Lead monoxide [1317-36-8] M 223.2, m 886°. Higher oxides were removed by heating under vacuum at 550° with subsequent cooling under vacuum. [Ray and Ogg J Am Chem Soc 78 5994 1956.]

Lead nitrate [10099-74-8] M 331.2, m 470°. Ppted twice from hot (60°) conc aqueous soln by adding HNO<sub>3</sub>. The ppte was sucked dry in a sintered-glass funnel, then transferred to a crystallising dish which was covered by a clock glass and left in an electric oven at 110° for several hours [Beck, Singh and Wynne-Jones Trans Faraday Soc 55 331 1959]. After 2 recrystns of ACS grade no metals above 0.001 ppm were detected.

Lead tetraacetate [546-67-8] M 443.4, m 175-180°,  $pK_1$  1.8,  $pK_2$  3.2,  $pK_3$  5.2,  $pK_4$  6.7. Dissolved in hot glacial acetic acid, any lead oxide being removed by filtration. White crystals of lead tetraacetate separated on cooling. Stored in a vacuum desiccator over  $P_2O_5$  and KOH for 24h before use.

Lissamine Green B {1-[bis-(4,4'-dimethylaminophenyl)methyl]-2-hydroxynaphthalene-3,6disulfonic acid sodium salt, Acid Green 50} [3087-16-9] M 576.6, m >200°(dec), CI 44090,  $\lambda$ max 633nm. Crystd from EtOH/water (1:1, v/v).

**Lissapol C (mainly sodium salt of 9-octadecene-1- sulfate)** [2425-51-6]. Refluxed with 95% EtOH, then filtered to remove insoluble inorganic electrolytes. The alcohol solution was then concentrated and the residue was poured into dry acetone. The ppte was filtered off, washed in acetone and dried under vacuum. [Biswas and Mukerji J Phys Chem 64 1 1960].

Lissapol LS (mainly sodium salt of anisidine sulfate) [28903-20-0]. Refluxed with 95% EtOH, then filtered to remove insoluble inorganic electrolytes. The alcohol solution was then concentrated and the residue was poured into dry acetone. The ppte was filtered off, washed in acetone and dried under vacuum. [Biswas and Mukerji J Phys Chem 64 1 1960].

Lithium (metal) [7439-93-2] M 6.9, m 180.5°, b 1342°, d 0.534. After washing with pet ether to remove storage oil, lithium was fused at 400° and then forced through a 10-micron stainless-steel filter with argon pressure. It was again melted in a dry-box, skimmed, and poured into an iron distillation pot. After heating under vacuum to 500°, cooling and returning to the dry-box for a further cleaning of its surface, the lithium was distd at 600° using an all-iron distn apparatus [Gunn and Green J Am Chem Soc 80 4782 1958].

Lithium acetate (2H<sub>2</sub>O) [546-89-4] M 102.0, m 54-56°. Crystallised from EtOH (5mL/g) by partial evaporation.

Lithium aluminium hydride [16853-85-3] M 37.9, m 125°(dec). Extracted with Et<sub>2</sub>O, and, after filtering, the solvent was removed under vacuum. The residue was dried at 60° for 3h, under high vacuum [Ruff J Am Chem Soc 83 1788 1961]. IGNITES in the presence of a small amount of water and reacts EXPLOSIVELY.

Lithium amide [7782-89-0] M 23.0, m 380-400°, d<sup>17.5</sup> 1.178. Purified by heating at 400° while NH<sub>3</sub> is passed over it in the upper of two crucibles (the upper crucible is perforated). The LiNH<sub>2</sub> will drip into the lower crucible through the holes in the upper crucible. The product is cooled in a stream of NH<sub>3</sub>. Protect it from air and moisture, store under N<sub>2</sub> in a clear glass bottle sealed with paraffin. Store small quantities so that all material is used once the bottle is opened. If the colour of the amide is yellow it should be destroyed as it is likely to have oxidised and to **EXPLODE.** On heating above 450° it is decomposed to Li<sub>2</sub>NH which is stable up to 750-800°. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 463 1963; Inorg Synth 2 135 1953.]

Lithium benzoate [553-54-8] M 128.1. from EtOH (13mL/g) by partial evaporation.

Lithium borohydride [16949-15-8] M 21.8, mCrystd 268°, b 380°(dec), d 0.66. Crystd from Et<sub>2</sub>O, and pumped free of ether at 90-100° during 2h [Schaeffer, Roscoe and Stewart J Am Chem Soc 78 729 1956].

Lithium bromide [7550-35-8] M 86.8, m 550°. Crystd several times from water or EtOH, then dried under high vacuum for 2 days at room temperature, followed by drying at 100°.

Lithium carbonate [554-13-2] M 73.9, m 552°, 618°. Crystd from water. Its solubility decreases as the temperature is raised.

Lithium chloride [7447-41-8] M 42.4, m 600°, 723°. Crystd from water (1mL/g) or MeOH and dried for several hours at 130°. Other metal ions can be removed by preliminary crystallisation from hot aqueous 0.01M disodium EDTA. Has also been crystallised from conc HCl, fused in an atmosphere of dry HCl gas, cooled under dry N<sub>2</sub> and pulverised in a dry-box. Kolthoff and Bruckenstein [*J Am Chem Soc* 74 2529 1952] ppted with ammonium carbonate, washed with Li<sub>2</sub>CO<sub>3</sub> five times by decantation and finally with suction, then dissolved in HCl. The LiCl solution was evaporated slowly with continuous stirring in a large evaporating dish, the dry powder being stored (while still hot) in a desiccator over CaCl<sub>2</sub>.

Lithium diisopropylamide [4111-54-0] M 107.1, b 82-84°/atm, 84°/atm, d<sup>22</sup> 0.722, flash point -6°. It is purified by refluxing over Na wire or NaH for 30min and then distilled into a receiver under

 $N_2$ . Because of the low boiling point of the amine a dispersion of NaH in mineral oil can be used directly in this purification without prior removal of the oil. It is **HIGHLY FLAMMABLE**, and is decomposed by air and moisture. [Org Synth 50 67 1970.]

Lithium dodecylsulfate [2044-56-6] M 272.3. Recrystd twice from absolute EtOH and dried under vacuum.

Lithium fluoride [7789-24-4] M 25.9, m 842°, 848°, b 1676°, 1681°, d 2.640. Possible impurities are LiCO<sub>3</sub>, H<sub>2</sub>O and HF. These can be removed by calcining at red heat, then pulverised with a Pt pestle and stored in a paraffin bottle. Solubility in H<sub>2</sub>O is 0.27% at 18°. It volatilises between 1100-1200°. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 235 1963].

Lithium formate (H<sub>2</sub>O) [6108-23-2 ( $H_2O$ ); 556-63-8 (anhydr)] M 70.0, d 1.46. Crystd from hot water (0.5mL/g) by chilling.

Lithium hydride. [7580-67-8] M 7.95, m 680°, d 0.76-0.77. It should be a white powder otherwise replace it. It darkens rapidly on exposure to air and is decomposed by  $H_2O$  to give  $H_2$  and LiOH, and reacts with lower alcohols. One gram in  $H_2O$  liberates 2.8L of  $H_2$  (Could be explosive).

Lithium hydroxide (H<sub>2</sub>O) [1310-66-3 (H<sub>2</sub>O); 1310-65-2 (anhydr)] M 42.0, m 471°, d 1.51, pK<sup>25</sup> 13.82. Crystd from hot water (3mL/g) as the monohydrate. Dehydrated at 150° in a stream of CO<sub>2</sub>-free air.

Lithium iodate [13765-03-2] M 181.9. Crystd from water and dried in a vacuum oven at 60°.

Lithium iodide [10377-51-2] M 133.8, m 469°, b 1171°, d 4.06. Crystd from hot water (0.5mL/g) by cooling in CaCl<sub>2</sub>-ice, or from acetone. Dried under vacuum over  $P_2O_5$  for 1h at 60° and then at 120°.

Lithium methylate (lithium methoxide) [865-34-9] M 38.0. Most probable impurity is LiOH due to hydrolysis by moisture. It is important to keep the sample dry. It can be dried by keeping in a vacuum at 60-80° under dry N<sub>2</sub> using an oil pump for a few hours. Store under N<sub>2</sub> in the cold. It should not have bands above 3000cm<sup>-1</sup>; IR has v<sub>KBr</sub> 1078, 2790, 2840 and 2930cm<sup>-1</sup>. [J Org Chem 21 156 1956.]

Lithium nitrate [7790-69-4] M 68.9, m 253°, d 2.38. Crystd from water or EtOH. Dried at 180° for several days by repeated melting under vacuum. If it is crystallised from water keeping the temperature above 70°, formation of trihydrate is avoided. The anhydrous salt is dried at 120° and stored in a vac desiccator over CaSO<sub>4</sub>. After 99% salt was recrystd 3 times it contained: metal (ppm) Ca (1.6), K (1.1), Mo (0.4), Na (2.2).

Lithium nitrite (H<sub>2</sub>O) [13568-33-7] M 71.0. Crystd from water by cooling from room temperature.

Lithium picrate [18390-55-1] M 221.0. Recrystd three times from EtOH and dried under vacuum at 45° for 48h [D'Aprano and Sesta J Phys Chem 91 2415 1987]. The necessary precautions should be taken in case of EXPLOSION.

Lithium perchlorate [7791-03-9] M 106.4,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from water or 50% aq MeOH. Rendered anhydrous by heating the trihydrate at 170-180° in an air oven. It can then be recrystd twice from acetonitrile and again dried under vacuum [Mohammad and Kosower J Am Chem Soc 93 2713 1971].

Lithium salicylate [552-38-5] M 144.1. Crystd from EtOH (2mL/g) by partial evaporation.

Lithium sulfate (anhydrous) [10377-48-7] M 109.9, loses H<sub>2</sub>O at 130° and m 859°, d 2.21. Crystd from H<sub>2</sub>O (4mL/g) by partial evaporation.

Lithium tetrafluoroborate [14283-07-9] M 93.7, pK<sup>25</sup> 13.82 (Li<sup>+</sup>), pK<sup>25</sup> -4.9 (for HBF<sub>4</sub>). Dissolve in THF just below its solubility, filter from insol material and evap to dryness in a vacuum below

50°. Wash the residue with dry  $Et_2O$ , and pass dry  $N_2$  gas over the solid and finally heat in an oven at 80-90°. Solubility in  $Et_2O$ : 1.9 (1.3)g in 100mL at 25°, in THF: 71g in 100mL at 25°. It is hygroscopic and is an **IRRITANT.** [J Am Chem Soc 74 5211 1952, 75 1753 1953.]

Lithium thiocyanate (lithium rhodanide) [556-65-0] M 65.0,  $pK^{25}$  -1.85 (for HSCN). It crystallises from H<sub>2</sub>O as the dihydrate but on drying at 38-42° it gives the monohydrate. It can be purified by allowing an aqueous soln to crystallise in a vac over P<sub>2</sub>O<sub>5</sub>. The crystals are collected, dried out in vacuum at 80°/P<sub>2</sub>O<sub>5</sub> in a stream of pure N<sub>2</sub> at 110°. [J Chem Soc 1245 1936.]

Lithium trimethylsilanolate (trimethylsilanol Li salt) [2004-14-0] M 96.1, m 120°(dec in air). Wash with Et<sub>2</sub>O and pet ether. Sublimes at 180°/1mm as fine transparent needles. [J Org Chem 17 1555 1952.]

**Magnesium** [7439-95-4] M 24.3, m 651°, b 1100°, d 1.739. Slowly oxidises in moist air and tarnishes. If dark in colour do not use. Shiny solid should be degreased by washing with dry Et<sub>2</sub>O, dry and keep in a N<sub>2</sub> atmosphere. It can be activated by adding a crystal of I<sub>2</sub> in the Et<sub>2</sub>O before drying and storing.

**Magnesium acetate** [142-72-3 (anhydr); 16674-78-5 (4 $H_2O$ )] **M 214.5, m 80°.** Crystd from anhydrous acetic acid, then dried under vacuum for 24h at 100°

Magnesium benzoate  $(3H_2O)$  [553-70-8] M 320.6, m ~200°. Crystd from water (6mL/g) between 100° and 0°.

Magnesium bromide (anhydrous) [7789-48-2] M 184.1, m 711°, d 3.72. Crystd from EtOH.

Magnesium chloride (6H<sub>2</sub>O) [7791-18-6] M 203.3, m ~100°(dec),  $pK_1^{25}$  10.3,  $pK_2^{25}$  12.2 (for Mg<sup>2+</sup> hydrolysis). Crystd from hot water (0.3mL/g) by cooling.

Magnesium dodecylsulfate [3097-08-3] M 555.1. Recrystd three times from EtOH and dried in a vacuum.

**Magnesium ethylate (magnesium ethoxide)** [2414-98-4] **M 114.4.** Dissolve ca 1g of solid in 12.8mL of absolute EtOH and 20mL of dry xylene and reflux in a dry atmosphere (use CaCl<sub>2</sub> in a drying tube at the top of the condenser). Add 10mL of absolute EtOH and cool. Filter solid under dry  $N_2$  and dry in a vacuum. Alternatively dissolve in absolute EtOH and pass through molecular sieves (40 mesh) under  $N_2$ , evap under  $N_2$ , and store in a tightly stoppered container. [J Am Chem Soc **68** 889 1964.]

**Magnesium D-gluconate** [3632-91-5] **M 414.6**,  $[\alpha]_{546}^{20} + 13.5^{\circ}$ ,  $[\alpha]_D^{20} + 11.3^{\circ}$  (c 1, H<sub>2</sub>O). Cryst from dilute EtOH to give *ca* trihydrate, and then dry at 98° in high vacuum. Insol in EtOH and solubility in H<sub>2</sub>O is 16% at 25°.

Magnesium iodate (4H<sub>2</sub>O) [7790-32-1] M 446.2. Crystd from water (5mL/g) between 100° and 0°.

Magnesium iodide [10377-58-9] M 278.1, m 634°. Crystd from water (1.2mL/g) by partial evapn in a desiccator.

**Magnesium ionophore I** (ETH 1117), (N, N'-diheptyl-N, N'-dimethyl-1, 4-butanediamide)[75513-72-3] M 340.6. Purified by flash chromatography (at 40 kPa) on silica and eluting with EtOHhexane (4:1). IR has v(CHCl<sub>3</sub>) 1630cm<sup>-1</sup>. [Helv Chim Acta 63 2271 1980.] It is a good magnesium selectophore compared with Na, K and Ca [Anal Chem 52 2400 1980].

Magnesium ionophore II (ETH 5214), [N,N''-octamethylene-bis(N'-heptyl-N"-methyl methylmalonamide)] [119110-37-1] M 538.8. Reagent (ca 700mg) can be purified by flash chromatography on Silica Gel 60 (30g) and eluting with CH<sub>2</sub>Cl<sub>2</sub>-Me<sub>2</sub>CO (4:1). [Anal Chem 61 574 1989.]

Magnesium lactate [18917-37-1] M 113.4. Crystd from water (6mL/g) between 100° to 0°.

**Magnesium nitrate (6H<sub>2</sub>O)** [13446-18-9] **M 256.4, m ~95°(dec).** Crystd from water (2.5mL/g) by partial evapn in a desiccator. After 2 recrystns ACS grade has: metal (ppm) Ca (6.2), Fe (8.4), K (2), Mo (0.6), Na (0.8), Se (0.02).

**Magnesium perchlorate (Anhydrone, Dehydrite)** [10034-81-8 (anhydr)] M 259.2, m >250°, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from water to give the *hexahydrate* M 331.3 [13346-19-0]. Coll, Nauman and West [J Am Chem Soc 81 1284 1959] removed traces of unspecified contaminants by washing with small portions of Et<sub>2</sub>O and drying in a vac (CARE). The anhydrous salt is commercially available as an ACS reagent, and is as efficient a dehydrating agent as  $P_2O_5$  and is known as "Dehydrite" or "Anhydrone". [Smith et al. J Am Chem Soc 44 2255 1922 and Ind Eng Chem 16 20 1924.] Hygroscopic, Keep in a tightly closed container. EXPLOSIVE in contact with organic materials, and is a SKIN IRRITANT.

Magnesium succinate [556-32-1] M 141.4. Crystd from water (0.5mL/g) between 100° and 0°.

**Magnesium sulfate (anhydrous)** [7487-88-9] **M 120.4, m 1127°.** Crystd from warm H<sub>2</sub>O (1mL/g) by cooling. Dry heptahydrate at ~250° until it loses 25% of its wt. Store in a sealed container.

Magnesium trifluoromethanesulfonate [60871-83-2] M 322.4, m >300°. Wash with  $CH_2Cl_2$  and dry at 125°/2h and 3mmHg. [Tetrahedron Lett 24 169 1983.]

**Magon [3-hydroxy-4-(hydroxyphenylazo)-2-naphthoyl-2,4-dimethylanilide;** Xylidyl Blue II] [523-67-1] M 411.5, m 246-247°. Suspend in H<sub>2</sub>O and add aqueous NaOH until it dissolves, filter and acidify with dil HC1. Collect the dye, dissolve in hot EtOH (sol is 100mg/L at ca 25°) concentrate to a small volume and allow to cool. Sol in H<sub>2</sub>O of the Na salt is 0.4mg/mL. [Anal Chim Acta 16 155 1957; Anal Chem 28 202 1956.]

Manganese (III) acetate  $(2H_2O)$  [19513-05-4] M 268.1, pK<sup>25</sup> 0.06 (for Mn<sup>3+</sup> hydrolysis). Wash the acetate with AcOH then thoroughly with Et<sub>2</sub>O and dry in air to obtain the dihydrate. The anhydrous salt can be made by stirring vigorously a mixt of the hydrated acetate (ca 6g) and Ac<sub>2</sub>O (22.5mL) and heat carefully (if necessary) until the mixture is clear. It is set aside overnight for the material to crystallise. Filter the solid, wash with Ac<sub>2</sub>O and dry over P<sub>2</sub>O<sub>5</sub>. The dihydrate can also be obtained from the di- and tetra- hydrate mixture of the divalent acetate by adding 500mL of Ac<sub>2</sub>O and 48g of the hydrated acetate and refluxing for 20min, then add slowly 8.0g of KMnO<sub>4</sub>. After refluxing for an additional 30min, the mixture was cooled to room temperature and 85mL of H<sub>2</sub>O added. It should be noted that larger amounts of H<sub>2</sub>O change the yield and nature of the manganese acetate and the yields of reactions that use this reagent, e.g. formation of lactones from olefines. The Mn(OAc)<sub>3</sub>.2H<sub>2</sub>O is then filtered off after 16h, washed with cold AcOH and air dried. [J Am Chem Soc **90** 5903, 5905 1968, Heiba et al. **91** 138 1969.]

Alternatively dissolve the salt (30g) in glacial acetic acid (200mL) by heating and filter. If crystals do not appear, the glass container should be rubbed with a glass rod to induce crystn which occurs within 1h. If not, allow to stand for a few days. Filter the cinnamon brown crystals which have a sliky lustre and dry over CaO. Keep away from moisture as it is decomposed by cold  $H_2O$ . [Lux in Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II, p 1469 1963; Williams and Hunter Can J Chem 54 3830 1976.]

**Manganese** (II) acetylacetone [14024-58-9] M 253.2, m  $\sim$ 250°. Purify by stirring 16g of reagent for a few min with 100mL absolute EtOH and filter by suction as rapidly as possible through coarse filter paper. Sufficient EtOH is added to the filtrate to make up for the loss of EtOH and to redissolve any solid that separates. Water (15mL) is added to the filtrate and the solution is evaporated with a stream of N<sub>2</sub> until reduced to half its vol. Cool for a few min and filter off the yellow crystals, dry under a stream of N<sub>2</sub>, then in a

vacuum at room temp for 6-8h. These conditions are important for obtaining the *dihydrate*. A vacuum to several mm of Hg or much lower pressure for several days produces the anhydrous complex. The degree of hydration can be established by determining the loss in weight of 100g of sample after heating for 4h at 100° and <20mmHg. The theoretical loss in weight for 2H<sub>2</sub>O is 12.5%. Material sublimes at 200°/2mm. It is soluble in heptane, MeOH, EtOH or  $C_6H_6$  at 30°. [*Inorg Synth* **6** 164 1960, **5** 105 1957.]

Manganese decacarbonyl  $Mn_2(CO)_{10}$  [10170-69-1] M 390.0, m 151-152°, 154-155°(sealed tube),  $d^{25}$  1.75. Golden yellow crystals which in the absence of CO begin to decompose at 110°, and on further heating yield a metallic mirror. In the presence of 3000psi of CO it does not decompose on heating to 250°. It is soluble in common organic solvents, insoluble in H<sub>2</sub>O, not very stable in air, to heat or UV light. Dissolves in a lot of  $C_{6}H_{6}$  and can be crystallised from it. It distils with steam at 92-100°. It can be purified by sublimation under reduced pressure (<0.5mm) at room temperature to give well formed golden yellow crystals. If the sample is orange coloured this sublimation leads to a mixture of golden-yellow and dark red crystals of the carbonyl and carbonyl iodide respectively which can be separated by hand picking under a microscope. Separate resublimations provide the pure compounds. POISONOUS [J Am Chem Soc 76 3831 1954, 80 6167 1958, 82 1325 1960].

Manganous acetate (4H<sub>2</sub>O) [6156-78-1 (4H<sub>2</sub>O); 638-38-0 (anhydr)] M 245.1, m 80°, d 1.59, pK<sup>25</sup> 10.59 (for  $Mn^{2+}$  hydrolysis). Crystd from water acidified with acetic acid.

Manganous bromide (anhydrous) [13446-03-2] M 214.8, m 695°;  $4H_2O$  [10031-20-6] M 286.8, m 64°(dec). Rose-red deliquescent crystals soluble in EtOH. The H<sub>2</sub>O is removed by heating at 100° then in HBr gas at 725° or dry in an atmosphere of N<sub>2</sub> at 200°.

Manganous chloride (4H<sub>2</sub>O) [13446-34-9; 7773-01-5 (anhydr)] M 197.9, m 58°, 87.5°, d 2.01. Crystd from water (0.3mL/g) by cooling.

Manganous ethylenebis(dithiocarbamate) [12427-38-2] M 265.3, pK<sub>Est</sub> ~ 3.0 (for --NCSSH). Crystd from EtOH.

Manganous lactate (3H<sub>2</sub>O) [51877-53-3] M 287.1. Crystd from water.

**Manganous sulfate** (H<sub>2</sub>O) [10034-96-5 (H<sub>2</sub>O); 15244-36-7 ( $xH_2O$ )] M 169.0, d 2.75. Crystd from water (0.9mL/g) at 54-55° by evaporating about two-thirds of the water. Dehydr at >400°.

**2-Mercaptopyridine** N-oxide sodium salt (pyridinethione or pyrithione sodium salt) [3811-73-2] M 149.1, m ~250°(dec),  $pK_1$  -1.95,  $pK_2$  4.65. When recrystd from water it assayed as 98.7% based on AgNO<sub>3</sub> titration [Krivis et al. Anal Chem 35 966 1963, see also Krivis et al. Anal Chem 48 1001 1976; and Barton and Crich J Chem Soc. Perkin Trans 1 1603, 1613 1986].

Mercuric acetate [1600-27-7] M 318.7,  $pK_1^{25}$  2.47,  $pK_2^{25}$  3.49 (for Hg<sup>2+</sup> hydrolysis). Crystd from glacial acetic acid. POISONOUS.

Mercuric bromide [7789-47-1] M 360.4, m 238.1°. Crystd from hot saturated ethanolic soln, dried and kept at 100° for several hours under vacuum, then sublimed. POISONOUS.

Mercuric chloride [7487-94-7] M 271.5, m 276°, b 304°, d 5.6. Crystd twice from distilled water, dried at 70° and sublimed under high vacuum. POISONOUS.

Mercuric cyanide [592-04-1] M 252.6, m 320°(dec), d 4.00. Crystd from water. POISONOUS.

Mercuric iodide (red) [7774-29-0] M 454.4, m 259°(yellow >130°), b ~350°(subl), d 6.3. Crystd from MeOH or EtOH, and washed repeatedly with distilled water. Has also been mixed thoroughly with excess 0.001M iodine solution, filtered, washed with cold distilled water, rinsed with EtOH and  $Et_2O$ , and dried in air. POISONOUS.

Mercuric oxide (yellow) [21908-53-2] M 216.6, m 500°(dec). Dissolved in HClO<sub>4</sub> and ppted with NaOH soln.

**Mercuric thiocyanate** [592-85-8] M 316.8, m 165°(dec),  $pK^{25}$  -1.85 (for HSCN). Recryst from H<sub>2</sub>O, and can form various crystal forms depending on conditions. Solubility in H<sub>2</sub>O is 0.069% at 25°, but is more soluble at higher temps. Decomposes to Hg above 165°. **Poisonous.** [J Phys Chem 35 1128 1931; Chem Ber 68 919 1935.]

Mercurous nitrate (2H<sub>2</sub>O) [7782-86-7 (2H<sub>2</sub>O); 7783-34-8 (H<sub>2</sub>O); 10415-75-5 (anhydr)] M 561.2, m 70°(dec), d 4.78,  $pK^{25}$  2.68 (for Hg<sub>2</sub><sup>2+</sup> hydrolysis). Solubility in H<sub>2</sub>O containing 1% HNO<sub>3</sub> is 7.7%. Recryst from a warm saturated soln of dilute HNO<sub>3</sub> and cool to room temp slowly to give elongated prisms. Rapid cooling gives plates. Colourless crystals to be stored in the dark. **POISONOUS.** [J Chem Soc 1312 1956.]

**Mercurous sulfate** [7783-36-0] **M 497.3, d 7.56.** Recrystallise from dilute  $H_2SO_4$ , and dry in a vacuum under  $N_2$  and store in the dark. Solubility in  $H_2O$  is 0.6% at 25°. **POISONOUS.** 

Mercury [7439-97-6] M 200.6, m -38.9°, b 126°/1mm, 184°/10mm, 261°/100mm, 356.9°/atm, d 13.534. After air had been bubbled through mercury for several hours to oxidise metallic impurities, it was filtered to remove coarser particles of oxide and dirt, then sprayed through a 4-ft column containing 10% HNO<sub>3</sub>. It was washed with distilled water, dried with filter paper and distilled under vacuum.

Mercury(II) bis(cyclopentadienyl) [18263-08-6] M 330.8. Purified by low-temp recrystn from Et<sub>2</sub>O.

Mercury dibromofluorescein {mercurochrome, merobromin,  $[2',7'-dibromo-4'-(hydroxy-mercurio)-fluorescein di-Na salt]} [129-16-8] M 804.8, m>300°. The Na salt is dissolved in the minimum vol of H<sub>2</sub>O, or the free acid suspended in H<sub>2</sub>O and dilute NaOH added to cause it to dissolve, filter and acidify with dilute HCl. Collect the ppte wash with H<sub>2</sub>O by centrifugation and dry in vacuum. The di Na salt can be purified by dissolving in the minimum volume of H<sub>2</sub>O and ppted by adding EtOH, filter, wash with EtOH or Me<sub>2</sub>CO and dry in a vacuum. Solubility in 95% EtOH is 2% and in MeOH it is 16%. [J Am Chem Soc 42 2355 1920.]$ 

Mercury orange [1-(4-chloromercuriophenylazo)-2-naphthol] [3076-91-3] M 483.3, m 291.5-293°(corr) with bleaching. Wash several times with boiling 50% EtOH and recrystallise from 1-butanol (0.9g/L of boiling alcohol). Fine needles insoluble in H<sub>2</sub>O but slightly soluble in cold alcohols, CHCl<sub>3</sub> and soluble in aqueous alkalis. [J Am Chem Soc 70 3522 1948.]

Mercury(II) trifluoroacetate [13257-51-7] M 426.6. Recrystd from trifluoroacetic anhydride/trifluoroacetic acid [Lan and Kochi J Am Chem Soc 108 6720 1986]. Very TOXIC and hygroscopic.

Metanil Yellow (3[{4-phenylamino}phenylazo]-benzenesulfonic acid) [587-98-4] M 375.4, pK<sub>Est</sub> <0. Salted out from water three times with sodium acetate, then repeatedly extracted with EtOH [McGrew and Schneider, J Am Chem Soc 72 2547 1950].

(Methoxycarbonylmethyl)triphenylphosphorane [methyl (triphenylphosphoranylidene)acetate] [2605-67-6] M 334.4, m 162-163°, 169-171°. Cryst by dissolving in AcOH and adding pet ether (b 40-50°) to give colorless plates. UV  $\lambda \max(A_{1mm}^{1\%})$ : 222nm (865) and 268nm (116) [Isler et al. Helv Chim Acta 40 1242 1957].

Methoxycarbonylmethyltriphenylphosphonium bromide [1779-58-4] M 415.3, m 163°, 165-170°(dec). Wash with pet ether (b 40-50°) and recryst from CHCl<sub>3</sub>/Et<sub>2</sub>O and dry in high vac at 65°. [Isler et al. Helv Chim Acta 40 1242 1957; Wittig and Haag Chem Ber 88 1654, 1664 1955.] Methoxymethyl trimethylsilane (trimethylsilylmethyl methyl ether) [14704-14-4] M 118.3, b 83°/740mm,  $d_4^{25}$  0.758,  $n_D^{25}$  1.3878. Forms an azeotrope with MeOH (b 60°). If it contains MeOH (check IR for bands above 3000cm<sup>-1</sup>) then wash with H<sub>2</sub>O and fractionate. A possible impurity could be chloromethyl trimethylsilane (b 97°/740mm). [J Am Chem Soc 70 4142 1948.]

1-Methoxy-2-methyl-1-trimethylsiloxypropene (dimethyl ketene methyl trimethylsilyl acetal) [31469-15-5] M 174.3, b 121-122°/0.35mm, 125-126°/0.4mm, 148-150°/atm, d 0.86. Add Et<sub>2</sub>O, wash with cold H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate Et<sub>2</sub>O, and distil oily residue in a vacuum. [J Organometal Chem 46 59 1972.]

trans-1-Methoxy-3-(trimethylsilyloxy)-1,3-butadiene (Danishefsky's diene) [54125-02-9] M 172.3, b 68-69°/14mm, 70-72°/16mm, d 0.885, n 1.4540. It may contain up to 1% of the precursor 4-methoxybut-4-ene-2-one. Easily distd through a Vigreux column in a vac and taking the middle fraction. [Danishefsky and Kitihara J Am Chem Soc 96 7807 1974; Danishefsky Acc Chem Res 14 400 1981.]

Methylarsonic acid [124-58-3] M 137.9, m 161°, pK<sub>1</sub><sup>25</sup> 1.54, pK<sub>2</sub><sup>25</sup> 6.31 [As(OH)<sub>2</sub>]. Crystd from abs EtOH.

Methyl dichlorosilane (dichloro methylsilane) [75-54-7] M 115.0, m -92.5°, b 41°/748mm, 40.9°/760mm, 40-45°/atm, d  $^{27}_{27}$ 1.105. Impurities are generally other chloromethyl silanes. Distilled through a conventional Stedman column of 20 theoretical plates or more. [Stedman column. A plain tube containing a series of wire-gauze discs stamped into flat, truncated cones and welded together, alternatively base-to-base and edge-to-edge, with a flat disc across each base. Each cone has a hole, alternately arranged, near its base, vapour and liquid being brought into intimate contact on the gauze surfaces (Stedman Can J Res B 15 383 1937)]. It should be protected from H<sub>2</sub>O by storing over P<sub>2</sub>O<sub>5</sub>. [Chem Ber 52 695 1919; J Am Chem Soc 68 9621946.]

Methylmercuric chloride [115-09-3] M 251.1, m 167°. Crystd from absolute EtOH (20mL/g).

Methyl Orange (sodium 4,4'-dimethylaminophenylazobenzenesulfonate) [547-58-0] M 327.3, pK 3.47. Crystd twice from hot water, then washed with a little EtOH followed by diethyl ether. Indicator: pH 3.1 (red) and pH 4.4 (yellow).

Methylphenyl dichlorosilane (dichloro methyl phenylsilane) [149-74-6] M 191.1, b 114-115°/50mm, 202-205°/atm, d 1.17. Purified by fractionation using an efficient column. It hydrolyses *ca* ten times more slowly than methyltrichlorosilane and *ca* sixty times more slowly than phenyltrichlorosilane. [J Phys Chem 61 1591 1957].

**Methylphosphonic acid** [993-13-5] **M 96.0, m 104-106°, 105-107°, 108°, pK\_1^{25} 2.12, pK\_2^{25} 7.29. If it tests for Cl<sup>-</sup>, add H<sub>2</sub>O and evaporate to dryness; repeat several times till free from Cl<sup>-</sup>. The residue solidifies to a wax-like solid. Alternatively, dissolve the acid in the minimum volume of H<sub>2</sub>O, add charcoal, warm, filter and evaporate to dryness in a vacuum over P<sub>2</sub>O<sub>5</sub>. [J Am Chem Soc 75 3379 1953.] The di-Na salt is prepared from 24g of acid in 50mL of dry EtOH and a solution of 23g Na dissolved in 400mL EtOH is added. A white ppte is formed but the mixture is refluxed for 30min to complete the reaction. Filter off and recrystallise from 50% EtOH. Dry crystals in a vacuum desiccator. [J Chem Soc 3292 1952.]** 

Methylphosphonic dichloride [676-97-1] M 132.9, m 33°, 33-37°, b 53-54°/10mm, 64-67°/20.5mm, 86°/44mm, 162°/760mm,  $d_4^{40}$  1.4382. Fractionally redistd until the purity as checked by hydrolysis and acidimetry for Cl<sup>-</sup> is correct and should solidify on cooling. [J Chem Soc 3437 1952; J Am Chem Soc 75 3379 1952; for IR see Can J Chem 34 1611 1956.]

Methyl Thymol Blue, sodium salt [1945-77-3] M 844.8, ε 1.89 x 10<sup>4</sup> at 435nm, pH 5.5. Starting material for synthesis is Thymol Blue. Purified as for Xylenol Orange on p. 387 in Chapter 4. Methyl trichlorosilane [75-79-6] M 149.5, b 13,7°/101mm, 64.3°/710.8mm, 65.5°/745mm, 66.1°/atm, d 1.263, n1.4110. If very pure distil before use. Purity checked by <sup>29</sup>Si nmr,  $\delta$  in MeCN is 13.14 with respect to Me<sub>4</sub>Si. Possible contaminants are other silanes which can be removed by fractional distillation through a Stedman column of >72 theoretical plates with total reflux and 0.35% take-off (see p. 441). The apparatus is under N<sub>2</sub> at a rate of 12 bubbles/min fed into the line using an Hg manometer to control the pressure. Sensitive to H<sub>2</sub>O. [J Am Chem Soc 73 4252 1951; J Org Chem 48 3667 1983.]

Methyl triethoxysilane [2031-67-6] M 178.31, b 142-144.5°/742mm, 141°/765mm, 141.5°/775mm, d 0.8911, n 1.3820. Repeated fractionation in a stream of N<sub>2</sub> through a 3' Heligrid packed Todd column (see p. 174). Hydrolysed by H<sub>2</sub>O and yields cyclic polysiloxanes on hydrolysis in the presence of acid in  $*C_6H_6$ . [J Am Chem Soc 77 1292, 3990 1955.]

Methyl trimethoxysilane [1185-55-3] M 136.2, b 102°/760mm, d 1.3687, n 1.3711. Likely impurities are 1,3-dimethyltetramethoxy disiloxane (b 31°/1mm) and cyclic polysiloxanes, see methyl triethoxysilane. [J Org Chem 16 1400 1952, 20 250 1955.]

**N-Methyl-N-trimethylsilylacetamide** [7449-74-3] M 145.3, b 48-49°/11mm, 84°/13mm, 105-107°/35mm (solid at room temp), d 0.90, n 1.4379. Likely impurity is Et<sub>3</sub>N.HCl which can be detected by its odour. If it is completely soluble in  $C_6H_6$ , then redistil, otherwise dissolve in this solvent, filter and evaporate first in a vacuum at 12mm then fractionate, all operations should be carried out in a dry N<sub>2</sub> atmosphere. [J Am Chem Soc 88 3390 1966; Chem Ber 96 1473 1963.]

Methyl trimethylsilylacetate [2916-76-9] M 146.3, b 65-68°/50mm, d 0.89. Dissolved in Et<sub>2</sub>O, shaken with 1M HCl, washed with H<sub>2</sub>O, aqueous saturated NaHCO<sub>3</sub>, H<sub>2</sub>O again, and dried (a ppte may be formed in the NaHCO<sub>3</sub> soln and should be drawn off and discarded). The solvent is distd off and the residue is fractionated through a good column. IR (CHCl<sub>3</sub>) v 1728cm<sup>-1</sup>. [J Org Chem 32 3535 1967, 45 237 1980.]

Methyl 2-(trimethylsilyl)propionate [55453-09-3] M 160.3, b 155-157°/atm, d 0.89. Dissolve in Et<sub>2</sub>O, wash with aqueous NaHCO<sub>3</sub>, H<sub>2</sub>O, 0.1M HCl, H<sub>2</sub>O again, dry (MgSO<sub>4</sub>), evaporated and distil. [J Chem Soc Perkin Trans 1 541 1985; Tetrahedron 39 3695 1983.]

Methyl triphenoxyphosphonium iodide [17579-99-6] M 452.2, m 146°. Gently heat the impure iodide with good grade Me<sub>2</sub>CO The saturated solution obtained is decanted rapidly from undissolved salt and treated with an equal volume of dry Et<sub>2</sub>O. The iodide separates as beautiful flat needles which are collected by centrifugation, washed several times with dry Et<sub>2</sub>O, and dried in a vacuum over P<sub>2</sub>O<sub>5</sub>. For this recrystn it is essential to minimise the time of contact with Me<sub>2</sub>CO and to work rapidly and with rigorous exclusion of moisture. If the crude material is to be used, it should be stored under dry Et<sub>2</sub>O, and dried and weighed *in vacuo* immediately before use. [J Chem Soc Perkin Trans 1 982 1974; J Chem Soc 224 1953.]

Methyl triphenylphosphonium bromide [1779-49-3] M 357.3, m 229-230°(corr), 227-229°, 230-233°. If the solid is sticky, wash with \*C<sub>6</sub>H<sub>6</sub> and dry in a vacuum over P<sub>2</sub>O<sub>5</sub>. [Marvel and Gall J Org Chem 24 1494 1959; Chem Ber 87 1318 1954; Milas and Priesing J Am Chem Soc 79 6295 1957; Wittig and Schöllkopf Org Synth 40 66 1960..] The iodide crystd from H<sub>2</sub>O has m 187.5-188.5° [J Chem Soc 1130 1953; Justus Liebigs Ann Chem 580 44 1953].

**N-Methyl-N-trimethylsilyl trifluoroacetamide** [24589-78-4] **M 199.3, b 78-79°/130mm.** Fractionate through a 40mm Vigreux column. Usually it contains *ca* 1% of methyl trifluoroacetamide and 1% of other impurities which can be removed by gas chromatography or fractionating using a spinning band column. [J Chromatogr 42 103 1969, 103 91 1975.]

Methyl vinyl dichlorosilane (dichloro methyl vinyl silane) [124-70-9] M 141.1, b 43-45.5°/11-11.5mm, 91°/742mm, 92.5°/743.2mm, 92.5-93°/atm, d 1.0917, n 1.444. Likely impurities are dichloromethylsilane, butadienyl-dichloromethylsilane. Fractionate through a column packed

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with metal filings (20 theoretical plates) at atmospheric pressure. [Izv Akad Nauk SSSR Ser Khim 1474 1957 and 767 1958.]

Milling Red SWB {1-[4-[4-toluenesulfonyloxy]phenylazo](3,3'dimethyl-1,1'-biphenyl)-4'-azo]-2-hydroxynaphthalene-6,8-disulfonic acid di-Na salt, Acid Red 114} [6459-94-5] M 830.8, m dec >250°, CI 23635,  $\lambda$ max ~514nm. Salted out three times with sodium acetate, then repeatedly extracted with EtOH. [McGrew and Schneider J Am Chem Soc 72 2547 1950.] See Solochrome Violet R on p. 352 in Chapter 4.

Milling Yellow G [51569-18-7]. Salted out three times with sodium acetate, then repeatedly extracted with EtOH. [McGrew and Schneider J Am Chem Soc 72 2547 1950.] See Solochrome Violet R on p. 352 in Chapter 4.

Molybdenum hexacarbonyl [13939-06-5] M 264.0, m 150°(dec), b 156°. Sublimed in a vacuum before use [Connor et al. J Chem Soc, Dalton Trans 511 1986].

Molybdenum hexafluoride [7783-77-9] M 209.9, b 35% 760mm. Purified by low-temperature trapto-trap distillation over predried NaF. [Anderson and Winfield J Chem Soc, Dalton Trans 337 1986.] Poisonous vapours.

Molybdenum trichloride [13478-18-7] M 202.3, m 1027°, d 3.74. Boiled with 12M HCl, washed with absolute EtOH and dried in a vacuum desiccator.

Molybdenum trioxide (molybdenum IV oxide,  $MoO_3$ ) [1313-27-5] M 143.9, m 795°, d 4.5. Crystd from water (50mL/g) between 70° and 0°.

Monocalcium phosphate  $(2H_2O)$  (monobasic) [7789-77-7  $(2H_2O)$ ; 7757-93-9 (anhydr)] M 154.1, m 200°(dec, loses H<sub>2</sub>O at 100°), d 2.2. Crystd from a near-saturated soln in 50% aqueous reagent grade phosphoric acid at 100° by filtering through fritted glass and cooling to room temperature. The crystals were filtered off and this process was repeated three times using fresh acid. For the final crystn the solution was cooled slowly with constant stirring to give thin plate crystals that were filtered off on fritted glass, washed free of acid with anhydrous acetone and dried in a vacuum desiccator [Egan, Wakefield and Elmore, J Am Chem Soc 78 1811 1956].

**Monoperoxyphthalic acid magnesium salt 6H<sub>2</sub>O.** (MMPP) [84665-66-7] M 494.7, m  $\sim$ 93°(dec). MMPP is a safer reagent than *m*-chloroperbenzoic acid because it is not as explosive and has advantages of solubility. It is sol in H<sub>2</sub>O, low mol wt alcohols, *i*-PrOH and DMF. The product of reaction, Mg phthalate, is sol in H<sub>2</sub>O. It has been used in aq phase to oxidise compds in e.g. CHCl<sub>3</sub> and using a phase transfer catalyst e.g. methyltrioctylammonium chloride [Brougham Synthesis 1015 1987]. The oxidising activity can be checked (as for perbenzoic acid in Silbert et al. Org Synth Coll Vol V 906 1973], and if found to be low it would be best to prepare afresh from phthalic anhydride (1mol), H<sub>2</sub>O<sub>2</sub> (1mol) and MgO at 20-25° to give MMPP. [Hignett, European Pat Appl 27 693 1981, Chem Abstr 95 168810 1981.]

Naphthalene Scarlet Red 4R [1-(4-sulfonaphthalene-1-azo)-2hydroxynaphthalene-6,8-disulfonic acid tri-Na salt, New Coccine, Acid Red 18] [2611-82-7] M 604.5, m >250°(dec), CI 16255,  $\lambda$ max 506nm. Dissolved in the minimum quantity of boiling water, filtered and enough EtOH was added to ppte *ca* 80% of the dye. This process was repeated until a soln of the dye in aqueous 20% pyridine had a constant extinction coefficient.

Naphthol Yellow S (citronin A, flavianic acid sodium salt, 8-hydroxy-5,7-dinitro-2naphthalene sulfonic acid disodium salt) [846-70-8] M 358.2, m dec on heating. Greenish yellow powder soluble in H<sub>2</sub>O. The *free sulfonic acid* can be recrystd from dil HCl (m 150°) or AcOH-EtOAc (m 148-149.5°). The disodium salt is then obtained by dissolving the acid in two equivalents of aqueous NaOH

and evaporating to dryness and drying the residue in a vacuum desiccator. The sodium salt can be recrystd from the minimum volume of  $H_2O$  or from EtOH [Dermer and Dermer J Am Chem Soc 61 3302 1939].

1,2-Naphthoquinone-4-sulfonic acid sodium salt (3,4-dihydro-3,4-dioxo-1-naphthlene sulfonic acid sodium salt) [521-24-4] M 260.2,  $pK_{Est} < 0$ . Yellow crystals from aqueous EtOH and dry at 80° in vacuo. Solubility in H<sub>2</sub>O is 5% [Org Synth Coll Vol III 633 1955; Danielson J Biol Chem 101 507 1933; UV: Rosenblatt et al. Anal Chem 27 1290 1955].

1-Naphthyl phosphate disodium salt [2183-17-7] M 268.1,  $pK_1^{25}$  0.97,  $pK_2^{25}$  5.85 (for free acid). The free acid has m 157-158° (from Me<sub>2</sub>CO/\*C<sub>6</sub>H<sub>6</sub>). The free acid is crystd several times by adding 20 parts of boiling \*C<sub>6</sub>H<sub>6</sub> to a hot solution of 1 part of free acid and 1.2 parts of Me<sub>2</sub>CO. It has m 157-158°. [J Am Chem Soc 77 4002 1955.] The monosodium salt was ppted from a soln of the acid phosphate in MeOH by addition of an equivalent of MeONa in MeOH. [J Am Chem Soc 72 624 1950.] See entry on p.550 in Chapter 6.

2-Naphthyl phosphate monosodium salt [14463-68-4] M 246.1, m 203-205°,  $pK_1^{25}$  1.25,  $pK_2^{25}$  5.83 (for free acid). Recrystd from H<sub>2</sub>O (10mL) containing NaCl (0.4g). The salt is collected by centrifugation and dried in a vac desiccator, m 203-205° (partially resolidifies and melts at 244°). Crystd from MeOH (m 222-223°). The free acid is recrystd several times by addn of 2.5 parts of hot CHCl<sub>3</sub> to a hot soln of the free acid (1 part) in Me<sub>2</sub>CO (1.3 parts), m 177-178°. [J Am Chem Soc. 73 5292 1951, 77 4002 1955.] See entry on p. 551 in Chapter 6.

Neodynium chloride  $6H_2O$  [13477-89-9] M 358.7, m 124°,  $pK_1^{25}$  8.43 (for Nd<sup>3+</sup> hydrolysis). Forms large purple prisms from conc solns of dilute HCl. Soluble in H<sub>2</sub>O (2.46 parts in 1 part of H<sub>2</sub>O) and EtOH.

**Neodynium nitrate** (6H<sub>2</sub>O) [16454-60-7] M 438.4, m 70-72°. Crystallises with 5 and 6 molecules of H<sub>2</sub>O from conc solutions in dilute HNO<sub>3</sub> by slow evaporation; 1 part is soluble in 10 parts of H<sub>2</sub>O.

**Neodymium oxide** [1313-97-9] M 336.5, m 2320°. Dissolved in HClO<sub>4</sub>, ppted as the oxalate with doubly recrystd oxalic acid, washed free of soluble impurities, dried at room temperature and ignited in a platinum crucible at higher than 850° in a stream of oxygen [Tobias and Garrett J Am Chem Soc 80 3532 1958].

**Neon** [7440-01-9] **M 20.2.** Passed through a copper coil packed with 60/80 mesh 13X molecular sieves which is cooled in liquid  $N_2$ , or through a column of Ascarite (NaOH-coated silica adsorbent).

Neopentoxy lithium [3710-27-8] M 94.1. Recrystd from hexane [Kress and Osborn J Am Chem Soc 109 3953 1987].

New Methylene Blue N (2,8-dimethyl-3,6-bis(ethylamino)phenothazinium chloride 0.5  $ZnCl_2$ ) [6586-05-6] M 416.1, m >200°(dec), pK<sub>1</sub> 3.54, pK<sub>2</sub> 4.82. Crystd from \*benzene/MeOH (3:1).

Nickel (II) acetate  $(4H_2O)$  [6018-89-9] M 248.9, d 1.744,  $pK_1^{2.5}$  8.94 (from Ni<sup>2+</sup> hydrolysis). Recryst from aqueous AcOH as the green tetrahydrate. Soluble in 6 parts of H<sub>2</sub>O. It forms lower hydrates and should be kept in a well closed container. [Z Anorg Allg Chem 343 92 1966.]

Nickel (II) acetylacetonate [3264-82-2] M 256.9, m 229-230°, b 220-235°/11mm,  $d^{17}$ 1.455. Wash the green solid with H<sub>2</sub>O, dry in a vacuum desiccator and recrystallise from MeOH. [J Phys Chem 62 440 1958.] The complex can be conveniently dehydrated by azeotropic distn with toluene and the crystals may be isolated by concentrating the toluene solution. [J Am Chem Soc 76 1970 1954.]

Nickel bromide [13462-88-9] M 218.5, m 963°(loses  $H_2O$  at ~ 200°). Crystd from dilute HBr (0.5mL/g) by partial evaporation in a desiccator.

Nickel chloride (6H<sub>2</sub>O) [7791-20-0 (6H<sub>2</sub>O); 69098-15-3 ( $xH_2O$ ); 7718-54-9 (anhydr)] M 237.7. Crystd from dilute HCl.

Nickel nitrate (6H<sub>2</sub>O) [13478-00-7] M 290.8, m 57°. Crystd from water (0.3mL/g) by partial evaporation in a desiccator.

Nickelocene [bis-(cyclopentadienyl)nickel II] [1271-28-9] M 188.9, m 173-174°(under N<sub>2</sub>). Dissolve in Et<sub>2</sub>O, filter and evaporate in a vacuum. Purify rapidly by recrystn from pet ether using a solid CO<sub>2</sub>-Me<sub>2</sub>CO bath, m 171-173°(in an evacuated tube). Also purified by vacuum sublimation. [J Am Chem Soc 76 1970 1954; J Inorg Nucl Chem 295, 110 1956.]

Nickel (II) phthalocyanine [14055-02-8] M 571.3, m >300°. Wash well with  $H_2O$  and boiling EtOH and sublime at high vacuum in a slight stream of  $CO_2$ . A special apparatus is used (see reference) with the phthallocyanine being heated to red heat. The sublimate is made of needles with an extremely bright red lustre. The powder is dull greenish blue in colour. [J Chem Soc 1719 1936.]

Nickel sulfate  $(7H_2O)$  [1010-98-1] M 280.9, m loses  $5H_2O$  at 100°, anhydr m at ~280°. Crystd from warm water (0.25mL/g) by cooling.

Nickel 5,10,15,20-tetraphenylporphyrin [14172-92-0] M 671.4,  $\lambda_{max}$  414(525)nm. Purified by chromatography on neutral (Grade I) alumina, followed by recrystn from CH<sub>2</sub>Cl<sub>2</sub>/MeOH [Yamashita J Phys Chem 91 3055 1987].

Niobium (V) chloride [10026-12-7] M 270.2, m 204.7-209.5°, b ~250°(begins to sublime at 125°), d 2.75. Yellow very deliquescent crystals which decompose in moist air to give HCl. Should be kept in a dry box flushed with N<sub>2</sub> in the presence of P<sub>2</sub>O<sub>5</sub>. Wash with CCl<sub>4</sub> and dry over P<sub>2</sub>O<sub>5</sub>. The yellow crystals usually contain a few small dirty white pellets among the yellow needles. These should be easily picked out. Upon grinding in a dry box, however, they turn yellow. NbCl<sub>5</sub> has been sublimed and fractionated in an electric furnace. [Inorg Synth 7 163 1963; J Chem Soc suppl 233 1949.]

Nitric acid [7697-37-2] M 63.0, m -42°, b 83°, d<sub>25</sub> 1.5027, [Constant boiling acid has composition 68% HNO<sub>3</sub> + 32% H<sub>2</sub>O, b 120.5°, d 1.41], pK<sup>25</sup> -1.27 (1.19). Obtained colourless (approx. 92%) by direct distn of fuming HNO<sub>3</sub> under reduced pressure at 40-50° with an air leak at the head of the fractionating column. Stored in a desiccator kept in a refrigerator. Nitrite-free HNO<sub>3</sub> can be obtained by vac distn from urea.

Nitric oxide [10102-43-9] M 30.0, b -151.8°. Bubbling through 10M NaOH removes NO<sub>2</sub>. It can also be freed from NO<sub>2</sub> by passage through a column of Ascarite followed by a column of silica gel held at -197°K. The gas is dried with solid NaOH pellets or by passing through silica gel cooled at -78°, followed by fractional distillation from a liquid N<sub>2</sub> trap. This purification does not eliminate nitrous oxide. Other gas scrubbers sometimes used include one containing conc H<sub>2</sub>SO<sub>4</sub> and another containing mercury. It is freed from traces of N<sub>2</sub> by a freeze and thaw method. **TOXIC**.

# *p*-Nitrobenzenediazonium fluoroborate [456-27-9] M 236.9. Crystd from water. Can be EXPLOSIVE when dry.

Nitrogen [7727-37-9] M 28.0, b -195.8°. Cylinder  $N_2$  can be freed from oxygen by passage through Fieser's soln [which comprises 2g sodium anthraquinone-2-sulfonate and 15g sodium hydrosulfite dissolved in 100mL of 20% KOH [Fieser, J Am Chem Soc 46 2639 1924] followed by scrubbing with saturated lead acetate soln (to remove any H<sub>2</sub>S generated by the Fieser soln), conc H<sub>2</sub>SO<sub>4</sub> (to remove moisture), then soda-lime (to remove any H<sub>2</sub>SO<sub>4</sub> and CO<sub>2</sub>). Alternatively, after passage through Fieser's solution, N<sub>2</sub> can be dried by washing with a soln of the metal ketyl from benzophenone and Na wire in absolute diethyl ether. [If ether vapour in N<sub>2</sub> is undesirable, the ketyl from liquid Na-K alloy under xylene can be used.]

Another method for removing  $O_2$  is to pass the nitrogen through a long tightly packed column of Cu turnings, the surface of which is constantly renewed by scrubbing it with ammonia (sg 0.880) soln. The gas is then

passed through a column packed with glass beads moistened with conc  $H_2SO_4$  (to remove ammonia), through a column of packed KOH pellets (to remove  $H_2SO_4$  and to dry the  $N_2$ ), and finally through a glass trap packed with chemically clean glass wool immersed in liquid  $N_2$ . Nitrogen has also been purified by passage over Cu wool at 723°K and Cu(II) oxide [prepared by heating Cu(NO<sub>3</sub>)<sub>2</sub>.6H<sub>2</sub>O at 903°K for 24h] and then into a cold trap at 77°K.

A typical dry purification method consists of a mercury bubbler (as trap), followed by a small column of silver and gold turnings to remove any mercury vapour, towers containing anhydrous  $CaSO_4$ , dry molecular sieves or  $Mg(ClO_4)_2$ , a tube filled with fine Cu turnings and heated to 400° by an electric furnace, a tower containing soda-lime, and finally a plug of glass wool as filter. Variations include tubes of silica gel, traps containing activated charcoal cooled in a Dry-ice bath, copper on Kieselguhr heated to 250°, and Cu and Fe filings at 400°.

2-Nitrophenol-4-arsonic acid (4-hydroxy-3-nitrophenylarsonic acid) [121-19-7] M 263.0,  $p K_{Est(1)} \sim 4.4 As(O)-(OH)-(O')$ ,  $p K_{Est(2)} \sim 7.4$  (phenolic OH),  $p K_{Est(3)} \sim 7.7$  (As(O)-2(O'). Crystd from water.

1-Nitroso-2-naphthol-3,6-disulfonic acid, di-Na salt, hydrate (Nitroso-R-salt) [525-05-3] M 377.3, m >300°,  $pK_{Est(1)}<0$  (SO<sub>3</sub><sup>-</sup>),  $pK_{Est(2)}\sim7$  (OH). Purified by dissolution in aqueous alkali and precipitation by addition of HCl.

Nitrosyl chloride [2696-92-6] M 65.5, b -5.5°. Fractionally distilled at atmospheric pressure in an allglass, low temperature still, taking the fraction boiling at -4° and storing it in sealed tubes.

**Nitrous oxide** [10024-97-2] **M 44.0, b -88.5°.** Washed with conc alkaline pyrogallol solution, to remove  $O_2$ ,  $CO_2$ , and  $NO_2$ , then dried by passage through columns of  $P_2O_5$  or Drierite, and collected in a dry trap cooled in liquid  $N_2$ . Further purified by freeze-pump-thaw and distn cycles under vacuum [Ryan and Freeman J Phys Chem **81** 1455 1977].

Nuclear Fast Red (1-amino-2,4-dihydroxy-5,10-anthraquinone-3-sulfonic acid Na Salt) [6409-77-4] M 357.3, m >290°(dec),  $\lambda_{max}$  518nm. A soln of 5g of the dye in 250mL of warm 50% EtOH was cooled to 15° for 36h, then filtered on a Büchner funnel, washed with EtOH until the washings were colourless, then with 100mL of diethyl ether and dried over P<sub>2</sub>O<sub>5</sub>. [Kingsley and Robnett Anal Chem 33 552 1961.]

### Octadecyl isonicotinate see hydrogen ionophore IV, ETH 1778 on p. 430.

Octadecyl trichlorosilane [112-04-9] M 387.9, b 159-162°/13mm, 185-199°/2-3mm,  $d_4^{30}$  0.98. Purified by fractional distillation. [J Am Chem Soc 69 2916 1947.]

Octadecyl trimethylammonium bromide [1120-02-1] M 392.5, m ~250°dec, 230-240°(dec). Cryst from EtOH or H<sub>2</sub>O (sol 1 in 1000parts). Very soluble in Me<sub>2</sub>CO. [J Am Chem Soc 68 714 1946.]

Octamethyl cyclotetrasiloxane [556-67-2] M 296.6, m 17-19°, 17.58°, 18.5°, b 74°/20 mm, 176.4°/760 mm,  $d_4^{29.3}$  0.9451,  $n_D^{30}$  1.3968. Solid has two forms, m 16.30° and 17.65°. Dry over CaH<sub>2</sub> and distil. Further fractionation can be effected by repeated partial freezing and discarding the liquid phase. [J Am Chem Soc 76 399 1954, 75 6313 1954.]

Octamethyl trisiloxane [107-51-7] M 236.5, m -80°, b 151.7°/747mm, 153°/760mm. Distil twice, the middle fraction from the first distillation is again distilled, and the middle fraction of the second distillation is used. [J Am Chem Soc 68 358, 691 1946, J Chem Soc 1908 1953.]

Octaphenyl cyclotetrasiloxane [546-56-5] M 793.2, m 201-202°, 203-204°, b 330-340°/1mm. Recryst from AcOH, EtOAc,  ${}^{*}C_{6}H_{6}$  or  ${}^{*}C_{6}H_{6}$ /EtOH. It forms two stable polymorphs and both forms as well as the mixture melt at 200-201°. There is a metastable form which melts at 187-189°. [J Am Chem Soc 67 2173 1945, 69 488 1947.]

Octyl trichlorosilane [5283-66-9] M 247.7, b 96.5°/10mm, 112°/15mm. 119°/28mm, 229°/760mm, d 1.0744, n 1.4453. Purified by repeated fractionation using a 15-20 theoretical plates glass column packed with glass helices. This can be done more efficiently using a spinning band column. The purity can be checked by analysing for Cl [ca 0.5-1g of sample is dissolved in 25mL of MeOH, diluted with H<sub>2</sub>O and titrated with standard alkali. [J Am Chem Soc 68 475 1946, 80 1737 1958.]

**Orange I [tropaeolin 000 Nr1, 4-(4-hydroxy-1-naphthylazo)benzenesulfonic acid sodium** salt] [523-44-4] M 350.3, m >260°(dec). Purified by dissolving in the minimum volume of  $H_2O$ , adding, with stirring, a large excess of EtOH. The salt separates as orange needles. It is collected by centrifugation or filtration, washed with absolute EtOH (3 x) and Et<sub>2</sub>O (2x) in the same way and dried in a vacuum desiccator over KOH. The free acid can be recrystallised from EtOH. [*Chem Ber 64* 86 1931.] The purity can be checked by titration with titanium chloride [J Am Chem Soc 68 2299 1946].

**Orange II** [tropaeolin 000 Nr2, 4-(2-hydroxy-1-naphthylazo)benzenesulfonic acid sodium salt] [633-96-5] M 350.3. Purification is as for Orange I. The solubility in H<sub>2</sub>O is 40g/L at 25°. [Helv Chim Acta 35 2579 1952.] Also purified be extracting with a small volume of water, then crystd by dissolving in boiling water, cooling to ca 80°, adding two volumes of EtOH and cooling. When cold, the ppte is filtered off, washed with a little EtOH and dried in air. It can be salted out from aqueous solution with sodium acetate, then repeatedly extracted with EtOH. Meggy and Sims [J Chem Soc 2940 1956], after crystallising the sodium salt twice from water, dissolved it in cold water (11mL/g) and conc HCl added to ppte the dye acid which was separated by centrifugation, redissolved and again ppted with acid. After washing the ppte three times with 0.5M acid it was dried over NaOH, recrystd twice from absolute EtOH, washed with a little Et<sub>2</sub>O, dried over NaOH and stored over conc H<sub>2</sub>SO<sub>4</sub> in the dark.

**Orange G** (1-phenylazo-2-naphthol-6,8-disulfonic acid di-Na salt) [1936-15-8] M 452.4,  $pK_{Est} \sim 9$ . Recryst from 75% EtOH, dry for 3h at 110° and keep in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub>. The free acid crystallises from EtOH or conc HCl in deep red needles with a green reflex. [J Am Chem Soc 48 2483 1923, J Chem Soc 292 1938.]

Orange RO {acid orange 8, 1,8-[bis(4-*n*-propyl-3-sulfophenyl-1-amino)]anthra-9,10quinone di-Na salt} [5850-86-2] M 364.4, CI 15575,  $\lambda$ max 490nm. Salted out three times with sodium acetate, then repeatedly extracted with EtOH.

Osmium tetroxide (osmic acid) [208/6-12-0] M 524.2, m 40.6°, b 59.4°/60 mm, 71.5°/100 mm, 109.3°/400 mm, 130°/760 mm, d 5.10, pK<sub>1</sub><sup>25</sup>7.2, pK<sub>2</sub><sup>25</sup>12.2, pK<sub>3</sub><sup>25</sup> 13.95,  $pK_4^{25}$  14.17 (H<sub>4</sub>OsO<sub>6</sub>). It is VERY TOXIC and should be manipulated in a very efficient fume cupboard. It attacks the eyes severely (use also face protection) and is a good oxidising agent. It is volatile and has a high vapour pressure (11mm) at room temp. It sublimes and dists well below its boiling point. It is sol in  ${}^{*}C_{6}H_{6}$ , H<sub>2</sub>O (7.24% at 25°), CCl<sub>4</sub> (375% at 25°), EtOH and Et<sub>2</sub>O. It is estimated by dissolving a sample in a glass stoppered flask containing 25mL of a solution of KI (previously saturated with CO<sub>2</sub>) and acidified with 0.35M HCl. After gentle shaking in the dark for 30min, the solution is diluted to 200mL with distilled  $H_2O$  satd with  $CO_2$  and titrated with standard thiosulfate using Starch indicator. This method is not as good as the gravimetric method. Hydrazine hydrochloride (0.1 to 0.3g) is dissolved in 3M HCl (10mL) in a glass stoppered bottle. After warming to 55-65°, a weighed sample of OsO4 solution is introduced, and the mixture is digested on a water bath for 1h. The mixture is transferred to a weighed glazed crucible and evaporated to dryness on a hot plate. A stream if  $H_2$  is started through the crucible and the crucible is heated over a burner for 20-30 min. The stream of  $H_2$  is continued until the crucible in cooled to room temperature, and then the H<sub>2</sub> is displaced by CO<sub>2</sub> in order to avoid rapid combustion of H<sub>2</sub>. Finally the crucible is weighed. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1603 1965; J Am Chem Soc **60** 1822 1938.]

§ Available commercially on a polymer support.

**Oxygen** [7782-44-7] **M 32.00, m -218.4°, b -182.96°, d<sup>-183</sup> 1.149, d<sup>-252.5</sup> 1.426.** Purified by passage over finely divided platinum at 673°K and Cu(II) oxide (see under nitrogen) at 973°, then condensed in liquid N<sub>2</sub>-cooled trap. **HIGHLY EXPLOSIVE in contact with organic matter.** 

**Palladium (II) acetate** [3375-31-3] M 244.5, m 205°dec,  $pK_1^{25}$  1.0,  $pK_2^{25}$  1.2 (for  $Pd_2^{2+}$ ). Recryst from CHCl<sub>3</sub> as purple crystals. It can be washed with AcOH and H<sub>2</sub>O and dried in air. Large crystals can be obtained by dissolving in  ${}^{*}C_6H_6$  and allowing to evaporate slowly at room temp. It forms green adducts with nitrogen donors, dissolved in KI soln but is insoluble in aqueous saturated NaCl, and NaOAc. Soluble in HCl to form  $PdCl_4^{2-}$ . [Chem Ind (London) 544 1964; J Chem Soc 658 1970.]

**Palladium (II) acetyl acetone** [14024-61-4] **M 304.6.** Recrystd from  ${}^{*}C_{6}H_{6}$ -pet ether and sublimed *in vacuo*. It is soluble in heptane,  ${}^{*}C_{6}H_{6}$  (1.2% at 20°, 2.2 at 40°), toluene (0.56% at 20°, 1.4% at 40°) and acetylacetone (1.2% at 20°, 0.05% at 40°). [J Inorg Nucl Chem 5 295 1957/8; Inorg Synth 5 105 1957.]

**Palladium (II) chloride** [7647-10-1] **M 177.3, m 678-680°.** The anhydrous salt is insoluble in  $H_2O$  and dissolves in HCl with difficulty. The dihydrate forms red *hygroscopic* crystals that are readily reduced to Pd. Dissolve in conc HCl through which dry  $Cl_2$  was bubbled. Filter this solution which contains  $H_2PdCl_4$  and  $H_2PdCl_6$  and on evaporation yields a residue of pure PdCl<sub>2</sub>. [Handbook of Preparative Inorganic Chemistry (Ed Brauer) Vol 2 1582 1965; Org Synth Coll Vol III 685 1955.]

**Palladium (II) cyanide** [2035-66-7] M 158.1. A yellow solid, wash well with H<sub>2</sub>O and dry in air. [*Inorg Chem* 2 245 1946]. **POISONOUS.** 

**Palladium (II) trifluoroacetate** [42196-31-6] M 332.4, m 210°(dec). Suspend in trifluoroacetic acid and evaporate on a steam bath a couple of times. The residue is then dried in vacuum (40-80°) to a brown powder. [J Chem Soc 3632 1965; J Am Chem Soc 102 3572 1980.]

**Pentafluorophenyl dimethylchlorosilane (Flophemesyl chloride)** [20082-71-7] M 260.7, b 89-90°/10mm,  $d_4^{30}$  1.403,  $n_D^{30}$  1.447. If goes turbid on cooling due to separation of some LiCl, then dissolve in Et<sub>2</sub>O, filter and fractionate. [J Chromatogr 89 225 1974, 132 548 1977,.]

**Perchloric acid** [7601-90-3] **M 100.5, d 1.665, pK^{25} -2.4 to -3.1 (HClO<sub>4</sub>).** The 72% acid has been purified by double distn from silver oxide under vacuum: this frees the acid from metal contamination. Anhydrous acid can be obtained by adding gradually 400-500mL of oleum (20% fuming H<sub>2</sub>SO<sub>4</sub>) to 100-120mL of 72% HClO<sub>4</sub> in a reaction flask cooled in an ice-bath. The pressure is reduced to 1mm (or less), with the reaction mixture at 20-25°. The temperature is gradually raised during 2h to 85°, the distillate being collected in a receiver cooled in Dry-ice. For further details of the distillation apparatus [see Smith J Am Chem Soc 75 184 1953]. HIGHLY EXPLOSIVE, a strong protective screen should be used at all times.

Phenylarsonic acid (benzenearsonic acid) [98-05-5] M 202.2, m 155-158°(dec),  $pK_1^{25}3.65$ ,  $pK_2^{25}8.77$ . Crystd from H<sub>2</sub>O (3mL/g) between 90° and 0°.

Phenylboric acid (benzeneboronic acid) [98-80-6] M 121.9, m ~43°, 215-216° (anhydride), 217-220°,  $pK_1^{25}$  8.83. It recrystallises from H<sub>2</sub>O, but can convert spontaneously to benzeneboronic anhydride or phenylboroxide on standing in dry air. Possible impurity is dibenzeneborinic acid which can be removed by washing with pet ether. Heating in an oven at 110°/760mm 1h converts it to the anhydride m 214-216°. Its solubility in H<sub>2</sub>O is 1.1% at 0° and 2.5% at 25° and in EtOH it is 10% (w/v). [Gilman and Moore J Am Chem Soc 80 3609 1958.] If the acid is required, not the anhydride, the acid (from recrystallisation in H<sub>2</sub>O) is dried in a slow stream of air saturated with H<sub>2</sub>O. The anhydride is converted to the acid by recrystallisation from H<sub>2</sub>O. The acid gradually dehydrates to the anhydride if left in air at room temperature with 30-40% relative humidity. The melting point is usually that of the anhydride because the acid dehydrates before it melts [Washburn et al. Org Synth Coll Vol IV 68 1963].

Phenyl dimethyl chlorosilane (DMPSCl, chlorodimethylphenylsilane) [768-33-2] M 170.7, b 79°/15mm, 85-87°/32mm, 196°/760mm, d 1.017, n 1.509. Fractionate through a 1.5 x 18 inch column packed with stainless steel helices; or a spinning band column. [J Am Chem Soc 74 386 1952; 70 1115 1948; J Chem Soc 494 1953.] Used for standardising MeLi or MeMgBr which form Me<sub>3</sub>PhSi, estimated by GC [Maienthal et al. J Am Chem Soc 76 6392 1954; House and Respess J Organomet Chem 4 95 1965.] TOXIC and MOISTURE SENSITIVE.

1,2-Phenylenephosphorochloridate (2-chloro-1,3,2-benzodioxaphosphole-2-oxide) [1499-17-8] M 190.5, m 52°, 58-59°, 59-61°, b 80-81°/1-2mm, 118°/10mm, 122°/12mm, 125°/16mm, 155°/33mm. Distil in a vacuum, sets to a colourless solid. It is soluble in pet ether, \*benzene and slightly soluble in  $Et_2O$ . [J Chem Soc (C) 2092 1970; Justus Liebigs Ann Chem 454 109 1927.]

Phenylmercuric hydroxide [100-57-2] M 294.7, m 195-203°. Crystd from dilute aqueous NaOH.

Phenylmercuric nitrate [8003-05-2] M 634.4, m 178-188°. Crystd from water.

**Phenylphosphinic acid [benzenephosphinic acid, PhPH(O)(OH)]** [1779-48-2] M 142.1, m 70°, 71°, 83-85°, 86°,  $pK_1^{25}$  1.75. Cryst from H<sub>2</sub>O (sol 7.7% at 25°). Purified by placing the solid in a flask covered with dry Et<sub>2</sub>O, and allowed to stand for 1 day with intermittent shaking. Et<sub>2</sub>O was decanted off and the process repeated. After filtration, excess Et<sub>2</sub>O was removed in vacuum. [Justus Liebigs Ann Chem 181 265 1876; Anal Chem 29 109 1957; NMR: J Am Chem Soc 78 5715 1956.]

**Phenylphosphonic acid** [1571-33-1] **M 158.1, m 164.5-166°, pK\_2^{25} 7.43** (7.07). Best recryst from H<sub>2</sub>O by concentrating an aqueous soln to a small volume and allowing to crystallise. Wash the crystals with ice cold H<sub>2</sub>O and dry in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub>. [J Am Chem Soc 78 1045 1954.]  $pK^{25}$  values in H<sub>2</sub>O are 7.07, and in 50% EtOH 8.26. [J Am Chem Soc 75 2209 1953.] [IR: Anal Chem 23 853 1951.]

Phenylphosphonic dichloride (P,P-dichlorophenyl phosphine oxide) [824-72-6] M 195.0, b 83-84°/1mm, 135-136°/23mm,  $d_4^{30}$  1.977,  $n_D^{30}$  1.5578. Fractionally distilled using a spinning band column. [J Am Chem Soc 76 1045 1954; NMR: J Am Chem Soc 78 3557, 5715 1956; IR: Anal Chem 23 853 1951.]

**Phenylphosphonous acid** [PhP(OH)<sub>2</sub>] [121-70-0] M 141.1, m 71°,  $pK_{Est} < 0$ ,  $pK^{17}$  2.1. Crystd from hot H<sub>2</sub>O.

**Phenylphosphonous dichloride** (**P,P-dichloro phenyl phosphine**) [644-97-3] **M 179.0, b 68-70°/1mm, 224-226°/atm, d\_4^{30} 1.9317, n\_D^{35} 1.5962.** Vacuum distilled by fractionating through a 20cm column packed with glass helices (better use a spinning band column) [*J Am Chem Soc* 73 755 1951; NMR: *J Am Chem Soc* 78 3557 1956; IR: Anal Chem 23 853 1951]. It forms a yellow Ni complex: Ni(C<sub>6</sub>H<sub>5</sub>Cl<sub>2</sub>P)<sub>4</sub> (**m** 91-92°, from H<sub>2</sub>O)[*J Am Chem Soc* 79 3681 1957] and a yellow complex with molybdenum carbonyl: Mo(CO)<sub>3</sub>.(C<sub>6</sub>H<sub>5</sub>Cl<sub>2</sub>P)<sub>3</sub> (**m** 106-110°dec) [*J Chem Soc* 2323 1959].

Phenyl phosphoro chloridate (diphenyl phosphoryl chloride) [2524-64-3] M 268.6, b 141°/1mm, 194°/13mm, 314-316/272mm,  $d_4^{30}$  1.2960,  $n_D^{35}$  1.5490. Fractionally distd in a good vac, better use a spinning band column. [J Am Chem Soc 81 3023 1959; IR: J Chem Soc 475, 481 1952.]

Phenyl phosphoryl dichloride [770-12-7] M 211.0, m -1°, b 103-104°/2mm, 110-111°/10mm, 130-134°/21mm, 241-243°/atm,  $d_4^{30}$  1.4160,  $n_D^{30}$  1.5216. Fractionally distilled under as good a vacuum as possible using an efficient fractionating column or a spinning band column. It should be redistilled if the IR is not very good [IR: J Chem Soc 475, 481 1952; J Am Chem Soc 60 750 1938, 80 727 1958]. HARMFUL VAPOURS.

Phenylthio trimethylsilane (trimethyl phenylthio silane) [4551-15-9] M 182.4, b 95-99°/12mm,  $d_4^{30}$  0.97. Purification is as for phenyl trimethyl silylmethyl sulfide on p. 450. Phenyl trimethoxylsilane (trimethoxysilyl benzene) [2996-92-1] M 198.3, b  $103^{\circ}/20$  mm, 130.5-131°/45mm,  $d_4^{35}$  1.022,  $n_D^{35}$  1.4698. Fractionate through an efficient column but note that it forms an azeotrope with MeOH which is a likely impurity. [J Am Chem Soc 75 2712 1953; J Gen Chem USSR (Engl Transl) 25 1079 1955.]

Phenyl trimethylsilane (trimethylphenylsilane) [768-32-1] M 150.3, b 67.3°/20mm, 98-99°/80mm, 170.6°/738mm,  $d_4^{25}$  0.8646. See trimethylphenylsilane on p. 489.

Phenyl trimethylsilylmethyl sulfide [(phenylthiomethyl)trimethylsilane] [17873-08-4] M 196.4, b 48°/0.04mm, 113-115°/12mm, 158.5°/52mm,  $d_4^{30}$  0.9671,  $n_D^{30}$  1.5380. If the sample is suspect then add H<sub>2</sub>O, wash with 10% aqueous NaOH, H<sub>2</sub>O again, dry (anhydrous CaCl<sub>2</sub>) and fractionally distil through a 2ft column packed with glass helices. [J Am Chem Soc 76 3713 1954.]

**Phosgene** [75-44-5] **M 98.9, b 8.2°/756mm.** Dried with Linde 4A molecular sieves, degassed and distilled under vacuum. This should be done in a closed system such as a vacuum line. **HIGHLY TOXIC**, should not be inhaled. If it is inhaled operator should lie still and made to breath ammonia vapour which reacts with phosgene to give urea.

**Phosphine** [7803-51-2] **M 34.0, m -133°, b -87.7°, pK -14, pK<sub>b</sub> 28**. Best purified in a gas line (in a vacuum) in an efficient fume cupboard. It is spontaneously flammable, has a strong odour of decayed fish and is **POISONOUS**. The gas is distd through solid KOH towers (two), through a Dry ice-acetone trap (-78°, to remove H<sub>2</sub>O, and P<sub>2</sub>H<sub>4</sub> which causes spontaneous ignition with O<sub>2</sub>), then through two liquid N<sub>2</sub> traps (-196°), followed by distn into a -126° trap (Dry ice-methylcyclohexane slush), allowed to warm in the gas line and then seal in ampoules preferably under N<sub>2</sub>. IR: v 2327 (m), 1121 (m) and 900 (m) cm<sup>-1</sup>. [Klement in *Handbook of Preparative Inorganic Chemistry (Ed. Brauer)* Vol I, pp. 525-530 1963; Gokhale and Jolly *Inorg Synth* **9** 56 1967.] PH<sub>3</sub> has also been absorbed into a soln of cuprous chloride in hydrochloric acid (when CuCl.PH<sub>3</sub> is formed). PH<sub>3</sub> gas is released when the soln is heated and the gas is purified by passage through KOH pellets and over then P<sub>2</sub>O<sub>5</sub>. The solubility is 0.26mL/1 mL of H<sub>2</sub>O at 20° and a crystalline hydrate is formed on releasing the pressure on an aq soln.

**Phosphonitrilic chloride (tetramer)** [1832-07-1] **M 463.9.** Purified by zone melting, then crystd from pet ether (b 40-60°) or *n*-hexane. [van der Huizen et al. J Chem Soc, Dalton Trans 1317 1986.]

**Phosphonitrilic chloride (trimer) (hexachlorocyclotriphosphazine)** [940-71-6] M 347.7, m 112.8°, 113-114°. Purified by zone melting, by crystallisation from pet.ether, *n*-hexane or \*benzene, and by sublimation. [van der Huizen et al. J Chem Soc, Dalton Trans 1311 1986; Meirovitch et al. J Phys Chem 88 1522 1984; Alcock et al. J Am Chem Soc 106 5561 1984; Winter and van de Grampel J Chem Soc, Dalton Trans 1269 1986.]

**Phosphoric acid** [7664-38-2] **M 98.0, m 42.3°, pK\_1^{25} 2.15, pK\_2^{25} 7.21, pK\_3^{25} 12.33. Pyrophosphate can be removed from phosphoric acid by diluting with distilled H<sub>2</sub>O and refluxing overnight. By cooling to 11° and seeding with crystals obtained by cooling a few millilitres in a Dry-ice/acetone bath, 85% orthophosphoric acid crystallises as H<sub>3</sub>PO<sub>4</sub>.H<sub>2</sub>O. The crystals are separated using a sintered glass filter. It has pKa^{25} values of 2.15, 7.20 and 12.37 in H<sub>2</sub>O.** 

**Phosphorus (red)** [7723-14-0] M 31.0, m 590°/43atm, ignites at 200°, d 2.34. Boiled for 15min with distilled H<sub>2</sub>O, allowed to settle and washed several times with boiling H<sub>2</sub>O. Transferred to a Büchner funnel, washed with hot H<sub>2</sub>O until the washings are neutral, then dried at 100° and stored in a desiccator.

**Phosphorus (white)** [7723-14-0] **M 31.0, m 590, d 1.82.** Purified by melting under dilute  $H_2SO_4^-$  dichromate (possible **carcinogen**) mixture and allowed to stand for several days in the dark at room temperature. It remains liquid, and the initial milky appearance due to insoluble, oxidisable material gradually disappears. The phosporus can then be distilled under vacuum in the dark [Holmes *Trans Faraday Soc* 58 1916]

1962]. Other methods include extraction with dry  $CS_2$  followed by evaporation of the solvent, or washing with 6M HNO<sub>3</sub>, then H<sub>2</sub>O, and drying under vacuum. **POISONOUS.** 

**Phosphorus oxychloride** [10025-87-3] **M 153.3, b 105.5°, n 1.461, d 1.675.** Distilled under reduced pressure to separate from the bulk of the HCl and the phosphoric acid, the middle fraction being distilled into ampoules containing a little purified mercury. These ampoules are sealed and stored in the dark for 4-6 weeks with occasional shaking to facilitate reaction of any free chloride with the mercury. The POCl<sub>3</sub> is then again fractionally distd and stored in sealed ampoules in the dark until used [Herber J Am Chem Soc 82 792 1960]. Lewis and Sowerby [J Chem Soc 336 1957] refluxed their distilled POCl<sub>3</sub> with Na wire for 4h, then removed the Na and again distilled. Use Na only with almost pure POCl<sub>3</sub> to avoid explosions. HARMFUL VAPOURS.

**Phosphorus pentabromide** [7789-69-7] **M 430.6, m <100°, b 106°(dec).** Dissolved in pure nitrobenzene at 60°, filtering off any insoluble residue on to sintered glass, then crystallised by cooling. Washed with dry  $Et_2O$  and removed the ether in a current of dry  $N_2$ . (All manipulations should be performed in a dry-box.) [Harris and Payne J Chem Soc 3732 1958]. Fumes in moist air because of hydrolysis. HARMFUL VAPOURS.

**Phosphorus pentachloride** [10026-13-8] **M 208.2, m 179-180°(sublimes).** Sublimed at 160-170° in an atmosphere of chlorine. The excess chlorine was then displaced by dry N<sub>2</sub> gas. All subsequent manipulations were performed in a dry-box [Downs and Johnson J Am Chem Soc 77 2098 1955]. Fumes in moist air. HARMFUL VAPOURS.

**Phosphorus pentasulfide** [1314-80-3] M 444.5, m 277-283°. Purified by extraction and crystallisation with  $CS_2$ , using a Soxhlet extractor. Liberates  $H_2S$  in moist air. HARMFUL VAPOURS.

**Phosphorus pentoxide** [1314-56-3] **M 141.9, m 562°, b 605°.** Sublimed at 250° under vacuum into glass ampoules. Fumes in moist air and reacts violently with water. **HARMFUL VAPOURS and attacks skin.** 

**Phosphorus sesquisulfide**  $P_4S_3$  [1314-85-8] M 220.1, m 172°. Extracted with CS<sub>2</sub>, filtered and evaple to dryness. Placed in H<sub>2</sub>O, and steam was passed through for an hour. The H<sub>2</sub>O was then removed, the solid was dried, followed by crystallisation from CS<sub>2</sub> [Rogers and Gross J Am Chem Soc 74 5294 1952].

**Phosphorus sulfochloride (phosphorus thiochloride)** [3982-91-0] M 169.4, m -35°, b 122-124°, 125°(corr),  $d_4^{30}$  1.64,  $n_D^{30}$  1.556. Possible impurities are PCl<sub>5</sub>, H<sub>3</sub>PO<sub>4</sub>, HCl and AlCl<sub>3</sub>. Gently mix with H<sub>2</sub>O to avoid a heavy emulsion, the product decolorises immediately and settles to the bottom layer. HARMFUL VAPOURS.

**Phosphorus tribromide** [7789-60-8] **M 270.7, m -41.5°, b 168-170°/725mm, 171-173°/atm, 172.9°/760mm(corr), d<sub>4</sub><sup>30</sup> 2.852.** It is decomposed by moisture, should be kept dry and is corrosive. Purified by distillation through an efficient fractionating column (see Whitmore and Lux J Am Chem Soc 54 3451] in a slow stream of dry N<sub>2</sub>, i.e. under strictly dry conditions. [Inorg Synth 2 147 1946; Org Synth Col Vol II 358 1943.] Dissolve in CCl<sub>4</sub>, dry over CaCl<sub>2</sub>, filter and distil. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) vol I 532 1963.] Store in sealed ampoules under N<sub>2</sub> and kept away from light. **HARMFUL VAPOURS.** 

**Phosphorus trichloride** [7719-12-2] M 137.3, b 76°, n 1.515, d 1.575. Heated under reflux to expel dissolved HCl, then distilled. It has been further purified by vacuum fractionation several times through a -45° trap into a receiver at -78°. HARMFUL VAPOURS.

**Phosphorus triiodide** [13455-01-1] **M 411.7, m 61°.** Decomposes in moist air and must be kept in a desiccator over CaCl<sub>2</sub>. It is crystallised from sulfur-free CS<sub>2</sub> otherwise the **m** decreases to ca 55°. It is best prepared freshly. [J Am Chem Soc 49 307 1927; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) vol I 541 1963.] HARMFUL VAPOURS.

12-Phosphotungstic acid [12501-23-4] M 2880.2, m ~96°. A few drops of conc HNO<sub>3</sub> were added to 100g of phosphotungstic acid dissolved in 75mL of water, in a separating funnel, and the soln was extracted with diethyl ether. The lowest of the three layers, which contained a phosphotungstic acid-ether complex, was separated, washed several times with 2M HCl, then with water and again extracted with ether. Evaporation of the ether, under vacuum with mild heating on a water bath gave crystals which were dried under vacuum and ground [Matijevic and Kerker, J Am Chem Soc 81 1307 1959].

**Phthalocyanine** [574-93-6] **M 514.6.** Purified by sublimation (two to three times) in an argon flow at 300-400Pa. Similarly for the Cu(II), Ni(II), Pb(II), VO(II) and Zn(II) phthalocyanine complexes.

**Platinum (II) acetylacetonate** [15170-57-7] M 393.3, m 249-252°. Recrystd from <sup>\*</sup>C<sub>6</sub>H<sub>6</sub> as yellow crystals and dried in air or in a vacuum desiccator. [Chem Ber 34 2584 1901.]

**Platinum (II) chloride** [10025-65-7] **M 266.0, d 5.87.** It is purified by heating at 450° in a stream of Cl<sub>2</sub> for 2h. Some sublimation occurs because the PtCl<sub>2</sub> sublimes completely at 560° as red (almost black) needles. This sublimate can be combined to the bulk chloride and while still at ca 450° it should be transferred to a container and cooled in a desiccator. A probable impurity is PtCl<sub>4</sub>. To test for this add a few drops of H<sub>2</sub>O (in which PtCl<sub>4</sub> is soluble) to the salt, filter and add an equal volume of saturated aqueous NH<sub>4</sub>Cl to the filtrate. If no ppte is formed within 1 min then the product is pure. If a ppte appears then the whole material should be washed with small volumes of H<sub>2</sub>O until the soluble PtCl<sub>4</sub> is removed. The purified PtCl<sub>2</sub> is partly dried by suction and then dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub>. It is insoluble in H<sub>2</sub>O but soluble in HCl to form chloroplatinic acid (H<sub>2</sub>PtCl<sub>4</sub>) by disproportionation. [Inorg Synth 6 209 1960.]

**Polystyrenesulfonic acid sodium salt**  $(-CH_2CH(C_6H_4SO_3Na)-)$  [25704-18-1]. Purified by repeated pptn of the sodium salt from aqueous soln by MeOH, with subsequent conversion to the free acid by passage through an Amberlite IR-120 ion-exchange resin. [Kotin and Nagasawa J Am Chem Soc 83 1026 1961.] Recrystd from EtOH. Also purified by passage through cation and anion exchange resins in series (Rexyn 101 cation exchange resin and Rexyn 203 anion exchange resin), then titrated with NaOH to pH 7. The sodium form of polystyrenesulfonic acid ppted by addition of 2-propanol. Dried in a vac oven at 80° for 24h, finally increasing to 120° prior to use. [Kowblansky and Ander J Phys Chem 80 297 1976.]

Pontacyl Carmine 2G (Acid Red 1, Amido Naphthol Red G, Azophloxine, 1-acetamido-8hydroxy-7-phenylazonaphthalene-3,7-disulfonic acid di-Na salt) [3734-67-6] M 510.4, CI 18050,  $\lambda$ max 532nm. Salted out three times with sodium acetate, then repeatedly extracted with EtOH. See Solochrome Violet R on p. 352 in Chapter 4. [McGrew and Schneider J Am Chem Soc 72 2547 1950.]

Pontacyl Light Yellow GX [Acid Yellow 17, 1-(2,5-dichloro-4-sulfophenyl]-3-methyl-4-(4-sulfophenylazo)-5-hydroxypyrazole di-Na Salt] [6359-98-4] M 551.3, CI 18965,  $\lambda max$ 400nm. Purification as for Pontacyl Carmine 2G above.

**Potassium (metal)** [7440-09-7] **M 39.1, m 62.3°, d 0.89.** Oil was removed from the surface of the metal by immersion in *n*-hexane and pure  $Et_2O$  for long periods. The surface oxide was next removed by scraping under ether, and the potassium was melted under vacuum. It was then allowed to flow through metal constrictions into tubes that could be sealed, followed by distillation under vacuum in the absence of mercury vapour (see Sodium). **EXPLOSIVE IN WATER.** 

**Potassium acetate** [127-08-2] M 98.2, m 292°, d 1.57, pK<sup>25</sup> 16 (for aquo K<sup>+</sup>). Crystd three times from water-ethanol (1:1) dried to constant weight in a vacuum oven, or crystd from anhydrous acetic acid and pumped dry under vacuum for 30h at 100°.

Potassium 4-aminobenzoate [138-84-1] M 175.2. Crystd from EtOH.

Potassium antimonyltartrate (H<sub>2</sub>O) [28300-74-5] M 333.9,  $[\alpha]_D$  +141° (c 2, H<sub>2</sub>O). Crystd from water (3mL/g) between 100° and 0°. Dried at 100°.

Potassium benzoate [582-25-2] M 160.2. Crystd from water (1mL/g) between 100° and 0°.

**Potassium bicarbonate** [298-14-6] **M 100.1.** Crystd from water at  $65-70^{\circ}$  (1.25mL/g) by filtering, then cooling to 15°. During all operations, CO<sub>2</sub> is passed through the stirred mixture. The crystals, sucked dry at the pump, are washed with distilled water, dried in air and then over H<sub>2</sub>SO<sub>4</sub> in an atmosphere of CO<sub>2</sub>.

**Potassium biiodate** [13455-24-8] **M 389.9.** Crystd three times from hot water (3mL/g), stirred continuously during each cooling. After drying at 100° for several hours, the crystals are suitable for use in volumetric analysis.

Potassium bisulfate [7646-93-7] M 136.2, m 214°. Crystd from H<sub>2</sub>O(1mL/g) between 100° and 0°.

Potassium borohydride [13762-51-1] M 53.9, m ~500°(dec). Crystd from liquid ammonia.

**Potassium bromate** [7758-01-2] **M 167.0, m 350°(dec at 370°), d 3.27.** Crystd from distilled  $H_2O(2mL/g)$  between 100° and 0°. To remove bromide contamination, a 5% soln in distilled  $H_2O$ , cooled to 10°, has been bubbled with gaseous chlorine for 2h, then filtered and extracted with reagent grade CCl<sub>4</sub> until colourless and odourless. After evaporating the aqueous phase to about half its volume, it was cooled again slowly to about 10°. The crystalline KBrO<sub>3</sub> was separated, washed with 95% EtOH and vacuum dried [Boyd, Cobble and Wexler J Am Chem Soc 74 237 1952]. Another way to remove Br<sup>-</sup> ions was by stirring several times in MeOH and then dried at 150° [Field and Boyd J Phys Chem 89 3767 1985].

**Potassium bromide** [7758-02-3] **M 119.0, m 734°, d 2.75.** Crystd from distilled water (1mL/g) between 100° and 0°. Washed with 95% EtOH, followed by  $Et_2O$ . Dried in air, then heated at 115° for 1h, pulverised and heated in a vacuum oven at 130° for 4h. Has also been crystd from aqueous 30% EtOH, or EtOH, and dried over  $P_2O_5$  under vacuum before heating in an oven.

**Potassium tert-butoxide** [865-47-4] M 112.2. It sublimes at 220°/1 Torr. Last traces of tert-BuOH are removed by heating at 150-160°/2mm for 1h. It is best prepared fresh; likely impurities are tert-BuOH, KOH and  $K_2CO_3$  depending on exposure to air. Its solubility at 25°-26° in hexane, toluene, Et<sub>2</sub>O, and THF is 0.27%, 2.27%, 4.34% and 25.0% repectively. [J Am Chem Soc 78 5938, 4364 1956.]

**Potassium carbonate** [584-08-7] **M 138.2, m 898°, d 2.3.** Crystd from water between 100° and 0°. After 2 recrystns tech grade had **B**, Li and Fe at 1.0, 0.04 and 0.01 ppm resp.

**Potassium chlorate** [3811-04-9] **M 122.6, m 368°.** Crystd from water (1.8mL/g) between 100° and 0°, and the crystals are filtered onto sintered glass.

**Potassium chloride** [7447-40-7] **M 74.6, m 771°, d 1.98.** Dissolved in conductivity water, filtered, and saturated with chlorine (generated from conc HCl and KMnO<sub>4</sub>). Excess chlorine was boiled off, and the KCl was ppted by HCl (generated by dropping conc HCl into conc H<sub>2</sub>SO<sub>4</sub>). The ppte was washed with water, dissolved in conductivity water at 90-95°, and crystd by cooling to about -5°. The crystals were drained at the centrifuge, dried in a vacuum desiccator at room temperature, then fused in a platinum dish under N<sub>2</sub>, cooled and stored in desiccator. Potassium chloride has also been sublimed in a stream of prepurified N<sub>2</sub> gas and collected by electrostatic discharge [Craig and McIntosh *Can J Chem* **30** 448 1952].

Potassium chromate [7789-00-6] M 194.2, m 975°, d 2.72,  $pK_1^{25}0.74$ ,  $pK_2^{25}6.49$  (for H<sub>2</sub>CrO<sub>4</sub>). Crystd from conductivity water (0.6g/mL at 20°), and dried between 135° and 170°.

Potassium cobalticyanide [13963-58-1] M 332.4, m dec on heating, d 1.91. Crystd from water to remove traces of HCN.

**Potassium cyanate** [590-28-3] **M 81.1, d 2.05, pK<sup>25</sup> 3.46 (for HCNO).** Common impurities include ammonia and bicarbonate ion (from hydrolysis). Purified by preparing a saturated aqueous solution at

50°, neutralising with acetic acid, filtering, adding two volumes of EtOH and keeping for 3-4h in an ice bath. (More EtOH can lead to co-precipitation of KHCO<sub>3</sub>.) Filtered, washed with EtOH and dried rapidly in a vacuum desiccator ( $P_2O_5$ ). The process is repeated [Vanderzee and Meyers J Chem Soc 65 153 1961].

**Potassium cyanide** [151-50-8] **M 65.1, m 634°, d 1.52.** A saturated solution in H<sub>2</sub>O-ethanol (1:3) at 60° was filtered and cooled to room temperature. Absolute EtOH was added, with stirring, until crystallisation ceased. The solution was again allowed to cool to room temperature (during 2-3h) then the crystals were filtered off, washed with absolute EtOH, and dried, first at 70-80° for 2-3h, then at 105° for 2h [Brown, Adisesh and Taylor J Phys Chem 66 2426 1962]. Also purified by vacuum melting and zone refining. **HIGHLY POISONOUS.** 

**Potassium dichromate** [7778-50-9] **M 294.2, m 398°(dec), d 2.68.** Crystd from water (1mL/g) between 100° and 0° and dried under vacuum at 156°. (Possible CARCINOGEN).

**Potassium dihydrogen citrate** [866-83-1] **M 230.2.** Crystd from water. Dried at 80°, or in a vacuum desiccator over Sicapent.

**Potassium dihydrogen phosphate** [7778-77-0] **M 136.1.** Dissolved in boiling distilled water (2mL/g), kept on a boiling water-bath for several hours, then filtered through paper pulp to remove any turbidity. Cooled rapidly with constant stirring, and the crystals were separated on to hardened filter paper, using suction, washed twice with ice-cold water, once with 50% EtOH, and dried at 105°. Alternative crystas are from water, then 50% EtOH, and again water, or from conc aqueous solution by addition of EtOH. Freed from traces of Cu by extracting its aqueous solution with diphenylthiocarbazone in CCl<sub>4</sub>, followed by repeated extraction with CCl<sub>4</sub> to remove traces of diphenylthiocarbazone.

Potassium dithionate [13455-20-4] M 238.3,  $pK_{Est(1)}$ -3.4,  $pK_2^{25}$ 0.49 (for dithionic acid). Crystd from water (1.5mL/g) between 100° and 0°.

**Potassium ethylxanthate** [140-89-6] M 160.3,  $m > 215^{\circ}(dec)$ . Crystd from absolute EtOH, ligroin-ethanol or acetone by addition of Et<sub>2</sub>O. Washed with ether, then dried in a desiccator.

**Potassium ferricyanide** [13746-66-2] **M 329.3, pK<sup>25</sup> <1 (for ferricyanide).** Crystd repeatedly from hot water (1.3mL/g). Dried under vacuum in a desiccator.

**Potassium ferrocyanide**  $(3H_2O)$  [14459-95-1] M 422.4,  $pK_3^{25}$  2.57,  $pK_4^{25}$  4.35 (for ferrocyanide) Crystd repeatedly from distilled water, never heating above 60°. Prepared anhydrous by drying at 110° over P<sub>2</sub>O<sub>5</sub> in a vacuum desiccator. To obtain the trihydrate, it is necessary to equilibrate in a desiccator over saturated aqueous soln of sucrose and NaCl. Can also be ppted from a saturated solution at 0° by adding an equal volume of cold 95% EtOH, standing for several hours, then centrifuging and washing with cold 95% EtOH. Finally sucked air dry with a water-pump. The anhydrous salt can be obtained by drying in a platinum boat at 90° in a slow stream of N<sub>2</sub> [Loftfield and Swift J Am Chem Soc 60 3083 1938].

Potassium fluoroborate [14075-53-7] M 125.9, m 530°. See potassium tetrafluoroborate on p. 458.

Potassium fluorosilicate [16871-90-2] M 220.3, d 2.3, pK 1.92 (for  $H_2SiF_6$ ). Crystd several times from conductivity water (100mL/g) between 100° and 0°.

**Potassium hexachloroiridate** (IV) [16920-56-2] M 483.1. Crystd from hot aqueous solution containing a few drops of HNO<sub>3</sub>.

Potassium hexachloroosmate (IV) [16871-60-6] M 481.1. Crystd from hot dilute aqueous HCl.

Potassium hexachloroplatinate (IV) [16921-30-5] M 486.0, m 250°(dec). Crystd from water (20mL/g) between  $100^{\circ}$  and  $0^{\circ}$ .

Potassium hexafluorophosphate [17084-13-8] M 184.1,  $pK_1^{25} \sim 0.5$ ,  $pK_2^{25} 5.12$  (for fluorophosphoric acid H<sub>2</sub>PO<sub>3</sub>F). Crystd from alkaline aqueous solution, using polyethylene vessels, or from 95% EtOH, and dried in a vacuum desiccator over KOH.

Potassium hexafluorozirconate ( $K_2ZrF_6$ ) [16923-95-8] M 283.4, d 3.48. Recrystd from hot water (solubility is 0.78% at 2° and 25% at 100°).

Potassium hydrogen fluoride [7789-29-9] M 78.1. Crystd from water.

Potassium hydrogen D-glucarate [18404-47-2] M 248.2, m 188°(dec). Crystd from water.

**Potassium hydrogen malate** [4675-64-3] M 172.2. A saturated aqueous solution at  $60^{\circ}$  was decolorised with activated charcoal, and filtered. The filtrate was cooled in water-ice bath and the salt was ppted by addition of EtOH. After being crystallised five times from ethanol-water mixtures, it was dried overnight at 130° in air [Eden and Bates J Res Nat Bur Stand 62 161 1959].

**Potassium hydrogen oxalate (H<sub>2</sub>O)** [127-95-7] M 137.1. Crystd from water by dissolving 20g in 100mL water at 60° containing 4g of potassium oxalate, filtering and allowing to cool to 25°. The crystals, after washing three or four times with water, are allowed to dry in air.

**Potassium hydrogen phthalate** [877-24-7] **M 204.2.** Crystd first from a dilute aqueous solution of  $K_2CO_3$ , then  $H_2O(3mL/g)$  between 100° and 0°. Before being used as a standard in volumetric analysis, analytical grade potassium hydrogen phthalate should be dried at 120° for 2h, then allowed to cool in a desiccator.

Potassium hydrogen *d*-tartrate [868-14-4] M 188.2,  $[\alpha]_{546}^{20}$  +37.5° (c 10, M NaOH). Crystd from water (17mL/g) between 100° and 0°. Dried at 110°.

**Potassium hydroxide (solution)** [1310-58-3] M 56.1,  $pK^{25}$  16 (for aquo K<sup>+</sup>). Its carbonate content can be reduced by rinsing KOH sticks rapidly with water prior to dissolving them in boiled out distilled water. Alternatively, a slight excess of saturated BaCl<sub>2</sub> or Ba(OH)<sub>2</sub> can be added to the soln which, after shaking well, is left so that the BaCO<sub>3</sub> ppte will separate out. Davies and Nancollas [Nature 165 237 1950] rendered KOH solutions carbonate free by ion exchange using a column of Amberlite IR-100 in the OH<sup>-</sup> form.

