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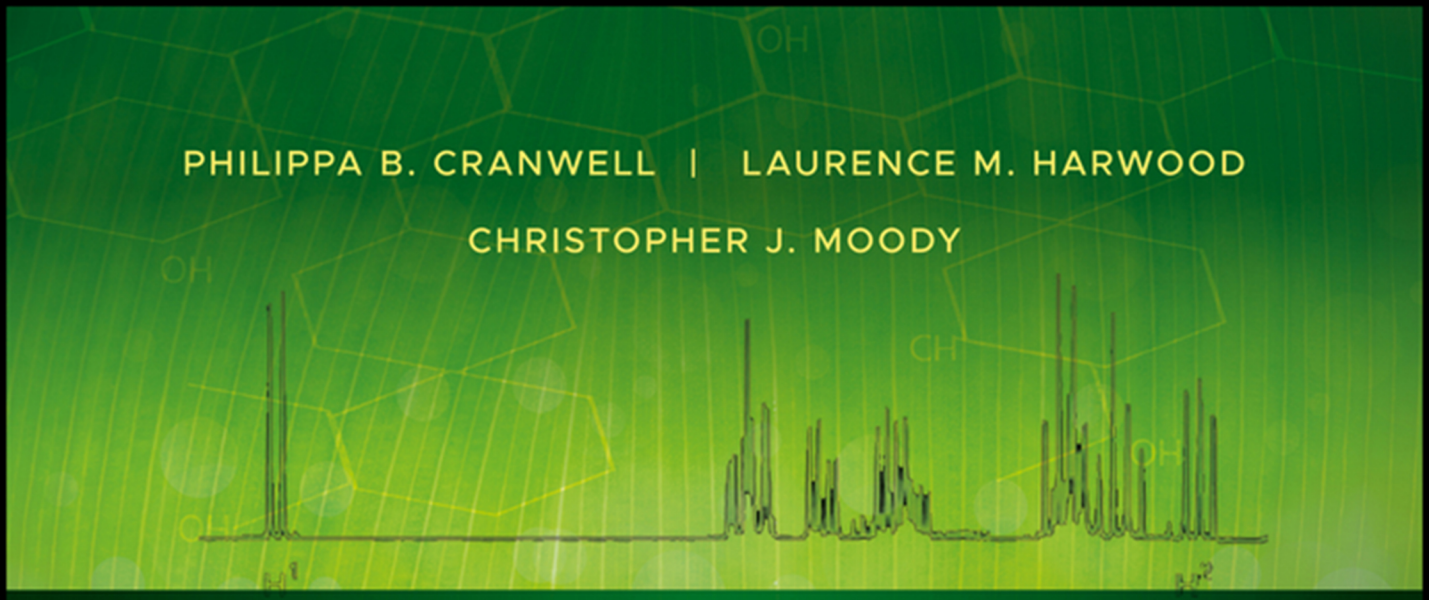

EXPERIMENTAL ORGANIC CHEMISTRY

THIRD EDITION

WILEY

Experimental Organic Chemistry

Experimental Organic Chemistry

Third Edition

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About the authors

Philippa B. Cranwell was born in Torquay, UK, and was educated at Torquay Girls' Grammar School and the University of Southampton. She carried out her PhD research at the University of Cambridge under the guidance of Steven Ley, and then undertook postdoctoral research at the ETH in Zürich, working with Erick Carreira, before taking up the position of Teaching Fellow, then Lecturer, at the University of Reading. Her research interests are within the area of organic chemistry, particularly with regard to the development of new reactions suitable for undergraduate students.

Laurence M. Harwood was born in Lincoln, UK, and was educated at the City Grammar School, then moving to Manchester University where he carried out his undergraduate studies and went on to carry out research under the supervision of Professor Hamish Sutherland, obtaining his PhD in 1978. After 2 years as a Royal Society Postdoctoral Fellow, working with Professor Marc Julia at the École Normale Supérieure in Paris, he returned to his first academic position at Manchester. In 1983, he was appointed to a lectureship at Oxford University and a fellowship at Merton College. In 1995 he moved to the Chair of Organic Chemistry at Reading. In 2001, he joined the team of Regional Editors for *Synlett*, in 2010 he was involved in the start-up company TechnoPep Ltd, in 2015 he took on the additional role of Director of the University of Reading Chemical Analysis Facility, and in 2017 he became the Associate Editor of SynOpen. His research interests range from natural product synthesis, through synthetic methodology, to synthesizing metal-selective ligands for use in nuclear waste treatment. His work has produced over 200 research publications and patents.

Christopher J. Moody was born in Manchester, UK, and was educated at Manchester Grammar School and King's College, London. He carried out his PhD research at the University of Liverpool under the supervision of Charles Rees, and spent a postdoctoral year at the ETH in Zürich working with Albert Eschenmoser, before taking up a post in industry at Roche. In 1979, he was appointed to a lectureship at Imperial College, London, renewing a collaboration with Charles Rees in parallel with establishing an independent research career. In 1990, he moved to the Chair of Organic Chemistry at Loughborough University, and in 1996 he was appointed Professor of Organic Chemistry at Exeter. He took up his present post as the Sir Jesse Boot Professor of Chemistry in the University of Nottingham in August 2005. His research interests range across organic chemistry, with a focus on the synthesis of biologically active molecules, particularly heterocyclic compounds and quinones. His work is reported in over 420 publications and patents.

Preface to the third edition

In its first incarnation, this book grew out of the conviction that highly developed practical skills, as well as a thorough grasp of theory, are the hallmark of a true organic chemist and that chemistry is illustrated more vividly by experiment than from a book or lecture course, when the facts can seem abstract and sterile. The original aim, therefore, was to produce a book containing safe, interesting experiments of varying complexity, together with all the associated technical instruction, which could be used in a variety of courses from the elementary to the advanced. With the goal of enthusing budding and current organic chemists, experiments were chosen to be more than just recipes for preparing a particular compound, or manipulative exercises. Rather, each experiment was associated with some important reaction, an interesting mechanism, or an underlying principle, without forgetting the practical skills to be acquired along the way. Within the constant and overriding demands for safety, the range of experiments was chosen to illustrate as many techniques and to cover as much organic chemistry as possible, in order to link up with lecture courses, and provide depth and relevance to the whole teaching programme.

So that was in the years running up to 1989 when the first edition appeared, to be followed by a second edition in 1999. Time has moved on, and this third edition of *Experimental Organic Chemistry*, arguably long overdue, has been born out of the recognition that much has happened in the field of organic chemistry since 1999, although the original aims espoused in the first edition still remain central.

Such progress has been made since 1989 that reactions and techniques that were once the domain of the specialist research laboratory – or indeed not even discovered when the first edition appeared – have now become commonplace in both academic and industrial environments – metal-catalysed cross-coupling reactions, metathesis, organocatalysis, microwave and flow chemistry are all now represented in the third edition. To this end, a new member has joined the writing team and it is doubtless that, without the professional ability, enthusiasm, verve and sheer determination to see the job finished by Dr Philippa Cranwell, this project would probably have withered and petered out. She is a very welcome addition to the team.

However, the third edition is not simply about the addition of new subject matter, but the removal of other material in recognition of the technical advances that have been made since this book was last updated. The almost immeasurable increase in computational power during the lifetime of this book has rendered much of the initial discussions of data storage and retrieval obsolete, as the power of the Internet reigns supreme and will only continue to evolve and gather force at an ever-increasing pace. As a result, most references to hardcopy data storage and retrieval have been removed, except for that last bastion of paper – the laboratory notebook – although it is recognized that, even here, its days are numbered.

If the Internet has changed for ever the way in which we obtain and exchange information, then technological advances combined with increased computing power have radically affected the way in which experimental data are measured and interpreted. This third edition contains expanded discussions of NMR and IR spectroscopic and mass spectrometric techniques that are now routine parts of the analytical arsenal of organic chemistry, while still retaining explanations of the fundamental principles of these techniques. UV spectroscopy is retained, even though it is recognized that this technique is rarely used in the research laboratory nowadays, except as a detection method in HPLC. So why have certain aspects of spectroscopic techniques been retained in the third edition? Quite simply, the more technology takes over, the more an analytical technique becomes a 'black box', so much so that the chemist may forget to question and challenge; accepting mutely, the data produced. Without a fundamental understanding and appreciation of a technique being used and its pitfalls and limitations, a scientist is treading on treacherous ground when carrying out spectroscopic analysis.

Nonetheless, some techniques described in the first edition and retained in the second have simply fallen out of practice and have been removed in recognition of standard practice in teaching and research laboratories at this time. However, it is not simply older practices that have been removed. In the second edition, microscale chemical techniques were included as, during that period, these were becoming popular in student teaching programmes in many universities. They now seem to have waned in popularity worldwide, so

microscale methodology and experimental procedures pertaining to student experiments have been removed, although small-scale protocols useful at the research level have been retained.