**Potassium iodate** [7758-05-6] **M 214.0, pK^{25} 0.80 (for HIO<sub>3</sub>).** Crystd twice from distilled water (3mL/g) between 100° and 0°, dried for 2h at 140° and cooled in a desiccator. Analytical reagent grade material dried in this way is suitable for use as an analytical standard.

**Potassium iodide** [7681-11-0] **M 166.0, pK<sup>25</sup> -8.56 (for HI).** Crystd from distilled water (0.5mL/g) by filtering the near-boiling soln and cooling. To minimise oxidation to iodine, the crystn can be carried out under N<sub>2</sub> and the salt is dried under vacuum over P<sub>2</sub>O<sub>5</sub> at 70-100°. Before drying, the crystals can be washed with EtOH or with acetone followed by pet ether. Has also been recrystallised from water/ethanol. After 2 recrystns ACS/USP grade had Li and Sb at <0.02 and <0.01 ppm resp.

Potassium ionophore I (valinomycin) [2001-95-8] M 111.3, m 186-187°, 190°,  $[\alpha]_D^{20}$  +31.0° (c 1.6, \*C<sub>6</sub>H<sub>6</sub>). See valinomycin on p. 573 in Chapter 6.

**Potassium isoamyl xanthate** [61792-26-5] **M 202.4, pK 1.82 (pK<sup>0</sup> 2.8 free acid).** Crystd twice from acetone-diethyl ether. Dried in a desiccator for two days and stored under refrigeration.

Potassium laurate [10124-65-9] M 338.4. Recrystd three times from EtOH [Neto and Helene J Phys Chem 91 1466 1987].

Potassium nickel sulfate ( $6H_2O$ ) [13842-46-1] M 437.1. Crystd from  $H_2O(1.7mL/g)$  between 75° and 0°.

**Potassium nitrate** [7757-79-1] **M 101.1, m 334°.** Crystd from hot  $H_2O$  (0.5mL/g) by cooling (cf KNO<sub>2</sub> below). Dried for 12h under vacuum at 70°. After 2 recrystns tech grade had < 0.001 ppm of metals.

Potassium nitrite [7758-09-0] M 85.1, m  $350^{\circ}(dec)$ ,  $pK^{20} 3.20$  (for HNO<sub>2</sub>). A saturated solution at 0° can be warmed and partially evaporated under vacuum, the crystals so obtained being filtered from the warm solution. (This procedure is designed to reduce the level of nitrate impurity and is based on the effects of temperature on solubility. The solubility of KNO<sub>3</sub> in water is 13g/100mL at 0°, 247g/100mL at 100°; for KNO<sub>2</sub> the corresponding figures are 280g/100mL and 413g/100mL.)

**Potassium nitrosodisulfonate** (Fremy's Salt) [14293-70-0] M 268.3. Yellow needles (dimeric) which dissolve in  $H_2O$  to give the violet monomeric free radical. Purified by dissolving (~12g) in 2M KOH (600mL) at 45°, filtering the blue soln and keeping it in a refrigerator overnight. The golden yellow crystals (10g) are filtd off, washed with MeOH (3x), then  $Et_2O$  and stored in a glass container in a vac over KOH. It is stable indefinitely when dry. [Cram and Reeves J Org Chem 80 3094 1958; Schenk Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I p. 505 1963.]

**Potassium nonafluorobutane sulfonate** [29420-49-3] **M 338.2.** Wash with H<sub>2</sub>O and dry in vacuum. The K salt when distilled with 100% H<sub>2</sub>SO<sub>4</sub> gives the free acid which can be distilled (**b** 105°/22mm, 210-212°/760mm) and then converted to the K salt. [J Chem Soc 2640 1957.]

Potassium oleate [143-18-0] M 320.6. Crystd from EtOH (1mL/g).

**Potassium osmate (VI) dihydrate** [19718-36-6] **M 368.4.** Hygroscopic **POISONOUS** crystals which are soluble in  $H_2O$  but insol in EtOH and  $Et_2O$ . It decomposes slowly in  $H_2O$  to form the tetroxide which attacks the eyes. The solid should be kept dry and in this form it is relatively safe. [Synthesis 610 1972.]

Potassium oxalate [6487-48-5] M 184.2, m 160°(dec), d 2.13. Crystd from hot water.

Potassium perchlorate [7778-74-7] M 138.6, m 400(dec), d 2.52,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from boiling water (5mL/g) by cooling. Dried under vacuum at 105°.

Potassium periodate (potassium metaperiodate) [7790-21-8] M 230.0, m 582°, d 3.62. Crystd from distilled water.

**Potassium permanganate** [7722-64-7] M 158.0, m 240(dec), d 2.7,  $pK^{25}$  -2.25 (for HMnO<sub>4</sub>). Crystd from hot water (4mL/g at 65°), then dried in a vacuum desiccator over CaSO<sub>4</sub>. Phillips and Taylor [J Chem Soc 4242 1962] cooled an aqueous solution of KMnO<sub>4</sub>, saturated at 60°, to room temperature in the dark, and filtered through a No.4 porosity sintered-glass filter funnel. The solution was allowed to evaporate in air in the dark for 12h, and the supernatant liquid was decanted from the crystals, which were dried as quickly as possible with filter paper.

**Potassium peroxydisulfate (potassium persulfate)** [7727-21-1] M 270.3. Crystd twice from distilled water (10mL/g) and dried at 50° in a vacuum desiccator.

**Potassium peroxymonosulfate (Oxone, potassium monopersulfate triple salt; 2KHSO<sub>5</sub>.KHSO<sub>4</sub>.K<sub>2</sub>SO<sub>4</sub>),** [37222-66-5, triple salt] [70693-62-8] **M 614.8.** This is a stable form of Caro's acid and should contain >4.7% of active oxygen. It can be used in EtOH/H<sub>2</sub>O and EtOH/AcOH/H<sub>2</sub>O solutions. If active oxygen is too low it is best prepared afresh from 1mole of KHSO<sub>5</sub>, 0.5moles of KHSO<sub>4</sub> and 0.5moles of K<sub>2</sub>SO<sub>4</sub>. [Kennedy and Stock J Org Chem 25 1901 1960; Stephenson US Patent 2,802,722 1957.] A rapid prepn of *Caro's acid* is made by stirring finely powdered potassium persulfate (M 270.3) into ice cold conc H<sub>2</sub>SO<sub>4</sub> (7mL) and when homogeneous add ice (40-50g). It is stable for several days if kept cold. Keep away from organic matter as it is a **STRONG OXIDANT**. A detailed prepn of **Caro's acid** (*hypersulfuric acid*,  $H_2SO_5$ , [7722-86-3]) in crystalline form m ~45° from  $H_2O_2$  and chlorosulfonic acid was described by Fehér in Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I p. 388 1963.

Potassium perrhenate (KReO<sub>4</sub>) [10466-65-6] M 289.3,  $pK^{25}$  -1.25 (for HReO<sub>4</sub>). Crystd from water (7mL/g), then fused in a platinum crucible in air at 750°.

**Potassium phenol-4-sulfonate** (4-hydroxybenzene-1-sulfonic acid K salt) [30145-40-5] M 212.3. Crystd several times from distilled water at 90°, after treatment with charcoal, by cooling to ca 10°. Dried at 90-100°.

**Potassium phthalimide (phthalimide K salt)** [1074-82-4] **M 185.2, m >300°**. The solid may contain phthalimide and  $K_2CO_3$  from hydrolysis. If too much hydrolysis has occurred (this can be checked by extraction with cold Me<sub>2</sub>CO in which the salt is insoluble, evaporation of the Me<sub>2</sub>CO and weighing the residue) it would be better to prepare it afresh. If little hydrolysis had occurred then recryst from a large volume of EtOH, and wash solid with a little Me<sub>e</sub>CO and dry in a continuous vacuum to constant weight. [Salzerg and Supriawski Org Synth Coll Vol I 119 1941; Raman and IR: Hase J Mol Struct 48 33 1978; Dykman Chem Ind (London) 40 1972; IR, NMR: Assef et al. Bull Soc Chim Fr II-167 1979.]

**Potassium picrate** [573-83-1] M 267.2. Crystd from water or 95% EtOH, and dried at room temperature in vacuum. It is soluble in 200 parts of cold water and 4 parts of boiling water. THE DRY SOLID EXPLODES WHEN STRUCK OR HEATED.

Potassium propionate [327-62-8] M 112.2. Crystd from water (30mL/g) or 95% EtOH.

Potassium reineckate [34430-73-4] M 357.5. Crystd from KNO<sub>3</sub> soln, then from warm water [Adamson J Am Chem Soc 80 3183 1958].

**Potassium (VI) ruthenate** [31111-21-4] **M 243.3.** Dissolve in H<sub>2</sub>O and evaporate until crystals are formed. The crystals are iridescent green prisms which appear red as thin films. Possible impurity is  $RuO_4$ ; in this case wash with CCl<sub>4</sub> (which dissolves  $RuO_4$ ). The concn of an aqueous solution of  $RuO_4^{2-}$  (orange colour) can be estimated from the absorbance at 385nm ( $\varepsilon$  1030 M<sup>-1</sup> cm<sup>-1</sup>), or at 460nm ( $\varepsilon$  1820 M<sup>-1</sup> cm<sup>-1</sup>). [*Can J Chem* **50** 3741 1972; *J Am Chem Soc* **74** 5012 1952; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1600 1965].

**Potassium selenocyanate** [3425-46-5] M 144.1. Dissolved in acetone, filtered and ppted by adding Et<sub>2</sub>O.

**Potassium sodium tartrate** (4H<sub>2</sub>O) [6381-59-5 (4H<sub>2</sub>O); 304-59-6 (R,R)] M 282.3. Crystd from distilled water (1.5mL/g) by cooling to  $0^{\circ}$ .

**Potassium sulfate** [7778-80-5] **M 174.3, m 1069°, d 2.67** Crystd from distilled water (4mL/g at 20°; 8mL/g at 100°) between 100° and 0°.

**Potassium d-tartrate** (H<sub>2</sub>O) [921-53-9, 6381-59-5] M 235.3, m loses H<sub>2</sub>O at 150°, d 1.98. Crystd from distilled water (solubility: 0.4mL/g at 100°; 0.7mL/g at 14°).

**Potassium tetrachloroplatinate(II)** [10025-99-7] **M 415.1, m 500°(dec).** Crystd from aqueous 0.75M HCl (20mL/g) between 100° and 0°. Washed with ice-cold water and dried.

**Potassium tetracyanopalladate (II)**  $3H_2O$  [10025-98-6] M 377.4. All operations should be carried out in an efficient fume cupboard - Cyanide is very POISONOUS Dissolve the complex (ca 5g) in a solution of KCN (4g) in H<sub>2</sub>O (75mL) with warming and stirring and evaporate hot till crystals appear. Cool, filter off the crystals and wash with a few drops of cold H<sub>2</sub>O. Further concentration of the mother liquors provides more crystals. The complex is recrystallised from H<sub>2</sub>O as the colourless trihydrate. It effloresces in

dry air and dehydrates at 100° to the monohydrate. The anhydrous salt is obtained by heating at 200°, but at higher temperatures it decomposes to (CN)<sub>2</sub>, Pd and KCN. [Inorg Synth 2 245 1946.]

Potassium tetrafluoroborate (potassium borofluoride) [14075-53-7] M 125.9, m 530°,  $d_4^{30}$  2.505, pK<sup>25</sup> -4.9 (for HBF<sub>4</sub>). Cryst from H<sub>2</sub>O (sol % (temp): 0.3 (3°), 0.45 (20°), 1.4 (40°), 6.27 (100°), and dry under vacuum. Non-hygroscopic salt. A 10% solution is transparent blue at 100°, green at 90° and yellow at 60°. [Chem Ber 65 535 1932; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol 1 223 1963.]

**Potassium tetraoxalate** (2H<sub>2</sub>O) [oxalic acid hemipotassium salt] [6100-20-5 (2H<sub>2</sub>O); 127-96-8 (anhydr)] M 254.2. Crystd from water below 50°. Dried below 60° at atmospheric pressure.

**Potassium tetraphenylborate** [3244-41-5] M 358.3. Ppted from a soln of KCl acidified with dilute HCl, then crystallised twice from acetone, washed thoroughly with water and dried at 110° [Findeis and de Vries Anal Chem 28 1899 1956]. It has also been recrystd several times from conductivity water.

**Potassium thiocyanate** [333-20-0] M 97.2, m 172°,  $pK^{25}$  -1.85 (for HSCN). Crystd from H<sub>2</sub>O if much chloride ion is present in the salt, otherwise from EtOH or MeOH (optionally by addition of Et<sub>2</sub>O). Filtered on a Büchner funnel without paper, and dried in a desiccator at room temperature before being heated for 1h at 150°, with a final 10-20min at 200° to remove the last traces of solvent [Kolthoff and Lingane J Am Chem Soc 57 126 1935]. Stored in the dark.

Potassium thiosulfate hydrate [13446-67-8; 10294-66-3 (75% aq soln)] M 190.3,  $pK_1^{25}$  0.6,  $pK_2^{25}$  1.74 (for  $H_2S_2O_3$ ) Crystd from warm water (0.5mL/g) by cooling in an ice-salt mixture.

**Potassium thiotosylate** [28519-50-8] M 226.4. Recrystallise from absolute EtOH and dry at 130°. In wet EtOH the *monohydrate* can be obtained. [J Gen Chem USSR (Engl Transl) 28 1345 1958.]

**Potassium trifluoroacetate** [2923-16-2] M 152.1, m 140-142°,  $pK^{25}$  0.52 (for CF<sub>3</sub>CO<sub>2</sub>H). To purify dissolve the salt in trifluoroacetic acid with *ca* 2% of trifluoroacetic anhydride, filter and evaporate carefully to dryness (avoid over heating), and finally dry in a vacuum at 100°. It can be recrystallised from trifluoroacetic acid (solubility in the acid is *ca* 50.1%). [J Am Chem Soc 74 4746 1952, 76 4285 1954; J Inorg Nucl Chem 9 166 1959.]

Potassium trimethylsilanolate (trimethylsilanol K salt) [10519-96-7] M 128.3, m 131-135° (cubic form),  $d^{25}$  1.11, 125° dec (orthorhombic form). Recryst from H<sub>2</sub>O and dried at 100°/1-2mm. [J Am Chem Soc 75 5615 1953; IR: J Org Chem 17 1555 1952.]

Potassium tungstate (*ortho*  $2H_2O$ ) [37349-36-3; 7790-60-5] M 362.1, m 921°, d 3.12,  $pK_1^{25}$  2.20,  $pK_2^{25}$  3.70 (for  $H_2WO_4$ ). Crystd from hot water (0.7mL/g).

**Praseodymium acetate** [6192-12-7] M 318.1. Recrystd several times from water [Ganapathyl J Am Chem Soc 109 3159 1986].

**Praseodymium trichloride (6H<sub>2</sub>O)** [10361-79-2] M 355.4,  $pK_1^{25}$  8.55 (for  $Pr^{3+}$  hydrol). Its 1M soln in 6M HCl was passed twice through a Dowex-1 anion-exchange column. The eluate was evaporated in a vac desiccator to about half its vol and allowed to crystallise [Katzin and Gulyas J Phys Chem 66 494 1962].

**Praseodymium oxide** ( $Pr_6O_{11}$ ) [12037-29-5] M 1021.4. Dissolved in acid, ppted as the oxalate and ignited at 650°.

**Propargyl triphenyl phosphonium bromide** [2091-46-5] M 381.4, m 179°. Recrystallises from 2-propanol as white plates. Also crystallises from EtOH, m 156-158°. IR has v 1440, 1110cm<sup>-1</sup> (P-C str). [Justus Liebigs Ann Chem 682 62 1965; J Org Chem 42 200 1977].

**Propenyloxy trimethylsilane** [1833-53-0] **M 130.3, b 93-95°/atm, d 0.786.** Purified by fractional distillation using a very efficient column at atmospheric pressure. Usually contains 5% of hexamethyldisiloxalane which boils at 99-101°, but is generally non-reactive and need not be removed. [J Am Chem Soc 71 5091 1952.] It has been distilled under N<sub>2</sub> through a 15cm column filled with glass helices. Fraction b 99-104° is further purified by gas chromatography through a Carbowax column (Autoprep A 700) at a column temperature of 87°, retention time is 9.5min. [J Organometal Chem 1 476 1963-4.]

1-Propenyltrimethylsilane (*cis and trans* mixture) [17680-01-2] M 114.3, b 85-88°,  $n_D^{20}$ 1.4121. Dissolve (~ 20g) in THF (200mL), shake with H<sub>2</sub>O (2x 300 mL), dry (Na<sub>2</sub>SO<sub>4</sub>) and fractionate. This is a mixture of *cis* and *trans* isomers which can be separated by gas chromatography on an AgNO<sub>3</sub> column (for prep: see Seyferth and Vaughan *J Organomet Chem* 1 138 1963) at 25° with He as carrier gas at 9psi. The *cis*-isomer has  $n_D^{25}$  1.4105 and the *trans*-isomer has  $n_D^{25}$  1.4062. [Seyferth et al. *Pure Appl Chem* 13 159 1966.]

**Pyridinium chlorochromate** [26299-14-9] **M 215.6, m 205°(dec).** Dry in a vacuum for 1h. It is not hygroscopic and can be stored for extended periods at room temp without change. If very suspect it can be readily prepared. [*Tetrahedron Lett* 2647 1975; Synthesis 245 1982.] § Available commercially on a polymer support.

**Pyridinium dichromate** [20039-37-6] M 376.2, m 145-148°, 152-153°. Dissolve in the minimum volume of H<sub>2</sub>O and add 5 volumes of cold Me<sub>2</sub>CO and cool to -20°. After 3h the orange crystals are collected, washed with a little cold Me<sub>2</sub>CO and dried in a vacuum. It is soluble in dimethylformamide (0.9g/mL at 25°), and in H<sub>2</sub>O, and has a characteristic IR with v 930, 875, 765 and 730cm<sup>-1</sup>. [*Tetrahedron Lett* 399 1979; Chem Ind (London) 1594 1969.] (Possible carcinogen). § Available commercially on a polymer support.

**3-(2-Pyridyl)-5,6-diphenyl-1,2,4-triazine-**p, p'-disulfonic acid, monosodium salt (H<sub>2</sub>O) [63451-29-6] M 510.5. Purified by recrystn from water or by dissolving in the minimum volume of water, followed by addition of EtOH to ppte the pure salt.

Pyrocatechol Violet (tetraphenolictriphenylmethanesulfonic acid Na salt) [115-41-3] M 386.4,  $\varepsilon$  1.4 x 10<sup>4</sup> at 445nm in acetate buffer pH 5.2-5.4, pK<sub>Est(1)</sub>>0 (SO<sub>3</sub>H), pK<sub>Est(2)</sub>~ 9.4, pK<sub>Est(3)</sub>~ 13. It was recrystd from glacial acetic acid. Very hygroscopic. Indicator standard for metal complex titrations. [Mustafin et al. Zh Anal Khim 22 1808 1967.]

**Pyrogallol Red (tetraphenolic xanthyliumphenylsulfonate)** [32638-88-3] M 418.4, m >300°(dec),  $\varepsilon$  4.3 x 10<sup>4</sup> at 542nm, pH 7.9-8.6, pK as above. Recrystd from aqueous alkaline solution (Na<sub>2</sub>CO<sub>3</sub> or NaOH) by precipitation on acidification [Suk Collect Czech Chem Commun 31 3127 1966].

Pyronin B [di-(3,6-bis(diethylamino)xanthylium chloride) diFeCl<sub>5</sub> complex] [2150-48-3] M 358.9 (Fe free), m 176-178° (diFe complex), CI 45010,  $\lambda$ max 555nm, pK<sup>25</sup> 7.7. Crystd from EtOH. Forms Fe stain.

**Quinolinium chlorochromate** [108703-35-1] M 265.6, m 127-130°. A yellow-brown solid which is stable in air for long periods. If it has deteriorated or been kept for too long, it is best to prepare it freshly. Add freshly distilled quinoline (13mL) to a mixture of chromic acid (CrO<sub>3</sub>) (10g) and  $\sim 5M$  HCl (11mL of conc HCl and 10mL of H<sub>2</sub>O) at 0°. A yellow-brown solid separates, it is filtered off on a sintered glass funnel, dried for 1h in a vacuum, and can be stored for extended periods without serious loss in activity. It is a good oxidant for primary alcohol in CH<sub>2</sub>Cl<sub>2</sub>. [Singh et al. Chem Ind (London) 751 1986; method of Corey and Suggs Tetrahedron Lett 2647 1975.]

# **Reinecke salt** see ammonium reineckate on p. 394.

**Resorufin** (7-hydroxy-3H-phenoxazine-3-one Na salt) [635-78-9] M 213.2,  $pK_1^{30}$  6.93,  $pK_2^{30}$ 9.26,  $pK_3^{30}$  10.0. Washed with water and recrystd from EtOH several times.

**Rhodium (II) acetate dimer (2H<sub>2</sub>O)** [15956-28-2] **M 478.0.** Dissolve 5g in boiling MeOH (*ca* 600mL) and filter. Concentrate to 400mL and chill overnight at *ca* 0° to give dark green crystals of the MeOH adduct. Concn of the mother liquors gives a further crop of  $[Rh(OAc)_2]_2$ .2MeOH. The adduct is then heated at 45° in vacuum for 2h (all MeOH is lost) to leave the emerald green crystals of the actetate. [*J Chem Soc (A)* 3322 1970.] Alternatively dissolve in glacial AcOH and reflux for a few hs to give an emerald green soln. Evaporate most of the AcOH on a steam bath then heat the residue at 120°/1h. Extract the residue with boiling Me<sub>2</sub>CO. Filter, concentrate to half its volume and keep at 0°/18h. Collect the crystals, wash with ice cold Me<sub>2</sub>CO and dry at 110°. It is soluble in most organic solvents with which it forms adducts including NMe<sub>3</sub> and Me<sub>2</sub>S and give solutions with different colours varying from green to orange and red. [UV: *Inorg Synth* 2 960 1963.]

**Rhodium (III) chloride** [10049-07-7] **M 209.3, m >100°(dec), b 717°.** Probable impurities are KCl and HCl. Wash solid well with small volumes of  $H_2O$  to remove excess KCl and KOH and dissolve in the minimum volume of conc HCl. Evaporate to dryness on a steam bath to give wine-red coloured RhCl<sub>3</sub>.3H<sub>2</sub>O. Leave on the steam bath until odour of HCl is lost - do not try to dry further as it begins to decompose above 100° to the oxide and HCL. It is not soluble in H<sub>2</sub>O but soluble in alkalis or CN solns and forms double salts with alkali chlorides. [Inorg Synth 7 214 1063.]

**Rhodizonic acid sodium salt** (5,6-dihydroxycyclohex-5-ene-1,2,3,4-tetraone di-Na salt) [523-21-7] M 214.0,  $pK_1^{30}$  4.1 (4.25),  $pK_2^{30}$  4.5 (4.72). The free acid, obtained by acidifiying and extracting with Et<sub>2</sub>O, drying (MgSO<sub>4</sub>), filtering, evaporating and distilling in vacuum (b 155-160°/14mm). The *free acid* solidifies on cooling and the colourless crystals can be recrystd from tetrahydrofuran-pet ether or \*C<sub>6</sub>H<sub>6</sub>. It forms a *dihydrate* m 130-140°. The pure di Na salt is formed by dissolving in 2 equivs of NaOH and evaporating in a vacuum. It forms violet crystals which give an orange soln in H<sub>2</sub>O that is unstable for extended periods even at 0°, and should be prepared freshly before use. Salts of rhodizonic acid cannot be purified by recrystn without great loss due to conversion to croconate, so that the original material must be prepared pure. It can be washed with NaOAc soln then EtOH to remove excess NaOAc dried under vacuum and stored in the dark. [UV and tautomerism: Schwarzenbach and Suter *Helv Chim Acta* 24 617 1941; Polarography: Preisler and Berger J Am Chem Soc 64 67 1942; Souchay and Taibouet J Chim Phys 49 C108 1952.]

Rose Bengal [Acid Red 94, 4,5,6,7-tetrachloro-2'.4',5',7'-tetraiodofluorescein di-Na or di-K salt] [di-Na salt 632-69-9] M 1017.7 (di-Na salt) [di-K salt 11121-48-5] M 1049.8 (di-K salt). This biological stain can be purified by chromatography on silica TLC using a 35:65 mix of EtOH/acetone as eluent.

**Rubidium bromide** [7789-39-1] **M 165.4, m 682°, b 1340°, d 3.35.** A white crystalline powder which crystallises from H<sub>2</sub>O (solubility: 50% in cold and 67% in boiling H<sub>2</sub>O to give a neutral soln). Also crystd from near-boiling water (0.5mL/g) by cooling to  $0^\circ$ .

Rubidium chlorate [13446-71-4] M 168.9, d 3.19. Crystd from water (1.6mL/g) by cooling from 100°.

**Rubidium chloride** [7791-11-9] **M 120.9, m 715°, d 2.80.** Crystd from water (0.7mL/g) by cooling to 0° from 100°.

Rubidium nitrate [13126-12-0] M 147.5, m 305°, d 3.11. Crystd from hot water (0.25mL/g) by cooling to room temperature.

**Rubidium perchlorate** [13510-42-4] **M 184.9, d 2.80, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>).** Crystd from hot water (1.6mL/g) by cooling to  $0^{\circ}$ .

**Rubidium sulfate** [7488-54-2] **M 267.0, m 1050°, d 6.31.** Crystd from water (1.2mL/g) between 100° and 0°.

Ruthenium (III) acetylacetonate [14284-93-6] M 398.4, m 240°(dec). Purified by recrystn from \*benzene. [J Am Chem Soc 74 6146 1952.]

Ruthenium (III) chloride  $(2H_2O)$  ( $\beta$ -form) [14898-67-0] M 207.4 + H<sub>2</sub>O, m >500°(dec), d 3.11, pK<sub>1</sub><sup>25</sup> 3.40 (for aquo Rh<sup>3+</sup> hydrolysis). Dissolve in H<sub>2</sub>O, filter and concentrate to crystallise in the absence of air to avoid oxidation. Evaporate the solution in a stream of HCl gas while being heated just below it boiling point until a syrup is formed and finally to dryness at 80-100° and dried in a vacuum over H<sub>2</sub>SO<sub>4</sub>. When heated at 700° in the presence of Cl<sub>2</sub> the insoluble  $\alpha$ -form is obtained [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1598 1965; J Org Chem 46 3936 1981].

**Ruthenium** (IV) oxide [12036-10-1] M 133.1, d 6.97. Freed from nitrates by boiling in distilled water and filtering. A more complete purification is based on fusion in a KOH-KNO<sub>3</sub> mix to form the soluble ruthenate and perruthenate salts. The melt is dissolved in water, and filtered, then acetone is added to reduce the ruthenates to the insoluble hydrate oxide which, after making a slurry with paper pulp, is filtered and ignited in air to form the anhydrous oxide [Campbell, Ortner and Anderson Anal Chem 33 58 1961].

**Ruthenocene** [bis-(cyclopentadienyl)ruthenium] [1287-13-4] M 231.2, m 195.5°, 199-210°. Sublime in high vacuum at 120°. Yellow crystals which can be recrystallised from CCl<sub>4</sub> as transparent plates. [J Am Chem Soc 74 6146 1952].

**Samarium (II) iodide** [32248-43-4] M 404.2, m 520°, b 1580. Possible impurity is  $SmI_3$  from which it is made. If present, grind solid to a powder and heat in a stream of pure  $H_2$ . The temperature (~ 500-600°) should be below the m (~ 628°) of  $SmI_3$ , since the molten compounds react very slowly. [Wetzel in Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II pp. 1149, 1150 1965.]

Selenious acid [7783-00-8] M 129.0, m 70°(dec), d 3.0,  $pK_1^{25}$  2.62,  $pK_2^{25}$  8.32 (H<sub>2</sub>SeO<sub>3</sub>). Crystd from water. On heating it loses water and SeO<sub>2</sub> sublimes.

Selenium [7782-49-2] M 79.0, m 217.4°, d 4.81. Dissolved in small portions in hot conc HNO<sub>3</sub> (2mL/g) filtered and evaporated to dryness to give selenious acid which was then dissolved in conc HCl. Passage of SO<sub>2</sub> into the solution ppted selenium (but not tellurium) which was filtered off and washed with conc HCl. This purification process was repeated. The selenium was then converted twice to the selenocyanate by treating with a 10% excess of 3M aqueous KCN, heating for half an hour on a sand-bath and filtering. Addition of an equal weight of crushed ice to the cold solution, followed by an excess of cold, conc HCl, with stirring (in a well ventilated fume hood because HCN is evolved) ppted selenium powder, which, after washing with water until colourless, and then with MeOH, was heated in an oven at 105°, then by fusion for 2h under vacuum. It was cooled, crushed and stored in a desiccator [Tideswell and McCullough J Am Chem Soc 78 3036 1956].

Selenium dioxide [7446-08-4] M 111.0, m 340°. Purified by sublimation, or by solution in HNO<sub>3</sub>, pptn of selenium which, after standing for several hours or boiling, is filtered off, then re-oxidised by HNO<sub>3</sub> and cautiously evaporated to dryness below 200°. The dioxide is dissolved in water and again evaporated to dryness.

Selenopyronine [85051-91-8] M 365.8,  $\lambda$ max 571nm ( $\varepsilon$  81,000). Purified as the hydrochloride from hydrochloric acid [Fanghanel et al. J Phys Chem 91 3700 1987].

Selenourea [630-10-4] M 123.0, m 214-215°(dec). Recrystd from water under nitrogen.

**Silica** [7631-86-9 (colloidal); 112945-52-5 (fumed)]. Purification of silica for high technology applications uses isopiestic vapour distillation from conc volatile acids and is absorbed in high purity water. The impurities remain behind. Preliminary cleaning to remove surface contaminants uses dip etching in HF or a mixture of HCl, H<sub>2</sub>O<sub>2</sub> and deionised water [Phelan and Powell Analyst **109** 1299 1984].

Silica gel [63231-67-4; 112926-00-8]. Before use as a drying agent, silica gel is heated in an oven, then cooled in a desiccator. Conditions in the literature range from heating at 110° for 15h to 250° for 2-3h. Silica gel has been purified by washing with hot acid (in one case successively with aqua regia, conc HNO<sub>3</sub>, then conc HCl; in another case digested overnight with hot conc H<sub>2</sub>SO<sub>4</sub>), followed by exhaustive washing with distilled water (one week in a Soxhlet apparatus has also been used), and prolonged oven drying. Alternatively, silica gel has been extracted with acetone until all soluble material was removed, then dried in a current of air, washed with distilled water and oven dried. Silica gel has also been washed successively with water, M HCl, water, and acetone, then activated at 110° for 15h.

Silicon monoxide [10097-28-6] M 44.1, m > 1700°, d 2.18. Purified by sublimation in a porcelain tube in a furnace at 1250° (4h) in a high vacuum (10<sup>-4</sup>mm) in a stream of N<sub>2</sub>. It is obtained as brownish black scales. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 696 1963.]

Silicon tetraacetate [562-90-3] M 264.3, m 110-111°, b 148°/5-6mm,  $pK_1^{25}9.7$ ,  $pK_2^{25}11.9$  (for H<sub>4</sub>SiO<sub>4</sub> free acid). It can be crystallised from mixtures of CCl<sub>4</sub> and pet ether or Et<sub>2</sub>O, or from acetic anhydride and then dried in a vacuum desiccator over KOH. Ac<sub>2</sub>O adheres to the crystals and is removed first by drying at room temp then at 100° for several hours. It is soluble in Me<sub>2</sub>CO, is very hygroscopic and effervesces with H<sub>2</sub>O. It decomposes at 160-170°. [Z Obshch Khim (Engl Transl) 27 985 1957; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 701 1963.]

Silicon tetrachloride [10026-04-7] M 169.9, m -70°, b 57.6°, d 1.483. Distd under vacuum and stored in sealed ampoules under N<sub>2</sub>. Very sensitive to moisture.

12-Silicotungstic acid (tungstosilicic acid;  $H_4SiW_{12}O_{40}$ ) [12027-43-9] M 2914.5. Extracted with diethyl ether from a solution acidified with HCl. The diethyl ether was evaporated under vacuum, and the free acid was crystallised twice [Matijevic and Kerker J Phys Chem 62 1271 1958].

Silver (metal) [7440-22-4] M 107.9, m 961.9°, b 2212°, d 10.5. For purification by electrolysis, see Craig et al. [J Res Nat Bur Stand 64A 381 1960].

Silver acetate [563-63-3] M 166.9,  $pK^{25} > 11.1$  (for aquo Ag<sup>+</sup> hydrolysis). Shaken with acetic acid for three days, the process being repeated with fresh acid, the solid then being dried in a vacuum oven at 40° for 48h. Has also been recrystallised from water containing a trace of acetic acid, and dried in air.

Silver bromate [7783-89-3] M 235.8, m dec on heating, d 5.21. Crystd from hot water (80mL/g).

Silver bromide [7785-23-1] M 187.8, m 432°, d 6.47. Purified from Fe, Mn, Ni and Zn by zone melting in a quartz vessel under vacuum.

Silver chlorate [7783-92-8] M 191.3, m 230°, b 270°(dec), d 4.43. Recrystd three times from water (10mL/g at 15°; 2mL/g at 80°).

Silver chloride [7783-90-6] M 143.3, m 455°, b 1550°, d 5.56. Recrystd from conc NH<sub>3</sub> solution.

Silver chromate [7784-01-2] M 331.8, d<sup>25</sup> 5.625, pK<sub>1</sub><sup>25</sup> 0.74, pK<sub>2</sub><sup>25</sup> 6.49 (for H<sub>2</sub>CrO<sub>4</sub>). Wash the red-brown powder with H<sub>2</sub>O, dry in a vacuum, then powder well and dry again in a vacuum at 90°/5h. Solubility in H<sub>2</sub>O is 0.0014% at 10°. [*J Org Chem* 42 4268 1977.]

Silver cyanide [506-64-9] M 133.9, m dec at 320°, d 3.95. POISONOUS white or grayish white powder. Stir thoroughly with H<sub>2</sub>O, filter, wash well with EtOH and dry in air in the dark. It is very insoluble in H<sub>2</sub>O (0.000023g in 100mL H<sub>2</sub>O) but is soluble in HCN or aqueous KCN to form the soluble  $Ag(CN)_2^{-2}$  complex. [Chem Ber 72 299 1939; J Am Chem Soc 52 184 1930.]

Silver diethyldithiocarbamate [1470-61-7] M 512.3,  $pK_1^{25}$  3.36 (for N, N-diethyldithiocarbamate). Purified by recrystn from pyridine. Stored in a desiccator in a cool and dark place.

Silver difluoride [7783-95-1] M 145.9, m 690°, d 4.7. Highly TOXIC because it liberates HF and  $F_2$ . Very hygroscopic and reacts violently with  $H_2O$ . It is a powerful oxidising agent and liberates  $O_3$  from dilute acids, and  $I_2$  from I<sup>-</sup> soln. Store in quartz or iron ampoules. White when pure, otherwise it is brown-tinged. Thermally stable up to 700°. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 241 1963.]

Silver fluoride [7775-41-9] M 126.9, m 435°, b ca 1150°, d 5.852. Hygroscopic solid with a solubility of 135g/100mL of H<sub>2</sub>O at 15°, and forms an insoluble basic fluoride in moist air. Purified by washing with AcOH and dry \*C<sub>6</sub>H<sub>6</sub>, then kept in a vacuum desiccator at room temperature to remove \*benzene and stored in opaque glass bottles. Flaky hygroscopic crystals which darken on exposure to light. It attacks bone and teeth. [J Chem Soc 4538 1952; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 240 1963.]

Silver iodate [7783-97-3] M 282.8, m >200°, d 5.53. Washed with warm dilute HNO<sub>3</sub>, then H<sub>2</sub>O and dried at 100°, or recrystd from NH<sub>3</sub> soln by adding HNO<sub>3</sub>, filtering, washing with H<sub>2</sub>O and drying at 100°.

Silver lactate [128-00-7] M 196.9, m ~ 100°. Recrystd from H<sub>2</sub>O by adding EtOH. The solid was collected washed with EtOH then Et<sub>2</sub>O and dried at 80° to give the dihydrate. White powder soluble in 15 parts of H<sub>2</sub>O but only slightly soluble in EtOH. [Justus Liebigs Ann Chem 63 89 1847; Helv Chim Acta 2 251 1919.]

Silver nitrate [7761-88-8] M 169.9, m 212°, b 444°(dec), d 4.35. Purified by recrystn from hot water (solubility of AgNO<sub>3</sub> in water is 992g/100mL at 100° and 122g/100mL at 0°). It has also been purified by crystn from hot conductivity water by slow addition of freshly distilled EtOH.

CAUTION: avoid using EtOH for washing the ppte; and avoid concentrating the filtrate to obtain further crops of AgNO<sub>3</sub> owing to the risk of EXPLOSION (as has been reported to us) caused by the presence of silver fulminate. When using EtOH in the purification the apparatus should be enveloped in a strong protective shield. [Tully, News Ed (Am Chem Soc) 19 3092 1941; Garin and Henderson J Chem Educ 47 741 1970; Bretherick, Handbook of Reactive Chemical Hazards 4th edn, Butterworths, London, 1985, pp 13-14.] Before being used as a standard in volumetric analysis, analytical reagent grade AgNO<sub>3</sub> should be finely powdered, dried at 120° for 2h, then cooled in a desiccator.

Recovery of silver residues as  $AgNO_3$  [use protective shield during the whole of this procedure] can be achieved by washing with hot water and adding 16M HNO<sub>3</sub> to dissolve the solid. Filter through glass wool and concentrate the filtrate on a steam bath until precipitation commences. Cool the solution in an ice-bath and filter the precipitated AgNO<sub>3</sub>. Dry at 120° for 2h, then cool in a desiccator in a vacuum. Store over  $P_2O_5$  in a vacuum in the dark. AVOID contact with hands due to formation of black stains.

Silver nitrite [7783-99-5] M 153.9, m 141°(dec), d 4.45. Crystd from hot conductivity water (70mL/g) in the dark. Dried in the dark under vacuum.

Silver(I) oxide [20667-12-3] M 231.7, m ~200°(dec), d 7.13. Leached with hot water in a Soxhlet apparatus for several hours to remove any entrained electrolytes.

Silver (II) oxide [1301-96-8] M 123.9, m >100°(dec),  $d^{25}$  7.22. Soluble in 40,000 parts of H<sub>2</sub>O, and should be protected from light. Stir with an alkaline solution of potassium peroxysulfate (K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>) at 85-

90°. The black AgO is collected, washed free from sulfate with  $H_2O$  made slightly alkaline and dried in air in the dark. [Inorg Synth 4 12 1953.]

Silver perchlorate (H<sub>2</sub>O) [14242-05-8 (H<sub>2</sub>O); 7783-93-9 (anhydr)] M 207.3, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Refluxed with \*benzene (6mL/g) in a flask fitted with a Dean and Stark trap until all the water was removed azeotropically (ca 4h). The soln was cooled and diluted with dry pentane (4mL/g of AgClO<sub>4</sub>). The ppted AgClO<sub>4</sub> was filtered off and dried in a desiccator over P<sub>2</sub>O<sub>5</sub> at 1mm for 24h [Radell, Connolly and Raymond J Am Chem Soc 83 3958 1961]. It has also been recrystallised from perchloric acid. [Caution due to EXPLOSIVE nature in the presence of organic matter.]

Silver permanganate [7783-98-4] M 226.8, d 4.49. Violet crystals which can be crystallised from hot H<sub>2</sub>O (sol is 9g/L at  $20^{\circ}$ ). Store in the dark. Oxidising agent, decomposed by light.

Silver sulfate [10294-26-5] M 311.8, m 652°, b 1085°(dec), d 5.45. Crystd form hot conc  $H_2SO_4$  contg a trace of HNO<sub>3</sub>, cooled and diluted with  $H_2O$ . The ppte was filtd off, washed and dried at 120°.

Silver thiocyanate [1701-93-5] M 165.9, m 265°(dec), d 3.746,  $pK^{25}$  -1.85 (for HSCN). Digest the solid salt with aqueous NH<sub>4</sub>NCS, wash thoroughly with H<sub>2</sub>O and dry at 110° in the dark. Soluble in dilute aqueous NH<sub>3</sub>. Dissolve in strong aqueous NH<sub>4</sub>NCS solution, filter and dilute with large volume of H<sub>2</sub>O when the Ag salt separates. The solid is washed with H<sub>2</sub>O by decantation until free from NCS<sup>-</sup> ions, collected, washed with H<sub>2</sub>O, EtOH and dried in an air oven at 120°. Alternatively dissolve in dilute aqueous NH<sub>3</sub> and single crystals are formed by free evaporation of the solution in air. [J Chem Soc 836, 2405 1932; IR and Raman: Acta Chem Scand 13 1607 1957; Acta Cryst 10 29 1957.]

Silver tosylate [16836-95-6] M 279.1. The anhydrous salt is obtained by recrystn from H<sub>2</sub>O. [Chem Ber 12 1851 1879.]

Silver trifluoroacetate [2966-50-9] M 220.9, m 251-255°. Extract the salt (Soxhlet) with Et<sub>2</sub>O. The extract is filtered and evaporated to dryness, then the powdered residue is completely dried in a vacuum desiccator over silica gel. Solubility in Et<sub>2</sub>O is 33.5g in 750mL. It can be recrystd from  $C_6H_6$  (sol: 1.9g in 30mL of  $C_6H_6$ ; and 33.5g will dissolve in 750mL of anhydrous Et<sub>2</sub>O). [J Org Chem 23 1545 1958; J Chem Soc 584 1951.] It is also soluble in trifluoroacetic acid (15.2% at 30°), toluene, o-xylene and dioxane [J Am Chem Soc 76 4285 1954].

Silver trifluoromethanesulfonate [2923-28-6] M 256.9. Recrystd twice from hot CCl<sub>4</sub> [Alo et al. J Chem Soc, Perkin Trans 1 805 1986].

**Sodium (metal)** [7440-23-5] **M 23.0, m 97.5°, d 0.97.** The metal was placed on a coarse grade of sintered-glass filter, melted under vacuum and forced through the filter using argon. The Pyrex apparatus was then re-evacuated and sealed off below the filter, so that the sodium could be distilled at 460° through a side arm and condenser into a receiver bulb which was then sealed off [Gunn and Green J Am Chem Soc 80 4782 1958]. **EXPLODES and IGNITES in water.** 

**Sodium acetate** [127-09-3] **M 82.0, m 324°, d 1.53.** Crystd from acetic acid and pumped under vacuum for 10h at 120°. Alternatively, crystd from aqueous EtOH, as the trihydrate. This material can be converted to the anhydrous salt by heating slowly in a porcelain, nickel or iron dish, so that the salt liquefies. Steam is evolved and the mass again solidifies. Heating is now increased so that the salt melts again. (NB: if it is heated too strongly, the salt chars.) After several minutes, the salt is allowed to solidify and cooled to a convenient temperature before being powdered and bottled (water content should now less than 0.02%).

**Sodium acetylide** [1066-26-8] **M 48.0.** It disproportionates at *ca* 180° to sodium carbide. It sometimes contains diluents, e.g. xylene, butyl ether or dioxane which can be removed by filtration followed by a vacuum at 65-60°/5mm. Alternatively the acetylide is purged with HC=CH at 100-125° to remove diluent. NaC<sub>2</sub>H adsorbs 2.2x, 2.0x and 1.6x its wt of xylene, butyl ether and dioxane respectively. Powdered NaC<sub>2</sub>H is yellow or yellow-gray in colour and is relatively stable. It can be heated to *ca* 300° in the absence of air. Although no

explosion or evolution of gas occurs, it turns brown due to disproportionation. At 170-190° in air it ignites slowly and burns smoothly. At 215-235° in air it flash-ignites and burns quickly. It can be dropped into a *slight* excess of H<sub>2</sub>O without flashing or burning but vigorous evolution of HC=CH (HIGHLY FLAMMABLE IN AIR) occurs. The sample had been stored in the absence of air for one year without deterioration. Due to the high flammability of HC=CH the salt should be stored dry, and treated with care. After long storage, NaC=CH can be redissolved in liquid NH<sub>3</sub> and used for the same purposes as the fresh material. However it may be slightly turbid due to the presence of moisture. [*J Org Chem* 22 649 1957; *J Am Chem Soc* 77 5013 1955; Inorg Synth 2 76, 81 1946; Org Synth 30 15 1950.] See p. 89, Chapter 4 for prepartion.

**Sodium alginate** [9005-38-3]. Freed from heavy metal impurities by treatment with ion-exchange resins (Na<sup>+</sup>-form), or with a dilute solution of the sodium salt of EDTA. Also dissolved in 0.1M NaCl, centrifuged and fractionally ppted by gradual addition of EtOH or 4M NaCl. The resulting gels were centrifuged off, washed with aq EtOH or acetone, and dried under vacuum. [Büchner, Cooper and Wassermann J Chem Soc 3974 1961.]

Sodium *n*-alkylsulfates. Crystd from EtOH/Me<sub>2</sub>CO [Hashimoto and Thomas J Am Chem Soc 107 4655 1985].

**Sodium amide** [7782-92-5] **M 39.0, m 210°.** It reacts violently with  $H_2O$  and is soluble in liquid  $NH_3$  (1% at 20°). It should be stored in wax-sealed container is small batches. It is very hygroscopic and absorbs  $CO_2$  and  $H_2O$ . If the solid is discoloured by being yellow or brown in colour then it should be destroyed as it can be highly **EXPLOSIVE.** It should be replaced if discoloured. It is best destroyed by covering with much toluene and slowly adding dilute EtOH with stirring until all the ammonia is liberated (FUME CUPBOARD). [Inorg Synth 1 74 1939; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 465 1963; Org Synth Coll Vol III, 778 1955.]

Sodium 4-aminobenzoate [555-06-6] M 159.1. Crystd from water.

Sodium 4-aminosalicylate  $(2H_2O)$  [6018-19-5] M 175.1. Crystd from water at room temperature (2mL/g) by adding acetone and cooling.

Sodium ammonium hydrogen phosphate [13011-54-6] M 209.1, m 79°(dec), d 1.55. Crystd from hot water (1mL/g).

Sodium amylpenicillin [575-47-3] M 350.4. Crystd from moist acetone or moist ethyl acetate.

Sodium anthraquinone-1,5-disulfonate  $(H_2O)$  [853-35-0] M 412.3. Separated from insoluble impurities by continuous extraction with water. Crystd twice from hot water and dried under vacuum.

Sodium anthraquinone-1-sulfonate (H<sub>2</sub>O) [107439-61-2] M 328.3. Crystd from hot water (4mL/g) after treatment with active charcoal, or from water by addition of EtOH. Dried under vacuum over CaCl<sub>2</sub>, or in an oven at 70°. Stored in the dark.

Sodium anthraquinone-2-sulfonate (H<sub>2</sub>O) [131-08-8] M 328.3. See 9,10-anthraquinone-2-sulfonic acid disodium salt on p. 395.

Sodium antimonyl tartrate [34521-09-0] M 308.8. Crystd from water.

Sodium arsenate (7H<sub>2</sub>O) [10048-95-0] M 312.0, m 50 (loses 5H<sub>2</sub>O), m 130°, d 1.88  $pK_1^{25}$ 2.22,  $pK_2^{25}$ 6.98 (for H<sub>3</sub>AsO<sub>4</sub>). Crystd from water (2mL/g).

Sodium azide [26628-22-8] M 65.0, m 300°(dec, explosive),  $pK^{25}$  4.72 (for HN<sub>3</sub>). Crystd from hot water or from water by the addition of absolute EtOH or acetone. Also purified by repeated crystn from an aqueous solution saturated at 90° by cooling it to 10°, and adding an equal volume of EtOH. The crystals were washed with acetone and the azide dried at room temperature under vacuum for several hours in an

Abderhalden pistol. [Das et al. J Chem Soc, Faraday Trans 1 78 3485 1982.] HIGHLY POISONOUS and potentially explosive.

Sodium barbitone (sodium 5,5-diethylbarbiturate) [144-02-5] M 150.1,  $pK_1^{25}$  3.99,  $pK_2^{25}$  12.5 (barbituric acid). Crystd from water (3mL/g) by adding an equal volume of EtOH and cooling to 5°. Dried under vacuum over  $P_2O_5$ .

Sodium benzenesulfinate [873-55-2] M 164.2, m >300°. See benzenesulfinic acid sodium salt on p. 400.

Sodium benzenesulfonate [515-42-4] M 150.1,  $pK_1^{25}$  0.70 (2.55) (for PhSO<sub>3</sub>H<sub>2</sub>). Crystd from EtOH or aqueous 70-100% MeOH, and dried under vacuum at 80-100°.

Sodium benzoate [532-32-1] M 144.1. Crystd from EtOH (12mL/g).

Sodium benzylpenicillin see N-benzylpenicillin sodium salt on p. 514 in Chapter 6.

Sodium bicarbonate [144-55-8] M 84.0, m  $\sim$ 50°(dec, -CO<sub>2</sub>). Crystd from hot water (6mL/g). The solid should not be heated above 40° due to the formation of carbonate.

Sodium bis(trimethylsilyl)amide (bexamethyl disilazane sodium salt) [1070-89-9] M 183.4, m 165-167°(sintering at 140°). It can be sublimed at 170°/2 Torr (bath temp 220-250°) onto a cold finger, and can be recrystd from  ${}^{*}C_{6}H_{6}$  (sol: 10g in 100mL at 60°). It is slightly soluble in Et<sub>2</sub>O and is decomposed by H<sub>2</sub>O. [*Chem Ber* 94 1540 1961.]

Sodium bisulfite [7631-90-5] M 104.1, d 1.48. Crystd from hot  $H_2O$  (1mL/g). Dried at 100° under vac for 4h.

**Sodium borate (borax)** [1330-43-4] **M 201.2, m 741°, d 2.37.** Most of the water of hydration was removed from the decahydrate by evacuation at 25° for three days, followed by heating to 100° and evacuation with a high-speed diffusion pump. The dried sample was then heated gradually to fusion (above 966°), allowed to cool gradually to 200°, then transferred to a desiccator containing  $P_2O_5$  [Grenier and Westrum J Am Chem Soc 78 6226 1956].

Sodium borate (decahydrate, hydrated borax) [1303-96-4] M 381.2, m 75°(loses 5H<sub>2</sub>O at 60°), d 1.73. Crystd from water (3.3mL/g) keeping below 55° to avoid formation of the pentahydrate. Filtered at the pump, washed with water and equilibrated for several days in a desiccator containing an aqueous solution saturated with respect to sucrose and NaCl. Borax can be prepared more quickly (but its water content is somewhat variable) by washing the recrystd material at the pump with water, followed by 95% EtOH, then Et<sub>2</sub>O, and air dried at room temperature for 12-18h on a clock glass.

**Sodium borohydride** [16940-66-2] **M 37.8, m ~400°(dec), d 1.07.** After adding NaBH<sub>4</sub> (10g) to freshly distilled diglyme (120mL) in a dry three-necked flask fitted with a stirrer, nitrogen inlet and outlet, the mixture was stirred for 30min at 50° until almost all of the solid had dissolved. Stirring was stopped, and, after the solid had settled, the supernatant liquid was forced under N<sub>2</sub> pressure through a sintered-glass filter into a dry flask. [The residue was centrifuged to obtain more of the solution which was added to the bulk.] The solution was cooled slowly to 0° and then decanted from the white needles that separated. The crystals were dried by pumping for 4h to give anhydrous NaBH<sub>4</sub>. Alternatively, after the filtration at 50° the solution was heated at 80° for 2h to give a white ppte of substantially anhydrous NaBH<sub>4</sub> which was collected on a sintered-glass filter under N<sub>2</sub>, then pumped at 60° for 2h [Brown, Mead and Subba Rao J Am Chem Soc 77 6209 1955].

NaBH<sub>4</sub> has also been crystd from isopropylamine by dissolving it in the solvent at reflux, cooling, filtering and allowing the solution to stand in a filter flask connected to a Dry-ice/acetone trap. After most of the solvent was passed over into the cold trap, crystals were removed with forceps, washed with dry diethyl ether and dried under vacuum. [Kim and Itoh *J Phys Chem* **91** 126 *1987*.] Somewhat less pure crystals were obtained more rapidly by using Soxhlet extraction with only a small amount of solvent and extracting for about 8h. The

crystals that formed in the flask were filtered off, then washed and dried as before. [Stockmayer, Rice and Stephenson J Am Chem Soc 77 1980 1955.] Other solvents used for crystallisation include water and liquid ammonia.

Sodium bromate [7789-38-0] M 150.9, m 381°, d 3.3. Crystd from hot water (1.1mL/g) to decrease contamination by NaBr, bromine and hypobromite. [Noszticzius et al. J Am Chem Soc 107 2314 1985.]

Sodium bromide [7647-15-6] M 102.9, m 747°, b 1390°, d 3.2. Crystd from water (0.86mL/g) between 50° and 0°, and dried at 140° under vacuum (this purification may not eliminate chloride ion).

Sodium 4-bromobenzenesulfonate [5015-75-8] M 258.7. Crystd from MeOH, EtOH or distd water.

Sodium tert-butoxide [865-48-5] M 96.1. It sublimes at 180°/1 Torr. Its solubility in tert-BuOH is 0.208M at 30.2° and 0.382M at 60°, and is quite soluble in tetrahydrofuran (32g/100g). It should not be used if it has a brown colour. [J Am Chem Soc 78 4364, 3614 1956, Inorg Synth 1 87 1939; IR: J Org Chem 21 156 1956.]

Sodium butyrate [156-54-7] M 110.1. Prepared by neutralisation of the acid and recrystn from EtOH.

Sodium cacodylate (3H<sub>2</sub>O) [124-65-2] M 214.0, m 60°. Crystd from aqueous EtOH.

Sodium carbonate [497-19-8] M 106.0, m 858°, d 2.5. Crystd from water as the decahydrate which was redissolved in water to give a near-saturated soln. By bubbling CO<sub>2</sub>, NaHCO<sub>3</sub> was ppted. It was filtered, washed and ignited for 2h at 280° [MacLaren and Swinehart J Am Chem Soc 73 1822 1951]. Before being used as a volumetric standard, analytical grade material should be dried by heating at 260-270° for 0.5h and allowed to cool in a desiccator. For preparation of primary standard sodium carbonate, see *Pure Appl Chem* 25 459 1969. After 3 recrystns tech grade had Cr, Mg, K, P, Al, W, Sc and Ti at 32, 9.4, 6.6, 3.6, 2.4, 0.6, 0.2 and 0.2 ppm resp; another technical source had Cr, Mg, Mo, P, Si, Sn and Ti at 2.6, 0.4, 4.2, 13.4, 32, 0.6, 0.8 ppm resp.

Sodium carboxymethylcellulose [9004-32-4]. Dialysed for 48h against distilled water.

Sodium cetyl sulfate [1120-01-0] M 344.5. See sodium hexadecylsulfate on p. 471.

Sodium chlorate [7775-09-9] M 106.4, m 248°, b >300°(dec), d 2.5. Crystd from hot water (0.5mL/g).

Sodium chloride [7647-14-5] M 58.4, m 800.7°, b 1413°, d 2.17. Crystd from saturated aqueous solution (2.7mL/g) by passing in HCl gas, or by adding EtOH or acetone. Can be freed from bromide and iodide impurities by adding chlorine water to an aqueous solution and boiling for some time to expel free bromine and iodine. Traces of iron can be removed by prolonged boiling of solid NaCl in 6M HCl, the crystals then being washed with EtOH and dried at *ca* 100°. Sodium chloride has been purified by sublimation in a stream of pre-purified N<sub>2</sub> and collected by electrostatic discharge [Ross and Winkler *J Am Chem Soc* 76 2637 1954]. For use as a primary analytical standard, analytical reagent grade NaCl should be finely ground, dried in an electric furnace at 500-600° in a platinum crucible, and allowed to cool in a desiccator. For most purposes, however, drying at 110-120° is satisfactory.

Sodium chlorite [7758-19-2] M 90.4, m ~180°(dec). Crystd from hot water and stored in a cool place. Has also been crystd from MeOH by counter-current extraction with liquid ammonia [Curti and Locchi Anal Chem 29 534 1957]. Major impurity is chloride ion; can be recrystallised from 0.001M NaOH.

Sodium 4-chlorobenzenesulfonate [5138-90-9] M 214.6, pK<sub>Est</sub> <0 (for SO<sub>3</sub>H). Crystd twice from MeOH and dried under vacuum.

Sodium 3-chloro-5-methylbenzenesulfonate [5138-92-1] M 228.7,  $pK_{Est} < 0$  (for SO<sub>3</sub>H). Crystd twice from MeOH and dried under vacuum.

Sodium chromate  $(4H_2O)$  [10034-82-9] M 234.0, m ~20°(for  $10H_2O$ ), d, 2.7,  $pK_1^{25}0.74$ ,  $pK_2^{25}6.49$  (for  $H_2CrO_4$ ). Crystd from hot water (0.8mL/g).

*dl*-Sodium creatine phosphate (4H<sub>2</sub>O) [922-32-7] M 327.1. See creatine phosphate di-Na salt on p. 523 in Chapter 6.

Sodium cyanate [917-61-3] M 65.0, m 550°,  $d_4^{20}$  1.893, pK<sup>25</sup> 3.47 (for HCNO). Colourless needles from EtOH. Solubility in EtOH is 0.22g/100g at 0°C. Soluble in H<sub>2</sub>O but can be recrystallised from small volumes of it.

Sodium cyanoborohydride [25895-60-7] M 62.8, m 240-242°(dec), d<sup>28</sup> 1.20. Very hygroscopic solid, soluble in H<sub>2</sub>O (212% at 29°, 121% at 88°), tetrahydrofuran (37% at 28°, 42.2% at 62°), very soluble in EtOH but insoluble in Et<sub>2</sub>O,  $^{*}C_{6}H_{6}$  and hexane. It is stable to acid up to pH 3 but is hydrolysed in 12N HCl. The rate of hydrolysis at pH 3 is 10<sup>-8</sup> that of NaBH<sub>4</sub>. The fresh commercially available material is usually sufficiently pure. If very pure material is required one of the following procedures must be used [Synthesis 135 1975]: (a) The NaBH<sub>3</sub>CN is dissolved in tetrahydrofuran (20% w/v), filtered and the filtrate is treated with a fourfold volume of CH<sub>2</sub>Cl<sub>2</sub>. The solid is collected and dried in a vacuum [Inorg Chem. 9 2146 1970].

Dissolve the NaBH<sub>3</sub>CN in dry MeNO<sub>2</sub>, filter, and pour the filtrate into a 10-fold volume of CCl<sub>4</sub> with vigorous stirring. The white ppte is collected, washed several times with CCl<sub>4</sub> and dried in a vacuum [*Inorg Chem* 9 624 1970]. (b) When the above procedures fail to give a clean product then dissolve the NaBH<sub>3</sub>CN (10g) in tetrahydrofuran (80mL) and add N MeOH/HCl until the pH is 9. Pour the solution with stirring into dioxane (250mL). The solution is filtered, and heated to reflux. A further volume of dioxane (150mL) is added slowly with swirling. The solution is cooled slowly to room temp then chilled in ice and the crystalline dioxane complex is collected, dried in a vacuum for 4h at 25°, then 4h at 80° to yield the amorphous dioxane-free powder is 6.7g with purity >98% [J Am Chem Soc 93 2897 1971]. The purity can be checked by iodometric titration [Anal Chem 91 4329 1969].

**Sodium** *p*-cymenesulfonate [77060-21-0] M 236.3. Dissolved in water, filtered and evaporated to dryness. Crystd twice from absolute EtOH and dried at 110°.

Sodium decanoate (sodium caproate) [1002-62-6] M 194.2. Neutralised by adding a slight excess of the free acid, recovering the excess acid by  $Et_2O$  extraction. The salt is crystd from solution by adding pure acetone, repeating the steps several times, then dried in an oven at ca 110° [Chaudhury and Awuwallia Trans Faraday Soc 77 3119 1981].

Sodium 1-decanesulfonate [13419-61-9] M 244.33. Recrystd from absolute EtOH and dried over silica gel.

Sodium *n*-decylsulfate [142-87-0] M 239.3. Rigorously purified by continuous  $Et_2O$  extraction of a 1% aqueous solution for two weeks.

Sodium deoxycholate (H<sub>2</sub>O) [302-95-4] M 432.6,  $[\alpha]_D^{20}$  +48° (c 1, EtOH). Crystd from EtOH and dried in an oven at 100°. The solution is freed from soluble components by repeated extraction with acid-washed charcoal.

Sodium dibenzyldithiocarbamate [55310-46-8] M 295.4, m 230°(dec),  $pK^{20}$  3.13 (for monobenzyldithiocarbamic acid). The free acid when recrystd twice from dry Et<sub>2</sub>O has m 80-82°. The Na salt is reppted from aqueous EtOH or EtOH by addition of Et<sub>2</sub>O or Me<sub>2</sub>CO [Anal Chem 50 896 1978]. The NH<sub>4</sub> salt has m 130-133°; Cu salt (yellow crystals) has m 284-286° and the Ti salt has m 64-70°.

Sodium 2,5-dichlorobenzenesulfonate [5138-93-2] M 249.0, pK<sub>Est</sub> <0 (for SO<sub>3</sub>H). Crystd from MeOH, and dried under vacuum.

Sodium dichromate [7789-12-0] M 298.0, m 84.6° (2H<sub>2</sub>O), 356° (anhydr); b 400°(dec),  $d_4^{25}$  2.348. Crystd from small volumes of H<sub>2</sub>O by evaporation to crystallisation. Solubility in H<sub>2</sub>O is 238% at 0° and 508% at boiling. Red dihydrate is slowly dehydrated by heating at 100° for long periods. It is deliquescent, a powerful oxidising agent-do not place in contact with skin- wash immediately as it is caustic. (Possible carcinogen).

Sodium diethyldithiocarbamate (3H<sub>2</sub>O) [20624-25-3] M 225.3, m 94-96°(anhydr), pK<sup>20</sup> 3.65 (diethyldithiocarbamic acid). Recrystd from water.

Sodium di(ethylhexyl)sulfosuccinate (Aerosol-OT) [577-11-7] M 444.6. Dissolved in MeOH and inorganic salts which ppted were filtered off. Water was added and the solution was extracted several times with hexane. The residue was evaporated to one fifth its original volume, \*benzene was added and azeotropic distillation was continued until no water remained. Solvent was then evaporated. The white solid was crushed and dried in vacuum over  $P_2O_5$  for 48h [El Seoud and Fendler J Chem Soc, Faraday Trans 1 71 452 1975].

Sodium diethyloxaloacetate [63277-17-8] M 210.2. Extracted several times with boiling  $Et_2O$  (until the solvent remained colourless) and then the residue was dried in air.

Sodium diformylamide [18197-26-7] M 95.0. Grind under dry tetrahydrofuran (fumehood), filter and wash with this solvent then dry in vacuum. [IR and prepn: Synthesis 122 1990; Chem Ber 100 355 1967, 102 4089 1969.]

Sodium dihydrogen orthophosphate (2H<sub>2</sub>O) [13472-35-0 (2H<sub>2</sub>O); 10049-21-5 (H<sub>2</sub>O); 7558-80-7 (anhydr)] M 156.0, m 60°(dec), d 1.91. Crystd from warm water (0.5mL/g) by chilling.

Sodium 2,2'-dihydroxy-1-naphthaleneazobenzene-5'-sulfonate [2092-55-9] M 354.3. See Solochrome Violet R on p. 352 in Chapter 4.

Sodium 2,4-dihydroxyphenylazobenzene-4'-sulfonate [547-57-9] M 304.2. Crystd from absolute EtOH.

Sodium p-(p-dimethylaminobenzeneazo)-benzenesulfonate [23398-40-5] M 327.3. Crystd from water.

**Sodium** *p*-**dimethylaminoazobenzene**-*o*'-**carboxylate** [845-10-3] **M 219.2.** Ppted from aqueous soln as the free acid which was recrystallised from 95% EtOH, then reconverted to the sodium salt.

**Sodium** *p*-**dimethylaminoazobenzene**-*p*'-**carboxylate** [845-46-5] **M 219.2.** Ppted from aqueous soln as the free acid which was recrystallised from 95% EtOH, then reconverted to the sodium salt.

Sodium 2,4-dimethylbenzenesulfonate [827-21-4] M 208.2. Crystd from MeOH and dried under vacuum.

Sodium 2,5-dimethylbenzenesulfonate [827-19-0] M 208.2. Dissolved in distilled water, filtered, then evaporated to dryness. Crystd twice form absolute EtOH or MeOH and dried at 110° under vacuum.

Sodium dimethyldithiocarbamate hydrate [128-04-1] M 143.2, m 106-108°, 120-122°,  $pK^{25}$ 3.36 (diethyldithiocarbamic acid). Crystallise from a small volume of H<sub>2</sub>O, or dissolve in minimum volume of H<sub>2</sub>O and add cold Me<sub>2</sub>CO and dry in air. The solution in Me<sub>2</sub>CO is ~50g/400mL. The dihydrate loses H<sub>2</sub>O on heating at 115° to give the hemi hydrate which decomposes on further heating [IR: Can J Chem. 34 1096 1956].

Sodium N,N-dimethylsulfanilate [2244-40-8] M 223.2, m >300°. Crystd from water.

Sodium dithionite  $(2H_2O)$  [7631-94-9] M 242.1, m 110°(loses  $2H_2O$ ), 267°(dec), d 2.19, pK<sub>Est(1)</sub>-3.4, pK<sub>2</sub><sup>25</sup>0.49 (for dithionic acid). Crystd from hot water (1.1mL/g) by cooling.

Sodium dodecanoate (sodium laurate) [629-25-4] M 222.3,  $pK^{20}$  5.3 (-COOH). Neutralised by adding a slight excess of dodecanoic acid, removing it by ether extraction. The salt is recrystd from aq soln by adding pure Me<sub>2</sub>CO and repeating the process (see sodium decanoate on p. 468). Also recrystd from MeOH.

Sodium 1-dodecanesulfonate [2386-53-0] M 272.4. Twice recrystd from EtOH.

Sodium dodecylbenzenesulfonate [25155-30-0] M 348.5. Recrystd from propan-2-ol.

**Sodium dodecylsulfate (SDS, sodium laurylsulfate)** [151-21-3] M 288.4, m 204-207°. Purified by Soxhlet extraction with pet ether for 24h, followed by dissolution in acetone:MeOH:H<sub>2</sub>O 90:5:5(v/v) and recrystn [Politi et al. J Phys Chem 89 2345 1985]. Also purified by two recrystns from absolute EtOH, aqueous 95% EtOH, MeOH, isopropanol or a 1:1 mixture of EtOH:isopropanol to remove dodecanol, and dried under vacuum [Ramesh and Labes J Am Chem Soc 109 3228 1987]. Also purified by foaming [see Cockbain and McMullen Trans Faraday Soc 47 322 1951] or by liquid-liquid extraction [see Harrold J Colloid Sci 15 280 1960]. Dried over silica gel. For DNA work it should be dissolved in excess MeOH passed through an activated charcoal column and evaporated until it crystallises out.

Also purified by dissolving in hot 95% EtOH (14mL/g), filtering and cooling, then drying in a vacuum desiccator. Alternatively, it was crystd from H<sub>2</sub>O, vacuum dried, washed with anhydrous Et<sub>2</sub>O, vacuum dried. These operations were repeated five times [Maritato J Phys Chem 89 1341 1985; Lennox and McClelland J Am Chem Soc 108 3771 1986; Dressik J Am Chem Soc 108 7567 1986].

**Sodium ethoxide** [141-52-6] **M 68.1.** Hygroscopic powder which should be stored under N<sub>2</sub> in a cool place. Likely impurity is EtOH which can be removed by warming at 60-80° under high vacuum. Hydrolysed by H<sub>2</sub>O to yield NaOH and EtOH. Other impurities, if kept in air for long periods are NaOH and Na<sub>2</sub>CO<sub>3</sub>. In this case the powder cannot be used if these impurities affect the reactivity and a fresh sample should be acquired [IR: J Org Chem **21** 156 1956].

Sodium ethylmercurithiosalicylate [54-64-8] M 404.8. Crystd from ethanol-diethyl ether

Sodium ethylsulfate [546-74-7] M 166.1. Recrystd three times from MeOH-Et<sub>2</sub>O and vacuum dried.

Sodium ferricyanide (H<sub>2</sub>O) [14217-21-1; 13601-19-9 (anhydr)] M 298.9,  $pK^{25} < 1$  (for ferricyanide). Crystd from hot water (1.5mL/g) or by precipitation from 95% EtOH.

Sodium ferrocyanide  $(10H_2O)$  [13601-19-9] M 484.1, m 50-80° (loses  $10H_2O$ ), 435°(dec), d 1.46,  $pK_3^{25}$  2.57,  $pK_4^{25}$  4.35 (for ferrocyanide). Crystd from hot water (0.7mL/g), until free of ferricyanide as shown by absence of Prussian Blue formation with ferrous sulfate soln.

**Sodium fluoride** [7681-49-4] **M 42.0, m 996°, b 1695°, d 2.56.** Crystd from water by partial evaporation in a vacuum desiccator,. or dissolved in water, and *ca* half of it ppted by addition of EtOH. Ppte was dried in an air oven at 130° for one day, and then stored in a desiccator over KOH.

Sodium fluoroacetate (mono) [62-74-8] M 100.0, m 200-205°(dec). A free flowing white TOXIC powder which is purified by dissolving in ca 4 parts of H<sub>2</sub>O and the pH is checked. If it is alkaline, add a few drops of FCH<sub>2</sub>CO<sub>2</sub>H to make the solution just acidic. Evaporate (fumehood) on a steam bath until crystals start to separate, cool and filter the solid off. More solid can be obtained by adding EtOH to the filtrate. Dry at 100° in vacuum. [J Chem Soc 1778 1948.]

Sodium fluoroborate [13755-29-8] M 109.8, m 384°, d 2.47, pK -4.9 (for fluoroboric acid  $H_3O^+BF_4^-$ ). Crystd from hot water (50mL/g) by cooling to 0°. Alternatively, purified from insoluble material by dissolving in a minimum amount of water, then fluoride ion was removed by adding conc lanthanum nitrate in excess. After removing lanthanum fluoride by centrifugation, the supernatant was passed

through a cation-exchange column (Dowex 50, Na<sup>+</sup>-form) to remove any remaining lanthanum [Anbar and Guttman *J Phys Chem* 64 1896 1960]. Also recrystd from anhydrous MeOH and dried in a vacuum at 70° for 16h. It is affected by moisture. [Delville et al. *J Am Chem Soc* 109 7293 1987.]

Sodium fluorosilicate [16893-85-9] M 188.1. Crystd from hot water (40mL/g) by cooling.

Sodium formaldehyde sulfoxylate dihydrate (sodium hydroxymethylsulfinate, Rongalite) [149-44-0] M 134.1, m 63-64° (dihydrate). Crystallises from  $H_2O$  as the dihydrate, decomposes at higher temperatures. Store in a closed container in a cool place. It is insoluble in EtOH and  $Et_2O$  and is a good reducing agent. [X-ray structure: J Chem Soc 3064 1955.] Note that this compound {HOCH<sub>2</sub>SO<sub>2</sub>Na} should not be confused with formaldehyde sodium bisulfite adduct {HOCH<sub>2</sub>SO<sub>3</sub>Na} from which it is prepared by reduction with Zn.

Sodium formate (anhydrous) [141-53-7] M 68.0, m 253°, d 1.92. A saturated aqueous solution at 90° (0.8mL water/g) was filtered and allowed to cool slowly. (The final temperature was above 30° to prevent formation of the hydrate.) After two such crystns the crystals were dried in an oven at 130°, then under high vacuum. [Westrum, Chang and Levitin J Phys Chem 64 1553 1960; Roecker and Meyer J Am Chem Soc 108 4066 1986.] The salt has also been recrystd twice from 1mM DTPA (diethylenetriaminepentaacetic acid which was recrystd 4x from MilliQ water and dried in a vac), then twice from water [Bielski and Thomas J Am Chem Soc 109 7761 1987].

Sodium D-gluconate [527-07-1] M 218.1, m 200-205°dec,  $[\alpha]_{546}^{20} + 14^{\circ}$ ,  $[\alpha]_D^{20} + 12$  (c 20, H<sub>2</sub>O). Crystallise from a small volume of H<sub>2</sub>O (sol 59g/100mL at 25°), or dissolve in H<sub>2</sub>O and add EtOH since it is sparingly soluble in EtOH. Insoluble in Et<sub>2</sub>O. It forms a Cu comples in alkaline soln and a complex with Fe in neutral solution. [J Am Chem Soc 81 5302 1959.]

**Sodium glycochenodeoxycholate** [16564-43-5] **M** 472.6. Dissolved in EtOH, filtered and concentrated to crystallisation, and recrystallised from a little EtOH.

**Sodium glycocholate** [863-57-0] **M 488.6.** Dissolved in EtOH, filtered and concentrated to crystallisation, and recrystallised from a little EtOH.

Sodium glycolate (2H<sub>2</sub>O) [2836-32-0] M 98.0. Ppted from aqueous solution by EtOH, and air dried.

Sodium hexadecylsulfate [1120-01-0] M 344.5. Recrystd from absolute EtOH or MeOH and dried in vac [Abu Hamdiyyah and Rahman J Phys Chem 91 1531 1987].

Sodium hexafluorophosphate [21324-39-0] M 167.9,  $pK_1^{25} \sim 0.5$ ,  $pK_2^{25} 5.12$  (for fluorophosphoric acid H<sub>2</sub>PO<sub>3</sub>F). Recrystd from acetonitrile and vacuum dried for 2 days at room temperature. It is an irritant and is hygroscopic. [Delville et al. J Am Chem Soc 109 7293 1987.]

Sodium hexanitrocobaltate III (Na<sub>3</sub>[Co(NO)<sub>6</sub>]) [13600-98-1] M 403.9. Dissolve (ca 60g) in H<sub>2</sub>O (300mL), filter to obtain a clear solution, add 96% EtOH (250mL) with vigorous stirring. Allow the ppte to settle for 2h, filter, wash with EtOH (4 x 25mL), twice with Et<sub>2</sub>O and dry in air [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1541 1965]. Yellow to brown yellow crystals which are very soluble in H<sub>2</sub>O, are decomposed by acid and form an insoluble K salt. Used for estimating K.

**Sodium hydrogen diglycollate** [50795-24-9] **M 156.1.** Crystd from hot water (7.5mL/g) by cooling to  $0^{\circ}$  with constant stirring, the crystals being filtered off on to a sintered-glass funnel and dried at  $110^{\circ}$  overnight.

Sodium hydrogen oxalate  $(2H_2O)$  [1186-49-8] M 130.0, m 100°(loses  $2H_2O$ ), b 200°(dec). Crystd from hot water (5mL/g) by cooling.

Sodium hydrogen succinate [2922-54-5] M 140.0. Crystd from water and dried at 110°.

Sodium hydrogen d-tartrate [526-94-3] M 190.1, m 100°(loses H<sub>2</sub>O), b 234°,  $[\alpha]_{546}$  +26° (c 1, H<sub>2</sub>O). Crystd from warm water (10mL/g) by cooling to 0°.

**Sodium hydroxide (anhydrous)** [1310-73-2] **M 40.0, m 323°, b 1390°, d 2.13.** Common impurities are water and sodium carbonate. Sodium hydroxide can be purified by dissolving 100g in 1L of pure EtOH, filtering the solution under vacuum through a fine sintered-glass disc to remove insoluble carbonates and halides. (This and subsequent operations should be performed in a dry, CO<sub>2</sub>-free box.) The soln is concentrated under vacuum, using mild heating, to give a thick slurry of the mono-alcoholate which is transferred to a coarse sintered-glass disc and pumped free of mother liquor. After washing the crystals several times with purified alcohol to remove traces of water, they are vacuum dried, with mild heating, for about 30h to decompose the alcoholate, leaving a fine white crystalline powder [Kelly and Snyder J Am Chem Soc 73 4114 1951].

Sodium hydroxide solutions (*caustic*),  $pK^{25}$  14.77. Carbonate ion can be removed by passage through an anion-exchange column (such as Amberlite IRA-400; OH<sup>-</sup>-form). The column should be freshly prepared from the chloride form by slow prior passage of sodium hydroxide soln until the effluent gives no test for chloride ions. After use, the column can be regenerated by washing with dilute HCl, then water. Similarly, other metal ions are removed when a 1M (or more dilute) NaOH soln is passed through a column of Dowex ion-exchange A-1 resin in its Na<sup>+</sup>-form.

Alternatively, carbonate contamination can be reduced by rinsing sticks of NaOH (analytical reagent quality) rapidly with  $H_2O$ , then dissolving in distilled  $H_2O$ , or by preparing a concentrated aqueous soln of NaOH and drawing off the clear supernatant liquid. (Insoluble Na<sub>2</sub>CO<sub>3</sub> is left behind.) Carbonate contamination can be reduced by adding a slight excess of conc BaCl<sub>2</sub> or Ba(OH)<sub>2</sub> to a NaOH soln, shaking well and allowing the BaCO<sub>3</sub> ppte to settle. If the presence of Ba in the soln is unacceptable, an electrolytic purification can be used. For example, sodium amalgam is prepared by the electrolysis of 3L of 30% NaOH with 500mL of pure mercury for cathode, and a platinum anode, passing 15 Faradays at 4Amps, in a thick-walled polyethylene bottle. The bottle is then fitted with inlet and outlet tubes, the spent soln being flushed out by CO<sub>2</sub>-free N<sub>2</sub>. The amalgam is then washed thoroughly with a large volume of deionised water (with the electrolysis current switched on to minimize loss of Na). Finally, a clean steel rod is placed in contact in the solution with the amalgam (to facilitate hydrogen evolution), reaction being allowed to proceed until a suitable concentration is reached, before being transferred to a storage vessel and diluted as required [Marsh and Stokes *Aust J Chem* **17** 740 *1964*].

Sodium 2-hydroxy-4-methoxybenzophenone-5-sulfonate [6628-37-1] M 330.3. Crystd from MeOH and dried under vacuum.

Sodium p-hydroxyphenylazobenzene-p'-sulfonate [2623-36-1] M 288.2. Crystd from 95% EtOH.

Sodium hypophosphite monohydrate [10039-56-2] M 106.0 (see pK of hypophosphorous acid). Dissolve in boiling EtOH, cool and add dry  $Et_2O$  till all the salt separates. Collect and dry in vacuum. It is soluble in 1 part of H<sub>2</sub>O. It liberates PH<sub>3</sub> on heating and can *ignite* spontaneously when heated. The anhydrous salt is soluble in ethylene glycol (33% w/w) and propylene glycol (9.7%) at 25°.

Sodium iodate [7681-55-2] M 197.9, m dec on heating, d 4.28. Crystd from water (3mL/g) by cooling.

**Sodium iodide** [7681-82-5] **M 149.9, m 660°, b 1304°, d 3.67.** Crystd from water/ethanol soln and dried for 12h under vacuum, at 70°. Alternatively, dissolved in acetone, filtered and cooled to -20°, the resulting yellow crystals being filtered off and heated in a vacuum oven at 70° for 6h to remove acetone. The NaI was then crystd from very dilute NaOH, dried under vacuum, and stored in a vacuum desiccator [Verdin *Trans Faraday Soc* 57 484 1961].

Sodium ionophore I (ETH 227) (N,N',N''-triheptyl-N,N',N''-trimethyl-4,4',4''-propylidynetris(3-oxabutyramide) [61183-76-4] M 642.0. It is purified (*ca* 200mg) by TLC on Kieselgel F<sub>254</sub> with CHCl<sub>3</sub>/Me<sub>2</sub>CO (1:1) as solvent, followed by HPLC (50mg) with an octadecyltrimethylsilane modified column (Mercksorb SI 100, 10µm) [IR, NMR, MS: *Helv Chim Acta* 59 2417 1976].

Sodium ionophore V (ETH 4120) [4-octadecanoyloxymethyl-N,N,N',N'-tetracyclohexyl-1,2-phenylenedioxydiacetamide] [129880-73-5] M 849.3. Purified by recrystn from EtOAc. [Preparation and properties: Anal Chim Acta 233 295 1990].

Sodium ionophore VI {bis[(12-crown-4)methyl]dodecyl methyl malonate} [80403-59-4] M 662.9. Purified by gel permeation or column chromatography. [Preparation and NMR data: J Electroanal Chem 132 99 1982.]

Sodium isopropylxanthate [140-93-2] M 158.2, pK 2.16 (for -S<sup>-</sup>). Crystd from ligroin/ethanol.

Sodium laurate [629-25-4] M 222.3. See sodium dodecanoate on p. 470.

Sodium RS-mandelate [114-21-6] M 174.1. Crystd from 95% EtOH.

Sodium 2-mercaptoethanesulfonate (MESNA) [19767-45-4] M 164.2,  $pK_1^{20}<0$  (SO<sub>3</sub><sup>-</sup>),  $pK_2^{20}$ 9.53 (SH). It can be recrystd from H<sub>2</sub>O and does not melt below 250°. It can be purified further by converting to the free acid by passing a 2M soln through an ion exchange (Amberlite IR-120) column in the acid form, evaporating the eluate in a vacuum to give the acid as a viscous oil (readily dec) which can be checked by acid and SH titration. It is then dissolved in H<sub>2</sub>O, carefully neutralised with aqueous NaOH, evaporated and recrystd from H<sub>2</sub>O [J Am Chem Soc 77 6231 1955].

Sodium metanilate [1126-34-7] M 195.2. Crystd from hot water.

Sodium metaperiodate (NaIO<sub>4</sub>) [7790-28-5] M 213.9, m ~300°(dec), d 4.17. Crystd from hot water.

Sodium metasilicate  $(5H_2O)$  [6834-92-0] M 212.1, m 1088°, d 2.4. Crystd from aqueous 5% NaOH solution.

Sodium methanethiolate [sodium methylmercaptide] [5188-07-8] M 70.1,  $pK^{25}$  10.33 (MeS<sup>-</sup>). Dissolve the salt (10g) in EtOH (10mL) and add Et<sub>2</sub>O (100mL). Cool and collect the ppte, wash it with Et<sub>2</sub>O and dry it in vacuum. It is a white powder which is very soluble in EtOH and H<sub>2</sub>O. [Bull Soc Chim Fr 3 2318 1936.]

Sodium methoxide [124-41-4] M 54.0. It behaves the same as sodium ethoxide. It is hygroscopic and is hydrolysed by moist air to NaOH and EtOH. Material that has been kept under  $N_2$  should be used. If erratic results are obtained, even with recently purchased NaOMe it should be freshly prepared thus: Clean Na (37g) cut in 1-3g pieces is added in small portions to stirred MeOH (800mL) in a 2L three necked flask equipped with a stirrer and a condenser with a drying tube. After all the Na has dissolved the MeOH is removed by distillation under vacuum and the residual NaOMe is dried by heating at 150° under vacuum and kept under dry  $N_2$  [Org Synth 39 51 1959].

Sodium 3-methyl-1-butanesulfonate [5343-41-9] M 174.1. Crystd from 90% MeOH.

Sodium molybdate  $(2H_2O)$  [10102-40-6] M 241.9, m 100°(loses  $2H_2O$ ), 687°, d 3.28, pK<sup>25</sup> 4.08 (for  $H_2MoO_4$ ). Crystd from hot water (1mL/g) by cooling to 0°.

Sodium monensin [22373-78-0] M 693.8. Recrystd from EtOH-H<sub>2</sub>O [Cox et al. J Am Chem Soc 107 4297 1985].

Sodium 1-naphthalenesulfonate [130-14-3] M 230.2. Recrystd from water or aqueous acetone [Okadata et al. J Am Chem Soc 108 2863 1986].

Sodium 2-naphthalenesulfonate [532-02-5] M 230.2. Crystd from hot 10% aqueous NaOH or water, and dried in a steam oven.

Sodium 2-naphthylamine-5,7-disulfonate [79004-97-0] M 235.4. Crystd from water (charcoal) and dried in a steam oven.

Sodium nitrate [7631-99-4] M 85.0, m 307°, b 380°, d 2.26. Crystd from hot water (0.6mL/g) by cooling to 0°, or from concentrated aqueous solution by addition of MeOH. Dried under vacuum at 140°. After 2 recrystns tech grade had K, Mg, B, Fe Al, and Li at 100, 29, 0.6, 0.4, 0.2 and 0.2 ppm resp.

Sodium nitrite [7632-00-0] M 69.0, m 271°, b 320°, d 2.17. Crystd from hot water (0.7mL/g) by cooling to 0°, or from its own melt. Dried over  $P_2O_5$ .

Sodium 1-octanesulfonate [5324-84-5] M 216.2. Recrystd from absolute EtOH. Sodium oleate [143-19-1] M 304.4, m 233-235°. Crystd from EtOH and dried in an oven at 100°.

**Sodium oxalate** [62-76-0] **M 134.0, m 250-270°(dec), d 2.34.** Crystd from hot water (16mL/g) by cooling to 0°. Before use as a volumetric standard, analytical grade quality sodium oxalate should be dried for 2h at 120° and allowed to cool in a desiccator.

Sodium palmitate [408-35-5] M 278.4, m, 270°, 285-201°. Crystd from EtOH, dried in an oven.

Sodium perchlorate (anhydrous) [7601-89-0] M 122.4, m 130°(for monohydrate), d 2.02,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Because its solubility in water is high (2.1g/mL at 15°) and it has a rather low temperature coefficient of solubility, sodium perchlorate is usually crystd from acetone, MeOH, water-ethanol or dioxane-water (33g dissolved in 36mL of water and 200mL of dioxane). After filtering and crystallising, the solid is dried under vacuum at 140-150° to remove solvent of crystn. Basic impurities can be removed by crystn from hot acetic acid, followed by heating at 150°. If NaClO<sub>4</sub> is ppted from distilled water by adding HClO<sub>4</sub> to the chilled solution, the ppte contains some free acid. **EXPLOSIVE** 

Sodium phenol-4-sulfonate (2H<sub>2</sub>O) (4-hydroxybenzenesulfonic acid Na salt) [825-90-1] M 232.2. Crystd from hot water (1mL/g) by cooling to 0°, or from MeOH, and dried in vacuum.

Sodium phenoxide [139-02-6] M 116.1, m 61-64°. Washed with  $Et_2O$ , then heated under vacuum to 200° to remove any free phenol.

Sodium phenylacetate [114-70-5] M 158.1. Its aqueous solution was evaporated to crystallisation on a steam bath, the crystals being washed with absolute EtOH and dried under vacuum at 80°.

Sodium *o*-phenylphenolate (4H<sub>2</sub>O) [132-27-4] M 264.3. Crystd from acetone and dried under vacuum at room temperature.

**Sodium phosphoamidate** [3076-34-4] **M 119.0.** Dissolved in water below 10°, and acetic acid added dropwise to pH 4.0 so that the monosodium salt was ppted. The ppte was washed with water and  $Et_2O$ , then air dried. Addition of one equivalent of NaOH to the solution gave the sodium salt, the solution being adjusted to pH 6.0 before use [Rose and Heald *Biochem J* 81 339 1961].

Sodium phytate (H<sub>2</sub>O) [myo-inositolhexakis(H<sub>2</sub>PO<sub>4</sub>) Na salt] [14306-25-3] M 857.9. Crystd from water.

Sodium piperazine-N, N'-bis(2-ethanesulfonate) H<sub>2</sub>O (PIPES-Na salt) [76836-02-7] M 364.3. Crystd from water and EtOH.

**Sodium polyacrylate (NaPAA)** [9003-04-7]. Commercial polyacrylamide was neutralised with an aqueous solution of NaOH and the polymer ppted with acetone. The ppte was redissolved in a small amount of water and freeze-dried. The polymer was repeatedly washed with EtOH and water to remove traces of low

molecular weight material, and finally dried in vacuum at 60° [Vink J Chem Soc, Faraday Trans 1 75 1207 1979]. Also dialysed overnight against distilled water, then freeze-dried.

**Sodium poly**( $\alpha$ -L-glutamate). It was washed with acetone, dried, dissolved in water and ppted with isopropanol at 5°. Impurities and low molecular weight fractions were removed by dialysis of the aqueous solution for 50h, followed by ultrafiltration through a filter impermeable to polymers of molecular weights greater the 10<sup>4</sup>. The polymer was recovered by freeze-drying. [Mori et al. J Chem Soc, Faraday Trans 1 2583 1978.]

Sodium propionate [137-40-6] M 96.1, m 287-289°. Recrystd from H<sub>2</sub>O (solubility 10%), and dried by heating at 100° for 4h. Solubility of anhydrous salt in MeOH is 13% at 15° and 13.77% at 68°. It is insoluble in  ${}^{*}C_{6}H_{6}$  and Me<sub>2</sub>CO. [J Chem Soc 1341 1934.]

Sodium pyrophosphate (10H<sub>2</sub>O) [13472-36-1] M 446.1, d 1.82,  $pK_1^{25}1.52$ ,  $pK_2^{25}2.36$ ,  $pK_3^{25}$ 6.60,  $pK_4^{25}9.25$  (for pyrophosphoric acid,  $H_4P_2O_7$ ). Crystd from hot  $H_2O$  and air dried at room temp.

Sodium selenate [13410-01-0] M 188.9,  $pK_1^{25} \sim 0$ ,  $pK_2^{25} 1.66$  (for selenic acid,  $H_2 SeO_4$ ). Crystd from water.

Sodium selenite [10102-18-8] M 172.9, m >350°,  $pK_1^{25}$  2.62,  $pK_2^{25}$  8.32 (for  $H_2$ SeO<sub>3</sub>). Crystd from water.

Sodium silicate solution [1344-09-8]  $pK_1^{25}9.51$ ,  $pK_2^{25}11.77$  (for silicic acid,  $H_4SiO_4$ ) Purified by contact filtration with activated charcoal.

Sodium succinate [150-90-3] M 162.1. See disodium succinate on p. 421.

Sodium sulfanilate [515-74-2] M 195.2. Crystd from water.

Sodium sulfate ( $10H_2O$ ) [7727-73-3 ( $10H_2O$ ); 7757-82-6 (anhydr)] M 322.2, m 32°(dec), 884° (anhydr), d 2.68 (anhydr). Crystd from water at 30° (1.1mL/g) by cooling to 0°. Sodium sulfate becomes anhydrous at 32°.

Sodium sulfide  $(9H_2O)$  [1313-84-4 (9H<sub>2</sub>O); 1313-82-2 (anhydr)] M 240.2, m ~50(loses H<sub>2</sub>O), 950(anhydr), d 1.43 (10H<sub>2</sub>O), 1.86 (anhydr). Some purification of the hydrated salt can be achieved by selecting large crystals and removing the surface layer (contaminated with oxidation products) by washing with distilled water. Other metal ions can be removed from Na<sub>2</sub>S solutions by passage through a column of Dowex ion-exchange A-1 resin, Na<sup>+</sup>-form. The hydrated salt can be rendered anhydrous by heating in a stream of H<sub>2</sub> or N<sub>2</sub> until water is no longer evolved. (The resulting cake should not be heated to fusion because it is readily oxidised.) Recryst from distilled water [Anderson and Azowlay J Chem Soc, Dalton Trans 469 1986].

**Sodium sulfite** [7757-83-7] **M 126.0, d 2.63.** Crystd from warm water (0.5mL/g) by cooling to 0°. Purified by repeated crystns from deoxygenated water inside a glove-box, finally drying under vacuum. [Rhee and Dasgupta J Phys Chem 89 1799 1985.]

Sodium R-tartrate (2H<sub>2</sub>O) [6106-24-7] M 230.1, m 120°(loses H<sub>2</sub>O), d 1.82. Crystd from warm dilute aqueous NaOH by cooling.

Sodium taurocholate [145-42-6] M 555.7. Purified by recrystn and gel chromatography using Sephadex LH-20.

Sodium tetradecylsulfate [1191-50-0] M 316.4. Recrystd from absolute EtOH [Abu Hamdiyyah and Rahman J Phys Chem 91 1531 1987].

Sodium tetrafluoroborate [13755-29-8] M 109.8, d 2.47, pK<sup>25</sup> -4.9 (for HBF<sub>4</sub>). See Sodium fluoroborate on p. 470.

Sodium tetrametaphosphate [13396-41-3] M 429.9,  $pK_1^{25}$  2.60,  $pK_2^{25}$  6.4,  $pK_3^{25}$  8.22,  $pK_4^{25}$  11.4 (tetrametaphosphoric acid,  $H_4P_4O_{12}$ ). Crystd twice from water at room temperature by adding EtOH (300g of Na<sub>4</sub>P<sub>4</sub>O<sub>12</sub>, H<sub>2</sub>O, 2L of water, and 1L of EtOH), washed first with 20% EtOH then with 50% EtOH and air dried [Quimby J Phys Chem 58 603 1954].

**Sodium tetraphenylborate [tetraphenyl boron Na]** [143-66-8] **M 342.2.** Dissolve in dry MeOH and add dry Et<sub>2</sub>O. Collect the solid and dry in a vacuum at  $80^{\circ}/2$ mm for 4h. Also can be extracted (Soxhlet) using CHCl<sub>3</sub> and crystallises from CHCl<sub>3</sub> as snow white needles. It is freely sol in H<sub>2</sub>O, Me<sub>2</sub>CO but insol in pet ether and Et<sub>2</sub>O. An aqueous soln has pH ~ 5 and can be stored for days at 25° or lower, and for 5 days at 45° without deterioration. Its solubility in polar solvents increases with decrease in temp [Justus Liebigs Ann Chem 574 195 1950]. The salt can also be recrystd from acetone-hexane or CHCl<sub>3</sub>, or from Et<sub>2</sub>O-cyclohexane (3:2) by warming the soln to ppte the compound. Dried in a vacuum at 80°. Dissolved in Me<sub>2</sub>CO and added to an excess of toluene. After a slight milkiness developed on standing, the mixture was filtered. The clear filtrate was evaporated at room temperature to a small bulk and again filtered. The filtrate was then warmed to 50-60°, giving clear dissolution of crystals. After standing at this temperature for 10min the mixture was filtered rapidly through a pre-heated Büchner funnel, and the crystals were collected and dried in a vacuum desiccator at room temperature for 3 days [Abraham et al. J Chem Soc, Faraday Trans 1 80 489 1984]. If the product gives a turbid aq solution, the turbidity can be removed by treating with freshly prepared alumina gel.

Sodium thioantimonate (Na<sub>3</sub>SbS<sub>4</sub>.9H<sub>2</sub>O, Schlippe's salt) [13776-84-6] M 481.1, m 87°, b 234°, d 1.81. Crystd from warm water (2mL/g) by cooling to 0°.

Sodium thiocyanate [540-72-7] M 81.1, m 300°,  $pK^{25}$  -1.85 (for HSCN). It is recrystd from EtOH or Me<sub>2</sub>CO and the mother liquor is removed from the crystals by centrifugation. It is very deliquescent and should be kept in an oven at 130° before use. It can be dried in vacuum at 120°/P<sub>2</sub>O<sub>5</sub> [*Trans Faraday Soc* 30 1104 1934]. Its solubility in H<sub>2</sub>O is 113% at 10°, 178% at 46°, 225.6% at 101.4°; in MeOH 35% at 15.8°, 51% at 48°, 53.5% at 52.3°; in EtOH 18.4% at 18.8°, 24.4% at 70.9°; and in Me<sub>2</sub>CO 6.85% at 18.8° and 21.4% at 56° [*J Chem Soc* 2282 1929].

Sodium thiocyanate has also been recrystd from water, acetonitrile or from MeOH using Et<sub>2</sub>O for washing, then dried at 130°, or dried under vacuum at 60° for 2 days. [Strasser et al. J Am Chem Soc 107 789 1985; Szezygiel et al. J Am Chem Soc 91 1252 1987.] (The latter purification removes material reacting with iodine.) Sodium thiocyanate solns can be freed from traces of iron by repeated batch extractions with Et<sub>2</sub>O.

Sodium thioglycolate [367-51-1] M 114.1. Crystd from 60% EtOH (charcoal). Hygroscopic.

Sodium thiosulfate (5H<sub>2</sub>O) [10102-17-7 (hydr); 7772-98-7 (anhydr)] M 248.2(anhydr), m 48(rapid heat), d 1.69,  $pK_1^{25}$  0.6,  $pK_2^{25}$  1.74 (for H<sub>2</sub>S<sub>2</sub>O<sub>3</sub>) Crystd from EtOH-H<sub>2</sub>O solns or from water (0.3mL/g) below 60° by cooling to 0°, and dried at 35° over P<sub>2</sub>O<sub>5</sub> under vacuum.

**Sodium** *p*-toluenesulfinate [824-79-3] M 178.2,  $pK^{25}$  2.80 (1.99)(for -SO<sub>2</sub><sup>-</sup>). Crystd from water (to constant UV spectrum), and dried under vacuum or extracted with hot \*benzene, then dissolved in EtOH-H<sub>2</sub>O and heated with decolorising charcoal. The solution was filtered and cooled to give crystals of the dihydrate.

Sodium *p*-toluenesulfonate [657-84-1] M 194.2,  $pK^{25}$  -1.34 (for -SO<sub>3</sub><sup>-</sup>). Dissolved in distilled water, filtered to remove insoluble impurities and evaporated to dryness. Then crystd from MeOH or EtOH, and dried at 110°. Its solubility in EtOH is not high (maximum 2.5%) so that Soxhlet extraction with EtOH may be preferable. Sodium *p*-toluenesulfonate has also been crystd from Et<sub>2</sub>O and dried under vacuum at 50°.

Sodium trifluoroacetate [2923-18-4] M 136.0, m 206-210°(dec),  $pK^{25}$  0.52 (for CF<sub>3</sub>CO<sub>2</sub><sup>-</sup>). A possible contaminant is NaCl. The solid is treated with CF<sub>3</sub>CO<sub>2</sub>H and evaporated twice. Its solubility in CF<sub>3</sub>CO<sub>2</sub>H is 13.1% at 29.8°. The residue is crystd from dil EtOH and the solid dried in vacuum at 100°. [J

Am Chem Soc 76 4285 1954.] It can be ppted from EtOH by adding dioxane, then crystd several times from hot absolute EtOH. Dried at 120-130%/1mm.

**Sodium 2,2',4-trihydroxyazobenzene-5'-sulfonate** [3564-26-9] **M 295.3.** Purified by precipitating the free acid from aqueous solution using concentrated HCl, then washing and extracting with EtOH in a Soxhlet extractor. Evaporation of the EtOH left the purified acid.

Sodium trimetaphosphate (6H<sub>2</sub>O) [7785-84-4] M 320.2, m 53°, d 1.79,  $pK_2^{25}$  1.64,  $pK_3^{25}$  2.07 (for trimetaphosphoric acid, H<sub>3</sub>P<sub>3</sub>O<sub>9</sub>). Ppted from an aq soln at 40° by adding EtOH. Air dried.

Sodium 2,4,6-trimethylbenzenesulfonate [6148-75-0] M 222.1. Crystd twice from MeOH and dried under vacuum.

Sodium trimethylsilanolate (sodium trimethylsilanol) [18027-10-6] M 112.2, m 230°(dec). It is very soluble in Et<sub>2</sub>O and <sup>\*</sup>C<sub>6</sub>H<sub>6</sub> but moderately soluble in pet ether. It is purified by sublimation at 130-150° in a high vacuum. [IR: J Am Chem Soc 75 5615 1953; J Org Chem 17 1555 1952.]

Sodium tripolyphosphate [7758-29-4] M 367.9,  $pK_1^{25} \sim 1$ ,  $pK_2^{25} 2.0$ ,  $pK_3^{25} 2.13$ ,  $pK_4^{25} 5.78$ ,  $pK_5^{25} 8.56$  (for tripolyphosphoric acid,  $H_5P_3O_{10}$ ). Purified by repeated pptn from aqueous solution by slow addition of MeOH and air dried. Also a solution of anhydrous sodium tripolyphosphate (840g) in water (3.8L) was filtered, MeOH (1.4L) was added with vigorous stirring to ppte Na<sub>5</sub>P<sub>3</sub>O<sub>10</sub>.6H<sub>2</sub>O. The ppte was collected on a filter, air dried by suction, then left to dry in air overnight. It was crystd twice more in this way, using a 13% aqueous solution (w/w), and leaching the crystals with 200mL portions of water [Watters, Loughran and Lambert J Am Chem Soc 78 4855 1956]. Similarly, EtOH can be added to ppte the salt from a filtered 12-15% aqueous solution, the final solution containing *ca* 25% EtOH (v/v). Air drying should be at a relative humidity of 40-60%. Heat and vac drying should be avoided. [Quimby J Phys Chem 58 603 1954.]

Sodium tungstate  $(2H_2O)$  [10213-10-2] M 329.9, m 698°, d 4.18,  $pK_1^{25}$  2.20,  $pK_2^{25}$  3.70 (for tungstic acid,  $H_2WO_4$ ). Crystd from hot water (0.8mL/g) by cooling to 0°.

**Sodium** m-xylenesulfonate [30587-85-0] **M** 208.2. Dissolved in distilled water, filtered, then evaporated to dryness. Crystd twice form absolute EtOH and dried at 110°.

Sodium p-xylenesulfonate [827-19-0] M 208.2. See sodium 2,5-dimethylbenzenesulfonate on p. 469.

Stannic chloride (tin IV chloride, stannic tetrachloride) [7646-78-8] M 260.5, m -33°, -30.2°, b 114°/760mm, d 2.23,  $pK^{25}$  14.15 (for aquo Sn<sup>4+</sup> hydrolysis). Fumes in moist air due to hydrate formation. Fractionate in a ground glass still and store in the absence of air. Possible impurities are SO<sub>2</sub> and HCl [Baudler Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I p. 729 1963]. It forms a solid pentahydrate [10026-06-9] which smells of HCl and is formed when the anhydrous salt is dissolved in a small vol of H<sub>2</sub>O. Also refluxed with clean mercury or P<sub>2</sub>O<sub>5</sub> for several hours, then distd under (reduced) N<sub>2</sub> pressure into a receiver containing P<sub>2</sub>O<sub>5</sub>. Finally redistd. Alternatively, distd from Sn metal under vacuum in an all-glass system and sealed off in large ampoules. Fumes in moist air. SnCl<sub>4</sub> is available commercially as 1M solns in CH<sub>2</sub>Cl<sub>2</sub> or hexane. HARMFUL VAPOURS.

Stannic iodide (SnI<sub>4</sub>) [7790-47-8] M 626.3, m 144°, b 340, d 4.46. Crystd from anhydrous CHCl<sub>3</sub>, dried under vacuum and stored in a vacuum desiccator. Sublimes at 180°.

Stannic oxide (SnO<sub>2</sub>) [18282-10-5] M 150.7, m 1630°, d 6.95. Refluxed repeatedly with fresh HCl until the acid showed no tinge of yellow. The oxide was then dried at 110°.

**Stannous bis-cyclopentadienyl** [26078-96-6] **M 248.9.** Purified by vacuum sublimation. Handled and stored under dry N<sub>2</sub>. The related thallium and indium compounds are similarly prepared.

Stannous chloride (anhydrous) [7772-99-8] M 189.6, m 247°, b 606°, d 3.95,  $pK_1^{25} 1.7$ ,  $pK_2^{25} 3.7$  (for aquo Sn<sup>2+</sup> hydrolysis). Analytical reagent grade stannous chloride dihydrate is dehydrated by adding slowly to vigorously stirred, redistilled acetic anhydride (120g salt per 100g of anhydride). (In a fume cupboard.) After *ca* an hour, the anhydrous SnCl<sub>2</sub> is filtered on to a sintered-glass or Büchner funnel, washed free from acetic acid wth dry Et<sub>2</sub>O (2 x 30mL), and dried under vacuum. It is stored in a sealed container. [Stephen J Chem Soc 2786 1930].

Strontium acetate [543-94-2] M 205.7, d 2.1, pK<sup>25</sup> 13.0 (for aquo Sr<sup>2+</sup> hydrolysis). Crystd from AcOH, then dried under vacuum for 24h at 100°.

Strontium bromide [10476-81-0] M 247.4, m 643°, d 4.22. Crystd from water (0.5mL/g).

Strontium chloride (6H<sub>2</sub>O) [1025-70-4] M 266.6, m 61°(rapid heating), 114-150°(loses 5H<sub>2</sub>O), 868°(anhydr). Crystd from warm water (0.5mL/g) by cooling to  $0^{\circ}$ .

Strontium chromate [7789-06-2] M 203.6, d 3.9,  $pK_1^{25}$  0.74,  $pK_2^{25}$  6.49 (for H<sub>2</sub>CrO<sub>4</sub>). Crystd from water (40mL/g) by cooling.

Strontium hydroxide (8H<sub>2</sub>O) [1311-10-0 (8H<sub>2</sub>O); 18480-07-4 (anhydr)] M 265.8, m 100<sup>o</sup>(loses H<sub>2</sub>O), d 1.90, m 375(anhydr), d 3.63 (anhydr). Crystd from hot water (2.2mL/g) by cooling to  $0^{\circ}$ .

Strontium lactate (3H<sub>2</sub>O) [29870-99-3] M 319.8, m 120°(loses 3H<sub>2</sub>O). Crystd from aq EtOH.

Strontium nitrate [10042-76-9] M 211.6, m 570°, b 645°, d 2.99. Crystd from hot water (0.5mL/g) by cooling to 0°.

Strontium oxalate (H<sub>2</sub>O) [814-95-9] M 193.6, m 150°. Crystd from hot water (20mL/g) by cooling.

Strontium salicylate [526-26-1] M 224.7. Crystd from hot water (4mL/g) or EtOH.

Strontium tartrate [868-19-9] M 237.7. Crystd from hot water.

Strontium thiosalicylate (5H<sub>2</sub>O) [15123-90-7] M 289.8. Crystd from hot water (2mL/g) by cooling to 0°.

Sulfamic acid [5329-14-6] M 97.1, m 205°(dec),  $pK^{25}$  0.99 (NH<sub>2</sub>SO<sub>3</sub>H). Crystd from water at 70° (300mL per 25g), after filtering, by cooling a little and discarding the first batch of crystals (about 25g) before standing in an ice-salt mixture for 20min. The crystals were filtered by suction, washed with a small quantity of ice water, then twice with cold EtOH and finally with Et<sub>2</sub>O. Air dried for 1h, then stored in a desiccator over Mg(ClO<sub>4</sub>)<sub>2</sub> [Butler, Smith and Audrieth *Ind Eng Chem (Anal Ed)* 10 690 1938]. For preparation of primary standard material see *Pure Appl Chem* 25 459 1969.

Sulfamide [7803-58-9] M 96.1, m 91.5°. Crystd from absolute EtOH.

Sulfur [7704-34-9] M 32.1, m between 112.8° and 120°, depending on form. Murphy, Clabaugh and Gilchrist [*J Res Nat Bur Stand* 64A 355 1960] have obtained sulfur of about 99.999% purity by the following procedure: Roll sulfur was melted and filtered through a coarse-porosity glass filter funnel into a 2L round-bottomed Pyrex flask with two necks. Conc H<sub>2</sub>SO<sub>4</sub> (300mL) was added to the sulfur (2.5Kg), and the mixture was heated to 150°, stirring continuously for 2h. Over the next 6h, conc HNO<sub>3</sub> was added in about 2mL portions at 10-15min intervals to the heated mixture. It was then allowed to cool to room temperature and the acid was poured off. The sulfur was rinsed several times with distilled water, then remelted, cooled, and rinsed several times with distd water again, this process being repeated four or five times to remove most of the acid entrapped in the sulfur. An air-cooled reflux tube (*ca* 40cm long) was attached to one of the necks of the flask, and a gas delivery tube (the lower end about 1in above the bottom of the flask) was inserted into the other. While the sulfur was boiled under reflux, a stream of helium or N<sub>2</sub> was passed through to remove any water, HNO<sub>3</sub> or H<sub>2</sub>SO<sub>4</sub>, as vapour. After 4h, the sulfur was cooled so that the reflux tube could be replaced by a bent air-cooled condenser. The sulfur was then distilled, rejecting the first and the final 100mL portions, and transferred in 200mL portions to 400mL glass cylinder ampoules (which were placed on their sides during solidification). After adding about 80mL of water, displacing the air with N<sub>2</sub>, and sealing the ampoule was cooled, and the water was titrated with 0.02M NaOH, the process being repeated until the acid content was negligible. Finally, entrapped water was removed by alternate evacuation to 10mm Hg and refilling with N<sub>2</sub> while the sulfur was kept molten. Other purifications include crystn from CS<sub>2</sub> (which is less satisfactory because the sulfur retains appreciable amounts of organic material), "benzene or "benzene/acetone, followed by melting and degassing. Has also been boiled with 1% MgO, then decanted, and dried under vacuum at 40° for 2 days over P<sub>2</sub>O<sub>5</sub>. [For purification of S<sub>6</sub>, "recryst. S<sub>8</sub>" and "Bacon-Fanelli sulfur" see Bartlett, Cox and Davis J Am Chem Soc 83 103, 109 1961.]

Sulfur dichloride [10545-99-0] M 103.0, m -78°, b 59°/760mm(dec), d 1.621. Twice distilled in the presence of a small amount of PCl<sub>3</sub> through a 12in Vigreux column, the fraction boiling between 55-61° being redistd (in the presence of PCl<sub>3</sub>), and the fraction distilling between 58-61° retained. (The PCl<sub>3</sub> is added to inhibit the decomposition of SCl<sub>2</sub> into S<sub>2</sub>Cl<sub>2</sub> and Cl<sub>2</sub>). The SCl<sub>2</sub> must be used as quickly as possible after distn, within 1h at room temperature, The sample contains 4% S<sub>2</sub>Cl<sub>2</sub>. On long standing this reaches 16-18%. HARMFUL VAPOURS.

Sulfur dioxide [7446-09-5] M 64.1, b -10°. Dried by bubbling through concentrated  $H_2SO_4$  and by passage over  $P_2O_5$ , then passed through a glass-wool plug. Frozen with liquid air and pumped to a high vacuum to remove dissolved gases. HARMFUL VAPOURS.

Sulfuric acid [7664-93-9] M 98.1, d 1.83,  $pK_1^{25} \sim -8.3$ ,  $pK_2^{25}$  1.99. Sulfuric acid, and also 30% fuming H<sub>2</sub>SO<sub>4</sub>, can be distilled in an all-Pyrex system, optionally from potassium persulfate. Also purified by fractional crystn of the monohydrate from the liquid. Dehydrates and attacks skin—wash immediately with H<sub>2</sub>O.

Sulfur monochloride (sulfur monochloride) [10025-67-9] M 135.0, m -77°; b 19.1°, 29-30°/12mm, 72°/100mm, 138°/760mm, d<sup>20</sup> 1.677,  $n_D^{20}$  1.67. Pungent, irritating golden yellow liquid. When impure its colour is orange to red due to SCl<sub>2</sub> formed. It fumes in moist air and liberates HCl, SO<sub>2</sub> and H<sub>2</sub>S in the presence of H<sub>2</sub>O. Distil and collect the fraction boiling above 137° at atmospheric pressure. Fractionate this fraction over sulfur at *ca* 12mm using ground glass apparatus (b 29-30°). Alternatively purify by distn below 60° from a mixture containing sulfur (2%) and activated charcoal (1%), under reduced pressure (e.g. 50mm). It is soluble in EtOH, \*C<sub>6</sub>H<sub>6</sub>, Et<sub>2</sub>O, CS<sub>2</sub> and CCl<sub>4</sub>. Store in a closed container in the dark in a refrigerator. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 371 1963.] HARMFUL VAPOURS.

Sulfur trioxide pyridine complex [26412-87-3] M 159.2, m 155-165°, 175°. Wash the solid with a little CCl<sub>4</sub>, then H<sub>2</sub>O to remove traces of pyridine sulfate, and dry over P<sub>2</sub>O<sub>5</sub> [Chem Ber 59 1166 1926; Synthesis 59 1979].

Sulfuryl chloride [7791-25-2] M 135.0, m -54.1°, b 69.3°/760mm,  $d_4^{20}$  1.67,  $n_D^{30}$  1.44. *Pungent, irritating colourless liquid.* It becomes yellow with time due to decomposition to SO<sub>2</sub> and HCl. Distil and collect fraction boiling below 75°/atm which is mainly SO<sub>2</sub>Cl<sub>2</sub>. To remove HSO<sub>3</sub>Cl and H<sub>2</sub>SO<sub>4</sub> impurities, the distillate is poured into a separating funnel filled with crushed ice and *briefly* shaken. The lower cloudy layer is removed, dried for some time in a desiccator over P<sub>2</sub>O<sub>5</sub> and finally fractionated at atmospheric pressure. The middle fraction boils at 69-70° and is pure SO<sub>2</sub>Cl<sub>2</sub>. It decomposes gradually in H<sub>2</sub>O to H<sub>2</sub>SO<sub>4</sub> and HCl. Reacts violently with EtOH and MeOH and is soluble in \*C<sub>6</sub>H<sub>6</sub>, toluene Et<sub>2</sub>O and acetic acid. [Handbook of Preparative Inorganic Chemistry (Ed Brauer) Vol I 383 1963; Inorg Synth 1 114 1939]. HARMFUL VAPOURS.

**Tantalium (V) chloride** (tantalium pentachloride) [7721-01-9] M 358.2, m 216.2°, 216.5-220°; b 239°/atm., d 3.68. Purified by sublimation in a stream of Cl<sub>2</sub>. Colourless

needles when pure (yellow when contaminated with even less than 1% of NbCl<sub>5</sub>). Sensitive to H<sub>2</sub>O, even in conc HCl it decomposes to tantalic acid. Sol in EtOH. [J Am Chem Soc 80 2952 1958; Handbook of Preparative Inorganic Chemistry (Ed Brauer) Vol II 1302 1965.]

Tantalium pentaethoxide [6074-84-6] M 406.3, b 147°/0.2mm, 202°/10mm,  $pK_1^{25}$  9.6,  $pK_2^{25}$  13.0 (for tantalic acid). Purified by distillation. It aggregates in  ${}^{*}C_6H_6$ , EtOH, MeCN, pyridine and disopropyl ether. [J Chem Soc 726 1955, 5 1956.]

Telluric acid [7803-68-1] M 229.6,  $pK_1^{25}$  7.70,  $pK_2^{25}$  11.04 (H<sub>6</sub>TaO<sub>6</sub>). Crystd once from nitric acid, then repeatedly from hot water (0.4mL/g).

**Tellurium** [13494-80-9] **M 127.6, m 450°.** Purified by zone refining and repeated sublimation to an impurity of less than 1 part in  $10^8$  (except for surface contamination by TeO<sub>2</sub>). [Machol and Westrum *J Am Chem Soc* 80 2950 1958.] Tellurium is volatile at 500°/0.2mm. Also purified by electrode deposition [Mathers and Turner *Trans Amer Electrochem Soc* 54 293 1928].

**Tellurium dioxide** [7446-07-3] **M 159.6, m 733°, d 6.04.** Dissolved in 5M NaOH, filtered and ppted by adding 10M HNO<sub>3</sub> to the filtrate until the soln was acid to phenolphthalein. After decanting the supernatant, the ppte was washed five times with distilled water, then dried for 24h at 110° [Horner and Leonhard J Am Chem Soc 74 3694 1952].

Terbium oxide [12037-01-3] M 747.7, pK<sup>25</sup> 8.16 (for Tb<sup>3+</sup> hydrolysis). Dissolved in acid, ppted as its oxalate and ignited at 650°.

**Tetraallyltin** (tetraallylstannane) [7393-43-3] M 283.0, b 52°/0.2mm, 69-70°/15mm, d 1.179, n 1.536. Possible contaminants are allyl chloride and allyltin chloride. Check <sup>1</sup>H NMR and IR [Fishwick and Wallbridge J Organometal Chem 25 69 1970], and if impure, dissolve in Et<sub>2</sub>O and shake with a 5% aq soln of NaF which ppts allyltin fluoride. Separate the Et<sub>2</sub>O layer, dry (MgSO<sub>4</sub>) and dist at ~ 0.2mm. It decomposes slightly on repeated distn. [O'Brien et al. *Inorg Synth* 13 75 1972; Fishwick et al. J Chem Soc (A) 57 1971.]

**Tetrabutylammonium borohydride** [33725-74-5] M 257.3, m 128-129°. Purified by recrystn from EtOAc followed by careful drying under vacuum at 50-60°. Samples purified in this way showed no signs of loss of *active* H after storage at room temperature for more than 1 year. Nevertheless samples should be stored at *ca* 6° in tightly stoppered bottles if kept for long periods. It is soluble in CH<sub>2</sub>Cl<sub>2</sub>. [J Org Chem 41 690 1976; Tetrahedron Lett 3173 1972.]

**Tetrabutylammonium chlorochromate** [54712-57-1] **M 377.9, m 184-185°.** Recrystd from EtOAc-hexane. IR v 920cm<sup>-1</sup> in CHCl<sub>3</sub> [Synthesis 749 1983]. Powerful oxidant.

**Tetrabutylammonium tetrafluoroborate** [429-42-5] M 329.3, m 161.8°, 161-163°,  $pK^{25}$  -4.9 (for HBF<sub>4</sub>). Recryst from H<sub>2</sub>O, aq EtOH or from EtOAc by cooling in Dry ice. Also recrystd from ethyl acetate/pentane or dry acetonitrile. Dried at 80° under vacuum. [Detty and Jones J Am Chem Soc 109 5666 1987; Hartley and Faulkner J Am Chem Soc 107 3436 1985.] Acetate m 118±2° (from BuCl); bromide m 118° (from EtOAc) and nitrate m 120° (from \*C<sub>6</sub>H<sub>6</sub>). [J Am Chem Soc 69 2472 1947, 77 2024 1955.]

Tetrabutyl orthotitanate monomer (titanium tetrabutoxide) [5593-70-4] M 340.4, b 142°/0.1mm, 134-136°/0.5mm, 160°/0.8mm, 174°/6mm, 189°/13mm,  $d_4^{35}$  0.993,  $n_D^{25}$  1.49. Dissolve in \*C<sub>6</sub>H<sub>6</sub>, filter if solid is present, evaporate and vacuum fractionate through a Widmer 24inch column. The ester hydrolyses when exposed to air to give hydrated ortho-titanic acid. Titanium content can be determined thus: weigh a sample (ca 0.25g) into a weighed crucible and cover with 10mL of H<sub>2</sub>O and a few drops of conc HNO<sub>3</sub>. Heat (hot plate) carefully till most of the H<sub>2</sub>O has evaporated. Cool and add more H<sub>2</sub>O (10mL) and conc HNO<sub>3</sub> (2mL) and evaporate carefully (no spillage) to dryness and ignite residue at 600-650°/1h. Weigh the residual TiO<sub>2</sub>. [J Chem Soc 2773 1952; J Org Chem 14 655 1949.]

Tetrabutyl tin (tin tetrabutyl) [1461-25-2] M 347.2, b 94.5-96°/0.28mm, 145°/11mm, 245-247°/atm,  $d_4^{20}$  1.05,  $n_D^{24}$  1.473. Dissolve in Et<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and distil under reduced pressure. Although it does not crystallise easily, once the melt has crystallised then it will recrystallise more easily. It is soluble in Et<sub>2</sub>O, Me<sub>2</sub>CO, EtOAc and EtOH but insoluble in MeOH and H<sub>2</sub>O and shows no apparent reaction with H<sub>2</sub>O. [J Org Chem 19 74 1954, J Chem Soc 1992 1954.]

Tetraethoxysilane (tetraethyl orthosilicate) [78-10-4] M 208.3, m -77°, b 165-166°/atm,  $d_4^{20}$  0.933,  $n_D^{25}$  1.382. Fractionate through an 80cm Podbielniak type column (see p. 141) with heated jacket and partial take-off head. Slowly decomposed by H<sub>2</sub>O, soluble in EtOH. It is flammable - irritates the eyes and mucous membranes. [J Am Chem Soc 78 5573 1956, cf J Chem Soc 5020 1952.]

Tetraethylammonium hexafluorophosphate [429-07-2] M 275.2, m >300°, 331°(dec),  $pK_1^{25} \sim 0.5$ ,  $pK_2^{25} 5.12$  (for fluorophosphoric acid  $H_2PO_3F$ ). Dissolve salt (0.8g) in hot  $H_2O$  (3.3mL) and cool to crystallise. Yield of prisms is 0.5g. Solubility in  $H_2O$  is 8.1g/L at 19° [*Chem Ber* 63 1067 1930].

**Tetraethylammonium tetrafluoroborate** [429-06-1] M 217.1, m 235°, 356-367°,  $pK^{25}$  -4.9 (for HBF<sub>4</sub>). Dissolve in hot MeOH, filter and add Et<sub>2</sub>O. It is soluble in ethylene chloride [*J Am Chem Soc* 69 1016 1947, 77 2025 1955]. See entry on p. 359 in Chapter 4.

**Tetraethyl lead** [78-00-2] **M 323.5, b 200°, 227.7°(dec), d 1.653, n 1.5198.** Its more volatile contaminants can be removed by exposure to a low pressure (by continuous pumping) for 1h at 0°. Purified by stirring with an equal volume of  $H_2SO_4$  (d 1.40), keeping the temperature below 30°, repeating this process until the acid layer is colourless. It is then washed with dilute Na<sub>2</sub>CO<sub>3</sub> and distilled water, dried with CaCl<sub>2</sub> and fractionally distd at low pressure under  $H_2$  or N<sub>2</sub> [Calingaert *Chem Rev* 2 43 1926]. VERY POISONOUS.

**Tetraethylsilane** [631-36-7] **M 144.3, b 153.8°/760mm, d\_4^{30} 0.77, n\_D^{30} 1.427.** Fractionate through a 3ft vacuum jacketted column packed with 1/4" stainless steel saddles. The material is finally percolated through a 2ft column packed with alumina and maintained in an inert atmosphere. [J Chem Soc 1992 1954; J Am Chem Soc 77 272 1955.]

**1.1.3.3-Tetraisopropyldisiloxane** [18043-71-5] M 246.5, b 129-130<sup>o</sup>/6mm,  $d_4^{30}$  0.89,  $n_D^{30}$  1.47. Fractionate under reduced pressure in a N<sub>2</sub> atm. [J Am Chem Soc 69 1500 1947.]

**Tetraisopropyl orthotitanate (titanium tetraisopropyl)** [546-68-9] **M 284.3, m 18.5°; b 80°/2mm, 78°/12mm, 228-229°/755mm.** Dissolve in dry  ${}^{*}C_{6}H_{6}$ , filter if a solid separates, evap and fractionate. It is hydrolysed by H<sub>2</sub>O to give solid Ti<sub>2</sub>O(*iso*-OPr)<sub>2</sub> **m** ca 48°. [J Chem Soc 2027, 1952, 469 1957.]

Tetrakis(diethylamino) titanium [(titanium tetrakis(diethylamide)] [4419-47-0] M 336.4, b 85-90°/0.1mm, 112°/0.1mm,  $d_4^{30}$  0.93,  $n_D^{30}$  1.54. Dissolve in \*C<sub>6</sub>H<sub>6</sub>, filter if a solid separates, evaporate under reduced pressure and distil. Orange liquid which reacts violently with alcohols. [J Chem Soc 3857 1960.]

**Tetrakis(hydroxymethyl)phosphonium chloride** [124-64-1] **M 190.6, m 151°**. Crystd from AcOH and dried at 100° in a vacuum. An 80% w/v aqueous solution has  $d_4^{20}$  1.33 [J Am Chem Soc 77 3923 1955].

**Tetrakis(triphenylphosphine) palladium** [14221-01-3] **M 1155.58, m 100-105°(dec).** Yellow crystals from EtOH. It is stable in air only for a short time, and prolonged exposure turns its colour to orange. Store in an inert atmosphere below room temp in the dark. [J Chem Soc 1186 1957.]

**Tetrakis(triphenylphosphine) platinum** [14221-02-4] **M 1244.3, m 118°.** Recrystd by adding hexane to a cold saturated solution in  ${}^{*}C_{6}H_{6}$ . It is soluble in  ${}^{*}C_{6}H_{6}$  and CHCl<sub>3</sub> but insoluble in EtOH and hexane. A less pure product is obtained if crystd by adding hexane to a CHCl<sub>3</sub> soln. Stable in air for several hours and completely stable under N<sub>2</sub>. [*J Am Chem Soc* 2323 1958.]

**Tetramethoxysilane** (tetramethyl orthosilicate) [681-84-5] M 152.2, m 4.5°, b 122°/760mm. Purification as for tetraethoxysilane. It has a vapour pressure of 2.5mm at 0°. [IR: J Am Chem Soc 81 5109 1959.]

**Tetramethylammonium borohydride** [16883-45-7] **M 89.0.** Recrystn from H<sub>2</sub>O three times yields ca 94% pure compound. Dry in high vacuum at 100° for 3h. The solubility in H<sub>2</sub>O is 48% (20°), 61% (40°); and in EtOH 0.5% (25°) and MeCN 0.4% (25°). It decompose slowly in a vacuum at 150°, but rapidly at 250°. The rate of hydrolysis of Me<sub>4</sub>N.BH<sub>4</sub> (5.8M) in H<sub>2</sub>O at 40° is constant over a period of 100h at 0.04% of original wt/h. The rate decreases to 0.02%/h in the presence of Me<sub>4</sub>NOH (5% of the wt of Me<sub>4</sub>N.BH<sub>4</sub>). [J Am Chem Soc 74 2346 1952.]

Tetramethylammonium hexafluorophosphate [558-32-7] M 219.1, m >300°,  $d_4^{25}$  1.617,  $pK_1^{25} \sim 0.5$ ,  $pK_2^{25}$  5.12 (for fluorophosphoric acid  $H_2PO_3F$ ). The salt (0.63g) is recrystd from boiling  $H_2O$  (76mL), yielding pure (0.45) Me<sub>4</sub>N.PF<sub>6</sub> after drying at 100°. It is a good supporting electrolyte. [*Chem Ber* 63 1067 1930.]

**Tetramethylammonium perchlorate** [2537-36-2] M 123.6, m>300°, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystallise twice from H<sub>2</sub>O and dry at 100° in an oven. Insol in most organic solvents. [J Chem Soc 1210 1933.]

**Tetramethylammonium triacetoxyborohydride** [109704-53-2] M 263.1, m 93-98°, 96.5-98°. If impure, wash with freshly distd  $Et_2O$  and dry overnight in a vac to give a free flowing powder. Check <sup>1</sup>H NMR, and if still suspect prepare freshly from  $Me_4NBH_4$  and AcOH in  $*C_6H_6$  and store away from moisture [Banus et al. J Am Chem Soc 74 2346 1952; Evans and Chipman Tetrahedron Lett 27 5939 1986]. It is an **IRRITANT** and **MOISTURE SENSITIVE**.

Tetramethylammonium triphenylborofluoride [437-11-6] M 392.2. Crystd from acetone or acetone/ethanol.

2,4,6,8-Tetramethylcyclotetrasiloxane [2370-88-9] M 240.5, m -69°, b 134°/750 mm, 134.5-134.9°/755 mm,  $d_4^{20}$  0.99,  $n_D^{20}$  1.3872. It is purified by repeated redistillation, and fractions with the required <sup>1</sup>H NMR data are collected. [J Gen Chem USSR (Engl Transl) 29 262 1959; J Am Chem Soc 68 962 1946].

1,1,3,3-Tetramethyldisiloxane [3277-26-7] M 134.3, b 70.5-71°/731mm, 71-72°/atm,  $d_4^{30}$ 0.75,  $n_D^{25}$  11.367. Possible impurity is 1,1,5,5-tetramethyl-3-trimethylsiloxytrisiloxane b 154-155°/733mm. Fractionate, collect fractions boiling below 80° and refractionate. Purity can be analysed by alkaline hydrolysis and measuring the volume of H<sub>2</sub> liberated followed by gravimetric estimation of silica in the hydrolysate. It is unchanged when stored in glass containers in the absence of moisture for 2-3 weeks. Small amounts of H<sub>2</sub> are liberated on long storage. *Care should be taken when opening a container due to pressure developed.* [J Am Chem Soc 79 974 1958; J Chem Soc 609 1958; IR: Z Anorg Chem 299 78 1959.]

*N,N,N'N'*-Tetramethylphosphonic diamide (methylphosphonic bis-dimethylamide) [2511-17-3] M 150.2, b 60.5°/0.6mm, 138°/32mm, 230-230°/atm,  $d_4^{30}$  1.0157,  $n_D^{30}$ 1.4539. Dissolve in heptane or ethylbenzene shake with 30% aqueous NaOH, stir for 1h, separate the organic layer and fractionate. [J Org Chem 21 413 1956]. IR has v 1480, 1460, 1300, 1184, 1065 and 988-970cm<sup>-1</sup> [Can J Chem 33 1552 1955].

**Tetramethylsilane** (TMS) [75-76-3] M 88.2, b 26.3°, n 1.359, d 0.639. Distilled from conc  $H_2SO_4$  (after shaking with it) or LiAlH<sub>4</sub>, through a 5ft vacuum-jacketted column packed with glass helices into an ice-cooled condenser, then percolated through silica gel to remove traces of halide.

2,4,6,8-Tetramethyl tetravinyl cyclotetrasiloxane [2554-06-5] M 344.7, m -43.5°, b 111-112°/10mm, 145-146°/13mm, 224-224.5°/758mm,  $d_4^{30}$  0.98,  $n_D^{30}$ 1.434. A 7mL sample was

distilled in a small Vigreux column at atmospheric pressure without polymerisation or decomposition. It is soluble in cyclohexane. [J Am Chem Soc 77 1685 1955.]

**Tetraphenylarsonium chloride hydrate** [507-28-8] **M 418.8, m 261-263°.** A neutralised aqueous soln was evaporated to dryness. The residue was extracted into absolute EtOH, evaporated to a small volume and ppted by addition of absolute  $Et_2O$ . It was again dissolved in a small volume of absolute EtOH or ethyl acetate and reppted with  $Et_2O$ . Alternatively purified by adding conc HCl to ppte the chloride dihydrate. Redissolved in water, neutralised with  $Na_2CO_3$  and evaporated to dryness. The residue was extracted with CHCl<sub>3</sub> and finally crystallised from CH<sub>2</sub>Cl<sub>2</sub> or EtOH by adding  $Et_2O$ . If the aqueous layer is somewhat turbid treat with Celite and filter through filter paper. **POISONOUS.** 

Tetraphenylarsonium iodide [7422-32-4] M 510.2. Crystd from MeOH. POISONOUS.

**Tetraphenylarsonium perchlorate** [3084-10-4] **M 482.8, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>).** Crystd from MeOH. **POISONOUS.** 

Tetraphenylboron potassium [3244-41-5] M 358.2. See potassium tetraphenylborate on p. 458.

**Tetraphenylphosphonium chloride** [2001-45-8] **M 374.9, m 273-275°.** Crystd from acetone. Dried at 70° under vacuum. Also recrystd from a mixture of 1:1 or 1:2 dichloromethane/pet ether, the solvents having been dried over anhydrous  $K_2CO_3$ . The purified salt was dried at room temperature under vasuum for 3 days, and at 170° for a further 3 days. *Extremely hygroscopic.* 

Tetraphenylsilane [1048-08-4] M 336.4, m 231-233°. Crystd from \*benzene.

**Tetraphenyltin** [595-90-4] **M 427.1, m 224-225°, 226°.** Yellow crystals from CHCl<sub>3</sub>, pet ether (b 77-120°), xylene or \*benzene/cyclohexane, and dried at 75°/20mm. [J Am Chem Soc 74 531 1952.]

**Tetrapropylammonium perchlorate** [15780-02-6] **M 285.8, m 238-240°, pK<sup>25</sup> -2.4 to -3.1** (for HClO<sub>4</sub>). Purified by recrystns from H<sub>2</sub>O or MeCN/H<sub>2</sub>O (1:4.v/v), and dried in an oven at 60° for several days, or in vacuum over P<sub>2</sub>O<sub>5</sub> at 100°. [Z Phys Chem 165A 245 1933, 144 281 1929, 140 97 1929.]

**Tetra-***n***-propylammonium perruthenate (TPAP, tetrapropyl tetraoxoruthenate)** [114615-82-6] **M 351.4, m 160°(dec).** It is a strong oxidant and may explode on heating. It can be washed with aq *n*propanol, then H<sub>2</sub>O and dried over KOH in a vac. It is stable at room temp but best stored in a refrigerator. It is sol in CH<sub>2</sub>Cl<sub>2</sub> and MeCN. [Dengel et al. *Transition Met Chem* **10** 98 1985; Griffith et al. J Chem Soc, Chem Commun 1625 1987.] § Polymer supported reagent is available commercially.

**Tetrasodium pyrene-1,3,6,8-tetrasulfonate** [59572-10-0] **M 610.5.** Recrystd from aqueous acetone [Okahata et al. J Am Chem Soc 108 2863 1986].

**Thallium (I) acetate** [563-68-8] M 263.4, m 126-128°, 127°,  $pK^{25}$  13.2 (for Tl<sup>+</sup>). Likely impurity is H<sub>2</sub>O because the white solid is deliquescent. Dry in a vacuum over P<sub>2</sub>O<sub>5</sub> or for several days in a desiccator, and store in a well closed container. 7.5g dissolve in 100g of liquid SO<sub>2</sub> at 0°, and *ca* 2mol% in AcOH at 25°. **POISONOUS.** [*Trans Faraday Soc* 32 1660 1936; *J Am Chem Soc* 52 516.]

**Thallous bromide** [7789-40-4] **M 284.3, m 460°.** Thallous bromide (20g) was refluxed for 2-3h with water (200mL) containing 3mL of 47% HBr. It was then washed until acid-free, heated to 300° for 2-3h and stored in brown bottles. **POISONOUS.** 

Thallous carbonate [6533-73-9] M 468.7, m 268-270°. Crystd from hot water (4mL/g) by cooling. POISONOUS.

Thallous chlorate [13453-30-0] M 287.8, d 5.05. Crystd from hot water (2mL/g) by cooling. POISONOUS.

**Thallous chloride** [7791-12-0] **M 239.8, m 429.9°, d 7.0.** Crystd from 1% HCl and washed until acid-free, or crystd from hot water (50mL/g), then dried at 140° and stored in brown bottles. Also purified by subliming in vacuum, followed by treatment with dry HCl gas and filtering while molten. (Soluble in 260 parts of cold water and 70 parts of boiling water). **POISONOUS.** 

Thallous hydroxide [12026-06-1] M 221.4, m 139°(dec),  $pK^{25}$  13.2 (for Tl<sup>+</sup>). Crystd from hot water (0.6mL/g) by cooling. POISONOUS.

Thallous iodide [7790-30-9] M 331.3, m 441.8°, b 824°, d 7.1. Refluxed for 2-3h with water containing HI, then washed until acid-free, and dried at 120°. Stored in brown bottles. POISONOUS.

Thallous nitrate [10102-45-1] M 266.4, m 206°, b 450°(dec), d 5.55. Crystd from warm water (1mL/g) by cooling to 0°. POISONOUS.

Thallous perchlorate [13453-40-2] M 303.8, pK<sup>25</sup> -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from hot water (0.6mL/g) by cooling. Dried under vacuum for 12h at 100° (protect from possible EXPLOSION).

Thallous sulfate [7446-18-6] M 504.8, m 633°, d 6.77. Crystd from hot water (7mL/g) by cooling, then dried under vacuum over  $P_2O_5$ . POISONOUS.

Thexyl dimethyl chlorosilane (dimethyl-[2,3-dimethyl-2-butyl] chlorosilane) [67373-56-2] M 178.8, b 55-56°/10mm, 158-159°/720mm,  $d_4^{20}$  0.970,  $n_D^{20}$  1.428. Purified by fractional distillation and stored in small aliquots in sealed ampoules. It is very sensitive to moisture and is estimated by dissolving an aliquot in excess of 0.1M NaOH and titrating with 0.1M HCl using methyl red as indicator. [Helv Chim Acta 67 2128 1984].

*N*-(Thexyl dimethylsilyl)dimethylamine (*N*-[2,3-dimethyl-2-butyl]dimethylsilyl dimethylamine) [81484-86-8] M 187.4, b 156-160%/720mm. Dissolve in hexane, filter, evaporate and distil. Colourless oil extremely sensitive to humidity. It is best to store small quatities in sealed ampoules after distillation. For estimation of purity crush an ampoule in excess 0.1N HCl and titrate the excess acid with 0.1M NaOH using methyl red as indicator. [*Helv Chim Acta* 67 2128 1984.]

**Thionyl chloride** [7719-09-7] M **119.0, b 77°, d 1.636.** Crude SOCl<sub>2</sub> can be freed from sulfuryl chloride, sulfur monochloride and sulfur dichloride by refluxing with sulfur and then fractionally distilling twice. [The SOCl<sub>2</sub> is converted to SO<sub>2</sub> and sulfur chlorides. The  $S_2Cl_2$  (b 135.6°) is left in the residue, whereas SCl<sub>2</sub> (b 59°) passes over in the forerun]. The usual purification is to distil from quinoline (50g SOCl<sub>2</sub> to 10g quinoline) to remove acid impurities, followed by distillation from boiled linseed oil (50g SOCl<sub>2</sub> to 20g of oil). Precautions must be taken to exclude moisture.

Thionyl chloride for use in organic syntheses can be prepared by distillation of technical SOCl<sub>2</sub> in the presence of diterpene (12g/250mL SOCl<sub>2</sub>), avoiding overheating. Further purification is achieved by redistillation from linseed oil (1-2%) [Rigby Chem Ind (London) 1508 1969]. Gas chromatographically pure material is obtained by distillation from 10% (w/w) triphenyl phosphite [Friedman and Wetter J Chem Soc (A) 36 1967; Larsen et al. J Am Chem Soc 108 6950 1986]. Harmful vapours.

Thorium chloride [10026-08-1] M 373.8,  $pK_1^{25}$  10.45,  $pK_2^{25}$  10.62,  $pK_3^{25}$  10.80,  $pK_4^{25}$  11.64 (for aquo Th<sup>4+</sup>). Freed from anionic impurities by passing a 2M soln of ThCl<sub>4</sub> in 3M HCl through a Dowex-1 anion-resin column. The eluate was partially evaporated to give crystals which were filtered off, washed with Et<sub>2</sub>O and stored in a desiccator over H<sub>2</sub>SO<sub>4</sub> to dry. Alternatively, a saturated solution of ThCl<sub>4</sub> in 6M HCl was filtered through quartz wool and extracted twice with ethyl, or isopropyl, ether (to remove iron), then evaporated to a small volume on a hot plate. (Excess silica ppted, and was filtered off. The filtrate was cooled to 0° and saturated with dry HCl gas.) It was shaken with an equal volume of Et<sub>2</sub>O, agitating with HCl gas, until the mixture becomes homogeneous. On standing, ThCl<sub>4</sub>.8H<sub>2</sub>O ppted and was filtered off, washed with Et<sub>2</sub>O and dried [Kremer J Am Chem Soc 64 1009 1942].

Thorium sulfate (4H<sub>2</sub>O) [10381-37-0] M 496.2, m 42°(loses H<sub>2</sub>O), d 2.8. Crystd from water.

Tin (powder) [7440-31-5] M 118.7. The powder was added to about twice its weight of 10% aqueous NaOH and shaken vigorously for 10min. (This removed oxide film and stearic acid or similar material sometimes added for pulverisation.) It was then filtered, washed with water until the washings were no longer alkaline to litmus, rinsed with MeOH and air dried. [Sisido, Takeda and Kinugama J Am Chem Soc 83 538 1961.]

Tin tetramethyl [594-27-4] M 178.8, m 16.5°, b 78.3°/740mm. It is purified by fractionation using a Todd column of 35-40 plates at atmospheric pressure (p. 177). The purity of the fractions can be followed by IR [J Am Chem Soc 77 6486 1955]. It readily dissolves stopcock silicone greases which give bands in the 8-10µ region. [J Am Chem Soc 76 1169 1954.]

**Titanium tetrabromide** [7789-68-6] **M 367.5, m 28.3°, b 233.5°, d 3.3.** Purified by distn. Distillate forms light orange hygroscopic crystals. Store in the dark under  $N_2$  preferably in sealed brown glass ampules. [Olsen and Ryan J Am Chem Soc 54 2215 1932.]

Titanium tetrachloride [7550-45-0] M 189.7, b 136.4°, 154°, d 1.730,  $pK_1^{25}$  0.3,  $pK_2^{25}$  1.8,  $pK_3^{25}$  2.1,  $pK_4^{25}$  2.4 (for aquo Ti<sup>4+</sup> hydrolysis). Refluxed with mercury or a small amount of pure copper turnings to remove the last traces of light colour [due to FeCl<sub>3</sub> and VCl<sub>4</sub>], then distilled under N<sub>2</sub> in an all-glass system, taking precautions to exclude moisture. Clabaugh, Leslie and Gilchrist [*J Res Nat Bur Stand* 55 261 1955] removed organic material by adding aluminium chloride hexahydrate as a slurry with an equal amount of water (the slurry being *ca* one-fiftieth the weight of TiCl<sub>4</sub>), refluxing for 2-6h while bubbling in chlorine, which was subsequently removed by passing a stream of clean dry air. The TiCl<sub>4</sub> was then distilled, refluxed with copper and again distilled, taking precautions to exclude moisture. Volatile impurities were then removed using a technique of freezing, pumping and melting. [Baxter and Fertig *J Am Chem Soc* 45 1228 1923; Baxter and Butler *J Am Chem Soc* 48 3117 1926.] HARMFUL VAPOURS.

**Titanium trichloride** [7705-07-9] **M 154.3, m >500°, pK\_1^{25} 2.55 (for hydrolysis of Ti<sup>3+</sup> to TiOH<sup>2+</sup>)**. Brown purple powder that is very reactive with H<sub>2</sub>O and pyrophoric when dry. It should be manipulated in a dry box. It is soluble in CH<sub>2</sub>Cl<sub>2</sub> and tetrahydrofuran and is used as a M solution in these solvents in the ratio of 2:1, and stored under N<sub>2</sub>. It is a powerful reducing agent. [*Inorg Synth* 6 52 1960; Synthesis 833 1989.]

**Titanocene dichloride** [1271-19-8] **M 248.9, m 260-280°(dec), 289.2°, 298-291°, d 1.60.** Bright red crystals from toluene or xylene-CHCl<sub>3</sub> (1:1) and sublimes at 190°/2mm. It is moderately soluble in EtOH and insoluble in Et<sub>2</sub>O,  $*C_6H_6$ , CS<sub>2</sub>, CCl<sub>4</sub>, pet ether and H<sub>2</sub>O. [IR: *J Am Chem Soc* 76 4281 1954; NMR and X-ray: Can J Chem 51 2609 1973, 53 1622 1975.]

**Titanyl sulfate** (TiOSO<sub>4</sub>.2H<sub>2</sub>O) [13825-74-6] M 160.0. Dissolved in water, filtered and crystd three times from boiling 45% H<sub>2</sub>SO<sub>4</sub>, washing with EtOH to remove excess acid, then with Et<sub>2</sub>O. Air dried for several hours, then oven dried at 105-110°. [Hixson and Fredrickson *Ind Eng Chem* 37 678 1945.]

**Tribenzyl chlorosilane** [18740-59-5] M 336.9, m 139-142°, 141-142°, b 300-360°/100 mm. It is recrystd three times from pet ether; slender colourless needles, m 141°, sparingly soluble in pet ether and soluble in Et<sub>2</sub>O. Does not fume in air but is decomposed by H<sub>2</sub>O to give *tribenzyl silanol* m 106° (from pet ether). [J Chem Soc 93 439 1908; J Org Chem 15 556 1950.]

**Tribenzyl phosphine** [76650-89-7] **M 304.4, m 96-101°, b 203-210°/0.5mm, pK**<sub>Est</sub>~8.8. Dissolve in Et<sub>2</sub>O, dry over Na<sub>2</sub>SO<sub>4</sub>, evap and distil in an inert atmosphere. Distillate solidifies on cooling and is sublimed at 140°/0.001mm. This has m 92-95°(evacuated capillary). When air is bubbled through an Et<sub>2</sub>O solution, it is oxidised to *tribenzyl phosphine oxide*, m 209-212° (evacuated capillary) (from Me<sub>2</sub>CO). [J Chem Soc 2835 1959.]

**Tri-***n***-butyl borate** [688-74-4] **M 230.2, b 232.4°, n 1.4092, d 0.857.** The chief impurities are *n*-butyl alcohol and boric acid (from hydrolysis). It must be handled in a dry-box, and can readily be purified by fractional distillation, under reduced pressure.

**Tri-***n***-butyl chlorosilane** [995-45-9] **M 234.9, b 93-94°/4.5mm, 134-139°/16mm, 250-252°/atm, 142-144°/29mm, d\_4^{20} 0.88, n\_D^{20} 1.447. Fractionate and store in small aliquots in sealed ampoules. [***J Am Chem Soc* **74 1361 1952;** *J Org Chem* **24 219 1959.]** 

Tri-*n*-butyl phosphate (butyl phosphate) [126-73-8] M 266.3, m -80°, b 47°/0.45 mm, 98°/0.1mm, 121-124°/3mm, 136-137°/5.5mm, 166-167°/17mm, 177-178°/27 mm, 289°/760atm (some dec),  $d_4^{20}$  0.980,  $n_D^{20}$  1.44249. The main contaminants in commercial samples are organic pyrophosphates, mono- and di- butyl phosphates and butanol. It is purified by washing successively with 0.2M HNO<sub>3</sub> (three times), 0.2M NaOH (three times) and water (three times), then fractionally distilled under vacuum. [Yoshida J Inorg Nucl Chem 24 1257 1962.] It has also been purified via its uranyl nitrate addition compound, obtained by saturating the crude phosphate with uranyl nitrate. This compound was crystd three times with *n*-hexane by cooling to -40°, and then decomposed by washing with Na<sub>2</sub>CO<sub>3</sub> and water. Hexane was removed by steam distn and the water was then evaporated under reduced pressure and the residue was distilled under reduced pressure. [Siddall and Dukes J Am Chem Soc 81 790 1959.]

Alternatively wash with water, then with 1% NaOH or 5% Na<sub>2</sub>CO<sub>3</sub> for several hours, then finally with water. Dry under reduced pressure and fractionate carefully under vacuum. Stable colourless oil, sparingly soluble in H<sub>2</sub>O (1mL dissolves in 165mL of H<sub>2</sub>O), but freely miscible in organic solvents. [*J Am Chem Soc* 74 4953 1952, 80 5441 1958; <sup>31</sup>P NMR: *J Am Chem Soc* 78 5715 1956; *J Chem Soc* 1488 1957.]

Tri-*n*-butyl phosphine [998-40-3] M 202.3, b 109-110°/10mm, 115-116°/12mm, 149.5°/50mm, 240.4-242.2°/atm,  $d_4^{20}$  0.822,  $n_D^{20}$  1.4463, pK<sub>Est</sub>~7.6. Fractionally distilled under reduced pressure in an inert atm (N<sub>2</sub>) through an 8" gauze packed column (b 110-111°/10mm) and redistilled in a vacuum and sealed in thin glass ampoules. It is easily oxidised by air to *tri-n-butylphosphine oxide*, b 293-296°/745mm. It has a characteristic odour, it is soluble in EtOH, Et<sub>2</sub>O, and \*C<sub>6</sub>H<sub>6</sub> but insoluble in H<sub>2</sub>O and is less easily oxidised by air than the lower molecular weight phosphines. It forms complexes, e.g. with CS<sub>2</sub> (1:1) m 65.5° (from EtOH). [J Chem Soc 33 1929, 1401 1956.]

**Tri-***n***-butyl phosphite** [102-85-2] **M 250.3, b 114-115°/5mm, 122°/12mm, 130°/17mm, 137°/26mm, d\_4^{20}0.926, n\_D^{20} 1.4924. Fractionate with an efficient column. Stable in air but is slowly hydrolysed by H<sub>2</sub>O. [J Chem Soc 1464 1940, 1488 1957; J Am Chem Soc 80 2358, 2999 1958.]** 

**Tri-n-butyl tin chloride** [1461-22-9] M 325.5, b 98-100°/0.4mm, 140-152°/10 mm, 172°/25mm,  $d_4^{20}$  1.21,  $n_D^{20}$  1.492. Fractionate in an inert atmosphere, and seal in small aliquots in glass ampoules. Sensitive to moisture. [*J Chem Soc* 1446 1947; *J Appl Chem* 6 93 1956.]

Tributyl tin hydride [688-73-3] M 291.1, b 76°/0.7mm, 81°/0.9mm,  $d_4^{20}$  1.098,  $n_D^{20}$  1.473. Dissolve in Et<sub>2</sub>O, add quinol (500mg for 300mL), dry over Na<sub>2</sub>SO<sub>4</sub>, filter, evaporate and distil under dry N<sub>2</sub>. It is a clear liquid if dry and decompose very slowly. In the presence of H<sub>2</sub>O traces of tributyl tin hydroxide are formed in a few days. Store in sealed glass ampoules in small aliquots. It is estimated by reaction with aq NaOH when H<sub>2</sub> is liberated. CARE: stored samples may be under pressure due to liberated H<sub>2</sub>. [J Appl Chem 7 366 1957.]

B-Trichloroborazine [933-18-6] M 183.1, m 87°, b 88-92°/21mm. Purified by distillation from mineral oil.

**Trichloromethyl trimethylsilane** (trimethylsilyl trichloromethane) [5936-98-1] M 191.6, m 130-132°, b 146-156°/749mm. It distils at atmospheric pressure without decomposition and readily sublimes at 70°/10mm. It has one peak in the <sup>1</sup>H NMR spectrum (CH<sub>2</sub>Cl<sub>2</sub>)  $\delta$ : 0.38. [Synthesis 626 1980.]

Tricyclohexylphosphine [2622-14-2] M 280.4, m 82-83°, pK<sub>Est</sub>~9.5. Recrystd from EtOH [Boert et al. J Am Chem Soc 109 7781 1987].

Triethoxysilane [998-30-1] M 164.3, m -170°, b 131.2-131.8°/atm, 131.5°/760mm,  $d_4^{20}$  0.98753,  $n_D^{20}$  1.4377. Fractionated using a column packed with glass helices of *ca* 15 theoretical plates in

an inert atmosphere. Store in aliquots in sealed ampoules because it is sensitive to moisture. [J Am Chem Soc 72 1377, 2032 1950; J Org Chem 13 280 1948.]

Triethylborane [97-94-9] M 146.0, b 118.6°, n 1.378, d 0.678. Distilled at 56-57°/220mm.

Triethyl borate [150-46-9] M 146.0, b 118°, n 1.378, d 0.864. Dried with sodium, then distilled.

**Triethyl phosphate** [78-40-0] M 182.2, b 40-42°/0.25-0.3mm, 98-98.5°/8-10 mm, 90°/10mm, 130°/55mm, 204°/680mm, 215-216°/760mm,  $d_4^{25}$  1.608,  $n_D^{20}$  1.4053. Dried by refluxing with solid BaO and fractionally distilled under reduced pressure. It is kept with Na and distilled. Stored in the receiver protected from light and moisture. Alternatively it is dried over Na<sub>2</sub>SO<sub>4</sub> and distilled under reduced pressure. The middle fraction is stirred for several weeks over anhydrous Na<sub>2</sub>SO<sub>4</sub> and again fractionated under reduced pressure until the specific conductance reached a constant low value of  $\kappa^{25}$  1.19 x  $10^8$ ,  $\kappa^{40}$  1.68 x  $10^8$ , and  $\kappa^{55}$  2.89 x  $10^8$  ohm<sup>-1</sup> cm<sup>-1</sup>. It has also been fractionated carefully under reduced pressure through a glass helices packed column. It is soluble in EtOH, Et<sub>2</sub>O and H<sub>2</sub>O (dec). [J Am Chem Soc 77 4767 1955, 78 6413, 3557 (P NMR) 1956; J Chem Soc 3582 1959, IR: J Chem Soc 475 1952 and Can J Chem 36 820 1958; Kosolapoff Organophosphorus Compounds, Wiley p. 258 1950.]

Triethylphosphine [554-70-1] M 118.2, b 100°/7mm, 127-128°/744mm,  $d_4^{15}$  0.812,  $n_D^{18}$  1.457, pK<sup>25</sup> 8.69 (also available as a 1.0M soln in THF). All operations should be carried out in an efficient fume cupboard because it is flammable, toxic and has a foul odour. Purified by fractional distn at atm pressure in a stream of dry N<sub>2</sub>, as it is oxidised by air to the oxide. In 300% excess of CS<sub>2</sub> it forms Et<sub>3</sub>PCS<sub>2</sub> (m 118-120° cryst from MeOH) which decomposes in CCl<sub>4</sub> to give Et<sub>3</sub>PS as a white solid m 94° when recryst from EtOH. [Sorettas and Isbell J Org Chem 27 273 1962; J Am Chem Soc 82 5791 1960; pK: Henderson and Streuli J Am Chem Soc 82 5791 1960; see also trimethylphosphine.] Store in a sealed vial under N<sub>2</sub>.

Alternatively, dissolve in  $Et_2O$  and shake with a solution of AgI and KI to form the insoluble complex. Filter off the complex, dry over  $P_2O_5$  and the  $Et_3P$  is regenerated by heating the complex in a tube attached to a vacuum system. [J Chem Soc 530 1953, 1828 1937; J Org Chem 27 2573 1962; Kosolapoff Organophosphorus Compounds, Wiley p. 31 1950.]

**Triethyl phosphite** [122-52-1] M 166.2, b 48-49°/11mm, b 52°/12mm, 57.5°/19mm, 157.9°/757mm,  $d_4^{20}$  0.9687,  $n_D^{20}$  1.4135. Treat with Na (to remove water and any dialkyl phosphonate), then decant and distil under reduced pressure, with protection against moisture or distil in vacuum through an efficient Vigreux column or a column packed with Penn State 0.16 x 0.16 in protruded nickel packing and a variable volume take-off head. [Org Synth Coll Vol IV 955 1963; J Am Chem Soc 78 5817 1956, 80 2999 1958; Kosolapoff Organophosphorus Compounds, Wiley p. 203 1950.]

Triethyl phosphonoacetate (triethyl carboxymethyl phosphonate) [867-13-0] M 224.2, b 83-84°/0.5mm, 103°/1.2mm, 143-144°/11mm, 260-262°/atm,  $d_4^{20}$  1.1215,  $n_D^{20}$  1,4310. Purified by fractional distn, preferably *in vacuo*. <sup>31</sup>P NMR has P resonance at 19.5 relative to orthophosphate. [Kosolapoff and Powell J Am Chem Soc 68 1103 1946; 72 4198 1950; Speziale and Freeman J Org Chem 23 1586 1958.]

Triethyl phosphonoformate [1474-78-8] M 210.2, b 70-72°/0.1mm, 122.5-123°/8mm, 130-131°/10mm, 138.2°/12.5mm,  $d_4^{20}$  1.22,  $n_D^{20}$  1.423. Dissolve in Et<sub>2</sub>O, shake with H<sub>2</sub>O (to remove any trace of NaCl impurity), dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and distil using an efficient fractionating column. [*Chem Ber* 57 1035 1924.]

**Triethyl 2-phosphonopropionate** [3699-66-9] **M 238.2, b 76-77°/0.2mm, 137-138.5°/17mm,**  $d_0^{20}$  **1.096,**  $n_D^{20}$  **1.432.** Purified by fractional distillation with high reflux ratio, preferably using a spinning band column. [*J Am Chem Soc* 4198 1950.]

## Purification of Inorganic and Metal-Organic Chemicals

Triethylsilane [617-86-7] M 116.3, b 105-107°, 107-108°, d 0.734. n 1.414. Refluxed over molecular sieves, then distilled. It was passed through neutral alumina before use [Randolph and Wrighton J Am Chem Soc 108 3366 1986].

Triethylsilyl-1,4-pentadiene (1,4-pentadien-3-yloxy-trimethylsilane) [62418-65-9] M 198.4, b 72-74°/12mm,  $d_4^{20}$  0.842,  $n_D^{20}$  1.439. Dissolve in pentane, wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate, and distil under vacuum. R<sub>F</sub> values on Kieselgel 60 are 0.15 (pentane) and 0.60 (\*C<sub>6</sub>H<sub>6</sub>). [IR, NMR, MS: *Helv Chim Acta* 64 2002 1981.]

Triethyltin hydroxide [994-32-1] M 222.9. Treated with HCl, followed by KOH, and filtered to remove diethyltin oxide [Prince J Chem Soc 1783 1959].

**Tri-n-hexylborane** [1188-92-7] **M 265.3.** Treated with hex-1-ene and 10% anhydrous  $Et_2O$  for 6h at gentle reflux under N<sub>2</sub>, then vacuum distilled through an 18in glass helices-packed column under N<sub>2</sub> taking the fraction **b** 130°/2.1mm to 137°/1.5mm. The distillate still contained some di-*n*-hexylborane [Mirviss J Am Chem Soc 83 3051 1961].

**Triiron dodecacarbonyl** [17685-52-8] **M 503.7, m 140°(dec).** It usually contains 10% by weight of MeOH as stabiliser. This can be removed by keeping in a vacuum at 0.5mm for at least 5h. It can be sublimed slowly at high vacuum and is soluble in organic solvents. [J Org Chem 37 930 1972, J Chem Soc 4632 1960; Inorg Synth 7 193 1963.]

Triisoamyl phosphate [919-62-0] M 308.4, b 143°/3mm. Purified by repeated crystallisation, from hexane, of its addition compound with uranyl nitrate. (see *tributyl phosphate*.) [Siddall J Am Chem Soc 81 4176 1959].

Triisobutyl phosphate [126-71-6] M 266.3, b 119-129°/8-12mm, 192°/760mm, d 0.962, n 1.421. Purified by repeated crystallisation, from hexane, of its addition compound with uranyl nitrate. (see tributyl phosphate.) [Siddall J Am Chem Soc 81 4176 1959.]

**Triisooctyl thiophosphate** [30108-39-5] **M 450.6.** Purified by passage of its solution in CCl<sub>4</sub> through a column of activated alumina.

**Triisopropyl phosphite** [116-17-6] **M 208.2, b 58-59°/7mm, n<sup>25</sup> 1.4082.** Distilled from sodium, under vacuum, through a column with glass helices. (This removes any dialkyl phosphonate).

Trimesitylphosphine [23897-15-6] M 388.5, m 205-206°, pK<sub>Est</sub>~8.0. Recrystd from EtOH [Boert et al. J Am Chem Soc 109 7781 1987].

Trimethallyl phosphate [14019-81-9] M 260.3, b 134.5-140°/5mm, n<sup>25</sup> 1.4454. Purified as for triisoamyl phosphate.

Trimethoxysilane [2487-90-3] M 122.2, m -114.8°, 81.1°/760mm, 84°/atm,  $d_4^{20}$  0.957,  $n_D^{20}$  1.359. Likely impurities are Si(OMe)<sub>4</sub> and H<sub>2</sub>Si(OMe)<sub>2</sub>. Efficient fractionation is essential for removing these impurities [IR: J Am Chem Soc 81 5109 1959].

Trimethyl borate (methylborate, trimethoxyboron) [121-43-7] M 103.9, b 67-68°/742mm,  $d_4^{20}$  0.928,  $n_D^{20}$  1.3610. Carefully fractionated through a gauze-packed column. Redistil and collect in weighed glass vials and seal. Keep away from moisture. It undergoes alkyl exchange with alcohols and forms azeotropes, e.g. with MeOH the azeotrope consists of 70% (MeO)<sub>3</sub>B and 30% MeOH with b 52-54°/atm, d 0.87. [J Chem Soc 2288 1952; Chem Ind (London) 53 1952; J Am Chem Soc 75 213 1953.] Also dried with Na, then distilled.

**Trimethyl boroxine** [823-96-1] M 125.5, b 80°/742mm, 79.3°/755mm,  $d_4^{20}$  0.902. Possible impurity is methylboronic acid. If present then add a few drops of conc H<sub>2</sub>SO<sub>4</sub> and distil immediately, then

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fractionate through an efficient column. [J Am Chem Soc 79 5179 1957; IR: Z Anorg Chem 272 303 1953.]

**Trimethyl chlorosilane (chlorotrimethylsilane)** [75-77-4] M 108.6, b 56-57°/atm, 58°/760mm, d 0.86, n 1.388. Likely impurities are other chlorinated methylsilanes, and tetrachlorosilane (b 57.6°), some of which can form azeotropes. To avoid the latter very efficient fractional distillation is required. It has been fractionated through a 12 plate glass helices packed column with only the heart-cut material used. It has also been fractionated through a 90cm, 19mm diameter Stedman column (see p. 441). Also purified by redistilling from CaH<sub>2</sub> before use. [J Am Chem Soc 70, 4254, 4258 1948; J Org Chem 23 50 1958.] FLAMMABLE and CORROSIVE.

**Trimethyloxonium tetrafluoroborate** [420-37-1] **M 147.9, m 141-143**°(sinters, open capillary), 179.6-180.0°(dec), 210-220°(dec). The salt must be a white crystalline solid  $\mathbf{m} \sim 179.6-180.0°$  (dec, sealed tube). Under a N<sub>2</sub> atmosphere (e.g. Dry Box), wash twice with CH<sub>2</sub>Cl<sub>2</sub> then twice with Nadried Et<sub>2</sub>O, and dry by passing dry N<sub>2</sub> over the salt until free from Et<sub>2</sub>O [Curphey Org Synth Coll Vol VI 1019 1988]. The oxonium salt purified in this way can be handled in air for short periods. The sample kept in a desiccator (Drierite) for 1 month at -20° had the same  $\mathbf{m}$ , and samples stored in this way for >1 year are satisfactory for alkylations. <sup>1</sup>H NMR in liq SO<sub>2</sub> in a sealed tube had a single peak at  $\delta 4.54$  (impurities have  $\delta$  at 3.39). [Meerwein Org Synth Coll Vol V 1096 1973.] If the sample looks good, dry in a vac desiccator for 2h (25°/1mm) and stored under N<sub>2</sub> at -20°. Melting point depends on heating rate.

**Trimethylphenylsilane** (phenyltrimethylsilane) [768-32-1] M 150.3, b 67.3°/20 mm, 170.6°/738mm,  $d_4^{25}$  0.8646, n 1.491. Fractionally distd at atm or reduced pressure (Podbielniak column, p.141) and estimated by GC with a column packed with Silicone Fluid No 710 on Chromosorb P support. [Gilman et al. J Org Chem 18 1743 1953; Maienthal et al. J Am Chem Soc 76 6392 1954; House and Respess J Organomet Chem 4 95 1965; J Am Chem Soc 71 2923 1949, 73 4770 1951, 75 2821 1953]

**Trimethyl phosphate** [5/2-56-1] **M 140.1, b 77°/12mm, 94°/22mm, 110°/60mm, 197.2°/atm, d\_4^{20} 1.0213, n\_D^{20} 1.3961**. Purified by fractionation through and efficient column at high reflux ratio. It is quite soluble in H<sub>2</sub>O, solubility is 1:1 at 25°. [*J Am Chem Soc* 74 2923 1952; IR: *J Chem Soc* 847 1952; Can J Chem 36 820 1958; Kosolapoff Organophosphorus Compounds, Wiley p. 258 1950.]

Trimethylphosphine [594-02-2] M 76.1, m -86°, b 38-39°/atm, pK<sup>25</sup> 8.65, (also available as a 1.0M soln in THF or toluene). All operations should be carried out in an efficient fume cupboard because it is flammable, toxic and has a foul odor. Distd at atm pressure in a stream of dry  $N_2$  (apparatus should be held together with springs to avoid loss of gas from increased pressure in the system) and the distillate run into a soln of AgI in aq KI whereby the complex [Me<sub>3</sub>PAgI]<sub>4</sub> separates steadily. Filter off the complex, wash with satd aq KI soln, then  $H_2O$  and dry in a vac desiccator over  $P_2O_5$ . The dry complex is heated in a flask (in a stream of dry  $N_2$ ) in an oil bath at 140°, when pure Me<sub>3</sub>P distils off (bath temp can be raised up to 260°). The vapour pressure of Me<sub>3</sub>P at 20° is 466mm and the **b** is 37.8° [Thomas and Eriks Inorg Synth 9 59 1967]. Alternatively, freshly distilled Me<sub>3</sub>P (6g) is shaken with a solution of AgI (13.2g, 1.1mol) in saturated aqueous KI solution (50mL) for 2h. A white solid, not wetted with H<sub>2</sub>O, separates rapidly. It is collected, washed with the KI solution, H<sub>2</sub>O, and dried [J Chem Soc 1829 1937]. The silver complex is stable if kept dry in the dark in which state it can be kept indefinitely.  $Me_3P$  can be generated from the complex when required. Store under  $N_2$  in a sealed container. It has been distd in a vacuum line at -78° in vacuo and condensed at -96° [IR and NMR: Crosbie and Sheldrick J Inorg Nucl Chem 31 3684 1969]. The pK<sup>22</sup> by NMR was 8.80 [Silver and Lutz J Am Chem Soc 83 786 1961; pK 8.65: Henderson and Strueuli J Am Chem Soc 82 5791 1960].

 $[Me_2PAgI]_4$  [12389-34-3] complex is a flammable solid which has m 140-142°. It is decomposed by heating gently in one arm of an inverted U tube. The other arm is kept in a freezing mixture. The complex dissociates and pure Me<sub>3</sub>P collects in the cold arm and is used at once. It should not be allowed to come in contact with air [*J Chem Soc* 708 1938]. The CS<sub>2</sub> complex has m 119° (cryst from 95% EtOH) and decomposes in CCl<sub>4</sub> to give Me<sub>3</sub>PS m 154° (from EtOH) [Sorettas and Isbell *J Org Chem* 27 273 1962].

Triphenylphosphine hydrochloride is unstable and volatilises at 75°/0.4mm (120°/14mm). [J Am Chem Soc 67 503 1945; IR: Trans Faraday Soc 40 41 1944; Kosolapoff Organophosphorus Compounds, Wiley p. 31 1950.]

**Trimethyl phosphite** [121-45-9] M 124.1, b 22°/23mm, 86-86.5°/351mm, 111-112°/760mm, 111°/atm,  $d_4^{20}$  1.0495,  $n_D^{20}$  1.408. Treated with Na (to remove water and any dialkyl phosphonate), then decanted and distilled with protection against moisture. It has also been treated with sodium wire for 24h, then distilled in an inert atmosphere onto activated molecular sieves [Connor et al. J Chem Soc, Dalton Trans 511 1986]. It has also been fractionally distilled using a spinning band column at high reflux ratio. It is a colourless liquid which is slowly hydrolysed by H<sub>2</sub>O. [J Am Chem Soc 80 2999 1958; IR: J Chem Soc 255 1950, P NMR: J Am Chem Soc 79 2719 1957; Kosolapoff Organophosphorus Compounds, , Wiley p. 203 1950.]

Trimethylsilyl acetamide [13435-12-6] M 131.3, m 38-43°, 52-54°, b 84°/13mm, 185-186°/atm. Repeated distillation in an inert atmosphere, all operations to be performed under anhydrous atmosphere. In the presence of moisture trimethylsilanol (b 31-34°/26mm) is formed and is a likely impurity (check by NMR). [Chem Ber 96 1473 1963.]

**Trimethylsilyl acetonitrile** (TMSAN) [18293-53-3] M 113.2, b 49-51°/10mm, 65-70°/20mm,  $d_4^{20}$  0.8729,  $n_D^{20}$  1.4420. Check if NMR and IR spectra are correct, if not dissolve in \*C<sub>6</sub>H<sub>6</sub> (10vols), wash with buffer (AcOH-AcONa pH *ca* 7) several times, dry (CaCl<sub>2</sub>), evaporate and distil. IR: v (CCl<sub>4</sub>) 2215 (CN) cm<sup>-1</sup>; NMR  $\delta$  (CCl<sub>4</sub>): 0.23 (s, 9H, SiMe<sub>3</sub>), and 1.53 (s, 2H, CH<sub>2</sub>CN). [J Chem Soc Perkin Trans 1 26 1979.]

**Trimethylsilyl azide** [4648-54-8] M 115.2, b 92-95°/atm, 95-99°/atm,  $d_4^{20}$  0.878,  $n_D^{20}$  1.441. Distil through a Vigreux column in a N<sub>2</sub> atmosphere maintaining the oil bath temperature thermostated at 135-140°. Check the purity by <sup>1</sup>H NMR [CHCl<sub>3</sub>,  $\delta$ : single peak at 13cps from Me<sub>4</sub>Si. Likely impurities are siloxane hydrolysis products. The azide is thermally stable even at 200° when it decomposes slowly without explosive violence. All the same it is advisable to carry out the distillation behind a thick safety screen in a fumehood because unforseen **EXPLOSIVE** azides may be formed on long standing. [Birkofer and Wagner Org Synth Coll Vol VI 1030 1988.]

**Trimethylsilyl chloroacetate** [18293-71-5] **M 166.7, m -20°, b 57-58°/14mm, 70-71°/ 30mm, 159°/760mm, d\_4^{20} 1.057, n\_D^{20} 11.4231.** Purified by repeated fractionation and taking the fractions with clean NMR spectra. [J Am Chem Soc 2371 1952.]

**Trimethylsilyl cyanide** [7677-24-9] **M 99.2, m 8-11°, 10.5-11.5°, 11-12°, 12-12.5°; b 54-55°/87mm, 67-71°/168mm, 114-117°/760mm, 118-119°/760mm, d\_4^{20} 0.79 n\_D^{20} 1.43916. Material should have only one sharp signal in the <sup>1</sup>H NMR (in CCl<sub>4</sub> with CHCl<sub>3</sub> as internal standard) \delta: 0.4 and IR with v at 2210cm<sup>-1</sup> [J Am Chem Soc 74 5247 1952, 77 3224 1955]; otherwise purify by fractionating through an 18 x 1/4 in column. [J Am Chem Soc 81 4493 1959.] It has also been carefully distilled using a 60cm vac jacketed column. If volume of sample is small the cyanide can be chased (in the distillation) with xylene that had be previously distilled over P<sub>2</sub>O<sub>5</sub>. [J Org Chem 39 914 1974.]** 

2-Trimethylsilyl-1,3-dithiane [13411-42-2] M 192.2, b 54.5°/0.17mm, 100°/8mm,  $d_4^{20}$  1.04,  $n_D^{20}$  1.533. Fractionally distil through an efficient column and collect the fractions that have the correct NMR and IR spectra. <sup>1</sup>H NMR (CCl<sub>4</sub>)  $\tau$  6.36 (SiMe<sub>3</sub>), 9.87 (SCHS) and dithiane H at 7 and 8 (ratio 1:9:4:2) from Me<sub>4</sub>Si; UV  $\lambda_{max}$  244nm ( $\epsilon$  711); sh 227nm ( $\epsilon$  800). [J Am Chem Soc 89 434 1967.]

Trimethylsilyl ethanol [2916-68-9] M 118.3, b 53-55°/11mm, 75°/41mm, 95°/100mm,  $d_4^{25}$  0.8254,  $n_D^{25}$  1.4220. If the NMR spectrum is not clean then dissolve in Et<sub>2</sub>O, wash with aqueous NH<sub>4</sub>Cl solution, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and distil. The 3,4-dinitrobenzoyl deriv has m 66° (from EtOH). [NMR: J Am Chem Soc 79 974 1957; Z Naturforsch 14b 137 1959.]

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**2-(Trimethylsilyl)ethoxymethyl chloride (SEMCl)** [76513-69-4] **M 166.7, b 57-59°/8mm, d 0.942, n 1.4350.** Dissolve in pentane, dry (MgSO<sub>4</sub>), evaporate and dist residual oil in a vac. Stabilise with 10ppm of diisopropylamine. Store under N<sub>2</sub> in a sealed container in a refrigerator. [Lipshutz and Pegram Tetrahedron Lett **21** 3343 1980.]

**2-(Trimethylsilyl)ethoxymethyltrimethylphosphonium chloride** [82495-75-8] M **429.0, m 140-142°.** Wash the solid with AcOH and recryst from CH<sub>2</sub>Cl<sub>2</sub>-EtOAc. Dry in a vacuum desiccator. *Hygroscopic.* <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : -0.2 (s, Me<sub>3</sub>Si), 0.8 (t, 8Hz, CH<sub>2</sub>Si), 3.83 (t, 8Hz, OCH<sub>2</sub>), 5.77 (d, J<sub>PH</sub> 4Hz, P<sup>+</sup>-CH<sub>2</sub>O) and 7.70 (m, aromatic H). [Justus Liebigs Ann Chem 1031 1983.]

**Trimethylsilylethyl phenylsulfone** (phenyl-2-trimethylsilylethylsulfone) [73476-18-3] M 242.4, m 52°. Dissolve in Et<sub>2</sub>O, wash with saturated HCO<sub>3</sub>, saturated NaCl, H<sub>2</sub>O and dried (MgSO<sub>4</sub>). Evaporation leaves residual crystals m 52°. [Tetrahedron Lett 23 1963 1982, J Org Chem 53 2688 1985.]

1-Trimethylsilyloxy-1,3-butadiene [6651-43-0] M 142.3, b 131°/760mm (mixt of isomers), 49.5°/25mm (E-isomer), d 0.8237, n 1.447. Purified by fractional distn and collecting the fractions with the required <sup>1</sup>H NMR. Store under N<sub>2</sub> — it is a flammable and moisture sensitive liquid. [Caseau et al. Bull Soc Chim Fr 16658 1972; Belge Patent 670,769, Chem Abstr 65 5487d 1966.]

1-(Trimethylsilyloxy)cyclopentene [19980-43-9] M 156.3, b 45°/11mm, 75-80°/20-21mm,  $d_4^{20}$  0.878,  $n_D^{20}$  1.441. If too impure as seen by the NMR spectrum then dissolve in 10 vols of pentane, shake with cold NaHCO<sub>3</sub>(3 x 500mL), then 1.5M HCl (200mL) and aqueous NaHCO<sub>3</sub> (200mL) again, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate and distil through a short Vigreux column. <sup>1</sup>H NMR: (CDCl<sub>3</sub>)  $\delta$ : 0.21 (s, 9H), 1.55 (m, 2H), 1.69 (m, 2H), 2.05 (br d, 4H) and 4.88 (br s, 1H). GLPC in a 6ft x 1/8in with 3% SP2100 on 100-120 mesh Supelcoport column should give one peak. [Org Synth Coll Vol VIII 460 1993.]

**2-(Trimethylsilyloxy)furan** [61550-02-5] **M 156.3, b 34-35°/9-10mm, 42-50°/17mm, 40-42°/25mm, d\_4^{20} 0.950, n\_D^{20} 1.436. Fractionally distilled using a short path column. <sup>1</sup>H NMR in CCl<sub>4</sub> has \delta: 4.90 (dd, J 1.3Hz, 3H), 6.00 (t, J 3Hz, 4H) and 6.60 (m, 5H). [Heterocycles 4 1663 1976.]** 

4-Trimethylsilyloxy-3-penten-2-one (cis) (acetylacetone enol trimethylsilyl ether) [13257-81-3] M 172.3, b 66-68°/4mm, 61-63°/5mm,  $d_4^{20}$  0.917,  $n_D^{20}$  1.452. Fractionally distilled and stored in glass ampoules which are sealed under N<sub>2</sub>. It hydrolyses readily in contact with moisture giving, as likely impurities, hexamethyldisiloxane and 2,4-pentanedione. [J Am Chem Soc 80 3246 1958.]

Trimethylsilyl isocyanate [1118-02-1] M 115.2, b 90-92°/atm, b 91.3-91.6°/atm,  $d_4^{20}$  0.850 n  $_D^{20}$  1.43943. Purified by repeated fractionation as for the isothiocyanate. [J Chem Soc 3077 1950.]

**Trimethylsilyl** isothiocyanate [2290-65-5] M 131.3, m -33°, b 142.6-143.1°/759 mm, 143.8°/760mm,  $n_D^{20}$  1.4809. The <sup>1</sup>H NMR spectrum should have only one peak, if not purify by repeated fractionation in an all glass system using a 50cm (4mm internal diameter) column without packing. [J Am Chem Soc 69 3049 1947; Chem Ber 90 1934 1957; Synthesis 51 1975.]

(Trimethylsilyl)methanol [3219-63-4] M 104.2, b 120-122°/754mm, 122-123°/768mm,  $d_4^{20}$  0.83  $n_D^{20}$  1.4176. If the NMR indicates impurities (should have only two signals) then dissolve in Et<sub>2</sub>O, shake with aqueous 5N NaOH, M H<sub>2</sub>SO<sub>4</sub>, saturated aqueous NaCl, dry (MgSO<sub>4</sub>) and distil using an efficient column at atmospheric pressure. The 3,5-dinitrobenzoate has m 70-70.5° (from 95% EtOH). [Huang and Wang Acta Chem Sin 23 291 1957, Chem Abs 52 19911 1958; Speier et al. J Am Chem Soc 81 1844 1959 and J Am Chem Soc 70 1117 1949.]

(Trimethylsilyl)methylamine (aminomethyl trimethylsilane) [18166-02-4] M 103.2, b 101.6°/735mm,  $d_4^{20}$  0.77,  $n_D^{20}$  1.416. A possible contaminant is hexamethyldisiloxane. Should have two <sup>1</sup>H NMR signals in CDCl<sub>3</sub>, if not, dissolve in <sup>\*</sup>C<sub>6</sub>H<sub>6</sub>, shake with 15% aq KOH, separate, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate and distil using a still of *ca* 10 theoretical plates. The water azeotrope has b 83°/735mm,

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hence it is important to dry the extract well. The hydrochloride has **m** 198/199<sup>o</sup> (from MeOH or Me<sub>2</sub>CO). [J Am Chem Soc **73** 3867 1951; NMR, IR: J Organometal Chem **44** 279 1972.]

**Trimethylsilylmethyl phenylsulfone** (phenyltrimethylsilylmethylsulfone) [17872-92-3] M 228.4, m 28-32°, b 121°/0.01mm, 160°/6mm,  $n_D^{20}$ 1.5250. Fractionate at high vacuum and recrystallise from pentane at -80°. If too impure (cf IR) dissolve in CH<sub>2</sub>Cl<sub>2</sub> (ca 800mL for 100g), wash with 2M aqueous NaOH (2 x 200mL), brine, dry, evaporate and distil. [J Chem Soc, Perkin Trans 1 1949 1985; IR and NMR: J Am Chem Soc 76 3713 1954.]

1-(Trimethylsilyl)-2-phenylacetylene (1-phenyl-2-trimethylsilylacetylene) [78905-09-6] M 174.3, b 45-46°/0.1mm, 67°/5mm, 87.5°/9mm, d 0.8961 n 1.5284. Dissolve in  $Et_2O$ , wash with H<sub>2</sub>O, dry and fractionate through a Todd column (see p. 174). [J.Am Chem Soc 80 5298 1958.]

3-(Trimethylsilyl)propyne [13361-64-3] M 112.3, b 99-100°/760mm, d 0.7581, n1.4091. Fractionally distilled and 0.5% of 2,6-di-*tert*-butyl-p-cresol added to stabilise it. [Doklady Acad Nauk USSR 93 293 1953; Chem Abs 48 13616 1954.]

1-Trimethylsilyl-1,2,4-triazole [18293-54-4] M 141.3, b 74°/12mm,  $d_4^{20}$  0.99,  $n_D^{20}$  1.4604. Fractionally distilled at atmospheric pressure in an inert atmosphere because it is moisture sensitive. [Chem Ber 93 2804 1960.]

Trimethylsilyl trifluoromethane (trifluoromethyl trimethylsilane) [81290-20-2] M 142.2, b 54-55°, 55-55.5°,  $d_4^{20}$  0.962,  $n_D^{20}$  1.332. Purified by distilling from trap to trap in a vacuum of 20mm using a bath at 45° and Dry ice-Me<sub>2</sub>CO bath for the trap. The liquid in the trap is then washed with ice cold H<sub>2</sub>O (3x), the top layer is collected, dried (Na<sub>2</sub>SO<sub>4</sub>), the liquid was decanted and fractionated through a helices packed column at atmospheric pressure. <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F, and <sup>29</sup>Si NMR can be used for assessing the purity of fractions. [*Tetrahedron Lett* 25 2195 1984; J Org Chem 56 984 1991.]

**Trimethyl vinyl silane** [754-05-2] M 100.2, b 54.4°/744mm, 55.5°/767mm, d(25,4) 0.6865,  $n_D^{25}$  1.3880. If the <sup>1</sup>H NMR spectrum shows impurities then dissolve in Et<sub>2</sub>O, wash with aq NH<sub>4</sub>Cl soln, dry over CaCl<sub>2</sub>, filter, evaporate and distil at atmospheric pressure in an inert atmosphere. It is used as a copolymer and may polymerise in the presence of free radicals. It is soluble in CH<sub>2</sub>Cl<sub>2</sub>. [J Org Chem 17 1379 1952.]

Trineopentyl phosphate [14540-59-1] M 320.4. Crystd from hexane.

**Tri-(4-nitrophenyl)phosphate** [3871-20-3] **M 461.3, m 155-156°, 156°, 156-158°, 157-159°**. It has been recrystd from AcOH, dioxane, AcOEt and Me<sub>2</sub>CO and dried in vacuum over  $P_2O_5$ . [J Am Chem Soc 72 5777 1950, 79 3741 1957.]

**Tri-n-octylphosphine oxide** [78-50-2] **M 386.7, m 59.5-60°, pK**<sub>Est</sub> <0. Mason, McCarty and Peppard [J Inorg Nuclear Chem 24 967 1962] stirred an 0.1M solution in \*benzene with an equal volume of 6M HCl at 40° in a sealed flask for 48h, then washed the \*benzene solution successively with water (twice), 5% aq Na<sub>2</sub>CO<sub>3</sub> (three times) and water (six times). The \*benzene and water were then evaporated under reduced pressure at room temperature. Zingaro and White [J Inorg Nucl Chem 12 315 1960] treated a pet ether solution with aqueous KMnO<sub>4</sub> (to oxidise any phosphinous acids to phosphinic acids), then with sodium oxalate, H<sub>2</sub>SO<sub>4</sub> and HCl (to remove any manganese compounds). The pet ether solution was slurried with activated alumina (to remove phosphinic acids) and recrystd from pet ether or cyclohexane at -20°. It can also be crystd from EtOH.

Triphenylantimony [603-36-1] M 353.1, m 52-54°. Recrystd from acetonitrile [Hayes et al. J Am Chem Soc 107 1346 1985].

Triphenylarsine [603-32-7] M 306.2, m 60-62°. Recrystd from EtOH or aqueous EtOH [Dahlinger et al. J Chem Soc, Dalton Trans 2145 1986; Boert et al. J Am Chem Soc 109 7781 1987].

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**Triphenylbismuth** (bismuth triphenyl) [603-33-8] M 440.3, m 75-76°, 77-78°, 78.5°,  $d_4^{98.5}$  1.6427(melt). Dissolve in EtOH, ppte with H<sub>2</sub>O, extract with Et<sub>2</sub>O, dry and evaporate when the residue crystallises. It has been recrystd from EtOH and Et<sub>2</sub>O-EtOH and is a stable compound. [J Chem Soc suppl p121 1949; Chem Ber 37 4620 1904; J Am Chem Soc 62 665 1940; UV: J Chem Phys 22 1430 1954.]

Triphenyl borane (borane triphenyl) [960-71-4] M 242.1, m 134-140°, 137°, 139-141°, 142-142.5°, 147.5-148°, 151°, b 203°/15mm. Recryst three times from  $Et_2O$  or  $C_6H_6$  under  $N_2$  and dry at 130°. It can be distilled in a high vacuum at 300-350°, and has been distilled (b 195-215°) in vacuum using a bath temp of 240-330°.  $N_2$  was introduced into the apparatus before dismantling. It forms complexes with amines. [Chem Ind (London) 1069 1957; Justus Liebigs Ann Chem 563 110 1949; J Am Chem Soc 57 1259 1935.]

Triphenylchlorostannane (triphenyltin chloride) [639-58-7] M 385.5, m 103-106°(dec). See triphenyltin chloride on p. 494.

Triphenyl phosphate [115-86-6] M 326.3, m 49.5-50°, b 245°/0.1mm. Crystd from EtOH.

**Triphenylphosphine** [603-35-0] M 262.3, m 77-78°, 79°, 79-81°, 80.5°, 80-81°, b >360°(in inert gas),  $d_4^{25}$  1.194,  $d_4^{80}$  1.075 (liq), pK 2.73. Crystd from hexane, MeOH, diethyl ether, CH<sub>2</sub>Cl<sub>2</sub>/hexane or 95% EtOH. Dried at 65°/<1mm over CaSO<sub>4</sub> or P<sub>2</sub>O<sub>5</sub>. Chromatographed through alumina using (4:1) \*benzene/CHCl<sub>3</sub> as eluent. [Blau and Espenson et al. J Am Chem Soc 108 1962 1986; Buchanan et al. J Am Chem Soc 108 1537 1986; Randolph and Wrighton J Am Chem Soc 108 3366 1986; Asali et al. J Am Chem Soc 109 5386 1987.] It has also been crystd twice from pet ether and 5 times from Et<sub>2</sub>O-EtOH to give m 80.5°. Alternatively, dissolve in conc HCl, and upon dilution with H<sub>2</sub>O it separates because it is weakly basic; it is then crystallised from EtOH-Et<sub>2</sub>O. It recrystallises unchanged from AcOH. [J Chem Soc Suppl. p121 1949; J Am Chem Soc 78 3557 1956.] 3Ph<sub>3</sub>P .4HCl crystallises when HCl gas is bubbled through an Et<sub>2</sub>O solution; it has m 70-73°, but recrystallises very slowly and is deliquescent. The HI, made by adding Ph<sub>3</sub>P to hydriodic acid is not hygroscopic and decomps at ~100°. The chlorate (1:1) salt has m 165-167°, but decomposes slowly at 100°. All salts hydrolyse in H<sub>2</sub>O to give Ph<sub>3</sub>P [IR, UV: J Am Chem Soc 80 2117 1958; pK: J Am Chem Soc 82 5791 1960; Kosolapoff, Organophosphorus Compounds, Wiley 1950]. § Available commercially on a polystyrene or polyethyleneglycol support.

**Triphenyl phosphine dibromide** [1034-39-5] **M 422.1, m 235°, 245-255°(dec).** Recrystd from MeCN-Et<sub>2</sub>O. Although it has been recrystd from EtOH, this is not recommended as it converts alcohols to alkyl bromides. It deteriorates on keeping and it is best to prepare it afresh. [Anderson and Freenor J Am Chem Soc **86** 5037 1964; Horner et al. Justus Liebigs Ann Chem **626** 26 1959.]

Triphenylphosphine oxide [791-28-6] M 278.3, m 152.0°, pK<sub>Est</sub> ~ -2.10 (aq H<sub>2</sub>SO<sub>4</sub>). Crystd from absolute EtOH. Dried *in vacuo*.

**Triphenyl phosphite** [101-02-0] **M 310.3, b 181-189°/1mm, d 1.183.** Its ethereal soln was washed successively with aqueous 5% NaOH, distilled water and saturated aqueous NaCl, then dried with  $Na_2SO_4$  and distilled under vacuum after evaporating the diethyl ether.

**Triphenylphosphorylidene acetaldehyde (formylmethylenetriphenylphosphorane)** [2136-75-6] **M 304.3, m 185-187°, 186-187°(dec).** Recryst from Me<sub>2</sub>CO, or dissolve in  $C_6H_6$ , wash with N NaOH, dry (MgSO<sub>4</sub>), evap, and cryst residue from Me<sub>2</sub>CO. It can be prepd from its precursor, formylmethyltriphenylphosphonium chloride (crystd from CHCl<sub>3</sub>/EtOAc), by tratment with Et<sub>3</sub>N and extraction with  $C_6H_6$ . [Tripett and Walker *Chem Soc* 1266 1961.]

Triphenyl silane [789-25-3] M 260.4, m 45°, b 148-151°/1mm. Purified by recrystn from MeOH. [J Am Chem Soc 81 5925 1959; Acta Chem Scand 9 947 1955; IR: J Am Chem Soc 76 5880 1954.]

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**Triphenylsilanol** (hydroxytriphenylsilane) [791-31-1] M 276.4, m 150-153°, 151-153°, 154-155°, 156°. It can be purified by dissolving in pet ether, passing through an Al<sub>2</sub>O<sub>3</sub> column, eluting thoroughly with CCl<sub>4</sub> to remove impurities and then eluting the silanol with MeOH. Evaporation gives crystals m 153-155°. It can be recrystallised from pet ether, CCl<sub>4</sub> or from \*benzene or Et<sub>2</sub>O-pet ether (1:1). It has also been recrystallised by partial freezing from the melt to constant melting point. [*J Am Chem Soc* 81 3288 1959; IR: *J Org Chem* 17 1555 1952 and *J Chem Soc* 124 1949.]

Triphenyltin chloride (chlorotriphenylstannane) [639-58-7] M 385.5, m 103-106°(dec), 108°(dec), b 240°/13.5mm. Purify by distillation, followed by recrystn from MeOH by adding pet ether (b 30-60°), m 105-106° [Chem Ber 67 1348 1934], or by crystn from Et<sub>2</sub>O [Krause Chem Ber 51 914 1918]. It sublimes in a vacuum. HIGHLY TOXIC.

**Triphenyltin hydroxide** [76-87-9] M 367.0, m 122-123.5°, 124-126°. West, Baney and Powell [J Am Chem Soc 82 6269 1960] purified a sample which was grossly contaminated with tetraphenyltin and diphenyltin oxide by dissolving it in EtOH, most of the impurities remaining behind as an insoluble residue. Evaporation of the EtOH gave the crude hydroxide which was converted to triphenyltin chloride by grinding in a mortar under 12M HCl, then evaporating the acid soln. The chloride, after crystallisation from EtOH, had m 104-105°. It was dissolved in  $Et_2O$  and converted to the hydroxide by stirring with excess aqueous ammonia. The ether layer was separated, dried, and evaporated to give triphenyltin hydroxide which, after crystn from EtOH and drying under vacuum, was in the form of white crystals (m 119-120°), which retained some cloudiness in the melt above 120°. The hydroxide retains water (0.1-0.5 moles of water per mole) tenaciously.

**Triphenyl vinyl silane** [18666-68-7] **M 286.5, m 58-59°, 57-59.5°, 67-68°, b 190-210°/3mm.** It has been recrystallised from EtOH, 95% EtOH, EtOH- ${}^{*}C_{6}H_{6}$ , pet ether (b 30-60°) and Et<sub>2</sub>O, and has been distilled under reduced pressure. [J Am Chem Soc 74 4582 1952; J Org Chem 17 1379 1952.]

Tri-*n*-propyl borate [688-71-1] M 188.1, b 175-177°, d 0.857, n 1.395. Dried with sodium and then distilled.

**Triquinol-8-yl phosphate** [52429-99-9] **M 479.4, m 193-197°, 202-203°**. Purified by recrystn from dimethylformamide. Purity was checked by paper chromatography,  $R_F 0.90$  [*i*-PrOH, saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, H<sub>2</sub>O; 2:79:19 as eluent]; IR (KBr) v 1620–1570 (C=C, C=N) and 1253 (P=O). [Bull Chem Soc Jpn 47 779 1974.]

**Tri-ruthenium dodecacarbonyl** [15243-33-1] **M 639.1, m 154-155°.** Recryst from  ${}^{*}C_{6}H_{6}$  or cyclohexane as orange-red crystals, and sublime at 80-100°/0.1mm. It has  $v_{CO}$  2062 and 2032. [J Chem Soc, Chem Commun 684 1966; J Chem Soc (A) 1238 1967; IR,UV: Angew Chem Int Ed Engl 7 427 1968.]

Tris-(2-biphenylyl) phosphate [132-28-5] M 554.6, m 115.5-117.5°. Crystd from MeOH containing a little acetone.

Tris(2,2'-bipyridine)ruthenium(II) dichloride  $(6H_2O)$  [50525-27-4] M 748.6. Recrystd from water then from MeOH [Ikezawa et al. J Am Chem Soc 108 1589 1986].

Tris-(1,2-dioxyphenyl)cyclotriphosphazine {trispiro[1,3,5,2,4,6-triazatriphosphorine]-2,2':-2,4":2,6"'-tris(1,3,2)benzodioxaphosphole} [311-03-5] M 459.0, m 244-245°, 245°, 245-246°. Recrystd from  ${}^{*}C_{6}H_{6}$  or chlorobenzene, then triple sublimed (175°/0.1mm, 200°/0.1mm, 230°/0.05mm). UV has  $\lambda_{max}$ nm (log ε): 276 (3.72), 271 (3.79) 266sh (3.68) and 209 (4.38) in MeCN. IR (v): 1270 (O-Ph), 1220 (P=N), 835 (P-O-Ph) and 745 (Ph) cm<sup>-1</sup>. [Alcock J Am Chem Soc 86 2591 1964; Alcock et al. J Am Chem Soc 98 5120 1976; Meirovitch J Phys Chem 88 1522 1984.]

(±)-Tris-(2-ethylhexyl)phosphate (TEHP, tri-isooctylphosphate, "trioctyl" phosphate, [78-42-2; 25103-23-5] M 434.6, b 186°/1mm, 219°/5mm, d<sup>25</sup> 0.92042, n 1.44464. TEHP, in an equal volume of diethyl ether, was shaken with aqueous 5% HCl and the organic phase was filtered to remove

traces of pyridine (used as a solvent during manufacture) as its hydrochloride. This layer was shaken with aqueous  $Na_2CO_3$ , then water, and the ether was distilled off at room temperature. The ester was filtered, dried for 12h at 100°/15mm, and again filtered, then shaken intermittently for 2 days with activated alumina (100g/L). It was decanted through a fine sintered-glass disc (with exclusion of moisture), and distd under vacuum. [French and Muggleton J Chem Soc 5064 1957.] \*Benzene can be used as a solvent (to give 0.4M soln) instead of ether. IR: 1702, 1701, 481 and 478cm<sup>-1</sup> [Bellamy and Becker J Chem Soc 475 1952]. The uranyl nitrate salt was purified by partial crystallisation from hexane [Siddall J Am Chem Soc 81 4176 1959].

Trisodium citrate  $(2H_2O)$  [68-04-2] M 294.1, m 150°(loses H<sub>2</sub>O). Crystd from warm water by cooling to 0°.

**Trisodium 8-hydroxy-1,3,6-pyrenetrisulfonate** [6358-69-6] **M 488.8, m >300(dec).** Purified by chromatography with an alumina column, and eluted with *n*-propanol-water (3:1, v/v). Recrystd from aqueous acetone (5:95, v/v) using decolorising charcoal.

**Trisodium 1,3,6-naphthalenetrisulfonate** [5182-30-9] **M 434.2.** The free acid was obtained by passage through an ion-exchange column and converted to the lanthanum salt by treatment with  $La_2O_3$ . This salt was crystallised twice from hot water. [The much lower solubility of  $La_2(SO_4)_3$  and its retrograde temperature dependence allows a good separation from sulfate impurity]. The lanthanum salt was then passed through an appropriate ion-exchange column to obtain the free acid, the sodium or potassium salt. (The sodium salt is *hygroscopic*). [Atkinson, Yokoi and Hallada J Am Chem Soc **83** 1570 1961.] Also recrystd from aqueous acetone [Okahata et al. J Am Chem Soc **108** 2863 1986].

**Trisodium orthophosphate** (12H<sub>2</sub>O) [10101-89-0] M 380.1,  $pK_1^{25}$  2.15,  $pK_2^{25}$  7.21,  $pK_3^{25}$  12.33 (for H<sub>3</sub>PO<sub>4</sub>). Crystd from warm dilute aqueous NaOH (1mL/g) by cooling to 0°.

Tris(2,4-pentandionate)aluminium [13963-57-0] M 324.3. See aluminum acetylacetonate on p. 390.

**Tris-(trimethylsilyl)silane** (TTMSS) [1873-77-4] M 248.7, b 73°/5mm, d 0.808, n 1.49. Purified by fractional distn and taking the middle cut. Store under  $N_2$  or Ar as it is an IRRITANT and **PYROPHORIC**. [Chatgilialoglu Acc Chem Res 25 188 1992; NMR: Gilman et al. J Organomet Chem 4 163 1965.]

Tritium [10028-17-8] M 6.0. Purified from hydrocarbons and <sup>3</sup>He by diffusion through the wall of a hot nickel tube [Landecker and Gray *Rev Sci Instrum* 25 1151 1954]. RADIOACTIVE.

**Tri**-*p*-tolyl phosphate [20756-92-7; 1330-78-5 (isomeric tritolyl phosphate mixture)] M 368.4, b 232-234°,  $d^{25}$  1.16484, n 1.56703. Dried with CaCl<sub>2</sub>, then distd under vacuum and percolated through a column of alumina. Passage through a packed column at 150°, with a counter-current stream of nitrogen, under reduced pressure, removed residual traces of volatile impurities.

Tri-o-tolylphosphine [6163-58-2] M 304.4, m 129-130°, pK<sub>Est</sub> <0. Crystd from EtOH [Boert et al. J Am Chem Soc 109 7781 1987].

**Tungsten** (rod) [7440-33-7] M 183.6. m 3410°, b 5900°, d 19.0. Cleaned with conc NaOH solution, rubbed with very fine emery paper until its surface was bright, washed with previously boiled and cooled conductivity water and dried with filter paper.

Tungsten hexacarbonyl [14040-11-0] M 351.9, d 2.650. Sublimed in vacuo before use [Connoe et al. J Chem Soc, Dalton Trans 511 1986].

Tungsten (VI) trichloride [13283-01-7] M 396.6, m 265°(dec), 275°, b 346°,  $d_4^{25}$  3.520,  $pK_1^{25}$  2.20,  $pK_2^{25}$  3.70 (for tungstic acid,  $H_2WO_4$ ). Sublimed in a stream of Cl<sub>2</sub> in a high temperature furnace and collected in a receiver cooled in a Dry Ice-acetone bath in an inert atmosphere because it is sensitive to moisture. It is soluble in CS<sub>2</sub>, CCl<sub>4</sub>, CHCl<sub>3</sub>, POCl<sub>3</sub>, \*C<sub>6</sub>H<sub>6</sub>, pet ether and Me<sub>2</sub>CO. Solns decompose on

standing. Good crystals can be obtained by heating WCl<sub>6</sub> in CCl<sub>4</sub> to  $100^{\circ}$  in a sealed tube, followed by slow cooling (tablets of four-sided prisms). Store in a desiccator over H<sub>2</sub>SO<sub>4</sub> in the dark. [Inorg Synth 3 163 1950, 9 1331967; Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol II 1417 1965.]

**Uranium hexafluoride** [7783-81-5] M 352.0, b 0°/17.4mm, 56.2°/765mm, m 64.8°, pK<sup>25</sup> 1.68 (for hydrolysis of U<sup>4+</sup> to UOH<sup>3+</sup>). Purified by fractional distillation to remove HF. Also purified by low temperature trap-to-trap distillation over pre-dried NaF [Anderson and Winfield J Chem Soc, Dalton Trans 337 1986].

**Uranium trioxide** [1344-58-7] **M 286.0, d 7.29.** The oxide was dissolved in HClO<sub>4</sub> (to give a uranium content of 5%), and the solution was adjusted to pH 2 by addition of dilute ammonia. Dropwise addition of 30% H<sub>2</sub>O<sub>2</sub>, with rapid stirring, ppted U(VI) peroxide, the pH being held constant during the pptn, by addition of small amounts of the ammonia soln. (The H<sub>2</sub>O<sub>2</sub> was added until further quantities caused no change in pH.) After stirring for 1h, the slurry was filtered through coarse filter paper in a Büchner funnel, washed with 1% H<sub>2</sub>O<sub>2</sub> acidified to pH 2 with HClO<sub>4</sub>, then heated at 350° for three days in a large platinum dish [Baes J Phys Chem 60 878 1956].

Uranyl nitrate (6H<sub>2</sub>O) [13520-83-7] M 502.1, m 60.2°, b 118°,  $pK^{25}$  5.82 (for aquo  $UO_2^{2+}$ ). Crystd from water by cooling to -5°, taking only the middle fraction of the solid which separated. Dried as the hexahydrate over 35-40% H<sub>2</sub>SO<sub>4</sub> in a vacuum desiccator.

**Vanadium** (metal) [7440-62-2] M 50.9, m 1910°, d 6.0. Cleaned by rapid exposure consecutively to HNO<sub>3</sub>, HCl, HF, de-ionised water and reagent grade acetone, then dried in a vacuum desiccator.

Vanadium (III) acetonylacetonate [13476-99-8] M 348.3, m 181-184°, 185-190°,  $pK_1^{25} 2.92$ ,  $pK_2^{25} 3.5$ (for aquo V<sup>3+</sup> hydrolysis). Crystd from acetylacetone as brown plates. It can be distilled in small quantities without decomposition. It is soluble in CHCl<sub>3</sub> and \*C<sub>6</sub>H<sub>6</sub> and evaporation of a CHCl<sub>3</sub> solution yields brown crystals which are washed with cold EtOH and dried in vacuum or at 100° in a CO<sub>2</sub> atmosphere. Under moist conditions it readily oxidises [V(AcAc)<sub>3</sub> to V(AcAc)<sub>2</sub>O]. [J Chem Soc 103 78 1913, Inorg Synth 5 105 1957; Anal Chem 30 526 1958; UV: J Am Chem Soc 80 5686 1958.]

Vanadyl acetylacetonate [3153-26-2] M 265.2, m 256-259°. Crystd from acetone.

Vanadyl trichloride (VOCl<sub>3</sub>) [7727-18-6] M 173.3, m-79.5°, b 124.5-125.5°/744mm, 127.16°/760mm, d<sup>0</sup> 1.854, d<sup>32</sup> 1.811. Should be lemon yellow in colour. If red it may contain VCl<sub>4</sub> and Cl<sub>2</sub>. Fractionally distil and then redistil over metallic Na but be careful to leave some residue because the residue can become **EXPLOSIVE** in the presence of the metal **USE A SAFETY SHIELD** and avoid contact with moisture. It readily hydrolyses to vanadic acid and HCl. Store in a tightly closed container or in sealed ampoules under N<sub>2</sub>. [Inorg Synth 1 106 1939, 4 80 1953.]