As in the previous two editions, the book is divided into two main sections – the first surveying aspects of safety, apparatus, purification and spectroscopic techniques, and the recording and retrieval of data, and the second containing the experimental procedures and appendices. As a result of the need to include examples of more recent synthetic methodologies, the experimental section has increased to 104 experimental procedures from the 86 contained in the second edition, almost back to the 105 contained in the first edition. More importantly, the range and choice of illustrative experiments more closely reflect the experimental environment in which today's organic chemists operate, from the fundamental to the more esoteric. As before, the experimental procedures have been further subdivided into chapters covering 'functional group interconversions', 'carbon–carbon bond-forming reactions' and 'projects', but an additional chapter covering 'enabling technologies' – microwave and flow chemistry – has been included. We are indebted to Associate Professor Nicholas Leadbeater of the University of Connecticut for providing procedures for the flow chemistry protocols contained in this chapter, and the Moody group at the University of Nottingham for the microwave chemistry protocols. Above all, we have continued to include examples of most of the important reaction types at varying levels of experimental difficulty, so that a concerted series of experiments might be designed that is tailored to the specific teaching needs of a class or an individual student.

Safety in the laboratory is, as always, the paramount consideration when choosing or retaining an experiment, and we have attempted to minimize potential hazards by avoiding toxic materials wherever possible and by highlighting in the text any possible hazards at appropriate points of the procedure. In addition, the scale of each standard experimental procedure has been kept as small as is commensurate with the level of difficulty, to minimize any adverse consequences of an accident, in addition to lessening disposal problems and cost. Nonetheless, health and safety regulations worldwide have become complex and sometimes contradictory, so the advice always is to assess the risk and validate all procedures with the local health and safety guidelines before commencing any experimental work.

Following feedback over the past 25 years or so, the experiments in this third edition have been included for their reproducibility and all have been independently assessed for such. Each experiment is preceded by a general discussion, outlining the aims and salient features of the investigation, and is followed by a series of problems designed to emphasize the points raised in the experiment. To emphasize safety aspects, make the greatest use of time available in the teaching laboratory and encourage forward planning, apparatus, instruments and chemicals required in the experiment are listed at the beginning of the procedure, together with an estimation of the amount of time necessary to complete the experiment. Extended periods of reflux or stirring have been avoided wherever possible and long experiments have been designed so that they have clear break points at roughly 3-hour intervals, indicated in margin notes in the procedure. The indicative degree of difficulty of each experiment is as follows:

1. Introductory-level experiments requiring little previous experience.
2. Longer experiments with the emphasis on developing basic experimental techniques.
3. Experiments using more complex techniques and spectroscopic analysis.
4. Research level.

Data on yields and melting points, useful hints and checkers' comments for each experiment, and guidelines for answers to all of the problems are available at the companion website: www.wiley.com/go/cranwell/EOC. Of course, almost all necessary data can be obtained from the Internet with a few clicks of a mouse or a few swipes of the finger. Nonetheless, some data tables are presented in appendices at the end of this book as we felt that these were likely to be of greatest use both to students working for their first degree and also to research workers.

In addition to those already mentioned, we would like to acknowledge others whose help has been fundamental in the production of this third edition. In alphabetical order, thanks go to Professor Matthew Almond (University of Reading), Professor Chris Braddock (Imperial College), Dr Geoff Brown (University of Reading), Professor Rainer Cramer (University of Reading), Dr Rob Haigh (University of Reading) and Associate Professor John Mckendrick (University of Reading). In addition, we reiterate our gratitude to all those individuals who gave their time, expertise and advice to assist with the production of the two preceding editions.

On the book production side, we would like to thank the Wiley team, in particular Jenny Cossham for her support, hard work and patience in making this third edition a reality, and Sarah Keegan for her dedication to seeing the project to completion.

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September 2016

About the companion website

This book is accompanied by a companion website:

www.wiley.com/go/cranwell/EOC

The website includes:

- PowerPoint files of all images in the book for downloading
- Instructor's Manual

Part 1

Laboratory practice

1

Safety in the chemical laboratory

The chemistry laboratory is a dangerous environment in which to work. The dangers are often unavoidable, since chemists regularly have to use hazardous materials. However, with sensible precautions, the laboratory is probably no more dangerous than your home, be it house or apartment, which, if you stop to think about it, also abounds with hazardous materials and equipment – household bleach, pharmaceutical products, herbicides and insecticides, natural or bottled gas, kitchen knives, diverse electrical equipment, the list goes on and on – all of which are taken for granted. In the same way that you learn to cope with the hazards of everyday life, so you learn good laboratory practice, which goes a long way to help minimize the dangers of organic chemistry.