Vinyl chlorosilane [75-94-5] M 161.5, b 17.7°/46.3mm, 82.9°/599.4mm, 92°/742mm, 91-91.5°/atm,  $d_4^{20}$  0.1.2717,  $n_D^{20}$  1.435. Fractionally distil at atmospheric pressure. It is H<sub>2</sub>O sensitive and is stored in the dark and is likely to polymerise. [*Chem Ber* 91 1805 1958, 92 1012 1959; *Anal Chem* 24 1827 1952]

**Vinylferrocene** (ferroceneylethene) [1271-51-8] M 212.1, m 51-52.5°, b 80-85°/0.2 mm. Dissolve in  $Et_2O$ , wash with  $H_2O$  and brine, dry (Na<sub>2</sub>SO<sub>4</sub>), evap to a small vol. Purify through an  $Al_2O_3$  (Spence grade H) column by eluting the yellow band with pet ether (b 40-60°). The low melting orange crystals which can be sublimed. The *tetracyanoethylene adduct* [49716-63-4] crysts from \*C<sub>6</sub>H<sub>6</sub>-pentane and has m 137-

Vinyltributylstannane (vinyltributyltin) [7486-35-3] M 317.1, b 104-106°/3.5mm, d 1.081, n 1.4751. Fractionate under reduced pressure and taking the middle fraction to remove impurities such as (*n*-Bu)<sub>3</sub>SnCl. [Seyferth and Stone J Am Chem Soc 79 515 1957.]

Rauch and Siegel J Organomet Chem 11 317 1968.]

**Water** [7732-18-5] M 18.0, m 0°, b 100°,  $pK^{25}$  14.00. Conductivity water (specific conductance *ca* 10<sup>-7</sup> mho) can be obtained by distilling water in a steam-heated tin-lined still, then, after adding 0.25% of solid NaOH and 0.05% of KMnO<sub>4</sub>, distilling once more from an electrically heated Barnstead-type still, taking the middle fraction into a Jena glass bottle. During these operations suitable traps must be used to protect against entry of CO<sub>2</sub> and NH<sub>3</sub>. Water only a little less satisfactory for conductivity measurements (but containing traces of organic material) can be obtained by passing ordinary distilled water through a mixed bed ion-exchange column containing, for example, Amberlite resins IR 120 (cation exchange) and IRA 400 (anion exchange), or Amberlite MB-1. This treatment is also a convenient one for removing traces of heavy metals. (The metals Cu, Zn, Pb, Cd and Hg can be tested for by adding pure concentrated ammonia to 10mL of sample and shaking vigorously with 1.2mL 0.001% dithizone in CCl<sub>4</sub>. Less than 0.1µg of metal ion will impart a faint colour to the CCl<sub>4</sub> layer.) For almost all laboratory purposes, simple distillation yields water of adequate purity, and most of the volatile contaminants such as ammonia and CO<sub>2</sub> are removed if the first fraction of distillate is discarded.

Xylenol Orange (sodium salt) [3618-43-7]. See entry on p. 387 in Chapter 4.

**Zinc** (dust) [7440-66-6] M 65.4. Commercial zinc dust (1.2Kg) was stirred with 2% HCl (3L) for 1min, (then the acid was removed by filtration), and washed in a 4L beaker with a 3L portion of 2% HCl, three 1L portions of distilled water, two 2L portions of 95% EtOH, and finally with 2L of absolute Et<sub>2</sub>O. (The wash solutions were removed each time by filtration.) The material was then dried thoroughly and if necessary, any lumps were broken up in a mortar.

Zinc (metal) [7440-66-6] M 65.4, m 420°, d 7.141. Fused under vacuum, cooled, then washed with acid to remove the oxide.

Zinc acetate  $(2H_2O)$  [5970-45-6] M 219.5, m 100°(loses  $2H_2O$ ), 237°, d 1.74, pK<sup>25</sup> 8.96 (for hydrolysis of Zn<sup>2+</sup> to ZnOH<sup>+</sup>). Crystd (in poor yield) from hot water or, better, from EtOH.

Zinc acetonylacetate [14024-63-6] M 263.6, m 138º. Crystd from hot 95% EtOH.

**Zinc bromide** [7699-45-8] **M 225.2, m 384, b 697.** Heated to  $300^{\circ}$  under vacuum (2 x  $10^{-2}$ mm) for 1h, then sublimed.

Zinc caprylate [557-09-5] M 351.8. Crystd from EtOH.

Zinc chloride [7646-85-7] M 136.3, m 283°, 290°. The anhydrous material can be sublimed under a stream of dry HCl, followed by heating to 400° in a stream of dry N<sub>2</sub>. Also purified by refluxing (50g) in dioxane (400mL) with 5g zinc dust, filtering hot and cooling to ppte ZnCl<sub>2</sub>. Crystd from dioxane and stored in a desiccator over P<sub>2</sub>O<sub>5</sub>. It has also been dried by refluxing in thionyl chloride. [Weberg et al. J Am Chem Soc 108 6242 1986.] Hygroscopic: minimal exposure to the atmosphere is necessary.

## Purification of Inorganic and Metal-Organic Chemicals

Zinc cyanide [557-21-1] M 117.4, m 800°(dec), d 1.852. It is a POISONOUS white powder which becomes black on standing if Mg(OH)<sub>2</sub> and carbonate are not removed in the preparation. Thus wash well with H<sub>2</sub>O, then well with EtOH, Et<sub>2</sub>O and dry in air at 50°. Analyse by titrating the cyanide with standard AgNO<sub>3</sub>. Other likely impurities are ZnCl<sub>2</sub>, MgCl<sub>2</sub> and traces of basic zinc cyanide; the first two salts can be washed out. It is soluble in aq KCN solns. However, if purified in this way Zn(CN)<sub>2</sub> is not reactive in the Gattermann synthesis. For this the salt should contain at least 0.33 mols of KCl or NaCl which will allow the reaction to proceed faster. [J Am Chem Soc 45 2375 1923, 60 1699 1938; Org Synth Coll Vol III 549 1955.]

Zinc diethyldithiocarbamate [14324-55-1] M 561.7, pK<sup>25</sup> 3.04 (for Et<sub>2</sub>NCS<sub>2</sub><sup>-</sup>). Crystd several times from hot toluene or from hot CHCl<sub>3</sub> by addition of EtOH.

Zinc dimethyldithiocarbamate [137-30-4] M 305.8, m 248-250°, pK<sup>25</sup> 3.36 (for Me<sub>2</sub>NCS<sub>2</sub><sup>-</sup>). Crystd several times from hot toluene or from hot CHCl<sub>3</sub> by addition of EtOH.

Zinc ethylenebis[dithiocarbamate] [12122-67-7] M 249.7. Crystd several times from hot toluene or from hot CHCl<sub>3</sub> by addition of EtOH.

Zinc fluoride [7783-49-5] M 103.4, m 872°, b 1500°, d<sup>25</sup> 5.00. Possible impurity is H<sub>2</sub>O which can be removed by heating at 100° or by heating to 800° in a dry atmosphere. Heating in the presence of NH<sub>4</sub>F produces larger crystals. It is sparingly sol in H<sub>2</sub>O (1.51g/100mL) but more sol in HCl, HNO<sub>3</sub> and NH<sub>4</sub>OH. It can be stored in glass bottles. [Handbook of Preparative Inorganic Chemistry (Ed. Brauer) Vol I 242 1963.]

Zinc formate (2H<sub>2</sub>O) [557-41-5] M 191.4, m 140<sup>o</sup>(loses H<sub>2</sub>O), d 2.21. Crystd from water (3mL/g).

Zinc iodide [10139-47-6] M 319.2, m 446, b 624°(dec), d 4.74. Heated to 300° under vacuum (2 x  $10^{-2}$ mm) for 1h, then sublimed.

Zinc RS-lactate (3H<sub>2</sub>O) [554-05-2; 16039-53-5 (L)] M 297.5. Crystd from water (6mL/g).

Zincon (o-[1-(2-hydroxy-5-sulfo)-3-phenyl-5-formazono]-benzoic acid) [135-52-4] M 459.4. Main impurities are inorganic salts which can be removed by treatment with dilute acetic acid. Organic contaminants are removed by refluxing with ether. It can be recrystd from dilute H<sub>2</sub>SO<sub>4</sub>. [Fichter and Schiess Chem Ber 33 751 1900.]

Zincon disodium salt (o-[1-(2-hydroxy-5-sulfo)-3-phenyl-5-formazono]-benzoic acid di-Na salt) [135-52-4; 56484-13-0] M 484.4, m ~250-260° (dec). Zincon soln is prepared by dissolving 0.13g of the powder in aqueous N NaOH (2mL diluted to 100mL with H<sub>2</sub>O). This gives a deep red colour which is stable for one week. It is a good reagent for zinc ions but also forms stable complexes with transition metal ions. [UV-VIS: Bush and Yoe Anal Chem 26 1345 1954; Hunter and Roberts J Chem Soc 820 1941; Platte and Marcy Anal Chem 31 1226 1959] The free acid has been recrystd from dilute H<sub>2</sub>SO<sub>4</sub>. [Fichter and Scheiss Chem Ber 33 751 1900.]

Zinc perchlorate (6H<sub>2</sub>O) [13637-61-1] M 372.4, m 105-107°,  $pK^{25}$  -2.4 to -3.1 (for HClO<sub>4</sub>). Crystd from water.

Zinc phenol-o-sulfonate (8H<sub>2</sub>O) [127-82-2] M 555.8. Crystd from warm water by cooling to 0°.

Zinc phthalocyanine [14320-04-8] M 580.9. Sublimed repeatedly in a flow of oxygen-free N<sub>2</sub>.

Zinc sulfate  $(7H_2O)$  [7446-20-0] M 287.5, m 100°(dec), 280°(loses all  $7H_2O$ ), >500(anhydr), d 1.97. Crystd from aqueous EtOH.

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Zinc trifluoromethanesulfonate [54010-75-2] M 363.5, m >300°. It should be dried at 125° for 2h at 3mm. It is soluble in CH<sub>2</sub>Cl<sub>2</sub> but insoluble in pet ether. [Tetrahedron Lett 24 169 1983.]

Zirconium (IV) proposide [23519-77-9] M 327.6, b 198°/0.03mm, 208°/0.1mm,  $d_4^{20}$  1.06,  $n_D^{20}$  1.454. Although it was stated that it could not be crystallised or sublimed even at  $150^{\circ}/10^{-4}$ mm [J Chem Soc 280 1951], the proposide has, when properly prepared, been purifed by distn in a high vacuum [J Chem Soc 2025 1953].

Zirconium tetrachloride [10026-11-6] M 233.0, m 300°(sublimes),  $pK_1^{25}$ -0.32,  $pK_2^{25}$ 0.06,  $pK_3^{25}$  0.35,  $pK_4^{25}$  0.46 (for hydrolysis of aquo Zr<sup>4-</sup>). Crystd repeatedly from conc HCl.

**Zirconocene chloride hydride** (bis[cyclopentadienyl]zirconium hydride chloride) (Schwartz reagent) [37342-97-5] M 257.9. It is a moisture and light sensitive compound. Its purity can be determined by reaction with a slight excess of Me<sub>2</sub>CO whereby the active H reacts to produce Cp<sub>2</sub>ZrClOPr<sup>i</sup> and the integrals of the residual Me<sub>2</sub>CO in the <sup>1</sup>H NMR will show how pure the sample is. The presence of Cp<sub>2</sub>ZrH<sub>2</sub> can be determined because it forms Cp<sub>2</sub>Zr(OPr<sup>i</sup>)<sub>2</sub>. For very active compound it is best to prepare freshly from the dichloride by reduction with Vitride [LiAl(OCH<sub>2</sub>CH<sub>2</sub>OH)<sub>2</sub>H<sub>2</sub>], the white ppte is filtered off, washed with tetrahydrofuran, \*C<sub>6</sub>H<sub>6</sub>, Et<sub>2</sub>O, dried in vacuum and stored under anhydrous conditions and in the dark. [IR: J Chem Soc, Chem Commun 1105 1969; J Am Chem Soc 96 8115 1974, 101 3521 1979; Synthesis 1 1988.]

Zirconocene dichloride (bis[cyclopentadienyl]zirconium dichloride) [1291-32-3] M 292.3, m 242-245°, 248°. Purified by recrystn from CHCl<sub>3</sub> or xylene, and dried in vacuum. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ : 6.52 from Me<sub>4</sub>Si. Store in the dark under N<sub>2</sub> as it is moisture sensitive. [IR, NMR, MS: Aust J Chem 18 173 1965; method of J Am Chem Soc 81 1364 1959; and references in the previous entry.]

Zirconyl chloride (6H<sub>2</sub>O) [7699-43-6] M 286.2, m 150°(loses 6H<sub>2</sub>O). Crystd repeatedly from 8M HCl as ZrOCl<sub>2</sub>.8H<sub>2</sub>O. On drying ZrOCl<sub>2</sub>.6H<sub>2</sub>O m 150°. The product was not free from hafnium.

Zirconyl chloride (8H<sub>2</sub>O) [13520-92-8] M 322.3, m 150°(loses  $6H_2O$ ), 210°(loses all  $H_2O$ ). 400°(anhydr dec), d 1.91. Recrystd several times from water [Ferragina et al. J Chem Soc, Dalton Trans 265 1986]. Recrystn from 8M HCl gives the octahydrate as white needles on concentrating. It is also formed by hydrolysing ZrCl<sub>4</sub> with water. After one recryst from  $H_2O$ , 99+% grade had Ag, Al, As, Cd, Cu, Hf, Mg, Na, Sc and V at 20, 1.8, 0.6, 0.6, 0.4, 8.4, 0.4, 2.4, 80 and 3 ppm resp.

# **CHAPTER 6**

# PURIFICATION OF BIOCHEMICALS AND RELATED PRODUCTS

Biochemicals are chemical substances produced by living organisms. They range widely in size, from simple molecules such as formic acid and glucose to macromolecules such as proteins and nucleic acids. Their *in vitro* synthesis is often impossibly difficult and in such cases they are available (if at all) only as commercial tissue extracts which have been subjected to purification procedures of widely varying stringency. The desired chemical may be, initially, only a minor constituent of the source tissue which may vary considerably in its composition and complexity. Recent advances in molecular biology have made it possible to produce substantial amounts of biological materials, which are present in nature in extremely small amounts, by recombinant DNA technology and expression in bacteria, yeast, insect and mammalian cells. The genes for these substances can be engineered such that the gene products, e.g. polypeptides or proteins, can be readily obtained in very high states of purity. However, many such products which are still obtained from the original natural sources are available commercially and may require further purification.

As a preliminary step the tissue might be separated into phases [e.g. whole egg into white and yolk, blood into plasma (or serum) and red cells], and the desired phase may be homogenised. Subsequent treatment usually comprises filtration, solvent extraction, salt fractionation, ultracentrifugation, chromatographic purification, gel filtration and dialysis. Fractional precipitation with ammonium sulfate gives crude protein species. Purification is finally judged by the formation of a single band of macromolecule (e.g. protein) on electrophoresis and/or analytical ultracentrifugation. Although these generally provide good evidence of high purity, none-the-less it does not follow that one band under one set of experimental conditions is an absolute indication of homogeneity.

During the past 20 or 30 years a wide range of methods for purifying substances of biological origin have become available. For small molecules (including many sugars and amino acids) reference should be made to Chapters 1 and 2. The more important methods used for large molecules, polypeptides and proteins in particular, comprise:

- 1. Centrifugation. In addition to centrifugation for sedimenting proteins after ammonium sulfate precipitation in dilute aqueous buffer, this technique has been used for fractionation of large molecules in a denser medium or a medium of varying density. By layering sugar solutions of increasing densities in a centrifuge tube, proteins can be separated in a sugar-density gradient by centrifugation. Smaller DNA molecules (e.g. plasmid DNA) can be separated from RNA or nuclear DNA by centrifugation in aqueous cesium chloride (ca 0.975g/mL of buffer) for a long time (e.g. 40h at 40,000 x g). The plasmid DNA band appears at about the middle of the centrifuge tube, and is revealed by the fluorescent pink band formed by the binding of DNA to ethidium bromide which is added to the CsCl buffer. Microfuges are routinely used for centrifugation in Eppendorf tubes (1.2-2mL) and can run up to speeds of 12,000 x g. Analytical centrifugation, which is performed under specific conditions in an analytical ultracentrifuge is very useful for determining purity, aggregation of protein subunits and the molecular weight of macromolecules. [D.Rickwood, T.C.Ford and J.Steensgaard Centrifugation: Essential Data Series, J Wiley & Sons, NY, 1994].
- 2. Gel filtration with polyacrylamide (mol wt exclusion limit from 3000 to 300,000) and agarose gel (mol wt exclusion limit 0.5 to  $150 \times 10^6$ ) is useful for separating macromolecules. In this technique high-molecular weight substances are too large to fit into the gel microapertures and pass rapidly through the matrix (with the void volume), whereas low molecular weight species enter these apertures and are held there for longer periods of time, being retarded by the column material in the equilibria, relative to the larger molecules. This method is also used for desalting solutions of macromolecules. Dry gels and crushed beads are also

useful in the gel filtration process. Selective retention of water and inorganic salts by the gels or beads (e.g. Sephadex G-25) results in increased concentration and purity of the protein fraction which moves with the void volume. (See also Chapter 1, pp 23, 41).

- 3. Ion exchange matrices are microreticular polymers containing carboxylic acid (e.g. Bio-Rad 70) or phosphoric acid (Pharmacia, Amersham Biosciences, Mono-P) exchange functional groups for weak acidic cation exchangers, sulfonic acid groups (Dowex 50W) for strong acidic cation exchangers, diethylaminoethyl (DEAE) groups for weakly basic anion exchangers and quaternary ammonium (QEAE) groups for strong anion exchangers. The old cellulose matrices for ion exchanges have been replaced by Sephadex, Sepharose or Fractogel which have more even particle sizes with faster and more reproducible flow rates. Some can be obtained in fine, medium or coarse grades depending on particle size. These have been used extensively for the fractionation of peptides, proteins and enzymes. The use of pH buffers controls the strength with which the large molecules are bound to the support in the chromatographic process. Careful standardisation of experimental conditions and similarly the very uniform size distribution of Mono beads has led to high resolution in the purification of protein solutions. MonoQ (Pharmacia, Amersham Biosciences) is a useful strong anion exchanger, and MonoS (Pharmacia, Amersham Biosciences) is a useful strong anion exchanger, and MonoS (Pharmacia, Amersham Biosciences) is a useful strong cation exchanger whereas MonoP is a weak cation exchanger. These have been successful with medium pressure column chromatography (FPLC, see below in 8). Chelex 100 binds strongly and removes metal ions from macromolecules. [See also Chapter 1, pp. 22-24.]
- 4. Hydroxylapatite is used for the later stages of purification of enzymes. It consists essentially of hydrated calcium phosphate which has been precipitated in a specific manner. It combines the characteristics of gel and ionic chromatography. Crystalline hydroxylapatite is a structurally organised, highly polar material which, in aqueous solution (in buffers) strongly adsorbs macromolecules such as proteins and nucleic acids, permitting their separation by virtue of the interaction with charged phosphate groups and calcium ions, as well as by physical adsorption. The procedure therefore is not entirely ion-exchange in nature. Chromatographic separations of singly and doubly stranded DNA are readily achievable whereas there is negligible adsorption of low molecular weight species.
- 5. Affinity chromatography is a chromatographic technique whereby the adsorbant has a particular and specific affinity for one of the components of the mixture to be purified. For example the adsorbant can be prepared by chemically binding an inhibitor of a specific enzyme (which is present in the crude complex mixture) to a matrix (e.g. Sepharose). When the mixture of impure enzyme is passed through the column containing the adsorbant, only the specific enzyme binds to the column. After adequate washing, the pure enzyme can be released from the column by either increasing the salt concentration (e.g. NaCl) in the eluting buffer or adding the inhibitor to the eluting buffer. The salt or inhibitor can then be removed by dialysis, gel filtration (above) or ultrafiltration (see below). [See W.H.Scouten, Affinity Chromatography: Bioselective Adsorption on Inert Matrices, J.Wiley & Sons, NY, 1981, ISBN 0471026492; H.Schott, Affinity Chromatography: Template Chromatography of Nucleic Acids and Proteins, Marcel Dekker, NY, 1984, ISBN 0824771117; P.Matejtschuk ed. Affinity Separations Oxford University Press 1997 ISBN 0199635501 (paperback); M.A.Vijayalakshmi, Biochromatography, Theory and Practice, Taylot & Francis Publ, 2002, ISBN 0415269032; and Chapter 1, p. 25.]
- 6. In the *Isoelectric focusing* of large charged molecules on polyacrylamide or agarose gels, slabs of these are prepared in buffer mixtures (e.g. ampholines) which have various pH ranges. When a voltage is applied for some time the buffers arrange themselves on the slabs in respective areas according to their pH ranges (prefocusing). Then the macromolecules are applied near the middle of the slab and allowed to migrate in the electric field until they reach the pH area similar to their isoelectric points and focus at that position. This technique can also be used in a chromatographic mode, chromatofocusing, whereby a gel in a column is run (also under HPLC conditions) in the presence of ampholines (narrow or wide pH ranges as required) and the macromolecules are then run through in a buffer. Capillary electrophoresis systems in which a current is applied to set the gradient are now available in which the columns are fine capillaries and are used for qualitative and quantitative purposes [See R.Kuhn and S.Hoffstetter-Kuhn, Capillary Electrophoresis: Principles and Practice, Springer-Verlag Inc, NY, 1993; P.Camilleri ed. Capillary Electrophoresis - Theory and Practice, CRC Press, Boca Raton, Florida, 1993; D.R.Baker, Capillary Electrophoresis, J Wiley & Sons, NY, 1995; P.G.Righetti, A.Stoyanov and M.Zhukov, The Proteome Revisited, Isoelectric Focusing; J.Chromatography Library Vol 63 2001, Elsevier, ISBN 0444505261.] The bands are eluted according to their isoelectric points. Isoelectric focusing standards are available which can be used in a preliminary run in order to calibrate the effluent from the column, or alternatively the pH of the effluent is recorded using a glass electrode designed for the purpose. Several efficient commercially available apparatus are available for separating proteins on a preparative and semi-preparative scale.
- 7. High performance liquid chromatography (HPLC) is liquid chromatography in which the eluting liquid is sent through the column containing the packing (materials as in 2-6 above, which can withstand higher than atmospheric pressures) under pressure. On a routine basis this has been found useful for purifying

### **Purification of Biochemicals and Related Products**

proteins (including enzymes) and polypeptides after enzymic digestion of proteins or chemical cleavage (e.g. with CNBr) prior to sequencing (using reverse-phase columns such as µ-Bondapak C18). Moderate pressures (50-300psi) have been found most satisfactory for large molecules (FPLC). [See Scopes Anal Biochem 114 8 1981; High Performance Liquid Chromatography and Its Application to Protein Chemistry, Hearn in Advances in Chromatography, 20 7 1982; B. A. Bidlingmeyer Practical HPLC Methodology and Applications, J Wiley & Sons, NY 1991; L.R.Snyder, J.L.GlajCh and J.J.Kirkland Practical HPLC Method Development, J Wiley & Sons, NY 1988; ISBN 0471627828; R.W.A.Oliver, HPLC of Macromolecules: A Practical Approach, 2nd Edn, Oxford University Press, 1998, T.Hanai, HPLC: A Practical Guide, Royal Society of Chemistry (UK), 1999, ISBN 084045155; P.Millner High Resolution Chromatography, Oxford University Press, 1999 ISBN 0199636486; see also Chapter 1, bibliography.]

- 8. Ultrafiltration using a filter (e.g. Millipore) can remove water and low-molecular weight substances without the application of heat. Filters with a variety of molecular weight exclusion limits not only allow the concentration of a particular macromolecule to be determined, but also the removal (by washing during filtration) of smaller molecular weight contaminants (e.g. salts, inhibitors or cofactors). This procedure has been useful for changing the buffer in which the macromolecule is present (e.g. from Tris-Cl to ammonium carbonate), and for desalting. Ultrafiltration can be carried out in a stirrer cell (Amicon) in which the buffer containing the macromolecule (particularly protein) is pressed through the filter, with stirring, under argon or nitrogen pressure (e.g. 20-60psi). During this filtration process the buffer can be changed. This is rapid (e.g. 2L of solution can be concentrated to a few mLs in 1 to 2h depending on pressure and filter). A similar application uses a filter in a specially designed tube (Centricon tubes, Amicon) and the filtration occurs under centrifugal force in a centrifuge (4-6000rpm at 0°/40min). The macromolecule (usually DNA) then rests on the filter and can be washed on the filter by centrifugation. The macromolecule is recovered by inverting the filter, placing a conical receiver tube on the same side where the macromolecule rests, filling the other side of the filter tube with eluting solution (usually a very small volume e.g. 100 µL), and during further centrifugation this solution passes through the filter and collects the macromolecule from the underside into the conical receiver tube.
- 9. Partial precipitation of a protein in solution can often be achieved by controlled addition of a strong salt solution, e.g ammonium sulfate. This is commonly the first step in the purification process. Its simplicity is offset by possible denaturation of the desired protein and the (sometimes gross) contamination with other proteins. It should therefore be carried out by careful addition of small aliquots of the powdered salt or concentrated solution (below 4°, with gentle stirring) and allowing the salt to be evenly distributed in the solution before adding another small aliquot. Under carefully controlled conditions and using almost pure protein it is sometimes possible to obtain the protein in crystalline form suitable for X-ray analysis (see below).
- 10. Dialysis. This is a process by which small molecules, e.g. ammonium sulfate, sodium chloride, are removed from a solution containing the protein or DNA using a membrane which is porous to small molecules. The solution (e.g. 10mL) is placed in a dialysis bag or tube tied at both ends, and stirred in a large excess of dialysing solution (e.g. 1.5 to 2 L), usually a weak buffer at ca 4°. The dialysing buffer is replaced with fresh buffer several times, e.g. four times in 24h. This procedure is similar to ultrafiltration (above) and allows the replacement of buffer in which the protein, or DNA, is dissolved. It is also possible to concentrate the solutions by placing the dialysis tube or bag in Sephadex G25 which allows the passage of water and salts from the inside of the bag thus concentrating the protein (or DNA) solution. Dialysis tubing is available from various distibutors but "Spectra/por" tubing (from Spectrum Medical Industries, Inc, LA) is particularly effective because it retains macromolecules and allows small molecules to dialyse out very rapidly thus reducing dialysing time considerably. This procedure is used when the buffer has to be changed so as to be compatible with the next purification or storage step, e.g. when the protein (or DNA) needs to be stored frozen in a particular buffer for extended periods.
- 11. Gel Electrophoresis. This is becoming a more commonly used procedure for purifying proteins, nucleic acids, nucleoproteins, polysaccharides and carbohydrates. The gels can be electroblotted onto membranes and the modern procedures of identifying, sequencing (proteins and nucleic acids) and amplifying (nucleic acids) on sub-micro scales have made this technique of separation a very important one. See below for polyacrylamide gel electrophoresis (PAGE), [D.Patel Gel Electrophoresis, J.Wiley-Liss, Inc., 1994; P.Jones and D.Rickwood, Gel Electrophoresis: Nucleic Acids, J.Wiley and Sons,1999 (paperback) ISBN 0471960438; D.M.Gersten and D.Gersten, Gel Electrophoresis: Proteins, J.Wiley and Sons Inc, 1996 ISBN 0471962651; R.Westermeier Electrophoresis in Practice, 3rd Edn, Wiley-VCH, NY, 2001, ISBN 3527303006].
- 12. Crystallisation. The ultimate in purification of proteins or nucleic acids is crystallisation. This involves very specialised procedures and techniques and is best left to the experts in the field of X-ray crystallography who provide a complete picture of the structure of these large molecules. [A. Ducruix and R. Giegé eds, Crystallisation of Nucleic Acids and Proteins: A Practical Approach, 2nd Edition, 2000,

Oxford University Press, ISBN 0199636788 (paperback); T.L.Blundell and L.N.Johnson Protein Crystallisation, Academic Press, NY, 1976; A.McPherson Preparation and Analysis of Protein Crystals, J.Wiley & Sons, NY, 1982; A.McPherson, Crystallisation of Biological Macromolecules, Cold Spring Harbour Laboratory Press, 2001 ISBN 0879696176.]

Other details of the above will be found in Chapters 1 and 2 which also contain relevant references.

Several illustrations of the usefulness of the above methods are given in the *Methods Enzymol* series (Academic Press) in which 1000-fold purifications or more, have been readily achieved. In applying these sensitive methods to macromolecules, reagent purity is essential. It is disconcerting, therefore, to find that some commercial samples of the widely used affinity chromatography ligand Cibacron Blue F3GA contained this dye only as a minor constituent. The major component appeared to be the dichlorotriazinyl precursor of this dye. Commercial samples of Procion Blue and Procion Blue MX-R were also highly heterogeneous [Hanggi and Cadd Anal Biochem 149 91 1985]. Variations in composition of sample dyes can well account for differences in results reported by different workers. The purity of substances of biological origin should therefore be checked by one or more of the methods given above. Water of high purity should be used in all operations. Double glass distilled water or water purified by a MilliQ filtration system (see Chapter 2) is most satisfactory.

Brief general procedures for the purification of polypeptides and proteins. Polypeptides of up to ca 1-2000 (10-20 amino acid residues) are best purified by reverse phase HPLC. The desired fractions that are collected are either precipitated from solution with EtOH or lyophilised. The purity can be checked by HPLC and identified by microsequencing (1-30 picomoles) to ascertain that the correct polypeptide was in hand. Polypeptides larger than these are sometimes classified as proteins, and are purified by one or more of the procedures described above. The purification of enzymes and functional proteins which can be identified by specific interactions is generally easier to follow because enzyme activities or specific protein interactions can be checked (by assaying) after each purification step. The commonly used procedures for purifying soluble proteins involve the isolation of an aqueous extract from homogenised tissues or extracts from ruptured cells from microorganisms or specifically cultured cells, for example, by sonication, freeze shocking or passage through a small orifice under pressure. Contaminating nucleic acids are removed by precipitation with a basic protein, e.g. protamine sulfate. The soluble supernatant is then subjected to fractionation with increasing concentrations of ammonium sulfate. The required fractions are then further purified by the procedures described in sections 2-9 above. If an affinity adsorbant has been identified then affinity chromatography can provide an almost pure protein in one step sometimes even from the crude extract. The rule of thumb is that a solution with a protein concentration of 1mg/mL has an absorbance  $A_{1cm}$  at 280nm of 1.0 units. Membrane-bound proteins are usually insoluble in water or dilute aqueous buffer and are obtained from the insoluble fractions, e.g. the microsomal fractions from the  $>100,000 \times g$  ultracentrifugation supernatant. These are solubilised in appropriate detergents, e.g. Mega-10 (nonionic), Triton X-100 (ionic) detergents, and purified by methods 2 to 8 (previous section) in the presence of detergent in the buffer used. They are assayed also in the presence of detergent or membrane lipids.

The purity of proteins is best checked by *polyacrylamide gel electrophoresis* (PAGE). The gels are either made or purchased as pre-cast gels and can be with uniform or gradient gel composition. Proteins are applied onto the gels via wells set into the gels or by means of a comb, and travel along the gel surface by means of the current applied to the gel. When the buffer used contains sodium dodecylsulfate (SDS) the proteins are denatured and the denatured proteins (e.g. as protein subunits) separate on the gels mainly according to their molecular sizes. These can be identified by running marker proteins, with a range of molecular weights, simultaneously on a track alongside the proteins under study. The protein bands are visualised by fixing the gel (20% acetic acid) and staining with Coomassie blue followed by silver staining if higher sensitivity is required. An Amersham-Pharmacia "Phast Gel Electrophoresis" apparatus is very useful for rapid analysis of proteins. It uses small precast polyacrylamide gels (two gels can be run simultaneously) with various uniform or gradient polyacrylamide concentrations as well as gels for isoelectric focusing. The gels are usually run for 0.5-1h and can be stained and developed (1-1.5h) in the same apparatus. The equipment can be used to electroblot the protein bands onto a membrane from which the proteins can be isolated and sequenced or subjected to antibody or other identification procedures. It should be noted that all purification procedures are almost always carried out at ca 4° in order to avoid denaturation or inactivation of the protein being investigated. Anyone contemplating the purification of a protein is referred to: Professor R.K.Scopes's monograph Protein Purification, 3rd edn, Springer-Verlag, New

York, 1994, ISBN 0387940723; M.L.Ladisch ed. Protein Purification - from Molecular Mechanisms to Largescale Processes, American Chemical Society, Washington DC, 1990; E.L.V.Harris and S.Angal, Protein Purification Applications - A Practical Approach, IRL Press, Oxford, 1990; J.C.Janson and L.Rydén, Protein Purification - Principles, High Resolution Methods and Applications, VCH Publ. Inc., 1989; ISBN 0895731223 R.Burgess, Protein Purification - Micro to Macro, A.R.Liss, Inc., NY, 1987; S.M.Wheelwright, Protein Purification: Design and Scale up of Downstream Processing, J Wiley & Sons, NY, 1994, references in the bibliography in Chapter 1, and selected volumes of Methods Enzymol, e.g. M.P.Deutscher ed. Guide to Protein Purification, Methods Enzymol, Academic Press, NY, Vol 182 1990, ISBN 0121820831; T.Palzkill, Proteomics, Kluwer Academic Publ, 2001, ISBN 0792375653; M.A.Vijayalakshmi, Biochromatography, Theory and Practice, Taylot & Francis Publ, 2002, ISBN 0415269032; J.S.Davies, Amino Acids, Peptides and Proteins Vol 32 2001, A Specialist Periodical Report, Royal Society of Chemistry, ISBN 0854042326; S.Roe, Protein Purification Techniques: A Practical Approach, 2nd Edn, Oxford University Press, 2001, ISBN 0199636737; T.Palmer, Enzymes, Biochemistry, Biotechnology, Clinical Chemistry, Horwood Publishing, 2001, ISBN 1898563780.

Brief general procedures for purifying DNA. Oligo-deoxyribonucleotides (up to ca 60-mers) are conveniently purified by HPLC (e.g. using a Bio-Rad MA7Q anion exchange column and a Rainin Instrument Co, Madison, Dynamax-300A C<sub>8</sub> matrix column) and used for a variety of molecular biology experiments. Plasmid and chromosomal DNA can be isolated by centrifugation in caesium chloride buffer (see section 1. centrifugation above), and then re-precipitated with 70% ethanol at -70° (18h), collected by centrifugation (microfuge) and dried in air before dissolving in TE (10mM TrisHCl, 1mM EDTA pH 8.0). The DNA is identified on an Agarose gel slab (0.5 to 1.0% DNA grade in 45mM Tris-borate + 1mM EDTA or 40mM Trisacetate + 1mM EDTA pH 8.0 buffers) containing ethidium bromide which binds to the DNA and under UV light causes it be visualised as pink fluorescent bands. Marker DNA (from  $\lambda$  phage DNA cut with the restriction enzymes Hind III and/or EcoRI ) are in a parallel track in order to estimate the size of the unknown DNA. The DNA can be isolated from their band on the gel by transfer onto a nitro-acetate paper (e.g. NA 45) electrophoretically, by binding to silica or an ion exchange resin, extracted from these adsorbents and precipitated with ethanol. The DNA pellet is then dissolved in TE buffer and its concentration determined. A solution of duplex DNA (or RNA) of 50µg/mL gives an absorbance of 1.0units at 260nm/1cm cuvette (single stranded DNA or RNA gives a value of 1.3 absorbance units). DNA obtained in this way is suitable for molecular cloning. For experimental details on the isolation, purification and manipulation of DNA and RNA the reader is referred to: J.Sambrook, E.F.Fritsch and T.Maniatis, Molecular Cloning - A Laboratory Manual, 2nd edn, (3 volumes), Cold Spring Harbor Laboratory Press, NY, 1989, ISBN 0879693096 (paperback); P.D.Darbre, Basic Molecular Biology: Essential Techniques, J.Wiley and Sons, 1998, ISBN 0471977055; J.Sambrook and D.W.Russell, Molecular Cloning - A Laboratory Manual, 3rd edn, (3 volumes), Cold Spring Harbor Laboratory Press, NY, 2001, ISBN 0079695773 (paperback), ISBN 0079695765 (cloth bound), also available on line; M.A.Vijayalakshmi, Biochromatography, Theory and Practice, Taylot & Francis Publ, 2002, ISBN 0415269032; A.Travers and M.Buckle, DNA-Protein Interactions: A Practical Approach, Oxford University Press, 2000, ISBN 0199636915 (paperback); R.Rapley and D.L.Manning eds RNA: Isolation and Characterisation Protocols, Humana Press 1998 ISBN 086034941; R.Rapley, The Nucleic Acid Protocols Handbook, Humana Press 2000 ISBN 0896038416 (paperback).

This chapter lists some representative examples of biochemicals and their origins, a brief indication of key techniques used in their purification, and literature references where further details may be found. Simpler low molecular weight compounds, particularly those that may have been prepared by chemical syntheses, e.g. acetic acid, glycine, will be found in Chapter 4. Only a small number of enzymes and proteins are included because of space limitations. The purification of some of the ones that have been included has been described only briefly. The reader is referred to comprehensive texts such as the *Methods Enzymol* (Academic Press) series which currently runs to more than 344 volumes and *The Enzymes* (3rd Edn, Academic Press) which runs to 22 volumes for methods of preparation and purification of proteins and enzymes. Leading references on proteins will be found in *Advances in Protein Chemistry* (59 volumes, Academic Press) and on enzymes will be found in *Advances in Enzymology* (72 volumes, then became *Advances in Enzymology and Related Area of Molecular Biology*, J Wiley & Sons). The *Annual Review of Biochemistry* (Annual Review Inc. Patlo Alto California) also is an excellent source of key references to the up-to-date information on known and new natural compounds, from small molecules, e.g. enzyme cofactors to proteins and nucleic acids.

Abbreviations of titles of periodical are defined as in the Chemical Abstracts Service Source Index (CASSI).

**Ionisation constants** of ionisable compounds are given as **pK** values (published from the literature) and refer to the **pKa** values at room temperature (~ 15°C to 25°C). The values at other temperatures are given as superscripts, e.g. **pK**<sup>25</sup> for 25°C. Estimated values are entered as **pK**<sub>Est(1)</sub>~ (see Chapter 1, p 6 for further information).

**Benzene**, which has been used as a solvent successfully and extensively in the past for reactions and purification by chromatography and crystallisation is now considered a **very dangerous substance** so it has to be used with extreme care. We emphasise that an alternative solvent to benzene (e.g. tolucne, toluene-petroleum ether, or a petroleum ether to name a few) should be used first. However, if benzene has to be used then all operations have to be performed in a well ventilated fumehood and precautions taken to avoid inhalation and contact with skin and eyes. Whenever benzene is mentioned in the text and asterisk e.g.  ${}^{*}C_{6}H_{6}$  or  ${}^{*}$  benzene, is inserted to remind the user that special precaution should be adopted.

Amino acids, carbohydrates and steroids not found below are in Chapter 4 (see also CAS Registry Numbers Index and General Index).

**Abrin A and Abrin B** [1393-62-0] M<sub>r</sub> 63,000-67,000. Toxic proteins from seeds of *Abras precatorius*. Purified by successive chromatography on DEAE-Sephadex A-50, carboxymethylcellulose, and DEAE-cellulose. [Wei et al. J Biol Chem 249 3061 1974.]

Acetoacetyl coenzyme A trisodium salt trihydrate [102029-52-7] M 955.6, pK<sub>1</sub> 4.0 (NH<sub>2</sub>), pK<sub>2</sub> 6.4 (PO<sub>4</sub><sup>-</sup>). The pH of solution (0.05g/mL H<sub>2</sub>O) is adjusted to 5 with 2N NaOH. This solution can be stored frozen for several weeks. Further purification can be carried out on a DEAE-cellulose formate column, then through a Dowex 50 (H<sup>+</sup>) column to remove Na ions, concentrated by lyophilisation and redissolved in H<sub>2</sub>O. Available as a soln of 0.05g/mL of H<sub>2</sub>O. The concn of acetoacetylcoenzyme A is determined by the method of Stern et al. J Biol Chem 221 15 1956. It is stable at pH 7-7.5 for several hours at 0° (half life ca 1-2h). At room temperature it is hydrolysed in ca 1-2h at pH 7-7.5. At pH 1.0/20° it is more stable than at neutrality. It is stable at pH 2-3/-17° for at least 6 months. [J Biol Chem 159 1961 1964; 242 3468 1967; Clikenbeard et al. J Biol Chem 250 3108 1975; J Am Chem Soc 75 2520 1953, 81 1265 1959; see Simon and Shemin J Am Chem Soc 75 2520 1953; Salem et al. Biochem J 258 563 1989.]

Acetobromo- $\alpha$ -D-galactose [3068-32-4] M 411.2, m 87°,  $[\alpha]_{546}^{20} + 255°$ ,  $[\alpha]_D^{20} + 210°$  (c 3, CHCl<sub>3</sub>). Purified as for the glucose analogue (see next entry). If the compound melts lower than 87° or is highly coloured then dissolve in CHCl<sub>3</sub> (*ca* 3 vols) and extract with H<sub>2</sub>O (2 vols), 5% aqueous NaHCO<sub>3</sub>, and again with H<sub>2</sub>O and dry over Na<sub>2</sub>SO<sub>4</sub>. Filter and evaporate in a vacuum. The partially crystalline solid or syrup is dissolved in dry Et<sub>2</sub>O (must be very dry) and recrystd by adding pet ether (b 40-60°) to give a white product. [McKellan and Horecker *Biochem Prep* 11 111 1960.]

Acetobromo- $\alpha$ -D-glucose [572-09-8] M 411.2, m 87-88°, 88-89°,  $[\alpha]_{546}^{20} + 230°$ ,  $[\alpha]_D^{20} + 195°$ (c 3, CHCl<sub>3</sub>). If nicely crystalline recryst from Et<sub>2</sub>O-pentane. Alternatively dissolve in diisopropyl ether (dried over CaCl<sub>2</sub> for 24hours, then over P<sub>2</sub>O<sub>5</sub> for 24hours) by shaking and warming (for as short a period as possible), filter warm. Cool to *ca* 45° then slowly to room temperature and finally at 5° for more than 2hours. Collect the solid, wash with cold dry diisopropyl ether and dry in a vacuum over Ca(OH)<sub>2</sub> and NaOH. Store dry in a desiccator in the dark. Solutions can be stabilised with 2% CaCO<sub>3</sub>. [Redemann and Niemann *Org Synth* 65 236 1987, Coll Vol III 11 1955.]

Acetoin dehydrogenase [from beef liver; acetoin NAD oxidoreductase] [9028-49-3]  $M_r$ 76000, [EC 1.1.1.5]. Purified via the acetone cake then Ca-phosphate gel filtration (unabsorbed), lyophilised and then fractionated through a DEAE-22 cellulose column. The Km for diacetyl in 40µM and for NADH it is 100µM in phosphate buffer at pH 6.1. [Burgos and Martin *Biochim Biophys Acta* 268 261 1972; 289 13 1972.]

(-)-3- $\beta$ -Acetoxy-5-etienic acid [3- $\beta$ -acetoxy-5-etiocholenic acid, androst-5-ene-17- $\beta$ -carboxylic acid] [51424-66-9] M 306.5, m 238-240°, 241-242°, 243-245°, 246-247°, [ $\alpha$ ]<sub>D</sub><sup>20</sup> -19.9° (c 1, Me<sub>2</sub>CO), -36° (c 1, Dioxane), -33.5° (CHCl<sub>3</sub>), pK<sub>Est</sub> ~ 4.7. It is purified by recrystn from Me<sub>2</sub>CO, Et<sub>2</sub>O-pentane, or AcOH, and dried in a vacuum oven (105°/20mm) and sublimed at high vacuum. [Staunton and Eisenbram Org Synth 42 4 1962; Steiger and Reichstein Helv Chim Acta 20 1404 1937.]

Acetylcarnitine chloride (2-acetoxy-3-carboxy-N,N,N-trimethylpropanamine HCl) [S(D +)-5080-50-2;  $R(L_{-})$ - 5061-35-8; RS 2504-11-2] M 239.7, m 181°, 197°(dec),  $[\alpha]_D^{25}$ -28° (c 2, H<sub>2</sub>O) for S-isomer, pK<sup>25</sup> 3.6. Recrystd from isopropanol. Dried over P<sub>2</sub>O<sub>5</sub> under high vacuum.

Acetylcholine bromide [66-23-9] M 226.1, m 143°, 146°. Hygroscopic solid but less than the hydrochloride salt. It crystd from EtOH as prisms. Some hydrolysis occurs in boiling EtOH particularly if it contains some  $H_2O$ . It can also be recryst from EtOH or MeOH by adding dry Et<sub>2</sub>O. [Acta Chem Scand 12 1492, 1497, 1502 1958.]

Acetylcholine chloride [60-31-1] M 181.7, m 148-150°, 151°. It is very sol in H<sub>2</sub>O (> 10%), and is very hygroscopic. If pasty, dry in a vacuum desiccator over H<sub>2</sub>SO<sub>4</sub> until a solid residue is obtained. Dissolve in abs EtOH, filter and add dry Et<sub>2</sub>O and the hydrochloride separates. Collect by filtration and store under very dry conditions. [J Am Chem Soc 52 310 1930.] The chloroplatinate crystallises from hot H<sub>2</sub>O in yellow needles and can be recrystd from 50% EtOH, m 242-244° [Biochem J 23 1069 1929], other m given is 256-257°. The perchlorate crystallises from EtOH as prisms m 116-117°. [J Am Pharm Assocn 36 272 1947.]

 $N^4$ -Acetylcytosine [14631-20-0] M 153.1, m >300°, 326-328°, pK<sub>Est(1)</sub> ~1.7, pK<sub>Est(2)</sub> ~10.0. If TLC or paper chromatography show that it contains unacetylated cytosine then reflux in Ac<sub>2</sub>O for 4h, cool at 3-4° for a few days, collect the crystals, wash with cold H<sub>2</sub>O, then EtOH and dry at 100°. It is insoluble in EtOH and difficulty soluble in H<sub>2</sub>O but crystallises in prisms from hot H<sub>2</sub>O. It is hydrolysed by 80% aq AcOH at 100°/1h. [Am Chem J 29 500 1903; UV: J Chem Soc 2384 1956; J Am Chem Soc 80 5164 1958.] It forms an Hg salt [J Am Chem Soc 79 5060 1957].

 $\beta$ -D-N-Acetylglucosaminidase [from M sexta insects] [9012-33-3] M<sub>r</sub> ~61,000, [EC 3.2.1.52]. Purified by chromatography on DEAD-Biogel, hydroxylapatite chromatography and gel filtration through Sephacryl S200. Two isoforms: a hexosaminidase EI with Km 177 $\mu$ M ( $V_{max}$  328 sec<sup>-1</sup>) and EII a chitinase with Km 160 $\mu$ M ( $V_{max}$  103 sec<sup>-1</sup>) with 4-nitrophenyl- $\beta$ -acetylglucosamine as substrate. [Dziadil-Turner Arch Biochem Biophys 212 546 1981.]

 $\beta$ -D-N-Acetylhexosaminidase A and B (from human placenta) [9012-33-3] M<sub>r</sub> ~61,000, [EC 3.2.1.52]. Purified by Sephadex G-200 filtration and DEAE-cellulose column chromatography. Hexosaminidase A was further purified by DEAE-cellulose column chromatography, followed by an ECTEOLA-cellulose column, Sephadex-200 filtration, electrofocusing and Sephadex G-200 filtration. Hexosaminidase B was purified by a CM-cellulose column, electrofocusing and Sephadex G-200 filtration. [Srivastava et al. J Biol Chem 249 2034 1974.]

N-Acetyl-D-lactosamine [2-acetylamino-O- $\beta$ -D-lactopyranosyl-2-deoxy-D-glucose] [32181-59-2] M 383.4, m 169-171°, 170-171°,  $[\alpha]_D^{18}$ +51.5°  $\rightarrow$  +28.8° (in 3h, c 1, H<sub>2</sub>O]. Purified by recrystn from MeOH (with 1 mol of MeOH) or from H<sub>2</sub>O. It is available as a soln of 0.5g /mL of H<sub>2</sub>O. [Zilliken J Biol Chem 271 181 1955.]

**O-Acetyl-\beta-methylcholine chloride** [Methacholine chloride, Amechol, Provocholine, 2acetoxypropyl-ammonium chloride] [62-51-1] M 195.7, m 170-173°, 172-173°. It forms white hygroscopic needles from Et<sub>2</sub>O and is soluble in H<sub>2</sub>O, EtOH and CHCl<sub>3</sub>. It decomposes readily in alkaline solns and slowly in H<sub>2</sub>O. It should be handled and stored in a dry atmosphere. The bromide is less hygroscopic and the *picrate* has m 129.5-131° (from EtOH). [racemate: Annis and Ely *Biochem J* 53 34 1953; IR of iodide: Hansen Acta Chem Scand 13 155 1959.]

*N*-Acetyl muramic acid [NAMA, *R*-2-(acetylamino)-3-*O*-(1-carboxyethyl)-2-deoxy-D-glucose] [10597-89-4] M 292.3, m ~125°(dec),  $[\alpha]_D^{20}$ +41.2° (c 1.5, H<sub>2</sub>O, after 24h), pK<sub>Est</sub> ~ 3.6. See muramic acid below.

N-Acetyl neuraminic acid (NANA, O-Sialic acid, 5-acetamido-3,5-dideoxy-D-glycero-Dglacto-2-nonulosonic acid, lactaminic acid) [131-48-6] M 309.3, m 159°(dec), 181-183°(dec), 185-187°(dec),  $[\alpha]_D^{25}$ -33° (c 2, H<sub>2</sub>O, l 2), pK 2.6. A Dowex-1x8 (200-400 mesh) in the formate form was used, and was prepd by washing with 0.1M NaOH, then 2N sodium formate, excess formate was removed by washing with H<sub>2</sub>O. N-Acetyl neuraminic acid in H<sub>2</sub>O is applied to this column, washed with H<sub>2</sub>O, then eluted with 2N formic acid at a flow rate of 1mL/min. Fractions (20mL) were collected and tested (Bial's orcinol reagent, cf Biochem Prep 7 1 1959). NANA eluted at formic acid molarity of 0.38 and the Bial positive fractions are collected and lyophilised. The residue is recrystd from aqueous AcOH: Suspend 1.35g of residue in AcOH, heat rapidly to boiling, add H<sub>2</sub>O dropwise until the suspension dissolves (do not add excess  $H_2O$ , filter hot and then keep at +5° for several hours until crystn is complete. Collect and dry in a vacuum over P<sub>2</sub>O<sub>5</sub>. Alternatively dissolve 1.35g of NANA in 14mL of H<sub>2</sub>O, filter, add 160mL of MeOH followed by 360mL of Et<sub>2</sub>O. Then add pet ether (b 40-60°) until heavy turbidity. Cool at 20° overnight. Yield of NANA is ca 1.3g. Dry over P<sub>2</sub>O<sub>5</sub> at 1mm vacuum and 100° to constant weight. It mutarotates in Me<sub>2</sub>SO:  $[\alpha]_{D}^{20}$  -115° (after 7min) to -32° (after 24h). It is available as aqueous soln (0.01g/mL). [IR and synthesis: Cornforth et al. Biochem J 68 57 1958; Zillikin and O'Brien Biochem Prep 7 1 1960; <sup>13</sup>C NMR and 1-13C synthesis: Nguyen, Perry J Org Chem 43 551 1978; Danishevski, DeNinno J Org Chem 51 2615 1986; Gottschalk, The Chemistry and Biology of Sialic Acids and Related Substances, Cambridge University Press, London, 1960.]

N-Acetyl neuraminic acid aldolase [from Clostridium perfringens, N-acetylneuraminic acid pyruvate lyase] [9027-60-5]  $M_r$  32,000 [EC 4.1.3.3]. Purified by extraction with H<sub>2</sub>O, protamine pptn, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pptn, Me<sub>2</sub>CO pptn, acid treatment at pH 5.7 and pptn at pH 4.5. The equilibrium constant for pyruvate + n-acetyl-D-mannosamine N-acetylneuraminidate at 37° is 0.64. The Km for Nacetylneuraminic acid is 3.9mM in phosphate at pH 7.2 and 37°. [Comb and Roseman Methods Enzymol 5 391 1962.] The enzyme from Hogg kidney (cortex) has been purified 1700 fold by extraction with H<sub>2</sub>O, protamine sulfate pptn, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pptn, heating between 60-80°, a second (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pptn and starch gel electrophoresis. The Km for N-acetylneuraminic acid is 1.5mM. [Brunetti et al. J Biol Chem 237 2447 1962.]

*N*-Acetyl penicillamine [D- 15537-71-0, DL-59-53-0] M 191.3, m 183°, 186-187° (DL-form), 189-190° (D-form), D-form  $[\alpha]_D^{25}$  +18° (c 1, 50% EtOH), pK<sub>Est(1)</sub>~3.0 (CO<sub>2</sub>H), pK<sub>Est(2)</sub>~ 8.0 (SH). Both forms are recrystd from hot H<sub>2</sub>O. A pure sample of the D-form was obtained after five recrystns. [Crooks in *The Chemistry of Penicillin* Clarke, Johnson and Robinson eds, Princeton University Press, 470 1949.]

*p*-Acetylphenyl sulfate potassium salt, [38533-41-4] M 254.3, m dec on heating, pK<sub>Est</sub> ~2,1. Purified by dissolving in the minimum vol of hot water (60°) and adding EtOH, with stirring, then left at 0° for 1h. Crystals were filtd off and recrystd from H<sub>2</sub>O until free of Cl and SO<sub>4</sub><sup>2-</sup> ions. Dried in a vac over P<sub>2</sub>O<sub>5</sub> at room temperature. It is a specific substrate for arylsulfatases which hydrolyse it to *p*-acetylphenol [ $\lambda$ max 327nm ( $\epsilon$  21700 M<sup>-1</sup>cm<sup>-1</sup>)] [Milsom et al. *Biochem J* 128 331 1972].

S-Acetylthiocholine bromide [25025-59-6] M 242.2, m 217-223°(dec). It is a hygroscopic solid which can be recrystd from ligroin-EtOH (1:1), dried and kept in a vacuum desiccator. Crystn from  ${}^{*}C_{6}H_{6}$ -EtOH gave m 227° or from propan-1-ol the m was 213°. [Acta Chem Scand 11 537 1957, 12 1481 1958.]

**S-Acetylthiocholine chloride** [6050-81-3] **M 197.7, m 172-173°** The chloride can be purified in the same way as the bromide, and it can be prepared from the iodide. A few milligrams dissolved in H<sub>2</sub>O can be purified by applying onto a Dowex-1 Cl<sup>-</sup> resin column (prepared by washing with N HCl followed by  $CO_3^{2-}$  free H<sub>2</sub>O until the pH is 5.8). After equilibration for 10min elution is started with  $CO_3^{2-}$  free distilled H<sub>2</sub>O and

### **Purification of Biochemicals and Related Products**

3mL fractions are collected and their OD at 229nm measured. The fractions with appreciable absorption are pooled and lyophilised at  $0.5^{\circ}$ . Note that at higher temps decomposition of the ester is appreciable; hydrolysis is appreciable at pH >10.5/20°. The residue is dried *in vacuo* over P<sub>2</sub>O<sub>5</sub>, checked for traces of iodine (conc H<sub>2</sub>SO<sub>4</sub> and heat, violet vapours are released), and recrystd from propan-1-ol. [*Clin Chim Acta* 2 316 1957.]

S-Acetylthiocholine iodide [1866-15-5] M 289.2, m 203-204°, 204°, 204-205°. Recrystd from propan-1-ol (or *iso*-PrOH, or EtOH/Et<sub>2</sub>O) until almost colourless and dried in a vacuum desiccator over  $P_2O_5$ . Solubility in  $H_2O$  is 1% w/v. A 0.075M (21.7mg/mL) solution in 0.1M phosphate buffer pH 8.0 is stable for 10-15 days if kept refrigerated. Store away from light. It is available as a 1% soln in  $H_2O$ . [Biochemical Pharmacology 7, 88 1961; IR: Hansen Acta Chem Scand 13 151 1959, 11 537 1957; Clin Chim Acta 2 316 1957; Zh Obshch Khim 22 267 1952.]

Actinomycin C (Cactinomycin) [8052-16-2] M ~1255. (A commercial mixture of Actinomycin C<sub>1</sub> ~5%, C<sub>2</sub>~30% and C<sub>3</sub>~65%). Actinimycin C<sub>1</sub> (native) crysts from EtOAc as red crystals, is sol in CHCl<sub>3</sub>, \*C<sub>6</sub>H<sub>6</sub> and Me<sub>2</sub>CO and has m 246-247°(dec),  $[\alpha]_D^{20}$ -328° (0.22, MeOH) and  $\lambda_{max}$  443nm ( $\epsilon$  25,000) and 240nm ( $\epsilon$  34,000). Actinimycin C<sub>2</sub> (native) crysts as red needles from EtOAc and has m 244-246°(dec),  $[\alpha]_D^{20}$ -325° (c 0.2, MeOH),  $\lambda_{max}$  443nm ( $\epsilon$  25,300) and ( $\epsilon$  33,400). Actinimycin C<sub>3</sub> (native) recryst from cyclohexane, or \*C<sub>6</sub>H<sub>6</sub>/MeOH/cyclohexane as red needles m 238-241° (dec),  $[\alpha]_D^{20}$ -321° (c 0.2, MeOH),  $\lambda_{max}$  443nm ( $\epsilon$  23,300). [Brockman and Lackner, Chem Ber 101 1312 1968.] It is light sensitive.

Actinomycin D (Dactinomycin) [50-76-0] M 1255.5, m 241-243°(dec),  $[\alpha]_D^{22}$ -296° (c 0.22, MeOH). Crystallises as bright red rhombic crystals from absolute EtOH or from MeOH-EtOH (1:3). It will also crystallise from EtOAc-cyclohexane (m 246-247° dec), CHCl<sub>3</sub>-pet ether (m 245-246° dec), and EtOAc-MeOH-\*C<sub>6</sub>H<sub>6</sub> (m 241-243° dec). Its solubility in MeCN is 1mg/mL.  $[\alpha]_D^{20}$  varies from -296° to -327° (c 0.2, MeOH).  $\lambda_{max}$  (MeOH) 445, 240nm (log  $\varepsilon$  4.43, 4.49),  $\lambda_{max}$  (MeOH, 10N HCl, 1:1) 477nm (log  $\varepsilon$  4.21) and  $\lambda_{max}$  (MeOH, 0.1N NaOH) 458, 344, 285 (log  $\varepsilon$  3.05, 4.28, 4.13). It is *HIGHLY* TOXIC, light sensitive and antineoplastic. [Bullock and Johnson, *J Chem Soc* 3280 1957.]

Acyl-coenzyme A Synthase [from beef liver] [9013-18-7] M<sub>r</sub> 57,000, [EC 6.2.1.2]. Purified by extraction with sucrose-HCO<sub>3</sub> buffer, protamine sulfate pptn, (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (66-65%) pptn at pH 4.35 and a second (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (35-60%) pptn at pH 4.35. It has Km 0.15mM (V<sub>rel</sub> 1.0) for octanoate; 0.41mM (V<sub>rel</sub> 2.37) for heptanoate and 1.59mM (V<sub>rel</sub> 0.63). Km for ATP is 0.5mM all at pH 9.0 in ethylene glycol buffer at 38°. [Jencks et al. J Biol Chem 204 453 1953; Methods Enzymol 5 467 1962.]

Acyl-coenzyme A Synthase (from yeast) [9012-31-1] [EC 6.2.1.1]. This enzyme has been purified by extraction into phosphate buffer pH 6.8-7.0 containing 2-mercaptoethanol and EDTA, protamine sulfate pptn, polyethylene glycol fractionation, Alumina  $\gamma$  gel filtration, concentration by (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pptn, Bio-Gel A-0.5m chromatography and DEAE-cellulose gradient chromatography. It has M<sub>r</sub> ~151,000, Km (apparent) 0.24mM (for acetate) and 0.035mM (for CoA); 1.2 mM (for ATP) and Mg<sup>2+</sup> 4.0mM. [Frenkel and Kitchens *Methods Enzymol* **71** 317 1981.]

Adenosine-5'-diphosphate [adenosine-5'-pyrophosphate, ADP] [58-64-0] M 427.2,  $[\alpha]_D^{25}$ -25.7° (c 2, H<sub>2</sub>O),  $pK_1^{25} < 2$  (PO<sub>4</sub>H),  $pK_2^{25} < 2$  (PO<sub>4</sub>H),  $pK_3^{25}$  3.95 (NH<sub>2</sub>),  $pK_4^{25}$  6.26 (PO<sub>4</sub>H). Characterised by conversion to the *acridine salt* by addition of alcoholic acridine (1.1g in 50mL), filtering off the yellow salt and recrystallising from H<sub>2</sub>O. The salt has m 215°(dec),  $\lambda_{max}$  259nm ( $\epsilon$  15,400) in H<sub>2</sub>O. [Baddiley and Todd J Chem Soc 648 1947, 582 1949, cf LePage Biochem Prep 1 1 1949; Martell and Schwarzenbach Helv Chim Acta 39 653 1956].

Adenosine-3'-monophosphoric acid hydrate [3'-adenylic acid, 3'-AMP] [84-21-9] M 347.3, m 197°(dec, as  $2H_2O$ ), 210°(dec), m 210°(dec),  $[\alpha]_{546}$  -50° (c 0.5, 0.5M Na<sub>2</sub>HPO<sub>4</sub>), pK<sub>1</sub><sup>25</sup> 3.65, pK<sub>2</sub><sup>25</sup> 6.05. It crystallises from large volumes of H<sub>2</sub>O in needles as the monohydrate, but is not very soluble in boiling H<sub>2</sub>O. Under acidic conditions it forms an equilibrium mixture of 2' and 3' adenylic acids *via* the 2',3'-cyclic phosphate. When heated with 20% HCl it gives a quantitative yield of furfural after 3hours, unlike 5'-adenylic acid which only gives traces of furfural. The yellow *monoacridine salt* has m 175°(dec) and

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the diacridine salt has m 177° (225°)(dec). [Brown and Todd J Chem Soc 44 1952; Takaku et al. Chem Pharm Bull Jpn 21 1844 1973; NMR: Ts'O et al. Biochemistry 8 997 1969.]

Adenosine-5'-monophosphoric acid monohydrate [5'-adenylic acid, 5'-AMP] [18422-05-4] M 365.2, m 178°, 196-200°, 200° (sintering at 181°),  $[\alpha]_D^{20}$  -47.5°,  $[\alpha]_{546}$  -56° (c 2, in 2% NaOH), -26.0° (c 2, 10% HCl), -38° (c 1, 0.5M Na<sub>2</sub>HPO<sub>4</sub>), pK<sub>1</sub><sup>25</sup> 3.89, pK<sub>2</sub><sup>25</sup> 6.14, pK<sub>3</sub><sup>25</sup> 13.1. It has been recrystd from H<sub>2</sub>O (fine needles) and is freely soluble in boiling H<sub>2</sub>O. Crysts also from H<sub>2</sub>O by addition of acetone. Purified by chromatography on Dowex 1 (in formate form), eluting with 0.25M formic acid. It was then adsorbed onto charcoal (which had been boiled for 15min with M HCl, washed free of chloride and dried at 100°), and recovered by stirring three times with isoamyl alcohol/H<sub>2</sub>O (1:9 v/v). The aqueous layer from the combined extracts was evaporated to dryness under reduced pressure, and the product was crystallised twice from hot H<sub>2</sub>O. [Morrison and Doherty *Biochem J* 79 433 1961]. It has  $\lambda_{max}$  259nm ( $\varepsilon$ 15,400) in H<sub>2</sub>O at pH 7.0. [Alberty et al. J Biol Chem 193 425 1951; Martell and Schwarzenbach Helv Chim Acta 39 653 1956]. The acridinium salt has m 208° [Baddiley and Todd J Chem Soc 648 1947; Pettit Synthetic Nucleotides, van Nostrand-Reinhold, NY, Vol 1 252 1972; NMR: Sarma et al. J Am Chem Soc 96 7337 1974; Norton et al. J Am Chem Soc 98 1007 1976; IR of diNa salt: Miles Biochem Biophys Acta 27 324 1958].

Adenosine 5"-[ $\beta$ -thio]diphosphate tri-lithium salt [73536-95-5] M 461.1. Purified by ionexchange chromatography on DEAE-Sephadex A-25 using gradient elution with 0.1-0.5M triethylammonium bicarbonate. [Biochem Biophys Acta 276 155 1972.]

Adenosine 5"-[ $\alpha$ -thio]monophosphate di-lithium salt [19341-57-2] M 375.2. Purified as for the diNa salt [Murray and Atkinson *Biochemistry* 7 4023 1968]. Dissolve 0.3g in dry MeOH (7mL) and M LiI (6mL) in dry Me<sub>2</sub>CO containing 1% of mercaptoethanol and the Li salt is ppted by adding Me<sub>2</sub>CO (75mL). The residue is washed with Me<sub>2</sub>CO (4 x 30mL) and dried at 55°/25mm.  $\lambda_{max}$  (HCl, pH 1.2) 257nm ( $\epsilon$ 14,800); (0.015M NaOAc, pH 4.8) 259nm ( $\epsilon$  14,800); and (0.015M NH<sub>4</sub>OH, pH 10.1) 259nm ( $\epsilon$  15,300).

Adenosine-5'-triphosphate (ATP) [56-65-5] M 507.2,  $[\alpha]_{546}$  -35.5 (c 1, 0.5 M Na<sub>2</sub>HPO<sub>4</sub>), pK<sub>1</sub><sup>25</sup> 4.00, pK<sub>2</sub><sup>25</sup> 6.48. Ppted as its barium salt when excess barium acetate soln was added to a 5% soln of ATP in water. After filtering off, the ppte was washed with distd water, redissolved in 0.2M HNO<sub>3</sub>, and again pptd with barium acetate. The ppte, after several washings with distd water, was dissolved in 0.2M HNO<sub>3</sub> and again slightly more 0.2M H<sub>2</sub>SO<sub>4</sub> than was needed to ppte all the barium as BaSO<sub>4</sub>, was added. After filtering off the BaSO<sub>4</sub>, the ATP was ppted by addition of a large excess of 95% ethanol, filtered off, washed several times with 100% EtOH and finally with dry diethyl ether. [Kashiwagi and Rabinovitch J Phys Chem 59 498 1955.]

S-(5'-Adenosyl)-L-homosysteine [979-92-0] M 384.4, m 202°(dec), 204°(dec), 205-207°(dec),  $[\alpha]_D^{25} + 93°$  (c 1, 0.2N HCl),  $[\alpha]_D^{23} + 44°$  (c 0.1, 0.05N HCl), (pK see SAM hydrochloride below). It has been recrystd several times from aqueous EtOH or H<sub>2</sub>O to give small prisms and has  $\lambda_{max}$  260nm in H<sub>2</sub>O. The *picrate* has m 170°(dec) from H<sub>2</sub>O. [Baddiley and Jameison J Chem Soc 1085 1955; de la Haba and Cantoni J Biol Chem 234 603 1959; Borchardt et al. J Org Chem 41 565 1976; NMR: Follmann et al. Eur J Biochem 47 187 1974.]

(-)-S-Adenosyl-L-methionine chloride (SAM hydrochloride) [24346-00-7] M 439.9, pK<sub>Est(1)</sub>~ 2.13, pK<sub>Est(2)</sub>~ 4.12, pK<sub>Est(3)</sub>~ 9.28. Purified by ion exchange on Amberlite IRC-150, and eluting with 0.1-4M HCl. [Stolowitz and Minch J Am Chem Soc 103 6015 1981.] It has been isolated as the trireineckate salt by adding 2 volumes of 1% solution of ammonium reineckate in 2% perchloric acid. The reineckate salt separates at once but is kept at 2° overnight. The salt is collected on a sintered glass funnel, washed with 0.5% of ammonium reineckate, dried (all operations at 2°) and stored at 2°. To obtain adenosylmethionine, the reineckate is dissolved in a small volume of methyl ethyl ketone and centrifuged at room temp to remove a small amount of solid. The clear dark red supernatant is extracted (in a separating funnel) with a slight excess of 0.1 N H<sub>2</sub>SO<sub>4</sub>. The aqueous phase is re-extracted with fresh methyl ethyl ketone until it is colourless. [Note that reineckates have UV absorption at 305nm ( $\epsilon$  15,000), and the optical density at 305nm is used to detect the presence of reineckate ions.] Methyl ethyl ketone is removed from the aqueous layer containing adenosylmethionine sulfate, the pH is adjusted to 5.6-6.0 and extracted with two volumes of Et<sub>2</sub>O. The *sulfate* is obtained by evaporating the aqueous layer in *vacuo*. The *hydrochloride* can be obtained in the same way but using HCl instead of  $H_2SO_4$ . SAM-HCl has a solubility of 10% in  $H_2O$ . The salts are stable in the cold at pH 4-6 but decompose in alkaline media. [Cantoni *Biochem Prep* 5 58 1957.] The purity of SAM can be determined by paper chromatography [Cantoni *J Biol Chem* 204 403 1953; *Methods Enzymol* 3 601 1957], and electrophoretic methods or enzymic analysis [Cantoni and Vignos J Biol Chem 209 647 1954].

L-Adrenaline [L-epinephrine, L(-)-(3,4-dihydroxyphenyl)-2-methylaminoethanol] [51-43-4] M 183.2, m 210°(dec), 211°(dec), 211-212°(dec), 215°(dec),  $[\alpha]$ \s(20,D) -52° (c 2, 5% HCl), pK<sub>1</sub><sup>25</sup> 8.88, pK<sub>2</sub><sup>25</sup> 9.90, pK<sub>3</sub><sup>25</sup> 12.0. It has been recrystd from EtOH + AcOH + NH<sub>3</sub> [Jensen J Am Chem Soc 57 1765 1935]. It is sparingly soluble in H<sub>2</sub>O, readily in acidic or basic solns but insoluble in aqueous NH<sub>3</sub>, alkali carbonate solns, EtOH, CHCl<sub>3</sub>, Et<sub>2</sub>O or Me<sub>2</sub>CO. It is readily oxidised in air and turns brown on exposure to light and air. Store in the dark under N<sub>2</sub>. Its pKa values in H<sub>2</sub>O are 8.88 and 9.90 [Lewis Br J Pharmacol Chemother 9 488 1954]. The hydrogen oxalate salt has m 191-192°(dec, evac capillary) after recrystn from H<sub>2</sub>O or EtOH [Pickholz J Chem Soc 928 1945].

Adrenolone hydrochloride [3',4'-dihydroxy-2-methylaminoacetophenone hydrochloride] [62-13-5] M 217.7, m 244-249°(dec), 248°(dec), 256°(dec), pK 5.5. It was purified by recrystn from EtOH or aqueous EtOH. [Gero J Org Chem 16 1222 1951; Kindler and Peschke Arch Pharm 269 581, 603 1931.]

ADP-Ribosyl transferase (from human placenta) [9026-30-6]. Purified by making an affinity absorbent for ADP-ribosyltransferase by coupling 3-aminobenzamide to Sepharose 4B. [Burtscher et al. Anal Biochem 152 285 1986.]

Agglutinin (from peanuts) [Arachis hypogaea] [1393-62-0]  $M_r$  134,900 (tetramer). Purified by affinity chromatography on Sepharose- $\zeta$ -aminocaproyl- $\beta$ -D-galactopyranosylamine. [Lotan et al. J Biol Chem 250 8518 1974.]

Alamethicin (from Tricoderma viridae). [27061-78-5] M 1964.3, m 259-260°, 275-270°,  $[\alpha]_D^{2^2}$ -45° (c 1.2, EtOH), pK 6.04 (aq EtOH). Recrystd from MeOH. [Panday et al. J Am Chem Soc 99 8469 1977.] The acetate [64918-47-4] has m 195-180° from MeOH/Et<sub>2</sub>O and the acetate-methyl ester [64936-53-4] has m 145-140° from aq MeOH.

Albumin (bovine and human serum) [9048-46-8 (bovine); 70024-90-7 (human)]  $M_r \sim 67,000$  (bovine), 69 000 (human), UV:  $A_{280nm}$  6.6 (bovine) and 5.3 (human) in H<sub>2</sub>O,  $[\alpha]_{546}^{25}$  -78.2° (H<sub>2</sub>O). Purified by soln in conductivity water and passage at 2-4° through two ion-exchange columns, each containing a 2:1 mixture of anionic and cationic resins (Amberlite IR-120, H-form; Amberlite IRA-400, OH-form). This treatment removed ions and lipid impurities. Care was taken to exclude CO<sub>2</sub>, and the soln was stored at -15°. [Möller, van Os and Overbeek *Trans Faraday Soc* 57 312 1961.] More complete lipid removal was achieved by lyophilising the de-ionised soln, covering the dried albumin (human serum) with a mixture of 5% glacial acetic acid (v/v) in iso-octane (previously dried with Na<sub>2</sub>SO<sub>4</sub>) and allowing to stand at 0° (without agitation) for upwards of 6h before decanting and discarding the extraction mixture, washing with iso-octane, re-extracting, and finally washing twice with iso-octane. The purified albumin was dried under vacuum for several hours, then dialyzed against water for 12-24h at room temperature, lyophilised, and stored at -10°C [Goodman *Science* 125 1296 1957]. It has be recrystd in high (35%) and in low (22%) EtOH solutions from Cohn's Fraction V.

The high EtOH recrystn was as follows: To 1 Kg of Fraction V albumin paste at  $-5^{\circ}$  was added 300mL of 0.4 M pH (pH 5.5) acetate buffer in 35% EtOH pre-cooled to  $-10^{\circ}$  and 430 mL of 0.1 M NaOAc in 25% EtOH also at  $-10^{\circ}$ . Best results were obtained by adding all of the buffer and about half of the NaOAc and stirring slowly for 1hour. The rest of the NaOAc was added when all the lumps had disintegrated. The mixture was set aside at  $-5^{\circ}$  for several days to crystallise. 35% EtOH (1 L) was then added to dilute the crystalline suspension and lower the ionic strength prior to centrifugation at  $-5^{\circ}$  (yield 80%). The crystals were further dissolved in 1.5 volumes of 15% EtOH-0.02M NaCl at  $-5^{\circ}$  and clarified by filtration through washed, calcined diatomaceous earth. This soln may be recrystd by re-adjusting to the conditions in the first crystallisation, or it may be recrystd at 22% EtOH with the aid of a very small amount of decanol (enough to give a final concn of 0.02%).

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Note that crystn from lower EtOH gave better purification (i.e. by removing globulins and carbohydrates) and producing a more stable product.

The low EtOH recrystn was as follows: To 1 Kg of Fraction V at -10° to -15° was added 500mL of 15% EtOH at -5°, stirred slowly until a uniform suspension was formed. 15% EtOH (500mL) and sufficient 0.2M NaHCO<sub>3</sub> soln at 0° to bring the pH (1:10 diln) to 5.3. This required 125-150mL. Some temp rise occurs and care must be taken to keep the temp  $< -5^{\circ}$ . If the albumin is incompletely dissolved a small amount of H<sub>2</sub>O was added (100mL at a time at 0°, allowing 15min between additions). Undissolved albumin can be easily distinguished from small amounts of undissolved globulins, or as the last albumin dissolves, the appearance of the soln changes from milky white to hazy grey-green in colour. Keep the soln at -5° for 12h and filter by suspending in 15g of washed fine calcined diatomaceous earth, and thus filtering using a Büchner funnel precoated with coarser diatomaceous earth. The filtrate may require two or more similar filtrations to give a clear soln. To crystallise the filtrate add through a capillary pipette, and with careful stirring, 1/100volume of a soln containing 10% decanol and 60% EtOH (at -10°), and seeded with the needle-type albumin crystals. After 2-3 days crystn is complete. The crystals are centrifuged off. These are suspended with gentle mechanical stirring in one third their weight of 0.005 M NaCl pre-cooled to  $0^{\circ}$ . With careful stirring, H<sub>2</sub>O (at  $0^{\circ}$ ) is added slowly in an amount equal to 1.7 times the weight of the crystals. At this stage there is about 7% EtOH and the temp cannot be made lower than -2.5° to -1°. Clarify and collect as above. [Cohn et al. J Am Chem Soc 69 1753 1947.1

Human serum albumin has been purified similarly with 25% EtOH and 0.2% decanol. The isoelectric points of bovine and human serum albumins are 5.1 and 4.9.

Amethopterin (Methotrexate, 4-amino-4-deoxy- $N^{10}$ -methylpteroyl-L-glutamic acid) [59-05-2] M 454.4, m 185-204°(dec),  $[\alpha]_D^{20} + 19°$  (c 2, 0.1N aq NaOH), pK<sub>1</sub> <0.5 (pyrimidine<sup>2+</sup>), pK<sub>2</sub> 2.5 (N5-Me<sup>+</sup>), pK<sub>3</sub> 3.49 ( $\alpha$ -CO<sub>2</sub>H), pK<sub>4</sub> 4.99 ( $\gamma$ -CO<sub>2</sub>H), pK<sub>5</sub> 5.50 (pyrimidine<sup>+</sup>). Commonest impurities are 10-methyl pteroylglutamic acid, 4-amino-10-methylpteroylglutamic acid, aminopterin and pteroylglutamic acid. Purified by chromatography on Dowex-1 acetate, followed by filtration through a mixture of cellulose and charcoal. It has been recrystd from aqueous HCl or by dissolution in the minimum volume of N NaOH and acidified until pptn is complete, filter or collect by centrifugation, wash with H<sub>2</sub>O (also by centrifugation) and dry at 100°/3mm. It has UV  $\lambda_{max}$  at 244 and 307nm ( $\epsilon$  17300 and 19700) in H<sub>2</sub>O at pH 1; 257, 302 and 370nm ( $\epsilon$  23000, 22000 and 7100) in H<sub>2</sub>O at pH 13. [Momle Biochem Prep 8 20 1961; Seeger et al. J Am Chem Soc 71 1753 1949.] It is a potent inhibitor of dihydrofolate reductase and used in cancer chemotherapy. [Blakley *The Biochemistry of Folic Acid and Related Pteridines* (North-Holland Publ Co., Amsterdam, NY) pp157-163 1969.] It is CARCINOGENIC, HANDLE WITH EXTREME CARE.

 $\alpha$ -Amino acids. All the  $\alpha$ -amino acids 'natural' configuration [S (L), except for cysteine which is R(L)] at the  $\alpha$ - carbon atom are available commercially in a very high state of purity. Many of the 'non-natural'  $\alpha$ amino acids with the [R(D)] configuration as well as racemic mixtures are also available and generally none require further purification before use unless they are of "Technical Grade'. The R or S enantiomers are optically active except for glycine which has two hydrogen atoms on the  $\alpha$ - carbon atom, but these are prochiral and enzymes or proteins do distinguish between them, e.g. serine hydroxymethyltransferase successfully replaces the pro- $\alpha$ - hydrogen atom of glycine with CH<sub>2</sub>OH (from formaldehyde) to make S-serine. The twenty common natural  $\alpha$ -amino acids are: **amino acid**, three letter abbreviation, one letter abbreviation, pK (-COOH) and pK (-NH<sub>3</sub><sup>+</sup>): Alanine, Ala, A, 2.34, 9.69; Arginine, Arg, R, 2.17, 9.04; Asparagine, Asn, N, 2.01, 8.80; Aspartic acid, Asp, D, 1.89, 9.60; Cysteine, Cys, C, 1.96, 8.18; Glutamine, Gln, Q, 2.17, 9.13; Glutamic acid, Glu, E, 2.19, 9.67; Glycine, Gly, G, 2.34, 9.60; Histidine, His, H, 1.8, 9.17; Isoleucine, Ile, I, 2.35, 9.68; Leucine, Leu, L, 2.36, 9.60; Lysine, Lys, K, 2.18, 8.95; Methionine, Met, M, 2.28, 9.20; Phenylalanine, Phe, F, 1.83, 9.12; Proline, Pro, P, 1.99, 10.96; Serine, Ser, S, 2.21, 9.15; Threonine, Thr, T, 2.11, 9.62; Tryptophan, Trp, W, 2.38, 9.39; Tyrosine, Tyr, Y, 2.2, 9.11, Valine, Val, V, 2.32, 9.61 repectively. Technical grade amino acids can be purified on ion exchange resins (e.g. Dowex 50W and eluting with a gradient of HCl or AcOH) and the purity is checked by TLC in two dimensions and stained with ninhydrin. (J.P.Greenstein and M.Winitz, Chemistry of the Amino Acids (3 Volumes), J.Wiley & Sons, NY, 1961; C.Cooper, N.Packer and K.Williams, Amino Acid Analysis Protocols, Humana Press, 2001, ISBN 0896036561). Recently codons for a further two amino acids have been discovered which are involved in ribosome-mediated protein synthesis giving proteins containing these amino acids. The amino acids are R(L)-selenocysteine [Stadtman Ann Rev Biochem 65 83 1996] and pyrrolysine [(4R, 5R)-4-substituted (with Me, NH<sub>2</sub> or OH) pyrroline-5-carboxylic acid] [Krzychi and Chan et al. Science 296 1459 and 1462 2002.] They are, however, rare at present and only found in a few microorganisms.

**9-Aminoacridine hydrochloride monohydrate (Acramine yellow, Monacrin)** [52417-22-8] M **248.7, m** >355°,  $pK_1^{20}$  **4.7,**  $pK_2^{20}$  **9.99.** Recrystd from boiling H<sub>2</sub>O (charcoal; 1g in 300 mL) to give pale yellow crystals with a neutral reaction. It is one of the most fluorescent substances known. At 1:1000 dilution in H<sub>2</sub>O it is pale yellow with only a faint fluorescence but at 1:100,000 dilution it is colourless with an intense blue fluorescence. [Albert and Ritchie Org Synth Coll Vol III 53 1955; Falk and Thomas Pharm J **153** 158 1944.] See entry in Chapter 4 for the free base.

(4-amino-4-deoxypteroyl-L-glutamic acid) [54-62-6] M 440.4, m 231-Aminopterin 235°(dec),  $[\alpha]_D^{20}$  +18° (c 2, 0.1N aq NaOH), pK<sub>1</sub> <0.5 (pyrimidine<sup>2+</sup>), pK<sub>2</sub> 2.5 (N5-Me<sup>+</sup>), pK<sub>3</sub> 3.49 (α-CO<sub>2</sub>H), pK<sub>4</sub> 4.65 (γ-CO<sub>2</sub>H), pK<sub>5</sub> 5.50 (pyrimidine<sup>+</sup>). Purified by recrystn from H<sub>2</sub>O, and has properties similar to those of methotrexate. It has UV at  $\lambda_{max}$  244, 290 and 355nm ( $\epsilon$  18600, 21300 and 12000) in H<sub>2</sub>O at pH 1; 260, 284 and 370nm (£ 28500, 26400 and 8600) in H<sub>2</sub>O at pH 13. [Seeger et al. J Am Chem Soc 71 1753 1949; Angier and Curran J Am Chem Soc 81 2814 1959; Blakley The Biochemistry of Folic Acid and Related Pteridines (North-Holland Publ Co., Amsterdam, NY) pp157-163 1969.] For small quantities chromatography on DEAE cellulose with a linear gradient of ammonium bicarbonate pH 8 and increasing the molarity from 0.1 to 0.4 and followed by UV is best. For larger quantities a near boiling solution of aminopterin (5g) in H<sub>2</sub>O (400mL) was slowly treated with small portions of MgO powder (~0.7g) calcined magnesia) with vigorous stirring until a small amount of MgO remained undissolved and the pH rises from 3-4 to 7-8. Charcoal (1g) is added to the hot solution, filtered at once through a large sintered glass funnel of medium porosity and lined with a hot wet pad of Celite (~2-3 mm thick). The filtrate is cooled in ice and the crystals of the Mg salt are collected by filtration and recrystd form boiling H<sub>2</sub>O (200mL) and the crystals washed with EtOH. The Mg salt is redissolved in boiling H<sub>2</sub>O (200mL) and carefully acidified with vigorous agitation with AcOH (2mL). Pure aminopterin (3g) separates in fine yellow needles (dihydrate) which are easily filtd. The filtrate is washed with cold  $H_2O$ , then  $Me_2CO$  and dried in vac. If a trace of impurity is still present as shown by DEAE cellulose chromatography, then repetition of the process will remove it, see UV above. [Loo J Med Chem 8 139 1965.] CARCINOGENIC

**3-Aminopyridine adenine dinucleotide** [21106-96-7] M 635.4 (see NAD for pK) Purified by ion exchange chromatography [Fisher et al. J Biol Chem 248 4293 1973; Anderson and Fisher Methods Enzymol 66 81 1980].

 $\alpha$ -Amino-thiophene-2-acetic acid 2-(2-thienyl)glycine [R(+)-65058-23-3; S(-)-4052-59-9; (-)-43189-45-3; RS(±)-21124-40-3] M 57.2, m 236-237° (R), 189-191°, 235-236° (S), 208-210°, 223-224° (dec)(RS),  $[\alpha]_{D}^{20}$  (+) and (-) 84° (c 1, 1% aq HCl),  $[\alpha]_{D}^{25}$  (+) and (-) 71° (c 1 H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 1.5, pK<sub>Est(2)</sub>~ 8.0. Recrystd by dissolving in H<sub>2</sub>O (1g in 3 mL), adjusting the pH to 5.5 with aq NH<sub>3</sub>, diluting with MeOH (20 mL), stirring, adjusting the pH to 5.5 and cooling to 0°. Also recrystd from small vols of H<sub>2</sub>O. [*R*-isomer: Nishimura et al. *Nippon Kagaku Zasshi* 82 1688 1961; S-isomer: Johnson and Panetta Chem Abstr 63 14869h 1965; Johnson and Hardcastle Chem Abstr 66 10930m 1967; RS-isomer:LiBassi et al. Gazz Chim Ital 107 253 1977.] The (±) N-acetyl derivative has m 191° (from H<sub>2</sub>O) [Schouteenten et al. Bull Soc Chim Fr II-248, II-252 1978].

4(6)-Aminouracil (4-amino-2,6-dihydroxypyrimidine) [873-83-6] M 127.1, m >350°,  $pK_1^{20}$ 0.00 (basic),  $pK_2^{20}$  8.69 (acidic),  $pK_3^{20}$  15.32 (acidic). Purified by dissolving in 3M aq NH<sub>3</sub>, filter hot, and add 3M formic acid until pptn is complete. Cool, filter off (or centrifuge), wash well with cold H<sub>2</sub>O, then EtOH and dry in air. Dry further in a vac at ~80°. [Barlin and Pfeiderer J Chem Soc (B) 1424 1971.]

Amylose [9005-82-7] ( $C_6H_{10}O_5$ )<sub>n</sub> (for use in iodine complex formation). Amylopectin was removed from impure amylose by dispersing in aqueous 15% pyridine at 80-90° (concn 0.6-0.7%) and leaving the soln stand at 44-45° for 7 days. The ppte was re-dispersed and recrystd during 5 days. After a further dispersion in 15% pyridine, it was cooled to 45°, allowed to stand at this temperature for 12hours, then cooled

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to 25° and left for a further 10hours. The combined ppte was dispersed in warm water, ppted with EtOH, washed with absolute EtOH, and vacuum dried [Foster and Paschall J Am Chem Soc 75 1181 1953].

Angiotensin (from rat brain) [70937-97-2] M 1524.8. Purified using extraction, affinity chromatography and HPLC [Hermann et al. Anal Biochem 159 295 1986].

Angiotensinogen (from human blood serum) [64315-16-8]. Purified by chromatography on Blue Sepharose, Phenyl-Sepharose, hydroxylapatite and immobilised 5-hydroxytryptamine [Campbell et al. *Biochem J* 243 121 1987].

Anion exchange resins. Should be conditioned before use by successive washing with water, EtOH and water, and taken through two  $OH^--H^+-OH^+$  cycles by successive treatment with N NaOH, water, N HCl, water and N NaOH, then washed with water until neutral to give the  $OH^-$  form. (See commercial catalogues on ion exchange resins).

**β-Apo-4'-carotenal** [12676-20-9] **M 414.7, m 139°**,  $A_{1cm}^{1\%}$  2640 at 461nm Recrystd from CHCl<sub>3</sub>/EtOH mixture or *n*-hexane. [Bobrowski and Das J Org Chem 91 1210 1987.]

**B-Apo-8'-carotenal** [1107-26-2] **M 414.7, m 136-139°.** Recrystd from CHCl<sub>3</sub>/EtOH mixture or *n*-hexane. [Bobrowski and Das J Org Chem **91** 1210 1987.]

**B-Apo-8'-carotenoic acid ethyl ester** [1109-11-1] M 526.8, m 134-138°,  $A_{1cm}^{1\%}$  2550 at 449nm. Crystd from pet ether or pet ether/ethyl acetate. Stored in the dark in an inert atmosphere at -20°.

**B-Apo-8'-carotenoic acid methyl ester** [16266-99-2] M 512.7, m 136-137°,  $A_{1 cm}^{1 \%}$  2575 at 446nm and 2160 at 471nm, in pet ether. Crystd from pet ether or pet ether/ethyl acetate. Stored in the dark in an inert atmosphere at -20°.

Apocodeine [641-36-1] M 281.3, m 124°, pK<sub>Est(1)</sub>~ 7.0, pK<sub>Est(2)</sub>~ 8.2. Crystd from MeOH and dried at 80°/2mm.

Apomorphine [58-00-4] M 267.3, m 195°(dec),  $pK_1^{15}$  7.20 (NH<sub>2</sub>),  $pK_2^{15}$  8.91 (phenolic OH). Crystd from CHCl<sub>3</sub> and pet ether, also from Et<sub>2</sub>O with 1 mol of Et<sub>2</sub>O which it loses at 100°. It is white but turns green in moist air or in alkaline soln. NARCOTIC

Apomorphine hydrochloride [41372-20-7] M 312.8, m 285-287°(dec),  $[\alpha]_D^{20}$ -48° (c 1 H<sub>2</sub>O). Cryst from H<sub>2</sub>O and EtOH. Crystals turn green on exposure to light. NARCOTIC

Aureomycin (7-chlorotetracycline) [57-62-5] M 478.5, m 172-174°(dec),  $[\alpha]_D^{23}$  -275° (MeOH), pK<sub>1</sub> 3.3, pK<sub>2</sub> 7.44, pK<sub>3</sub> 9.27. Dehydrated by azeotropic distn of its soln with toluene. On cooling anhydrous material crystallises out and is recrystd from \*C<sub>6</sub>H<sub>6</sub>, then dried under vacuum at 100° over paraffin wax. (If it is crystd from MeOH, it contains MeOH which is not removed on drying.) [Stephens et al. J Am Chem Soc 76 3568 1954; Biochem Biophys Res Commun 14 137 1964].

Aureomycin hydrochloride (7-chlorotetracycline hydrochloride) [64-72-2] M 514.0, m 234-236°(dec),  $[\alpha]_D^{25}$ -23.5° (H<sub>2</sub>O). Purified by dissolving 1g rapidly in 20mL of hot water, cooling rapidly to 40°, treating with 0.1mL of 2M HCl, and chilling in an ice-bath. The process is repeated twice. Also recrystd from Me<sub>2</sub>NCHO + Me<sub>2</sub>CO. [Stephens et al. J Am Chem Soc 76 3568 1954; UV: McCormick et al. J Am Chem Soc 79 2849 1975.]

Avidin (from egg white) [1405-69-2]  $M_r \sim 70,000$ . Purified by chromatography of an ammonium acetate soln on CM-cellulose [Green *Biochem J* 101 774 1966]. Also purified by affinity chromatography on 2-iminobiotin-6-aminohexyl-Sepharose 4B [Orr *J Biol Chem* 256 761 1981]. It is a biotin binding protein.

Azurin (from *Pseudomonas aeruginosa*) [12284-43-4]  $M_r$  30,000. Material with  $A_{625/A280} = 0.56$  was purified by gel chromatography on G-25 Sephadex with 5mM phosphate pH 7 buffer as eluent [Cho et al. J *Phys Chem* 91 3690 1987]. It is a blue Cu protein used in biological electron transport and its reduced form is obtained by adding a slight excess of Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub>. [See *Structure and Bonding* Springer Verlag, Berlin 23 1 1975.]

**Bacitracin** (Altracin, Topitracin) [1405-87-4] M 1422.7,  $[\alpha]_D^{23} + 5^{\circ}$ (H<sub>2</sub>O). It has been purified by carrier displacement using *n*-heptanol, *n*-octanol and *n*-nonanol as carriers and 50% EtOH in 0.1 N HCl. The pure material gives one spot with R<sub>F</sub> ~0.5 on paper chromatography using AcOH:*n*-BuOH: H<sub>2</sub>O (4:1:5). [Porath Acta Chem Scand 6 1237 1952.] It has also been purified by ion-exchange chromatography. It is a white powder soluble in H<sub>2</sub>O and EtOH but insoluble in Et<sub>2</sub>O, CHCl<sub>3</sub> and Me<sub>2</sub>CO. It is stable in acidic soln but unstable in base. (Abraham and Bewton *Biochem J* 47 257 1950; Synthesis: Munekata et al. *Bull Chem Soc Jpn* 46 3187, 3835 1973.]

 $N^{6}$ -Benzyladenine [1214-39-7] M 225.3, m 231-232°, 232.5°(dec), pK<sub>Est(1)</sub>~ 4.2, pK<sub>Est(2)</sub>~ 10.1. Purified by recrystn from aqueous EtOH. It has  $\lambda_{max}$  at 207 and 270nm (H<sub>2</sub>O), 268 nm (pH 6), 274nm (0.1 N HCl) and 275nm (0.1 N NaOH). [Daly *J Org Chem* 21 1553 1956; Bullock et al. *J Am Chem Soc* 78 3693 1956.]

 $N^6$ -Benzyladenosine [4294-16-0] M 357.4, m 177-179°, 185-187°,  $[\alpha]_D^{25}$ -68.6° (c 0.6, EtOH)(see above entry for pK). Purified by recrystn from EtOH. It has  $\lambda_{max}$  266nm (aq EtOH-HCl) and 269 nm (aqueous EtOH-NaOH). [Kissman and Weiss J Org Chem 21 1053 1956.]

**N-Benzylcinchoninium chloride** (9S-benzyl-9-hydroxycinchoninium chloride) [69221-14-3] M 421.0,  $[\alpha]_D^{20}$  +169° (c 0.4, H<sub>2</sub>O), pK<sub>Est</sub> ~ 5. Recrystd from isoPrOH, toluene or small volumes of H<sub>2</sub>O. Good chiral phase transfer catalyst [Julia et al. J Chem Soc Perkin Trans 1 574 1981; Hughes et al. J Am Chem Soc 106 446 1984; Hughes et al. J Org Chem 52 4745 1987]. See cinchonine below.

**R**-(-)-**N**-Benzylcinchonidinium chloride [69257-04-1] M 421.0, m 212-213° (dec),  $[\alpha]_D^{20}$ -175.4°, -183° (c 5, 0.4, H<sub>2</sub>O), pK<sub>Est</sub> ~5. Dissolve in minimum volume of H<sub>2</sub>O and add absolute Me<sub>2</sub>CO. Filter off and dry in a vacuum. Also recrystd from hot EtOH or EtOH-Et<sub>2</sub>O. (A good chiral phase transfer catalyst - see above) [Colonna et al. J Chem Soc Perkin Trans 1 547 1981, Imperali and Fisher J Org Chem 57 757 1992]. See cinchonidine below.

N-Benzylpenicillin sodium salt [69-57-8] M 356.37, m 215° (charring and dec), 225° (dec),  $[\alpha]_D^{20}$  +269° (c 0.7, MeOH),  $[\alpha]_D^{25}$  +305° (c 1, H<sub>2</sub>O), pK<sup>25</sup> 2.76 (4.84 in 80% aq EtOH)(for free acid). Purified by dissolving in a small volume of MeOH (in which it is more soluble than EtOH) and treating gradually with ~5 volumes of EtOAc. This gives an almost colourless crystalline solid (rosettes of clear-cut needles) and recrystallising twice more if slightly yellow in colour. The salt has also been conveniently recrystd from the minimum amount of 90% Me<sub>2</sub>CO and adding an excess of absolute Me<sub>2</sub>CO. A similar procedure can be used with wet n-BuOH. If yellow in colour then dissolve (~3.8g) in the minimum volume of H<sub>2</sub>O (3mL), add n-BuOH and filter through a bed of charcoal. The salt forms long white needles on standing in a refrigerator overnight. More crystals can be obtained on concentrating the mother liquors in vacuo at 40°. A further recrystn (without charcoal) yields practically pure salt. A good preparation has ~600 Units/mg. The presence of  $H_2O$  in the solvents increases the solubility considerably. The solubility in mg/100mL at 0° is 6.0 (Me<sub>2</sub>CO), 15.0 (Me<sub>2</sub>CO + 0.5% H<sub>2</sub>O), 31.0 (Me<sub>2</sub>CO + 1.0% H<sub>2</sub>O), 2.4 (methyl ethyl ketone), 81.0 (n-butanol) and 15.0 (dioxane at 14°). Alternatively it is dissolved in H<sub>2</sub>O (solubility is 10%), filtered if necessary and ppted by addition of EtOH and dried in a vacuum over  $P_2O_5$ . A sample can be kept for 24h at 100° without loss of physiological activity. [IR: Anal Chem 19 620 1947; The Chemistry of Penicillin [Clarke, Johnson and Robinson eds.] Princeton University Press, Princeton NJ, Chapter V 85 1949.]

Other salts, e.g. the **potassium salt** can be prepared from the Na salt by dissolving it (147mg) ice-cold in  $H_2O$  acidified to pH 2, extracting with  $Et_2O$  (~50mL), wash once with  $H_2O$ , and extract with 2mL portions of 0.3% KHCO<sub>3</sub> until the pH of the extract rose to ~6.5 (~7 extractns). The combined aqueous extracts are

lyophilised and the white residue is dissolved in *n*-BuOH (1mL, absolute) with the addition of enough H<sub>2</sub>O to effect soln. Remove insoluble material by centrifugation and add absolute *n*-BuOH to the supernatant. Crystals should separate on scratching, and after 2.5h in a refrigerator they are collected, washed with absolute *n*-BuOH and EtOAc and dried (yield 51.4mg). The *potassium salt* has **m** 214-217° (dec) (block preincubated at 200°; heating rate of 3°/min) and  $[\alpha]_D^{22}$  +285° (c 0.748, H<sub>2</sub>O). The *free acid* has **m** 186-187° (MeOH-Me<sub>2</sub>CO), 190-191° (H<sub>2</sub>O)  $[\alpha]_D^{25}$  +522°.

(+)-Bicuculine [R-6(5,6,7,8-tetrahydro-6-methyl-1,3-dioxolo[4,5-g]isoquinolon-5-yl)-furo-[3,4-c]-1,3-benzodioxolo-8(6H)-one] (485-49-4] M 367.4, m 177°, 193-195°, 193-197°, 215°,  $[\alpha]_D^{20} + 126°$  (c 1, CHCl<sub>3</sub>),  $[\alpha]_{546}^{20} + 159°$  (c 1, CHCl<sub>3</sub>), pK 4.84. Recrystallises from CHCl<sub>3</sub>-MeOH as plates. Crystals melt at 177° then solidify and re-melt at 193-195° [Manske Canad J Research 21B 13 1943]. It is soluble in CHCl<sub>3</sub>, \*C<sub>6</sub>H<sub>6</sub>, EtOAc but sparingly soluble in EtOH, MeOH and Et<sub>2</sub>O. [Stereochem: Blaha et al. Collect Czech Chem Commun 29 2328 1964; Snatzke et al. Tetrahedron 25 5059 1969; Pharmcol: Curtis et al. Nature 266 1222 1970].

L-erythro-Biopterin (2-amino-4-hydroxy-6-[{1R,2S}-1,2-dihydroxypropyl]pteridine) [22150-76-1] M 237.2, m >300°(dec),  $[\alpha]_{546}^{20}$  -65° (c 2.0, M HCl),  $pK_1^{25}$ 2.23(2.45),  $pK_2^{25}$ 7.89(8.05). Purified by chromatography on Florisil washed thoroughly with 2M HCl, and eluted with 2M HCl. The fractions with the UV-fluorescent band are evapd *in vacuo* and the residue recrystd. Biopterin is best recrystd (90% recovery) by dissolving in 1% aq NH<sub>3</sub> (*ca* 100 parts), and adding this soln dropwise to an equal vol of M aq formic acid at 100° and allowing to cool at 4° overnight. It is dried at 20° to 50°/01mm in the presence of P<sub>2</sub>O<sub>5</sub>. [Schircks, Bieri and Viscontini *Helv Chim Acta* 60 211 1977; Arrnarego, Waring and Paal Aust J Chem 35 785 1982.] Also crystd from *ca* 50 parts of water or 100 parts of hot 3M aq HCl by adding hot 3M aq NH<sub>3</sub> and cooling. It has UV:  $\lambda_{max}$  at 212, 248 and 321nm (log  $\varepsilon$  4.21, 4.09 and 3.94) in H<sub>2</sub>O at pH 0.0; 223infl, 235.5, 274.5 and 345nm (log  $\varepsilon$  4.07inflexion, 4.10, 4.18 and 3.82) in H<sub>2</sub>O at pH 5.0; 221.5, 254.5 and 364nm (log  $\varepsilon$  3.92, 4.38 and 3.84) in H<sub>2</sub>O at pH 10.0 [Sugimoto and Matsuura Bull Chem Soc Jpn 48 3767 1875].