The experiments in this book have been carefully chosen to exclude or restrict the use of exceptionally hazardous materials, while still highlighting and exemplifying the major reactions and transformations of organic chemistry. However, most chemicals are harmful in some respect, and the particular hazards associated with the materials **should not be ignored**. Unfortunately, it has not been possible to exclude totally the use of some chemicals, such as chloroform and dichloromethane, which are described as 'cancer suspect agents', but if handled correctly with proper regard for the potential hazard, there is no reason why such compounds cannot be used in the organic chemistry laboratory. Ultimately, laboratory safety lies with the individual; *you* are responsible for carrying out the experiment in a safe manner without endangering yourself or other people, and therefore it is *your* responsibility to learn and observe the essential safety rules of the chemical laboratory.

Prior to starting any experiment, a risk assessment should be prepared to identify the hazards, the likelihood of harm and any steps you can undertake to reduce the level of risk. The material safety data sheets (MSDSs) for any chemicals you are planning to use will provide valuable information. The risk assessment should also consider the end product and any intermediates that may be produced, as these may have hazardous properties.

Experimental Organic Chemistry, Third Edition. Philippa B. Cranwell, Laurence M. Harwood and Christopher J. Moody.

Companion website: www.wiley.com/go/cranwell/EOC

Legislation varies between the United Kingdom, Europe and the United States, therefore the references given in this section are generally for the UK only. Further information for a UK laboratory can be found at the following websites:

http://www.hse.gov.uk/coshh/basics/assessment.htm
http://www.hse.gov.uk/risk/controlling-risks.htm

1.1 Essential rules for laboratory safety

The essential rules for laboratory safety can be expressed under two simple headings: **ALWAYS** and **NEVER**.

Most of these rules are common sense and need no further explanation. Indeed, if asked to name the single most important factor that contributes towards safety in the laboratory, the answer is simple: common sense.

ALWAYS

- familiarize yourself with the laboratory safety procedures
- wear eye protection and a laboratory coat
- dress sensibly
- wash your hands before leaving the laboratory
- read the instructions carefully before starting any experiment
- check that the apparatus is assembled correctly
- handle all chemicals with great care
- keep your working area tidy
- attend to spills immediately
- ask your instructor if in doubt
- carry out a risk assessment

NEVER

- eat or drink in the laboratory
- smoke in the laboratory
- apply makeup in the laboratory
- inhale, taste or sniff chemicals
- fool around or distract your neighbours
- run in the laboratory
- work alone
- carry out unauthorized experiments

1.1.1 Laboratory safety procedures

Your laboratory will have certain safety procedures with which you must be familiar. Some of these procedures are legal requirements; others will have been laid down by the department. Make sure you know:

- where all the exits to the laboratory are, in the event of an evacuation because of fire or other incident;
- the precise location of fire extinguishers, fire blankets, sand buckets, safety showers and eye-wash stations;
- what type the fire extinguishers are and how to operate them, especially how to remove the safety pin.

If you are unsure of which type of extinguisher to use then do not attempt to fight the fire; the use of an incorrect type can, and probably will, make things worse.

1.1.2 Eye protection

You must wear eye protection at all times in the laboratory. Even if you are just writing in your notebook, your neighbour may be handling hazardous materials. The use of corrosive chemicals is not the only hazard for eyes, as many solvents are just as painful and irritating. Eyes are particularly vulnerable to damage from sharp objects such as broken glass and from chemicals, and therefore must always be protected to prevent permanent damage. Protection should be in the form of approved safety goggles or safety glasses (http://www.hse.gov.uk/foi/internalops/oms/2009/03/om200903app3.pdf). Ordinary prescription glasses do not provide adequate protection, since they do not have side shields and may not have shatter-proof lenses. If you are going to do a lot of laboratory work, it is probably worth obtaining a pair of safety glasses fitted with prescription lenses. Alternatively, wear goggles over your normal glasses for full protection. Contact lenses are often forbidden in chemical laboratories, because in the event of an accident, chemicals can get under the lens and damage the eye before the lens can be removed. Even if contact lenses are permitted, then you must wear well-fitting goggles for protection. Inform your instructor, the laboratory staff and your neighbours that you are wearing contact lenses so that they know what to do in case of accident. Although no experiments in this book require them, full face shields should be worn for particularly hazardous operations. If a chemical does get into the eye, you must take swift action. The appropriate action is discussed in Section 1.4.5.