D-(+)-Biotin (vitamin H, hexahydro-2-oxo-1*H*-thieno[3,4-d]imidazole-4-pentanoic acid) [58-85-5] M 244.3, m 229-231°, 230.2°(dec), 230-231°, 232-234°(dec),  $[\alpha]_{546}^{20}$  +108°,  $[\alpha]_D^{20}$  +91.3° (c 1, 0.1N NaOH), pK<sub>Est</sub> ~ 4.8. Crystd from hot water in fine long needles with a solubility of 22 mg/100mL at 25°. Its solubility in 95% EtOH is 80 mg/100 mL at 25°. Its isoelectric point is at pH 3.5. Store solid and solutions under sterile conditions because it is susceptible to mould growth. [Confalone J Am Chem Soc 97 5936 1975; Wolf et al. J Am Chem Soc 67 2100 1945; Synthesis: Ohuri and Emoto Tetrahedron Lett 2765 1975; Harris et al. J Am Chem Soc 66 1756 1944.] The (+)-methyl ester has m 166-167° (from MeOH-Et<sub>2</sub>O),  $[\alpha]_D^{22}$  +57° (c 1, CHCl<sub>3</sub>) [du Vigneaud et al. J Biol Chem 140 643, 763 1941]; the (+)-S-oxide has m 200-203°,  $[\alpha]_D^{20}$  +130° (c 1.2, 0.1N NaOH) [Melville J Biol Chem 208 495 1954]; the SS-dioxide has m 274-275°(dec, 268-270°) and the SS-dioxide methyl ester has m 239-241° (from MeOH-Et<sub>2</sub>O) [Hofmann et al. J Biol Chem 141 207, 213 1941.]

**D-(+)-Biotin hydrazide** [66640-86-6] M 258.4, m 238-240°, 245-247°,  $[\alpha]_D^{20} + 66°$  (c 1, Me<sub>2</sub>NCHO). Wash the material with H<sub>2</sub>O, dry, wash with MeOH then Et<sub>2</sub>O, dry, and recrystallise from hot H<sub>2</sub>O (clusters of prisms) [Hofmann et al. J Biol Chem 144 513 1942].

D-(+)-Biotin N-hydroxysuccinimide ester (+-biotin N-succinimidyl ester) [35013-72-0] M 342.4, m 210°, 212-214°,  $[\alpha]_D^{20}+53°$  (c 1, Me<sub>2</sub>NCHO). Recrystd from refluxing isoPrOH and dried in a vacuum over P<sub>2</sub>O<sub>5</sub> + KOH. [Jasiewicz et al. *Exp Cell Biol* 100 213 1976.]

**D-(+)-Biotin 4-nitrophenyl ester** [33755-53-2] M 365.4, m 160-163°, 163-165°, [ $\alpha$ ]<sub>D</sub><sup>25</sup>+47° (c 2, Me<sub>2</sub>NCHO containing 1% AcOH). It has been recrystd by dissolving 2g in 95% EtOH (30mL), heated to dissolve, then cooled in an ice-water bath. The crystals are collected, washed with ice-cold 95% EtOH (5mL) and dried over P<sub>2</sub>O<sub>5</sub>. The R<sub>F</sub> on silica plates (CHCl<sub>3</sub>:MeOH-19:1) is 0.19 [Bodanszky and Fagan J Am Chem Soc 99 235 1977].

N-(+)-Biotinyl-4-aminobenzoic acid [6929-40-4] M 363.4, m 295-297°, 295-300°,  $[\alpha]_D^{23}$ +56.55° (c 0.5, 0.1N NaOH), pK<sub>Est</sub> ~4.0. Dissolve in NaHCO<sub>3</sub> soln, cool and ppte by adding N HCl. Collect the solid, dry at 100° and recrystallise from MeOH. Note that it is hydrolysed by aq 3M, 1M and 0.2M HCl at 120°, but can be stored in 5% aq NaHCO<sub>3</sub> at -20° without appreciable hydrolysis [Knappe et al. *Biochem* Zeitschrift 338 599 1963; J Am Chem Soc 73 4142 1951; Bayer and Wilchek Methods Enzymol 26 1 1980]

**N-Biotinyl-6-aminocaproic** N-succinimidyl ester [72040-63-2] M 454.5, m 149-152°. Dissolve ~400mg in dry propan-2-ol (~25mL) with gentle heating. Reduce the volume to ~10mL by gentle boiling and allow the soln to cool. Decant the supernatant carefully from the white crystals, dry the crystals in a vacuum over  $P_2O_5$  at 60° overnight. Material gives one spot on TLC. [Costello et al. Clin Chem 25 1572 1979; Kincaid et al. Methods Enzymol 159 619 1988.]

*N*-(+)-Biotinyl-6-aminocaproyl hydrazide (biotin-6-aminohexanoic hydrazide) [109276-34-8] M 371.5, m 189-191°, 210°,  $[\alpha]_D^{20}$  +23° (c 1, Me<sub>2</sub>NCHO). Suspend in ice-water (100mg/mL), allow to stand overnight at 4°, filter and dry the solid in a vacuum. Recrystd from isoPrOH. R<sub>F</sub> 0.26 on SiO<sub>2</sub> plate using CHCl<sub>3</sub>-MeOH (7:3) as eluent. [O'Shannessy et al. Anal Biochem 163 204 1987.]

N-(+)-Biotinyl-L-lysine (Biocytin) [576-19-2] M 372.5, m 228.5°, 228-230° (dec), 241-243°, 245-252° (dec, sintering at 227°),  $[\alpha]_D^{2.5}+53°$  (c 1.05, 0.1 N NaOH). Recrystd rapidly from dilute MeOH or Me<sub>2</sub>CO. Also recrystd from H<sub>2</sub>O by slow evaporation or by dissolving in the minimum volume of H<sub>2</sub>O and adding Me<sub>2</sub>CO until solid separates. It is freely soluble in H<sub>2</sub>O and AcOH but insoluble in Me<sub>2</sub>CO. [Wolf et al. J Am Chem Soc 76 2002 1952, 72 1048 1050.] It has been purified by chromatography on superfiltrol-Celite, Al<sub>2</sub>O<sub>3</sub> and by countercurrent distribution and then recrystd [IR: Peck et al. J Am Chem Soc 74 1991 1952]. The hydrochloride can be recrystd from aqueous Me<sub>2</sub>CO + HCl and has m 227° (dec).

2-(4-Biphenylyl)-5-phenyl-1,3,4-oxadiazole [852-38-0] M 298.4, m 166-167°, 167-170°. Recrystd from toluene. It is a good scintillation material [Brown et al. Discussion Faraday Soc 27 43 1959].

2,5-Bis(4-biphenylyl)-1,3,4-oxadiazole (BBOD) [2043-06-3] M 374.5, m 229-230°, 235-238°. Recrystd from heptane or toluene. It is a good scintillant. [Hayes et al. J Am Chem Soc 77 1850 1955.]

4,4-Bis(4-hydroxyphenyl)valeric acid [diphenolic acid] [126-00-1] M 286.3, m 168-171°, 171-172°, pK<sub>Est(1)</sub>~ 4.8 (CO<sub>2</sub>H), pK<sub>Est(2)</sub>~ 7.55 (OH), pK<sub>Est(3)</sub>~9.0 (OH). When recrystd from \*C<sub>6</sub>H<sub>6</sub> the crystals have 0.5 mol of \*C<sub>6</sub>H<sub>6</sub> (m 120-122°) and when recrystd from toluene the crystals have 0.5 mol of toluene. Purified by recrystn from hot H<sub>2</sub>O. It is sol in Me<sub>2</sub>CO, AcOH, EtOH, propan-2-ol, methyl ethyl ketone. It is also recrystallised from AcOH, heptane-Et<sub>2</sub>O or Me<sub>2</sub>CO + \*C<sub>6</sub>H<sub>6</sub>. It has  $\lambda_{max}$  225 and 279nm in EtOH. The methyl ester has m 87-89° (aqueous MeOH to give the trihydrate). [Bader and Kantowicz J Am Chem Soc 76 4465 1954.]

**Bis(2-mercaptoethyl)sulfone (BMS)** [145626-87-5] **M 186.3, m 57-58°, pK\_1^{25}7.9, pK\_2^{25}9.0**. Recrystd from hexane as white fluffy crystals. Large amounts are best recrystd from de-oxygenated H<sub>2</sub>O (charcoal). It is a good alternative reducing agent to dithiothreitol. Its IR (film) has v 2995, 2657, 1306, 1248, 1124 and 729 cm<sup>-1</sup>. The synthetic intermediate *thioacetate* has **m** 82-83° (white crystals from CCl<sub>4</sub>). The *disulfide* was purified by flash chromatography on SiO<sub>2</sub> and elution with 50% EtOAc-hexane and recrystd from hexane, **m** 137-139°. [Lamoureux and Whitesides J Org Chem **58** 633 1993.]

**Bombesin** (2-L-glutamin-3-6-L-asparaginealytesin) [31362-50-2] M 619.9. Purified by gel filtration on a small column of Sephadex G-10 and eluted with 0.01 M AcOH. This procedure removes lower molecular weight contaminants which are retarded on the column. The procedure should be repeated twice and the material should now be homogeneous on electrophoresis, and on chromatography gives a single active spot which is negative to ninhydrin but positive to Cl<sub>2</sub> and iodoplatinate reagents.  $R_F$  on paper chromatography (*n*-BuOH-pyridine-AcOH-H<sub>2</sub>O (37.5: 25:7.5: 30) is 0.55 for Bombesin and 0.65 for Alytin. [Bernardi *Experientia* **B 27** 872 1971; **A 27** 166 1971.] The hydrochloride has **m** 185°(dec) (from EtOH)  $[\alpha]_D^{24}$  -20.6° [c 0.65, Me<sub>2</sub>NCHO-(Me<sub>2</sub>N)<sub>3</sub>PO (8:2)].

**Bradykinin** [ArgProProGlyPheSerProPheArg] [5979-11-3]  $M_r$  1,240.4. Purified by ionexchange chromatography on CMC (O-carboxymethyl cellulose) and partition chromatography on Sephadex G-25. Purity was checked by paper chromatography using BuOH:AcOH:H<sub>2</sub>O (4:1:5) as eluent. [Park et al. Can J Biochem 56 92 1978; ORD and CD: Bodanszky et al. Experientia 26 948 1970; activity: Regoli and Barabé Pharmacol Rev 32 1 1980.]

Brefeldin A [1-R-2c,15c-dihydroxy-7t-methyl-(1r,13t)-6-oxa-bicyclo[11.3.0]hexadeca-3t,11t-dien-5-one, Decumbin] [20350-15-6] M 280.4, m 200-202°, 204°, 204-205°,  $[\alpha]_D^{22}$ +95° (c 0.81, MeOH). Isolated from *Penicillium brefeldianum* and recrystd from aqueous MeOH-EtOAc or MeOH. Solubility in H<sub>2</sub>O is 0.6mg/mL, 10mg/mL in MeOH and 24.9mg/mL in EtOH. The *O*-acetate recrystallises from Et<sub>2</sub>O-pentane and has m 130-131°,  $[\alpha]_D^{22}$  +17° (c 0.95, MeOH). [Sigg Helv Chim Acta 47 1401 1964; UV and IR: Härri et al. Helv Chim Acta 46 1235 1963; total synthesis: Kitahara et al. Tetrahedron 3021 1979; X-ray : Weber et al. Helv Chim Acta 54 2763 1971.]

**Bromelain** (anti-inflammatory Ananase from pineapple) [37189-34-7] M<sub>r</sub> ~33 000, [EC 3.4.33.4]. This protease has been purified *via* the acetone powder, G-75 Sephadex gel filtration and Bio-Rex 70 ion-exchange chromatography and has  $A_{1cm}^{1\%}$  20.1 at 280nm. The protease from pineapple hydrolyses benzoyl glycine ethyl ester with a Km (app) of 210mM and k<sub>cat</sub> of 0.36 sec<sup>-1</sup>. [Murachi Methods Enzymol 19 273 1970; Balls et al. Ind Eng Chem 33 950 1941.]

**5-Bromo-2'-deoxyuridine** [59-14-3] M 307.1, m 193-197°(dec), 217-218°,  $[\alpha]_D^{25}$ -41° (c 0.1, H<sub>2</sub>O), pK<sup>25</sup> ~ 8.1. Recrystd from EtOH or 96% EtOH. It has  $\lambda_{max}$  279 nm at pH 7.0, and 279 nm (log  $\varepsilon$  3.95) at pH 1.9. Its R<sub>F</sub> values are 0.49, 0.46 and 0.53 in *n*-BuOH-AcOH-H<sub>2</sub>O (4:1:1), *n*-BuOH-EtOH-H<sub>2</sub>O (40:11:19) and *i*-PrOH-25% aq NH<sub>3</sub>-H<sub>2</sub>O (7:1:1) respectively. [*Nature* 209 230 1966; Collect Czech Chem Comm 29 2956 1964.]

6-Bromo-2-naphthyl- $\alpha$ -D-galactopyranoside [25997-59-5] M 385.2, m 178-180°, 224-226°, 225°,  $[\alpha]_D^{28}$  +60° (c 1.2, pyridine). It was prepared from penta-O-acetyl-D-galactoside and 6-bromo-2-naphthol and ZnCl<sub>2</sub> The resulting tetra-acetate (2g) was hydrolysed by dissolving in 0.3N KOH (100mL) and heated until the soln was clear, filtered and cooled to give colourless crystals of the  $\alpha$ -isomer which are collected and recrystd twice from hot MeOH. The high specific rotation is characteristic of the  $\alpha$ -isomer. The *tetra-acetate* has m 155-156° [ $\alpha$ ]<sub>D</sub><sup>20</sup> +60° (c 1, CHCl<sub>3</sub>) [Dey and Pridham *Biochem J* 115 47 1969] [reported m 75-85°, [ $\alpha$ ]<sub>D</sub><sup>24</sup> +94° (c 1.3, dioxane), Monis et al. J Histochem Cytochem 11 653 1963].

**5-Bromouridine** [957-75-5] M 323.1, m 215-217°, 217-218°,  $[\alpha]_D^{25}$ -4.1° (c 0.1, H<sub>2</sub>O), pK<sup>25</sup> 8.1. Recrystd from 96% EtOH. UV  $\lambda_{max}$  279nm (log  $\varepsilon$  3.95) in H<sub>2</sub>O pH 1.9. R<sub>F</sub> in *n*-BuOH:AcOH:H<sub>2</sub>O (4:4:1) is 0.49; in *n*-BuOH:EtOH:H<sub>2</sub>O (40:11:9) is 0.46 and in isoPrOH:25%NH<sub>3</sub>:H<sub>2</sub>O (7:1:2) is 0.53 using Whatman No 1 paper. [Prystas and Sorm Collect Czech Chem Commun 29 2956 1964.]

Brucine [357-57-3 (anhydr), 5892-11-5 ( $4H_2O$ )] M 430.5, m 178-179°,  $[\alpha]_{546}^{20}$  -149.9° (anhydrous; c 1, in CHCl<sub>3</sub>), pK<sub>1</sub><sup>15</sup> 2.50, pK<sub>2</sub><sup>15</sup> 8.16 (pK<sub>2</sub><sup>25</sup> 8.28). Crystd once from water or aq Me<sub>2</sub>CO, as tetrahydrate, then suspended in CHCl<sub>3</sub> and shaken with anhydrous Na<sub>2</sub>SO<sub>4</sub> (to dehydrate the brucine, which then dissolves). Ppted by pouring the soln into a large bulk of dry pet ether (b 40-60°), filtered and heated to 120° in a high vacuum [Turner J Chem Soc 842 1951]. VERY POISONOUS

a-Brucine sulfate (hydrate) [4845-99-2] M 887.0, m 180°(dec). Crystd from water.

Butyryl choline iodide [(2-butyryloxyethyl)trimethyl ammonium iodide] [2494-56-6] M 301.7, m 85-89°, 87°, 93-94°. Recrystd from isoPrOH or Et<sub>2</sub>O. [Tammelin Acta Chem Scand 10 145 1956.] The perchlorate has m 72° (from isoPrOH). [Aldridge Biochem J 53 62 1953.]

**S-Butyryl thiocholine iodide** [(2-butyrylmercaptoethyl)trimethyl ammonium iodide] [1866-16-6] **M 317.2, m 173°, 173-176°.** Recrystd from propan-1-ol and dried *in vacuo*; store in the dark under N<sub>2</sub>. The bromide has m 150° (from Me<sub>2</sub>CO) or m 140-143° (from butan-1-ol). [Gillis Chem and Ind (London) 111 1957; Hansen Acta Chem Scand 11 537 1957.] **L-Canavanine sulfate** (from jackbean, O-guanidino-L-homoserine) [2219-31-0] M 274.3, m 160-165°(dec), 172°(dec),  $[\alpha]_D^{18.5} + 19.8°$  (c 7, H<sub>2</sub>O),  $pK_1^{25}7.40$  (CO<sub>2</sub>H),  $pK_2^{25}$ 9.25 ( $\alpha$ -NH<sub>2</sub>),  $pK_3^{25}$  11.5 (guanidinoxy). Recrystd by dissolving (~1g) in H<sub>2</sub>O (10mL), and adding with stirring 0.5 to 1.0 vols of 95% EtOH whereby crystals separate. These are collected, washed with Me<sub>2</sub>CO-EtOH (1:1) and dried over P<sub>2</sub>O<sub>5</sub> in a vacuum. [Hunt and Thompson *Biochem Prep* 13 416 1971; Feacon and Bell *Biochem J* 59 221 1955.]

**Carbonic anhydrase** (carbinate hydrolase) [9001-03-0]  $M_r$  31,000 [EC 4.2.1.1]. Purified by hydroxylapatite and DEAE-cellulose chromatography [Tiselius et al. Arch Biochem Biophys 65 132 1956, Biochim Biophys Acta 39 218 1960], and is then dialysed for crystn. A 0.5 to 1% soln of the enzyme in 0.05 M Tris-HCl pH 8.5 was dialysed against 1.75M soln of (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> in the same buffer, and this salt soln was slowly increased in salt concn by periodic removal of small amounts of dialysate and replacement with an equal volume of 3.5M (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>. The final salt concn in which the DEAE-cellulose fractions which gave beautiful birefringent suspensions of crystals ranged from 2.4 to 2.7M, and appeared first as fine crystals then underwent transition to thin fragile plates. Carbonic anhydrase is a Zn enzyme which exists as several isoenzymes of varying degrees of activity [J Biol Chem 243 6474 1968; crystal structure: Nature, New Biology 235 131 1972; see also P.D. Boyer Ed. The Enzymes Academic Press NY, pp 587-665 1971].

**Carboxypeptidase A** (from bovine pancreas, peptidyl-L-aminoacid lyase) [11075-17-5]  $M_r$ 34,600 [EC 3.4.17.1]. Purified by DEAE-cellulose chromatography, activation with trypsin and dialysed against 0.1M NaCl, yielding crystals. It is recrystd by dissolving in 20 mL of M NaCl and dialysed for 24hours each against the following salts present in 500mL of 0.02M sodium veronal pH 8.0: ,0.5M NaCl, 0.2M NaCl and 0.15M NaCl. The last dialysate usually induces crystn. If it does not crystallise then dialyse the last soln against 0.02M sodium veronal containing 0.10M NaCl. Only 2 or 3 recrystns are required to attain maximum activity. [Cox et al. *Biochemistry* 3 44 1964.] Enzyme activity is measured by hydrolysing hippuryl-Lphenylalanine (or phenylacetic acid) and observing the rate of change of optical density at 254nm (reaction extinction coefficient is ~0.592 cm<sup>2</sup>/µmole at pH 7.5 [Bergmyer *Methods in Enzymatic Analysis* (Academic Press) 1 436 1974].

Carminic acid  $(7-\alpha-D-glucopyranosyl-9,10-dihydro-3,5,6,8-tetrahydroxy-1-methyl-9,10$ dioxo-2-anthracene carboxylic acid, Neutral Red 4: CI 75470) [1260-17-9] M 492.4, m $120°(dec), <math>[\alpha]_{654}^{15}$  +51.6° (H<sub>2</sub>O), (several phenolic pKs). Forms red prisms from EtOH. It gives a red colour in Ac<sub>2</sub>O and yellow to violet in acidic solution. UV:  $\lambda_{max}$  (H<sub>2</sub>O) 500nm ( $\epsilon$  6,800); (0.02N HCl) 490-500nm ( $\epsilon$  5,800) and (0.0001N NaOH) 540nm ( $\epsilon$  3,450). IR:  $\nu_{max}$  (Nujol) 1708s, 1693s, 1677m,1648m, 1632m, 1606s, 1566s, 1509 cm<sup>-1</sup>. Periodate oxidation is complete after 4h at 0° with the consumption of 6.2 mols. The *tetra-O-methyl carminate* has m 186-188° (yellow needles from \*C<sub>6</sub>H<sub>6</sub> + pet ether). [IR: Ali and Haynes J Chem Soc 1033 1959; Bhatia and Venkataraman Indian J Chem 3 (2) 92 1965; Synthesis: Davis and Smith Biochem Prep 4 38 1955.]

Carnitine ( $\alpha$ -hydroxy- $\beta$ -N,N,N-trimethylaminopropionic acid) [R(+)- 541-14-0; S(L-) 541-15-1; RS 461-06-3] M 161.2, m R or S isomer 197-198°(dec), 210-212°(dec), RS isomer 195-197°,  $[\alpha]_{546}^{20}$  (+) and (-) 36° (c 10, H<sub>2</sub>O), pK<sup>25</sup> 3.6. The S(L) isomer is levocarnitine, Vitamin B<sub>7</sub>. The R or S isomers crystallise from EtOH + Me<sub>2</sub>CO (hygroscopic). The R or S hydrochlorides crystallise from hot EtOH and have m 142°(dec). The RS isomer crystallises from hot EtOH (hygroscopic). The RS hydrochloride crystallises in needles from hot EtOH and has m 196°(dec).

L-Carnosine ( $\beta$ -alanyl-L-histidine) [305-84-0] M 226.2, m 258-260°(dec), 260°(capillary tube), 262°(dec),  $[\alpha]_D^{25} + 20.5°$  (c 1.5, H<sub>2</sub>O),  $pK_1^{25}$  2.64,  $pK_2^{25}$  6.83,  $pK_3^{25}$  9.51. Likely impurities: histidine,  $\beta$ -alanine. Crystd from water by adding EtOH in excess. Recrystd from aqueous EtOH by slow addition of EtOH to a strong aqueous soln of the dipeptide. Its solubility in H<sub>2</sub>O is 33.3% at 25°. [Vinick and Jung J Org Chem 48 392 1983; Turner J Am Chem Soc 75 2388 1953; Sifford and du Vigneaud J Biol Chem 108 753 1935.]

 $\alpha$ -Carotene [7488-99-5] M 536.9, m 184-188°,  $[\alpha]_{643}^{20}$  +385° (c 0.08, \*C<sub>6</sub>H<sub>6</sub>)  $\lambda_{max}$  422, 446, 474 nm, in hexane,  $A_{1cm}^{1\%}$  2725 (at 446nm), 2490 (at 474nm). Purified by chromatography on columns of calcium hydroxide, alumina or magnesia. Crystd from CS<sub>2</sub>/MeOH, toluene/MeOH, diethyl ether/pet ether, or acetone/pet ether. Stored in the dark, under inert atmosphere at -20°.

all-trans- $\beta$ -Carotene [7235-40-7] M 536.9, m 178-179°, 179-180°, 180°, 181°, 183° (evac capillary),  $\varepsilon_{1cm}^{1\%}$  2590 (450nm), 2280 (478nm), in hexane. It forms purple prisms when crystd from \*C<sub>6</sub>H<sub>6</sub>-MeOH and red rhombs from pet ether. Its solubility in hexane is 0.1% at 0°. It is oxygen sensitive and should be stored under N<sub>2</sub> at -20° in the dark. It gives a deep blue colour with SbCl<sub>3</sub> in CHCl<sub>3</sub>. UV: (\*C<sub>6</sub>H<sub>6</sub>) 429infl,  $\lambda_{max}$  454 and 484nm. The principal peak at 454nm has  $A_{1cm}^{1\%}$  2000. [Synthesis: Surmatis and Ofner J Org Chem 26 1171 1961; Milas et al. J Am Chem Soc 72 4844 1950.]  $\beta$ -Carotene was also purified by chromatography (Al<sub>2</sub>O<sub>3</sub> activity I-II) - it was dissolved in pet ether-\*C<sub>6</sub>H<sub>6</sub> (10:1), applied to the column and eluted with pet ether-EtOH, the desired fraction was evaporated and the residue recrystd from \*C<sub>6</sub>H<sub>6</sub>-MeOH as violet-red plates. [UV: Inhoffen et al. Justus Liebigs Ann Chem 570 54,68 1950; Review: Fleming Selected Organic Synthesis (J Wiley, Lond) pp. 70-74 1973.] Alternatively it can be purified by chromatography on a magnesia column, thin layer of Kieselguhr or magnesia. Crystd from CS<sub>2</sub>/MeOH, Et<sub>2</sub>O/pet ether, acetone/pet ether or toluene/MeOH. Stored in the dark, under inert atmosphere, at -20°. Recrystd from 1:1 EtOH/CHCl<sub>3</sub> [Bobrowski and Das J Phys Chem 89 5079 1985; Johnston and Scaiano J Am Chem Soc 108 2349 1986].

γ-Carotene [472-93-5, 10593-83-6] M 536.9,  $A_{1cm}^{1\%}$  (λmax) 2055 (437nm), 3100 (462nm), 2720 (494nm) in hexane. Purified by chromatography on alumina or magnesia columns. Crystd from \*C<sub>6</sub>H<sub>6</sub>/MeOH (2:1). Stored in the dark, under inert atmosphere, at 0°.

 $\xi$ -Carotene [38894-81-4] M 536.9, m 38-42°,  $\lambda_{max}$  378, 400, 425nm,  $A_{1cm}^{1\%}$  ( $\lambda$ max) 2270 (400nm), in pet ether. Purified by chromatography on 50% magnesia-HyfloSupercel, developing with hexane and eluting with 10% EtOH in hexane. It was crystd from toluene/MeOH. [Gorman et al. J Am Chem Soc 107 4404 1985.] Stored in the dark under inert atmosphere at -20°.

 $\lambda$ -Carrageenan [9064-57-7, 9000-07-1 ( $\kappa$  + little of  $\lambda$ )]. This D-galactose-anhydro-D or L-galactoside polysaccharide is ppted from 4g of Carrageenan in 600mL of water containing 12g of KOAc by addn of EtOH. The fraction taken, ppted between 30 and 45% (v/v) EtOH. [Pal and Schubert J Am Chem Soc 84 4384 1962.]

**Cation exchange resins.** Should be conditioned before use by successive washing with water, EtOH and water, and taken through two  $H^+$ -OH<sup>-</sup>-H<sup>+</sup> cycles by successive treatment with M HCl, water, M NaOH, water and M HCl, then washed with water until neutral to give the H<sup>+</sup> form. (See commercial catalogues on ion exchange resins).

Cathepsin B (from human liver) [9047-22-7] M<sub>r</sub> 27,500 [EC 3.4.22.1]. Purified by affinity chromatography on the semicarbazone of Gly-Phe-glycinal-linked to Sepharose 4B, with elution by 2,2'-dipyridyl disulfide [Rich et al. *Biochem J* 235 731 1986; *Methods Enzymol* 80 551 1981].

**Cathepsin D** (from bovine spleen) [9025-26-7]  $M_r$  56,000, [EC 3.4.23.5]. Purified on a CM column after ammonium sulfate fractionation and dialysis, then starch-gel electrophoresis and by ultracentrifugal analysis. Finally chromatographed on a DEAE column [Press et al. *Biochem J* 74 501 1960].

Cephalosporin C potassium salt [28240-09-7] M 453.5,  $[\alpha]_D^{20} + 103^\circ$  (H<sub>2</sub>O), pK<sub>1</sub> <2.6, pK<sub>2</sub> 3.1, pK<sub>3</sub> 9.8. Purified by dissolving in the minimum volume of H<sub>2</sub>O (filter) and adding EtOH until separation of solid is complete. A soln is stable in the pH range 2.5-8. It has UV  $\lambda_{max}$  is 260nm (log  $\varepsilon$  3.95) in H<sub>2</sub>O. The Ba salt has  $[\alpha]_D^{20} + 80^\circ$  (c 0.57, H<sub>2</sub>O) [Woodward et al. J Am Chem Soc 88 852 1966; Abraham and Newton Biochem J 79 377 1961; Hodgkin and Maslen Biochem J 79 402 1961; see also Quart Reviews Chem Soc London 21 231 1967].

Ceruloplasmin (from human blood plasma) [9031-37-2]  $M_r$  134,000. This principle Cu transporter (90-90% of circulating Cu) is purified by precipitation with polyethylene glycol 4000, batchwise adsorption and elution from QAE-Sephadex, and gradient elution from DEAE-Sepharose CL-6B. Ceruloplasmin

was purified 1640-fold. Homogeneous on anionic polyacrylamide gel electrophoresis (PAGE), SDS-PAGE, isoelectric focusing and low speed equilibrium centrifugation. [Oestnuizen Anal Biochem 146 1 1985; Cohn et al. J Am Chem Soc 68 459 1946.]

**Chemokines.** These are small proteins formed from longer precursors and are chemoattractants for lymphocytes and lymphoid organs. They are characterised by having cysteine groups in specific relative positions. The two largest families are the  $\alpha$  and  $\beta$  families that have four cysteine residues arranged (C-X-C) and (C-C) respectively. The mature chemokines have ~70 amino acids with internal cys S-S bonds and attract myeloid type cells *in vitro*. The  $\gamma$ -family (Lymphotactin) has only two cys residues. The  $\delta$ -family (Neurotactin, Fractalkine) has the C-C-X-X-C sequence (*ca* 387 amino acids), binds to membrane promoting adhesion of lymphocytes. The soluble domain of human Fractalkine chemoattracts monocytes and T cells. Several chemokines are available commercially (some prepared by recombinant DNA techniques) including 6Ckine/exodus/SLC which belongs to the  $\beta$ -family with 6 cysteines (110 amino acids mature protein), as the name implies (C-C-C-C-X....X-C-C) and homes lymphocytes to secondary lymphoid organs with lymphocyte adhesion antitumor properties. Other chemokines available are C10 ( $\beta$ CC) and Biotaxin. Several chemokine receptors and antibodies are available commercially and can generally be used without further purification. [Murphy 'Molecular biology of lymphocyte chemoattractant receptors' in *Ann Rev Immunol* 12 593 *1994*.]

**Chirazymes.** These are commercially available enzymes e.g. lipases, esterases, that can be used for the preparation of a variety of optically active carboxylic acids, alcohols and amines. They can cause regio and stereospecific hydrolysis and do not require cofactors. Some can be used also for esterification or transesterification in neat organic solvents. The proteases, amidases and oxidases are obtained from bacteria or fungi, whereas esterases are from pig liver and thermophilic bacteria. For preparative work the enzymes are covalently bound to a carrier and do not therefore contaminate the reaction products. Chirazymes are available form Roche Molecular Biochemicals and are used without further purification.

Chlorambucil [4-{bis(2-chloroethyl)amino}benzene)butyric acid] [305-03-3] M 304.2, m 64-66°, pK<sub>1</sub> 5.8 (6.0 at 66°, 50% aq Me<sub>2</sub>CO), pK<sub>2</sub> 8.0. It is recrystd from pet ether (flat needles) and has a solubility at 20° of 66% in EtOH, 40% in CHCl<sub>3</sub>, 50% in Me<sub>2</sub>CO but is insoluble in H<sub>2</sub>O [Everett et al. J Chem Soc 2386 1953]. CARCINOGEN.

**Chloramphenicol** [Amphicol,  $1R, 2R \cdot (-) \cdot 2 \cdot \{2, 2 \cdot dichloroacetylamino\} \cdot 1 \cdot \{4 \cdot nitrophenyl\}$ propan-1,3-diol] [56-75-7] M 323.1, m 149-151°, 150-151°, 151-152°,  $[\alpha]_D^{20} + 20.5°$  (c 3, EtOH),  $[\alpha]_D^{25} \cdot 25.5°$  (EtOAc). Purified by recrystn from H<sub>2</sub>O (sol 2.5mg/mL at 25°) or ethylene dichloride as needles or long plates and by sublimation at high vacuum. It has  $A_{1cm}^{1\%}$  298 at  $\lambda_{max}$ 278nm and it is slightly soluble in H<sub>2</sub>O (0.25%) and propylene glycol (1.50%) at 25° but is freely soluble in MeOH, EtOH, BuOH, EtOAc and Me<sub>2</sub>CO. [Relstock et al. J Am Chem Soc 71 2458 1949; Confroulis et al. J Am Chem Soc 71 2463 1949; Long and Troutman J Am Chem Soc 71 2469, 2473 1949, Ehrhart et al. Chem Ber 90 2088 1957.]

Chloramphenicol palmitate [530-43-8] M 561.5, m 90°,  $[\alpha]_D^{26}$  +24.6° (c 5, EtOH). Crystd from \*benzene.

2-Chloroadenosine [146-77-0] M 301.7, m 145-146°(dec), 147-149°(dec),  $pK_{Est(1)} \sim 0.5$ ,  $pK_{Est(2)} \sim 7.6$ . Purified by recrystn from H<sub>2</sub>O (~1% in cold) and has  $\lambda_{max}$  at 264 nm (pH 1 and 7) and 265 nm (pH 13) in H<sub>2</sub>O. [Brown and Weliky J Org Chem 23 125 1958; Schaeffer and Thomas J Am Chem Soc 80 3738 1958; IR: Davoll and Lewy J Am Chem Soc 74 1563 1952.]

Chlorophylls a and b see entries on p. 167 in Chapter 4.

6-Chloropurine riboside (6-chloro-9- $\beta$ -D-ribofuranosyl-9H-purine) [2004-06-0] M 286.7, m 158-162°(dec), 165-166°(sintering At 155°), 168-170°(dec),  $[\alpha]_D^{26}$ -45° (c 0.8, H<sub>2</sub>O). Purified by suspending the dry solid (~12 g) in hot MeOH (130 mL) and then adding enough hot H<sub>2</sub>O (~560 mL) to cause solution, filter and set aside at 5° overnight. The colourless crystals of the riboside are filtered off, washed with Me<sub>2</sub>CO, Et<sub>2</sub>O and dried at 60°/0.1mm. More material can be obtained from the filtrate by evapn to

**Chromomycin** A<sub>3</sub> [7059-24-7] M 1183.3, m 185°dec,  $[\alpha]_D^{23}$ -57° (c 1, EtOH). Dissolve reagent (10g) in EtOAc and add to a column of Silica Gel (Merck 0.05-0.2microns, 4x70cm) in EtOAc containing 1% oxalic acid. Elute with EtOAc+1% oxalic acid and check fractions by TLC. Pool fractions, wash with H<sub>2</sub>O thoroughly, dry and evaporate. Recryst from EtOAc. The *hepta-acetate* has m 214°,  $[\alpha]_D^{23}$ -20° (c 1, EtOH). [*Tetrahedron* 23 421 1967; J Am Chem Soc 91 5896 1969.]

 $\alpha$ -Chymotrypsin [9004-07-3] M<sub>r</sub> ~25000 [EC 3.4.21.1]. Crystd twice from four-tenths saturated ammonium sulfate soln, then dissolved in 1mM HCl and dialysed against 1mM HCl at 2-4°. The soln was stored at 2° [Lang, Frieden and Grunwald J Am Chem Soc 80 4923 1958].

Cinchonidine [485-71-2] M 294.4, m 210.5°,  $[\alpha]_{546}^{20}$  -127.5° (c 0.5, EtOH),  $pK_1^{15}$  4.17,  $pK_2^{15}$  8.4. Crystd from aqueous EtOH. For *N*-benzyl chloride see entry in Chapter 6.

Cinchonine [118-10-5] M 294.4, m 265°,  $[\alpha]_{546}^{20}$  +268° (c 0.5, EtOH),  $pK_1^{15}$  4.28,  $pK_2^{15}$  8.35. Crystd from EtOH or diethyl ether. For *N*-benzyl chloride see entry in Chapter 6.

Citranaxanthin [3604-90-8] M 456.7, m 155-156°,  $A_{1cm}^{1\%}$  ( $\lambda$ max) 410 (349nm), 275 (466nm) in hexane. Purified by chromatography on a column of 1:1 magnesium oxide and HyfloSupercel (diatomaceous filter aid). Crystd from pet ether. Stored in the dark, under inert atmosphere, at 0°.

Citric acid cycle components (from rat heart mitochondria). Resolved by anion-exchange chromatography [LaNoue et al. J Biol Chem 245 102 1970].

**Clonidine hydrochloride** [Catapres, 2-(2,6-dichloroanilino)-2-imidazoline hydrochloride] [4205-91-8] M 266.6, m 305°, pK 5.88 (free base). It is recrystd from EtOH-Et<sub>2</sub>O and dried in a vacuum (solubility in H<sub>2</sub>O is 5%). It has a pKa of 5.88. The *free base* has m 124-125° and is recrystallised from hexane. [Jen et al. J Med Chem 18 90 1975; NMR: Jackman and Jen J Am Chem Soc 97 2811 1975.]

Clostripain [9028-00-6] [EC 3.4.22.8]  $M_r \sim 55,000$ . Isolated from Clostridium histolyticum callogenase by extraction in pH 6.7 buffer, followed by hydroxylapatite chromatography with a 0.1-0.2 M phosphate gradient, then Sephadex G-75 gel filtration with 0.05M phosphate pH 6.7, dialysis and a second hydroxylapatite chromatography (gradient elution with 0.1M  $\rightarrow$  0.3M phosphate, pH 6.7). It has proteinase and esterase activity and is assayed by hydrolysing *n*-benzoyl-L-arginine methyl ester. [Mitchell and Harrington J Biol Chem 243 4683 1968, Methods Enzymol 19 635 1970.]

Cloxacillin sodium salt (sodium 3-o-chlorophenyl-5-methyl-4-isoxazolyl penicillin monohydrate) [642-78-4] M 457.9, m 170°,  $[\alpha]_D^{20} + 163°$  (H<sub>2</sub>O pH 6.0-7.5), pK<sub>Est</sub> ~ 2.8 (COOH). Purified by dissolving in isoPrOH containing 20% of H<sub>2</sub>O, and diluting with isoPrOH to a water content of 5% and chilled, and recrystd again in this manner. The sodium salt is collected and dried at 40° in air to give the colourless monohydrate. It is soluble in H<sub>2</sub>O (5%), MeOH, EtOH, pyridine and ethylene glycol. [Doyle et al. J Chem Soc 5838 1963; Naylor et al. Nature 195 1264 1962.]

 $\beta$ -Cocaine {2 $\beta$ -carbomethoxy-3- $\beta$ -benzoxytropane, methyl [1*R*-(*exo*,*exo*)]-3-(benzoyloxy)-2-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate} [50-36-2] M 303.4, m 98°, b 187-188°/0.1mm,  $[\alpha]_D^{20}$  -15.8° (c 4, CHCl<sub>3</sub>), pK<sup>24</sup> 8.39. Crystallises from EtOH and sublimes below 90° in a vacuum in a non-crystalline form.

Cocarboxylase tetrahydrate (aneurine pyrophosphoric acid tetrahydrate, thiamine pyrophosphoric acid tetrahydrate) [136-09-4] M 496.4, m 220-222°(sinters at 130-140°), 213-214°, pK<sub>Est(1)</sub>~2, pK<sub>Est(2)</sub>~6, pK<sub>Est(3)</sub>~9. Recrystd from aqueous Me<sub>2</sub>CO. [Wenz et al. Justus Liebigs Ann Chem 618 210 1958; UV: Melnick J Biol Chem 131 615 1939; X-ray: Carlisle and Cook Acta Cryst (B) 25 1359 1969.] The hydrochloride salt has m 242-244°(dec), 241-243°(dec) or 239-240°(dec) and is

recrystd from aqueous HCl + EtOH, EtOH containing HCl or HCl + Me<sub>2</sub>CO. [Weijlard J Am Chem Soc 63 1160 1941; Synthesis: Weijlard and Tauber J Am Chem Soc 60 2263 1938.]

Codeine [76-57-3] M 299.4, m 154-156°,  $[\alpha]_D^{20}$  -138° (in EtOH), pK<sup>25</sup> 8.21. Crystd from water or aqueous EtOH. Dried at 80°.

**Coenzyme A trihydrate** [85-61-0] **M 821.6, pK<sub>1</sub> 4.0 (adenine NH<sub>2</sub>), pK<sub>2</sub> 6.5 (PO<sub>4</sub>H), pK<sub>3</sub> 9.6 (SH). White powder best stored in an inert atmosphere in the dark in sealed ampoules after drying** *in* **vacuo over P<sub>2</sub>O<sub>5</sub> at 34°. It has UV: \lambda\_{max} 259 nm (\varepsilon 16,800) in H<sub>2</sub>O. [Buyske et al. J Am Chem Soc 76 3575 1954.] It is sol in H<sub>2</sub>O but insol in EtOH, Et<sub>2</sub>O and M<sub>2</sub>CO. It is readily oxidised in air and is best kept as the more stable** *trilithium salt* **[Moffat and Khorana J Am Chem Soc 83 663 1961; see also Beinert et al. J Biol Chem 200 384 1953; De Vries et al. J Am Chem Soc 72 4838 1950; Gregory et al. J Am Chem Soc 74 854 1952 and Baddiley Adv Enzymol 16 1 1955].** 

Coenzyme  $Q_0$  (2,3-Dimethoxy-5-methyl-1,4-benzoquinone, 3,4-dimethoxy-2,5-toluquinone, fumigatin methyl ether) [605-94-7] M 182.2, m 56-58°, 58-60°, 59°. It crystallises in red needles from pet ether (b 40-60°) and can be sublimed in high vacuum with a bath temperature of 46-48° [Ashley, Anslow and Raistrick J Chem Soc 441 1938; UV in EtOH: Vischer J Chem Soc 815 1953; UV in cyclohexane: Morton et al. Helv Chim Acta 41 2343 1858; Aghoramurthy et al. Chem Ind (London) 1327 1954].

Coenzyme Q<sub>4</sub> (Ubiquinone-4, 2,3-dimethoxy-5-methyl-6-[3,7,11,15-tetramethyl-hexadeca-2t,6t,10t,14-tetraenyl]-[1,4]benzoquinone [4370-62-1] M 454.7, m 30°, 33-45°,  $A_{1cm}^{1\%}$  (275nm) 185. A red oil purified by TLC chromatography on SiO<sub>2</sub> and eluted with Et<sub>2</sub>O-hexane. Purity can be checked by HPLC (silica column using 7% Et<sub>2</sub>O-hexane). It has  $\lambda_{max}$  270 nm ( $\varepsilon$  14,800) in pet ether. [NMR and MS: Naruta J Org Chem 45 4097 1980; cf Morton Biochemical Spectroscopy (Adam Hilger, London, 1975) p 491]. It has also been dissolved in MeOH/EtOH (1:1 v/v) and kept at 5° until crystals appear [Lester and Crane Biochim Biophys Acta 32 497 1958].

Coenzyme Q<sub>9</sub> (Ubiquinone-9, 2,3-dimethoxy-5-methyl-6-[3,7,11,15,19,23,27,31,35nonamethyl-hexatriaconta-2t,6t,10t,14t,18t,22t,26t,30t,34-nonaenyl]-1,4-benzoquinone) [303-97-9] M 795.3, m 40.5-42.5°, 44-45°, 45°. Yellow crystals purified by recrystn from pet ether and by TLC chromatography on SiO<sub>2</sub> and eluted with Et<sub>2</sub>O-hexane. Purity can be checked by HPLC (silica column using 7% Et<sub>2</sub>O-hexane). It has  $\lambda_{max}$  270nm ( $\varepsilon$  14,850) in pet ether. [NMR and MS: Naruta J Org Chem 45 4097 1980; Le et al. Biochem Biophys Acta 32 497 1958; cf Morton Biochemical Spectroscopy (Adam Hilger, London, 1975) p 491; IR: Lester et al. Biochim Biophys Acta 33 169 1959; UV: Rüegg et al. Helv Chim Acta 42 2616 1959; Shunk J Am Chem Soc 81 5000 1959.]

Coenzyme Q<sub>10</sub> (Ubiquinone-10, 2,3-dimethoxy-5-methyl-6-[3,7,11,15,19,23,27,31,35,-39decamethyl-tetraconta-2t,6t,10t,14t,18t,22t,26t,30t,34t,38-decaenyl]-1,4-benzoquinone) [303-98-0] M 795.3, m 48-49°,49°, 49.5-50.5°, 50°. Purified by recrystn from EtOH, EtOH + Me<sub>2</sub>CO or Et<sub>2</sub>O-EtOH and by chromatography on silica gel using isoPrOH-Et<sub>2</sub>O (3:1) to give orange crystals. It has  $\lambda_{max}$  270nm ( $\varepsilon$  15,170) in pet ether. [Terao et al. J Org Chem 44 868 1979; NMR and MS: Naruta et al. J Org Chem 45 4097 1980; IR: Lester et al. Biochem Biophys Acta 42 1278 1959, NMR: Planta et al. Helv Chim Acta 42 1278 1959; cf Morton Biochemical Spectroscopy (Adam Hilger, London, 1975) p 491].

Colcemide (Demecocine) [477-30-5] M 371.4, m 182-185°, 183-185°,  $[\alpha]_D^{20}$ -129° (c 1, CHCl<sub>3</sub>). It has been purified by chromatography on silica and eluting with CHCl<sub>3</sub>-MeOH (9:1) and recrystn from EtOAc-Et<sub>2</sub>O and forms yellow prisms. UV in EtOH has  $\lambda_{max}$  243nm ( $\varepsilon$  30,200) and 350nm ( $\varepsilon$  16,3000). [Synthesis, IR, NMR, MS: Capraro and Brossi *Helv Chim Acta* 62 965 1979.]

Colchicine [64-86-8] M 399.5, m 155-157°(dec),  $[\alpha]_{546}^{20}$  -570° (c 1, H<sub>2</sub>O), pK<sup>20</sup> 1.85. Commercial material contains up to 4% desmethylcolchicine. Purified by chromatography on alumina, eluting with CHCl<sub>3</sub> [Ashley and Harris J Chem Soc 677 1944]. Alternatively, an acetone solution on alkali-free alumina has been used, and eluting with acetone [Nicholls and Tarbell J Am Chem Soc 75 1104 1953]. Colchicoside [477-29-2] M 547.5, m 216-218°. Crystd from EtOH.

Colicin E (from *E.coli*) [11032-88-5]. Purified by salt extraction of extracellular-bound colicin followed by salt fractionation and ion-exchange chromatography on a DEAE-Sephadex column, and then by CM-Sephadex column chromatography [Schwartz and Helinski J Biol Chem 246 6318 1971].

Collagenase (from human polymorphonuclear leukocytes) [9001-12-1]  $M_r$  68,000-125,000 [EC 3.4.24.3]. Purified by using N-ethylmaleimide to activate the enzyme, and wheat germ agglutininagarose affinity chromatography [Callaway et al. *Biochemistry* 25 4757 1986].

Compactin [73573-88-3] M 390.5, m 151-153°,  $152^{\circ}$ ,  $[\alpha]_D^{22} + 283°$  (c 0.48, acetone). Purified by recrystn from aqueous EtOH. UV:  $\lambda_{max}$  230, 237 and 246nm (log  $\varepsilon$  4.28, 4.30 and 4.11); IR (KBr): v 3520, 1750 (lactone CO) and 1710 (CO ester) cm<sup>-1</sup>. [Clive et al. J Am Chem Soc 110 6914 1988; Synthesis review: Rosen and Heathcock Tetrahedron 42 4909 1986; IR, NMR, MS: Brown et al. J Chem Soc Perkin Trans 1 1165 1976.]

Convallatoxin ( $\alpha$  cardenolide mannoside) [508-75-8] M 550.6, m 238-239°,  $[\alpha]_D^{25} 9.4°$  (c 0.7, dioxane). Crystd from EtOAc. *Tetra-acetate* has m 238-242° (MeOH/Et<sub>2</sub>O),  $[\alpha]_D^{25}$ -5° (CHCl<sub>3</sub>).

Copper-zinc-superoxide dismutase (from blood cell haemolysis) [9054-89-1]  $M_r \sim 32,000$ [EC 1.15.1.1]. Purified by DEAE-Sepharose and copper chelate affinity chromatography. The preparation was homogeneous by SDS-PAGE, analytical gel filtration chromatography and by isoelectric focusing [Weselake et al. Anal Biochem 155 193 1986; Fridovich J Biol Chem 244 6049 1969].

**Coproporphyrin I** [531-14-6] M 654.7,  $\lambda_{max}$  591, 548, 401nm in 10% HCl. Crystd from pyridine/glacial acetic acid. The *dihydrochloride* [69477-27-6] has M 727.7 and  $\lambda_{max}$  395nm in water.

Corticosterone (11 $\beta$ , 21-dihydroxypregn-4-en-3,20-dione) [50-22-6] M 346.5, m 180-181°, 180-182°, 181-184°,  $[\alpha]_D^{15} + 223°$  (c 1.1, EtOH),  $[\alpha]_D^{23-25} + 194°$  (c 0.1, dioxane). Purified by recrystn from Me<sub>2</sub>CO (trigonal plates), EtOH or isoPrOH. UV  $\lambda_{max}$  at 240nm, and gives an orange-yellow soln with strong fluorescence on treatment with concentrated H<sub>2</sub>SO<sub>4</sub>. Insoluble in H<sub>2</sub>O but soluble in organic solvents. [Reichstein and Euw Helv Chim Acta 21 1197 1938, 27 1287 1944; Mason et al. J Biol Chem 114 613 1936; ORD: Foltz et al. J Am Chem Soc 77 4359 1955; NMR: Shoolery and Rogers J Am Chem Soc 80 5121 1958.] The 21-O-benzoyl derivative has m 201-202° [Reichstein Helv Chim Acta 20 953 1937].

**Corticotropin** [92307-52-3] **polypeptide**  $M_r \sim 4697$ . Extract separated by ion-exchange on CMcellulose, desalted, evapd and lyophilised. Then run on gel filtration (Sephadex G-50) [Lande et al. *Biochemical Preparations* 13 45 1971; Esch et al. *Biochem Biophys Res Commun* 122 899 1984].

Cortisol see hydrocortisone on p. 541.

Cortisone [53-06-5] M 360.5, m 230-231°,  $[\alpha]_{546}^{20}$  +225° (c 1, in EtOH). Crystd from 95% EtOH or acetone.

Cortisone-21-acetate [50-04-4] M 402.5, m 242-243°,  $[\alpha]_{546}^{20}$  +227° (c 1, in CHCl<sub>3</sub>). Crystd from acetone.

Creatine (H<sub>2</sub>O) (*N*-guanidino-*N*-methylglycine) [6020-87-7] M 131.1, m 303°,  $pK_1^{25}2.63$ ,  $pK_2^{25}14.3$ . Likely impurities are creatinine and other guanidino compounds. Crystd from water as monohydrate. Dried under vacuum over P<sub>2</sub>O<sub>5</sub> to give anhydrous material.

**Creatine phosphate di Na, 4H<sub>2</sub>O salt (phosphocreatine)** [922-32-7] M 327.1,  $pK_1^{27}$  2.7,  $pK_2^{27}$  4.58,  $pK_3^{27} \sim 12$ . To 3-4g of salt in H<sub>2</sub>O (220mL) is added 4 vols of EtOH with thorough stirring and allowed to stand at 20° for 12hrs (this temp is critical as crystals did not readily form at 23° or 25°). The salt first appears as oily droplets which slowly settle and crystallise. After 12hrs the supernatant is clear. Stirring

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and scratching the flask containing the filtrate brings out additional (0.3-1g) crystals if the salt is kept at 20° for 12hrs. Filter at room temp, wash with 3 x 5mL of ice-cold 90% EtOH then 5mL of abs EtOH and dry in a vac desiccator (Drierite or CaCl<sub>2</sub>) for 16-30hrs. The hexahydrate (plates) is converted to the tetrahydrate salt (needles) in vac at -10°. [Ennor and Stocken *Biochem Prep* 5 9 1957; *Biochem J* 43 190 1958.]

Creatinine (2-imino-1-methyl-4-oxoimidazolidine) [60-27-5] M 113.1, m 260°(dec),  $pK_1^{25}$ 4.80,  $pK_2^{25}$ 9.2. Likely impurities are creatine and ammonium chloride. Dissolved in dilute HCl, then neutralised by adding ammonia. Recrystd from water by adding excess of acetone.

Crotaline (monocrotaline, 12,13-dihydroxy-(13 $\beta$ -14 $\beta$ H)-14,19-dihydro-20-norcrotalanan-11,15-dione) [315-22-0] M 325.4, m 196-197°(dec), 197-198°(dec), 203°(dec),  $[\alpha]_D^{20}$ -55° (c 1, EtOH). It forms prisms from absolute EtOH and recrystallises also from CHCl<sub>3</sub>. UV in 96% EtOH has  $\lambda_{max}$  217nm (log  $\varepsilon$  3.32). [Adams et al. J Am Chem Soc 74 5612 1952; Culvenor and Smith Aust J Chem 10 474 1957.] The hydrochloride has m 212-214° (from MeOH-Et<sub>2</sub>O) and  $[\alpha]_D^{28}$ -38.4° (c 5, H<sub>2</sub>O) [Adams and Gianturco J Am Chem Soc 78 1922 1956]. The picrate has m 230-231.5°(dec) [Adams et al. J Am Chem Soc 74 5614 1952].

 $\alpha$ -Cyclodextrin (H<sub>2</sub>O) [10016-20-3] M 972.9, m >280°(dec),  $[\alpha]_{546}$  +175° (c 10, H<sub>2</sub>O). Recrystd from 60% aq EtOH, then twice from water, and dried for 12hours in a vacuum at 80°. Also purified by pptn from water with 1,1,2-trichloroethylene. The ppte was isolated, washed and resuspended in water. This was boiled to steam distil the trichloroethylene. The soln was freeze-dried to recover the cyclodextrin. [Armstrong et al. J Am Chem Soc 108 1418 1986].

**B-Cyclodextrin** (H<sub>2</sub>O) [7585-39-9] M 1135.0, m >300°(dec),  $[\alpha]_{546}$  +170° (c 10, H<sub>2</sub>O). Recrystd from water and dried for 12hours in a vacuum at 110°, or 24hours in a vacuum at 70°. The purity was assessed by TLC on cellulose with a fluorescent indicator. [Taguchi, J Am Chem Soc 108 2705 1986; Tabushi et al. J Am Chem Soc 108 4514 1986; Orstam and Ross J Phys Chem 91 2739 1987.]

**D**-(*R*-natural) and L-(*S*-non-natural) Cycloserine (2-amino-3-isoxazolidone) [*R*- 68-41-7 and S- 339-72-0] **M** 102.1, **m** 145-150° (dec), 154-155°, 155-156° (dec), 156° (dec),  $[\alpha]_D^{25}$  (+) and (-) 137° (c 5, 2N NaOH),  $pK_1^{10}$  4.5,  $pK_2^{10}$  7.74,  $pK_1^{25}$  4.50,  $pK_2^{25}$  7.43,  $pK_1^{50}$  4.44,  $pK_2^{50}$  7.20. Purified by recrystn from aqueous EtOH or MeOH or aqueous NH<sub>3</sub> + EtOH or isoPrOH. Also recrystd from aqueous ammoniacal soln at pH 10.5 (100mg/mL) by diluting with 5 volumes of isopropanol and then adjusting to pH 6 with acetic acid. An aqueous soln buffered to pH 10 with Na<sub>2</sub>CO<sub>3</sub> can be stored in a refrigerator for 1 week without decomposition. UV:  $\lambda_{max}$  226nm ( $A_{1cm}^{1\%}$  4.02). The *tartrate salt* has **m** 165-166° (dec), 166-168° (dec), and  $[\alpha]_D^{24}$  -41° (c 0.7, H<sub>2</sub>O). [Stammer et al. J Am Chem Soc **79** 3236 1959; UV: Kuehl J Am Chem Soc **77** 2344 1955.]

Cystamine dihydrochloride [2,2'-diaminodiethylene disulfide dihydrochloride, 2,3'-dithiobis(ethylamine) dihydrochloride] [56-17-7] M 225.2, m 219-220°(dec),  $pK_1^{30}$  8.82,  $pK_2^{30}$ 9.58. Recrystd by dissolving in EtOH containing a few drops of dry EtOH-HCl, filtering and adding dry Et<sub>2</sub>O. The solid is dried in a vacuum and stored in dry and dark atmosphere. It has been recrystd from EtOH (solubility: 1g in 60mL of boiling EtOH) or MeOH (plates). The *free base* has b 90-100°/0.001mm, 106-108°/5mm and 135-136°/atm,  $d_4^{20}$  1.1559,  $n_D^{20}$  1.5720. [Verly and Koch *Biochem J* 58 663 1954; Gonick et al. *J Am Chem Soc* 76 4671 1954; Jackson and Block *J Biol Chem* 113 137 1936].] The dihydrobromide has m 238-239° (from EtOH-Et<sub>2</sub>O) [Viscontini Helv Chim Acta 36 835 1953].

S,S-(L,L)-Cystathionine (S-2-amino-2-carboxyethyl-L-homocysteine, L-2-amino-4[(2-amino-2-carboxyethyl)thio]butyric acid) [56-88-2] M 222.3, m >300°, dec at 312° with darkening at 270°,  $[\alpha]_D^{20}$  +23.9° (c 1, M HCl). Could be converted to the *HCl* salt by dissolving in 20% HCl and carefully basifying with aqueous NH<sub>3</sub> until separation is complete. Filter off and dry in a vacuum. It forms prisms from H<sub>2</sub>O. The *dibenzoyl* derivative has m 229° (from EtOH). [IR: Greenstein and Winitz Chemistry of the Amino Acids (J Wiley) Vol 3 2690 1961 and Tallan et al. J Biol Chem 230 707 1958; Synthesis: du Vigneaud et al. J Biol Chem 143 59 1942; Anslow et al. J Biol Chem 166 39 1946.]

[Prepn: Weiss and Stekol J Am Chem Soc 73 2497 1951; see also du Vigneaud et al. J Biol Chem 143 60 1942; Biological synthesis: Greenberg Methods Enzymol 5 943 1962.]

Cysteamine (2-aminoethanethiol, 2-mercaptoethylamine) [60-23-1] M 77.2, m 97-98.5°, 98-99°, 99-100°,  $pK_1^0$  9.15,  $pK_2^0$  11.93,  $pK_1^{30}$  8.42,  $pK_2^{30}$  10.83. Soluble in H<sub>2</sub>O giving an alkaline reaction and it has a disagreeable odour. Likely impurity is the disulfide, cystamine which is not soluble in alkaline solution. Under a N<sub>2</sub> atmosphere dissolve in EtOH, evaporate to dryness and wash the white residue with dry pet ether, then sublime at 0.1mm and store under N<sub>2</sub> (out of contact with air) at 0-10° in the dark. Its  $HgCl_2$  (2:3) complex has m 181-182° (from H<sub>2</sub>O), and its picrate has m 125-126°. [Mills and Bogert J Am Chem Soc 57 2328 1935, 62 1173 1940; Baddiley and Thain J Chem Soc 800 1952; Shirley Preparation of Organic Intermediates (J. Wiley) Vol 3 189 1951; Barkowski and Hedberg J Am Chem Soc 109 6989 1987.]

**Cysteamine hydrochloride** [156-57-0] **M 113.6, m 70.2-70.7°, 70-72°**. Purified by recrystn from EtOH. It is freely soluble in H<sub>2</sub>O and should be stored in a dry atmosphere. [Mills and Bogert J Am Chem Soc **62** 1177 1940.] The picrate has **m** 125-126°, see previous entry for free base.

(±)-Cysteic acid (3-sulfoalanine, 1-amino-3-sulfopropionic acid) [13100-82-8, 3024-83-7] M 169.2, m 260°(dec). Likely impurities are cystine and oxides of cysteine. Crystd from water by adding 2 volumes of EtOH. When recrystd from aqueous MeOH it has m 264-266°, and the anhydrous acid has m ~260°(dec). [Chapeville and Formageot *Biochim Biophys Acta* 26 538 1957; J Biol Chem 72 435 1927.]

R(L)-Cysteic acid (H<sub>2</sub>O) [23537-25-9] M 187.2, m 275-280° (dec), 289°,  $[\alpha]_D^{20} + 8.66°$  (c 7.4, H<sub>2</sub>O, pH 1) and +1.54° (H<sub>2</sub>O, pH 13), pK<sub>1</sub><sup>25</sup> 1.9 (SO<sub>3</sub>H), pK<sub>2</sub><sup>25</sup> 8.7 (CO<sub>2</sub>H), pK<sub>3</sub><sup>25</sup> 12.7 (NH<sub>2</sub>). Likely impurities are cystine and oxides of cysteine. Crystd from water by adding 2 volumes of EtOH. When recrystd from aqueous MeOH it has m 264-266°, and the anhydrous acid has m ~260°(dec). [Chapeville and Formageot *Biochim Biophys Acta* 26 538 1957; *J Biol Chem* 72 435 1927.]

**D-(S)- and L-(R)- Cysteine** (S- and R-2-amino-3-mercaptopropionoic acid) [S(+)-: 921-01-7]and R(-)-: 52-90-4] M 121.2, m 230°, 240° (dec),  $[\alpha]_D^{20}(+)$  and (-) 7.6° (c 2, M HCl) and (+) and (-) 10.1° (c 2, H<sub>2</sub>O, pH 10),  $pK_1^{25}$  1.92 (CO<sub>2</sub>),  $pK_2^{25}$  8.35 (NH<sub>2</sub>),  $pK_3^{25}$  10.46 (SH). Purified by recrystn from H<sub>2</sub>O (free from metal ions) and dried in a vacuum. It is soluble in H<sub>2</sub>O, EtOH, Me<sub>2</sub>CO, EtOAc, AcOH, \*C<sub>6</sub>H<sub>6</sub> and CS<sub>2</sub>. Acidic solns can be stored under N<sub>2</sub> for a few days without deterioration. [For synthesis and spectra see Greenstein and Winitz Chemistry of the Amino Acids (J. Wiley) Vol 3 p1879 1961.]

L-Cysteine hydrochloride (H<sub>2</sub>O) [52-89-1] M 175.6, m 175-178° (dec),  $[\alpha]_D^{25}$  +6.53° (5M HCl). Likely impurities are cystine and tyrosine. Crystd from MeOH by adding diethyl ether, or from hot 20% HCl. Dried under vacuum over P<sub>2</sub>O<sub>5</sub>. *Hygroscopic*.

(±)-Cysteine hydrochloride [10318-18-0] M 157.6. Crystd from hot 20% HCl; dried under vacuum over  $P_2O_5$ .

L-Cystine [56-89-3] M 240.3,  $[\alpha]_D^{18.5}$ -229° (c 0.92 in M HCl),  $pK_1^{25}$  1.04 (1.65),  $pK_2^{25}$  2.05 (2.76),  $pK_3^{25}$  8.00 (7.85),  $pK_4^{25}$  10.25 (8.7, 9.85). Cystine disulfoxide was removed by treating an aqueous suspension with H<sub>2</sub>S. The cystine was filtered off, washed with distilled water and dried at 100° under vacuum over P<sub>2</sub>O<sub>5</sub>. Crystd by dissolving in 1.5M HCl, then adjusting to neutral pH with ammonia. Likely impurities are D-cystine, meso-cystine and tyrosine.

Cytidine [65-46-3] M 243.2, m 210-220°(dec), 230°(dec), 251-252°(dec),  $[\alpha]_{546}^{20}$  +37° (c 9, H<sub>2</sub>O),  $[\alpha]_D^{20}$ +29° (c 9, H<sub>2</sub>O), pK 3.85. Crystd from 90% aqueous EtOH. Also has been converted to the *sulfate* by dissolving (~200mg) in a soln of EtOH (10mL) containing H<sub>2</sub>SO<sub>4</sub> (50mg), whereby the salt crystallises out. It is collected, washed with EtOH and dried for 5hours at 120°/0.1mm. The *sulfate* has m 225°. The *free base* can be obtained by shaking with a weak ion-exchange resin, filtering, evaporating and recrystallising the residue from EtOH as before. [Fox and Goodman J Am Chem Soc 73 3256 1956; Fox and

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Shugar Biochim Biophys Acta 9 369 1952; see Prytsas and Sorm in Synthetic Procedures in Nucleic Acid Chemistry (Zorbach and Tipson Eds) Vol 1 404 1973.]

Cytisine see entry in Chapter 4.

Cytochalasin B (from dehydrated mould matter) [14930-96-2] M 479.6. Purified by MeOH extraction, reverse phase C18 silica gel batch extraction, selective elution with 1:1 v/v hexane/tetrahydrofuran, crystn, subjected to TLC and recrystallised [Lipski et al. Anal Biochem 161 332 1987].

Cytochrome  $c_1$  (from horse, beef or fishes' heart, or pigeon breast muscle) [9007-43-6] M ~ 13,000. Purified by chromatography on CM-cellulose (CM-52 Whatman) [Brautigan et al. Methods Enzymol 53D 131 1978]. It has a high PI (isoelectric point) and has been purified further by adsorption onto an acidic cation exchanger, e.g. Amberlite IRC-50 (polycarboxylic) or in ground form Amberlite XE-40 (100-200 mesh) or Decalso-F (aluminium silicate), where the non-cytochrome protein is not adsorbed and is readily removed. The cytochrome is eluted using a soln containing 0.25g ions/L of a univalent cation at pH 4.7 adsorbed onto the NH<sub>4</sub><sup>+</sup> salt of Amberlite IRC-50 at pH 7, washed with H<sub>2</sub>O and then with 0.12M NH<sub>4</sub>OAc to remove non-cytochrome protein. When the cytochrome begins to appear in the eluate then the NH<sub>4</sub>OAc concn is increased to 0.25 M. The fractions with *ca* Fe = 0.465—0.467 are collected, dialysed against H<sub>2</sub>O and adsorbed onto a small IRC-50 column and eluted with 0.5M NH<sub>4</sub>OH, then dialysed and lyophilised. (A second fraction (II) can be eluted from the first resin with 0.5M NH<sub>4</sub>OH but is discarded). [Keilin and Hartree Biochem Prep 1 1 1952; Margoliash Biochem Prep 8 33 1957.]

Cytochrome c has been recrystd as follows: The above eluate (ca 100mL) is dialysed against  $H_2O$  (10 vols) at 4º for 24 h (no more), then passed through an XE-40 column (2 x 1 cm above) which is equilibrated with 0.1M NH<sub>4</sub>OAc pH 7.0. The column is washed with 0.1% (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pH 8.0 and the dark red resin in the upper part of the column is collected and in 0.1% (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> pH 8.0 transferred to another column (7 mm diameter) and the cytochrome c is eluted with 5%  $(NH_4)_2SO_4$  pH 8.0. More than 98% of the red colour is collected in a volume of ca 4mL in a weighed centrifuge tube. Add a drop of octanol, 0.43g of  $(NH_4)_2SO_4/g$  of soln. When the salt has dissolved ascorbic acid (5mg), add a few drops of 30% NH<sub>3</sub> and keep the soln at 10° for 10min (turns lighter colour due to reduction). Then add finely powdered (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> in small portions (stir with a glass rod) until the soln becomes turbid. Stopper the tube tightly, and set aside at 15-25° for 2 days while the cytochrome c separates as fine needles or rosettes. Further (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (20mg) are added per mL of suspension and kept in the cold for a few days to complete the crystallisation. The crystals are collected by centrifugation (5000xg), suspended in saturated  $(NH_4)_2SO_4$  (pH 8.0 at 10°) then centrifuged again. For recrystin the crystals are dissolved in the least volume of H<sub>2</sub>O, one drop of ammonia and 1 mg of ascorbic acid are added and the above process is repeated. The yield of twice recrystd cytochrome c from 2Kg of muscle is ca 200 mg but this varies with the source and freshness of the muscle used. The crystals are stored as a solid after dialysis against 0.08M NaCl or 0.1M sodium buffer and lyophilising, or as a suspension in saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> at 0°. [Hagihara et al. Biochem Prep 6 1 1958.] Purity of cytochrome c: This is checked by the ratio of the absorbance at 500nm (reduced form) to 280nm (oxidised form), i.e.  $\varepsilon_{500}/\varepsilon_{280}$  should be between 1.1 and 1.28, although values of up to 1.4 have been obtained for pure preparations.

For the preparation of the reduced form see Margoliash Biochem Prep 5 33 1957 and Yonetani Biochem Prep 11 19 1966.

Cytochrome from *Rhodospirillum rubrum*. ( $\varepsilon_{270}/\varepsilon_{551}$  0.967). Purified by chromatography on a column of CM-Whatman cellulose [Paleus and Tuppy Acta Chem Scand 13 641 1959].

Cytochrome c oxidase (from bovine heart mitochondria). [9001-16-5]  $M_r$  100,000/haeme, [EC 1.9.3.1]. Purified by selective solubilisation with Triton X-100 and subsequently with lauryl maltoside; finally by sucrose gradient centrifugation [Li et al. *Biochem J* 242 417 1978].

Also purified by extraction in 0.02 M phosphate buffer (pH 7.4) containing 2% of cholic acid (an inhibitor which stabilises as well as solubilises the enzyme) and fractionated with  $(NH_4)_2SO_4$  collecting the 26-33% saturation cut and refractionating again and collecting the 26-33% saturation fraction. The pellet collected at 10,000xg appears as an oily paste. The cholate needs to be removed to activate the enzyme as follows: The ppte is dissolved in 10mL of 0.1M phosphate buffer pH 7.4, containing 1% of Tween-80 and dialysed against 1L of 0.01 M PO<sub>4</sub> buffer (pH 7.4) containing 1% of Tween-80 for 10 h at 0° and aliquoted. The enzyme is

stable at 0° for 2 weeks and at -15° for several months. It is assayed for purity (see reference) by oxidation of reduced cytochrome c (Km 10µM). [Yonetani *Biochem Prep* 11 14 1966; J Biol Chem 236 1680 1961.]

Cytokines see chemokines, interferons, interleukins.

Cytosine [71-30-7] M 111.1, m 320-325° (dec), pK<sub>1</sub><sup>25</sup>4.6, pK<sub>2</sub><sup>25</sup>12.1. Crystd from water.

Cytosine-1- $\beta$ -O-arabinofuranoside (Cytarabin) [147-94-4] M 243.2, m ~220°(dec), 212-213.5°,  $[\alpha]_D^{20}$ +155° (c 1, H<sub>2</sub>O), pK<sup>25</sup> 4.3. Purified by recrystn from aqueous EtOH. It has  $\lambda_{max}$  212 and 279nm at pH 2 and 272nm at pH 12. [Walwick et al. Proc Chem Soc (London) 84 1959.]

**N-Decanoyl-N-methylglucamine** (Mega-10, N-D-glucidyl-N-methyl deconamide) [85261-20-7] M 349.5, m 91-93°, 92°. Possible impurities are decanoic acid and N-methylglycamine. The former is removed by grinding the solid with Et<sub>2</sub>O and then with pet ether and dried over  $P_2O_5$ . Twice recryst from MeOH-Et<sub>2</sub>O by dissolving in the minimum volume of MeOH and adding Et<sub>2</sub>O and drying in a vacuum. To remove the glycamine the solid (800mg) is dissolved in hot H<sub>2</sub>O (10mL) and set aside. Mega-10 crystallises in colourless needles. These are filtered off and dried in a vacuum to constant weight. It is a good non-ionic non-hygroscopic detergent with a critical micelle concentration (CMC) of 7.4mM (0.26%) in 0.1M Tris-HCl pH 7.4 at 25°. [Hildreth Biochem J 207 363 1982.]

Demeclocycline hydrochloride (7-chloro-6-demethyltetracycline hydrochloride, Clortetrin) [64-73-3] M 501.3, m 174-178°(dec, for sesquihydrate),  $[\alpha]_D^{25} \cdot 258°$  (c 0.5, 0.1N H<sub>2</sub>SO<sub>4</sub>), pK 4.45 [H<sub>2</sub>O-Me<sub>2</sub>NCHO (1:1)]. Crystd from EtOH-Et<sub>2</sub>O or H<sub>2</sub>O and dried in air [McCormick et al. J Am Chem Soc 79 4561 1957; Dobrynin et al. Tetrahedron Lett 901 1962].

**2'-Deoxyadenosine** (adenine 2'-deoxyriboside) [16373-93-6] M 269.3, m 187-189°, 189-191°,  $[\alpha]_D^{20} - 25°$  (c 0.5, H<sub>2</sub>O),  $[\alpha]_{589}^{25} - 26°$ ,  $[\alpha]_{310}^{25} - 206°$  (c 0.5, H<sub>2</sub>O), pK<sup>20</sup> 3.79. Purified by recrystn from H<sub>2</sub>O (as hydrated crystals; solubility of mono-hydrate is 1.1% in H<sub>2</sub>O at 20°). It has  $\lambda_{max}$  258nm (pH 1), 260nm (pH 7) and 261nm (pH 13). [Ness and Fletcher J Am Chem Soc 81 4752 1959; Walker and Butler Can J Chem 34 1168 1956.] The 3',5'-O-diacetyl derivative has m 151-152° (recrystd from EtOAc-pet ether).

**3'-Deoxyadenosine** (Cordycepin, adenine 3'-deoxyriboside) [73-03-0] M 251.2, m 225-226°, 225-229°,  $[\alpha]_D^{20}$ -47° (H<sub>2</sub>O), pK<sub>Est</sub> ~ 4.8. It forms needles from EtOH, *n*-BuOH and *n*-PrOH, and from H<sub>2</sub>O as the mono-hydrate. It has  $\lambda_{max}$  260nm ( $\epsilon$  14,600) in EtOH. The picrate has m 195°(dec, yellow crystals from H<sub>2</sub>O). [Kaczka et al. Biochim Biophys Acta 14 456 1964; Todd and Ulbricht J Chem Soc 3275 1960; Lee et al. J Am Chem Soc 83 1906 1961; Walton et al. J Am Chem Soc 86 2952 1964.]

11-Deoxycorticosterone acetate (21-acetoxy-4-pregnen-3,20-dione) [56-47-3] M 372.5, m 154-159°, 154-160°, 155-157°, 155-161°,  $[\alpha]_D^{20} + 174°$  (c 1, dioxane),  $[\alpha]_D^{22-24} + 196°$  (c 1, CHCl<sub>3</sub>). Recrystallises from EtOH as needles or Me<sub>2</sub>CO-hexane, and sublimes at high vacuum. Partly soluble in MeOH, Me<sub>2</sub>CO, Et<sub>2</sub>O and dioxane but insoluble in H<sub>2</sub>O. [Romo et al. J Am Chem Soc 79 5034 1957; NMR: Shoolery and Rogers J Am Chem Soc 80 5121 1959.]

2'-Deoxycytidine monohydrate [951-77-9] M 245.2, m 119-200°, 207-209°, 213-215°,  $[\alpha]_D^{25}$ +78° (c 0.4, N NaOH),  $[\alpha]_D^{23}$ +57.6° (c 2, H<sub>2</sub>O), pK 4.25. Purified by recrystn from MeOH-Et<sub>2</sub>O or EtOH and dried in air. [NMR: Miles J Am Chem Soc 85 1007 1963; UV: Fox and Shugar Biochim Biophys Acta 9 369 1952.] The hydrochloride crystallises from H<sub>2</sub>O-EtOH and has m 174°(dec, 169-173°) [Walker and Butler Can J Chem 34 1168 1956.] The picrate has m 208°(dec). [Fox et al. J Am Chem Soc 83 4066 1961.]

2'-Deoxycytidine 5'-monophosphoric acid (deoxycytidylic acid) [1032-65-1] M 307.2, m 170-172°(dec), 183-184°(dec), 183-187°(dec),  $[\alpha]_D^{21} + 35°$  (c 0.2, H<sub>2</sub>O), pK<sub>1</sub> 4.6, pK<sub>2</sub> 6.6.

Recrystd from H<sub>2</sub>O or aqueous EtOH and dried in a vacuum. [Volkin et al. J Am Chem Soc 73 1533 1951; UV: Fox et al. J Am Chem Soc 75 4315 1953; IR: Michelson and Todd J Chem Soc 3438 1954.]

2'-Deoxyguanosine monohydrate (9-[2-deoxy- $\beta$ -D-ribofuranosyl]guanidine) [961-07-9] M 285.3, m ca 200°(dec),  $[\alpha]_D^{20}+37.5^\circ$  (c 2, H<sub>2</sub>O),  $[\alpha]_D^{14}$ -47.7° (c 0.9, N NaOH), pK<sub>Est(1)</sub>~ 3.3, pK<sub>Est(2)</sub>~ 9.2. Recryst from H<sub>2</sub>O as the monohydrate. [Brown and Lythgoe J Chem Soc 1990 1950; Levene and London J Biol Chem 81 711 1929, 83 793 1929]; UV: Hotchkiss J Biol Chem 175 315 1948; ORD: Levendahl and James Biochim Biophys Acta 26 89 1957.] The 3',5'-di-O-acetyl derivative cryst from aqueous EtOH has m 222°(dec),  $[\alpha]_D^{18}$ -38° (c 0.3, 10% aq EtOH) [Hayes et al. J Chem Soc 808, 813 1955].

**2'-Deoxyinosine** [890-38-0] M **252.2, m 206°(dec), 218-220°(dec),**  $[\alpha]_D^{2.5} - 2.1°$  (c 2, N NaOH),  $[\alpha]_D^{21.5}$  (c 1, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 8.9, pK<sub>Est(2)</sub>~ 12.4. Purified by recrystn from H<sub>2</sub>O. [Brown and Lythgoe J Chem Soc 1990 1950; UV: : MacNutt Biochem J 50 384 1952.]

**5-Deoxy-5-(methylthio)adenosine** [2457-80-9] M 297.3, m 210-213°(dec), 211°, 212°, 213-214°,  $[\alpha]_D^{20}$ -23.7° (c 0.02, pyridine),  $[\alpha]_D^{20}$ -8° (c 1, 5% aq NaOH),  $[\alpha]_D^{25}$ +15° (c 0.4-1.0, 0.3N aq AcOH),  $pK_{Est}$ ~3.5. It has been recrystif from H<sub>2</sub>O and sublimed at 200°/0.004mm. [v.Euler and Myrbäck Z physiol Chem 177 237 1928; Weygand and Trauth Chem Ber 84 633 1951; Baddiley et al. J Chem Soc 2662 1953.] The hydrochloride has m 161-162° [Kuhn and Henkel Hoppe Seyler's Z Physiol Chem 269 41 1941]. The picrate has m 183°(dec) (from H<sub>2</sub>O).

**Deoxyribonucleic acid** (from plasmids). Purified by two buoyant density ultracentrifugations using ethidium bromide-CsCl. The ethidium bromide was extracted with  $Et_2O$  and the DNA was dialysed against buffered EDTA and lyophilised. [Marmur and Doty *J Mol Biol* 5 109 1962; Guerry et al. *J Bacteriol* 116 1064 1973.] See p. 504.

3'-Deoxythymidine {2',3'-dideoxythymidine,  $1-[(2r)-5c-hydroxymethyltetrahydro(2r)-furyl]-5-methylpyrimidine-2,4-dione} [3416-05-5] M 226.2, m 145°, 149-151°, <math>[\alpha]_D^{26}+18°$  (c 1, H<sub>2</sub>O), pK<sub>Est</sub> ~ 9.2. Recrystd from Me<sub>2</sub>CO + MeOH. [Michelson and Todd J Chem Soc 816 1955.]

**2'-Deoxyuridine**  $[1-(\beta-D-erythro-2-deoxypentofuranosyl)-1H-pyrimidine-2,4-dione] [951-78 0] M 228.2, m 163°, 163-163.5°, 165-167° 167°, <math>[\alpha]_D^{26} + 30°$  (c 2, H<sub>2</sub>O),  $[\alpha]_D^{22} + 50°$  (c 1, N NaOH), pK<sup>25</sup> 9.3. Forms needles from absolute EtOH or 95% EtOH. [Dekker and Todd *Nature* 166 557 1950; Brown et al. J Chem Soc 3035 1958; NMR Jardetzky J Am Chem Soc 83 2919 1961; Fox and Shugar Biochim Biophys Acta 9 369 1952; UV: MacNutt Biochem J 50 384 1952.]

3'-Deoxyuridine {1-[(2R)-5c-hydroxymethyltetrahydro(2r)furyl]-5-methylpyrimidin-2,4dione, 2'.3'-dideoxythymidine} [7057-27-4, 3416-05-5] M 226.2, m 149-151°,  $[\alpha]_D^{20}$ +18° (c 1, H<sub>2</sub>O), pK<sub>Est</sub> ~ 9.3. Recrystd from Me<sub>2</sub>CO + MeOH and dried in a vacuum. [Michelson and Todd J Chem Soc 816 1955.]

**Dermatan sulfate (condroitin sulfate B from pig skin)** [54328-33-5 (Na salt)]. Purified by digestion with papain and hyaluronidase, and fractionation using aqueous EtOH. [Gifonelli and Roden *Biochem* Prep 12 1 1968.]

**Desthiobiotin** [533-48-2] **M 214.3, m 156-158°**,  $[\alpha]_D^{20}$  +10.5° (c 2, H<sub>2</sub>O), pK<sub>Est</sub> ~2.8. Crystd from H<sub>2</sub>O or 95% EtOH.

**Dextran** [9004-54-0]  $M_r$  6,000-220,000. Solutions keeps indefinitely at room temperature if 0.2mL of Roccal (10% alkyldimethylbenzylammonium chloride) or 2mg phenyl mercuric acetate are added per 100mL solution. [Scott and Melvin Anal Biochem 25 1656 1953.]

**Diacetone-D-Glucose** (1,2:5,6-di-O-isopropylidene- $\alpha$ -D-glucofuranoside) [582-52-5] M 260.3, m 107-110°, 110.5°, 111-113°, 112°,  $[\alpha]_D^{15}$ -18.4° (c 1, H<sub>2</sub>O). It crystallises from Et<sub>2</sub>O, (needles), pet ether or \*C<sub>6</sub>H<sub>6</sub> and sublimes *in vacuo*. It is sol in 7 vols of H<sub>2</sub>O and 200 vols of pet ether at their

N,N'-Diacetylchitobiose (2-acetyl-O<sup>4</sup>-[2-acetylamino-2-deoxy-β-D-glucopyranosyl]-2deoxy-D-glucose) [35061-50-8] M 424.4, m 245-247°(dec), 251.5-252.5°, 260-262°,  $[\alpha]_D^{25}$  +39.5° (extrapolated) → +18.5° (after 60 min, c 1, H<sub>2</sub>O). Recrystd from aqueous MeOH or aqueous EtOH + 1,2-dimethoxyethane. [Zilliken et al. J Chem Soc 77 1296 1955.]

**1,8-Diazafluorenone** (cyclopenta[1.2-b:4,3-b']dipyridin-9-one) [54078-29-4] M 182.2, m 205°, 229-231°, pK<sub>Est</sub> ~ 2.6. Recrystd from Me<sub>2</sub>CO. The oxime has m 119-200°. [Druey and Schmid Helv Chim Acta 33 1080 1950.]

**Di- and tri-carboxylic acids**. Resolution by anion-exchange chromatography. [Bengtsson and Samuelson Anal Chim Acta **44** 217b 1969.]

**Digitonin** [11024-24-1] **M 1229.3, m >270°(dec),**  $[\alpha]_{546}^{20}$  -63° (c 3, MeOH). Crystd from aqueous 85% EtOH or MeOH/diethyl ether.

**Digitoxigenin** [143-62-4] **M 374.5, m 253°,**  $[\alpha]_{546}^{20}$  +21° (c 1, MeOH). Crystd from aqueous 40% EtOH.

D(+)-Digitoxose [527-52-6] M 148.2, m 112°,  $[\alpha]_{546}^{20}$  +57° (c 1, H<sub>2</sub>O). Crystd from MeOH/diethyl ether, or ethyl acetate.

Dihydrofolate reductase (from Mycobacterium phlei) [9002-03-3]  $M_r \sim 18,000$  [EC 1.5.1.3]. Purified by ammonium sulfate pptn, then fractionated on Sephadex G-75 column, applied to a Blue Sepharose column and eluted with 1mM dihydrofolate. [Al Rubeai and Dole *Biochem J* 235 301 1986.]

7,8-Dihydrofolic acid (7,8-dihydropteroyl-L-glutamic acid, DHFA) [4033-27-6] M 443.4, pK<sub>1</sub> 2.0 (basic 10-NH), pK<sub>2</sub> 2.89 (2-NH<sub>2</sub>), pK<sub>3</sub> 3.45 ( $\alpha$ -CO<sub>2</sub>H), pK<sub>4</sub> 4.0 (basic 5N), pK<sub>5</sub> 4.8 ( $\gamma$ -CO<sub>2</sub>H), pK<sub>6</sub> 9.54 (acidic 3NH). Best purified by suspending (1g mostly dissolved)) in ice-cold sodium ascorbate (300mL of 10% at pH 6.0 [prepared by adjusting the pH of 30g of sodium ascorbate in 150mL of H<sub>2</sub>O by adding 1N NaOH dropwise using a glass electrode till the pH is 6.0]). This gave a clear solution with pH ~5. While stirring at 0° add N HCl dropwise slowly (0.1mL/min) until the pH drops to 2.8 when white birefringent crystals separate. These are collected by centrifugation (1000xg for 5min), washed 3x with 0.001N HCl by centrifugation and decantation. The residue is then dried in a vacuum (0.02mm) over P<sub>2</sub>O<sub>5</sub> (change the P<sub>2</sub>O<sub>5</sub> frequently at first) and KOH at 25° in the dark. After 24hours the solid reaches constant weight.

For the assay of *dihydrofolate reductase* (see below): suspend ~66.5mg of DHFA in 10mL of 0.001M HCl containing 10mM dithiothreitol (DTT stock made from 154mg in 10mL H<sub>2</sub>O making 0.1M), shake well and freeze in 400µL aliquots. Before use mix 400µL of this suspension with 0.1M DTT (200µL, also made in frozen aliquots), and the mixture is diluted with 200µL of 1.5M Tris-HCl pH 7.0 and 1.2mL of H<sub>2</sub>O (making a total volume of ~2mL) to give a clear solution. To estimate the concentration of DHFA in this solution, dilute 20µL of this solution to 1mL with 0.1M Tris-HCl pH 7.0 and read the OD at 282nm in a 1cm pathlength cuvette.  $\varepsilon$  at 282nm is 28,000M<sup>-1</sup>cm<sup>-1</sup>. [Reyes and Rathod *Methods Enzymol* **122** 360 1986.]

**Dihydropteridine reductase (from sheep liver)** [9074-11-7]  $M_r$  52,000 [EC 1.6.99.7]. Purified by fractionation with ammonium sulfate, dialysed *versus* tris buffer, adsorbed and eluted from hydroxylapatite gel. Then run through a DEAE-cellulose column and also subjected to Sephadex G-100 filtration. [Craine et al. J Biol Chem 247 6082 1972.]

Dihydropteridine reductase (from human liver) [9074-11-7] Mr 52,000 [EC 1.6.99.7]. Purified to homogeneity on a naphthoquinone affinity adsorbent, followed by DEAE-Sephadex and CM-Sephadex

chromatography. [Firgaira, Cotton and Danks, *Biochem J* 197 31 1981.] [For other dihydropteridine reductases see Armarego et al. *Med Res Rev* 4(3) 267 1984.]

**DL**-erythro-Dihydrosphingosine (dl-erythro-2-aminooctadecan-1,3-diol) [3102-56-5] M 301.5, m 85-86°, 85-87°, pK<sub>Est</sub> ~ 8.8. Purified by recrystn from pet ether-EtOAc or CHCl<sub>3</sub>. The ( $\pm$ )-*N*-dichloroacetyl derivative has m 142-144° (from MeOH). [Shapiro et al. J Am Chem Soc 80 2170 1958; Shapiro and Sheradsky J Org Chem 28 2157 1963.] The D-isomer crystallises from pet ether-Et<sub>2</sub>O and has m 78.5-79°, [ $\alpha$ ]<sub>546</sub><sup>28</sup> +6° (CHCl<sub>3</sub> + MeOH, 10:1). [Grob and Jenny Helv Chim Acta 35 2106 1953, Jenny and Grob Helv Chim Acta 36 1454 1953.]

Dihydrostreptomycin sesquisulfate [5490-27-7] M 461.4, m 250°(dec), 255-265°(dec),  $[\alpha]_D^{20}$ -92.4° (c 1, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 9.5 (NMe), pK<sub>Est(2,3)</sub>~ 13.4 (guanidino). It crystallises from H<sub>2</sub>O with MeOH, *n*-BuOH or methyl ethyl ketone. The crystals are not hygroscopic like the amorphous powder, however both forms are soluble in H<sub>2</sub>O but the amorphous solid is about 10 times more soluble than the crystals. The *free base* also crystallises from H<sub>2</sub>O-Me<sub>2</sub>CO and has  $[\alpha]_D^{26}$ -92° (aqueous solution pH 7.0). [Solomons and Regina *Science* 109 515 1949; Wolf et al. *Science* 109 515 1949; McGilveray and Rinehart J Am Chem Soc 87 4003 1956].

3-(3,4-Dihydroxyphenyl)-L-alanine (DOPA, EUODOPA) [59-92-7, 5796-17-8] M 197.2, m 275°(dec), 267-268°(dec), 284-286°(dec), ~295°(dec),  $[\alpha]_D^{13}$ -13.1° (c 5.12, N HCl),  $pK_1^{25}$ 2.32 (CO<sub>2</sub>H),  $pK_2^{25}$ 8.72 (NH<sub>2</sub>),  $pK_3^{25}$  9.96 (OH),  $pK_4^{25}$  11.79 (OH). Likely impurities are vanillin, hippuric acid, 3-methoxytyrosine and 3-aminotyrosine. Recryst from large vols of H<sub>2</sub>O as colourless white needles; solubility in H<sub>2</sub>O is 0.165%, but it is insoluble in EtOH, \*C<sub>6</sub>H<sub>6</sub>, CHCl<sub>3</sub>, and EtOAc. Also crystd by dissolving in dilute HCl and adding dilute ammonia to give pH 5, under N<sub>2</sub>. Alternatively, crystd from dil aqueous EtOH. It is rapidly oxidised in air when moist, and darkens; particularly in alkaline solution. Dry in a vacuum at 70° in the dark, and store in a dark container preferably under N<sub>2</sub>.  $\lambda_{max}$  220.5nm (log  $\varepsilon$  3.79) and 280nm (log  $\varepsilon$  3.42) in 0.001N HCl. [Yamada et al. *Chem Pharm Bull Jpn* 10 693 1962; Bretschneider et al. *Helv Chim Acta* 56 2857 1973; NMR: Jardetzky and Jardetzky J Biol Chem 233 383 1958.]

**3,4-Dihydroxyphenylalanine-containing proteins**. Boronate affinity chromatography is used in the selective binding of proteins containing 3,4-dihydroxyphenylalanine to a *m*-phenylboronate agarose column and eluting with 1M NH<sub>4</sub>OAc at pH 10. [Hankus et al. *Anal Biochem* **150** 187 *1986*.]

3-(3,4-Dihydroxyphenyl)-2-methyl-L-alanine [methyldopa, 2-amino-3-(3,4-dihydroxyphenyl)-2-methylpropionic acid] [555-30-6] M 238.2, m >300°, 300-301°(dec),  $pK_1^{25} 2.2$ ,  $pK_2^{25} 9.2$ ,  $pK_3^{25} 10.6$ ,  $pK_4^{25} 12.0$ . Recrystd from H<sub>2</sub>O. [Reinhold et al. J Org Chem 33 1209 1968.] The L-isomer forms a sesquihydrate from H<sub>2</sub>O m 302-304° (dec), and the anhydrous crystals are hygroscopic,  $[\alpha]_D^{23}$  -4.0° (c 1, 0.1N HCl),  $[\alpha]_{546}$  +154.5° (c 5, CuSO<sub>4</sub> solution). It has  $\lambda_{max}$  281nm ( $\varepsilon$  2780). Solubility in H<sub>2</sub>O at 25° is ~10mg/mL and the pH of an aqueous solution is ~5.0. It is almost insoluble in most organic solvents. [Stein et al. J Am Chem Soc 77 700 1955.]

(±)-7-(2,3-Dihydroxypropyl)theophylline (Diprophylline, Dyphylline) [479-18-5] M 254.3, m 158°, 160-164°, 161°, 161-164°, pK<sub>Est</sub> ~ 8.7. Recrystd from EtOH or H<sub>2</sub>O. Solubility in H<sub>2</sub>O is 33% at 25°, in EtOH it is 2% and in CHCl<sub>3</sub> it is 1%.  $\lambda_{max}$  (H<sub>2</sub>O) 273nm ( $\varepsilon$  8,855). [Roth Arch Pharm 292 234 1959.] The 4-nitrobenzoyl derivative has m 178° [Oshay J Chem Soc 3975 1956].

3,5-Diiodo-L-thyronine (3,5-diiodo-4-[4-hydroxyphenoxy]-1-phenylalanine) [1041-01-6] M 525.1, m 255°(dec), 255-257°(dec),  $[\alpha]_D^{22} + 26^\circ$  [2N HCl-EtOH (1:2)],  $pK_1^{20} 3.25$ ,  $pK_2^{20} 5.32$ ,  $pK_3^{20} 9.48$ . Recrystd from EtOH. [Chambers et al. J Chem Soc 3424 1949.]

3,5-Diiodo-L-tyrosine dihydrate [300-39-0] M 469.0, m 199-210°, 202°(dec),  $[\alpha]_D^{20} + 2.89°$  (c 4.9, 4% HCl),  $pK_1^{25}$  2.12,  $pK_2^{25}$  6.48,  $pK_3^{25}$  7.82. It forms crystals from H<sub>2</sub>O [solubility (g/L): 0.204 at 0°, 1.86 at 50°, 5.6 at 75° and 17.0 at 100°]. Also recrysts from 50% or 70% EtOH. When boiled in EtOH the crystals swell and on further boiling a gelatinous ppte is formed [Harrington *Biochem J* 22 1434 1928; Jurd J Am Chem Soc 77 5747 1955]. Also crystd from cold dilute ammonia by adding acetic acid to pH 6. 1,2-Dilauroyl-sn-glycero-3-phosphoethanolamine ( $\pm$ -dilauroyl- $\alpha$ -cephalin, 3-sn-phosphatidylethanolamine 1,2-didodecanoyl) [59752-57-7] M 579.8, m 210°, pK<sub>Est(1)</sub>~ 5.8 (PO<sub>4</sub>H), pK<sub>Est(2)</sub>~ 10.5 (NH<sub>2</sub>). Recrystd from EtOH or tetrahydrofuran. [Bevan and Malkin J Chem Soc 2667 1951; IR: Bellamy and Beecher J Chem Soc 728 1953.]

1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride [1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride] see entry on p. 212 in Chapter 4.

**1,2-Dimyristoyl-sn-glycero-3-phosphocholine monohydrate** (dimyristoyl-L- $\alpha$ -lecithin) [18194-24-6] M 696.0,  $[\alpha]_D^{24} + 7^\circ$  (c 8, EtOH-CHCl<sub>3</sub> 1:1 for  $\alpha_1$  form), pK<sub>Est</sub> ~ 5.8 (PO<sub>4</sub>). Three forms  $\alpha_1$ ,  $\alpha_2$  and  $\beta'$ . Recryst from aqueous EtOH or EtOH-Et<sub>2</sub>O. Solubility at 22-23° in Et<sub>2</sub>O is 0.03%, in Me<sub>2</sub>CO it is 0.06% and in pyridine it is 1.3%. [Baer and Kates J Am Chem Soc 72 942 1950; Baer and Maurakas J Am Chem Soc 74 158 1952; IR: Marinetti and Stotz J Am Chem Soc 76 1347 1954.] The S-isomer with 1 H<sub>2</sub>O is recryst from 2,6-dimethylheptan-4-one and has m 226-227° (sintering at 90-95°), and  $[\alpha]_D -7^\circ$  (c 6, MeOH-CHCl<sub>3</sub> 1:1). [Baer and Mattin J Biol Chem 193 835 1951.]

(±)-1,2-Dimyristoyl-sn-glycero-3-phosphoethanolamine (dimyristoyl- $\alpha$ --kephalin) [998-07-2] M 635-9, m 207°, pK<sub>Est(1)</sub>~ 5.8 (PO<sub>4</sub>H), pK<sub>Est(2)</sub>~ 10.5 (NH<sub>2</sub>). Recrystd from EtOH [Bevan and Malkin J Chem Soc 2667 1951]. The *R*-isomer has m 195-196° (sintering at 130-135°) after recrystn from CHCl<sub>3</sub>-MeOH,  $[\alpha]_D^{26}$  +6.7° (c 8.5, CHCl<sub>3</sub>-AcOH 9:1). [Baer Can J Biochem Physiol 35 239 1957; Baer et al. J Am Chem Soc 74 152 1952.]

S-1,2-Dipalmitin [761-35-3] M 568.9, m 68-69°  $[\alpha]_D^{20}$ -2.9° (c 8, CHCl<sub>3</sub>),  $[\alpha]_{546}^{20}$ +1.0° (c 10, CHCl<sub>3</sub>/MeOH, 9:1). Crystd from chloroform/pet ether.

*R***-Dipalmitoyl-sn-glycero-3-phosphatidic** acid [7091-44-3] M 648.9,  $[\alpha]_D^{26} + 4^{\circ}$  (c 10, CHCl<sub>3</sub>), pK<sub>Est(1)</sub>~ 1.6, pK<sub>Est(2)</sub>~ 6.1. Recrystd from Me<sub>2</sub>CO at low temp. At 21° it is soluble in \*C<sub>6</sub>H<sub>6</sub> (4.2%), pet ether (0.01%), MeOH (2%), EtOH (2.5%), AcOH (1.3%), Me<sub>2</sub>CO (1.76%), and Et<sub>2</sub>O (1.5%). [Baer J Biol Chem 189 235 1951.]

**R-1,2-Dipalmitoyl-sn-glycero-3-phosphocholine monohydrate** (dipalmitoyl- $\alpha$ -L-lecithin) [63-89-8] M 752.1, m sinters at 120°,  $[\alpha]_D^{25} + 7.0°$  (c 5.6, abs CHCl<sub>3</sub>), pK<sub>Est</sub> ~ 5.8 (PO<sub>4</sub>). It has three crystn forms  $\alpha_1$ ,  $\alpha_2$  and  $\beta'$  which change at 60-70° and at 229° respectively. In order to obtain a fine powder, ~2 g are dissolved in CHCl<sub>3</sub> (15mL) and pet ether (b 35-60°) is added and the soln evaporated to dryness *in vacuo* <20°, and then dried at 0.1mm over CaCl<sub>2</sub>. [Baer and Maurukas J Am Chem Soc 74 158 1952; Baer and Kates J Biol Chem 185 615 1950.]

*d*,*l*- $\beta\gamma$ -Dipalmitoylphosphatidyl choline [2797-68-4] M 734.1, m 230-233°, pK<sub>Est</sub> ~ 5.8 (PO<sub>4</sub>). Recrystd from chloroform and dried for 48h at 10<sup>-5</sup> torr [O'Leary and Levine J Phys Chem 88 1790 1984].

**Dipeptidyl aminopeptidase (from rat brain)** [9031-94-1] [EC 3.4.11.10]. Purified about 2000fold by column chromatography on CM-cellulose, hydroxylapatite and Gly-Pro AH-Sepharose. [Imai et al. J Biochem (Tokyo) 93 431 1983.]

**1,2-Distearoyl-sn-glycerol** [1429-59-0] **M 625.0.** The dl-form recrystallises from CHCl<sub>3</sub>-pet ether (b 40-60°), **m** 59.5° ( $\alpha$  form) and 71.5-72.5° ( $\beta$  form). Recrystn from solvents (e.g. EtOH, MeOH, toluene, Et<sub>2</sub>O) gives the higher melting form and resolidification gives the lower melting forms. [IR: Chapman J Chem Soc 4680 1958, 2522 1956; .] The S-isomer is recrystd from CHCl<sub>3</sub>-pet ether and has **m** 76-77°, [ $\alpha$ ]<sub>D</sub><sup>24</sup> -2.8° (c 6, CHCl<sub>3</sub>). [Baer and Kates J Am Chem Soc 72 942 1950.]