Contact lenses

1.1.3 Dress

Dress sensibly in the laboratory. The laboratory is no place to wear your best clothes, since however careful you are, small splashes of chemicals or acids are inevitable. For this reason, shorts or short skirts are unsuitable for laboratory work and are forbidden in many institutions. A laboratory coat

should always be worn, and loose-fitting sleeves that might catch on flasks and other equipment should be rolled back. Long hair is an additional hazard, and should always be tied back. Proper shoes should be worn; there may be pieces of broken glass on the laboratory floor, and sandals do not provide adequate protection from glass or from chemical spills.

1.1.4 Equipment and apparatus

Never attempt to use any equipment or apparatus unless you fully understand its function. This is particularly true of items such as vacuum pumps, rotary evaporators and cylinders of compressed gas, where misuse can lead to the damage of expensive equipment, your experiment being ruined or, most serious of all, an accident. Remember the golden rule:

If in doubt, ask.

Before assembling the apparatus for your experiment, check that the glassware is clean and free from cracks or imperfections. Always check that the apparatus is properly clamped, supported and correctly assembled *before* adding any chemicals. Again, if in any doubt as to how to assemble the apparatus, ask.

1.1.5 Handling chemicals

Chemicals are hazardous because of their toxic, corrosive, flammable or explosive properties. Examples of the various categories of hazardous chemicals are given in the next section, but all chemicals should always be handled with great care. The major hazard in the organic chemistry laboratory is fire. Most organic compounds will burn when exposed to an open flame and many, particularly solvents that are often present in large quantities in the laboratory, are highly flammable. A serious solvent fire can raise the temperature of the laboratory to well over 100 °C within minutes of it starting. Good laboratory practice demands that there should be no open flames in the organic chemistry laboratory. Steam baths, heating mantles and hotplates should be used wherever possible to heat reaction mixtures and solvents. **Never** transfer a flammable liquid without checking that there are no open flames in the vicinity. Remember that solvent vapour is heavier than air and will therefore travel along bench tops and down into sinks and drains; never pour flammable solvents down the sink.

Always check for flammable solvents before lighting a burner

Never pour flammable solvents down the sink

Avoid inhaling the vapours from organic compounds at all times, and whenever possible use a reliable fume hood. The use of a good fume hood is essential for operations involving particularly toxic materials and for reactions that evolve irritating or toxic vapours.

Wear gloves when handling corrosive chemicals

Avoid skin contact with chemicals at all times. This is particularly important when handling corrosive acids and chemicals that are easily absorbed through the skin. It is best to wear disposable gloves that offer appropriate protection to the chemicals being handled (see MSDS for information); this minimizes the risk of chemicals coming into contact with the skin, but you must always be alert to the risk of seepage under the glove

that will exacerbate the dangers due to the material being held in close contact with the skin. The risk is also reduced by good housekeeping, ensuring that your bench and areas around the balance are kept clean and tidy. When highly corrosive or toxic chemicals are being handled, thin disposable gloves are inadequate and thick protective gloves must be worn. However, remember to remove gloves before leaving the laboratory; **do not contaminate door handles and other surfaces with soiled gloves.**

The gloves you use need to be appropriate for the task being undertaken. There are breakthrough times and chemical compatibility tests that will determine what to wear.

For the legislation surrounding chemical/microorganism gloves within Europe, see EN 374 (http://www.hse.gov.uk/foi/internalops/oms/2009/03/om200903app5.pdf).

1.1.6 Spills

All chemical spills should be cleared up immediately. Always wear gloves when dealing with a spill. Solids can be swept up and put in an appropriate waste container. Liquids are more difficult to deal with. Spilled acids must be neutralized with solid sodium hydrogen carbonate or sodium carbonate, and alkalis must be neutralized with sodium bisulfate. Neutral liquids can be absorbed with sand or paper towels, although the use of sand is strongly advised, since paper towels are not appropriate for certain spills. **Generation of gases as a result of using water or a damp paper towel could occur.**

If the spilled liquid is very volatile, it is often best to clear the area and let the liquid evaporate. When highly toxic chemicals are spilt, alert your neighbours, inform your instructor and ventilate and clear the area immediately.