1,2-Distearoyl-sn-glycero-3-phosphoethanolamine (distearoyl- $\alpha$ -kephalin) [1069-79-0] M 748.1, m 180-182° (*R*-form, sintering at 130-135°), m 196° (± form), pK<sub>Est(1)</sub>~ 5.8 (PO<sub>4</sub>H), pK<sub>Est(2)</sub>~ 10.5 (NH<sub>2</sub>). The *R*-form is recrystd from CHCl<sub>3</sub>-MeOH and the ±-form is recrystd from EtOH. [Bevan and Malkin J Chem Soc 2667 1951; Baer Can J Biochem Physiol 81 1758 1959.] **Dolichol (from pig liver)** [11029-02-0]  $C_{80}$ - $C_{105}$  polyprenols. Cryst 6 times from pet ether/EtOH at -20°C. Ran as entity on a paper chromatogram on paraffin impregnated paper, with acetone as the mobile phase. [Burgos *Biochem J* 88 470 1963.]

Domoic acid [4-(2-carboxyhexa-3,5-dienyl)-3-carboxymethylproline] [14277-97-5] M 311.3, m 215°, 217°,  $[\alpha]_D^{20}$ -108° (c 1,H<sub>2</sub>O), pK<sub>1</sub> 2.20 (2-CO<sub>2</sub>H), pK<sub>2</sub> 3.72 (CO<sub>2</sub>H), pK<sub>3</sub> 4.93 (3-CH<sub>2</sub>CO<sub>2</sub>H), pK<sub>4</sub> 9.82 (NH). The acid (~300 mg) is purifed on a Dowex 1 column (3.5 x 40 mm, 200-400 mesh, acetate form), washed with H<sub>2</sub>O until neutral, then eluted with increasing concentrations of AcOH (8L) from 0 to 0.25M. The fraction containing domoic acid (in 50mL) is collected, evaporated to dryness under reduced pressure and recrystd from aqueous EtOH. Glutamate and Kainate receptor agonist. [Impellizzeri et al. *Phytochemistry* 14 1549 1975; Takemoto and Diago Arch Pharm 293 627 1960.]

**DNA** (deoxyribonucleic acids). The essential structures of chromosomes are DNA and contain the genetic "blue print" in the form of separate genes. They are made up of the four deoxyribonucleic acids (nucleotides): adenylic acid, guanylic acid, cytidylic acid and thymidylic acid (designated A, G, C, T respectively) linked together by their phosphate groups in ester bonds between the 3' and 5' hydroxy groups of the 2'-deoxy-D-ribose moiety of the nucleotides. The chains form a double stranded spiral (helix) in which the two identical nucleotide sequences run antiparallel with the heterocyclic bases hydrogen bonded (A..T, G..C) forming the "ladder" between the strands. Short sequences of DNA are available commercially, are commercially custom made or synthesised in a DNA synthesiser and purified by HPLC. Their purity can be checked by restriction enzyme cleavage followed by gel electophoresis, or directly by gel electrophoresis or analytical HPLC. Commercial DNAs are usually pure enough for direct use but can be further purified using commercially available kits involving binding to silica or other matrices and eluting with tris buffers.

Dopamine- $\beta$ -hydroxylase (from bovine adrenal medulla) [9013-38-1] M<sub>r</sub> ~290,000, [EC 1.14.17.1]. The Cu-containing glycoprotein enzyme has been isolated by two procedures. The first is an elaborate method requiring extraction, two (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> fractionations, calcium phosphate gel filtration, EtOH fractionation, DEAE-cellulose chromatography followed by two Sephadex-G200 gel filtrations giving enzyme with a specific activity of 65 Units/mg. [Friedman and Kaufman J Biol Chem 240 4763 1965; Rush et al. Biochem Biophys Res Commun 61 38 1974.] The second procedure is much gentler and provides good quality enzyme. Sedimented chromaffin vesicles were lysed in 10 volumes of 5mM K-phosphate buffer pH 6.5 using a loosely fitting Teflon-glass homogeniser. The mixture is centrifuged at 40,000xg/0.5 h and the supernatant is diluted with an equal volume of 100mM phosphate buffer (pH 6.5) containing 0.4M NaCl. This lysate is applied to a concanavelin A-Sepharose column (4 x 0.7cm) which had been equilibrated with 50 mM of phosphate buffer (pH 6.5 + 0.2M NaCl) with a flow rate of ~ 0.3 mL/min. The column is washed thoroughly with the buffer until  $OD_{280nm}$  is 0.005. The enzyme is then eluted with the same buffer containing 10%  $\alpha$ methyl-D-mannoside (flow rate 0.1 mL/min) and the enzyme is collected in twenty column volumes. The pooled eluate is concentrated by ultrafiltration in an Amicon Diaflo stirrer cell using an XM100A membrane. The concentrated enzyme is dialysed against 50 mM phosphate buffer (pH 6.5) containing 0.1% NaCl. The enzyme gives one band (+ two very weak band) on disc gel electrophoresis indicating better than 93% purity (67% fold purification) and has a specific activity of 5.4Units/mg. [Rush et al. Biochem Biophys Res Commun 57 1301 1974; Stewart and Klinman Ann Rev Biochem 57 551 1988.]

**Ellipticine** (5,11-dimethylpyrido[4,3:b]carbazole) [519-23-3] M 246.3, m 311-315°(dec), 312-314°(dec), pK 5.78 (80% aq methoxyethanol). This DNA intercalator is purified by recrystn from CHCl<sub>3</sub> or MeOH and dried *in vacuo*. The UV  $\lambda_{max}$  values in aqueous EtOH-HCl are at 241, 249, 307, 335 and 426nm. [Marini-Bettolo and Schmutz Helv Chim Acta 42 2146 1959.] The methiodide has m 360°(dec), with UV  $\lambda_{max}$  (EtOH-KOH) 223, 242, 251, 311, 362 and 432nm. [Goodwin et al. J Am Chem Soc 81 1903 1959.]

Enniatin A [11113-62-5] M 681.9, m 122-122.5°,  $[\alpha]_D^{18}$ -92° (c 0.9, CHCl<sub>3</sub>). A cyclic peptidic ester antibiotic which is recrystd from EtOH/water but is deactivated in alkaline soln. [Ovchinnikov and Ivanov in *The Proteins* (Neurath and Hill eds) Academic Press, NY, Vol V pp. 365 and 516 1982.]

(-)-Ephedrine (1R, 2S-2 - methylamino-1-phenylpropanol) [299-42-3] M 165.2, m ~34°, 36°, 38.1°, b 126-129°/7mm, 225-227°/760mm, d<sup>22</sup> 1.0085,  $[\alpha]_D^{26}$  -42° (c 4, 3% HCl),  $[\alpha]_D^{22.5}$  +15.1° (c 0.8, H<sub>2</sub>O), -9.36° (c 3, MeOH), pK<sup>22</sup> 9.58 (pK<sup>25</sup> 8.84 in 80% aq methoxy-ethanol). Purified by vacuum distn (dehydrates) and forms waxy crystals or granules, and may pick up 0.5 H<sub>2</sub>O. The presence of H<sub>2</sub>O raises its m to 40°. [Moore and Taber *J Amer Pharm Soc* 24 211 1935.] The anhydrous base recrystd from dry ether [Fleming and Saunders *J Chem Soc* 4150 1955]. It gradually decomposes on exposure to light and is best stored in an inert atmosphere in the dark (preferably at -20°). Sol in H<sub>2</sub>O is 5%, in EtOH it is 1% and it is soluble in CHCl<sub>3</sub>, Et<sub>2</sub>O and oils. It has pKa values in H<sub>2</sub>O of 10.25 (0°) and 8.69 (60°) [Everett and Hyne *J Chem Soc* 1136 1958; Prelog and Häflinger *Helv Chim Acta* 33 2021 1950] and pKa<sup>25</sup> 8.84 in 80% aqueous methoxyethanol [Simon *Helv Chim Acta* 41 1835 1958]. The hydrochloride has m 220° (from EtOH-Et<sub>2</sub>O) and [ $\alpha$ ]<sub>20</sub><sup>20</sup> -38.8° (c 2, EtOH). [IR: Chatten and Levi Anal Chem 31 1581 1959.] The anhydrous base crystallises from Et<sub>2</sub>O [Fleming and Saunders *J Chem Soc* 4150 1955].

(+)-Ephedrine hydrochloride (1S-2R-2-methylamino-1-phenylpropan-1-ol hydrochloride) [24221-86-1] M 201.7, m 216-219°,  $[\alpha]_D^{20}$  +34° (c 11.5, H<sub>2</sub>O). Recryst from EtOH-Et<sub>2</sub>O. The free base recrystallises from \*C<sub>6</sub>H<sub>6</sub> with m 40-41° (Skita et al. Chem Ber 66 974 1933].

Erythromycin A [114-07-8] M 733.9, m 133-135°(dec), 135-140°, 137-140°,  $[\alpha]_D^{20}$ -75° (c 2, EtOH), pK 8.9. It recrystallises from H<sub>2</sub>O to form hydrated crystals which melt at *ca* 135-140°, resolidifies and melts again at 190-193°. The m after drying at 56°/8mm is that of the **anhydrous** material at 137-140°. Its solubility in H<sub>2</sub>O in ~2mg/mL. The *Hydrochloride* has m 170°, 173° (from aq EtOH, EtOH-Et<sub>2</sub>O). [Flynn et al. J Am Chem Soc 76 3121 1954; constitution : Wiley et al. J Am Chem Soc 79 6062 1957].

β-Estradiol (1,3,5-estratrien-3,17β-diol) [50-28-2] M 272.4, m 173-179°, 176-178°,  $[\alpha]_D^{20}$  +76° to +83° (c 1, dioxane). Purified by chromatography on SiO<sub>2</sub> (toluene-EtOAc 4:1) and recrystd from CHCl<sub>3</sub>-hexane or 80% EtOH. It is stable in air and insoluble in H<sub>2</sub>O and is ppted by digitonin. UV  $\lambda_{max}$  at 225 and 280 nm. [Oppolzer and Roberts *Helv Chim Acta* 63 1703 1980.]

β-Estradiol-6-one (1,3,5-estratriene-3,17β-diol-6-one) [571-92-6] M 359.4, m 278-280°, 281-283°,  $[\alpha]_D^{20}$  +4.2° (c 0.7, EtOH). It forms plates from EtOH. The 3,17-diacetate has m 173-175° after recrystn from aqueous EtOH. [Longwell and Wintersteiner J Biol Chem 133 219 1940.] The UV has  $\lambda_{max}$  255 and 326nm in EtOH [Slaunwhite et al. J Biol Chem 191 627 1951].

Ethidium bromide [1239-45-8] M 384.3, m 260-262°. Crystd from MeOH or EtOH [Lamos et al. J Am Chem Soc 108 4278 1986]. Sol in H<sub>2</sub>O is 1%. POSSIBLE CARCINOGEN.

Ethoxyquin (1,2-dihydro-6-ethoxy-2,2,4-trimethylquinoline) [91-53-2] M 217.3, b 169°/12-13mm,  $d_4^{20}$  1.000, pK<sub>Est</sub> ~ 5.8. Purified by fractional distn *in vacuo* and solidifies to a glass. [Knoevenagel Chem Ber 54 1723, 1730 1921]. The *methiodide* has m 179° (from EtOH) and the *1*-phenylcarbamoyl derivative has m 146-147° (from EtOH). [Beaver et al. J Am Chem Soc 79 1236 1957.]

17- $\alpha$ -Ethynylestradiol [57-63-6] M 296.4, m 141-146°, 145-146°,  $[\alpha]_D^{20} + 4°$  (c 1, CHCl<sub>3</sub>). It forms a hemihydrate on recrystn from MeOH-H<sub>2</sub>O. It dehydrated on melting and re-melts on further heating at m 182-184°. UV  $\lambda_{max}$  at 281nm ( $\epsilon$  2040) in EtOH. Solubility is 17% in EtOH, 25% in Et<sub>2</sub>O, 20% in Me<sub>2</sub>CO, 25% in dioxan and 5% in CHCl<sub>3</sub>. [Petit and Muller Bull Soc Chim Fr 121 1951.] The diacetyl derivative has m 143-144° (from MeOH) and  $[\alpha]_D^{20} + 1°$  (c 1, CHCl<sub>3</sub>) [Mills et al. J Am Chem Soc 80 6118 1958].

**Exonucleases.** Like the endonucleases they are restriction enzymes which act at the 3' or 5' ends of linear DNA by hydrolysing off the nucleotides. Although they are highly specific for hydrolysing nucleotides at the 3' or 5' ends of linear DNA, the number of nucleotides cleaved are time dependent and usually have to be estimated from the time allocated for cleavage. Commercially available exonucleases are used without further purification.

**Farnesol** (trans-trans-3,7,11-trimethyl-2,6,10-dodecatrien-1-ol) [106-28-5] M 222.4, b 111°/0.35mm, 126-127°/0.5mm, 142-143°/2mm,  $d_4^{20}$  0.8871,  $n_D^{25}$  1.4870. Main impurity is the cis-trans isomer. Purified by gas chromatography using a 4ft x 0.125in 3%OV-1 column at 150°. [Corey et al. J Am Chem Soc 92 6637 1970; Popjak et al. J Biol Chem 237 56 1962.] Also purifed through a 14-in Podbielniak column at 11°/0.35mm (see p. 141). Alternatively it has been purified by gas chromatography using SF96 silicone on Fluoropak columns or Carbowax 20M on Fluoropak or base-washed 30:60 firebrick (to avoid decomp of alcohol, prepared by treating the firebrick with 5N NaOH in MeOH and washed with MeOH to pH 8) at 210° with Helium carrier gas at 60 mL/min flow rate. The diphenylcarbamoyl derivative has m 61-63° (from MeOH) and has IR band at 3500 cm<sup>-1</sup>. [Bates et al. J Org Chem 28 1086 1963.]

Farnesyl pyrophosphate [13058-04-3; E, E: 372-97-4] M 382.3,  $pK_{Est(1)} \sim 2$ ,  $pK_{Est(2)} \sim 2$ ,  $pK_{Est(3)} \sim 3.95$ ,  $pK_{Est(4)} \sim 6.26$ . Purified by chromatography on Whatman No3 MM paper in a system of isopropanol-isobutanol-ammonia-water (40:20:1:30) (v/v). Stored as the Li or NH4 salt at 0°.

Ferritin (from human placenta) [9007-73-2]  $M_r \sim 445,000$  (Fe free protein). The purification of this major iron binding potein was achieved by homogenisation in water and precipitating with ammonium sulfate, repeating the cycle of ultracentrifuging and molecular sieve chromatography through Sephadex 4B column. Isoelectric focusing revealed a broad spectrum of impurities which were separated by ion-exchange chromatography on Sephadex A-25 and stepwise elution. [Konijn et al. Anal Biochem 144 423 1985.]

**Fibrinogen (from human plasma)** [9001-32-5]  $M_r$  341,000. A protein made up of  $2A\alpha$ , 2B $\beta$  and  $2\gamma$  subunits connected by disulfide bridges. Possible impurity is plasminogen. Purified by glycine pptn [Mosesson and Sherry *Biochemistry 5* 2829 1966] to obtain fractions 1-2, then further purified [Blombäck and Blombäck *Arkiv Kemi* 10 415 1956] and contaminating plasminogen is removed by passage through a lysine-Sepharose column. Such preparations were at least 95% clottable as determined by Mosesson and Sherry's method (above ref.) in which the OD<sub>280</sub> was measured before and after clotting with 5 Units/mL of thrombin (> 3000U/mg). All fibrinogen preps were treated with calf intestinal alkaline phosphatase to convert any fibrinogen peptide-AP to fibrinogen peptide-A by removing serine-bound phosphate. Solutions are then lyophilised and stored at -20°. [Higgins and Shafer J Biol Chem 256 12013 1981.] It is sparingly soluble in H<sub>2</sub>O. Aqueous solns are viscous with isoelectric point at pH 5.5. Readily denatured by heating above 56° or by chemical agents, e.g. salicylaldehyde, naphthoquinone sulfonates, ninhydrin or alloxan. [Edsall et al. J Am Chem Soc 69 2731 1947; Purification: Cama et al. Naturwissenschaften 48 574 1961; Lorand and Middlebrook Science 118 515 1953; cf. Fuller in Methods Enzymol 163 474 1988.]

For plasminogen-deficient fibrinogen from blood plasma, the anticoagulated blood was centrifuged and the plasma was frozen and washed with saline solution. Treated with charcoal and freeze-thawed. Dialysed versus Tris/NaCl buffer. [Maxwell and Nikel Biochem Prep 12 16 1968.]

**Fibronectin** (from human plasma) [86088-83-7]  $M_r \sim 220,000$ . This glycoprotein contains 5-12% of carbohydrate. It has been purified by glycine fractionation and DEAE-cellulose chromatography. Material is dissolved in 0.25M Tris-phosphate buffer pH 7.0, diluted to 20% and glycine added gradually till 2.1M when the temperature falls to below 15°. The ppte contains mainly fibrinogen. The supernatant is discarded and the ppte is treated with an equal volume of H<sub>2</sub>O, cooled (to 0°) and ppted by adding EtOH to 16% (v/v) at -4°. The ppte contains some CI (Cold Insoluble) globulin, fibronectin and small quantities of other proteins. To remove these the ppte is dissolved in 0.25M Tris-phosphate buffer (pH 7.0) *ca* 0.5% and purified by DEAE-cellulose chromatography after diluting the buffer to 0.05M buffer. [Morrison et al. J Am Chem Soc 70 3103 1948; Mosesson and Umfleet J Biol Chem 245 5728 1970; Mosesson and Amrani Blood 56 145 1980; Akiyama and Yamada Adv Enzymol 59 51 1987.]

Flavin adenine dinucleotide (di-Na,  $2H_2O$  salt, FAD) [146-14-5] M 865.6, [ $\alpha$ ]<sub>546</sub> -54° (c 1, H<sub>2</sub>O). Small quantities, purified by paper chromatography using *tert*-butyl alcohols/water, cutting out the main spot and eluting with water. Larger amounts can be ppted from water as the uranyl complex by adding a slight excess of uranyl acetate to a soln at pH 6.0, dropwise and with stirring. The soln is set aside overnight in the cold, and the ppte is centrifuged off, washed with small portions of cold EtOH, then with cold, peroxide-free diethyl ether. It is dried in the dark under vacuum over P<sub>2</sub>O<sub>5</sub> at 50-60°. The uranyl complex is suspended in water and, after adding sufficient 0.01M NaOH to adjust the pH to 7, the ppte of uranyl hydroxide is removed by

centrifugation [Huennekens and Felton *Methods Enzymol* **3** 954 1957]. It can also be crystd from water. Should be kept in the dark. More recently it was purified by elution from a DEAE-cellulose (Whatman DE 23) column with 0.1M phosphate buffer pH 7, and the purity was checked by TLC. [Holt and Cotton, *J Am Chem Soc* **109** 1841 1987.]

Flavin mononucleotide (Na, 2H<sub>2</sub>O salt, FMN) [130-40-5] M 514.4, pK<sub>1</sub> 2.1 (PO<sub>4</sub>H<sub>2</sub>), pK<sub>2</sub> 6.5 (PO<sub>4</sub>H<sup>-</sup>), pK<sub>3</sub> 10.3 (CONH), fluorescence  $\lambda$ max 530nm (870nm for reduced form). Purified by paper chromatography using *tert*-butanol-water, cutting out the main spot and eluting with water. Also purified by adsorption onto an apo-flavodoxin column, followed by elution and freeze drying Crystd from acidic aqueous soln. [Mayhew and Strating Eur J Biochem 59 539 1976.]

**4-Fluoro-7-nitrobenzofurazan** (4-fluoro-7-nitrobenzo-2-oxa-1,3-diazole) [29270-56-2] M 183.1, m 52.5-53.5°, 53-56°, 53.5-54.5°. Purified by repeated recrystn from pet ether (b 40-60°). On treatment with MeONa in MeOH it gave 4-methoxy-7-nitrobenzo-2-oxa-1,3-diazole m 115-116°. [Nunno et al. J Chem Soc (C) 1433 1970.] It is a very good fluorophore for amino acids [Imai and Watanabe Analyt Chim Acta 130 377 1981], as it reacts with primary and secondary amines to form fluorescent adducts with  $\lambda_{ex}$ 470nm and  $\lambda_{em}$  530nm. It gives a glycine derivative with m 185-187° [Miyano et al. Anal Chim Acta 170 81 1985].

**4-Fluoro-3-nitrophenylazide** [28166-06-5] **M 182.1, m 53-55°, 54-56°.** Dissolve in Et<sub>2</sub>O, dry over MgSO<sub>4</sub>, filter, evaporate and recryst the residue from pet ether (b 20-40°) to give orange needles. Store in a stoppered container at ~0°. The NMR has  $\delta$  7.75 (m 1H) and 7.35 (m 2H) in CDCl<sub>3</sub>. [Hagedorn et al. J Org Chem **43** 2070 1978.]

**2-Fluorophenylalanine** [R(+)-97731-02-7; S(-)-19883-78-4] M 183.2, m 226-232°, 231-234°,  $[\alpha]_D^{25}(+)$  and (-) 15° (c 2, H<sub>2</sub>O pH 5.5),  $pK_1^{24}$  2.12,  $pK_2^{24}$  9.01. Recryst from aqueous EtOH. The *hydrochloride* has m 226-231°(dec), and the *N*-acetyl derivative has m 147-149° (from aqueous EtOH). [Bennett and Nieman J Am Chem Soc 72 1800 1950.]

**4-Fluorophenylalanine** [R(+)- 18125-46-7; S(-)- 1132-68-9] **M 183.2, m 227-232°**,  $[\alpha]_D^{25}(+)$  and (-) **24°** (c **2**, H<sub>2</sub>**O**),  $pK_1^{24}$ **2.13**,  $pK_2^{24}$ **9.05**. It is recrystid from aqueous EtOH. The R-*N*-acetyl derivative has **m** 142-145°,  $[\alpha]_D^{25}$ -38.6° (c 8, EtOH). [Bennett and Nieman J Am Chem Soc **72** 1800 1950.]

5-Fluoro-L-tryptophan monohydrate [16626-02-1] M 240.2, m >250°(dec),  $[\alpha]_D^{20}$  +5.5° (c 1, 0.1N HCl), pK<sub>Est(1)</sub>~ 2.5 (CO<sub>2</sub>H), pK<sub>Est(2)</sub>~ 9.4 (NH<sub>2</sub>), pK<sub>Est(3)</sub>~16 (indole-NH). Recrystd from aqueous EtOH.

5-Fluorouridine (5-fluoro-1-β-D-ribofuranosyl-1*H*-pyrimidine-2,4-dione) [316-46-1] M 262.2, m 180-182°, 182-184°,  $[\alpha]_D^{20}$  +18° (c 1, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 8.0, pK<sub>Est(2)</sub>~ 13. Recrystd from EtOH-Et<sub>2</sub>O and dried at 100° in a vacuum. UV:  $\lambda_{max}$  269nm (pH 7.2, H<sub>2</sub>O), 270nm (pH 14, H<sub>2</sub>O). [Liang et al. *Mol Pharmacol* 21 224 1982.]

**5-Fluorouracil** (5-fluoropyrimidinedi-2,4-[1*H*,3*H*]-one) [51-21-8] M 130.1, m 282-283°(dec), 282-286°(dec),  $pK_1^{25}$  8.04,  $pK_2^{25}$  13.0. Recrystd from H<sub>2</sub>O or MeOH-Et<sub>2</sub>O, and sublimed at 190-200°/0.1mm or 210-230°/0.5mm. UV:  $\lambda_{max}$  265-266nm ( $\varepsilon$  7070). [Barton et al. J Org Chem 37 329 1972; Duschinsky and Pleven J Am Chem Soc 79 4559 1957.]

Fluram (Fluorescamine, 4-phenyl-spiro[furan-2(3H)-1-phthalan]-3,3'-dione) [38183-12-9] M 278.3, m 153-155°, 154-155°. A non-fluorescent reagent that reacts with primary amines to form highly fluorescent compounds. Purified by dissolving (~1g) in Et<sub>2</sub>O- ${}^{*}C_{6}H_{6}$  (1:1, 180 mL), wash with 1% aq NaHCO<sub>3</sub> (50mL), dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate in a vacuum. Dissolve the residue in warm CH<sub>2</sub>Cl<sub>2</sub> (5mL), dilute with Et<sub>2</sub>O (12mL) and refrigerate. Collect the solid and dry in a vacuum. IR (CHCl<sub>3</sub>): v 1810, 1745, 1722, 1625 and 1600 cm<sup>-1</sup>, and NMR (CDCl<sub>3</sub>):  $\delta$  8.71 (s, -OHC=). [Weigele et al. J Am Chem Soc 94 5927 1972, J Org Chem 41 388 1976; Methods Enzymol 47 236 1977.]

Folic acid (FA, pteroyl-S-glutamic acid) [75708-92-8] M 441.4, m >250°(dec),  $[\alpha]_D^{25} + 23°$ (c 0.5, 0.1N NaOH), pK<sub>1</sub> 2.35 (protonation N10), pK<sub>2</sub> 2.75 (protonation N1), pK<sub>3</sub> 3.49 ( $\alpha$ -CO<sub>2</sub>H), pK<sub>4</sub> 4.65 ( $\gamma$ -CO<sub>2</sub>H), pK<sub>5</sub> 8.80 (acidic N3). If paper chromatography indicates impurities then recrystallise from hot H<sub>2</sub>O or from dilute acid [Walker et al. J Am Chem Soc 70 19 1948]. Impurities may be removed by repeated extraction with *n*-BuOH of a neutral aqueous solns of folic acid (by suspending in H<sub>2</sub>O and adding N NaOH till the solid dissolves then adjusting the pH to ~7.0-7.5) followed by pptn with acid, filtration, and recrystn form hot H<sub>2</sub>O. [Blakley Biochem J 65 331 1975; Kalifa, Furrer, Bieri and Viscontini Helv Chim Acta 61 2739 1978.] Chromatography on cellulose followed by filtration through charcoal has also been used to obtain pure acid. [Sakami and Knowles Science 129 274 1959.] UV:  $\lambda_{max}$  247 and 296nm ( $\epsilon$  12800 and 18700) in H<sub>2</sub>O pH 1.0; 282 and 346nm ( $\epsilon$  27600 and 7200) in H<sub>2</sub>O pH 7.0; 256, 284 and 366nm ( $\epsilon$  24600, 24500 and 8600) in H<sub>2</sub>O pH 13 [Rabinowitz in The Enzymes (Boyer et al. Eds 2 185 1960].

Follicle Stimulating Hormone (FSH, follitropin) [9002-68-0]  $M_r \sim 36,000$ . Purified by Sephadex G100 gel filtration followed by carboxymethyl-cellulose with NH<sub>4</sub>OAc pH 5.5. The latter separates luteinising hormone from FSH. Solubility in H<sub>2</sub>O is 0.5%. It has an isoelectric point of 4.5. A soln of 1mg in saline (100mL) can be kept at 60° for 0.5h. Activity is retained in a soln at pH 7-8 for 0.5h at 75°. The activity of a 50% aq EtOH soln is destroyed at 60° in 15 min. [Bloomfield et al. *Biochim Biophys Acta* 533 371 1978; Hartree *Biochem J* 100 754 1966; Pierce and Parsons Ann Rev Biochem 50 465 1981.]

**Fructose-1,6-diphosphate (trisodium salt)** [38099-82-0] M 406.1,  $pK_3^{25}$  6.14,  $pK_4^{25}$  6.93 (free acid). For purification via the acid strychnine salt, see Neuberg, Lustig and Rothenberg [Arch Biochem 3 33 1943]. The calcium salt can be partially purified by soln in ice-cold M HCl (1g per 10mL) and repptn by dropwise addition of 2M NaOH: the ppte and supernatant are heated on a boiling water bath for a short time, then filtered and the ppte is washed with hot water. The magnesium salt can be pptd from cold aqueous soln by adding four volumes of EtOH.

**Fructose-6-phosphate** [643-13-0] **M 260.1**,  $[\alpha]_D^{21}$ +2.5 (c 3, H<sub>2</sub>O), pK<sup>25</sup> 5.84. Crystd as the barium salt from water by adding four volumes of EtOH. The barium can be removed by passage through the H<sup>+</sup> form of a cation exchange resin and the free acid collected by freeze-drying.

6-Furfurylaminopurine (Kinetin) [525-79-1] M 215.2, m 266-267°, 269-271°, 270-272°, 272° (sealed capillary),  $pK_1 < 1$ ,  $pK_2$  3.8,  $pK_3$  10. Platelets from EtOH and sublimes at 220°, but is best done at lower temperatures in a good vacuum. It has been extracted from neutral aqueous solns with Et<sub>2</sub>O. [Miller et al J Am Chem Soc 78 1375 1956; Bullock et al. J Am Chem Soc 78 3693 1956.]

Fusaric acid (5-n-butylpyridine-2-carboxylic acid) [536-69-6] M 179.2, m 96-98°, 98°, 98-100°, 101-103°, pK<sub>1</sub> 5.7, pK<sub>2</sub> 6.16 (80% aq methoxyethanol). Dissolve in CHCl<sub>3</sub>, dry (Na<sub>2</sub>SO<sub>4</sub>), filter, evaporate and recrystallise the residue from 50 parts of pet ether (b 40-60°) or EtOAc, then sublime *in vacuo*. The copper salt forms bluish violet crystals from H<sub>2</sub>O and has m 258-259°. [Hardegger and Nikles Helv Chim Acta 39 505 1956; Schreiber and Adam Chem Ber 93 1848 1960; NMR and MS: Tschesche and Führer Chem Ber 111 3500 1978.]

Fuschin (Magenta I, rosaniline HCl) [632-99-5] M 337.9, m >200°(dec). See rosaniline hydrochloride on p. 349 in Chapter 4.

**D-Galactal** [21193-75-9] M 146.2, m 100°, 100-102°, 104°, 103-106°,  $[\alpha]_D^{20}$ -21.3° (c 1, MeOH). Recryst from EtOAc, EtOH or EtOAc + MeOH. [Overend et al. J Chem Soc 675 1950; Wood and Fletcher J Am Chem Soc 79 3234 1957; Distler and Jourdian J Biol Chem 248 6772 1973.] **B-Galatosidase (from bovine testes)** [9031-11-2]  $M_r$  510,000, [EC 3.2.1.23]. Purified 600-fold by ammonium sulfate precipitation, acetone fractionation and affinity chromatography on agarose substituted with terminal thio- $\beta$ -galactopyranosyl residues. [Distlern and Jourdian J Biol Chem 248 6772 1973.]

Gangcyclovir [9-{(1,3-dihydroxy-2-propoxy)methyl}guanine; 2-amino-1,9-{(2-hydroxy-1-hydroxymethyl)-ethoxymethyl}-6H-purin-6-one; Cytovene; Cymeva(e)n(e)] [82410-32-0] M 255.2, m >290°(dec), >300°(dec), monohydrate m 248-249°(dec),  $pK_{Est(1)} \sim -1.1$ ,  $pK_{Est(2)} \sim 4.1$ ,  $pK_{Est(3)} \sim 9.7$ . Recryst from MeOH. Alternatively dissolve ~90g of reagent in 700mL of distilled H<sub>2</sub>O, filter and cool (ca 94% recovery). UV:  $\lambda_{max}$  in MeOH 254nm ( $\varepsilon$  12,880), 270sh nm ( $\varepsilon$  9040), solubility in H<sub>2</sub>O at 25° is 4.3mg/mL at pH 7.0. ANTIVIRAL. [Ogilvie et al. Can J Chem 60 3005 1982; Ashton et al. Biochem Biophys Res Commun 108 1716 1982; Martin et al. J Med Chem 26 759 1983.]

Geranylgeranyl pyrophosphate [6699-20-3 ( $NH_4$  salt)] M 450.5,  $pK_{Est(1)} < 2$ ,  $pK_{Est(2)} < 2$ ,  $pK_{Est(3)} \sim 3.95$ ,  $pK_{Est(4)} \sim 6.26$ . Purified by counter-current distribution between two phases of a butanol/isopropyl ether/ammonia /water mixture (15:5:1:19) (v/v), or by chromatography on DEAE-cellulose (linear gradient of 0.02M KCl in 1mM Tris buffer, pH 8.9). Stored as a powder at 0°.

Geranyl pyrophosphate [763-10-0 ( $NH_4$  salt)] M 314.2,  $pK_{Est(1)} < 2$ ,  $pK_{Est(2)} < 2$ ,  $pK_{Est(3)} < 3.95$ ,  $pK_{Est(4)} < 6.26$ . Purified by paper chromatography on Whatman No 3 MM paper in a system of isopropyl alcohol/isobutyl alcohol/ammonia/water (40:20:1:39), RF 0.77-0.82. Stored in the dark as the ammonium salt at 0°.

Gitoxigenin  $(3\beta, 14, 16\beta, 21$ -tetrahydroxy-20(22)norcholenic acid lactone) [545-26-6] M 390.5, m 223-226°, 234°, 239-240° (anhydrous by drying at 60°),  $[\alpha]_D^{20} + 30°$  (c 1, MeOH). Recrystn from aqueous EtOH produces plates of the sesquihydrate which dehydrate on drying at 100° *in vacuo*. It has also been recrystd from Me<sub>2</sub>CO-MeOH and from EtOAc the crystals contain 1 mol of EtOAc with  $[\alpha]_D^{21}$ +24.8° (c 1, dioxane). It has UV has  $\lambda_{max}$  at 310, 485 and 520nm in 96% H<sub>2</sub>SO<sub>4</sub>. On heating with ethanolic HCl it yields *digitaligenin* with loss of H<sub>2</sub>O. [Smith J Chem Soc 23 1931.]

Gliotoxin (3*R*-6*t*-hydroxy-3-hydroxymethyl-2-methyl-(5*at*)-2,3,6,10-tetrahydro-5*aH*-3,10*ac*-epidisulfido[1,2-*a*]-indol-1,4-dione) [67-99-2] M 326.4, m 191-218°(dec), 220°(dec), 221°(dec),  $[\alpha]_D^{20}$ -254° (c 0.6, CHCl<sub>3</sub>),  $[\alpha]_D^{25}$ -270° (c 1.7, pyridine). Purified by recrystn from MeOH. Its solubility in CHCl<sub>3</sub> is 1%. The *dibenzoyl* derivative has m 202° (from CHCl<sub>3</sub>-MeOH). [Glister and Williams Nature 153 651 1944; Elvidge and Spring J Chem Soc Suppl 135 1949; Johnson et al. J Am Chem Soc 65 2005 1943; Bracken and Raistrick Biochem J 41 569 1947.]

**Glucose oxidase (from** Aspergillus niger) [9001-37-0] M<sub>r</sub> 186,000, [EC 1.1.3.4]. Purified by dialysis against deionized water at 6° for 48hours, and by molecular exclusion chromatography with Sephadex G-25 at room temperature. [Holt and Cotton J Am Chem Soc 109 1841 1987.]

Glucose-1-phosphate [59-56-3] M 260.1,  $[\alpha]_D^{25} + 120^\circ$  (c 3, H<sub>2</sub>O),  $[\alpha]_D^{20} + 78^\circ$  (c 4, H<sub>2</sub>O of di-K salt), pK<sub>1</sub> 1.11, pK<sub>2</sub> 6.13 [pK<sup>25</sup> 6.50]. Two litres of 5% aq soln was brought to pH 3.5 with glacial acetic acid (+ 3g of charcoal, and filtered). An equal volume of EtOH was added, the pH was adjusted to 8.0 (glass electrode) and the soln was stored at 3° overnight. The ppte was filtered off, dissolved in 1.2L of distd water, filtered and an equal volume of EtOH was added. After standing at 0° overnight, the crystals were collected at the centrifuge, and washed with 95% EtOH, then absolute EtOH, ethanol/diethyl ether (1:1), and diethyl ether. [Sutherland and Wosilait, *J Biol Chem* 218 459 1956.] Its barium salt can be crystd from water and EtOH. Heavy metal impurities can be removed by passage of an aqueous soln (*ca* 1%) through an Amberlite IR-120 column (in the appropriate H<sup>+</sup>, Na<sup>+</sup> or K<sup>+</sup> forms). *Di-K salt* cryst as 2H<sub>2</sub>O from EtOH.

**Glucose-6-phosphate** [acid 156-73-5; Ba salt 58823-95-3; Na salt 54010-71-8] M 260.1, m 205-207°(dec) mono Na salt,  $[\alpha]_{546}^{20} + 41°$  (c 5, H<sub>2</sub>O), pK<sub>1</sub> 1.65, pK<sub>2</sub> 6.11, pK<sub>3</sub><sup>25</sup> 11.71 [-C<sub>1</sub>(OH)O<sup>-</sup>]. Can be freed from metal impurities as described for glucose-1-phosphate. Sol of Na Salt is 5% in H<sub>2</sub>O at 20°. Its barium salt can be purified by solution in dilute HCl and pptn by neutralising the soln. The ppte is washed with small volumes of cold water and dried in air.

Glucose-6-phosphate dehydrogenase [9001-40-5] Mr 128,000 (from Baker's yeast), 63,300 (from rat mammary gland) [EC 1.1.1.49]. The enzyme is useful for measuring pyridine nucleotides in enzyme recycling. The enzyme from Baker's yeast has been purified by  $(NH_4)_2SO_4$  fractionation, Me<sub>2</sub>CO pptn, a second (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> fractionation, concentration by DEAE-SF chromatography, a third (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> fractionation and recrystn. Crystn is induced by addition of its coenzyme NADP, which in its presence causes rapid separation of crystals at  $(NH_4)_2SO_4$  concentration much below than required to ppte the amorphous enzyme. To recryst, the crystals are dissolved in 0.01M NADP (pH 7.3) with (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> at 0.55 saturation and the crystals appear within 10 to 60 min. After standing for 2-3 days (at 4°) the (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> is increased to 0.60 of saturation and more than 80% of the activity in the original crystals is recovered in the fresh crystals. [Noltmann et al. J Biol Chem 236 1255 1961]. Large amounts can be obtained from rat livers. The livers are extracted with 0.025M phosphate buffer (pH 7.5), and ppted with 3M (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (70% of activity). The ppte is dissolved in 3volumes of 0.025M phosphate (pH 7.5), dialysed against this buffer + 0.2mM EDTA at 4° for 5h, then diluted to 1% protein and the nucleic acids ppted by addition of 0.4volumes of 1% protamine sulfate.  $(NH_{4})_{2}SO_{4}$  is added to a concentration of 2M (pH adjusted to 7.0 with NH<sub>3</sub>), the ppte is discarded and the supernatant is adjusted to 2.8M  $(NH_4)_2SO_4$ , dialysed, protein adjusted to 1% and treated with Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> gel. The gel is added in three steps (1.5mL of 0.4% gel/mL per step) and the gel is removed by centrifugation after each addn. The third gel adsorbed 50% of the activity. The gel is eluted with 0.2M phosphate (pH 7.4, 40mL/g of gel; 60% recovery). The extract is ppted in 3volumes with  $(NH_4)_2SO_4$  (adjusted to 4M) to give enzyme with an activity of 30µmoles/mg of protein x hour. [Lowry et al. J Biol Chem 236 2746 1961.] Km values for the yeast enzyme are 20µM for G-6P and 2µM for NADP (Tris pH 8.0, 10<sup>-2</sup> M MgCl<sub>2</sub>, 38°) [Noltmann and Kuby The Enzymes VII 223 1963].

L-Glutathione (reduced form,  $\gamma$ -L-glutamyl-L-cysteinyl-glycine) [70-18-8] M 307.3, m 188-190°(dec), 195°(dec),  $[\alpha]_D^{20}$ -20.1° (c 1, H<sub>2</sub>O),  $pK_1^{25}$ 2.12 (CO<sub>2</sub>H),  $pK_2^{25}$ 3.59 (CO<sub>2</sub>H),  $pK_3^{25}$ 8.75 (NH<sub>2</sub>),  $pK_4^{25}$ 9.65 (10.0, SH). Crystd from 50% aq EtOH, dry in a vac and store below 5°. Alternatively recrystd from aqueous EtOH under N<sub>2</sub>, and stored dry in a sealed container below 4°. It is soluble in H<sub>2</sub>O. [Weygand and Geiger *Chem Ber* 90 634 1957; Martin and Edsall *Bull Soc Chim Fr* 40 1763 1958; *Biochem Prep* 2 87 1952.]

**L-Glutathione** (oxidised) [27025-41-8] M 612.6, m 175-195°,  $[\alpha]_D^{20}$ -98° (c 2, H<sub>2</sub>O), pK<sub>1</sub> 3.15, pK<sub>2</sub> 4.03, pK<sub>3</sub> 8.75. Purified by recrystn from 50% aq EtOH. Its solubility in H<sub>2</sub>O is 5%. Store at 4°. [Li et al. J Am Chem Soc 76 225 1954; Berse et al. Can J Chem 37 1733 1959.]

**Glutathione S-transferase (human liver)** [50812-37-8]  $M_r$  25,000, [EC 2.5.1.18]. Purified by affinity chromatography using a column prepared by coupling glutathione to epoxy-saturated Sepharose. After washing contaminating proteins the pure transferase is eluted with buffer containing reduced glutathione. The solution is then concentrated by ultrafiltration, dialysed against phosphate buffer at pH ~7 and stored in the presence of dithiothreitol (2mM) in aliquots at <-20°. [Simons and Vander Jag Anal Biochem 52 334 1977.]

**Glyceraldehyde-3-phosphate dehydrogenase** [9001-50-7]  $M_r$  144,000, [EC 1.2.1.12]. Purified from rabbit muscle by extraction with 0.03N KOH and ppted with (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (0.52 of saturation). The clear supernatant was adjusted to pH 7.5 and NH<sub>3</sub> was added dropwise to pH 8.2-8.4. Crystals appear sometimes even without seeding. The crystals are dissolved in H<sub>2</sub>O, filtered to remove suspended material and 2 volumes of saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> at pH 8.2-8.4 is added. After 1hour the crystals appear. Recrystallise in the same way. [Cori et al. J Biol Chem 173 605 1948; Furfine and Velick J Biol Chem 240 844 1965, The Enzymes 7 243 1963; Lui and Huskey Biochemistry 31 6998 1992.] The Km values are: NADH (3.3 $\mu$ M) and 1,3diphosphoglycerate (8x10<sup>-7</sup>M) in pH 7.4 imidazole buffer at 26°, NAD (13 $\mu$ M), glyceraldehyde-3-P (90 $\mu$ M), P<sub>i</sub> (2.9x10<sup>-4</sup>M), and arsenate (69 $\mu$ M) in 8.6 M NaHCO<sub>3</sub> buffer at 26°. [Orsi and Cleland Biochemistry 11 102 1972.]

Glycerol kinase (from Candida mycoderma, E coli, rat or pigeon liver glycerokinase) [9030-66-4]  $M_r 251,000$ , [EC 2.7.1.30]. Commercial enzyme has been dialysed against 2mM Hepes, 5mM dithiothreitol and 0.3mM EDTA, followed by several changes of 20mM Hepes and 5mM dithiothreitol prior to storage under N<sub>2</sub> at -20°. [Knight and Cleland Biochemistry 28 5728 1989.] The enzyme from pigeon liver was purified by acid-pptn (acetate buffer at pH 5.1), (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> fractionation, heat treatment (60°/ 1 h),

calcium phosphate gel filtration, a second  $(NH_4)_2SO_4$  fractionation, dialysis, elution of inert proteins and crystn. This was done by repeatedly extracting the ppte from the last step with 0.05M sodium pyrophosphate (pH 7.5) containing 1mM EDTA and 0.2M  $(NH_4)_2SO_4$  was added. Careful addition of solid  $(NH_4)_2SO_4$  to this soln lead to crystn of the enzyme. Recrystn was repeated. The enzyme is activated by  $Mg^{2+}$  and  $Mn^{2+}$  ions and is most stable in solns in the pH 4.5-5.5 range. The stability is greatly increased in the presence of glycerol. It has Km for glycerol of 60 $\mu$ M and for ATP 9 $\mu$ M in glycine buffer pH 9.8 and 25°. [Kennedy *Methods Enzymol* 5 476 *1962*.]

L-Glycerol-3-phosphate dehydrogenase (GDH, from rabbit muscle) [9075-65-4]  $M_r$  78,000 [EC 1.1.1.8]. Recrystd by adding (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> till 0.45 saturation at pH 5.5 at 4° and the small amount of ppte is removed then satd (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> is added dropwise from time to time over several days in the cold room. The crystals are collected and recrystd until they have maximum activity. The enzyme is stable in half saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> for several weeks at 4°. The equilibrium [dihydroxyacetone][NADH][H<sup>+</sup>]/[G-3-P][NAD] is 1.0 x 10<sup>-12</sup>M in Tris buffer at 25°. It uses NAD ten times more efficiently than NADP. The Km for G-3-P is 1.1 x 10<sup>-4</sup>M, for NAD it is 3.8 x 10<sup>-4</sup>M and for dihydroxyacetone it is 4.6 x 10<sup>-4</sup>M in phosphate buffer pH 7.0 and at 23.3°. Dihydroxyacetone phosphate and fructose-1,6-diphosphate are inhibitors. [Branowski J Biol Chem 180 515 1949, The Enzymes 7 85 1963; Young and Pace Arch Biochem Biophys 75 125 1958; Walsh and Sallach Biochemistry 4 1076 1965.]

L- $\alpha$ -Glycerol phosphocholine (Cadmium Chloride)<sub>x</sub> complex [64681-08-9] M 257.2 + (183.3)<sub>x</sub>, pK<sub>Est</sub> ~ 5.5. Glycerol phosphocholine is purified via the CdCl<sub>2</sub> complex which is purified by four recrystns from 99% EtOH by standing at 0° for 1h. The white ppte is collected, washed with EtOH, Et<sub>2</sub>O and dried in a vacuum. The amorphous Cd complex can be converted to the crystalline form [C<sub>8</sub>H<sub>20</sub>O<sub>6</sub>NP.CdCl<sub>2</sub>.3H<sub>2</sub>O] by dissolving 34.4g in H<sub>2</sub>O (410mL) and 99% EtOH (1650mL total) added slowly with stirring and allowing the clear soln to stand at 25° for 12hours, then at 5° for 12h. The crystallised complex is filtered off, washed with cold 80% EtOH and dried in air. Glycerol phosphocholine can be recovered from the complex by dissolving in H<sub>2</sub>O (2% soln), passing through an ion-exchange column (4.9 x 100cm, of 1vol IRC-50 and 2vol of IR-45). The effluent is concentrated to a thick syrup at 45°. It is dried further at 50°/P<sub>2</sub>O<sub>5</sub>/48h. The vitreous product (~8.25g) is dissolved in 99% EtOH (50mL) and the clear soln is cooled at 5°, whereby crystals appear, and then at -15° for 16h. The crystals are filtered off, washed with 99% EtOH, and Et<sub>2</sub>O then dried at 50° in a vacuum over P<sub>2</sub>O<sub>5</sub>. It can be recryst from 99.5% EtOH, long prisms) which are *hygroscopic* and must be handled in a H<sub>2</sub>O-free atmosphere [Tattrie and McArthur Biochem Prep **6** 16 1958; Baer and Kates J Am Chem Soc **70** 1394 1948 ; Acta Cryst **21** 79, 87 1966].

Glycine anhydride (2,5-diketopiperazine) [106-57-0] M 114.1, m 309-310°, 311-312°(dec),  $\sim$ 315°(dec), pK<sub>1</sub> -4.45, pK<sub>2</sub> -2.16 (pK<sub>2</sub> -1.94 in AcOH). Recryst from H<sub>2</sub>O (plates) and can be sublimed (slowly) at 260° or at 140-170°/0.5mm. The *dihydrochloride* has m 129-130°, is prepd by dissolving in conc HCl and on adding EtOH to crystallisation point; dried in a vac. The *bis-1-naphthylurethane* has m 232°(dec), and the *diperchlorate* has m 117° (*hygroscopic*). [MS: Johnstone J Chem Soc Perkin Trans 1 1297 1975; NMR: Blaha and Samek Collect Czech Chem Commun 32 3780 1967; Sauborn J Phys Chem 36 179 1932; Corey J Am Chem Soc 60 1599 1938.]

Glycocyamine (N-guanylglycine) [352-97-6] M 117.1, m 280-284°(dec), >300°, pK<sup>25</sup> 2.86 (NH<sub>3</sub><sup>+</sup>). Recrystd from 15 parts of hot H<sub>2</sub>O, or by dissolving in slightly more than the calculated amount of 2N HCl and ppting by adding an equivalent of 2N NaOH, filtering washing with cold H<sub>2</sub>O and drying first *in vacuo* then at 60° *in vacuo*. The *hydrochloride* has m 200°(dec) after recrystn from aqueous HCl as plates. The *picrate* forms needles from hot H<sub>2</sub>O and has m 210°(dec). [Brand and Brand Org Synth Coll Vol III 440 1955; Failey and Brand J Biol Chem 102 768 1933; King J Chem Soc 2375 1930.]

Glycodeoxycholic acid monohydrate  $(N-[3\alpha-12\alpha-dihydroxy-5\beta-cholan-24-oyl]glycine)$ [360-65-6] M 467.6, m 186-177°(dec), 187-188°,  $[\alpha]_D^{23} + 45.9°$  (c 1, EtOH), pK<sub>Est</sub> ~ 4.4. Recrystallises from H<sub>2</sub>O or aqueous EtOH with 1 mol of H<sub>2</sub>O and dried at 100° *in vacuo*. Solubility in EtOH is 5%. [UV: Lindstedt and Sjövall Acta Chem Scand 11 421 1957.] The Na salt is recrystd from EtOH/Et<sub>2</sub>O, m 245-250°,  $[\alpha]_D^{23} + 41.2°$  (c 1, H<sub>2</sub>O) [Wieland Hoppe Seyler's Z Physiol Chem 106 181 1919; Cortese J Am Chem Soc 59 2532 1937]. **D(+)-Glycogen** [9005-79-2] **M 25,000-100,000, m 270-280°(dec),**  $[\alpha]_{546}$  +216° (c 5, H<sub>2</sub>O). A 5% aqueous soln (charcoal) was filtered and an equal volume of EtOH was added. After standing overnight at 3° the ppte was collected by centrifugation and washed with absolute EtOH, then EtOH/diethyl ether (1:1), and diethyl ether. [Sutherland and Wosilait *J Biol Chem* 218 459 1956.]

Glycogen synthase (from bovine heart) [9014-56-6]  $M_r$  60,000, [EC 2.4.1.11]. Purified by pptn of the enzyme in the presence of added glycogen by polyethylene glycol, chromatography on DEAE-Sephacel and high speed centrifugation through a sucrose-containing buffer. [Dickey-Dunkirk and Kollilea Anal Biochem 146 199 1985.]

**Gramicidin A** (a pentadecapeptide from *Bacillus brevis*) [11029-61-1] m ~229-230°(dec). Purified by countercurrent distribution from  ${}^{*}C_{6}H_{6}$ -CHCl<sub>3</sub>, MeOH-H<sub>2</sub>O (15:15:23:7) with 5000 tubes. Fractions were examined by UV (280nm) of small aliquots. Separation from Gramicidin C and other material occurred after 999 transfers. [Gross and Witkop *Biochemistry* 4 2495 1965; Bauer et al. *Biochemistry* 11 3266 1972.] Purified finally by recrystn from EtOH-H<sub>2</sub>O and dried at 100°/10<sup>-2</sup> mm over KOH and forms platelets m 229-230°. Almost insoluble in H<sub>2</sub>O (0.6%) but soluble in lower alcohols, dry Me<sub>2</sub>CO, dioxane, acetic acid and pyridine. The commercial material is more difficult to crystallise than the synthetic compound. [Sarges and Witkop J Am Chem Soc 86 1861, 87 2011, 2020 1965.] It has characteristic  $[\alpha]_D^{20} + 27.3°$  (c 1.3, MeOH) and UV  $\lambda_{max}$  282nm ( $\varepsilon$  22,100). The N-carbamoyldeformyl gramicidine A pptes from EtOAc-pet ether (b 40-60°).

**Gramicidin C** (gramicidin S, a pentadecapeptide from *Bacillus brevis*) [9062-61-7]. Same as Gramicidin A since they are isolated together and separated. [Sarges and Witkop *Biochemistry* 4 2491 1965; Hunter and Schwartz "Gramicidins" in *Antibotics I* (Gotlieb and Shaw Eds) Springer-Verlag, NY, p.642 1967; as well as references above for Gramicidin A.]

Gramicidin S 2HCl (from *Bacillus brevis* Nagano) [15207-30-4] M 1214.4, m 277-278°(dec),  $[\alpha]_D^{24}$ -289° (c 0.4, 70% aq EtOH). Crysts in prisms from EtOH + aq HCl.

Gramicidin S [113-73-5] M 1141.4, m 268-270°,  $[\alpha]_D^{25}$ -290° (c 0.5, EtOH + 30mM aq HCl [7:3]]. Crystd from EtOH. *Di-HCl* [15207-30-4] cryst from EtOH (+ few drops of HCl) has m 277-278°.

**N-Guanyltyramine hydrochloride** [60-20-8] **M 215.7, m 218°, pK<sub>1</sub> 10.2 (phenolic OH), pK<sub>2</sub> 12.4 (guanidino N).** Purified on a phosphocellulose column and eluted with a gradient of aqueous NH<sub>3</sub> (0-10%). The second major peak has the characteristic tryptamine spectrum and is collected, lyphilised to give white crystals of the *dihydrate* which dehydrates at 100°. It has UV  $\lambda_{max}$  at 274.5nm ( $\epsilon$  1310) in 0.1N NaOH and 274.5nm ( $\epsilon$  1330) at pH 7.0. Excitation  $\lambda_{max}$  is at 280nm and emission  $\lambda_{max}$  is at 330nm. [Mekalanos et al. J Biol Chem 254 5849 1979.]

**Haemoglobin** A (from normal human blood) [9008-02-0]  $M_r \sim 64,500$ , amorphous. Purified from blood using CM-32 cellulose column chromatography. [Matsukawa et al. J Am Chem Soc 107 1108 1985.] For the purification of the  $\alpha$  and  $\beta$  chains see Hill et al. Biochem Prep 10 55 1963.

Harmaline (7-methoxy-1-methyl-4,9-dihydro-3*H*- $\beta$ -carboline, 4,9-dihydro-7-methoxy-1methyl-3*H*-pyrido[3,4-*b*]indole) [304-21-2] M 214.3, m 229-230°, 229-231°, 235-237° (after distn at 120-140°/10<sup>-3</sup>), pK<sub>1</sub> 4.2. Recrystd from MeOH and sublimed at high vacuum. It has UV in MeOH has  $\lambda_{max}$  218, 260 and 376nm (log  $\varepsilon$  4.27, 3.90 and 4.02 respectively); IR (Nujol) v 1620, 1600, 1570 and 1535cm<sup>-1</sup> and in CHCl<sub>3</sub> v 1470 and 1629cm<sup>-1</sup>. [Spenser Can J Chem 37 1851 1959; Marion et al. J Am Chem Soc 73 305 1951; UV Prukner and Witkop Justus Liebigs Ann Chem 554 127 1942.] The hydrochloride dihydrate has m 234-236°(dec), the picrate has m 228-229° (sinters at 215°) from aqueous EtOH, and the N-acetate forms needles m 204-205°.

Hematin (ferrihaeme hydroxide) [15489-90-4] M 633.5, m 200°(dec), pK<sub>Est</sub> ~ 4. Crystd from pyridine. Dried at 40° in vacuo.

Hematoporphyrin (3,3'-[7,12-bis-(1-hydroxyethyl)-3,8,13,17-tetramethyl-porphyrin-2,18diyl]-dipropionic acid) [14459-29-1] M 598.7, pK<sub>Est</sub> ~4.8. Purified by dissolving in EtOH and $adding H<sub>2</sub>O or Et<sub>2</sub>O to give deep red crystals. Also recrystd from MeOH. UV has <math>\lambda_{max}$  at 615.5, 565, 534.4 and 499.5nm in 0.1 N NaOH, and 597, 619, 634,653, 683 and 701nm in 2 N HCl. [Falk Porphyrins and Metalloporphyrins Elsevier, NY, p 175 1964.] It is used in the affinity chromatographic purification of Heme proteins [Olsen Methods Enzymol 123 324 1986.] The O-methyl-dimethyl ester has m 203-206° (from CHCl<sub>3</sub>-MeOH) and the O,O'-dimethyl-dimethyl ester has m 145° (from CHCl<sub>3</sub>-MeOH). [Paul Acta Chem Scand 5 389 1951.]

Hematoporphyrin dimethyl ester [33070-12-1] M 626.7, m 212°. Crystd from CHCl<sub>3</sub>/MeOH.

Hematoxylin ( $\pm$ -11bc-7,11b-dihydroindeno[2,1-c]-chromen-3,4-6ar-9,10-pentaol) [517-28-2] M 302.3, m 200°(dec), 210-212°(dec). Recrystd from H<sub>2</sub>O (as trihydrate) in white-yellow crystals which become red on exposure to light and then melt at 100-120°. It has been recrystd from Me<sub>2</sub>CO-<sup>\*</sup>C<sub>6</sub>H<sub>6</sub>. Crystd also from dil aqueous NaHSO<sub>3</sub> until colourless. Soluble in alkali, borax and glycerol. Store in the dark below 0°. [Morsingh and Robinson *Tetrahedron* 26 182 1970; Dann and Hofmann *Chem Ber* 98 1498 1955.]

Hemin (ferriproptoporphyrin IX chloride) [16009-13-5] M 652.0, m sinters at 240°, pK<sub>Est</sub> ~4.8. It is purified by recrystn from AcOH. Also heme (5g) is shaken in pyridine (25mL) till it dissolves, then CHCl<sub>3</sub> (40mL) is added, the container is stoppered and shaken for 5min (releasing the stopper occasionally). The soln is filtered under slight suction, and the flask and filter washed with a little CHCl<sub>3</sub> (15mL). During this period, AcOH (300mL) is heated to boiling and saturated aqueous NaCl (5mL) and conc HCl (4mL) are added. The CHCl<sub>3</sub> filtrate is poured in a steady stream, with stirring, into the hot AcOH mixture and set aside for 12hours. The crystals are filtered off, washed with 50% aqueous AcOH (50mL), H<sub>2</sub>O (100mL), EtOH (25mL), Et<sub>2</sub>O and dried in air. [Fischer Org Synth Coll Vol III 442 1955.]

Heparin (from pig intestinal mucosa) [9005-49-6]  $M_r \sim 3,000$ , amorphous,  $[\alpha]_D^{20} \sim +55^{\circ}$  (H<sub>2</sub>O). Most likely contaminants are mucopolysaccharides including heparin sulfate and dermatan sulfate. Purified by pptn with cetylpyridinium chloride from saturated solutions of high ionic strength. [Cifonelli and Roden *Biochem Prep* 12 12 1968.]

Heparin (sodium salt) [9041-08-1]  $M_r \sim 3000$  (low Mol Wt, Bovine), amorphous,  $[\alpha]_D^{20}$  +47° (c 1.5, H<sub>2</sub>O). Dissolved in 0.1M NaCl (1g/100mL) and ppted by addition of EtOH (150mL).

Histones (from S4A mouse lymphoma). Purification used a macroprocess column, heptafluorobutyric acid as solubilising and ion-pairing agent and an acetonitrile gradient. [McCroskey et al. Anal Biochem 163 427 1987.]

Hyaluronidase [9001-54-1, 37326-33-3] M<sub>r</sub> 43,000 (bovine testes), 89,000 (bacterial), [EC 3.2.1.35]. Purified by chromatography on DEAE-cellulose prior to use. [Distler and Jourdain J Biol Chem 248 6772 1973.]

Hydrocortisone (11β,17α,21-trihydroxy-pregn-4-ene-3,20-dione) [50-23-7] M 362.5, m 212-213°, 214-217°, 218-221°, 220-222°,  $[α]_D^{22}$ +167° (c 1, EtOH). Recryst from EtOH or isoPrOH. It is bitter tasting and has UV  $λ_{max}$  at 242 nm (log ε 4.20). Its solubility at 25° is: H<sub>2</sub>O (0.28%), EtOH (1.5%), MeOH (0.62%), Me<sub>2</sub>CO (0.93%), CHCl<sub>3</sub> (0.16%), propylene glycol (1.3%) and Et<sub>2</sub>O (0.35%). It gives an intense green colour with conc H<sub>2</sub>SO<sub>4</sub>. [Wendler et al. J Am Chem Soc 72 5793 1950.]

Hydrocortisone acetate (21-acetoxy-11 $\beta$ ,17 $\alpha$ -trihydroxy-pregn-4-ene-3,20-dione) [50-03-3] M 404.5, m 218-221.5°, 221-223°, 222-225°,  $[\alpha]_D^{25}$ +166° (c 0.4, dioxane), +150.7° (c 0.5, Me<sub>2</sub>CO). Recrystd from Me<sub>2</sub>CO-Et<sub>2</sub>O or aqueous Me<sub>2</sub>CO as somewhat hygroscopic monoclinic crystals. UV has  $\lambda_{max}$  242 nm ( $A_{1cm}^{1\%}$  390) in MeOH. Its solubility at 25° is: H<sub>2</sub>O (0.001%), EtOH (0.45%), MeOH (0.04%), Me<sub>2</sub>CO (1.1%), CHCl<sub>3</sub> (0.5%), Et<sub>2</sub>O (0.15%) and is very soluble in Me<sub>2</sub>NCHO. [Wendler et al. J Am Chem Soc 74 3630 1952; Antonucci et al. J Org Chem 18 7081 1953.] (+)-Hydroquinidine anhydrous (9S-6'-methoxy-10,11-dihydrocinchonan-9-ol) [1435-55-8] M 326.4, m 168-169°, 169°, 169-170°, 171-172°,  $[\alpha]_D^{20} + 231°$  (c 2, EtOH), +299° (c 0.82, 0.1N H<sub>2</sub>SO<sub>4</sub>), pK<sub>Est</sub> ~ 8.8. Forms needles from EtOH and plates from Et<sub>2</sub>O. Slightly soluble in Et<sub>2</sub>O and H<sub>2</sub>O but readily soluble in hot EtOH. [Heidelberger and Jacobs J Am Chem Soc 41 826 1919; King J Chem Soc 523 1946.] The hydrochloride has m 273-274°,  $[\alpha]_D^{26} + 184°$  (c 1.3, MeOH) and is very soluble in MeOH and CHCl<sub>3</sub>, but less soluble in H<sub>2</sub>O, EtOH and less soluble in dry Me<sub>2</sub>CO. [Kyker and Lewis J Biol Chem 157 707 1945; Emde Helv Chim Acta 15 557 1932.]

Hydroquinine [522-66-7] M 326.4, m 168-171°, 171.5°,  $[\alpha]_D^{16}$ +143° (c 1.087, EtOH), pK<sup>15</sup> 8.87. Recrystd from EtOH. [Rabe and Schultz Chem Ber 66 120 1933.]

**19-Hydroxy-4-androsten-3,17-dione** [510-64-5] **M 302.4, m 167-169°, 168-170°, 169-170°, 172-173°,**  $[\alpha]_D^{20}$  +190° (c 1, CHCl<sub>3</sub>). Recryst from Me<sub>2</sub>CO-hexane or Et<sub>2</sub>O-hexane. It has UV  $\lambda_{max}$  at 242nm in EtOH or MeOH. The *19-acetoxy* derivative has  $[\alpha]_D^{26}$  +185° (CHCl<sub>3</sub>) and  $\lambda_{max}$  237.5nm in EtOH. [Ehrenstein and Dünnenberger J Org Chem 21 774 1956.]

3-Hydroxy butyrate dehydrogenase (from *Rhodopseudomonas spheroides*) [9028-38-0] M<sub>r</sub> ~85,000, [EC 1.1.1.30], amorphous. Purified by two sequential chromatography steps on two triazine dye-Sepharose matrices. [Scavan et al. *Biochem J* 203 699 1982.]

**25-Hydroxycholesterol** (cholest-5-en-3 $\beta$ ,25-diol) [2140-46-7] M 402.7, m 177-179°, 178-180°, 181.5-182.5°,  $[\alpha]_D^{25}$ -39° (c 1.05, CHCl<sub>3</sub>). Forms colourless needles from MeOH. [Schwartz *Tetrahedron Lett* 22 4655 1981.] The  $3\beta$ -acetoxy derivative has m 142-142.8° (from Me<sub>2</sub>CO),  $[\alpha]_D^{25}$ -40.4° (c 2, CHCl<sub>3</sub>). The  $3\beta$ ,25-diacetyl derivative has m 119-120.5° (from MeOH),  $[\alpha]_D^{25}$ -35.5° (CHCl<sub>3</sub>). [Dauben and Bradlow J Am Chem Soc 72 4248 1950; Ryer et al. J Am Chem Soc 72 4247 1950.]

18-Hydroxy-11-deoxycorticosterone (18,21-dihydroxypregn-4-en-3,20-dione tautomeric with 18,20-epoxy-20,21-dihydroxypregn-4-en-3-one) [379-68-0] M 346.5, m 168-170°, 171-173°, 191-195°, 200-205°,  $[\alpha]_D^{20}$ +151° (c 1, CHCl<sub>3</sub>). Recrystn from Et<sub>2</sub>O-Me<sub>2</sub>CO gave crystals m 200-205°, when recryst from M<sub>2</sub>CO it had m 191-195°. It has UV  $\lambda_{max}$  at 240nm. The 21-O-acetoxy-18-hydroxy derivative has m 158-159° (from Et<sub>2</sub>O-\*C<sub>6</sub>H<sub>6</sub>) and the 21-O-acetoxy-18,20-epoxy derivative has m 149-154° (from Et<sub>2</sub>O). [Kahnt et al. Helv Chim Acta 38 1237 1955; Pappo J Am Chem Soc 81 1010 1959.]

**R**-(-)-2-Hydroxy-3,3-dimethyl- $\gamma$ -butyrolactone (3-hydroxy-4,4-dimethyl-4,5-dihydrofuran-2-one, D-pantolactone) [599-04-2] M 130.1, m 89-91°, 90.5-91.5°, 91°, 92-93°, b 120-122°/15mm,  $[\alpha]_{D}^{20}$ -28° (c 5, MeOH),  $[\alpha]_{D}^{20}$ -51° (c 3, H<sub>2</sub>O). Recrystallise from Et<sub>2</sub>O-pet ether, disopropyl ether or \*C<sub>6</sub>H<sub>6</sub>-pet ether and sublime at 25°/0.0001mm. It hydrolyses readily to the hydroxy-acid and racemises when heated above 145°. The *Brucine salt* has m 211-212° (from EtOH). [Kuhn and Wieland *Chem Ber* 73 1134 1940; and Stiller et al. J Am Chem Soc 62 1779 1940; Bental and Tishler J Am Chem Soc 68 1463 1946.]

(±)-Ibotenic acid monohydrate ( $\alpha$ -[3-hdyroxy-5-isoxazolyl]-glycine,  $\alpha$ amino-3-hydroxy-5-isoxazoleacetic acid) [2552-55-8] M 176.1, m 144-146° (monohydrate), 151-152° (anhydrous), 148-151°, pK<sub>1</sub> 2, pK<sub>2</sub> 5.1, pK<sub>3</sub> 8.2. It has been converted to the ammonium salt (m 121-123° dec) dissolved in H<sub>2</sub>O and passed through an Amberlite IR 120 resin (H<sup>+</sup> form) and eluted with H<sub>2</sub>O. The acidic fractions were collected, evaporated to dryness and the residue recrystd from H<sub>2</sub>O as the monohydrate (m 144-146°). The anhydrous acid is obtained by making a slurry with MeOH, decanting and evaporating to dryness and repeating the process twice more to give the anhydrous acid (m 151-152°). Recrystn from H<sub>2</sub>O gives the monohydrate. [Nakamura *Chem Pharm Bull Jpn* 19 46 1971.] The *ethyl ester* forms needles when crystd from a small volume of Et<sub>2</sub>O and has m 78-79° and IR (CHCl<sub>3</sub>) with v 3500-2300 (OH), 1742 (ester CO), 1628, 1528cm<sup>-1</sup>, and UV with  $\lambda_{max}$  (EtOH) at 206nm ( $\epsilon$  7080). The hydrazide has m 174-175° (from MeOH) with IR (KBr) 1656 (C=O)cm<sup>-1</sup>. **2-Iminothiolane hydrochloride** (2-iminotetrahydrothiophene) [4781-83-3] M 137.6, m 187-192°, 190-195°, 193-194°, 202-203°, pK <2 (free base). Recryst from MeOH-Et<sub>2</sub>O (m 187-192°) but after sublimation at ~180°/0.2mm the melting point rose to 202-203°. It has NMR with  $\delta$  2.27 (2H, t), 3.25 (2H, t) and 3.52 (2H, t) in (CD<sub>3</sub>)<sub>2</sub>SO. [King et al. *Biochemistry* 17 1499 1978.] The *free base* is purifed by vacuum distn (b 71-72°/6mm) with IR (film) with v 1700 (C=N)cm<sup>-1</sup> and NMR (CDCl<sub>3</sub>) with  $\delta$  at 3.58 (2H, t) and 2.10-2.8 (4H, m). The *free base* is stable on storage but slowly hydrolyses in aqueous solns with half lives at 25° of 390h at pH 9.1, 210h at pH 10 and 18 h at pH 11. [Alagon and King *Biochemistry* 19 4343 1980.]

trans-Indol-3-ylacrylic acid [1204-06-4] M 187.2, m 190-195°(dec), 195°(dec), 196°(dec), 195-196°(dec), pK<sub>Est</sub> ~ 4.2. Recrystd from AcOH, H<sub>2</sub>O or EtOAc-cyclohexane. UV in MeOH has  $\lambda_{max}$ at 225, 274 and 325nm. [Shaw et al. J Org Chem 23 1171 1958; constitution: Rappe Acta Chem Scand 18 818 1964; Moffatt J Chem Soc 1442 1957; Kimming et al. Hoppe Seyler's Z Physiol Chem 371 234 1958.]

**3-Indolylbutyric acid** [133-32-4] **M 203.2, m 120-123°, 123-125°, 124°, pK 4.84.** Recrystd from H<sub>2</sub>O. It is soluble in EtOH, Et<sub>2</sub>O and Me<sub>2</sub>CO but insoluble in CHCl<sub>3</sub>. [Bowman and Islip Chem Ind London 154 1971; Jackson and Manske J Am Chem Soc 52 5029 1930; Albaum and Kaiser Am J Bot 24 420 1937.] UV has  $\lambda_{max}$  278 and 320nm in isoPrOH [Elvidge Quart J Pharm Pharmacol 13 219 1940]. The methyl ester has m 73-74° (from \*C<sub>6</sub>H<sub>6</sub>-pet ether) and b 230°/6mm [Bullock and Hand J Am Chem Soc 78 5854 1951]. Also recrystd from EtOH/water [James and Ware J Phys Chem 89 5450 1985].

**3-Indolylpyruvic acid** [392-12-1] **M 203.2, m~210°(dec), 208-210°(dec), 219°(dec), pK**<sub>Est</sub> ~ **2.4.** Recrystd from Me<sub>2</sub>CO-\*C<sub>6</sub>H<sub>6</sub>, EtOAc-CHCl<sub>3</sub>, Me<sub>2</sub>CO-AcOH (crystals with 1 molecule of AcOH) and dioxane-\*C<sub>6</sub>H<sub>6</sub> (with 0.5 molecule of dioxane) [Shaw et al. J Org Chem 23 1171 1958; Kaper and Veldstra Biochim Biophys Acta 30 401 1958]. The ethyl ester has m 133° (from Et<sub>2</sub>O) and its 2,4-dinitro-phenylhydrazone has m 255° (from Me<sub>2</sub>CO). [Baker J Chem Soc 461 1946.]

*myo*-Inositol (cyclohexane[1r, 2c, 3c, 4t, 5c, 6t]-hexol) [87-89-8] M 180.2, m 218° (dihydrate), 225-227°, 226-230°. Recrystd from aq 50% ethanol or H<sub>2</sub>O forming a dihydrate, or anhydrous crystals from AcOH. The dihydrate is efflorescent and becomes anhydrous when heated at 100°. The anhydrous crystals are not hygroscopic. Solubility in H<sub>2</sub>O at 25° is 14%, at 60° it is 28%, slightly soluble in EtOH but insoluble in Et<sub>2</sub>O. [Ballou and Anderson J Am Chem Soc 75 748 1953; Anderson and Wallis J Am Chem Soc 70 2931 1948.]

Interferons [ $\alpha$ IFN,  $\beta$ IFN and  $\gamma$ IFN]. Interferons are a family of glycosylated proteins and are cytokines which are produced a few hours after cells have been infected with a virus. Interferons protect cells from viral infections and have antiviral activities at very low concentrations (~3 x 10<sup>-4</sup> M, less than 50 molecules are apparently sufficient to protect a single cell). Double stranded RNA are very efficient inducers of IFNs. There are three main types of IFNs. The  $\alpha$ IFNs are synthesised in lymphocytes and the  $\beta$ IFNs are formed in infected fibroblasts. The  $\alpha$  and  $\beta$  families are fairly similar consisting of *ca* 166 to 169 amino acids. Although  $\gamma$ IFNs are also small glycosylated proteins (*ca* 146 amino acids), they are different because they are not synthesised after viral infections but are produced by lymphocytes when stimulated by **mitogens** (agents that induced cell division).

Several of these IFNs of mouse and human lymphocytes and fibroblasts are available commercially and have been best prepared in quantity by recombinant DNA procedures because they are produced in very small amounts by the cells. The commercial materials do not generally require further purification for their intended purposes. [Pestkas, Interferons and Interferon standards and general abbreviations, *Methods Enzymol*, Wiley & Sons, **119** 1986, ISBN 012182019X; Lengyel, Biochemistry of interferons and their actions, *Ann Rev Biochem* **51** 251-282 1982; De Maeyer and De Maeyer-Guignard, Interferons in *The Cytokine Handbook*, 3rd Edn, Thomson et al. Eds, pp. 491-516 1998 Academic Press, San Diego, ISBN 0126896623.]

Interleukin (from human source). Purified using lyophilisation and desalting on a Bio-Rad P-6DC desalting gel, then two steps of HPLC, first with hydroxylapatite, followed by a TSK-125 size exclusion column. [Kock and Luger J Chromatogr 296 293 1984.]

Interleukin-2 (recombinant human) [94218-72-1] M<sub>r</sub> ~15,000, amorphous. Purified by reverse phase HPLC. [Weir and Sparks *Biochem J* 245 85 1987; Robb et al. *Proc Natl Acad Sci USA* 81 6486 1984.]

**Interleukins** (IL-1, IL-2 —IIL18]. Interleukins are cytokines which cause a variety of effects including stimulation of cell growth and proliferation of specific cells, e.g. stem cells, mast cells, activated T cells, colony stimulating factors etc, as well as stimulating other ILs, prostaglandins release etc. They are small glycosylated proteins (*ca* 15 kD, 130-180 amino acids produced from longer precursors) and are sometimes referred to by other abbreviations, e.g. IL-2 as TCGF (T cell growth factor), IL-3 as multi-CSF (multilineage colony stimulating factor, also as BPA, HCSF, MCSF and PSF). They are produced in very small amounts and are commercially made by recombinant DNA techniques in bacteria or Sf21 insect cells. Interleukins for human (h-IL), mouse (m-IL) and rat (r-IL) are available and up to IL-18 are available commercially in such purity that they can be used directly without further refinement, particularly those that have been obtained by recombinant DNA procedures which are specific. As well as the interleukins, a variety of antibodies for specific IL reactions are available for research or IL identification. [Symons et al. Lymphokines and Interferons, *A Practical Approach*, Clemens et al. Eds, p. 272 *1987*; IRL Press, Oxford, ISBN 1852210354, 1852210362; Thomson et al. Eds, *The Cytokine Handbook*, 3rd Edn, *1998*; Academic Press, San Diego, ISBN 0126896623.]

Iodonitrotetrazolium chloride (2[4-iodophenyl]-3-[4-nitrophenyl]-5-phenyl-2H-tetrazolium chloride) [146-68-9] M 505.7, m 229°(dec), ~245°(dec). Recrystd. from H<sub>2</sub>O, aqueous EtOH or EtOH-Et<sub>2</sub>O. Alternatively dissolve in the minimum volume of EtOH and add Et<sub>2</sub>O; or dissolve in hot H<sub>2</sub>O (charcoal), filter and ppte by adding conc HCl. Filter solid off and dry at 100°. Solubility in H<sub>2</sub>O at 25° is 0.5%, and in hot MeOH-H<sub>2</sub>O (1:1) it is 5%. [Fox and Atkinson J Am Chem Soc 72 3629 1950.]

**Iodonitrotetrazolium violet-Formazan** [7781-49-9] M 471.3, m 185-186°. Dissolve in boiling dioxane (20g in 300mL), add H<sub>2</sub>O (100mL) slowly, cool, filter and dry *in vacuo* at 100°. Its solubility in CHCl<sub>3</sub> is ~1%. [UV: Fox and Atkinson J Am Chem Soc 72 3629 1950.]

**5-Iodouridine** (5-iodo-1-[ $\beta$ -D-ribofuranosyl]-pyrimidine-2,4(1*H*)-dione) [1024-99-3] M 370.1, m 205-208°(dec), 210-215°(dec),  $[\alpha]_D^{20}$ -23.5° (c 1, H<sub>2</sub>O), pK<sup>20</sup> 8.5. Recrystd from H<sub>2</sub>O and dried *in vacuo* at 100°. UV has  $\lambda_{max}$  289nm (0.01N HCl) and 278nm (0.01N NaOH). [Prusoff et al. *Cancer Res* 13 221 1953.]

**3-Isobutyl-1-methylxanthine** (3-isobutyl-1-methylpurine-2,6-dione) [28822-58-4] M 222.3, m 199-210°, 202-203°, pK<sub>Est</sub> ~ 6.7 (acidic NH). Recrystd from aqueous EtOH.

Isopentenyl pyrophosphate [358-71-4] M 366.2,  $pK_{Est(1)} < 2$ ,  $pK_{Est(2)} < 2$ ,  $pK_{Est(3)} - 3.95$ ,  $pK_{Est(4)} - 6.26$ . Purified by chromatography on Whatman No 1 paper using *tert*-butyl alcohol/formic acid/water (20:5:8,  $R_F 0.60$ ) or 1-propanol/ammonia/water (6:3:1.  $R_F 0.48$ ). Also purified by chromatography on a DEAE-cellulose column or a Dowex-1 (formate form) ion-exchanger using formic acid and ammonium formate as eluents. A further purification step is to convert it to the monocyclohexylammonium salt by passage through a column of Dowex-50 (cyclohexylammonium form) ion-exchange resin. Can also be converted into its lithium salt.

**DL-Isoserine** (±-3-amino-2-hydroxypropionic acid) [632-12-2] M 105.1, m 250-252°(dec), 235°(dec), 237°(dec), 245°(dec), pK<sub>1</sub><sup>25</sup> 2.78 (acidic), pK<sub>2</sub><sup>25</sup> 9.27 (basic). Recrystd from H<sub>2</sub>O or 50% aqueous EtOH. It has an isoelectric pH of 6.02. [Rinderknocht and Niemann J Am Chem Soc 75 6322 1953; Gundermann and Holtmann Chem Ber 91 160 1958; Emerson et al. J Biol Chem 92 451 1931.] The hydrobromide has m 128-130° (from aqueous HBr) [Schöberl and Braun Justus Liebigs Ann Chem 542 288 1939].

Isoxanthopterin (2-amino-4,7-dihydroxypteridine) [529-69-1] M 179.4, m>300°,  $pK_1^{20}$  -0.5 (basic),  $pK_2^{20}$  7.34 (acidic),  $pK_3^{20}$  10.06 (acidic). Purified by repeated pptn from alkaline solutions by acid (preferably AcOH), filter, wash well with H<sub>2</sub>O then EtOH and dried at 100°. Purity is checked by paper chromatography [R<sub>F</sub> 0.15 (*n*-BuOH, AcOH, H<sub>2</sub>O, 4:1:1); 0.33 (3% aq NH<sub>4</sub>OH). [Goto et al. Arch Biochem

Biophys 111 8 1965.] For biochemistry see Blakley Biochemistry of Folic Acid and Related Pteridines North Holland Publ Co, Amsterdam 1969.]

**Kanamycin B** (Bekanamycin, 4-0-[2,6-diamino-2,6-dideoxy- $\alpha$ -D-glucopyranosyl]-6-0-[3-amino-3-deoxy- $\alpha$ -D-glucopyranosyl]-2-deoxystreptamine) [4696-76-8, 29701-07-3 (sulfate salt)] M 483.5, m 170-179°(dec), 178-182°(dec),  $[\alpha]_D^{18} + 130°$  (c 0.5, H<sub>2</sub>O), pK 7.2. A small quantity (24mg) can be purified on a small Dowex 1 x 2 column (6 x 50mm), the correct fraction is evapd to dryness and the residue crystd from EtOH containing a small amount of H<sub>2</sub>O. [Umezawa et al. Bull Chem Soc Jpn 42 537 1969.] It has been crystd from H<sub>2</sub>O by dissolving ~1g in H<sub>2</sub>O (3mL), adding Me<sub>2</sub>NCHO (3mL) setting aside at 4° overnight, The needles are collected and dried to constant weight at 130°. It has also been recrystd from aq EtOH. It is slightly sol in CHCl<sub>3</sub> and isoPrOH. [IR: Wakazawa et al. J Antibiot 14A 180, 187 1961; Ito et al. J Antibiot 17 A 189 1964.]

**Lactate dehydrogenase** (from dogfish, Beef muscle) [9001-60-9] M<sub>r</sub> 140,000 [EC 1.1.1.27]. 40-Fold purification by affinity chromatography using Sepharose 4B coupled to 8-(6aminohexyl)amino-5'-AMP or -NAD<sup>+</sup>. [Lees et al. Arch Biochem Biophys 163 561 1974; Pesce et al. J Biol Chem 239 1753 1964.]

Lactoferrin (from human whey). Purified by direct adsorption on cellulose phosphate by batch extraction, then eluted by a stepped salt and pH gradient. [Foley and Bates Anal Biochem 162 296 1987.]

Lecithin (1,2-diacylphosphatidylcholine mixture) [8002-43-5] M ~600-800, amorphous. From hen egg white. Purified by solvent extraction and chromatography on alumina. Suspended in distilled water and kept frozen until used [Lee and Hunt J Am Chem Soc 106 7411 1984, Singleton et al. J Am Oil Chem Soc 42 53 1965]. For purification of commercial egg lecithin see Pangborn [J Biol Chem 188 471 1951].

Lectins (proteins and/or glycoproteins of non-immune origin that agglutinate cells, from seeds of *Robinia pseudoacacia*), M ~100,000. Purified by pptn with ammonium sulfate and dialysis; then chromatographed on DE-52 DEAE-cellulose anion-exchanger, hydroxylapatite and Sephacryl S-200. [Wantyghem et al. *Biochem J* 237 483 1986.]

Leucopterin (2-amino-5,8-dihydropteridine-4,6,7(1*H*)-trione) [492-11-5] M 195.1, m >300° (dec),  $pK_1^{20}$ -1.66,  $pK_2^{20}$ 7.56,  $pK_3^{20}$ 9.78,  $pK_4^{20}$ 13.6. Purified by dissolving in aqueous NaOH, stirring with charcoal, filtering and precipitating by adding aqueous HCl, then drying at 100° in a vacuum. It separates with 0.5 moles of H<sub>2</sub>O. Its solubility in H<sub>2</sub>O is 1g/750 litres [Albert et al. J Chem Soc 4219 1952; Albert and Wood J Appl Chem (London) 2 591 1952; Pfleiderer Chem Ber 90 2631 1957].

DL- $\alpha$ -Lipoamide (±-6,8-thioctic acid amide, 5-[1,2]-dithiolan-3-ylvaleric acid amide) [3206-73-3] M 205.3, m 124-126°, 126-129°, 130-131°. Recrystd from EtOH and has UV with  $\lambda_{max}$ 331nm in MeOH. [Reed et al. J Biol Chem 232 143 1958; IR: Wagner et al. J Am Chem Soc 78 5079 1956.]

DL- $\alpha$ -Lipoic acid (±-6,8-thioctic acid, 5-[1,2]-dithiolan-3-ylvaleric acid) [1077-28-7] M 206.3, m 59-61°, 60.5-61.5° and 62-63°, b 90°/10<sup>-4</sup>mm, 150°/0.1mm, pK<sup>25</sup> 4.7. It forms yellow needles from cyclohexane or hexane and has been distd at high vacuum, and sublimes at ~90° and very high vacuum. Insoluble in H<sub>2</sub>O but dissolves in alkaline soln. [Lewis and Raphael J Chem Soc 4263 1962; Soper et al. J Am Chem Soc 76 4109; Reed and Niu J Am Chem Soc 77 416 1955; Tsuji et al. J Org Chem 43 3606 1978; Calvin Fed Proc USA 13 703 1954.] The S-benzylthiouronium salt has m 153-154° (evacuated capillary; from MeOH), 132-134°, 135-137° (from EtOH). The d- and l- forms have m 45-47.5° and  $[\alpha]_{2}^{23} \pm 113°$  (c 1.88,  $C_{6}H_{6}$ ) and have UV in MeOH with  $\lambda_{max}$  at 330nm ( $\epsilon$  140). Lipoprotein lipase (from bovine skimmed milk) [9004-02-8] [EC 3.1.1.34]. Purified by affinity chromatography on heparin-Sepharose [Shirai et al. Biochim Biophys Acta 665 504 1981].

Lipoproteins (from human plasma). Individual human plasma lipid peaks were removed from plasma by ultracentrifugation, then separated and purified by agarose-column chromatography. Fractions were characterised immunologically, chemically, electrophoretically and by electron microscopy. [Rudel et al. *Biochem J* 13 89 1974.]

Lipoteichoic acids (from gram-positive bacteria) [56411-57-5]. Extracted by hot phenol/water from disrupted cells. Nucleic acids that were also extracted were removed by treatment with nucleases. Nucleic resistant acids, proteins, polysaccharides and teichoic acids were separated from lipoteichoic acids by anion-exchange chromatography on DEAE-Sephacel or by hydrophobic interaction on octyl-Sepharose [Fischer et al. *Eur J Biochem* 133 523 1983].

D-Luciferin (firefly luciferin, S-2[6-hydroxybenzothiazol-2-yl]-4,5-dihydrothiazol-4carboxylic acid), [2591-17-5] M 280.3, m 189.5-190°(dec), 196°(dec), 201-204°, 205-210°(dec, browning at 170°),  $[\alpha]_D^{22}$ -36° (c 1.2, DMF), pK<sub>Est(1)</sub>~ 1.2 (benzothiazole-N), pK<sub>Est(2)</sub>~ 1.6 (thiazolidine-N), pK<sub>Est(3)</sub>~ 6.0 (CO<sub>2</sub>H), pK<sub>Est(4</sub>) 8.5 (6OH). Recrystallises as pale yellow needles from H<sub>2</sub>O, or MeOH (83mg from 7mL). It has UV  $\lambda_{max}$  at 263 and 327nm (log  $\varepsilon$  3.88 and 4.27) in 95% EtOH. The Na salt has a solubility of 4mg in 1 mL of 0.05M glycine. [White et al. J Am Chem Soc 83 2402 11961, 85 337 1963; UV and IR: Bitler and McElroy Arch Biochem 72 358 1957; Review: Cormier et al. Fortschr Chem Org Naturst 30 1 1973.]

Lumiflavin (7,8,10-trimethylbenzo[g]pteridine-2,4(3H,10H)-dione) [1088-56-8] M 256.3, m 330°(dec), 340°(dec), pK 10.2. Forms orange crystals upon recrystn from 12% aqueous AcOH, or from formic acid. It sublimes at high vacuum. It is freely soluble in CHCl<sub>3</sub>, but not very soluble in H<sub>2</sub>O and most organic solvents. In H<sub>2</sub>O and CHCl<sub>3</sub> soln it has a green fluorescence. UV has  $\lambda_{max}$  at 269, 355 and 445nm ( $\varepsilon$  38,800, 11,700 and 11,800 respectively) in 0.1N NaOH and 264, 373 and 440nm ( $\varepsilon$  34,700, 11,400 and 10,400 respectively) in 0.1N HCl while UV in CHCl<sub>3</sub> has  $\lambda_{max}$  at 270, 312, 341, 360, 420, 445 and 470nm. [Hemmerich et al. Helv Chim Acta 39 1242 1956; Holiday and Stern Chem Ber 67 1352 1834; Yoneda et al. Chem Pharm Bull Jpn 20 1832 1972; Birch and Moye J Chem Soc 2622 1958; Fluorescence: Kuhn and Moruzzi Chem Ber 67 888 1934.]

**Magnesium protoporphyrin dimethyl ester** [14724-63-1] M 580.7. Crude product dissolved in as little hot dry  ${}^{*}C_{6}H_{6}$  as possible and left overnight at room temperature to cryst. [Fuhrhop and Graniek *Biochem Prep* 13 55 1971.]

 $\alpha$ -Melanotropin [581-05-5] (13 amino acids peptide),  $[\alpha]_D^{25}$ -58.5° (c 0.4, 10% aq AcOH). Extract separated by ion-exchange on carboxymethyl cellulose, desalted, evapd and lyophilised, then chromatographed on Sephadex G-25. [Lande et al. *Biochem Prep* 13 45 1971.]

**B-Melanotropin**. [9034-42-8] (18-22 amino acids peptide), amorphous. Extract separated by ionexchange on carboxymethyl cellulose, desalted, evapd and lyophilised, then chromatographed on Sephadex G-25. [Lande et al. *Biochem Prep* 13 45 1971.]

6-Mercaptopurine monohydrate [6112-76-1] M 170.2, m 314-315°(dec), ~315°(dec), 313-315°(dec),  $pK_1^{20}$  7.77,  $pK_2^{20}$  10.84. Recrystallises from H<sub>2</sub>O as yellow crystals of the monohydrate which become anhydrous on drying at 140°. It has UV  $\lambda_{max}$  at 230 and 312nm ( $\epsilon$  14,000 and 19,600) in 0.1N NaOH; 222 and 327nm ( $\epsilon$  9,2400 and 21,300), and 216 and 329nm ( $\epsilon$  8,740 and 19,300) in MeOH. [Albert and Brown J Chem Soc 2060 1954; IR: Brown and Mason J Chem Soc 682 1957; UV: Fox et al. J Am Chem Soc 80 1669 1958; UV: Mason J Chem Soc 2071 1954.]

6-Mercaptopurine-9-β-D-ribofuranoside [574-25-4] M 284.3, m 208-210°(dec), 210-211°(dec), 220-223°(dec), 222-224°(dec),  $[\alpha]_D^{25}$ -73° (c 1, 0.1N NaOH), pK 7.56. Recrystd from H<sub>2</sub>O or EtOH. It has UV λ<sub>max</sub> in H<sub>2</sub>O at 322nm (pH 1), 320 nm (pH 6.7) and 310nm (pH 13). [IR: Johnson et al. J Am Chem Soc 80 699 1958; UV: Fox et al. J Am Chem Soc 80 1669 1958.]

Metallothionein (from rabbit liver) [9038-94-2]. Purified by precipitation to give Zn- and Cdcontaining protein fractions and running on a Sephadex G-75 column, then isoelectric focusing to give two protein peaks [Nordberg et al. *Biochem J* 126 491 1972].

Methadone hydrochloride (2-dimethylamino-4-ethoxycarbonyl-4,4-diphenylbutane HCl) [1095-90-5] M 345.9, m 241-242°, pK<sub>2</sub><sup>25</sup>8.94, pK<sub>2</sub><sup>20</sup> 10.12 (free base). Crystd from EtOH.

Methoxantin coenzyme (PQQ, pyrrolo quinoline quinone, 2,7,9-tricarboxy-1H-pyrrolo-[2,3-f]-quinoline-4,5-dione, 4,5-dihydro-4,5-dioxo-1H-pyrrolo[2,3-f]quinoline-2,7,9-tricarboxylic acid) [72909-34-3] M 330.2, m 220°(dec). Efflorescent yellow-orange needles on recrystn from H<sub>2</sub>O by addition of Me<sub>2</sub>CO, or better from a supersaturated aqueous soln, as it forms an acetone adduct. [Forrest et al. Nature 280 843 1979.] It has also been purified by passage through a C-18 reverse phase silica cartridge or a silanised silica gel column in aqueous soln whereby methoxantin remains behind as a red-orange band at the origin. This band is collected and washed thoroughly with dilute aqueous HCl (pH 2) and is then eluted with MeOH-H<sub>2</sub>O (7:3) and evapd *in vacuo* to give the coenzyme as a red solid. It has also been purified by dissolving in aqueous 0.5M K<sub>2</sub>CO<sub>3</sub> and acidified to pH 2.5 whereby PQQ pptes as a deep red solid which is collected and dried *in vacuo*. Methoxantin elutes at 3.55 retention volumes from a C18 µBondapak column using H<sub>2</sub>O-MeOH (95:5) + 0.1% AcOH pH 4.5. It has UV  $\lambda_{max}$  at 247 and 330nm (shoulder at 270nm) in H<sub>2</sub>O and  $\lambda_{max}$  at 250 and 340nm in H<sub>2</sub>O at pH 2.5. With excitation at  $\lambda_{ex}$  365nm it has a  $\lambda_{max}$  emission at 483nm. The <sup>13</sup>C NMR has  $\delta$ : 113.86, 122.76, 125.97, 127.71, 130.68, 137.60, 144.63, 146.41, 147.62, 161.25, 165.48, 166.45, 173.30 and 180.00.

When a soln in 10% aqueous MeCO is adjusted to pH 9 with aqueous NH<sub>3</sub> and kept at 25° for 30 min, the *acetone adduct* is formed; UV has  $\lambda_{max}$  at 250, 317 and 360nm (H<sub>2</sub>O, pH 5.5) and with  $\lambda_{ex}$  at 360nm it has max fluorescence at  $\lambda_{max}$  at 465nm; and the <sup>13</sup>C NMR [(CD<sub>3</sub>)<sub>2</sub>SO, TMS] has  $\delta$ : 29.77, 51.06, 74.82, 111.96, 120.75, 121.13, 125.59, 126.88, 135.21, 139.19, 144.92, 161.01, 161.47, 165.17, 168.61, 190.16 and 207.03. It also forms a *methanol adduct*.

When it is reacted with Me<sub>2</sub>SO<sub>4</sub>-K<sub>2</sub>CO<sub>3</sub> in dry Me<sub>2</sub>NCHO at 80° for 4h, it forms the *trimethyl ester* which has m 265-267°(dec) [260-263°(dec)] after recrystn from hot MeCN (orange crystals) with UV  $\lambda_{max}$  at 252 and 344nm (H<sub>2</sub>O) and 251, 321 and 373nm (in MeOH; MeOH adduct ?). [Duine et al. *Eur J Biochem* 108 187 1980; Duine et al. *Adv Enzymology* 59 169 1987; Corey and Tramontano J Am Chem Soc 103 5599 1981; Gainor and Weinreb J Org Chem 46 4319 1981; Hendrickson and de Vries J Org Chem 17 1148 1982; McKenzie, Moody and Reese J Chem Soc Chem Commun 1372 1983.]

Methyl benzylpenicillinate [653-89-4] M 348.3, m 97°,  $[\alpha]_D^{20}$ +328° (c 1, MeOH). Crystd from CCl<sub>4</sub>.

5-Methylphenazinium methyl sulfate [299-11-6] M 306.3, m 155-157° (198°dec by rapid heating). It forms yellow prisms from EtOH (charcoal). Solubility in  $H_2O$  at 20° is 10%. In the presence of aqueous KI it forms a *semiquinone* which crystallises as blue leaflets from EtOH. [Wieland and Roseen Chem Ber 48 1117 1913; Voriskova Collect Czech Chem Commun 12 607 1947; Bülow Chem Ber 57 1431 1924.]

1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (MPTP) [23007-85-4] M 209.7, m 196-198°, pK<sub>Est</sub> ~ 9.3. Purified by recrystn from Me<sub>2</sub>CO + isoPrOH. The free base has b 137-142°/0.8 mm,  $n_D^{25}$  1.5347. [Schmidle and Mansfield J Am Chem Soc 78 425 1956; Defeudis Drug Dev Res 15 1 1988.]

6-α-Methylprednisolone (Medrol, 11β,17-21-trihydroxy-6α-methylpregna-1,4-dien-3,20dione) [83-43-2] M 347.5, m 226-237°, 228-237°, 240-242°,  $[\alpha]_D^{24}$ +91° (c 0.5, dioxane). Recrystd from EtOAc. UV has  $\lambda_{max}$  in 95% EtOH 243nm (ε 14,875). The 21-acetoxy derivative has m 205208° (from EtOAc),  $[\alpha]_D^{24}$  +95° (c 1, CHCl<sub>3</sub>). [Spero et al. J Am Chem Soc **78** 6213 1956; Fried et al. J Am Chem Soc **81** 1235 1959; <sup>1</sup>H NMR: Slomp and McGarvey J Am Chem Soc **81** 2200 1959.]

5-Methyltetrahydrofolic acid disodium salt (prefolic A) [68792-52-9] M 503.4, pK<sub>1</sub> 2.4 (N10 protonation), pK<sub>2</sub> 2.7 (pyrimidine N1 protonation), pK<sub>3</sub> 3.5 ( $\alpha$ -CO<sub>2</sub>H), pK<sub>4</sub> 4.9 ( $\gamma$ -CO<sub>2</sub>H), pK<sub>5</sub> 5.6 (N5-Me), pK<sub>6</sub> 8.5 (3NHCO acidic). Check purity by measuring UV at pH 7.0 (use phosphate buffer) and it should have  $\lambda_{max}$  290nm and  $\lambda_{min}$  245nm with a ratio of A<sub>290</sub>/A<sub>250</sub> of 3.7. This ratio goes down to 1.3 as oxidation to the dihydro derivative occurs. The latter can be reduced back to the tetrahydro compound by reaction with 2-mercaptoethanol at room temp. If oxidation had occurred then the compound should be chromatographed on DEAE-cellulose (~0.9 milliequiv/g, in AcO<sup>-</sup> form) in (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> (1.5 M) and washed with 1M NH<sub>4</sub>OAc containing 0.01M mercaptoethanol till free from UV absorption and then washed with 0.01M mercaptoethanol and 1M NH<sub>4</sub>OAc containing 0.01M mercaptoethanol and the fractions with absorption at 290nm are collected. These are evapd under reduced pressure at 25° and traces of NH<sub>4</sub>OAc and H<sub>2</sub>O are removed at high vacuum/25° (~24-48h). The residue is dissolved in the minimum volume of 0.01M mercaptoethanol and an equivalent of NaOH is added to convert the acid to the diNa salt and evaporated to dryness at high vacuum/25°. The product should have  $\lambda_{max}$  290nm ( $\epsilon$  32,000) in pH 7.0 buffer. [Sakami *Biochem Prep* 10 103 1963.]

5-Methyltryptamine hydrochloride (3-[2-aminoethyl]-5-methylindole hydrochloride) [1010-95-3] M 210.7, m 289-291°(dec), 290-292°,  $pK_{Est(1)} \sim -3$  (protonation of ring NH),  $pK_{Est(2)} \sim 9.0$  (CH<sub>2</sub>NH<sub>2</sub>),  $pK_{Est(3)} \sim 10.9$  (acidic indole NH). Recryst d from H<sub>2</sub>O. The free base has m 93-95° (from \*C<sub>6</sub>H<sub>6</sub>-cyclohexane), and the picrate has m 243°(dec) (from EtOH). [Young J Chem Soc 3493 1958; Gaddum et al. Quart J Exp Physiol 40 49 1955; Röhm Hoppe Seyler's Z Physiol Chem 297 229 1954.]

4-Methylumbelliferone( $\beta$ ) hydrate (7-hydroxy-4-methylcoumarin) [90-33-5] M 194.2, m 185-186°, 185-188°, 194-195°, pK<sub>Est</sub> ~ 10.0 (phenolic OH). Purified by recrystn from EtOH. It is insoluble in cold H<sub>2</sub>O, slightly soluble in Et<sub>2</sub>O and CHCl<sub>3</sub>, but soluble in MeOH and AcOH. It has blue fluorescence in aqueous EtOH, and has UV  $\lambda_{max}$  221, 251 and 322.5nm in MeOH. IR has v 3077 br, 1667, 1592, 1385, 1267, 1156, 1130 and 1066 cm<sup>-1</sup>. The acetate has m 153-154°. [Woods and Sapp J Org Chem 27 3703 1962.]

**4-Methylumbellifer-7-yl-\alpha-D-glucopyranoside** [17833-43-1] M 338.3, m 221-222°,  $[\alpha]_{\rm D}^{20}$ 237° (c 3, H<sub>2</sub>O). Recrystd from hot H<sub>2</sub>O.

**4-Methylumbellifer-7-yl-\beta-D-glucopyranoside** [18997-57-4] M 338.3, m 210-212°, 211°,  $[\alpha]_D^{20}$ -61.5° (c 2, pyridine), -89.5° (c 0.5, H<sub>2</sub>O for half hydrate). Recrystallises as the half hydrate from hot H<sub>2</sub>O. [Constantzas and Kocourek Collect Czech Chem Commun 24 1099 1959; De Re et al. Ann Chim (Rome) 49 2089 1959.]

**1-Methyluric acid** [708-79-2] **M 182.1, m >350°, pK<sub>1</sub> 5.75 (basic), pK<sub>2</sub> 10.6 (acidic).** Recrystd from H<sub>2</sub>O. [Bergmann and Dikstein *J Am Chem Soc* 77 691 1955.] It has UV  $\lambda_{max}$  at 231 and 283. nm (pH 3) and 217.5 and 292.5nm (pH >12) [Johnson *Biochem J* 5 133 1952].

Mevalonic acid lactone [674-26-0] M 130.2, m 28°, b 145-150°/5mm. Purified via the dibenzylethylenediammonium salt (m 124-125°) [Hofmann et al. J Am Chem Soc 79 2316 1957], or by chromatography on paper or on Dowex-1 (formate) column. [Bloch et al. J Biol Chem 234 2595 1959.] Stored as N,N'-dibenzylethylenediamine (DBED) salt, or as the lactone in a sealed container at 0°.

Mevalonic acid 5-phosphate [1189-94-2] M 228.1,  $pK_{Est(1)} \sim 1.5$  (PO<sub>4</sub>H<sub>2</sub>),  $pK_{Est(2)} \sim 4.4$  (CO<sub>2</sub>H),  $pK_{Est(3)} \sim 6.31$  (PO<sub>4</sub>H<sup>-</sup>). Purified by conversion to the *tricyclohexylammonium salt* (m 154-156°) by treatment with cyclohexylamine. Crystd from water/acetone at -15°. Alternatively, the phosphate was chromatographed by ion-exchange or paper (Whatman No 1) in a system isobutyric acid/ammonia/water (66:3:30; R<sub>F</sub> 0.42). Stored as the cyclohexylammonium salt.

Mevalonic acid 5-pyrophosphate [1492-08-6] M 258.1,  $pK_{Est(1)} < 2$ ,  $pK_{Est(2)} < 2$ ,  $pK_{Est(3)} < 3.95$ (PO<sub>4</sub>),  $pK_{Est(4)}$  4.4 (CO<sub>2</sub>H),  $pK_{Est(5)} < 6.26$  (PO<sub>4</sub>). Purified by ion-exchange chromatography on Dowex-1 formate [Bloch et al. J Biol Chem 234 2595 1959], DEAE-cellulose [Skilletar and Kekwick, Anal Biochem 20 171 1967], on by paper chromatography [Rogers et al. Biochem J 99 381 1966]. Likely impurities are ATP and mevalonic acid phosphate. Stored as a dry powder or as a slightly alkaline (pH 7-9) soln at -20°.

Mithramycin A (Aureolic acid, Plicamycin) [18378-89-7] M 1085.2, m 180-183°,  $[\alpha]_D^{20}$ -51° (c 0.3, EtOH), pK<sub>Est</sub> ~ 9.2. Purified from CHCl<sub>3</sub>, and is soluble in MeOH, EtOH, Me<sub>2</sub>CO, EtOAc, Me<sub>2</sub>SO and H<sub>2</sub>O, and moderately soluble in CHCl<sub>3</sub>, but is slightly soluble in \*C<sub>6</sub>H<sub>6</sub> and Et<sub>2</sub>O. Fluorescent antitumour agent used in flow cytometry. [Thiem and Meyer *Tetrahedron* 37 551 1981; NMR: Yu et al. *Nature* 218 193 1968.]

**Mitomycin** C [50-07-7] **M 334.4, m >360°, pK**<sub>Est(2)</sub>~ **8.0.** Blue-violet crystals form  ${}^{*}C_{6}H_{6}$ -pet ether. It is soluble in Me<sub>2</sub>CO, MeOH and H<sub>2</sub>O, moderately soluble in  ${}^{*}C_{6}H_{6}$ , CCl<sub>4</sub> and Et<sub>2</sub>O but insoluble in pet ether. It has UV  $\lambda_{max}$  at 216, 360 and a weak peak at 560nm in MeOH. [Stevens et al. J Med Chem 8 I 1965; Shirahata and Hirayama J Am Chem Soc 105 7199 1983.]

Muramic acid [R-2(2-amino-2-deoxy-D-glucose-3-yloxy)-propionic acid] [1114-41-6] M 251.2, m 145-150°(dec), 152-154°(dec), 155°(dec),  $[\alpha]_{D}^{25}$  +109° (c 2, H<sub>2</sub>O), +165.0° (extrapolated to 0 time)  $\rightarrow +123^{\circ}$  [after 3h (c 3, H<sub>2</sub>O)], pK<sub>Est(1)</sub>~ 3.8 (CO<sub>2</sub>), pK<sub>Est(2)</sub>~ 7.7 (NH<sub>2</sub>). It has been recrystd from H<sub>2</sub>O or aqueous EtOH as monohydrate which loses H<sub>2</sub>O at  $80^{\circ}$  in vacuo over P<sub>2</sub>O<sub>5</sub>. Sometimes contains some NaCl. It has been purified by dissolving 3.2g in MeOH (75mL), filtered from some insoluble material, concentrated to ~10mL and refrigerated. The colourless crystals are washed with absolute MeOH. This process does not remove NaCl; to do so the product is recrystd from a equal weight of  $H_2O$  to give a low yield of very pure acid (0.12g). On paper chromatography 0.26µg give one ninhydrin positive spot after development with 75% phenol (R<sub>F</sub> 0.51) or with sec-BuOH-HCO<sub>2</sub>O-H<sub>2</sub>O (7:1:2) (R<sub>F</sub> 0.30). [Matsushima and Park Biochem Prep 10 109 1963; J Org Chem 27 3581 1962.] The acid has been also purified by dissolving 990mg in 50% aqueous EtOH (2mL), cooling, collecting the colourless needles on a sintered glass funnel and dried over P2O5 at 80°/0.1mm to give the anhydrous acid. [Lambert and Zilliken Chem Ber 93 2915 1960.] Alternatively the acid is dissolved in a small volume of  $H_2O$ , neutralised to pH 7 with ion exchange resin beads (IR4B in OH<sup>-</sup> form), filtered, evaporated and dried. The residue is recrystd from 90% EtOH (v/v) and dried as above for 24h. [Strange and Kent *Biochem J* 71 333 1959.] The *N*-acetyl derivative has  $m \sim 125^{\circ}$  (dec) and  $[\alpha]_{D}^{20} + 41.2^{\circ}$  after 24h (c 1.5, H<sub>2</sub>O). [Watanabe and Saito J Bacteriol 144 428 1980.]

Muscimol (pantherine, 5-aminoethyl-3[2h]-isoxazolone) [2763-96-4] M 114.1, m 170-172°(dec), 172-174°(dec), 172-175°, 175°, 176-178°(dec),  $pK_{Est(1)}$ ~ 6 (acidic, ring 2-NH),  $pK_{Est(2)}$ ~ 8 (CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>). Recrystd from MeOH-tetrahydrofuran or EtOH and sublimed at 110-140° (bath) at 10<sup>-4</sup> mm and gives a yellow spot with ninhydrin which slowly turns purple [NMR: Bowden et al. J Chem Soc (C) 172 1968]. Also purified by dissolving in the minimum volume of hot H<sub>2</sub>O and adding EtOH dropwise until cloudy, cool, and colourless crystals separate; IR: v 3445w, 3000-2560w br, 2156w, 1635s and 1475s cm<sup>-1</sup>. [NMR: Jager and Frey Justus Liebigs Ann Chem 817 1982.] Alternatively it has been purified by two successive chromatographic treatments on Dowex 1 x 8 with the first elution with 2M AcOH and a second with a linear gradient between 0—2M AcOH and evaporating the desired fractions and recrystallising the residue from MeOH. [McCarry and Savard Tetrahedron Lett 22 5153 1981; Nakamura Chem Pharm Bull Jpn 19 46 1971.]

Mycophenolic acid (6-[1,3-dihydro-7-hydroxy-5-methoxy-4-methyl-1-oxoisobenzofuran-6yl]-4-methylhex-4-enoic acid) [24280-93-1] M 320.3, m 141°, 141-143°,  $pK_{Est(1)}$ ~ 2.5 (CO<sub>2</sub>H),  $pK_{Est(2)}$ ~ 9.5 (phenolic OH). Purified by dissolving in the minimum volume of EtOAc, applying to a silica gel column (0.05-0.2 mesh) and eluting with a mixture of EtOAc + CHCl<sub>3</sub> + AcOH (45:55:1) followed by recrystn from heptane-EtOAc, from aqueous EtOH or from hot H<sub>2</sub>O and drying *in vacuo*. It is a weak dibasic acid moderately soluble in Et<sub>2</sub>O, CHCl<sub>3</sub> and hot H<sub>2</sub>O but weakly soluble in  ${}^{*}C_{6}H_{6}$  and

## Purification of Biochemicals and Related Products

toluene. [Birch and Wright Aust J Chem 22 2635 1969; Canonica et al. J Chem Soc Perkin Trans 1 2639 1972; Birkinshaw, Raistrick and Ross Biochem J 50 630 1952.]

**Myoglobin** (from sperm whale muscle). [9047-17-0]  $M_r \sim 17,000$ . Purified by CM-cellulose chromatography and Sephadex G-50 followed by chromatography on Amberlite IRC-50 Type III or BioRex 70 (<400mesh). The crystalline product as a paste in saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> at pH 6.5-7.0 may be stored at 4° for at least 4 years unchanged, but must not be kept in a freezer. [Anres and Atassi *Biochemistry* 12 942 1980; Edmundson *Biochem Prep* 12 41 1968.]

Myricetin (Cannabiscetin, 3,3',4',5,5',7-hexahydroxyflavone) [529-44-2] M 318.2, m >300°, 357°(dec) (polyphenolic  $pK_{Est}$ ~8-11). Recrystd from aq EtOH (m 357° dec, as monohydrate) or Me<sub>2</sub>CO (m 350° dec, with one mol of Me<sub>2</sub>CO) as yellow crystals. Almost insol in CHCl<sub>3</sub> and AcOH. The *hexaacetate* has m 213°. [Hergert J Org Chem 21 534 1956; Spada and Cameroni Gazzetta 86 965, 975 1956; Kalff and Robinson J Chem Soc 127 181 1925.]

**Nalidixic acid** (1-ethyl-7-methyl-1,8-naphthyridin-4-one-3-carboxylic acid) [389-08-2] M 232.3, m 226.8-230.2°, 228-230°, 229-230°, pK 6.0. Crystd from H<sub>2</sub>O or EtOH as a pale buff powder. It is soluble at 23° in CHCl<sub>3</sub> (3.5%), toluene (0.16%), MeOH (0.13%), EtOH (0.09%), H<sub>2</sub>O (0.01% and Et<sub>2</sub>O (0.01%). It inhibits nucleic acid and protein synthesis in yeast. [Lesher et al. J Med and Pharm Chem 5 1063 1962.]

Naloxone hydrochloride hydrate (Narcan, 1-N-propenyl-7,8-dihydro-14-hydroxymorphinan-6-one hydrochloride) [51481-60-8] M 399.9, m 200-205°,  $[\alpha]_D^{20}$ -164° (c 2.5, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 6 (N-propenyl), pK<sub>Est(2)</sub>~ 9.6 (phenolic OH). This opiate antagonist has been recryst from EtOH + Et<sub>2</sub>O or H<sub>2</sub>O. It is soluble in H<sub>2</sub>O (5%) and EtOH but insoluble in Et<sub>2</sub>O. The free base has m 184° (177-178°) after recrystn from EtOAc,  $[\alpha]_D^{20}$ -194.5° (c 0.93, CHCl<sub>3</sub>). [Olofson et al. Tetrahedron Lett 1567 1977; Gold et al. Med Res Rev 2 211 1982.]

Naltrexone hydrochloride dihydrate (1-N-cyclopropylmethyl-7,8-dihydro-14-hydroxymorphinan-6-one hydrochloride) [16676-29-2] M 413.9, m 274-276°,  $[\alpha]_D^{20}$ -173° (c 1, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 6 (N-cyclopropylmethyl), pK<sub>Est(2)</sub>~ 9.6 (phenolic OH). This narcotic antagonist has been purified by recrystn from MeOH and dried air. The *free base* has m 168-170° after recrystn from Me<sub>2</sub>CO. [Cone et al. J Pharm Sci 64 618 1975; Gold et al. Med Res Rev 2 211 1982.]

**α-Naphthoflavone** (7,8-benzoflavone) [604-59-1] M 272.3, m 153-155°, 155°, pK 8-9 (phenolic OH). Recrystd from EtOH or aqueous EtOH. [IR: Cramer and Windel Chem Ber 89 354 1956; UV Pillon and Massicot Bull Soc Chim Fr 26 1954; Smith J Chem Soc 542 1946; Mahal and Venkataraman J Chem Soc 1767 1934.] It is a competitive inhibitor of human estrogen synthase. [Kellis and Vickery Science 225 1032 1984.]

Naphthol AS-acetate (3-acetoxynaphthoic acid anilide) [1163-67-3] M 305.3, m 152°, 160°. Recrystd from hot MeOH and dried *in vacuo* over P<sub>2</sub>O<sub>5</sub>. It is slightly soluble in AcOH, EtOH, CHCl<sub>3</sub> or \*C<sub>6</sub>H<sub>6</sub>. It is a fluorogenic substrate for albumin esterase activity. [Chen and Scott Anal Lett 17 857 1984.] At  $\lambda_{ex}$  320nm it had fluorescence at  $\lambda_{em}$  500nm. [Brass and Sommer Chem Ber 61 1000 1928.]

1-Naphthyl phosphate disodium salt [2183-17-7] M 268.1,  $pK_1^{26}$  0.97,  $pK_2^{26}$  5.85 (for free acid). Purified through an acid ion-exchange column (in H<sup>+</sup> form) to give the *free acid* which is obtained by freeze drying and recrystn from Me<sub>2</sub>CO + \*C<sub>6</sub>H<sub>6</sub>, or by adding 2.5 vols of hot CHCl<sub>3</sub> to a hot soln of 1 part acid and 1.2 parts Me<sub>2</sub>CO and cooling (m 155-157°, 157-158°). The acid is dissolved in the minimum volume of H<sub>2</sub>O to which 2 equivalents of NaOH are added and then freeze dried, or by adding the equivalent amount of MeONa in MeOH to a soln of the acid in MeOH and collecting the Na salt, washing with cold MeOH then Et<sub>2</sub>O and drying in a vacuum. [Friedman and Seligman J Am Chem Soc 72 624 1950; Chanley and Feageson J

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Am Chem Soc 77 4002 1955.] It is a substrate for alkaline phosphatase [Gomori Methods Enzymol 4 381 1957, 128 212 1968], and prostatic phosphatase [Babson Clin Chem 30 1418 1984]. See entry on p. 444.

2-Naphthyl phosphate monosodium salt [14463-68-4] M 246.2, m 296° (sintering at 228°),  $pK_1^{26}$  1.28,  $pK_2^{26}$  5.53 (for free acid). The *free acid* is purified as for the preceding 1-isomer and has m 176-177°, 177-178° after recrystn from CHCl<sub>3</sub> + Me<sub>2</sub>CO as the 1-isomer above. It is neutralised with one equivalent of NaOH and freeze dried or prepared as the 1-isomer above. Its solubility in H<sub>2</sub>O is 5%. It also forms a 0.5 Na.1 H<sub>2</sub>O salt which has m 203-205° (244°?). [Friedman and Seligman J Am Chem Soc 72 624 1950; Chanley and Fegeason J Am Chem Soc 77 4002 1955.] See entry on p. 444 in Chapter 5.

D(+)-Neopterin [2009-64-5] M 253.2, m >300°(dec),  $[\alpha]_{546}^{20}$  +64.5° (c 0.14, 0.1M HCl),  $[\alpha]_D^{25}$  +50.1° (c 0.3, 0.1N HCl), pK<sub>1</sub> 2.23 (basic), pK<sub>2</sub> 7.89 (acidic). Purified as biopterin. Also purified on a Dowex 1 x 8 (formate form) column and eluted with 0.03M ammonium formate buffer pH 8.0 then pH 7.2. The fluorescent neopterin fraction is evapd under reduced pressure leaving neopterin and ammonium formate (the latter can be sublimed out at high vacuum). The residue is stirred for 24h with EtOH and the solid is collected and recrystd from H<sub>2</sub>O [Viscontini et al. *Helv Chim Acta* 53 1202 1970; see Wachter et al. Eds *Neopterin* W de Guyter, Berlin 1992].

 $\beta$ -Nicotinamide adenine dinucleotide (diphosphopyridine nucleotide, NAD, DPN) [53-84-9] M 663.4, [α]<sup>23</sup><sub>D</sub>-34.8° (c 1, H<sub>2</sub>O), pK<sub>1</sub> 2.2 (PO<sub>4</sub>H), pK<sub>2</sub> 4.0 (adenine NH<sub>2</sub>), pK<sub>3</sub> 6.1 (PO<sub>4</sub><sup>-</sup>). Purified by paper chromatography or better on a Dowex-1 ion-exchange resin. The column was prepared by washing with 3M HCl until free of material absorbing at 260nm, then with water, 2M sodium formate until free of chloride ions and, finally, with water. NAD, as a 0.2% soln in water, adjusted with NaOH to pH 8, was adsorbed on the column, washed with water, and eluted with 0.1M formic acid. Fractions with strong absorption at 360nm were combined, acidified to pH 2.0 with 2M HCl, and cold acetone (ca 5L/g of NAD) was added slowly and with constant agitation. It was left overnight in the cold, then the ppte was collected in a centrifuge, washed with pure acetone and dried under vacuum over CaCl<sub>2</sub> and paraffin wax shavings [Kornberg Methods Enzymol 3 876 1957]. Purified by anion-exchange chromatography [Dalziel and Dickinson Biochemical Preparations 11 84 1966.] The purity is checked by reduction to NADH (with EtOH and yeast alcohol dehydrogenase) which has  $\varepsilon_{340mn}$  6220 M<sup>-1</sup>cm<sup>-1</sup>. [Todd et al. J Chem Soc 3727,3733 1957.] [pKa, Lamborg et al. J Biol Chem 231 685 1958.] The free acid crystallises from aq Me<sub>2</sub>CO with 3H<sub>2</sub>O and has m 140-142°. It is stable in cold neutral aqueous solns in a desiccator (CaCl<sub>2</sub>) at 25°, but decomposes at strong acid and alkaline pH. Its purity is checked by reduction with yeast alcohol dehydrogenase and EtOH to NADH and noting the OD at 340nm. Pure NADH has  $\varepsilon_{340}$  6.2 x  $10^4 M^{-1} cm^{-1}$ , i.e. 0.1µmole of NADH in 3mL and in a 1cm path length cell has an OD at 340nm of 0.207.

β-Nicotinamide adenine dinucleotide reduced di-Na salt trihydrate (reduced diphosphopyridine nucleotide sodium salt, NADH) [606-68-8] M 763.5, pK as for NAD. This coenzyme is available in high purity and it is advised to buy a fresh preparation rather than to purify an old sample as purification will invariably lead to a more impure sample contaminated with the oxidised form (NAD). It has UV  $\lambda_{max}$  at 340nm ( $\varepsilon$  6,200 M<sup>-1</sup>cm<sup>-1</sup>) at which wavelength the oxidised form NAD has no absorption. At 340 nm a 0.161mM solution in a 1cm (pathlength) cell has an absorbance of 1.0 unit. The purity is best checked by the ratio A<sub>280nm</sub>/A<sub>340nm</sub> ~2.1, a value which increases as oxidation proceeds. The dry powder is stable indefinitely at -20°. Solutions in aqueous buffers at pH ~7 are stable for extended periods at -20° and for at least 8h at 0°, but are oxidised more rapidly at 4° in a cold room (e.g. almost completely oxidised overnight at 4°). [UV: Drabkin J Biol Chem 175 563 1945; Fluorescence: Boyer and Thorell Acta Chem Scand 10 447 1956; Redox: Rodkey J Biol Chem 234 188 1959; Schlenk in The Enzymes 2 250, 268 1951; Kaplan in The Enzymes 3 105, 112 1960.] Deuterated NADH, i.e. NADD, has been purified through the anion exchange resin AG-1 x 8 (100-200 mesh, formate form) and through a Bio-Gel P-2 column. [Viola, Cook and Cleland Anal Biochem 96 334 1979.]

 $\beta$ -Nicotinamide adenine dinucleotide phosphate (NADP, TPN) [53-59-8] M 743.4, pK<sub>1</sub> 1.1 (PO<sub>4</sub>H<sub>2</sub>), pK<sub>2</sub> 4.0 (adenine NH<sub>2</sub>), pK<sub>3</sub> 6.1 (PO<sub>4</sub><sup>-</sup>). Purified by anion-exchange chromatography in much the same way as for NAD [Dalziel and Dickinson *Biochem J* 95 311 1965; *Biochemical Preparations* 11 87 1966]. Finally it is purified by dissolving in H<sub>2</sub>O and precipitating with 4 volumes of Me<sub>2</sub>CO and dried *in* 

vacuo over P<sub>2</sub>O<sub>5</sub>. It is unchanged by storing *in vacuo* at 2°. [Hughes et al. J Chem Soc 3733 1957, Schuster and Kaplan J Biol Chem **215** 183 1955.] Deuterated NADPH, i.e. NADPD, has been purified through the anion exchange resin AG-1 x 8 (100-200 mesh, formate form) and through a Bio-Gel P-2 column.  $\lambda_{min}$  259nm ( $\epsilon$  18.000) at pH 7.0. [Viola, Cook and Cleland Anal Biochem **96** 334 1979.]

β-Nicotinamide adenine dinucleotide phosphate reduced tetrasodium salt (reduced diphosphopyridine nucleotide phosphate sodium salt, NADPH) [2646-71-1] M 833.4, pK as for NADP. Mostly similar to NADH above.

β-Nicotinamide mononucleotide (NMN) [1094-61-7] M 334.2,  $[\alpha]_D^{23}$ -38.3° (c 1, H<sub>2</sub>O), pK<sub>Est</sub> ~ 6.1 (PO<sub>4</sub>°). Purified by passage through a Dowex 1 (Cl<sup>-</sup> form), washed with H<sub>2</sub>O until no absorbance at 260 nm. The tubes containing NMN are pooled, adjusted to pH 5.5-6 and evapd *in vacuo* to a small volume. This is adjusted to pH 3 with dilute HNO<sub>3</sub> in an ice bath and treated with 20 volumes of Me<sub>2</sub>CO at 0-5°. The heavy white ppte is collected by centrifugation at 0°. It is best stored wet and frozen or can be dried to give a gummy residue. It has  $\lambda_{max}$  266nm (ε 4600) and  $\lambda_{min}$  249nm (ε 3600) at pH 7.0 (i.e. no absorption at 340nm). It can be estimated by reaction with CN<sup>-</sup> or hydrosulfite which form the 4-adducts equivalent to NADH) which has UV  $\lambda_{max}$  340nm (ε 6200). Thus after reaction an OD<sub>340</sub> of one is obtained from a 0.1612mM soln in a 1cm path cuvette. [Plaut and Plaut *Biochem Prep* 5 56 1957; Maplan and Stolzenbach *Methods Enzymol* 3 899 1957; Kaplan et al. J Am Chem Soc 77 815 1955.]

(-)-Nicotine (1-methyl-2[3-pyridyl]-pyrrolidine) [54-11-5] M 162.2, b 123-125°/17 mm, 246.1°/730.5mm, 243-248°/atm (partial dec),  $d_4^{20}$  1.097,  $n_D^{20}$  1.5280,  $[\alpha]_D^{20}$  - 169° (c 1, Me<sub>2</sub>CO), pK<sub>1</sub><sup>15</sup> 6.16 (pyridine N<sup>+</sup>), pK<sub>2</sub><sup>15</sup> 10.96 (pyrrolidine N<sup>+</sup>). Very pale yellow hygroscopic oil with a characteristic odour (tobacco extract) with browns in air on exposure to light. Purifed by fractional distn under reduced pressure in an inert atmosphere. A freshly distd sample should be stored in dark sealed containers under N<sub>2</sub>. It is a strong base, at 0.05 M soln it has a pH of 10.2. Very soluble in organic solvents. It is soluble in H<sub>2</sub>O and readily forms salts. [UV: Parvis J Chem Soc 97 1035 1910; Dobbie and Fox J Chem Soc 103 1194 1913.] The hydrochlorides (mono- and di-) form deliquescent crystals soluble in H<sub>2</sub>O and EtOH but insoluble in Et<sub>2</sub>O. It has also been purified via the ZnCl<sub>2</sub> double salt. [Ratz Monatsh Chem 26 1241 1905; Biosynthesis: Nakan and Hitchinson J Org Chem 43 3922 1978.] The picrate has m 218° (from EtOH). POISONOUS.

(±)-Nicotine [22083-74-5] M 162.2, b 242.3°/atm,  $d_4^{20}$  1.082 (pK see above). Purified by distn. Its solubility in EtOH is 5%. The *picrate* forms yellow needles from hot H<sub>2</sub>O and has m 218°. The *methiodide* has m 219° (from MeOH).

Nisin [1414-45-5] M 3354.2. Polypeptide from S. lactis. Crystd from EtOH. [Berridge et al. Biochem J 52 529 1952; synthesis by Fukase et al. Tetrahedron Lett 29 795 1988.]

**2-Nitrophenyl-\beta-D-galactopyranoside** [369-07-3] M 301.3, m 185-190°, 193°, 193-194°,  $[\alpha]_D^{18}$ -51.9° (c 1, H<sub>2</sub>O). Purified by recrystn from EtOH. [Seidman and Link J Am Chem Soc 72 4324 1950; Snyder and Link J Am Chem Soc 75 1758 1953]. It is a chromogenic substrate for  $\beta$ -galactosidases [Jagota et al. J Food Sci 46 161 1981].

4-Nitrophenyl- $\alpha$ -D-galactopyranoside [7493-95-0] M 301.3, m 166-169°, 173°,  $[\alpha]_D^{25} + 248$  (c 1, H<sub>2</sub>O). Purified by recrystn from H<sub>2</sub>O or aqueous EtOH. The monohydrate has m 85° which resolidifies and melts at 151-152° (the hemihydrate) which resolidifies and melts again at 173° as the anhydrous form. Drying the monohydrate at 60° yields the hemihydrate and drying at 100° gives the anhydrous compound. The tetraacetate has m 147° after drying at 100°. [Jermyn Aust J Chem 15 569 1962; Helfreich and Jung Justus Liebigs Ann Chem 589 77 1954.] It is a substrate for  $\alpha$ -galactosidase [Dangelmaier and Holmsen Anal Biochem 104 182 1980].

**4-Nitrophenyl-\beta-D-galactopyranoside** [3150-24-1] M 301.3, m 178°, 178-181°,181-182°,  $[\alpha]_D^{20}$ -83° (c 1, H<sub>2</sub>O). Purified by recrystn from EtOH. [Horikoshi J Biochem (Tokyo) 35 39 1042;

Goebel and Avery J Exptl Medicine 50 521 1929; Snyder and Link J Am Chem Soc 75 1758.] It is a chromogenic substrate for  $\beta$ -galactosidases [Buoncore et al. J Appl Biochem 2 390 1980].

4-Nitrophenyl- $\alpha$ -D-glucopyranoside [3767-28-0] M 301.3, m 206-212°, 216-217° (sinters at 210°),  $[\alpha]_D^{20}$  +215° (c 1, H<sub>2</sub>O). Purified by recrystn from H<sub>2</sub>O, MeOH or EtOH. [Jermyn Aust J Chem 7 202 1954; Montgomery et al. J Am Chem Soc 64 690 1942.] It is a chromogenic substrate from  $\alpha$ -glucosidases [Oliviera et al. Anal Biochem 113 1881981], and is a substrate for glucansucrases [Binder and Robyt Carbohydr Res 124 2871983]. It is a chromogenic substrate for  $\beta$ -glucosidases [Weber and Fink J Biol Chem 255 9030 1980].

4-Nitrophenyl-β-D-glucopyranoside [2492-87-7] M 301.2, m 164°, 164-165°, 165°,  $[α]_D^{20}$ -107° (c 1, H<sub>2</sub>O). Purified by recrystn from EtOH or H<sub>2</sub>O. [Montgomery et al. J Am Chem Soc 64 690 1942; Snyder and Link J Am Chem Soc 75 1758 1953.]

Nonactin [6833-84-7] M 737.0, m 147-148°,  $[\alpha]_D^{20}$  0° (±2°) (c 1.2, CHCl<sub>3</sub>). This macrotetrolide antibiotic was rerystd from MeOH as colourless needles, and dries at 90°/20h/high vacuum. [Helv Chim Acta 38 1445 1955, 55 1371 1972; Tetrahedron Lett 3391 1975.]

*N*-Nonanoyl-*n*-methylglucamine (Mega-9) [85261-19-4] M 335.4, m 87-89°. A non-ionic detergent purified as *n*-decanoyl-*N*-methylglucamine above. [Hildreth *Biochem J* 207 363 1982.]

Nonyl- $\beta$ -D-glucopyranoside [69984-73-2] M 306.4, m 67.5-70°,  $[\alpha]_D^{20}$ -34.4° (c 5, H<sub>2</sub>O),  $[\alpha]_D^{25}$ -28.8° (c 1, MeOH). Purified by recrystn from Me<sub>2</sub>CO and stored in well stoppered containers as it is hygroscopic. [Pigman and Richtmyer J Am Chem Soc 64 369 1942.] It is a UV transparent non-ionic detergent for solubilising membrane proteins [Schwendener et al. Biochem Biophys Res Commun 100 1055 1981.]

L-Noradrenaline (Adrenor, R-2-amino-1-[3,4-dihydroxyphenyl]ethan-1-ol, L-norepinephrine) [51-41-2, 69815-49-2 (bitartrate salt)] M 169.2, m 216.5-218°(dec), ~220-230°(dec),  $[\alpha]_D^{20}$ -45° (c 5, N HCl),  $[\alpha]_D^{25}$ 37.3° (c 5, 1 equiv aqueous HCl),  $pK_1^{25}$ 5.58 (phenolic OH),  $pK_2^{25}$ 8.90 (phenolic OH),  $pK_3^{25}$ 9.78 (NH<sub>2</sub>). Recrystd from EtOH and stored in the dark under N<sub>2</sub>. [pKa, Lewis Brit J Pharmacol Chemother 9 488 1954; UV: Bergström et al. Acta Physiol Scand 20 101 1950; Fluorescence: Bowman et al. Science NY 122 32 1955; Tullar J Am Chem Soc 70 2067 1948.] The L-tartrate salt monohydrate has m 102-104.5°,  $[\alpha]_D^{25}$ -11° (c 1.6, H<sub>2</sub>O), after recrystn from H<sub>2</sub>O or EtOH.

L-Noradrenaline hydrochloride (Arterenol) [329-56-6] M 205.6, m 145.2-146.4°, ~150°(dec),  $[\alpha]_D^{25}$ -40° (c 6, H<sub>2</sub>O), pK see above. Recrystd from isoPrOH and stored in the dark as it is oxidised in the presence of light (see preceding entry). [Tullar J Am Chem Soc 70 2067 1948.]

Novobiocin  $(7-[O^3-carbamoyl-5-O^4-dimethyl-\beta-L-lyso-6-desoxyhexahydropyranosyloxy]-4-hydroxy-3[4-hydroxy-3-{3-methylbut-2-enyl}-benzyl-amino]-8-methylcoumarin) [303-81-1] M 612.6, two forms m 152-156° and m 172-174°, 174-178°, <math>\lambda_{max}$  at 330nm (acid EtOH), 305nm (alk EtOH),  $[\alpha]_D^{25}$ -63° (c 1, EtOH),  $pK_1$  4.03 (4.2),  $pK_2$  9.16. Crystd from EtOH and stored in the dark. It has also been recrystd from Me<sub>2</sub>CO-H<sub>2</sub>O. [Hoeksema et al. J Am Chem Soc 77 6710 1955; Kaczka et al. J Am Chem Soc 77 9404 1955.]

The sodium salt [1476-53-5] M 634.6, m 210-215°, 215-220°(dec), 222-229°,  $[\alpha]_D^{25}$ -38° (c 1, H<sub>2</sub>O) has been recrystd from MeOH, then dried at 60°/0.5mm. [Sensi, Gallo and Chiesa, Anal Chem 29 1611 1957; Kaczka et al. J Am Chem Soc 78 4126 1956.]

**5'-Nucleotidase** (from Electric ray, Torpedo sp) [9027-73-0] [EC 3.1.3.5], amorphous. Purified by dissolving in Triton X-100 and deoxycholate, and by affinity chromatography on concanavalin A-Sepharose and AMP-Sepharose [Grondal and Zimmerman Biochem J 245 805 1987].

Nucleotide thiophosphate analogues. The preparation and purification of  $[^{3}H]ATP\gamma S$ ,  $[^{3}H]GTP\gamma S$ ,  $s^{6}ITP\gamma S$  (6-thioinosine),  $c|^{6}ITP\gamma S$  (6-chloroinosine) and  $[^{3}H]ATP\gamma S$  are described and the general purification

was achieved by chromatography of the nucleotide thiophosphates in the minimum volume of  $H_2O$  placed onto a DEAE-Sephadex A25 column and eluting with a linear gradient of triethylammonium bicarbonate (0.1 to 0.6M for G and I nucleotides and 0.2 to 0.5M for A nucleotides). [Biochim Biophys Acta 276 155 1972.]

Nystatin dihydrate (Mycostatin, Fungicidin) [1400-61-9] M 962.1, m dec>160° (without melting by 250°),  $[\alpha]_D^{25}$ -7° (0.1N HCl in MeOH), -10° (AcOH), +12° (Me<sub>2</sub>NCHO), +21° (pyridine). Light yellow powder with the following solubilities at ~28°: MeOH (1.1%), ethylene glycol (0.9%), H<sub>2</sub>O (0.4%), CCl<sub>4</sub> (0.12%), EtOH (0.12%), CHCl<sub>3</sub> (0.05%) and \*C<sub>6</sub>H<sub>6</sub> (0.03%). Could be ppted from MeOH soln by addition of H<sub>2</sub>O. Aqueous suspensions of this macrolide antifungal antibiotic are stable at 100°/10min at pH 7.0 but decomposes rapidly at pH <2 and >9, and in the presence of light and O<sub>2</sub>. [Birch et al. *Tetrahedron Lett* 1491, 1485 1964; Weiss et al. *Antibiot Chemother* 7 374 1957.] It contains a mixture of components A<sub>1</sub>, A<sub>2</sub> and A<sub>3</sub>.

**Octyl-B-D-glucopyranoside** [29836-26-8] M 292.4, m 62-65°, 63.8-65°,  $[\alpha]_D^{20}$ -34° (c 4, H<sub>2</sub>O). Purified by recrystn from Me<sub>2</sub>CO. It is *hygroscopic* and should be stored in a well stoppered container. [Noller and Rockwell J Am Chem Soc 60 2076 1938; Pigman and Richtmyer J Am Chem Soc 64 369 1942.] It is a UV transparent non-ionic dialysable detergent for solubilising membrane proteins. The  $\alpha$ -D-isomer with  $[\alpha]_D^{20}$ +118° (c 1, MeOH) has similar solubilising properties. [Lazo and Quinn Anal Biochem 102 68 1980; Stubbs et al. Biochim Biophys Acta 426 46 1976.]

Orcine monohydrate (3,5-dihydroxytoluene) [6153-39-5] M 142.2, m 56°, 56-58°, 58°, b 147°/5 mm,  $pK_1^{20}$  9.48 (9.26),  $pK_2^{20}$  11.20 (11.66). Purified by recrystn from H<sub>2</sub>O as the monohydrate. It sublimes *in vacuo* and the *anhydrous* compound has m 106.5-108° (110°, 108°). Also can be recrystd from CHCl<sub>3</sub> (plates) or \*C<sub>6</sub>H<sub>6</sub> (needles or prisms). [UV: Kiss et al. *Bull Soc Chim Fr* 275 1949; Adams et al. J Am Chem Soc 62 732 1940.]

**Orosomucoid** (glycoprotein  $\alpha_1$  acid, from human plasma) [66455-27-4] M<sub>r</sub> 42000-44000, amorphous. Purified by passage through a carboxymethyl cellulose column and through a Sephadex G-25 column. [Aronson et al. J Biol Chem 243 4564 1968.]

**Orotic acid Li salt H<sub>2</sub>O** (1-carboxy-4,6-dihydroxypyrimidine Li salt H<sub>2</sub>O) [5266-20-6] M 180.0, m >300°, pK<sub>1</sub> 2.8 (CO<sub>2</sub>H), pK<sub>2</sub> 9.4 (OH), pK<sub>3</sub> >13 (OH) (for free acid). It is soluble in H<sub>2</sub>O at 17° and 100°. Best to acidify an aqueous soln, isolating the free acid which is recrystd from H<sub>2</sub>O (as monohydrate) m 345-347° (345-346°), then dissolving in EtOH, adding an equivalent amount of LiOH in EtOH and evaporating. Its solubility in H<sub>2</sub>O is 1.28% (17°) and 2.34% (100°). [Bachstez Chem Ber 63 1000 1930; Johnson and Shroeder J Am Chem Soc 54 2941 1932; UV: Shugar and Fox Biochim Biophys Acta 9 199 1952.]

**Oxacillin sodium salt** (5-methyl-3-phenyl-4-isoxazolylpenicillin sodium salt) [1173-88-2] **M 423.4, m 188°(dec),**  $[\alpha]_D^{20} + 29°$  (c 1, H<sub>2</sub>O), pK<sub>Est</sub> ~ 2.7. This antibiotic which is stable to penicillinase is purified by recrystn from isoPrOH and dried *in vacuo*. Its solubility in H<sub>2</sub>O at 25° is 5%. [Doyle et al. *Nature* 192 1183 1961.]

**Oxolinic acid** (5-ethyl-5,8-dihydro-8-oxo-1,3-dioxolo[4,5-g]quinoline-3-carboxylic acid) [14698-29-4] M 261.2, m 313-314°(dec), 314-316°(dec), pK<sub>Est</sub> ~ 2.3. Purified by recrystn from aqueous Me<sub>2</sub>CO or 95% EtOH. It has UV  $\lambda_{max}$  220, (255.5sh), 259.5, 268, (298sh, 311sh), 321 and 326nm [ $\epsilon$  14.8, (36.8sh), 38.4, 38.4, (6.4sh, 9.2sh), 10.8 and 11.2 x 10<sup>3</sup>]. [Kaminsky and Mettzer J Med Chem 11 160 1968.]

**Oxytocin** [50-56-6] **M 1007.2, m dec on heating,**  $[\alpha]_D^{22}$ -26.2° (c 0.53, N AcOH). A cyclic nonapeptide which was purified by countercurrent distribution between solvent and buffer. It is soluble in H<sub>2</sub>O, *n*-BuOH and isoBuOH. [Bodanszky and du Vigneaud *J Am Chem Soc* 81 2504 1959; Cash et al. *J Med Pharm Chem* 5 413 1962; Sakakibara et al. *Bull Chem Soc Jpn* 38 120 1965; solid phase synthesis: Bayer and

Hagenmyer Tetrahedron Lett 2037 1968.] It was also synthesised on a solid phase matrix and finally purified as follows: A Sephadex G-25 column was equilibrated with the aqueous phase of a mixture of 3.5% AcOH (containing 1.5% of pyridine) + n-BuOH +  $C_6H_6$  (2:1:1) and then the organic phase of this mixture was run through. A soln of oxytocin (100mg) in H<sub>2</sub>O (2mL) was applied to the column which was then eluted with the organic layer of the above mixture. The fractions containing the major peak [as determined by the Folin-Lowry protein assay [Fryer et al. Anal Biochem 153 262 1986] were pooled, diluted with twice their vol of H<sub>2</sub>O, evaporated to a small vol and lyophilised to give oxytocin as a pure white powder (20mg, 508 U/mg). [Ives Can J Chem 46 2318 1968.]

**Palmitoyl coenzyme A** [1763-10-6] M 1005.9. Possible impurities are palmitic acid, S-palmitoyl thioglycolic acid and S-palmitoyl glutathione. These are removed by placing *ca* 200mg in a centrifuge tube and extracting with Me<sub>2</sub>CO (20mL), followed by two successive extractions with Et<sub>2</sub>O (15mL) to remove S-palmitoyl thioglycolic acid and palmitic acid. The residue is dissolved in H<sub>2</sub>O (4 x 4 mL), adjusted to pH 5 and centrifuged to remove insoluble S-palmitoyl glutathione and other insoluble impurities. To the clear supernatant is added 5% HClO<sub>4</sub> (6mL) whereby S-palmitoyl CoA pptes. The ppte is washed with 0.8% HClO<sub>4</sub> (10mL) and finally with Me<sub>2</sub>CO (3 x 5mL) and dried *in vacuo*. It is stable for at least one year in dry form at 0° in a desiccator (dark). Solns are stable for several months at -15°. Its solubility in H<sub>2</sub>O is 4%. The adenine content is used as the basis of purity with  $\lambda_{max}$  at 260 and 232nm ( $\varepsilon$  6.4 x 10<sup>6</sup> and 9.4 x 10<sup>6</sup> cm<sup>2</sup>/mol respectively). Higher absorption at 232nm would indicate other thio ester impurities, e.g. S-palmitoyl glutathione, which absorb highly at this wavelength. Also PO<sub>4</sub> content should be determined and acid phosphate can be titrated potentiometrically. [Seubert *Biochem Prep* 7 80 *1960*; Srer et al. *Biochim Biophys Acta* 33 31 *1959*; Kornberg and Pricer J Biol Chem 204 329, 345 *1953*.]

**3-Palmitoyl-sn-glycerol** (*R*-glycerol-1-palmitate, L- $\beta$ -palmitin) [32899-41-5] M 330.5, d<sup>27.3</sup> **0.9014, m 66.5°** ( $\alpha$ -form), 74° ( $\beta$ '-form) and 77° ( $\beta$ -form). The stable  $\beta$ -form is obtained by crystn from EtOH or Skellysolve B and recrystn from Et<sub>2</sub>O provides the  $\beta$ '-form. The  $\alpha$ -form is obtained on cooling the melt. [Malkin and el Sharbagy J Chem Soc 1631 1936; Chapman J Chem Soc 58 1956; Luton and Jackson J Am Chem Soc 70 2446 1948.]

**Pancuronium bromide**  $(2\beta,16\beta-dipiperidino-5\alpha-androstan-3\alpha,17\beta-diol diacetate dimetho$ bromide) [15500-66-0] M 732.7, m 212-215°, 215°. Odourless crystals with a bitter taste which arepurified through acid-washed Al<sub>2</sub>O<sub>3</sub> and eluted with isoPrOH-EtOAc (3:1) to remove impurities (e.g. themonomethobromide) and eluted with isoPrOH to give the pure bromide which can be recrystd from CH<sub>2</sub>Cl<sub>2</sub>-Me<sub>2</sub>CO or isoPrOH-Me<sub>2</sub>CO. It is soluble in H<sub>2</sub>O (50%) and CHCl<sub>3</sub> (3.3%) at 20°. It is a non-depolarisingmuscle relaxant. [Buckett et al. J Med Chem 16 1116 1973.]

**D-Panthenol** (Provitamin B, R-2,4-dihydroxy-3,3-dimethylbutyric acid 3-hydroxypropylamide) [81-13-0] M 205.3, b 118-120°/0.02mm,  $d_{20}^{20}$  1.2,  $n_D^{20}$  1.4935,  $[\alpha]_D^{20}$  (c 5, H<sub>2</sub>O). Purified by distn *in vacuo*. It is a slightly *hygroscopic* viscous oil. Soluble in H<sub>2</sub>O and organic solvent. It is hydrolysed by alkali and strong acid. [Rabin J Am Pharm Assoc (Sci Ed) 37 502 1948; Bonati and Pitré Farmaco Ed Scient 14 43 1959.]

*R*-(+)-Pantothenic acid sodium salt (*N*-[2,4-dihydroxy-3,3-dimethylbutyryl]  $\beta$ -alanine Na salt) [867-81-2] M 241.2,  $[\alpha]_D^{25} + 27.1^\circ$  (c 2, H<sub>2</sub>O), pK<sup>25</sup> 4.4 (for free acid). Crystd from EtOH, very hygroscopic (kept in sealed ampoules). The free acid is a viscous hygroscopic oil with  $[\alpha]_D^{25} + 37.5^\circ$  (c 5, H<sub>2</sub>O), easily destroyed by acids and bases.

**R**-(+)-Pantothenic acid Ca salt [(D(+)-137-08-6; 63409-48-3] M 476.5, m 195-196°, 200-201°,  $[\alpha]_D^{20} + 28.2^\circ$  (c 5, H<sub>2</sub>O). Crysts in needles from MeOH, EtOH or isoPrOH (with 0.5mol of isoPrOH). Moderately hygroscopic. The S-benzylisothiuronium salt has m 151-152° (149° when crystd from Me<sub>2</sub>CO). [Kagan et al. J Am Chem Soc 79 3545 1957; Wilson et al. J Am Chem Soc 76 5177 1954; Stiller and Wiley J Am Chem Soc 63 1239 1941.]

**Papain** [9001-73-4]  $M_r \sim 21,000$ , [EC 3.4.22.2], amorphous. A suspension of 50g of papain (freshly ground in a mortar) in 200mL of cold water was stirred at 4° for 4h, then filtered through a Whatman No 1 filter paper. The clear yellow filtrate was cooled in an ice-bath while a rapid stream of H<sub>2</sub>S was passed through it for 3h, and the suspension was centrifuged at 2000rpm for 20min. Sufficient cold MeOH was added slowly and with stirring to the supernatant to give a final MeOH concn of 70 vol%. The ppte, collected by centrifuged, and the enzyme again ppted with MeOH. The process was repeated four times. [Bennett and Niemann J Am Chem Soc 72 1798 1950.] Papain has also been purified by affinity chromatography on a column of Gly-Gly-Tyr-Arg-agarose [Stewart et al. J Am Chem Soc 109 3480 1986].

Papaverine hydrochloride (6,7-dimethoxy-1-veratrylisoquinoline hydrochloride) [61-25-6] M 375.9, m 215-220°, 222.5-223.5°(dec), 231°,  $pK^{25}$  6.41. Recrystd from H<sub>2</sub>O and sublimed at 140°/0.1mm. Solubility in H<sub>2</sub>O is 5%. [Saunders and Srivastava J Pharm Pharmacol 3 78 1951; Biggs Trans Faraday Soc 50 800 1954.] The free base has m 148-150° [Bobbitt J Org Chem 22 1729 1957].

**Pargyline hydrochloride** (Eutonyl, N-methyl-n-propargylbenzylamine hydrochloride) [306-07-0] M 195.7, m 154-155°, 155°,  $pK^{25}$  6.9. Recrystd from EtOH-Et<sub>2</sub>O and dried *in vacuo*. It is very soluble in H<sub>2</sub>O, in which it is unstable. The *free base* has b 101-103°/11mm. It is a glucuronyl transferase inducer and a monoamine oxidase inhibitor. [von Braun et al. Justus Liebigs Ann Chem 445 205 1928; Yeh and Mitchell Experientia 28 298 1972; Langstrom et al. Science 225 1480 1984.]

**Pectic acid** [9046-40-6]  $M_r$  (C<sub>6</sub>H<sub>8</sub>O<sub>6</sub>)<sub>n</sub> ~500,000, amorphous,  $[\alpha]_D + 250^\circ$  (c 1, 0.1M NaOH). Citrus pectic acid (500g) was refluxed for 18h with 1.5L of 70% EtOH and the suspension was filtered hot. The residue was washed with hot 70% EtOH and finally with ether. It was dried in a current of air, ground and dried for 18h at 80° under vacuum. [Morell and Link J Biol Chem 100 385 1933.] It can be further purified by dispersing in water and adding just enough dilute NaOH to dissolve the pectic acid, then passing the soln through columns of cation- and anion-exchange resins [Williams and Johnson Ind Eng Chem (Anal Ed) 16 23 1944], and precipitating with two volumes of 95% EtOH containing 0.01% HCl. The ppte is worked with 95% EtOH, then Et<sub>2</sub>O, dried and ground.

**Pectin** [9000-69-5]  $M_r$  25,000-100,000, amorphous. Dissolved in hot water to give a 1% soln, then cooled, and made about 0.05M in HCl by addition of conc HCl, and ppted by pouring slowly, with vigorous stirring into two volumes of 95% EtOH. After standing for several hours, the pectin is filtered onto nylon cloth, then redispersed in 95% EtOH and stood overnight. The ppte is filtered off, washed with EtOH/Et<sub>2</sub>O, then Et<sub>2</sub>O and air dried.

D-(-)-Penicillamine (*R*-3-mercapto-D-valine, 3,3-dimethyl-D-cysteine, from natural penicillin) [52-67-5] M 149.2, m 202-206°, 214-217°,  $[\alpha]_D^{21}$ -63° (c 1, N NaOH or pyridine),  $pK_1^{20}$  2.4 (CO<sub>2</sub>H),  $pK_2^{20}$  8.0 (SH),  $pK_3^{20}$  10.68 (NH<sub>2</sub>). The melting point depends on the rate of heating (m 202-206° is obtained by starting at 195° and heating at 2°/min). It is soluble in H<sub>2</sub>O and alcohols but insoluble in Et<sub>2</sub>O, CHCl<sub>3</sub>, CCl<sub>4</sub> and hydrocarbon solvents. Purified by dissolving in MeOH and adding Et<sub>2</sub>O slowly. Dried *in vacuo* and stored under N<sub>2</sub>. [Weight et al. Angew Chem, Int Ed Engl 14 330 1975; Cornforth in The Chemistry of Penicillin (Clarke, Johnson and Robinson Eds) Princeton Univ Press, 455 1949; Polymorphism: Vidler J Pharm Pharmacol 28 663 1976.] The D-S-benzyl derivative has m 197-198° (from H<sub>2</sub>O),  $[\alpha]_D^{17}$  -20° (c 1, NaOH), -70° (N HCl).

L-(-)-Penicillamine [1113-41-3] M 149.2, m 190-194°, 202-206°, 214-217°,  $[\alpha]_D^{21}$ +63° (c 1, N NaOH or pyridine). Same as preceding entry for its enantiomer.

**D-Penicillamine disulfide hydrate** (S,S'-di-[D-penicillamine] hydrate) [20902-45-8] M 296.4 + aq, m 203-204°(dec), 204-205°(dec),  $[\alpha]_D^{23}$  +27° (c 1.5, N HCl), -82° (c 0.8, N NaOH), pK<sub>Est(1)</sub>~ 2.4 (CO<sub>2</sub>), pK<sub>Est(2)</sub>~ 10.7 (NH<sub>2</sub>). Purified by recrytn from EtOH or aqueous EtOH. [Crooks in *The Chemistry of Penicillin* (Clarke, Johnson and Robinson Eds) Princeton Univ Press, 469 1949; Use as a thiol reagent for proteins: Garel Eur J Biochem 123 513 1982; Süs Justus Liebigs Ann Chem 561 31 1948.] Pepsin [9001-75-6]  $M_r$  31,500(human), 6000(hog) [EC 3.4.23.1]. Rechromatographed on a column of Amberlite CG-50 using a pH gradient prior to use. Crystd from EtOH. [Richmond et al. *Biochim Biophys Acta* 29 453 1958; Huang and Tang, J Biol Chem 244 1085 1969, 245 2189 1970.]

Pertussis toxin (from Bordetella pertussis) [70323-44-3] M<sub>r</sub> 117,000. Purified by stepwise elution from 3 columns comprising Blue Sepharose, Phenyl Sepharose and hydroxylapatite, and SDS-PAGE [Svoboda et al. Anal Biochem 159 402 1986; Biochemistry 21 5516 1982; Biochem J 83 295 1978.]

**2-Phenylethyl-\beta-D-thiogalactoside** [63407-54-5] **M 300.4, m 108°,**  $[\alpha]_D^{23}$ -32.2° (c 5, MeOH). Recryst from H<sub>2</sub>O and dried in air to give the 1.5.H<sub>2</sub>O and has **m** 80°. Anhydrous surfactant is obtained by drying at 78° over P<sub>2</sub>O<sub>5</sub>. [Heilfrich and Türk Chem Ber 89 2215 1856.]

**Phenyl-** $\beta$ **-D-galactopyranoside** [2818-58-8] **M 256.3, m 153-54°, 146-148°, 155-156°(dried at 105°),**  $[\alpha]_D^{2\circ}$  **-42° (c 1, H<sub>2</sub>O).** Recrystd from H<sub>2</sub>O as 0.5H<sub>2</sub>O. [Conchie and Hay *Biochem J* **73** 327 1959; IR: Whistler and House Analyt Chem 25 1463 1953.] It is an acceptor substrate for fucosyltransferase [Chester et al. Eur J Biochem 69 583 1976].

**Phenyl-** $\beta$ -**D**-glucopyranoside [1464-44-4] M 256.3, m 174-175° 174-176°, 176°,  $[\alpha]_D^{20}$ -72.2° (c 1 for dihydrate, H<sub>2</sub>O). Recrystd from H<sub>2</sub>O as 2H<sub>2</sub>O and can be dried *in vacuo* at 100°/P<sub>2</sub>O<sub>5</sub>. Dry preparation has  $[\alpha]_D^{25}$ -70.7° (c 2, H<sub>2</sub>O). [Robertson and Waters J Chem Soc 2729 1930; IR: Bunton et al. J Chem Soc 4419 1955; Takahashi Yakugaku Zasshi (J Pharm Soc Japan) 74 7436 1954; Whixtler and House Anal Chem 25 1463; UV: Lewis J Am Chem Soc 57 898 1935.] It is a substrate for  $\beta$ -D-glucosidase [deBryne Eur J Biochem 102 257 1979].

**Phenylmercuric acetate (PhHgOAc)** [62-38-4] M 336.7, m 148-151°, 149°, 151.8-152.8°. Small colourless lustrous prisms from EtOH. Its solubility in H<sub>2</sub>O is 0.17% but it is more soluble in EtOH, Me<sub>2</sub>CO and \*C<sub>6</sub>H<sub>6</sub>. [Maynard J Am Chem Soc 46 1510 1925; Coleman et al. J Am Chem Soc 59 2703 1937; J Am Pharm Assoc 25 752 1936.] See PhHgOH and PhHgNO<sub>3</sub>.PhHgOH on p. 449 in Chapter 5.

**Phenylmethanesulfonyl fluoride (PMSF)** [329-98-6] **M 174.2, m 90-91°, 92-93°**. Purified by recrystn from  ${}^{*}C_{6}H_{6}$ , pet ether or CHCl<sub>3</sub>-pet ether. [Davies and Dick J Chem Soc 483 1932; cf Tullock and Coffman J Org Chem 23 2016 1960.] It is a general protease inhibitor (specific for trypsin and chymotrypsin) and is a good substitute for diisopropylphosphoro floridate [Fahrney and Gould J Am Chem Soc 85 997 1963].

[9001-78-9] M<sub>r</sub> ~40,000 (bovine liver), Phosphatase alkaline (alkaline phosphatase) ~140,000 (bovine intestinal mucosa), 80,000 (E.coli) [EC 3.1.3.1]. The E.coli supernatant in sucrose (20%, 33mM) in Tris-HCl pH 8.0 was purified through a DEAE-cellulose column and recrystallised. To the column eluates in 0.125M NaCl is added MgCl<sub>2</sub> (to 0.01M) and brought to 50% saturation in  $(NH_4)_2SO_4$  by adding the solid (0.20g/mL). The mixture is centrifuged to remove bubbles and is adjusted to pH 8.0 (with 2N NaOH). Saturated (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> at pH 8.0 is added dropwise until the soln becomes faintly turbid (-61% saturation). It is set aside at room temp for 1h (turbidity will increase). The mixture is placed in an ice bath for several minutes when turbidity disappears and a clear soln is obtained. It is then placed in a large ice bath at  $0^{\circ}$  (~5L) and allowed to warm slowly to room temperature in a dark room whereby crystals are formed appearing as a silky sheen. The crystals are collected by centrifugation at 25° if necessary. The crystalline solns are stable at room temperature for many months. They can be stored at 0°, but are not stable when frozen. Cysteine at 10<sup>-3</sup>M and thioglycolic acid at 10<sup>-4</sup>M are inhibitory. Inhibition is reversed on addition of Zn<sup>2+</sup> ions. Many organic phosphates are good substrates for this phosphatase. [Molamy and Horecker Methods Enzymol 9 639 1966; Torriani et al. Methods Enzymol 12b 212 1968; Engstrom Biochim Biophys Acta 92 71 1964.]

Alkaline phosphatase from rat *osteosarcoma* has been purified by acetone pptn, followed by chromatography on DEAE-cellulose, Sephacryl S-200, and hydroxylapatite. [Nair et al. Arch Biochem Biophys **254** 18 1987.]

3-sn-Phosphatidylethanolamine (L- $\alpha$ -cephalin, from Soya bean) [39382-08-6] M<sub>r</sub> ~600-800, amorphous, pK<sub>Est(1)</sub>~ 5.8 (PO<sub>4</sub><sup>-</sup>), pK<sub>Est(2)</sub>~ 10.5 (NH<sub>2</sub>). Purified by dissolving in EtOH, adding Pb(OAc)<sub>2</sub>.3H<sub>3</sub>O (30g in 100mL H<sub>2</sub>O) until excess Pb<sup>2+</sup> is present. Filter off the solid. Pass CO<sub>2</sub> gas through the soln until pptn of PbCO<sub>3</sub> ceases. Filter the solid off and evaporate (while bubbling CO<sub>2</sub>) under vacuum. An equal volume of  $H_2O$  is added to the residual oil extracted with hexane. The hexane extract is washed with  $H_2O$  until the aqueous phase is free from Pb [test with dithizone (2 mg in 100 mL CCl<sub>4</sub>; Feigel Spot Tests Vol I, Elsevier p. 10 1954]. The hexane is dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and evaporated to give a yellow waxy solid which should be dried to constant weight *in vacuo*. It is practically insoluble in  $H_2O$  and  $Me_2CO$ , but freely soluble in CHCl<sub>3</sub> (5%) and Et<sub>2</sub>O, and slightly soluble in EtOH. [Schofield and Dutton *Biochem Prep* 5 5 1957.]

**O-Phosphocolamine** 2-aminoethyl dihydrogen phosphate) [1071-23-4] M 141.1, m 237-240°, 242.3°, 234.5-244.5°, 244-245°(capillary),  $pK_1^{20} < 1.5$  (PO<sub>4</sub>H<sub>2</sub>),  $pK_2^{20} 5.77$  (PO<sub>4</sub>H<sup>-</sup>),  $pK_3^{20}$  10.26 (NH<sup>+</sup>). Purified by recrystn from aqueous EtOH as a hydrate (m 140-141°). Its solubility in H<sub>2</sub>O is 17% and 0.003% in MeOH or EtOH at 22°. [Fölisch and Österberg J Biol Chem 234 2298 1959; Baer aand Staucer Can J Chem 34 434 1956; Christensen J Biol Chem 135 399 1940.] It is a potent inhibitor of ornithine decarboxylase [Gilad and Gilad Biochem Biophys Res Commun 122 277 1984].

**Phosphoenolpyruvic acid monopotassium salt (KPEP)** [4265-07-0] M 206.1,  $pK_1^{25}$  3.4 (CO<sub>2</sub>),  $pK_2^{25}$  6.35 (PO<sub>4</sub>H<sup>-</sup>) (for free acid). It is purified via the monocyclohexylamine salt (see next entry). The salt (534mg) in H<sub>2</sub>O (10mL) is added to Dowex 50Wx4 H<sup>+</sup> form (200-400 mesh, 2mL, H<sub>2</sub>O washed) and stirred gently for 30min and filtered. The resin is washed with H<sub>2</sub>O (6mL) and the combined solns are adjusted to pH 7.4 with 3N KOH (~1.4mL) and the volume adjusted to 18.4mL with H<sub>2</sub>O to give a soln of 0.1M KPEP which can be lyophilised to a pure powder and is very good for enzyme work. It has been recrystd from MeOH-Et<sub>2</sub>O. [Clark and Kirby *Biochem Prep* 11 103 1966; Wold and Ballou J Biol Chem 227 301 1957; Cherbuliez and Rabinowitz Helv Chim Acta 39 1461 1956.]

The triNa salt [5541-93-5] M 360.0, is purified as follows: the salt (1g) is dissolved in MeOH (40mL) and dry  $Et_2O$  is added in excess. The white crystals are collected and dried over  $P_2O_5$  at 20°. [Chem Ber 92 952 1959.]

**Phosphoenolpyruvic acid tris(cyclohexylamine) salt** [35556-70-8] M 465.6, m 155-180°(dec). Recrystd from aqueous Me<sub>2</sub>CO and dried in a vacuum. At 4° it is stable for >2 years and has IR at 1721cm<sup>-1</sup> (C=O). [Wold and Ballou J Biol Chem 227 301 1957; Clark and Kirby Biochem Prep 11 103 1966 for the monocyclohexylamine salt.]

**D-3-Phosphoglyceric acid disodium salt (D-glycerate 3-phosphate di-Na salt)** [80731-10-8]**M 230.0,**  $[\alpha]_D^{25} + 7.7^{\circ}$  (c 5, H<sub>2</sub>O), -735° (in aq NH<sup>4</sup><sub>4</sub> molybdate), pK<sub>Est(1)</sub>~1.0 (PO<sub>4</sub>H<sub>2</sub>), pK<sub>Est(2)</sub>~ 6.66 (PO<sub>4</sub>H<sup>-</sup>) (for free acid). Best purified by conversion to the Ba salt by pptn with BaCl<sub>2</sub> which is recryst three times before conversion to the sodium salt. The Ba salt (9.5g) is shaken with 200mL of a 1:1 slurry of Dowex 50 (Na<sup>+</sup> form) for 2h. The mixture is filtered and the resin washed with H<sub>2</sub>O (2 x 25mL). The combined filtrates (150mL) are adjusted to pH 7.0 and concentrated *in vacuo* to 30-40mL and filtered if not clear. Absolute EtOH is added to make 100mL and then *n*-hexane is added whereby a white solid and/or a second phase separates. When set aside at room temperature complete pptn of the Na salt as a solid occurs. The salt is removed by centrifugation, washed with Me<sub>2</sub>CO, dried in air then in an oven at 55° to give a stable powder (4.5g). It did not lose weight when dried further over P<sub>2</sub>O<sub>5</sub> at 78°/8h. The high rotation in the presence of (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub> is not very sensitive to the concentration of molybdate or pH as it did not alter appreciably in 1/3 volume between 2.5 to 25% (w/v) of molybdate or at pH values ranging between 4 and 7. [Cowgill *Biochim Biophys Acta* 16 613 1955; Embdan, Deuticke and Kraft Hoppe Seyler's Z Physiol Chem **230** 20 1934.]

**Phospholipids.** For the removal of ionic contaminants from raw zwitterionic phospholipids, most lipids were purified twice by mixed-bed ionic exchange (Amberlite AB-2) of methanolic solutions. (About 1g of lipid in 10mL of MeOH). With both runs the first 1mL of the eluate was discarded. The main fraction of the solution was evaporated at 40°C under dry N<sub>2</sub> and recryst three times from *n*-pentane. The resulting white powder was dried for about 4h at 50° under reduced pressure and stored at 3°. Some samples were purified by mixed-bed ion exchange of aqueous suspensions of the crystal/liquid crystal phase. [Kaatze et al. J Phys Chem **89** 2565 1985.]

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**Phosphoproteins (various).** Purified by adsorbing onto an iminodiacetic acid substituted agarose column to which was bound ferric ions. This chelate complex acted as a selective immobilised metal affinity adsorbent for phosphoproteins. [Muszyfiska et al. *Biochemistry* 25 6850 1986.]

5'-Phosphoribosyl pyrophosphate synthetase (from human erythrocytes, or pigeon or chicken liver) [9015-83-2]  $M_r$  60,000, [EC 2.7.6.1]. Purified 5100-fold by elution from DEAE-cellulose, fractionation with ammonium sulfate, filtration on Sepharose 4B and ultrafiltration. [Fox and Kelley J Biol Chem 246 5739 1971; Flaks Methods Enzymol 6 158 1963; Kornberg et al. J Biol Chem 15 389 1955.]

**O-Phospho-L-serine** [407-41-0] M 185.1, m 175-176°,  $[\alpha]_D^{20} + 4.3^\circ$  (c 3.2, H<sub>2</sub>O), +16.2° (c 3.2, 2N HCl),  $pK_1^{25} < 1$  (PO<sub>4</sub>H<sub>2</sub>),  $pK_2^{25} 2.08$  (CO<sub>2</sub>H),  $pK_3^{25} 5.65$  (PO<sub>4</sub>H<sup>-</sup>),  $pK_4^{25} 9.74$  (NH<sub>3</sub><sup>+</sup>). Recrystd by dissolving 10g in H<sub>2</sub>O (150mL) at 25°, stirring for up to 20min. Undissolved material is filtered off (Büchner) and 95% EtOH (85mL) is added dropwise during 4min, and set aside at 25° for 3h then at 3° overnight. The crystals are washed with 95% EtOH (100mL) then dry Et<sub>2</sub>O (50mL) and dried in a vacuum (yield 6.5g). A further quantity (1.5mg) can be obtained by keeping the mother liquors and washings at -10° for 1 week. The *DL-isomer* has m 167-170°(dec) after recrystn from H<sub>2</sub>O + EtOH or MeOH. [Neuhaus and Korkes *Biochem Prep* 6 75 1958; Neuhaus and Byrne J Biol Chem 234 113 1959; IR: Fölsch and Mellander Acta Chem Scand 11 1232 1957.]

**O-Phospho-L-threonine (L-threonine-O-phosphate)** [1114-81-4] M 199.1, m 194°(dec),  $[\alpha]_D^{24}$ -7.37° (c 2.8, H<sub>2</sub>O) (pK as above). Dissolve in the minimum volume of H<sub>2</sub>O, add charcoal, stir for a few min, filter and apply onto a Dowex 50W (H<sup>+</sup> form) then elute with 2N HCl. Evaporate the eluates under reduced pressure whereby the desired fraction produced crystals of the phosphate which can be recrystal from H<sub>2</sub>O-MeOH mixtures and the crystals are then dried *in vacuo* over P<sub>2</sub>O<sub>5</sub> at ~80°. [de Verdier Acta Chem Scand 7 196 1953.]

**O-Phospho-L-tyrosine** (L-tyrosine-O-phosphate) [21820-51-9] M 261.2, m 225°, 227°, 253°,  $[\alpha]_D^{20}$ -5.5° (c 1, H<sub>2</sub>O), -9.2° (c 1, 2N HCl), pK<sub>Est(1)</sub>~ 1.6 (PO<sub>4</sub>H<sub>2</sub>), pK<sub>Est(2)</sub>~ 2.02 (CO<sub>2</sub>H), pK<sub>Est(3)</sub>~ 5.65 (PO<sub>4</sub>H<sup>-</sup>), pK<sub>Est(4)</sub> 9.2 (NH<sub>3</sub><sup>+</sup>). Purified by recrystn from H<sub>2</sub>O or H<sub>2</sub>O + EtOH. [Levene and Schormüller J Biol Chem 100 583 1933; Posternak and Graff Helv Chim Acta 28 1258 1945.]

Phytol (d-3,7R,11R,15-tetramethylhexadec-2-en-1-ol) [150-86-7] M 296.5, b 145°/0.03mm, 150-151°/0.06mm, 202-204°/10mm,  $d_4^{25}$  0.8497,  $n_D^{25}$  1.437,  $[\alpha]_D^{22}$ +0.06° (neat). Purified by distn under high vacuum. It is almost insoluble in H<sub>2</sub>O but soluble in most organic solvents. It has UV  $\lambda_{max}$  at 212nm (log  $\varepsilon$  3.04) in EtOH and IR v at 3300 and 1670cm<sup>-1</sup>. [Demole and Lederer Bull Soc Chim Fr 1128 1958; Burrell J Chem Soc (C) 2144 1966; Bader Helv Chim Acta 34 1632 1951.]

**D-Pipecolinic acid** (*R*-piperidine-2-carboxylic acid) [1723-00-8] M 129.2, m 264°(dec), 267°(dec), ~280°(dec),  $[\alpha]_D^{19} + 26.2°$  (c 2, H<sub>2</sub>O),  $[\alpha]_D^{25} + 35.7°$  (H<sub>2</sub>O),  $pK_1^{20}$  2.29 (CO<sub>2</sub>H),  $pK_2^{20}$  10.77 (NH<sup>+</sup>). Recrystallises as platelets from EtOH and is soluble in H<sub>2</sub>O. The hydrochloride has m 256-257°(dec) from H<sub>2</sub>O and  $[\alpha]_D^{25} + 10.8°$  (c 2, H<sub>2</sub>O). [Lukés et al. Collect Czech Chem Commun 22 286 1957; Bayerman Recl Trav Chim Pays-Bas 78 134 1959; Asher et al. Tetrahedron Lett 22 141 1981.]

**L-Pipecolinic acid** (S-piperidine-2-carboxylic acid) [3105-95-1] M 129.2, m 268°(dec), 271°(dec), ~280°(dec),  $[\alpha]_D^{20}$ -26° (c 4, H<sub>2</sub>O),  $[\alpha]_D^{25}$ -34.9° (H<sub>2</sub>O). Recryst from aqueous EtOH and sublimes as needles in a vacuum. It is sparingly soluble in absolute EtOH, Me<sub>2</sub>CO and CHCl<sub>3</sub> but insoluble in Et<sub>2</sub>O. The hydrochloride has m 258-259°(dec, from MeOH) and  $[\alpha]_D^{25}$ -10.8° (c 10, H<sub>2</sub>O). [Fujii and Myoshi Bull Chem Soc Jpn 48 1241 1975.]

Piperidine-4-carboxylic acid (isonipecotic acid) [498-94-2] M 129.2, m 336°(dec, darkens at ~300°),  $pK_{Est(1)}$ ~ 4.3 (CO<sub>2</sub>H),  $pK_{Est(2)}$ ~ 10.6 (NH<sup>+</sup>). Recrystallises from H<sub>2</sub>O or EtOH as needles. The hydrochloride recrystallises from H<sub>2</sub>O or aqueous HCl and has m 293°dec (298°dec, 300°dec). [Wibaut Recl Trav Chim Pays-Bas 63 141 1944; IR: Zacharius et al. J Am Chem Soc 76 2908 1954.]

**Pituitary Growth Factor** (from human pituitary gland) [336096-71-0]. Purified by heparin and copper affinity chromatography, followed by chromatography on carboxymethyl cellulose (Whatman 52). [Rowe et al. *Biochemistry* 25 6421 1986.]

Plasmids. These are circular lengths of DNA which invade bacteria or other cells e.g. insect cells, yeast cells, and have sequences which are necessary for their replication using enzymes and other ingredients, e.g. nucleotides, present in the cells. They contain engineered, or already have, genes which produce enzymes that provide the cells with specific antibiotic resistance and are thus useful for selecting bacteria containing specific plasmids. Plasmids have been extremely useful in molecular biology since they can be very easily identified (from their size or the sizes of the DNA fragments derived from their restriction enzyme digests) and can be readily engineered in vitro (outside the cells). Genes coding for specific enzymes or other functional proteins can be inserted into these plasmids which have DNA sequences that allow the expression of large quantities of bacteria or non-bacterial (e.g. human) proteins. They have also been engineered in such a way as to produce 'fusion proteins' (in which the desired protein is fused with a specific "reporter, marker or carrier protein" which will facilitate the isolation of the desired protein (e.g. by binding strongly to a nickel support) and then the desired protein can be cleaved from the eluted fusion protein and obtained in very pure form. A large number of plasmids with a variety of sequences for specific purposes are commercially available in very pure form. They can be used to infect cells and can be isolated and purified from cell extracts in large amounts using a number of available procedures. These procedures generally involve lysis of the cells (e.g. with alkaline sodium dodecylsulfate, SDS), separation from nuclear DNA, precipitation of plasmid DNA from the cell debris, adsorbing it on columns which specifically bind DNA, and then eluting the DNA from the column (e.g. with specific Tris buffers as recommended by the suppliers) and precipitating it (e.g. with Tris buffer in 70% EtOH at -70°C) The purity is checked in agarose gel (containing ethidium bromide to visualise the DNA) by electrophoresis. A large number of plasmids are now commercially available (see Clontech GmbH, http://www.clontech.com; Invitrogen http://www.invitrogen.com, among other suppliers) used as vectors for bacterial, mammalian, yeast and baculovirus expression.

**Podophylotoxin** [518-28-5] **M** 414,4, **m** 181-181°, 183-184°, 188-189°,  $[\alpha]_D^{20}$  - 132° (c 1, CHCl<sub>3</sub>). Recrystallises form \*C<sub>6</sub>H<sub>6</sub> (with 0.5C<sub>6</sub>H<sub>6</sub>), EtOH-\*C<sub>6</sub>H<sub>6</sub>, aqueous EtOH (with 1-1.5H<sub>2</sub>O, **m** 114-115°) and CH<sub>2</sub>Cl<sub>2</sub>-pentane. When dried at 100°/10 mm it has **m** 183-184°. [UV: Stoll et al. *Helv Chim Acta* 37 1747 1954; IR: Schecler et al. J Org Chem 21 288 1956.] Inhibitor of microtubule assembly [Prasad et al. Biochemistry 25 739 1986].

**Polyethylene glycol** [25322-68-3] M<sub>r</sub> various, from ~200 to ~35,000. May be contaminated with aldehydes and peroxides. Methods are available for removing interfering species. [Ray and Purathingal Anal Biochem 146 307 1985.]

**Polypeptides.** These are a string of  $\alpha$ -amino acids usually with the natural S(L) [L-cysteine is an exception and has the R absolute configuration] or sometimes "unnatural" R(D) configuration at the  $\alpha$ -carbon atom. They generally have less than ~100 amino acid residues. They can be naturally occurring or, because of their small size, can be synthesised chemically from the desired amino acids. Their properties can be very similar to those of small proteins. Many are commercially available, can be custom made commercially or locally with a peptide synthesiser. They are purified by HPLC and can be used without further purification. Their purity can be checked as described under proteins.

Porphobilinogen (5-amino-4-carboxymethyl-1*H*-pyrrole-3-propionic acid) [487-90-1] M 226.2, m 172-175°(dec), 175-180°(dec, darkening at 120-130°),  $pK_1$  3.70 (4-CH<sub>2</sub>CO<sub>2</sub>H),  $pK_2$  4.95 (3-CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H),  $pK_3$  10.1 (NH<sup>+</sup>). Recrystallises as the monohydrate (pink crystals) from dil NH<sub>4</sub> OAc solns of pH 4, and is dried *in vacuo*. The hydrochloride monohydrate has m 165-170°(dec) (from dilute HCl). [Jackson and MacDonald Can J Chem 35 715 1957, Westall Nature 170 614 1952; Bogarad J Am Chem Soc 75 3610 1953.]

**Porphyrin a (from ox heart)** [5162-02-1] M 799.0, m dec on heating. Purified on a cellulose powder column followed by extraction with 17% HCl and fractionation with HCl. [Morell et al. Biochem J 78]

793 1961.] Recrystd from CHCl<sub>3</sub>/Pet ether or Et<sub>2</sub>O/\*C<sub>6</sub>H<sub>6</sub> [detailed UV-VIS and NMR date: Caughey et al. J Biol Chem **250** 7602 1975; Lemberg Adv Enzymol **23** 265 1961].

**Prazosin hydrochloride** (2[4-{(2-furoyl)piperazin-1-yl}4-amino-6,7-dimethoxyquinazoline hydrochloride) [19237-84-4] M 419.9, m 278-280°, 280-282°, pK 6.5. It is recrystd by dissolving in hot MeOH adding a small volume of MeOH-HCl (dry MeOH saturated with dry HCl gas) followed by dry Et<sub>2</sub>O until crystn is complete. Dry *in vacuo* over solid KOH till odour of HCl is absent. It has been recrystd from hot H<sub>2</sub>O, the crystals were washed with H<sub>2</sub>O, and the H<sub>2</sub>O was removed azeotropically with CH<sub>2</sub>Cl<sub>2</sub>, and dried in a vacuum. [NMR and IR: Honkanen et al. *J Heterocycl Chem* 17 797 1980; cf Armarego and Reece Aust J Chem 34 1561 1981.] It is an antihypertensive drug and is an  $\alpha_1$ -adrenergic antagonist [Brosman et al. Proc Natl Acad Sci USA 82 5915 1985].

Prednisolone acetate (21-acetoxypregna-1,4-diene-11 $\beta$ -17 $\alpha$ -diol-3,20-dione) [52-21-1] M 402.5, m 237-239°, 240-242°, 240-243°, 244°, [ $\alpha$ ]<sub>D</sub><sup>20</sup>+116° (c 1, dioxane). Recrystd from EtOH, Me<sub>2</sub>CO, Me<sub>2</sub>CO-hexane, and has UV  $\lambda_{max}$  at 243nm in EtOH. [Joly et al. Bull Soc Chim Fr 366 1958; Herzog et al. J Am Chem Soc 77 4781 1955.]

Primaquine diphosphate (RS- 8-[4-amino-1-methylbutylamino]-6-methoxyquinoline diphosphate) [63-45-6] M 455.4, m 197-198°, 204-206°,  $pK_{Est(1)}$ ~ 3.38 (ring N<sup>+</sup>),  $pK_{Est(2)}$ ~ 10.8 NH<sub>3</sub><sup>+</sup>). It forms yellow crystals from 90% aq EtOH and is moderately soluble in H<sub>2</sub>O. The oxalate salt has m 182.5-185° (from 80% aq EtOH) and the free base is a viscous liquid b 165-170°/0.002mm, 175-177°/2mm. [Elderfield et al. J Am Chem Soc 68 1526 1964; 77 4817 1955.]

**Procaine hydrochloride** (Novocain, 2-diethylaminoethyl-4-aminobenzoate) [51-05-8] M 272.8, m 153-156°, 154-156°, 156°,  $pK_{Est(1)} \sim 2.52$  (NH<sub>2</sub><sup>+</sup>)  $pK_2^{20}$  9.0 (Et<sub>2</sub>N<sup>+</sup>). Recrystd from aqueous EtOH. It has solubility at 25° in H<sub>2</sub>O (86.3%), EtOH (2.6%) and Me<sub>2</sub>CO (1%), it is slightly soluble in CHCl<sub>3</sub> but is almost insoluble in Et<sub>2</sub>O. The anhydrous *free base* is recrystd from ligroin or Et<sub>2</sub>O and has m 61°. [Einhorn *Justus Liebigs Ann Chem* 371 125 1909; IR: Szymanski and Panzica J Amer Pharm Assoc 47 443 1958.]

L-Propargylglycine (S-2-aminopent-4-ynoic acid) [23235-01-0] M 113.1, m 230°(dec starting at 210°),  $[\alpha]_D^{20}$ -35° (c 1, H<sub>2</sub>O), -4° (c 5, 5N HCl), pK<sub>Est(1)</sub>~ 2.3 (CO<sub>2</sub>H), pK<sub>Est(2)</sub>~ 9.8 (NH<sub>2</sub>). The acid crystallises readily when ~4g in 50mL H<sub>2</sub>O is treated with abs EtOH at 4°/ 3hrs, and is collected washed with cold abs EtOH and Et<sub>2</sub>O and dried in vac. Also recrystallises from aqueous Me<sub>2</sub>CO, R<sub>F</sub> on SiO<sub>2</sub> TLC plates with *n*-BuOH-H<sub>2</sub>O-AcOH (4:1:1) is 0.26. The *racemate* has m 238-240°. [Leukart et al. *Helv Chim Acta* 59 2181 1976; Eberle and Zeller *Helv Chim Acta* 68 1880 1985; Jansen et al. *Recl Trav Chim Pays-Bas* 88 819 1969.] It is a suicide inhibitor of  $\gamma$ -cystathionase and other enzymes [Washtier and Abeles *Biochemistry* 16 2485 1977; Shinozuka et al. *Eur J Biochem* 124 377 1982].

**Propidium iodide** (3,8-diamino-5-(3-diethylaminopropyl)-6-phenylphenantridinium iodide methiodide) [25535-16-4] M 668.4, m 210-230°(dec),  $pK_{Est(1)}$ ~ 4 (aniline NH<sub>2</sub>),  $pK_{Est(2)}$ ~ 8.5 (EtN<sub>2</sub>). Recrystd as red crystals from H<sub>2</sub>O containing a little KI. It fluoresces strongly with nucleic acids. [Eatkins J Chem Soc 3059 1952.] TOXIC.

*R***-Propranalol hydrochloride** (*R*-1-isopropylamino-3-(1-naphthyloxy)-2-propanol HCl) [13071-11-9] M 295.8, m 192°, 193-195°,  $[\alpha]_D^{20} \cdot 25°$  (c 1, EtOH), pK<sup>20</sup> 9.5 (for free base). Recryst from *n*-PrOH or Me<sub>2</sub>CO. It is soluble in H<sub>2</sub>O and EtOH but is insoluble in Et<sub>2</sub>O, \*C<sub>6</sub>H<sub>6</sub> or EtOAc. The *racemate* has m 163-164°, and the *free base* recryst from cyclohexane has m 96°. [Howe and Shanks Nature 210 1336 1966.] The S-isomer (below) is the physiologically active isomer.

S-Propranalol hydrochloride (S-1-isopropylamino-3-(1-naphthyloxy)-2-propanol HCl) [4199-10-4] M 295.8, m 192°, 193-195°,  $[\alpha]_D^{20} + 25°$  (c 1, EtOH) pK<sup>20</sup> 9.5. See preceding entry for physical properties. The is the active isomer which blocks isoprenaline tachycardia and is a  $\beta$ -adrenergic blocker. [Leclerc et al. *Trends Pharmacol Sci* 2 18 1981; Howe and Shanks *Nature* 210 1336 1966.]

**Protamine kinase (from rainbow trout testes)** [37278-10-7] [EC 2.7.1.70]. Partial purification by hydoxylapatite chromatography followed by biospecific chromatography on nucleotide coupled Sepharose 4B (the nucleotide was 8-(6-aminohexyl)amine coupled cyclic-AMP). [Jergil et al. *Biochem J* 139 441 1974.]

**Protamine sulfate (from herring sperm)** [9007-31-2]  $[\alpha]_D^{22}$ -85.5° (satd H<sub>2</sub>O), pK 7.4-8.0. A strongly basic protein (white powder, see pK) used to ppte nucleic acids from crude protein extracts. It dissolved to the extent of 1.25% in H<sub>2</sub>O. It is freely soluble in hot H<sub>2</sub>O but separates as an oil on cooling. It has been purified by chromatography on an IRA-400 ion-exchange resin in the SO<sub>4</sub><sup>2-</sup> form and washed with dilute H<sub>2</sub>SO<sub>4</sub>. Eluates are freeze-dried under high vacuum below 20°. This method is used to convert proteamine and protamine hydrochloride to the sulfate. [UV: Rasmussen Hoppe Seyler's Z Physiol Chem 224 97 1934; Ando and Sawada J Biochem (Tokyo) 49 252 1961; Felix and Hashimoto Hoppe Seyler's Z Physiol Chem 330 205 1963]

Protease nexin (From cultured human fibroblasts) [148263-58-5]. Purified by affinity binding of protease nexin to dextran sulfate-Sepharose. [Farrell et al. *Biochem J* 237 707 1986.]

**Proteins.** These are usually naturally occurring (or deliberately synthesised in microorganisms, e.g. bacteria, insect cells, or animal tissues), and are composed of a large number of  $\alpha$ -S (L)amino acids residues (except for L-cysteine which has the *R* absolute configuration), selected from the 20 or so natural amino acids, in specific sequences and in which the  $\alpha$ -amino group forms an amide (peptide) bond with the  $\alpha$ -carboxyl group of the neighboring amino acid. The number of residues are usually upwards of 100. Proteins with less than 100 amino acids are better referred to as **polypeptides**. Aqueous soluble proteins generally fold into ball-like structures mainly with hydrophilic residues on the outside of the "balls" and hydrophobic residues on the inside. Proteins can exist singly or can for dimers, trimers, tetramers etc, consisting of similar or different protein subunits. They are produced by cells for a large variety of functions, e.g. enzymology, reaction mediation as in regulation of DNA synthesis or chaperonins for aiding protein folding, formation of pores in membranes for transport of ions or organic molecules, or for intra or inter cellular signalling etc. The purity of proteins can be checked in denaturing (SDS, sodium dodecylsulfate) or non-denaturing polyacrylamide gels using electrophoresis (PAGE), and staining appropriately (e.g. with Coommassie Blue, followed by silver staining for higher sensitivity). If the protein is partly impure then it should be purified further according to the specific literature procedures for the individual protein (see specific proteins in the *Methods Enzymol*, Wiley series).

Proteoglycans (from cultured human muscle cells). Separated by ion-exchange HPLC using a Biogel TSK-DEAE 5-PW analytical column. [Harper et al. Anal Biochem 159 150 1986.]

**Prothrombin** (Factor II, from equine blood plasma) [9001-26-7]  $M_r$  72,000. Purified by two absorptions on a barium citrate adsorbent, followed by decomposition of the adsorbents with a weak carboxylic cation-exchanger (Amberlite IRF-97), isoelectric pptn (pH 4.7-4.9) and further purification by chromatography on Sephadex G-200 or IRC-50. Finally recrystd from a 1% soln adjusted to pH 6.0-7.0 and partial lyophilisation to *ca* 1/5 to 1/10th vol and set aside at 2-5° to crystallise. Occasionally seeding is required. [Miller *Biochem Prep* 13 49 1971.]

**Protoporphyrin IX** (3,18-divinyl-2,7,13,17-tetramethylporphine-8,12-dipropionic acid, ooporphyrin) [553-12-8] M 562.7, pK<sub>Est</sub> ~ 4.8. Purified by dissolving (4g) in 98-100% HCOOH (85mL), diluting with dry Et<sub>2</sub>O (700mL) and keeping at 0° overnight. The ppte is collected and washed with Et<sub>2</sub>O then H<sub>2</sub>O and dried in a vacuum at 50° over P<sub>2</sub>O<sub>5</sub>. It has been recrystd from aqueous pyridine and from Et<sub>2</sub>O as monoclinic, brownish-yellow prisms. UV  $\lambda_{max}$  values in 25% HCl are 557.2, 582.2 and 602.4nm. It is freely soluble in ethanolic HCl, AcOH, CHCl<sub>3</sub>, and Et<sub>2</sub>O containing AcOH. It forms sparingly soluble diNa and diK salts. [Ramsey *Biochem Prep* 3 39 1953; UV: Holden Aust J. Exptl Biol and Med Sci 15 412 1937; Garnick J Biol Chem 175 333 1948; IR: Falk and Willis Aust J Sci Res [A] 4 579 1951.]

The **Dimethyl ester** [5522-66-7] **M 590.7, m 228-230°**, is prepared by dissolving (0.4g) in CHCl<sub>3</sub> (33mL) by boiling for a few min, then diluting with boiling MeOH (100mL) and refrigerating for 2 days. The crystals are collected, washed with CHCl<sub>3</sub>-MeOH (1:9) and dried at 50° in a vacuum (yield 0.3g). UV has  $\lambda_{max}$  631, 576, 541, 506 and 407nm in CHCl<sub>3</sub> and 601, 556 and 406nm in 25% HCl. [Ramsey *Biochem Prep* **3** 39 1953.]

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**Prymnesin** (toxic protein from phytoflagellate *Pyrymnesium parvum*) [11025-94-8]. Purified by column chromatography, differential soln and pptn in solvent mixtures and differential partition between diphasic mixtures. The product has at least 6 components as observed by TLC. [Ulitzur and Shilo *Biochim Biophys Acta* 301 350 1970.]

Pterin-6-carboxylic acid (2-amino-4-oxo-3,4-dihydropteridine-6-carboxylic acid) [948-60-7] M 207.2, m >360°,  $pK_1^{20}$  1.43,  $pK_2^{20}$  2.88,  $pK_3^{20}$  7.72. Yellow crystals by repeated dissolution in aqueous NaOH and adding aqueous HCl. It has UV with  $\lambda_{max}$  at 235, 260 and 265nm ( $\varepsilon$  11000, 10500 and 9000) in 0.1N HCl and 263 and 365nm ( $\varepsilon$  20500 and 9000) in 0.1N NaOH. [UV: Pfleiderer et al. Justus Liebigs Ann Chem 741 64 1970; Stockstad et al. J Am Chem Soc 70 5 1948; Fluorescence: Kavanagh and Goodwin Arch Biochem 20 315 1949.]

**Purine-9-** $\beta$ -ribifuranoside (Nebularin) [550-33-4] M 252.2, m 178-180°, 181-182°,  $[\alpha]_D^{25}$ -48.6° (c 1, H<sub>2</sub>O), -22° (c 0.8, 0.1N HCl) and -61° (c 0.8, 0.1N NaOH), pK 2.05. Recrystd from butanone + MeOH or EtOH and forms a MeOH photo-adduct. It is a strong inhibitor of adenosine deaminase [EC 3.5.4.4]. [Nair and Weichert *Bioorg Chem* 9 423 1980; Löfgren et al. Acta Chem Scand 7 225 1953; UV: Brown and Weliky J Biol Chem 204 1019 1953.]

**Puromycin dihydrochloride** (*O*-methyl-1-tyrosine[ $N^6$ , $N^6$ -dimethylaminoadenosin-3'-ylamide]) [58-58-2] M 616.5, m 174°,  $[\alpha]_D^{25}$ -11° (free base in EtOH), pK<sub>1</sub> 6.8, pK<sub>2</sub> 7.2. Purified by recrystn from H<sub>2</sub>O. The *free base* has m 175.5-177° (172-173°) (from H<sub>2</sub>O). The *sulfate* has m 180-187° dec (from H<sub>2</sub>O), and the *picrate monohydrate* has m 146-149° (from H<sub>2</sub>O). [Baker et al. *J Am Chem Soc* 77 1 1955; Fryth et al. *J Am Chem Soc* 80 3736 1958.] It is an inhibitor of aminopeptidase and terminates protein synthesis [Reboud et al. *Biochemistry* 20 5281 1981].

**Pyridoxal hydrochloride** [65-22-5] M 203.6, m 176-180°(dec),  $pK_1^{20}$  4.23 (3-OH),  $pK_2^{20}$  8.7 (**Pyridinium**<sup>+</sup>),  $pK_3^{20}$  13.04 (CH<sub>2</sub>OH?). Dissolve in water and adjust the pH to 6 with NaOH. Set aside overnight to crystallise. The crystals are washed with cold water, dried in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> and stored in a brown bottle at room temperature. [Fleck and Alberty J Phys Chem 66 1678 1962.]

**Pyridoxal-5'-phosphate monohydrate** (PLP, codecarboxylase) [54-47-7] M 265.2,  $pK_1^{25} < 2.5$  (PO<sub>4</sub>),  $pK_2^{25} 4.14$  (3-OH),  $pK_3^{25} 6.20$  (PO<sub>4</sub>),  $pK_4^{25} 8.69$  (pyridinium<sup>+</sup>). It has been purified by dissolving 2g in H<sub>2</sub>O (10-15mL, in a dialysis bag a third full) and dialysing with gentle stirring against 1L of H<sub>2</sub>O (+ two drops of toluene) for 15h in a cold room. The dialysate is evaporated to 80-100mL then lyophilised. Lemon yellow microscopic needles of the monohydrate remain when all the ice crystals have been removed. The purity is checked by paper chromatography (in EtOH or *n*-PrOH-NH<sub>3</sub>) and the spot(s) visualised under UV light after reaction with *p*-phenylene diamine, NH<sub>3</sub> and molybdate. Solutions stored in a freezer are 2-3% hydrolysed in 3-weeks. At 25°, only 4-6% hydrolysis occurs even in N NaOH or HCl, and 2% is hydrolysed at 37° in 1 day - but is complete at 100° in 4h. Best stored as dry solid at -20°. In aqueous acid the solution is colourless but is yellow in alkaline solutions. It has UV  $\lambda_{max}$  at 305nm ( $\varepsilon$  1100) and 380nm ( $\varepsilon$  6550) in 0.1 N NaOH; 330nm ( $\varepsilon$  2450) and 388nm ( $\varepsilon$  4900) in 0.05M phosphate buffer pH 7.0 and 295nm ( $\varepsilon$  6700) in 0.1N HCl. [Peterson et al. *Biochemical Preparations* 3 34, 119 1953.] The oxime dec at 229-230° and is practically insoluble in H<sub>2</sub>O, EtOH and Et<sub>2</sub>O. The O-methyloxime decomposes at 212-213°. [Heyl et al J Am Chem Soc 73 3430 1951.] It has also been purified by column chromatography through Amberlite IRC-50 (H<sup>+</sup>) [Peterson and Sober J Am Chem Soc 76 169 1954].

**Pyridoxamine hydrochloride** [5103-96-8, 524-36-7 (free base)] **M 241.2, m 226-227**<sup>o</sup>(dec),  $pK_1^{25}$ **3.54 (3-OH), pK\_2^{25} 8.21 (ring N<sup>+</sup>), pK\_3^{25} 10.63 (NH<sub>2</sub>).** Crystd from hot MeOH. The free base crysts from EtOH, has **m** 193-193.5<sup>o</sup> [Harris et al. J Biol Chem 154 315 1944, J Am Chem Soc 66 2088 1944].

Pyridoxine hydrochloride see Vitamin B<sub>6</sub>.

**Pyruvate kinase isoenzymes** (from Salmonella typhimurium) [9001-59-6]  $M_r$  64,000, [EC 2.7.1.40], amorphous. Purified by  $(NH_4)_2SO_4$  fractionation and gel filtration, ion-exchange and affinity chromatography. [Garcia-Olalla and Garrido-Pertierra Biochem J 241 573 1987.]

Quinacrine [Atebrine, 3-chloro-9(4-diethylamino-1-methyl)butylamino-7methoxy)acridine] dihydrochloride. [69-05-6] M 472.9, m 248-250°(dec),  $pK_1^{30}$  -6.49 (aq H<sub>2</sub>SO<sub>4</sub>),  $pK_2^{30}$  7.73 (ring NH<sup>+</sup>),  $pK_3^{30}$  10.18 (Et<sub>2</sub>N). Cryst from H<sub>2</sub>O (sol 2.8% at room temp) as yellow crystals. Slightly sol in MeOH and EtOH. Antimalarial, antiprotozoal and intercalates DNA. [Wolfe Antibiot 3 (Springer-Verlag) 203 1975.]

Quisqualic acid (3-[3,5-dioxo-1,2,4-oxadiazolin-2-yl]-L-alanine) [52809-07-1] M 189.1, m 190-191°,  $[\alpha]_D^{20}+17°$  (c 2, 6M HCl),  $pK_{Est(1)}\sim 2.1$  (CO<sub>2</sub>H),  $pK_{Est(2)}\sim 8.9$  (NH<sub>2</sub>). It has been purified by ion-exchange chromatography on Dowex 50W (x 8, H<sup>+</sup> form), the desired fractions are lyophilised and recrystd from H<sub>2</sub>O-EtOH. It has IR (KBr) v: 3400-2750br, 1830s, 1775s, 1745s and 1605s cm<sup>-1</sup>; and <sup>1</sup>H NMR (NaOD/D<sub>2</sub>O, pH 13)  $\delta$ : 3.55-3.57 (1H m, X of ABX, H-2), 3.72-3.85 (2H, AB of ABX, H-3), <sup>13</sup>C NMR (D<sub>2</sub>O)  $\delta$ : 50.1t, 53.4d, 154.8s, 159.7s and 171.3s. [Baldwin et al. J Chem Soc, Chem Commun 256 1985.] It is a quasiqualate receptor agonist [Joels et al. Proc Natl Acad Sci USA 86 3404 1989].

**Renal dipeptidase** (from porcine kidney cortex) [9031-96-3] M<sub>r</sub> 47,000 [EC 3.4.13.11]. Purified by homogenising the tissue, extracting with Triton X-100, elimination of insoluble material, and ion-exchange, size exclusion and affinity chromatography. [Hitchcock et al. Anal Biochem 163 219 1987.]

**Restriction enzymes (endonucleases).** These are enzymes which cleave double stranded DNA (linear or circular) at specific nucleotide sequences within the DNA strands which are then used for cloning (by ligating bits of DNA sequences together) or used for identifying particular DNA materials, e.g. plasmids, genes etc. A very large number of restriction enzymes are now available commercially and are extensively used in molecular biology. They are highly specific for particular nucleotide arrangements and are sensitive to the reaction conditions, e.g. composition of the medium, pH, salt concentration, temperature etc, which have to be strictly adhered to. The enzymes do not require further purification and the reaction conditions are also provided by the suppliers from which the necessary reaction media can also be purchased (see commercial catalogues).

Retinal (Vitamin A aldehyde), Retinoic acid (Vitamin A acid), Retinyl acetate, Retinyl palmitate see entries in Chapter 4.

**Reverse transcriptase (from avian or murine RNA tumour viruses)** [9068-38-6] [EC 2.7.7.49]. Purified by solubilising the virus with non-ionic detergent. Lysed virions were adsorbed on DEAE-cellulose or DEAE-Sephadex columns and the enzyme eluted with a salt gradient, then chromatographed on a phosphocellulose column and enzyme activity eluted in a salt gradient. Purified from other viral proteins by affinity chromatography on a pyran-Sepharose column. [Verna *Biochim Biophys Acta* 473 1 1977; Smith *Methods Enzymol* 65 560 1980; see commercial catalogues for other transcriptases.]

**Riboflavin** [83-88-5] M 376.4, m 295-300°(dec),  $[\alpha]_D$  -9.8° (H<sub>2</sub>O), -125° (c 5, 0.05N NaOH), pK<sub>1</sub> 1.7, pK<sub>2</sub> 9.69 (10.2, acidic NH). Crystd from 2M acetic acid, then extracted with CHCl<sub>3</sub> to remove lumichrome impurity. [Smith and Metzler *J Am Chem Soc* 85 3285 1963.] Has also been crystd from water. (See also p. 575.)

**Riboflavin-5'-phosphate (Na salt, 2H<sub>2</sub>O)** [130-40-5] **M 514.4.** See flavin mononucleotide (FMN) on p. 535.

**D-(+)-Ribonic acid-** $\gamma$ -lactone [5336-08-3] M 148.12, m 80°, 84-86°,  $[\alpha]_D^{20} + 18.3°$  (c 5, H<sub>2</sub>O). Purified by recrystn from EtOAc. The *tribenzoate* has m 54-56° (from AcOH),  $[\alpha]_D^{25} + 27°$  (c 2.37, Me<sub>2</sub>NCHO) and the 3,5-O-*benzylidene* derivative has m 230-231.5° (needles from Me<sub>2</sub>CO-pet ether),  $[\alpha]_D^{25} - 177°$  (CHCl<sub>3</sub>). [Chen and Joulié J Org Chem 49 2168 1984; Zinner and Voigt J Carbohydr Res 7 38 1968.]

**Ribonuclease** (from human plasma) [9001-99-4]  $M_r \sim 13,700$ , [EC 3.1.27.5], amorphous. Purified by  $(NH_4)_2SO_4$  fractionation, followed by PC cellulose chromatography and affinity chromatography (using Sepharose 4B to which (G)<sub>n</sub> was covalently bonded). [Schmukler et al. J Biol Chem 250 2206 1975.]

**RNA** (ribonucleic acids). Ribonucleic acids are like DNA except that the 2'-deoxy-D-ribose moiety is replaced by a D-ribose moiety and the fourth nucleotide thymidylic acid (T) is replaced by uridylic acid (U). RNA does not generally form complete douplex molecules like DNA, i.e. it is generally monomeric, except in certain viruses. The two main classes of RNA are **messenger-RNA** (mRNA) and **transfer-RNA** (tRNA). mRNA transcribed from the DNA gene followed by the splicing out of the non-coding nucleotides (of the introns) and codes for a specific gene. There are many different tRNAs, at least one of which links to a specific  $\alpha$ -amino acid, that bind to the mRNA via the ribosome (a set of proteins) to the RNA triplets (three nucleotides) which code for the particular  $\alpha$ -amino acids. An enzyme then joins the  $\alpha$ -amino acids of two adjacent tRNA- $\alpha$ -amino acid ribosome complexes bound to the mRNA to form a peptide bond. Thus peptide bonds and consequently polypeptides and proteins coded by the DNA via the respective mRNA are produced. Martin et al. [Biochem J 89 327 1963] dissolved RNA (5g) in 90mL of 0.1mM EDTA, then homogenised

with 90mL of 90% (w/v) phenol in water using a Teflon pestle. The suspension was stirred vigorously for 1h at room temperature, then centrifuged for 1h at 0° at 25000rpm. The lower (phenol) layer was extracted four times with 0.1mM EDTA and the aqueous layers were combined, then made 2% (w/v) with respect to AcOK and 70% (v/v) with respect to EtOH. After standing overnight at -20°, the ppte was centrifuged down, dissolved in 50mL of 0.1mM EDTA, made 0.3M in NaCl and left 3 days at 0°. The purified RNA was then centrifuged down at 10000xg for 30min, dissolved in 100mL of 0.1mM EDTA, dialysed at 4° against water, and freeze-dried. It was stored at -20° in a desiccator. Michelson [J Chem Soc 1371 1959] dissolved 10g of RNA in water, added 2M ammonia to adjust the pH to 7, then dialysed in Visking tubing against five volumes of water for 24h. The process was repeated three times, then the material after dialysis was treated with 2M HCl and EtOH to ppte the RNA which was collected, washed with EtOH, ether and dried [see commercial catalogues for further examples].

Ricin (toxin from Castor bean *Ricinus communis*) [A chain 96638-28-7; B chain 96638-29-8]  $M_r \sim 60,000$ , amorphous. Crude ricin, obtained by aqueous extraction and  $(NH_4)_2SO_4$  pptn, was chromatographed on a galactosyl-Sepharose column with sequential elution of pure ricin. The second peak was due to ricin agglutinin. [Simmons and Russell Anal Biochem 146 206 1985.] Inhibitor of protein synthesis. EXTREMELY DANGEROUS, USE EXTREME CARE [instructions accompany product].

**Rifampicin** (**Rifampin**) [13292-46-1] **M 823.0, m 183-185°, pK<sub>1</sub> 1.7, pK<sub>2</sub> 7.9.** This macrolide antibiotic crystallises form Me<sub>2</sub>CO in red-orange plates. It has UV  $\lambda_{max}$  237, 255,334, and 475nm ( $\epsilon$  33,200, 32,100, 27,000 and 15,400) at pH 7.38. It is stable in Me<sub>2</sub>SO and H<sub>2</sub>O. Freely soluble in most organic solvents and slightly soluble in H<sub>2</sub>O at pH <6. [Binda et al. Arzneim.-Forsch 21 1907 1971.] It inhibits cellular RNA synthesis without affecting DNA [Calvori et al. Nature 207 417 1965].

**Rifamycin B** [13929-35-6] **M** 755.8, m 300° (darkening at 160-164°),  $[\alpha]_D^{20}$ -11° (MeOH), pK<sub>1</sub> 2.60, pK<sub>2</sub> 7.76. It forms yellow needles from \*C<sub>6</sub>H<sub>6</sub>. It has solubility in H<sub>2</sub>O (0,027%), MeOH (2.62%) and EtOH (0.44%). It has UV  $\lambda_{max}$  223, 304 and 245nm ( $A_{1cm}^{1\%}$  555, 275 and 220). [Oppolzer and Prelog Helv Chim Acta 56 2287 1973; Oppolzer et al. Experientia 20 336 1964; X-ray: Brufani et al. Experientia 20 339 1964.]

**Rifamycin SV sodium salt** [15105-92-7] **M 719.8, m 300°(darkening >140°),**  $[\alpha]_D^{20} - 4^\circ$  (**MeOH**), **pK**<sub>Est</sub> ~ 7.8. Yellow orange crystals from Et<sub>2</sub>O-pet ether or aq EtOH, very soluble in MeOH, EtOH, Me<sub>2</sub>CO and EtOAc, soluble in Et<sub>2</sub>O and HCO<sub>3</sub>, slightly soluble in H<sub>2</sub>O and pet ether. Its UV has  $\lambda_{max}$  at 223, 314 and 445nm ( $A_{1cm}^{1\%}$  586, 322 and 204) in phosphate buffer pH 7. [NMR: Bergamini and Fowst Arzneim.-Forsch 15 951 1965.]

**Saccharides.** Resolved by anion-exchange chromatography. [Walberg and Kando Anal Biochem 37 320 1970.]

Sarcosine anhydride [5076-82-4] M 142.2, m 146-147°, pK<sub>Est(1)</sub>~-4.2, pK<sub>Est(2)</sub>~-1.9. Crystd from water, EtOH or ethyl acetate. Dried in vacuum at room temperature.

(-)-Scopolamine hydrobromide  $3H_2O$  ( $6\beta,7\beta$ -epoxy- $3\alpha$ -tropanyl S(-)-tropate HBr, hyoscine HBr) [114-49-8] M 438.3, m 193-194°, 195°, 195-199°,  $[\alpha]_D^{25}$ -25°(c 5, H<sub>2</sub>O), pK<sup>20</sup> 8.15. Recrystd from Me<sub>2</sub>CO, H<sub>2</sub>O or EtOH-Et<sub>2</sub>O and dried. Soluble in H<sub>2</sub>O (60%) and EtOH (5%) but insol in Et<sub>2</sub>O and slightly in CHCl<sub>3</sub>. The hydrochloride has m 300° (from Me<sub>2</sub>CO). The free base is a viscous liquid which forms a crystalline hydrate with m 59° and  $[\alpha]_D^{20}$ -28° (c 2.7, H<sub>2</sub>O). Readily hydrolysed in dilute acid or base. [Meinwald J Chem Soc 712 1953; Fodor Tetrahedron 1 86 1957.]

Seleno-DL-methionine ( $\pm 2$ -amino-4-methylselanylbutyric acid) [2578-28-1] M 196.1, m 265°(dec), 267-269°(dec), 270° (see pKs of methionine). Crystallises in hexagonal plates from MeOH and H<sub>2</sub>O. [Klosterman and Painter J Am Chem Soc 69 2009 1949.] The L-isomer is purified by dissolving in H<sub>2</sub>O, adjusting the pH to 5.5 with aqueous NH<sub>3</sub>, evaporating to near-dryness, and the residue is washed several times with absolute EtOH till solid is formed and then recrystd from Me<sub>2</sub>CO. It has m 266-268°(dec), 275°(dec),  $[\alpha]_{D}^{25}$ +18.1°(c 1, N HCl). [Pande et al. J Org Chem 35 1440 1970.]

Serotonin hydrochloride (5-HT, 3-[2-aminoethyl]-5-hydroxyindole HCl) [153-98-0] M 212.7, m 167-168°, 178-180°,  $pK_1^{25}$  4.9,  $pK_2^{25}$  9.8 (10.0, NH<sub>2</sub>),  $pK_3^{25}$  11.1 (5-OH),  $pK_4^{25}$  18.25 (acidic indole NH). Purified by recrystn from EtOH-Et<sub>2</sub>O or Et<sub>2</sub>O to give the hygroscopic salt. Store in the dark as it is light sensitive. The *free base* has m 84-86° (from Et<sub>2</sub>O). The 5-benzyloxy derivative has m 84-86° (from Et<sub>2</sub>O). [Ek and Witkop J Am Chem Soc 76 5579 1954; HamLin and Fischer J Am Chem Soc 73 5007 1951.] The picrate 1H<sub>2</sub>O has m 196-197.5° (dec with sintering at 160-165°) after recrystn from Et<sub>2</sub>O. Serotonin is a natural neurotransmitter [Chuang Life Sci 41 1051 1987].

Sinigrin monohydrate (Myronate K) [64550-88-5] M 415.5, m 125-127°, 127-129°,  $[\alpha]_D^{20}$ -17° (c 0.2, H<sub>2</sub>O), pK<sub>Est</sub> <0. Purified by recryst three times from EtOH and once from MeOH. The tetraacetate has m 193-195°,  $[\alpha]_D^{20}$ -16° (c 0.14, H<sub>2</sub>O). [Benn et al. J Chem Soc, Chem Commun 445 1965; Kjaer et al. Acta Chem Scand 10 432 1956; Marsh et al. Acta Cryst (Sect B) 26 1030 1970.] It is a  $\beta$ -D-thioglucopyranoside substrate for thiogluconidase [MacLeod and Rossiter Phytochem 25 1047 1986].

α-Solanine (solan-5-en-3β-yl-[ $O^3$ -β-D-glucopyranosyl- $O^2$ -α-L-rhamnopyranosyl-β-D-galacto -pyranoside]) [20562-02-1] M 868.1, m 285°(dec), 286°(dec) (sintering >190°), [α]<sub>2</sub><sup>20</sup> -58° (c 0.8, pyridine), pK<sup>15</sup> 6.66. Recrystd from EtOH, 85% aqueous EtOH, MeOH or aqueous MeOH as dihydrate m 276-278°. Solubility in H<sub>2</sub>O is 25mg/L and 5% in pyridine, but it is very soluble in Et<sub>2</sub>O and CHCl<sub>3</sub>. The hydrochloride is gummy or amorphous but has been crystd (m ~212° dec). It has insecticidal properties. [Kuhn et al. Chem Ber 88 1492 1955.]

**Somatostatin** [38916-34-6] **M 1637.9**,  $[\alpha]_D^{25}$ -36° (c 0.57, 1% AcOH). A tetradecapeptide which is purified by gel filtration on Sephadex G-25, eluting with 2N AcOH, and then by liquid partition chromatography on Sepahdex G-25 using *n*-BuOH-AcOH-H<sub>2</sub>O (4:1:5) and has  $R_F = 0.4$ . It is a brain growth hormone releasing-inhibiting factor which has also been synthesised. [Burgus et al. *Proc Natl Acad Sci USA* **70** 684 1973; Sorantakis and McKinley *Biochem Biophys Res Commun* 54 234 1973; Hartridt et al. *Pharmazie* 37 403 1982.]

Spectinomycin dihydrochloride pentahydrate (Actinospectacin) [21736-83-4] M 495.3, m 205-207°(dec),  $[\alpha]_D^{20}$  +14.8° (c 0.4, H<sub>2</sub>O), pK<sub>1</sub> 6.95, pK<sub>2</sub> 8.70. Purified from aqueous Me<sub>2</sub>CO and is soluble in H<sub>2</sub>O, MeOH and dilute acid and base but only slightly soluble in Me<sub>2</sub>CO, EtOH, CHCl<sub>3</sub> and \*C<sub>6</sub>H<sub>6</sub>. The *free base* is an amorphous solid, m 184-194° with  $[\alpha]_D^{20}$  -20° (H<sub>2</sub>O). [Wiley et al. J Am Chem Soc 93 2652 1963; X-ray: Cochran et al. J Chem Soc Chem Commun 494 1972.] It is an aminoglycoside antibiotic which interacts with 16S ribosomal RNA [Moazet and Noller Nature 327 389 1987]; and is used for the treatment of gonorrhea [Rinehart J Infect Dis 119 345 1969].

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**D-Sphingosine** (2S,3S-D-erythro-2-aminooctadec-4t-ene-1,3-diol from bovine brain) [123-78-4] M 299.5, m 79-82°, 82° 82.5° (softens at ~70°),  $[\alpha]_D^{22}$ -3.4° (c 2, CHCl<sub>3</sub>), pK<sub>Est</sub> ~ 8.8. Purified by recrystn from EtOAc, Et<sub>2</sub>O or pet ether (60-80°) It is insoluble in H<sub>2</sub>O but is soluble in Me<sub>2</sub>CO, EtOH and MeOH. It has IR bands at 1590 and 875 cm<sup>-1</sup>, and is characterised as the tribenzoate m 122-123° (from 95% EtOH). [Tipton Biochem Prep 9 127 1962.]

Spirilloxanthin [34255-08-8] M 596.9, m 216-218°,  $\lambda_{max}$  463, 493, 528 nm,  $\epsilon_{1cm}^{1\%}$  2680 (493 nm) in pet ether (b 40-70°). Crystd from CHCl<sub>3</sub>/pet ether, acetone/pet ether, \*C<sub>6</sub>H<sub>6</sub>/pet ether or \*C<sub>6</sub>H<sub>6</sub>. Purified by chromatography on a column of CaCO<sub>3</sub>/Ca(OH)<sub>2</sub> mixture or deactivated alumina. [Polgar et al. Arch Biochem Biophys 5 243 1944.] Stored in the dark in an inert atmosphere, at -20°.

Squalane (Cosbiol, 2,6,10,15,19,23-hexamethyltetracosane, perhydrosqualene) [111-01-3] M 422.8, m -38°, b 176°/0.05mm, 210-215°/1mm, 274°/10mm,  $\sim 350°/760$ mm,  $d_4^{20}$  0.80785,  $n_D^{20}$  1.416. Purified by fractional distn *in vacuo* or evap distn. Soluble in pet ether, \*C<sub>6</sub>H<sub>6</sub>, Et<sub>2</sub>O and CHCl<sub>3</sub>, slightly sol in alcohols, Me<sub>2</sub>CO and AcOH but insol in H<sub>2</sub>O [Staudinger and Leupold *Helv Chim Acta* 15 223 1932; Sax and Stross Anal Chem 29 1700 1951; Mandai et al. Tetrahedron Lett 22 763 1981].

Squalene (all-trans-2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene) [111-02-4] M 410.7, m ~75°, b 203°/0.1mm, 213°/1mm, 285°/25mm, d<sup>25</sup> 0.8670, n 1.4905. Crystd repeatedly from Me<sub>2</sub>CO (1.4mL/g) using a Dry-ice bath, washing the crystals with cold acetone, then freezing the squalene under vacuum. Squalene was further purified by passage through a column of silica gel or chromatographed on activated alumina, using pet ether as eluent and stored in vac in the dark. Dauben et al. [J Am Chem Soc 74 4321 1952] purified squalene via its hexachloride and is bactericidal. [Capstack et al. J Biol Chem 240 3258 1965; Krishna et al. Arch Biochem Biophys 114 200 1966; Heilbron and Thompson J Chem Soc 883 1929; Karrer et al. Helv Chim Acta 13 1084 1930; UV: Farmer et al. J Chem Soc 544 1943.]

Starch [9005-84-9] M (162.1)<sub>n</sub>. Defatted by Soxhlet extraction with Et<sub>2</sub>O or 95% EtOH. For fractionation of starch into "amylose" and "amylopectin" fractions, see Lansky et al. [J Am Chem Soc 71 4066 1949].

Sterigmatocystin (3a,12c-dihydro-8-hydroxy-6-methoxy-3*H*-furo[3',2',:4,5]furo[2,3-c]xanthen-7-one) [10048-13-2] M 324.3, m 246°, 247-248°,  $[\alpha]_D^{20}$ -398° (c 0.1, CHCl<sub>3</sub>), pK<sub>Est</sub> ~ 8.0. Recrystd from amyl acetate, Me<sub>2</sub>CO or EtOH and sublimed *in vacuo*. It has UV  $\lambda_{max}$  at 208, 235, 249 and 329nm (log  $\varepsilon$  4.28, 4.39, 4.44 and 4.12). [UV: Bullock et al. J Chem Soc 4179, 1962; UV, IR: Holker and Mulheirn J Chem Soc Chem Commun 1576, 1576 1968; Birkinshaw and Hammady Biochem J 65 162 1957.] This mycotoxin induces bone marrow changes in mice [Curry et al. Mutation Res 137 111 1984].

Stigmatellin A (2-[4,6-dimethoxy-3,5,11-trimethyltridecatri-7t,9t,11t-enyl]-8-hydroxy-5,7-dimethoxy-3-methyl-4H-1-benzopyran-4-one) [91682-96-1] M 514.6, m 128-130°,  $[\alpha]_D^{20}$ +38.5° (c 2.3, MeOH), pK<sub>Est</sub> ~7 (phenolic OH). It is stable in aqueous soln at neutral pH but decomposes at pH <5. Purified by recrystn from toluene-hexane). It has UV  $\lambda_{max}$ : nm ( $\varepsilon$ ) 248sh (41000), 258 (59500) 267 (65500), 279 (41400) and 335 (5200) in MeOH; 249sh (45600), 258 (60000), 268 (72700), 277 (54100), 320 (2500) and 370 (3000) in MeOH + 1 drop of N KOH; 243sh (29300), 264 (63200), 274 (64100), 283sh (45800), 329 (4800) and 420 (21000) in MeOH + 6N HCl; and IR (CHCl<sub>3</sub>) v: 3550m, 1645chs, 1635ss, 1620ss, 1590s, 1510m and 905m cm<sup>-1</sup>. It gives colour reactions at 110° with vanillin/H<sub>2</sub>SO<sub>4</sub> (grey), Ce(IV)/(NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (yellow) and phosphomolybdate (blue-grey). [Höfle et al. Justus Liebigs Ann Chem 1882 1984.] It inhibits electron transport [Jagow and Link Methods Enzymol 126 253 1986; Robertson et al. Biochemistry 32 1310 1933], and has antibiotic properties [Kunze et al. J Antibiot 37 454 1984]. The 7t,9t,11c-isomer is Stigmatellin B.

Streptomycin sulfate [3810-74-0] M 1457.4,  $[\alpha]_D^{20}$ -84.3° (c 3, H<sub>2</sub>O), pK<sub>Est(1)</sub>~ 9.5 (MeNH), pK<sub>Est(2,3)</sub>~ 13.4 (guanidino). Recrystd from H<sub>2</sub>O-EtOH, washed with a little EtOH, Et<sub>2</sub>O and dried in a vacuum. [UV and IR: Grove and Randall Antibiotics Monographs 2 163 1855; Heuser et al. J Am Chem Soc 75 4013 1953, Kuehl et al. J Am Chem Soc 68 1460 1946; Regna et al. J Biol Chem 165 631 1946.] During protein synthesis it inhibits initiation and causes misreading of mRNA [Zierhut et al. Eur J Biochem 98 577 1979; Chandra and Gray Methods Enzymol 184 70 1990].

Streptonigrin (nigrin, 5-amino-6-[7-amino-5,8-dihydro-6-methoxy-5,8-dioxo-2-quinolinyl]-4-[2-hydroxy-3,4-dimethoxyphenyl]-3-methyl-2-pyridinecarboxylic acid) [3930-19-6] M 506.5, m 262-263°, 275°(dec), pK 6.3 (1:1 aq dioxane). Purified by TLC on pH 7-buffered silica gel (made from a slurry of Silica Gel 60 and 400mL of 0.05M phosphate buffer pH 7.0) and eluted with 5% MeOH/CHCl<sub>3</sub>. The extracted band can then be recrystd from Me<sub>2</sub>CO or dioxane as almost black plates or needles. It is soluble in pyridine, Me<sub>2</sub>NCHO, aqueous NaHCO<sub>3</sub> (some dec), and slightly soluble in MeOH, EtOH, EtOAc and H<sub>2</sub>O. It has UV  $\lambda_{max}$  248, 375-380nm ( $\epsilon$  38400 and 17400). [Weinreb et al. J Am Chem Soc 104 536 1982; Rao et al. J Am Chem Soc 85 2532 1963.] It is an antineoplastic and causes severe bone marrow depression [Wilson et al. Antibiot Chemother 11 147 1961].

Streptozotocin (*N*-[methylnitrosocarbamoyl]- $\alpha$ -D-glucosamine, streptozocin) [18883-66-4] M 265.2, m 111-114°(dec), 114-115°(dec), 115°(dec with evolution of gas),  $[\alpha]_D^{20} \sim +39°$ (H<sub>2</sub>O, may vary due to mutarotation). Recrystd from 95% EtOH and is soluble in H<sub>2</sub>O, MeOH and Me<sub>2</sub>CO. It has UV  $\lambda_{max}$  228nm ( $\epsilon$  6360) in EtOH. The *tetraacetate* has m 111-114°(dec),  $[\alpha]_D^{25} +41°$  (c 0.78, 95% EtOH) after recrystn from EtOAc. [Herr et al. *J Am Chem Soc* 89 4808 1967; NMR: Wiley et al. *J Org Chem* 44 9 1979.] It is a potent methylating agent for DNA [Bennett and Pegg Cancer Res 41 2786 1981].

Subtilisin (from *Bacillus subtilis*) [9014-01-1] [EC 3.4.21.62]. Purified by affinity chromatography using 4-(4-aminophenylazo)phenylarsonic acid complex to activated CH-Sepharose 4B. [Chandraskaren and Dhar *Anal Biochem* 150 141 1985].

Succinyl coenzyme A trisodium salt [108347-97-3] M 933.5. If it should be purified further then it should be dissolved in H<sub>2</sub>O (0.05g/mL) adjusted to pH 1 with 2M H<sub>2</sub>SO<sub>4</sub> and extracted several times with Et<sub>2</sub>O. Excess Et<sub>2</sub>O is removed from the aqueous layer by bubbling N<sub>2</sub> through it and stored frozen at pH 1. When required the pH should be adjusted to 7 with dilute NaOH and used within 2 weeks (samples should be frozen). Succinyl coenzyme A is estimated by the hydroxamic acid method [*J Biol Chem* 242 3468 1967]. It is more stable in acidic than in neutral aqueous solutions. [*Methods Enzymol* 128 435 1986.]

**2-Sulfobenzoic cyclic anhydride** (2,1-benzoxathiazol-3-one 1,1-dioxide) [81-08-3] M 184.2, m 126-127°, 129.5°, 130°, b 184-186°/18mm. If the sample has hydrolysed extensively (presence of OH band in the IR) then treat with an equal bulk of SOCl<sub>2</sub> reflux for 3h (CaCl<sub>2</sub> tube), evaporate and distil residue in a vacuum, then recrystd from  $C_6H_6$ , Et<sub>2</sub>O- $C_6H_6$  or CHCl<sub>3</sub> (EtOH free by passing through Al<sub>2</sub>O<sub>3</sub>, or standing over CaCl<sub>2</sub>). [Clarke and Breger Org Synth Coll Vol I 495 1948.] Used for modifying  $\zeta$ amino functions of lysyl residues in proteins [Bagree et al. FEBS Lett 120 275 1980]. (see entry on p. 126.)

Syrexin (from bovine liver). Purified by  $(NH_4)_2SO_4$  pptn, then by pH step elution from chromatofocusing media in the absence of ampholytes. [Scott et al. Anal Biochem 149 163 1985.]

**Taurodeoxycholic acid sodium salt monohydrate** (*n*-[desoxycholyl)taurine Na salt  $H_2O$ ) [1180-95-6] M 539.7, m 171-175°,  $[\alpha]_D^{23} + 37°$  (c 1,  $H_2O$ ), pK 1.4 (free acid). The salt is recryst from EtOH-Et<sub>2</sub>O. Its solubility in  $H_2O$  is 10%. The free acid has m 141-144°. [Norman Ark Kemi 8 331 1956.] It forms mixed micelles and solubilises some membrane proteins [Hajjar et al. J Biol Chem 258 192 1983].

Terramycin (oxytetracycline) [79-57-2] M 460.4 (anhy), 496.5 (2H<sub>2</sub>O), sinters at 182°, melts at 184-185°(dec),  $[\alpha]_D^{20}$ -196.6° (equilibrium in 0.1M HCl), -2.1° (equilibrium in 0.1M NaOH). Crystd (as dihydrate) from water or aqueous EtOH.

**2,2:5',2"-Terthiophene** [1081-34-1] **M 248.4, m 92-93°, 94-95°, 94-94.5°, 94-96°.** Recrystd from MeOH,  ${}^{*}C_{6}H_{6}$ , pet ether or MeOH. [UV: Zechmeister and Sease J Am Chem Soc 69 273 1947; Steinkopf et al. Justus Liebigs Ann Chem 546 180 1941.] Phototoxic nematocide [Cooper and Nitsche Bioorg Chem 13 36 1985; Chan et al. Phytochem 14 2295 1975]. See also Terthiophene on p. 356 in Chapter 4.

Tetracycline [60-54-8] M 444.4, m 172-174°(dec),  $[\alpha]_{546}^{20}$  + 270° (c 1, MeOH), pK<sub>1</sub><sup>25</sup> 3.30, pK<sub>2</sub><sup>25</sup> 7.68, pK<sub>3</sub><sup>25</sup> 9.69. Crystd from toluene.

Tetracycline hydrochloride [64-75-5] M 480.9, m 214°(dec), 215-220°,  $[\alpha]_D^{25}$ -258° (c 0.5, 0.1N HCl),  $[\alpha]_D^{20}$ -245° (c 1, MeOH), pK<sub>1</sub> 1.4 (enolic OH), pK<sub>2</sub> 7.8 (phenolic OH), pK<sub>3</sub> 9.6 (Me<sub>2</sub>N). Recrystd from MeOH + *n*-BuOH or *n*-BuOH + HCl. It is insoluble in Et<sub>2</sub>O and pet ether. It has UV  $\lambda_{max}$  at 270 and 366nm in MeOH. [Gottstein et al. J Am Chem Soc 81 1198 1959; Conover et al. J Am Chem Soc 84 3222 1962.]

(BH<sub>4</sub>.2HCl, 6R-2-amino-4-hydroxy-6-6R-Tetrahydro-erythro-biopterin dihydrochloride [{1R,2S}-1,2-dihydroxypropyl]-5,6,7,8-tetrahydropteridine 2HCl) [69056-38-8] M 316.2, m 245-246°(dec), [α]<sup>25</sup><sub>D</sub> -6.8° (c 0.67, 0.1N HCl), pK<sub>1</sub> 1.37 (pyrimidine<sup>+</sup>), pK<sub>2</sub> 5.6 (5-NH<sup>+</sup>), pK<sub>3</sub> 10.6 (acidic, 3NH). Recrystn from HCl enriches BH<sub>4</sub> in the natural 6R isomer. Dissolve the salt (~6g) in conc HCl (15mL) under gentle warming then add EtOH (30mL) dropwise, chill and collect the colourless needles (67%, up to 99% if mother liquors are concentrated), and dried in vacuo immediately over  $P_2O_5$  and KOH. Stores indefinitely at -20° in a dry atmosphere, Better store in sealed ampoules under dry  $N_2$ . It can be recrystd from 6N aqueous HCl. It has UV  $\lambda_{max}$  (2N HCl) 264nm ( $\epsilon$  16770; pH 3.5 phosphate buffer) 265nm (£ 13900); (pH 7.6) 297nm (£ 9500) and 260nm sh (£ 4690). It has been separated from the 6R-isomer by HPLC on a Partisil-10SCX column using 30mM ammonium phosphate buffer (pH 3.0) containing 3mM NaHSO<sub>3</sub> (2mL/min flow rate; 275nm detector) with retention times of 5.87min (6R) and 8.45min (6S). It is stable in acidic soln and can be stored for extended periods at -20° in 0.04M HCl. Above pH 7 the neutral species are obtained and these are readily oxidised by oxygen in the solvent to quinonoid species and then further oxidation and degradation occurs at room temperatures. These changes are slower at 0°. The sulfate salt can be obtained by recrystn from 2M  $H_2SO_4$  and is less soluble than the hydrochloride salt. The 6R-2, 5, 1', 2'tetraacetylbiopterin derivative has m 292° (dec) after recrystn from MeOH (100 parts) and  $[\alpha]_{589}^{20}$  -144° (c 0.5, CHCl<sub>3</sub>), [\alpha]<sup>20</sup><sub>589</sub> +12.8° (c 0.39, Me<sub>2</sub>SO). [NMR, UV: Matsuura et al. Heterocycles 23 3115 1985; Viscontini et al. Helv Chim Acta 62 2577 1979; Armarego et al. Aust J Chem 37 355 1984.]

Tetrahydrofolic acid dihydrochloride 2H<sub>2</sub>O (THFA, 65- or 6RS- 5,6,7,8-tetrahydrofolic acid 2HCl 2H<sub>2</sub>O, 5,6,7,8-tetrahydropteroyl-L-glutamic acid 2HCl 2H<sub>2</sub>O) [135-16-0] M 544.4, m >200°(dec),  $[\alpha]_D^{27}$ +16.9° (H<sub>2</sub>O pH 7.0 + 2-mercaptoethanol), pK<sub>1</sub> 1.7 (pyrimidine N<sup>+</sup>), pK<sub>2</sub> 2.4 (10N<sup>+</sup>), pK<sub>3</sub> 3.5 (α-CO<sub>2</sub>H), pK<sub>4</sub> 4.9 (γ-CO<sub>2</sub>H), pK<sub>5</sub> 5.6 (5-NH<sup>+</sup>), pK<sub>6</sub> 10.4 (acidic, 3NH). Very high quality material is now available commercially and should be a white powder. It can be dried over P<sub>2</sub>O<sub>5</sub> in a vacuum desiccator and stored in weighed aliquots in sealed ampoules. It is stable at room temp in sealed ampoules for many months and for much more extended periods at -10°. When moist it is extremely sensitive to moist air whereby it oxidises to the yellow 7,8-dihydro derivative. In soln it turns yellow in colour as it oxidises and then particularly in the presence of acids it turns dark reddish brown in colour. Hence aqueous solutions should be frozen immediately when not in use. It is always advisable to add 2mercaptoethanol (if it does not interfere with the procedure) which stabilises it by depleting the soln of  $O_2$ . The sulfate salt is more stable but then it is much less soluble. The best way to prepare standard solns of this acid is to dissolve it in the desired buffer and estimate the concentration by UV absorption in pH 7 buffer at 297nm ( $\epsilon$  22,000 M<sup>-1</sup>cm<sup>-1</sup>). If a sample is suspect it is not advisable to purify it because it is likely to deteriorate further as "dry box" conditions are necessary. Either a new sample is purchased or one is freshly prepared from folic acid. It has pKa values of -0.1, 4.3 and 9.0. [Hafeti et al. Biochem Prep 7 89 1960; UV: Mathews and Huennekens J Biol Chem 235 3304 1960; Osborn and Huennekens J Biol Chem 233 969 1958; O'Dell et al. J Am Chem Soc 69 250 1947; Blakley Biochem J 65 331 1957; Asahi Yakugaku Zasshi (J Pharm Soc Japan) 79 1548 1959.]

5,6,7,8-Tetrahydropterin sulfate (2-amino-5,6,7,8-tetrahydropteridin-4-one  $H_2SO_4$ ) [20350-44-1] M 265, m >200°(dec),  $pK_1^{25}$  1.3 (pyrimidine +),  $pK_2^{25}$  5.6 (5-NH+),  $pK_3^{25}$  10.6 (acidic, 3NH). If it has become too strongly violet in colour then it may need reducing again. Best to check the UV absorption in N HCl where it has a peak at ~265nm which drops sharply to zero having no absorption at *ca* 340nm. The presence of absorption at 340nm indicated oxidation to quinonoid or 7,8-dihydropterin. If the absorption is weak then dissolve in the minimum volume of anhydrous trifluoroacetic acid (fume hood) add charcoal, filter, then add one or two drops of N H<sub>2</sub>SO<sub>4</sub> followed by dry Et<sub>2</sub>O at 0°, allow the white tetrahydro

#### Purification of Biochemicals and Related Products

salt to settle and collect, and wash with dry Et<sub>2</sub>O, by centrifugation. Dry the residue in a vacuum desiccator over P<sub>2</sub>O<sub>5</sub> and KOH. Store in aliquots in the dark at <0°. It has UV  $\lambda_{max}$  at 265nm ( $\epsilon$  16980) at pH -1.0 (dication); 219nm ( $\epsilon$  23440) and 266nm ( $\epsilon$  12880) at pH 3.5 (monocation); 220nm ( $\epsilon$  18620), [260nm ( $\epsilon$  4270)sh] and 299nm ( $\epsilon$  9330) at pH 8.0 (neutral species); and 218nm ( $\epsilon$  10000), [240nm ( $\epsilon$  5500)sh] and 287nm ( $\epsilon$  5500) at pH 13 (anion). [Blakley *Biochem J* 72 707 1959; Asahi Yakugaku Zasshi (J Pharm Soc Jpn) 79 1557 1959; Pfleiderer in *Pterins and Folate* (Benkovic and Blakley Eds) J Wiley Vol 2 p97 1985.]

Thiamine monophosphate chloride  $1H_2O$  (Aneurine monophosphate chloride) [532-40-1] M 416.8, m 193°(dec), 200°(dec), 200-203°(dec), pK<sub>1</sub> 2.40, pK<sub>2</sub> 4.80, pK<sub>3</sub> 6.27, pK<sub>4</sub> 9.65, pK<sub>5</sub> 10.20. Purified by recrystn from aqueous HCl, EtOH slightly acidified with HCl, EtOH-Me<sub>2</sub>CO, H<sub>2</sub>O, or H<sub>2</sub>O-EtOH + Et<sub>2</sub>O. Dissolve in a small volume of H<sub>2</sub>O and mix with EtOH + Me<sub>2</sub>CO (1:1) to give the HCl.H<sub>2</sub>O as crystals. Filter, wash with Et<sub>2</sub>O and dry in a vacuum. The *chloride hydrochloride*, m 215-217°(dec) is obtained when crystd from aqueous HCl. [Wenz et al. Justus Liebigs Ann Chem 618 2280 1958, Viscontini et al. Helv Chim Acta 34 1388 1951, Leichssenring and Schmidt Chem Ber 95 767 1962; McCormick and Wright Methods Enzymol 18A 141, 147 1970.]

**Thiamphenicol** (1*R*,2*R*-2-[2,2-dichloroacetylamino]-1-[4-methanesulfonylphenyl]-propan-1,3-diol) [15318-45-3 (D-threo), 90-91-5] M 356.2, m 163-166°, 165.2-165.6°, 165-166°,  $[\alpha]_D^{25}$ +15.6° (c 2, EtOH), pK 7.2. Recrystd from H<sub>2</sub>O or CHCl<sub>3</sub>. UV  $\lambda_{max}$  224, 266 and 274nm ( $\epsilon$ 13700, 800 and 700) in 95% EtOH. The *IS*,2*S*-isomer [14786-51-7] has m 164.3-166.3° (from H<sub>2</sub>O + EtOAc + pet ether) and  $[\alpha]_D^{25}$ -12.6° (c 1, EtOH); and the racemate *IRS*,2*RS* Racefenical [15318-45-3]] has m 181-183° (sinter at 180-183°) from CHCl<sub>3</sub>-EtOAc-pet ether. [Cutler et al. *J Am Chem Soc* 74 5475, 5482 1952; UV: Nachod and Cutler *J Am Chem Soc* 74 1291 1952; Suter et al. *J Am Chem Soc* 75 4330 1953; Cutler et al. *J Am Pharm Assoc* 43 687 1954.]

Thiazolyl blue tetrazolium bromide (MTT, 3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyl-2Htetrazolium bromide) [298-93-1, 2348-71-2] M 414.3, m 171°. It is recrystd by dissolving in MeOH containing a few drops of HBr and then adding dry Et<sub>2</sub>O to complete the crystn, wash the needles with Et<sub>2</sub>O and dry in a vacuum desiccator over KOH. [Beyer and Pyl Chem Ber 87 1505 1954.]

**2-Thiocytosine** (4-amino-2-mercaptopyrimidine) [333-49-3] M 127.2, m 236-237°(dec), 285-290°(dec),  $pK_1^{20}$  3.90 (NH<sub>2</sub>),  $pK_2^{20}$  11.10 (SH). It is recrystd from hot H<sub>2</sub>O and dried at 100° to constant weight. [Brown J Appl Chem (London) 9 203 1959; Russell et al. J Am Chem Soc 71 2279 1949.] It is used in transcription and translation studies [Rachwitz and Scheit Eur J Biochem 72 191 1977.]

**6-Thioguanine** [154-42-7] **M 167.2, m >300°, pK\_1^{23} 8.2 (SH), pK\_2^{23} 11.6 (acidic, 9-NH).** Recrystd from H<sub>2</sub>O as needles. It has UV  $\lambda_{max}$  at 258 and 347nm (H<sub>2</sub>O, pH 1) and 242, 270 and 322nm (H<sub>2</sub>O, pH 11). [Elion and Hitchings *J Am Chem Soc* 77 1676 1955; Fox et al. *J Am Chem Soc* 80 1669 1958.] It is an antineoplastic agent [Kataoka et al. Cancer Res 44 519 1984].

**Thrombin (from bovine blood plasma)** [9002-04-4]  $M_r$  32,600 [EC 3.4.4.13]. Purified by chromatography on a DEAE-cellulose column, while eluting with 0.1M NaCl, pH 7.0, followed by chromatography on Sephadex G-200. Final preparation was free from plasminogen and plasmin. [Yin and Wessler J Biol Chem 243 112 1968.]

Thrombin from bovine blood was purified by chromatography using p-chlorobenzylamino- $\varepsilon$ -aminocaproyl agarose, and gel filtration through Sephadex G-25. [Thompson and Davie Biochim Biophys Acta 250 210 1971.]

Thrombin from various species was purified by precipitaion of impurities with rivanol. [Miller Nature 184 450 1959.]

L-Thyroxine sodium salt (5H<sub>2</sub>O) [6106-07-6] M 888.9,  $[\alpha]_{546}^{20}$  +20° (c 2, 1M HCl + EtOH, 1:4). Crystd from absolute EtOH and dried for 8h at 30°/1mm.

D-Thyroxine {O-[3,5-diiodo-4-oxyphenyl]-3,5-diiodo-D-(-)-tyrosine, 3,3',5,5'-tetra-iodo-D-thyronine} [51-49-0] M 776.9, m 235°(dec), 235-236°(dec), 340°(dec),  $[\alpha]_D^{20}+4.5°$  (c 3, aq

0.2N NaOH in 70% EtOH),  $[\alpha]_D^{20}$ -17° (c 2, aq N HCl + EtOH 1:4),  $pK_1^{25}$  2.2 (CO<sub>2</sub>H),  $pK_2^{25}$  8.40 (OH),  $pK_3^{25}$  10,1 (NH<sub>2</sub>). Recrystd from H<sub>2</sub>O as needles or from an ammonical soln by dilution with H<sub>2</sub>O, MeOH or Me<sub>2</sub>CO. Also purified by dissolving ~6.5 g in a mixture of MeOH (200mL) and 2N HCl (20mL), add charcoal, filter then add NaOAc soln to pH 6 and on standing the thyroxine separates, is washed with MeOH then Me<sub>2</sub>CO and dried *in vacuo*. The *N*-formyl-D-thyroxine derivative has **m** 210° and  $[\alpha]_{546}^{21}$  -26.9° (c 5, EtOH). The racemate ±-thyroxine has **m** 256° and is purified in the same way. [Nahm and Siedel Chem Ber 96 1 1963; Salter Biochem J 24 471 1930.]

L-Thyroxine (*O*-[3,5-diiodo-4-oxyphenyl]-3,5-diiodo-L-(+)-tyrosine, 3,3',5,5'-tetraiodo-Dthyronine) [51-48-9] M 776.9, m 229-230°(dec), ~235°(dec), 237°(dec),  $[\alpha]_D^{22}$ -5.1° (c 2, aq N NaOH + EtOH 1:2),  $[\alpha]_D^{22}$ +15° (c 5, aq N HCl in 95% EtOH 1:2),  $[\alpha]_D^{22}$ +26° (EtOH/1M aq HCl; 1:1) (pK 6.6). Purification is the same as for the D-isomer above. Likely impurities are tyrosine, iodotyrosine, iodothyroxines and iodide. Dissolve in dilute ammonia at room temperature, then crystd by adding dilute acetic acid to pH 6. The *N*-formyl-L-thyroxine has m 214°(dec) and  $[\alpha]_{546}^{21}$  +27.8° (c 5, EtOH). [Harington et al. Biochem J 39 164 1945; Nahm and Siedel Chem Ber 96 1 1963; Reineke and Turner J Biol Chem 161 613 1945; Chalmers et al. J Chem Soc 3424 1949.]

Tissue inhibitor of metalloproteins (TIMP, from human blood plasma),  $M_r \sim 30,000$ . Purified by a [anti-human amniotic fluid-TIMP]-Sepharose immuno-affinity column eluted with 50mM glycine/HCl pH 3.0 buffer that is 0.5M in NaCl then by gel filtn [Cawston et al. *Biochem J* 238 677 1986].

dl- $\alpha$ -Tocopherol (see vitamin E) [59-02-9] M 430.7,  $A_{1 \text{ cm}}^{1 \%}$  74.2 at 292 nm in MeOH. Dissolved in anhydrous MeOH (15mL/g) cooled to -6° for 1h, then chilled in a Dry-ice/acetone bath, crystn being induced by scratching with a glass rod.

γ-Tocopherol (3,4-dihydro-2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)-2*H*-benzopyran-6ol) [54-28-4] M 416.7, m -30°, b 200-210°/0.1mm,  $d_4^{20}0.951$ ,  $n_D^{20}1.505$ ,  $[\alpha]_D^{20}-2.4^\circ$ (EtOH). Purified by distn at high vacuum and stored in dark ampoules under N<sub>2</sub>. UV  $\lambda_{max}$  298nm ( $A_{1cm}^{1\%}$ 92.8). It is insoluble in H<sub>2</sub>O but soluble in organic solvents. The allophanate (used for separating isomers) has m 136-138°,  $[\alpha]_D^{18}$  +3.4° (CHCl<sub>3</sub>). [Baxter et al. J Am Chem Soc 65 9181943; Emerson et al. Science 83 421 1936, J Biol Chem 113 319 1936.]

Tolylene-2,4-diisocyanate (toluene-2,4-diisocyanate). [584-84-9] M 174.2, m 19.5-21.5°, 20-22°, 28°, b 126°/11mm, 124-126°/18mm, 250°/760mm. It is purified by fractionation in a vacuum and should be stored in a dry atmosphere. It is soluble in organic solvents but reacts with H<sub>2</sub>O, alcohols (slowly) and amines all of which could cause explosive polymerisation. It darkens on exposure to light. It has a sharp pungent odour, is TOXIC and is IRRITATING TO THE EYES. [Siefken Justus Liebigs Ann Chem 562 75, 96, 127 1949; Bayer Angew Chem 59 257 1947.] It is a reagent for covalent crosslinking of proteins [Wold Methods Enzymol 25 623 1972.]

Tomatidine  $(5\alpha, 20\beta, 22\alpha, 25\beta, 27$ -azaspirostan-3 $\beta$ -ol) [77-59-8] M 415.7, m 202-206°,  $[\alpha]_D^{20}$  +5.9° (c 1, MeOH),  $[\alpha]_D^{20}$ +8° (CHCl<sub>3</sub>). Forms plates from EtOAc. Also purified by dissolving 80mg in \*C<sub>6</sub>H<sub>6</sub> and applying to an Al<sub>2</sub>O<sub>3</sub> column (3.0g) and eluting with \*C<sub>6</sub>H<sub>6</sub>, evaporating and recrystallising three times from EtOAc. The hydrochloride has m 265-270° from EtOH and  $[\alpha]_D^{25}$ -5° (MeOH). [IR: Uhle J Am Chem Soc 83 1460 1961; Kessar et al. Tetrahedron 27 2869 1971; Schreiber and Adams Experientia 17 13 1961.]

Tomatine (225,255-3β,β-lycotetraosyloxy-5α-spirosolan) [17406-45-0] M 1034.2, m 263-268°(dec), 290-291°(evac capillary), 283.5-287°(dec), 272-277°(dec), 300-305°(dec),  $[α]_D^{20}$ -18° to -34° (c 0.55, pyridine). Recrystd from MeOH, EtOH, aqueous EtOH or dioxane + NH<sub>3</sub>. It is almost insoluble in pet ether, Et<sub>2</sub>O or H<sub>2</sub>O. [Reichstein Angew Chem 74 887 1962.]

*N*-Tosyl-L-lysine chloromethyl ketone (3*S*-1-chloro-3-tosylamino-7-amino-2-heptanone HCl) [4272-74-6] M 369.3, m 150-153°(dec), 156-158°(dec), ~165°(dec),  $[\alpha]_D^{20}$ -7.3° (c 2, H<sub>2</sub>O), pK<sub>Est</sub> ~ 10.6 (7-NH<sub>2</sub>). The hydrochloride slowly crystallises from a conc soln in absolute EtOH,

#### Purification of Biochemicals and Related Products

thinned with EtOH-Et<sub>2</sub>O for collection and dried *in vacuo*. It is a suicide enzyme inhibitor [Matsuda et al. *Chem Pharm Bull Jpn* **30** 2512 1982; Shaw et al. *Biochemistry* **4** 2219 1965].

**Transferrin (from human or bovine serum)** [11096-37-0] M<sub>r</sub>~80,000. Purified by affinity chromatography on phenyl-boronate agarose followed by DEAE-Sephacel chromatography. The product is free from haemopexin. [Cook et al. Anal Biochem 149 349 1985; Aisen and Listowsky Ann Rev Biochem 49 357 1980.]

**Trehalase** (from kidney cortex) [9025-52-9] [EC 3.2.1.28]. Purified by solubilising in Triton X-100 and sodium deoxycholate, and submitting to gel filtration, ion-exchange chromatography, conA-Sepharose chromatography, phenyl-Sepharose CL-4B hydrophobic interaction chromatography, Tris-Sepharose 6B affinity and hydrolyapatite chromatography. Activity was increased 3000-fold. [Yoneyama Arch Biochem Biophys 255 168 1987.]

**Trifluoperazine dihydrochloride (10-[3-{4-methyl-1-piperazinyl}propyl]-2-trifluoro-methylphenothiazine 2HCl)** [440-17-5] M 480.4, m 240-243°, 242-243°, pK<sub>1</sub> 3.9, pK<sub>2</sub> 8.1. Recrystd from abs EtOH dried *in vacuo* and stored in tightly stoppered bottles because it is *hygroscopic*. It is soluble in H<sub>2</sub>O but insoluble in  ${}^{*}C_{6}H_{6}$ , Et<sub>2</sub>O and alkaline aqueous soln. It has UV  $\lambda_{max}$  at 258 and 307.5nm (log  $\varepsilon$  4.50 and 3.50) in EtOH (neutral species). [Craig et al. J Org Chem 22 709 1957.] It is a calmodulin inhibitor [Levene and Weiss J Parmacol Exptl Ther 208 454 1978], and is a psychotropic agent [Fowler Arzneim.-Forsch 27 866 1977].

**T4-RNA ligase (from bacteriophage-infected** *E.coli*)  $M_r$  **43,500 [EC 6.5.1.3** for RNA lyase]. Purified by differential centrifugation and separation on a Sephadex A-25 column, then through hydroxylapatite and DEAE-glycerol using Aff-Gel Blue to remove DNAase activity. (Greater than 90% of the protein in the enzyme preparation migrated as a single band on gradient polyacrylamide gels containing SDS during electrophoresis.) [McCoy et al. *Biochim Biophys Acta* **562** 149 *1979*.]

**Tubercidin** (7-deazaadenosine) [69-33-0] M 266.3, m 247-248°,  $[\alpha]_D^{17}$ -67° (50% aq AcOH), pK<sup>10</sup> 5.2-5.3. Forms needles from hot H<sub>2</sub>O. It is soluble in H<sub>2</sub>O (0.33%), MeOH (0.5%) and EtOH 0.05%). It has UV  $\lambda_{max}$  270nm ( $\epsilon$  12100) in 0.001N NaOH. The *picrate* has m 229-231°(dec). [Tolman et al. J Am Chem Soc 91 2102 1969; Mizuno et al. J Org Chem 28 3329 1963, IR: Anzai et al. J Antibiot (Japan) [9] 10 201 1957.]

**Tunicamycin** [11089-65-9] **m** 234-235°(dec),  $[\alpha]_D^{20} + 52°$  (c 0.5, pyridine),  $pK_{Est} \sim 9.4$ . The components are purified by recrystallising 3 times from hot glass-distilled MeOH and the white crystals are dissolved in 25% aqueous MeOH and separated on a Partisil ODS-10µ column (9.4 x 25 cm) [Magnum-9 Whatman] using a 260 nm detector. The column was eluted with MeOH:H<sub>2</sub>O mixture adjusted to 1:4 (v/v) then to 2:4 (v/v). The individual components are recovered and lyophilised. Ten components were isolated and all were active (to varying extents) depending on the lengths of the aliphatic side-chains. The mixture has UV  $\lambda_{max}$  205 and 260nm ( $A_{1cm}^{1\%}$  230 and 110). Stable in H<sub>2</sub>O at neutral pH but unstable in acidic soln. It inhibits protein glycosylation. [Mahoney and Duskin J Biol Chem 254 6572 1979; Elnein Trends Biochem Sci 6 219 1981; Takatsuki J Antibiot 24 215 1971.]

**Ubiquinol-cytochrome c reductase** (from beef heart mitochondria) [9027-03-6] [EC 1.10.2.2]. Purified in Triton X-100 by solubilising the crude enzyme with Triton X-100, followed by hydroxylapatite and gel chromatography. The minimum unit contains nine polypeptide subunits of  $M_r 6000 - 49000$  kD. [Engel et al. Biochim Biophys Acta 592 211 1980.]

Uracil, uridine and uridine nucleotides. Resolved by ion-exchange chromatography AG1 (Cl<sup>-</sup> form). [Lindsay et al. Anal Biochem 24 506 1968.]

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Uridine 5'-diphosphoglucose pyrophosphorylase (from rabbit skeletal muscle) [9029-22-6]  $M_r$  350,000, [EC 2.7.7.9]. Purified by two hydrophobic chromatographic steps and gel filtration. [Bergamini et al. Anal Biochem 143 35 1984.] Also purified from calf liver by (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (40-58%) pptn, Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> gel filtration, DEAE-cellulose chromatography and recrystn by dialysis against increasing concentrations of (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> (from 10%) in 0.02M TEA (at 2.5% increments) until at 20% (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> it crystallises out [Hansen et al. Methods Enzymol 8 248 1966].

Uridine 5'-(1-thio) monophosphate [15548-52-4, 18875-72-4 (Abs Stereochem specified)] and Uridine 5'-( $\alpha$ -thio) diphosphate [RS( $\alpha$ -P) 27988-67-6; R( $\alpha$ -P) 72120-52-6], pK<sub>Est(1)</sub>~ 6.4, pK<sub>Est(2)</sub>~ 9.5 The Et<sub>3</sub>N salt was purified by dissolving ~4g in 500mL of H<sub>2</sub>O (add a drop or two of Et<sub>3</sub>N if it does not dissolve) and chromatographed by applying to a column (3 x 30cm) of DEAE-Sephadex A-25 and eluted with a 1.4L linear gradient of Et<sub>3</sub>NH.HCO<sub>3</sub> from 0.05 to 0.55M, pH 7.8 and 4°. The product eluted between 0.2-0.3M Et<sub>3</sub>N.HCO<sub>3</sub>. Pooled fractions were evaporated and the residue was twice taken up in EtOH and evaporated to dryness to remove the last traces of Et<sub>3</sub>NH.HCO<sub>3</sub>. <sup>31</sup>P NMR: P<sub> $\alpha$ </sub> is a doublet at -40.81 and -40.33, and P<sub> $\beta$ </sub> at 7.02ppm, J<sub> $\alpha,\beta$ </sub> 32.96Hz. [Biochemistry 18 5548 1979.]

Uridylic acid (di-Na salt) [27821-45-0] M 368.2, m 198.5°,  $pK_3^{25}$  6.63,  $pK_4^{20}$  9.71. Crystd from MeOH.

**Urokinase (from human urine)** [9039-53-6]  $M_r$  53,000, [EC 3.4.21.31]. Crystn of this enzyme is induced at pH 5.0 to 5.3 (4°) by careful addition of NaCl with gentle stirring until the soln becomes turbid (silky sheen). The NaCl concentration is increased gradually (over several days) until 98% of saturation is achieved whereby the urokinase crystallises as colourless thin brittle plates. It can be similarly recrystd to maximum specific activity [104K CTA units/mg of protein (Sherry et al. J Lab Clin Med 64 145 1964)]. [Lesuk et al. Science 147 880 1965; NMR: Bogusky et al. Biochemistry 28 6728 1989.] It is a plasminogen activator [Gold et al. Biochem J 262 1989].

(+)-Usnic acid (2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyldibenzofuran-1,3(2H,9bH)-dione) [7562-61-0, 125-46-2] M 344.3, m 201-204°, 203-206°,  $[\alpha]_{546}^{20}$  +630° (c 0.7, CHCl<sub>3</sub>), pK<sub>1</sub> 4.4, pK<sub>2</sub> 8.8, pK<sub>3</sub> 10.7. This very weak acid is the natural form which is recrystd from Me<sub>2</sub>CO, MeOH or \*C<sub>6</sub>H<sub>6</sub>. At 25° it is soluble in H<sub>2</sub>O (<0.01%), Me<sub>2</sub>CO (0.77%), EtOAc (0.88%), MeOCH<sub>2</sub>CH<sub>2</sub>OH (0.22%) and furfural (7.32%). [Curd and Robertson J Chem Soc 894 1937; Barton and Brunn J Chem Soc 603 1953; resolution: Dean et al. J Chem Soc 1250 1953; synthesis: Barton et al. J Chem Soc 538 1956.]

(-)-Usnic acid (2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyldibenzofuran-1,3(2H,9bH)-dione) [6159-66-6, 7562-61-0] M 344.3, m 201-204°, 204°,  $[\alpha]_D^{20}$ -495° (c 0.9, CHCl<sub>3</sub>). Properties almost similar to those of the preceding entry.

Ustilagic acid (Ustizeain B, di-D-glucosyldihydroxyhexadecanoic acid) [8002-36-6] M ~780, m 146-147°,  $[\alpha]_D^{23}$  +7° (c 1, pyridine), pK ~ 4.9. It is a mixture of partly acetylated di-D-glucosyldihydroxyhexadecanoic acid which crysts from diethyl ether. Also purified from the culture by dissolving in hot MeOH, filtering and concentrating by blowing a current of air until the soln becomes turbid, then heating to 50° and adding 4 vols of H<sub>2</sub>O (also at 50°) and allowing to cool very slowly. Filter off the white solid and dry in air. [Lemieux et al. Can J Chem 29 409, 415 1951; Can J Biochem Physiol 33 289 1955.]

**Valinomycin** (Potassium ionophore I) [2001-95-8] M 111.3, m 186-187°, 190°,  $[\alpha]_D^{20} + 31.0°$  (c 1.6, \*C<sub>6</sub>H<sub>6</sub>). Recryst from dibutyl ether or Et<sub>2</sub>O. Dimorphic, modification A crystallises from *n*-octane, and modification B crystallises from EtOH/H<sub>2</sub>O. Soluble in pet ether, CHCl<sub>3</sub>, AcOH, BuOAc and Me<sub>2</sub>CO. [J Am Chem Soc 97 7242 1975; UV, IR and NMR see Chem Ber 88 57 1955.]

(±)-Verapramil hydrochloride (5-[N-{3,4-dimethoxyphenylethyl}methylamino]-2-[3,4-dimethoxyphenyl]-2-isopropylvaleronitrile HCl) [23313-68-0] M 491.1, m 138.5-140.5°,

 $pK_{Est} \sim 10.6$ . Purified by dissolving in EtOH, filtering (if insoluble particles are present) and adding Et<sub>2</sub>O, filtering the salt, washing with Et<sub>2</sub>O and drying *in vacuo*. It has the following solubilities: hexane (0.001%), CH<sub>2</sub>Cl<sub>2</sub> (~10%), MeOH (~10%) EtOH (20%) and H<sub>2</sub>O (8.3%). It has UV  $\lambda_{max}$  232 and 278nm. The *free base* is a viscous yellow oil b 243-246°/0.01mm (n<sub>D</sub><sup>25</sup> 1,5448) and is almost insol in H<sub>2</sub>O but sol in organic solvents. It is a Ca channel antagonist and is a coronary vasodilator. [Ramuz Helv Chim Acta 58 2050 1975; Harvey et al. Biochem J 257 95 1989.]

Veratridine (3-veratroylveracevine) [71-62-5] M 673.8, pK<sub>Est</sub> ~7 (quinolizidine N). A n alkaloid neurotoxin purified from veratrine. [McKinney et al. Anal Biochem 153 33 1986.]

Vinblastine sulfate (vincaleucoblastine) [143-67-9] M 909.1, m 284-285°,  $[\alpha]_D^{25}$ -28° (c 1, MeOH), pK<sub>1</sub> 5.4, pK<sub>2</sub> 7.4. Purified by recrystn from H<sub>2</sub>O and dried *in vacuo*. [Neuss et al. J Am Chem Soc 86 1440 1964.] The free base is recrystd from MeOH or EtOH and has m 210-212°, 211-216°,  $[\alpha]_D^{25}$ +42° (CHCl<sub>3</sub>); and has UV  $\lambda_{max}$  214 and 259nm (log  $\varepsilon$  4.73 and 4.21). The dihydrochloride dihydrate has m 244-246°. [Bommer et al. J Am Chem Soc 86 1439 1964.] It is a monoamine oxidase inhibitor [Keun Son et al. J Med Chem 33 1845 1990].

Vincristine sulfate (22-oxovincaleucoblastine sulfate) [2068-78-2] M 925.1, m 218-220°,  $[\alpha]_D^{25}$  +26.2° (CH<sub>2</sub>Cl<sub>2</sub>), pK<sub>1</sub> 5.0, pK<sub>2</sub> 7.4 (in 33% aq Me<sub>2</sub>NCHO). Recryst from MeOH. It has UV  $\lambda_{max}$  220, 255 and 296nm (log  $\varepsilon$  4.65, 4.21 and 4.18). It is a monoamine oxidase inhibitor and is used in cancer research [Son et al. J Med Chem 33 1845 1990; Horio et al. Proc Natl Acad Sci USA 85 3580 1988].

**Viomycin sulfate** (Viocin, Tuberactinomycin B) [37883-00-4] M 685.7, m 266°(dec),  $[\alpha]_D^{17}$ -29.5° (c 1, H<sub>2</sub>O), pK<sub>1</sub> 7.2 (8.2), pK<sub>2</sub> 10.3. Crystd from H<sub>2</sub>O-EtOH and dried in a vacuum. Dry material is hygroscopic and should be stored dry. The UV has  $\lambda_{max}$  at 268 and 285nm (log  $\varepsilon$  4.4 and 4.2) in H<sub>2</sub>O. [Kitigawa et al. Chem Pharm Bull Jpn 20 2176 1972.] The hydrochloride forms hygroscopic plates with m 270°(dec),  $[\alpha]_D^{18}$ -16.6° (c 1, H<sub>2</sub>O) with  $\lambda_{max}$  268nm (log  $\varepsilon$  4.5) in H<sub>2</sub>O; 268nm (log  $\varepsilon$  4.4) in 0.1N HCl and 285nm (log  $\varepsilon$  4.3) in 0.1N NaOH.

Vitamin A acid [Retinoic acid, 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexenyl)-2,4,6,8nonatetraen-1-oic acid] [302-79-4] M 300.4, m 180-181°, 180-182°,  $pK_{Est} \sim 4.2$ . Purified by chromatography on silicic acid columns, eluting with a small amount of EtOH in hexane. Dissolve in Et<sub>2</sub>O, wash with H<sub>2</sub>O, dry (Na<sub>2</sub>SO<sub>4</sub>), evaporate and the solid residue crystd from MeOH (0.53g /3.5mL MeOH to give 0.14g) or EtOH. Also recrystd from *i*-PrOH, or as the *methyl ester* from MeOH. UV in MeOH has  $\lambda_{max}$ 351nm ( $\epsilon$  45,000). 9-Cis-acid forms yellow needles from EtOH, m 189-190°, UV in MeOH has  $\lambda_{max}$  343nm ( $\epsilon$  36,500) and 13-cis-acid forms red-orange plates from *i*-PrOH, m 174-175°, UV has  $\lambda_{max}$  345nm ( $\epsilon$  39,800). Store in the dark, in an inert atmosphere, at 0° [Robeson et al. J Am Chem Soc 77 4111 1955].

Vitamin A alcohol (retinol) [68-26-8] M 286.5,  $A_{1cm}^{1\%}$  ( $\lambda max$ )(all-trans) 1832 (325 nm), (13cis) 1686 (328nm), (11-cis) 1230 (319 nm), (9-cis) 1480 (323 nm), (9,13-di-cis) 1379 (324 nm), (11,13-di-cis) 908 (311 nm) in EtOH. Purified by chromatography on columns of waterdeactivated alumina eluting with 3-5% acetone in hexane. Separation of isomers is by TLC plates on silica gel G, developed with pet ether (low boiling)/methyl heptanone (11:2). Stored in the dark, under nitrogen, at 0°, as in diethyl ether, acetone or ethyl acetate. [See Gunghaly et al. Arch Biochem Biophys 38 75 1952.]

Vitamin A aldehyde [all-trans-retinal; 3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexenyl)-2,4,6,8-nonatetraen-1-al] [116-31-4] M 284.4, m 61-64°. Separated from retinol by column chromatography on water-deactivated alumina. Eluted with 1-2% acetone in hexane, or on TLC plates of silica gel G development. It crystallises from pet ether or *n*-hexane as yellow-orange crystals, and the UV in hexane has  $\lambda_{max}$  373nm ( $A_{1cm}^{1\%}$  1,548) [368nm ( $\varepsilon$  48000)]. It is an **irritant** and is light sensitive. Store in sealed ampoules under N<sub>2</sub>. The **semicarbazone** forms yellow crystals from CHCl<sub>3</sub>-Et<sub>2</sub>O or EtOH, m 199-201°(dec). The 9-cis-isomer [514-85-2] and the 13-cis-isomer [472-86-6] [ $\lambda_{max}$  375nm ( $\varepsilon$  1250) in EtOH] are also available commercially.

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Vitamin B<sub>1</sub> Hydrochloride [Aneurine hydrochloride, Thiamine hydrochloride,  $3{(4-amino-2-methyl-5-pyrimidinyl)methyl}-4-methylthiazolium chloride monohydrochloride] [67-03-8] M 337.3, m 248°(dec), 249-250°, monohydrate m 135°(dec), pK<sub>1</sub><sup>25</sup> 4.8, pK<sub>2</sub><sup>25</sup> 9.2. Crystallises from 95% EtOH (sol, ca 1%). The monohydrate is dehydrated by drying at 100° in vacuo over H<sub>2</sub>SO<sub>4</sub>, but is hygroscopic and picks up one mol. of H<sub>2</sub>O readily. It can be sterilised at 100° if the pH of the solution is below 5.5. The nitrate has m 196-200°(dec) and is more stable than the hydrochloride. The picrolonate crystallises from H<sub>2</sub>O and is dimorphic, m 164-165° and 228-229°(dec). [Todd and Bergel J Chem Soc 364, 367 1937; J Am Chem Soc 58 1063, 1504 1936, 59 526 1937.]$ 

Vitamin B<sub>2</sub> [Riboflavin, Lactoflavin, 6,7-dimethyl-9-(D-1'-ribityl)isoalloxazine] [83-88-5]M 376.4, m 278-282°(dec with darkening at 240°), 281-282°,  $[\alpha]_D^{25}$  -112° to -122° (c 2.5, 0.02M NaOH),  $[\alpha]_D^{20}$ -59° (c 0.23, AcOH), pK<sub>1</sub> 1.7, pK<sub>2</sub> 9.69 (10.2). It crystallises from H<sub>2</sub>O as a yellow-orange powder in three different forms with differing amounts of H<sub>2</sub>O. It melts if placed in an oil bath at 250°, but decomposes at 280° if heated at a rate of 5°/min. Solubility in H<sub>2</sub>O is 1g in 3000-15000mL depending on the crystal structure. Sol in EtOH at 25° is 4.5mg in 100mL. Store in the dark because it is decomposed to lumichrome by UV light.

Vitamin B<sub>6</sub> hydrochloride (adermine, pyridoxine HCl, 3-hydroxy-4,5-bis[hydroxymethyl]-2-methylpyridine HCl) [58-56-0] M 205.6, m 208-208.5°, 208-209°(dec), 209-210°(dec), 205-212° (sublimes),  $pK_1^{25}$ 5.0 (3-OH),  $pK_2^{25}$ 8.96 (pyridinium<sup>+</sup>). Purified by recrystn form EtOH-Me<sub>2</sub>CO, *n*-BuOH or MeOH-Et<sub>2</sub>O. Its solubility in H<sub>2</sub>O is 22% and in EtOH it is 1.1%. It is insoluble in Et<sub>2</sub>O and CHCl<sub>3</sub>. Acidic aqueous solns are stable at 120°/30 min. The *free base* has m 159-160° after recrystn from Me<sub>2</sub>CO and sublimation at 140-145°/0.0001mm. It has UV  $\lambda_{max}$  at 290nm ( $\epsilon$  84000) in 0.1N aqueous HCl and 253 and 325nm ( $\epsilon$  3700 and 7100). [Khua and Wendt Chem Ber 71 780 1938, 72 311 1939; Harris and Folkers J Am Chem Soc 61 1242 1939; Harris et al. J Am Chem Soc 62 3198 1940.] See also Pyridoxal-5'-phosphate H<sub>2</sub>O above.

Vitamin B<sub>12</sub> (cyanocobalamine,  $\alpha$ -[5,6-dimethylbenzimidazolyl]cyano cobamide) [68-19-9] M 1355.4, m darkens at 210-220° and does not melt below 300°, [ $\alpha$ ]  $^{23}_{656}$ -59° (H<sub>2</sub>O). Crystd from de-ionized H<sub>2</sub>O, solubility in H<sub>2</sub>O is 1g/80g and dried under vacuum over Mg(ClO<sub>4</sub>)<sub>2</sub>. The dry red crystals are hygroscopic and can absorb ~12% of H<sub>2</sub>O. A soln at pH 4.5-5 can be autoclaved for 20min at 120° without dec. Aqueous solns are stabilised by addition of (NH<sub>4</sub>)<sub>2</sub>SO<sub>4.</sub> [Golding Comprehensive Organic Chem Vol 5 (Ed. Haslam; Pergamon Press, NY, 1979) pp 549-584.]

Alternatively an aqueous soln of the coenzyme was concentrated, if necessary in a vacuum at 25° or less, until the concentration was 0.005 to 0.01M (as estimated by the OD at 522 nm of an aliquot diluted with 0.01M Kphosphate buffer pH 7.0). If crystals begin to form on the walls of the container they should be re-dissolved with a little H<sub>2</sub>O. The concentrated soln is placed in a glass stoppered flask and diluted with 5vols of Me<sub>2</sub>CO. After 2-3h at 3° it is centrifuged (10,000xg/10 min) in Me<sub>2</sub>CO-insol plastic tubes to remove some amorphous ppte. The clear supernatant is inoculated with a small crystal of the vitamin and allowed to crystallise overnight at 3°. Crystals are formed on the walls and the bottom of the container. A further 2vols of Me<sub>2</sub>CO are added and set aside at  $3^{\circ}$  to further crystallise. Crystallisation is followed by observing the OD<sub>522</sub> of the supernatant. When the OD falls to 0.27 then ca 94% of the crystals have separated. The supernatant is decanted (saved for obtaining a second crop) and the crystals are washed with a little cold 90% aqueous Me<sub>2</sub>CO (2 x), 100% Me<sub>2</sub>CO (2 x), Et<sub>2</sub>O (2 x) at which time the crystals separated from the glass walls. Allow to settle and remove residual Et<sub>2</sub>O with a stream of dry N<sub>2</sub>. The process can be repeated if necessary. The crystals can be dried in air or in a vacuum for 2h over silica gel at 100° with an 8-9% weight loss. [Barker et al. Biochem Prep 10 33 1963.] This material gives a single spot of paper chromatography [see Weissbach et al. J Biol Chem 235 1462 1960.] The vitamin is soluble in H<sub>2</sub>O (16.4mM at 24°, 6.4mM at 1°), in EtOH and PhOH but insol in Me<sub>2</sub>CO, Et<sub>2</sub>O, CH<sub>2</sub>Cl<sub>2</sub> and dioxane. UV:  $\lambda_{max}$  260, 375 and 522nm ( $\varepsilon$  34.7 x 10<sup>6</sup>, 10.9 x 10<sup>6</sup> and 8.0 x 10<sup>6</sup> / mole) in H<sub>2</sub>O. The dry crystals are stable for months in the dark, but aqueous solns decompose on exposure to VIS or UV light or alkaline CN<sup>-</sup>, but stable in the dark at pH 6-7. The vitamin is inactivated by strong acids or alkalies. [Barker et al. J Biol Chem 235 480 1960; see also Vitamin  $B_{12}$  (Zagalak and Friedrich Eds) W de Gruyter, Berlin 1979.]

Vitamin C see ascorbic acid entry on p. 116 in Chapter 4.

Vitamin D<sub>2</sub> [50-14-6] M 396.7, m 114-116°,  $[\alpha]_{546}^{20}$  +122° (c 4, EtOH) Converted into their 3,5-dinitrobenzoyl esters, and crystd repeatedly from acetone. The esters were then saponified and the free vitamins were isolated. [Laughland and Phillips Anal Chem 28 817 1956.]

Vitamin D<sub>3</sub> [67-97-0] 384.6, m 83-85°,  $[\alpha]_{546}^{20}$  +126° (c 2, EtOH). Converted into their 3,5dinitrobenzoyl esters, and crystd repeatedly from acetone. The esters were then saponified and the free vitamins were isolated. [Laughland and Phillips Anal Chem 28 817 1956.]

Vitamin E  $(2R,4'R,8'R-\alpha$ -tocopherol, natural active isomer) [59-02-9] M 430.7, m 2.5-3.5°, b 200-220°/0.1mm, 200°/0.005mm,  $d_4^{25}$  0.950,  $n_D^{25}$  1.5045,  $[\alpha]_D^{25}$  +3.58° (c 1.1, \*C<sub>6</sub>H<sub>6</sub>). Viscous yellow oil which is distd at high vacuum. It has  $\lambda_{max}$  294nm ( $E_{1cm}^{1\%}$  71). It is oxygen and light sensitive and is best stored as its stable acetate which is purified by evaporative distn at b 180-200°(bath temp)/0.7mm,  $[\alpha]_D^{25}$  +3.3° (c 5.1, EtOH). [NMR: Cohen et al. *Helv Chim Acta* 64 1158 1981; Burton and Ingold Acc Chem Res 19 194 1986; Karrer et al. *Helv Chim Acta* 21 520 1938.]

Vitamin E acetate (DL- $\alpha$ -tocopheryl acetate) [7695-91-2] M 472.8, m -27.5°, b 194-196°/0.01mm, 222-224°/0.3mm,  $d_4^{20}$  0.958,  $n_D^{20}$  1.4958. It is a viscous liquid which is purified by distn under high vacuum in an inert atm and stored in sealed ampoules in the dark. It is considerably more stable to light and air than the parent unacetylated vitamin. It is insoluble in H<sub>2</sub>O but freely soluble in organic solvents. All eight stereoisomers have been synthesised. The commercially pure *d*- $\alpha$ -*tocopheryl acetate* (2R,4'R,8'R) has b 180-200°/0.7mm and  $[\alpha]_D^{20}$ +3.9° (c 5, EtOH). [Cohen et al. *Helv Chim Acta* 64 1158 1981.]

Vitamin K<sub>1</sub> (2-methyl-3-phytyl-1,4-naphthoquinone) [84-80-0] M 450.7, m -20°, b 141-140/0.001mm, b 140-145°/10<sup>-3</sup> mm,  $d_{25}^{25}$  0.967,  $n_D^{25}$  1.527,  $[\alpha]_D^{20}$ -0.4° (c 57.5, \*C<sub>6</sub>H<sub>6</sub>). Yellow viscous oil, which can be distd at high vacuum practically unchanged. Insoluble in H<sub>2</sub>O, but soluble in common organic solvents. Store in the dark under N<sub>2</sub>, oxygen sensitive.  $A_{1cm}^{1\%}$  328 at 248nm. [J Am Chem Soc 61 2557 1939, 76 4592 1954; Helv Chim Acta 27 225 1954.]

Vitamin K<sub>3</sub> (2-methyl-1,4-naphthoquinone, Menadione, Menaphthone) [58-27-5] M 172.2, m 105-106°, 105-107°. Recrystd from 95% EtOH, or MeOH after filtration. Bright yellow crystals which are decomposed by light. Solubility in EtOH is 1.7% and in  ${}^{*}C_{6}H_{6}$  it is 10%. It **IRRITATES** the mucous membranes and skin. [Fieser J Biol Chem 133 391 1940.]

**Xanthine** (2,6-dihydroxypurine, purine-2,6(1*H*,3*H*)dione) [69-89-6] M 152.1, pK<sub>1</sub> 0.8 [protonation of imidazole 7(9)NH], pK<sub>2</sub> 7.44 [monoanion 1(3)NH], pK<sub>3</sub> 11.12 [dianion 1,3-N<sup>2</sup>]. The monohydrate separates in a microcryst form on slow acidification with acetic acid of a solution of xanthine in dil NaOH. Also ppted by addition of conc NH<sub>3</sub> to its soln in hot 2N HCl (charcoal). After washing with H<sub>2</sub>O and EtOH, it is dehydrated on heating above 125°. Sol in H<sub>2</sub>O is 1 in 14,000 at 16° and 1 in 1,500 and separates as plates from boiling H<sub>2</sub>O. It has no m, but the *perchlorate* has m 262-264° [Lister *Heterocyclic Compounds, Fused Pyrimidines—Purines Part II*, Ed. Brown, J.Wiley & Sons, 1971].

Xanthopterin monohydrate (2-amino-4,6-dihydroxypteridine, 2-amino-pteridin-4,6(1H,5H)dione) [5979-01-1 ( $H_2O$ ), 119-48-8 (anhydr)] M 197.2, m <300°, pK<sub>1</sub> 1.6 (basic), pK<sub>2</sub> 6.59 (acidic), pK<sub>3</sub> 9.31 (acidic)(anhydrous species), and pK<sub>1</sub> 1.6 (basic), pK<sub>2</sub> 8.65 (acidic), pK<sub>3</sub> 9.99 (acidic)(7,8-hydrated species). Purification as for isoxanthopterin. Crystd by acidifying an ammoniacal soln, and collecting by centrifugation followed by washing with EtOH, ether and drying at 100° in vacuo. Paper chromatography R<sub>F</sub> 0.15 (*n*-PrOH, 1% aq NH<sub>3</sub>, 2:1), 0.36 (*n*-BuOH,AcOH, H<sub>2</sub>O, 4:1:1) and 0.47 (3% aq NH<sub>3</sub>). [Inoue and Perrin J Chem Soc 260 1962; Inoue Tetrahedron 20 243 1964; see also Blakley Biochemistry of Folic Acid and Related Pteridines North Holland Publ Co, Amsterdam 1969.] **Xanthotoxin** (Methoxalen, 9-methoxyfuro[3,2-g][1]benzopyran-7-one) [298-81-7] M 216.2, m 146-148°, 148°, 148-149°. Purified by recrystn from  ${}^{*}C_{6}H_{6}$ -pet ether (b 60-80°) as silky needles, EtOH-Et<sub>2</sub>O as rhombic prisms or hot H<sub>2</sub>O as needles. It is soluble in aqueous alkali due to ring opening of a lactone but recyclises upon acidification. It has UV  $\lambda_{max}$  in EtOH at 219, 249 and 300nm (log  $\varepsilon$ 4.32, 4.35 and 4.06) and <sup>1</sup>H NMR in CDCl<sub>3</sub> with  $\delta$  at 7.76 (d, 1H, J 10 Hz), 7.71 (d, 1H, J 2.5 Hz), 7.38 (s, 1H), 6.84 (d, 1H, J 2.5 Hz), 6.39 (d, 1H, J 10 Hz) and 4.28 (s, 3H). [Nore and Honkanen J Heterocycl Chem 17 985 1980.] It is a DNA intercalator and is used in the treatment of dermal diseases [Tessman et al. *Biochemistry* 24 1669 1985.]

Xylanase (from Streptomyces lividans) [37278-89-0] M<sub>r</sub> 43,000 [EC 3.2.1.8]. Purified by anion-exchange chromatography on an Accell QMA column and finally by HPLC using a ProteinPak DEAE 5PW anion-exchange column. Solutions were stored frozen at -70°. [Morosoli et al. Biochem J 239 587 1986; Wong et al. Microbiol Rev 52 305 1988.]

**Zeatin** (trans-N<sup>6</sup>-[4-hydroxy-3-methylbut-2-en-1-yl]adenine) [1637-39-4] M 219.3, m 207-208, 209-209.5°, pK<sub>1</sub> 4.4 (basic), pK<sub>2</sub> 9.8 (acidic). Purified by recrystn from EtOH or H<sub>2</sub>O. The UV has  $\lambda_{max}$  at 207 and 275nm ( $\epsilon$  1400 and 14650) in 0.1N aqueous HCl; 212 and 270nm ( $\epsilon$  17050 and 16150) in aqueous buffer pH 7.2; 220 and 276nm ( $\epsilon$  15900 and 14650) in 0.1N aq NaOH. The picrate has m 192-194° (from H<sub>2</sub>O) from which zeatin can be recovered by treatment with Dowex 1 x 8 (200-400 mesh, OH<sup>-</sup> form). [Letham et al. Aust J Chem 22 205 1969; Proc Chem Soc (London) 230 1964; Shaw and Wilson Proc Chem Soc (London) 231 1964.] It is a cell division factor (plant growth regulator) [Letham and Palni Ann Rev Plant Physiol 34 163 1983] and inhibits mitochondrial function [Miller Plant Physiol 69 1274 1982]. Its 9-riboside is a cytokine [McDonald and Morris Methods Enzymol 100 347 1985].

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Yohimbine 388

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Zone refining 16

50-00-0	245	53-16-7	231	57-47-6	231	60-18-4	383
50-01-1	253	53-19-0	166	57-48-7	246		
						60-19-5	383
50-02-2	187	53-41-8	113	57-50-1	354	60-20-8	540
50-03-3	541	53-59-8	551	57-53-4	282	60-23-1	525
50-04-4	523	53-70-3	191	57-55-6	338	60-24-2	282
50-07-7	549						
		53-84-9	551	57-57-8	339	60-27-5	524
50-14-6	576	53-96-3	82	57-62-5	513	60-29-7	204
50-22-6	523	54-06-8	98	57-63-6	533	60-31-1	506
50-23-7	541	54-11-5	552	57-67-0	354	60-34-4	293
50-27-1	231	54-28-4	571	57-68-1	354	60-35-5	81
50-28-2	533	54-43-0	186	57-83-0	338	60-46-8	212
50-29-3	134	54-47-7	563	57-85-2	356	60-54-8	569
50-30-6	197	54-62-6	512	57-87-4	230		
						60-56-0	282
50-32-8	123	54-64-8	470	57-88-5	170	60-80-0	115
50-33-9	328	54-85-3	272	57-91-0	317	60-81-1	333
50-36-2	521	54-92-2	273	57-94-3	383	60-82-2	333
50-50-0	317	54-95-5	303				
				57-97-6	213	61-25-6	556
50-55-5	348	54-96-6	190	58-89-9	255	61-54-1	382
50-56-6	554	55-21-0	119	58-00-4	513	61-72-3	281
50-69-1	349	55-22-1	272	58-08-2	152	61-73-4	292
50-70-4	352	55-55-0	288	58-15-1			
					110	61-78-9	106
50-71-5	100	56-03-1	132	58-18-4	301	61-78-2	132
50-76-0	508	56-04-2	302	58-22-0	356	61-82-5	111
50-78-2	92	56-06-4	189	58-27-5	576	61-90-5	278
50-79-3	197	56-10-0	106	58-46-8			
					356	62-13-5	510
50-81-7	116	56-12-2	104	58-55-9	366	62-23-7	310
50-84-0	196	56-17-7	524	58-56-0	575	62-38-4	557
50-85-1	173	56-18-8	189	58-58-2	563	62-44-2	86
50-89-5	369	56-23-1	205	58-61-7	98	62-51-1	
							506
50-98-6	230	56-23-5	157	58-63-9	269	62-53-3	113
50-99 <b>-</b> 7	251	56-34-8	359	58-64-0	508	62-54-4	407
51-05-8	561	56-40-6	102	58-85-5	515	62-55-5	367
51-17-2	122	56-45-1	351	58-86-6	387	62-56-6	369
51-20-7	142	56-47-3	527	58-90-2	358	62-57-7	107
51-21-8	535	56-49-5	290	58-96-8	384	62-74-8	470
51-28-5	221	56-54-2	346	59-00-2	386	62-75-9	217
51-34-3	267	56-55-3	119	59-02-9	571	62-76-0	474
51-35-4	265	56-57-5	313	59-02-9	576	63-42-3	277
51-36-5	197	56-65-5	509	59-05-2	511	63-68-3	284
51-41-2	553	56-75-7	520	59-14-3	517	63-74-1	354
51-43-4	230	56-81-5	252	59-23-4	250	63-89-8	
							531
51-43-4	510	56-82-6	252	59-31-4	266	63-91-2	327
51-44-5	197	56-84-8	116	59-46-1	338	63-92-3	326
51-45-6	258	56-85-9	251	59-49-4	126	64-04-0	325
51-48-9	571	56-86-0	251	59-50-7	164	64-10-8	333
51-49-0	570	56-87-1	280	59-51-8	284		231
						64-17-5	
51-52-5	341	56-88-2	524	59-52-9	209	64-18-6	246
51-55-8	116	56-89-3	525	59-53-0	507	64-19-7	83
51-60-5	308	56-92-8	258	59-56-3	537	64-20-0	363
51-67-2	383	56-93-9	131				
				59-66-5	83	64-67-5	205
51-78-5	109	57-06-7	102	59-67-6	308	64-69-7	269
51-79-6	235	57-09-0	158	59-85-8	411	64-72-2	513
52-21-1	561	57-10-3	255	59-88-1	330	64-73-3	527
52-39-1	99	57-11-4	353	59-92-7	530	64-75-5	569
52-52-8	105	57-13-6	383	59-96-1	326	64-85-7	186
52-67-5	556	57-14-7	216	60-00-4	237	64-86-8	522
52-89-1	525	57-24-9	353	60-09-3	103	65-22-5	563
52-90-4	525	57-27-2	303	60-10-6	227	65-45-2	350
53-03-2	337	57-41-0	225	60-11-7	212		
						65-46-3	525
53-06-5	523	57-44-3	202	60-12-8	330	65-49-6	111

65-71-4	369	71-55-6	374	75-56-9	341	77-85-0	382
65-82-7	91	71-62-5	574	75-57-0	363	77-86-1	381
65-85-0	122	71-67-0	405	75-58-1	363	77-92-9	171
66-22-8	383	71-91-0	359	75-59-2	363	77-95-2	346
66-23-9	506	72-18-4	385	75-60-5	405	77-99-6	378
66-27-3	294	72-19-5	369	75-62-7	142	78-00-2	481
66 <b>-</b> 71-7	324	72-40-2	106	75-63-8	142	78-09-1	360
66-84-2	251	72-43-5	285	75-64-9	145	78-10-4	481
		72-43-5	285 99	75-65-0	145	78-11-5	321
66-99-9	304					78-27-3	242
67-03-8	575	72-54-8	134	75-66-1	298		
67-42-5	238	72-55-9	134	75-71-8	198	78-28-4	297
67-43-6	203	72-80-0	199	75-72-9	169	78-40-0	487
67-47-0	263	73-03-0	527	75-73-0	157	78-42-2	494
67-48-1	170	73-22-3	383	75-76-3	482	78-46-6	417
67-51-6	219	73-24-5	97	75-77-4	489	78-50-2	492
67-52-7	118	73-32-5	272	75-78-5	419	78-53-5	418
67-56-1	284	74-11-3	161	75-79-6	442	78-59-1	273
67-63-0	273	74-31-7	226	75-83-2	214	78-61-1	117
67-64-1	84	74-39-5	309	75-84-3	218	78-71-7	134
67-66-3	163	74-79-3	115	75-85-4	112	78-76-2	137
67-68-5	219	74-82-8	283	75-86-5	84	78-77-3	271
67-71-0	219	74-83-9	289	75-87-6	159	78-78-4	289
67-72-1	255	74-84-0	231	75-89-8	377	78-79-5	273
67-96-9	207	74-85-1	237	75-91-2	148	78-82-0	272
67-97-0	576	74-86-2	89	75-94-5	496	78-83-1	298
67-99-2	537	74-87-3	290	75-97-8	150	78-84-2	272
68-04-2	495	74-88-4	294	75-98-9	337	78-85-3	283
68-05-3	359	74-89-5	288	76-01-7	320	78-86-4	162
68-11-1	367	74-90-8	430	76-03-9	374	78-87-5	200
68-12-2	215	74-96-4	234	76-05-1	376	78-90-0	338
		74-90-4	338	76-06-2	167	78-93-0	144
68-19-9	575	74-98-0	338 341	76-09-5	336	78-93-0	302
68-26-8	574				358		
68-41-7	524	75-00-3	235	76-12-0		78-95-5	160
68-81-9	180	75-03-6	239	76-13-1	375	78-98-8	293
68-81-5	269	75-04-7	234	76-16-4	256	79-00-5	374
68-94-0	265	75-05-8	85	76-19-7	316	79-01-6	374
69-05-6	564	75-07-0	81	76-24-4	100	79-05-0	339
69-33-0	572	75-08-1	231	76-37-9	360	79-06-1	95
69-57-8	514	75-09-2	198	76-39-1	296	79-07-2	160
69-65-8	281	75-11-6	208	76-57-3	522	79-08-3	136
69-72-7	350	75-12-7	245	76-59-5	142	79-09-4	339
69-89-6	576	75-15-0	156	76-60-8	138	79-10-7	95
69-93-2	384	75-18-3	219	76-73-3	351	79-11-8	160
70-11-1	136	75-19-4	182	76-74-4	322	79-14-1	252
70-18-8	538	75-21-8	238	76-75-2	283	79-15-2	136
70-23-5	235	75-22-9	404	76-83-5	381	79-16-3	287
70-26-8	318	75-24-1	392	76-84-6	381	79-19-6	369
70-34-8	221	75-25-2	138	76-86-8	412	79-20-9	287
70-47-3	116	75-26-3	274	76-87-9	494	79-24-3	311
70-47-5	368	75-28-5	271	76-93-7	122	79-27-6	356
70-49-3	370	75-29-6	274	77-06-5	250	79-29-8	214
70-55-5	110	75-30-9	274	77-09-8	326	79-31-2	272
70-09-9	265	75-33-2	339	77-21-4	240	79-33-4	277
70-70-2	203	75-34-3	198	77-26-9	102	79-34-5	358
71-00-1	270	75-34-3	198 88	77-47-4	255	79-34-3	169
71-00-1	238 340	75-44-5	450	77-48-5	193	79-39-0	283
	540 527	75-44-5	430 269	77-48-5	296	79-40-3	283
71-30-7			209 378	77-49-6	290 158	79-40-3 79-41-4	283
71-36-3	143	75-50-3 75-52-5		77-55-2 77-59-8	571	79-41-4	285 196
71-41-0	111		311				
71-43-2	119	75-54-7	441	77-71-4	216	79-44-7	215

79-46-9	313	83-40-9	173	86-74-8	156	89-82-7	342
79-49-2	320	83-43-2	547	86-84-0	307	89-86-1	207
79-57-2	568	83-44-3	186	86-87-3	306	89-98-5	160
79-58-3	349	83-46-5	351	86-88-4	307	90-00-6	240
79-63-0	277	83-48-7	353	86-93-1	331	90-01-7	260
79-69-6	270	83-49-8	267	86-98-6	200	90-02-8	350
79-74-3	190	83-56-7	208	87-13-8	204	90-04-0	113
79-77-6	270	83-60-3	348	87-17-2	350	90-05-1	253
79-81-2	348	83-67-0	366	87-32-1	93	90-11-9	140
80-05-7	274	83-72-7	264	87-41-2	334	90-12-0	295
80-11-5	296	83-73-8	208	87-42-3	168	90-13-1	165
80-15-9	175	83-74-9	267	87-48-9	139	90-15-3	305
80-43-3	201	83-88-5	575	87-51-4	258	90-19-7	348
80-46-6	112	84-11-7	324	87-52-5	253	90-20-0	108
80-48-8	302	84-12-8	325	87-56-9	304	90-26-6	328
80-40-0	369	84-15-1	355	87-61-6	374	90-30-2	331
80-62-6	294	84-16-2	257	87-62-7	213	90-33-5	548
80-70-6	364	84-17-3	202	87-66-1	345	90-41-5	104
80-72-8	348	84-21-9	508	87-68-3	323	90-43-7	<b>26</b> 0
80-78-4	351	84-24-2	334	87-72-9	115	90-44-8	115
80-91-1	338	84-54-8	288	87-73-0	349	90-45-9	103
80-92-2	338	84-58-2	197	87-81-0	355	90-46-0	387
	169	84-65-1	115	87-85-4	256	90-47-1	386
80-97-7							
81-07-2	122	84-66-2	205	87-86-5	320	90-52-8	107
81-08-3	126	84-68-4	196	87-87-6	206	90-65-3	319
81-13-0	555	84-74-2	195	87-88-7	159	90-80-2	251
81-14-1	276	84-79-7	277	87-89-8	543	90-82-4	341
81-16-3	307	84-80-0	576	88-04-0	162	90-90-4	137
81-23-2	186	84-86-6	305	88-06-2	375	90-91-5	570
81-24-3	355	84-88-8	266	88-14-2	249	90-93-7	134
81-24-5	170	84-89-9	306	88-15-3	92	90-94-8	303
81-27-6	351	85-01-8	324	88-16-4	161	90-96-0	210
81-31-2	386	85-02-9	124	88-19-7	370	90-98-2	197
81-54-9	342	85-18-7	169	88-21-1	318	90-99-3	225
81-61-8	346	85-31-4	367	88-27-7	194	91-00-9	225
81-64-1	347	85-32-5	253	88-30-2	377	91-01-0	121
81-77-6	268	85-41-6	334	88-31-1	368	91-02-1	126
81-81-2	386	85-44-9	334	88-58-4	195	91-10-1	211
							193
81-84-5	305	85-46-1	305	88-65-3	137	91-13-4	
81-88-9	348	85-47-2	304	88-67-5	269	91-15-6	334
81-92-5	326	85-52-9	125	88-72-2	314	91-16-7	210
81-93-6	326	85-61-0	522	88-73-3	165	91-17-8	184
82-02-0	276	85-66-5	342	88-74-4	309	91-18-9	341
82-05-3	119	85-83-6	354	88-75-5	312	91-19-0	347
82-22-4	115	85-84-7	120	88-88-0	335	91-20-3	304
82-24-6	103	85-85-8	345	88-89-1	335	91-22-5	347
	288		354	88-99-3	334	91-23-6	309
82-38-2		85-86-9					
82-57-5	386	85-98-3	203	89-01-0	342	91-40-7	327
82-58-6	279	86-00-0	310	89-05-4	345	91-48-5	329
82-62-2	374	86-28-2	235	89-25-8	297	91-52-1	210
82-68-8	320	86-29-3	224	89-32-7	345	91-53-2	533
82-71-3	353	86-34-0	326	89-51-0	258	91-56-5	270
82-86-0	81	86-35-1	240	89-52-1	88	91-57-6	295
82-94-0	293	86-38-4	199	89-56-5	173	91-58-7	165
83-07-8	103	86-42-0	111	89-57-6	111	91-59-8	306
83-12-5	331	86-48-6	306	89-61-2	199	91-60-1	368
83-30-7	377	86-55-5	305	89-63-4	165	91-62-3	300
83-32-9	81	86-57-7	312	89-65 <b>-</b> 6	271	91-63-4	300
83-34-1	294	86-59-9	347	89-69-0	374	91-64-5	173
83-38-5	196	86-73-7	243	89-73 <b>-</b> 6	350	91-65-6	203

91-66-7	202	94-36-0	125	97-00-7	162	99-30-9	199
91-94-1	196	94-41-7	119	97-02-9	220	99-32-1	159
92-06-8	355	94-53-1	337	97-23-4	199	99-33-2	221
92-24-0	304	94-59-7	350	97-30-3	293	99-34-3	221
92-29-5	259	94-62-2	337	97-39-2	227	99-35-4	380
92-29-3	346	94-67-7	350	97-41-6	236	99-54-7	199
92-35-3	367	94-74-6	164	97-44-9	<i>390</i>	99-55-8	296
92-41-1	304	94-75-7	200	97-53-0	242	99-56-9	312
92-51-3	131	95-03-4	164	97-56-3	103	99-57-0	109
92-52-4	132	95-13-6	268	97-59-6	99	99-61-6	309
92-59-1	128	95-14-7	124	97-62-1	239	99-65-0	220
92-61-5	350	95-15-8	124	97-63-2	239	99-73-0	140
92-62-6	338	95-20-5	294	97-65-4	275	99-76-3	<i>293</i>
92-66-0	137	95-45-4	216	97-67-6	280	99-77-4	240
92-67-1	104	95-47-6	387	97-88-1	149	99-81-0	140
92-69-3	260	95-48-7	173	97-90-5	237	99-87-6	183
92-70-6	306	95-49-8	169	97-93-8	391	99-90-1	136
92-71-7	225	95-50-1	196	97-94-9	487	99-92-3	103
92-76-2	263	95-51-2	160	97-95-0	235	99-93-4	259
92-77-3	263	95-52-3	245	97-97-2	160	99-94-5	371
92-82-0	325	95-53-4	371	98-00-0	249	99-96-7	260
92-82-0	386	95-54-5	329	98-01-1	249	99-97-8	200
	326		109		368	99-99-0	315
92-84-2		95-55-6		98-03-3			
92-85-3	366	95-56-7	140	98-05-5	448	100-00-5	165
92-86-4	192	95-57-8	166	98-06-6	146	100-01-6	309
92-87-5	121	95-63-6	378	98-08-8	377	100-02-7	312
92-91-1	327	95-64-7	213	98-09-9	121	100-06-1	285
92-92-2	132	95-65-8	218	98-11-3	121	100-09-4	285
92-94-4	356	95-71-6	371	98-15-7	161	100-10-7	212
93-00-5	307	95-73-8	201	98-29-3	147	100-11-8	310
93-04-9	286	95-75-0	201	98-48-6	120	100-13-0	314
93-07-2	210	95-76-1	196	98-50-0	396	100-14-1	310
93-08-3	91	95-77-2	199	98-51-1	151	100-15-2	296
93-09-4	305	95-80-7	370	98-53-3	148	100-16-3	313
93-10-7	346	95-83-0	167	98-54-4	150	100-17-4	309
93-11-8	305	95-84-1	106	98-56-6	161	100-19-6	309
93-15-2	242	95-87-1	218	98-58-8	137	100-20-9	355
93-17-4	258	95-88-5	168	98-59-9	370	100-21-0	355
93-18-5	233	95-93-2	363	98-60-2	161	100-22-1	364
93-20-9	307	95-94-3	358	98-79-3	345	100-23-2	217
93-25-4	286	95-95-4	374	98-80-6	448	100-25-4	220
93-31-9	371	96-09-3	353	98-82-8	174	100-26-5	344
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603-54-3	226	612-14-6	120	620-24-6	260	627-06-5	303
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604-09-1	265	612-62-4	168	620-50-8	215	627-21-4	322
604-35-3	170	612-71-5	381	621-02-3	227	627-83-8	238
604-44-4	165	612-94-2	331	621-09-0	224	627-84-9	238
604-53-5	132	612-95-3	332	621-23-8	378	627-93-0	211
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604-68-2	251	613-12-7	288	621-42-1	<i>83</i>	628-02-4	155
604-69-3	251	613-31-0	206	621-59-0	275	628-13-7	344
604-88-6	255	613-78-5	307	621-66-9	262	628-28-4	150
605-49-1	196	614-75-5	264	621-82-9	171	628-41-1	178
605-60-7	314	614-80-2	83	621-84-1	127	628-63-7	111
605-69-6	221	615-18-9	162	622-15-1	225	628-63-7	322
605-94-7	522	615-20-3	161	622-21-9	201	628-81-9	148
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629-04-9	254	637-44-5	331	687-38-7	253	765-43-5	183
629-05-0	317	637-59-2	332	688-71-1	494	766-39-2	217
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629-14-1	238	637-84-3	377	688-74-4	485	767-15-7	105
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629-31-2	254	637-92-3	148	693-02-7	257	768-33-2	449
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629-45-8	148	638-38-0	439	693-65-2	112	768-91-2	288
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629-97-0	228	640-60-8	333	696-54-8	344	769-42-6	213
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633-71-6	263	658-78-6	313	723-62-6	114	804-63-7	347
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634-36-6	378	661-69-8	428	741-03-7	359	814-68-6	95
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634-66-2	358	666-99-9	98	754-05-2	492	814-81-3	415
634-67-3	374	670-54-2	359	754-34-7	323	814-95-9	478
634-83-3	358	672-15-1	258	758-96-3	219	818-08-6	418
634-90-2	358	673-40-5	137	759-24-0	203	818-88-2	350
634-93-5	374	673-84-7	217	760-21-4	235	819-83-0	421
635-21-1	104	674-26-0	548	760-32-7	418	821-06-7	192
635-51-8	332	674-76-0	297	760-93-0	283	821-48-7	133
635-65-4	132	674-82-8	209	761-35-3	531	822-23-1	316
635-78-9	460	674-82-8	276	761-65-9	195	822-36-6	294
635-93-8	169	675-20-7	384	762-21-0	202	822-67-3	180
636-04-4	367	676-97-1	441	762-62-9	218	823-18-7	178
636-09-0	205	677-53-6	367	762-72-1	390	823-76-7	89
636-30-6	374	677-69-0	254	763-29-1	297	823-96-1	488
636-70-4	375	680-31-9	428	763-10-0	537	824-07-9	354
636-73-7	344	681-84-5	482	764-13-6	216	824-35-1	408
636-98-6	269	684-16-2	255	764-35-2	258	824-72-6	449
637-01-4	364	685-87-0	203	764-85-2	319	824-79-3	476
637-39-8	375	685-91-6	202	765-30-0	183	824-94-2	285

825-90-1         474         880.52.4         96         960.71.4         493         1074.82.4         457           826.73.3         124         882.06.4         311         961.07-9         528         1076.22.8         303           826.74.4         385         882.33-7         225         961.68.2         221         1076.33.6         201           827.14.0         469         886.38.4         225         975.17.7         330         1077.85.7         455           827.54.3         307         902.47.6         221         981.40.8         405         1081.34.1         556           825.51.3         96         915.35.5         254         992.55.6         400         1083.44.3         311           830.01.5         312         917.23.7         366         993.13.5         441         1085.92.3         417           830.81.9         306         91.92.0         488         995.45.9         466         1094.61.7         527           831.61.8         229         92.06.61         252         996.70.3         362         1095.90.5         547           835.64.3         264         919.62.0         488         995.45.9         466         10045.90.5 <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th>								
	825-90-1	474	880-52-4	96	960-71-4	493	1074-82-4	457
826-74-4         385         882-33-7         225         961-68-2         221         1076-43-3         1/20           827-19-0         469         886-38-4         225         975-17-7         330         1077-68-9         411           827-51-1         469         880-38-0         528         977-96-8         203         1079-66-9         411           827-51-3         307         902-47-6         521         981-40-8         405         1081-34-1         566           828-01-3         265         914-45-4         357         998-38-8         348         1081-34-1         568           828-01-3         265         917-63-1         468         994-33-5         441         1085-92-3         417           830-03-5         312         917-70-4         434         994-89-8         423         1088-50-8         546           830-81-6         268         919-62-0         488         994-59-9         486         1094-17-5         527           835-64-3         264         921-05-1         255         996-50-9         486         1094-17-5         527           835-64-3         264         921-07-1         525         996-50-9         486         1096-11-7								
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853-68-9       395       930-88-1       294       1003-03-8       182       1115-84-0       295         860-22-0       431       931-19-1       335       1003-67-4       335       1116-76-3       380         863-57-0       471       931-88-4       181       1003-73-2       335       1116-76-3       380         865-34-9       436       932-90-1       1/9       1003-78-7       2/9       1116-98-9       147         865-47-4       453       933-18-6       486       1005-24-9       155       1118-12-3       151         865-47-4       453       933-52-8       363       1005-56-7       329       1118-12-3       151         866-83-1       454       935-30-8       155       1007-32-5       128       1119-94-4       228         866-97-7       356       935-31-9       177       1007-42-7       258       1110-01-0       471         867-13-0       487       935-56-8       97       1008-72-6       399       1120-01-0       471         867-17-9       261       938-55-6       213       1010-95-3       548       1120-46-1       415         868-19-9       478       937-14-4       166					1002-62-6		1114-41-6	
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CHEMISTRY

# PURIFICATION OF LABORATORY CHEMICALS

## FIFTH EDITION

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### Christina L.L. Chai

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- The only complete source that covers the purification of laboratory chemicals that are commercially available in such an easy-to-use format
- Provides purification procedures for commercially available chemicals and biochemicals
- Includes an extremely useful compilation of ionisation constants

Now in its fifth edition, Purification of Laboratory Chemicals continues to provide laboratory scientists with a manual for purifying and increasing the purity of modern commercially available chemical substances.

The authors have written and revised six chapters that describe the aspects of purification and properties of chemical substances. In addition to detailing physical methods and procedures such as crystallization, distillation, chromatography, etc., the authors also address chemical methods and procedures used in purification including conversion to specific derivatives or complexes and regeneration of the original material in a much-purified form.

The book also outlines recent developments in synthesis (e.g., combinatorial chemistry, solid support chemistry, fluorous chemistry) and the corresponding purification procedures that will provide many of the commercially supplied chemical substances in years to come. Additionally, interesting perspective about the future of purification is provided by the authors, based on their years of experience.

The bulk of the book contains purification procedures (taken from the literature) of individual entries for commercially available organic compounds, inorganic and metal-organic compounds, and biochemical and related compounds respectively. The entries are accessible in alphabetical order, and in most cases synonymous names and/or abbreviations are included as well as the CAS (Chemical Abstracts Service) Registry Numbers. The physical properties have been entered, such as the molecular weight, melting and boiling points, and specific rotations if substances are optically active. Rapid purification procedures for common solvents have also been included after the respective extensive procedures.

New to this edition, the ionisation constants in the form of pK have been entered for ionisable compounds. These are followed by procedures, used to purify the substances, in most cases to analytical purity. An index of CAS Registry Numbers with the respective page numbers of the entries has been added as well, making it easy to locate any substance irrespective of which chapter it is in, and also rapidly telling the reader whether there is a purification procedure for that substance in this book.



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