If you are unsure of how to proceed then seek advice, as you could make things worse.

1.2 Hazardous chemicals

One of the fundamental rules of laboratory safety requires you to read the instructions before starting any experiment. In Europe, hazard symbols must conform to the Globally Harmonized System for labelling and packing (http://www.unece.org/trans/danger/publi/ghs/pictograms.html). Some examples of the commonly used symbols are shown in Fig. 1.1, and examples of each type of hazardous chemical are given in the following sections.

1.2.1 Flammable reagents

Always follow the general guidelines (Section 1.1.5) when handling flammable reagents.

Solvents constitute the major flammable material in the organic chemistry laboratory. The following organic solvents are all commonly used and are highly flammable: hydrocarbons such as *hexane*, *light petroleum* (*petroleum*

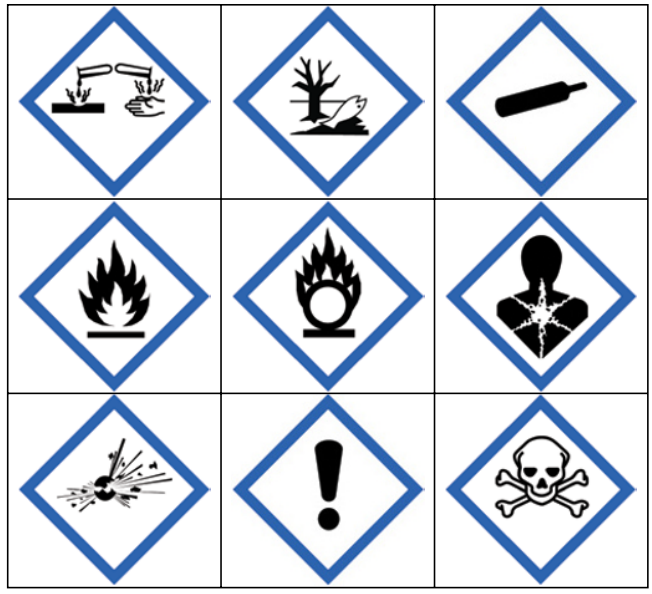

Fig. 1.1 Common hazard warning signs. Source: Reproduced from www.unece.org/trans/danger/publi/ghs/pictograms.html.

ether), *benzene* and *toluene*; alcohols such as *ethanol* and *methanol*; esters such as *ethyl acetate*; ketones such as *acetone*.

Ethers require a special mention because of their tendency to form explosive peroxides on exposure to air and light. *Diethyl ether* and *tetrahydrofuran* are particularly prone to this and should be handled with great care. In addition, diethyl ether has a very low flash point and has a considerable narcotic effect.

Carbon disulfide is so flammable that even the heat from a steam bath can ignite it. The use of this solvent should be avoided at all times.

Additionally, some gases, notably *hydrogen*, are highly flammable, as are some solids, particularly finely divided metals such as *magnesium* and *transition metal catalysts*. Some solids such as *sodium* and *lithium aluminium hydride* are described as flammable because they liberate hydrogen on reaction with water.

1.2.2 Explosive reagents

Some chemicals constitute explosion hazards because they undergo explosive reactions with water or other common substances. The alkali metals are common examples: *sodium metal* reacts violently with water; *potassium metal* reacts explosively with water.

Other compounds contain the seeds of their own destruction. This usually means that the molecule contains a lot of oxygen and/or nitrogen atoms, and can therefore undergo internal redox reactions, or eliminate a stable molecule such as N_2. Such compounds are often highly shock sensitive and constitute a considerable explosion hazard, particularly when dry. Examples include *polynitro compounds*, *picric acid*, *metal acetylides*,

azides, *diazo compounds*, *peroxides* and *perchlorate salts*. These are avoided in procedures described in this book.

If you have to use potentially explosive reagents, wear a face mask and work on the smallest scale possible and behind a shatter-proof screen. Never do so without consulting an instructor and alert others before commencing the procedure.

1.2.3 Oxidizers

Oxidizers are an additional hazard in the chemical laboratory, since they can cause fires simply by coming into contact with combustible material such as paper.

Nitric and *sulfuric acids*, in addition to being highly corrosive, are both powerful oxidizers.

Reagents such as *bleach*, *ozone*, *hydrogen peroxide*, *peracids*, *chromium(VI) oxide* and *potassium permanganate* are all powerful oxidizers.

1.2.4 Corrosive reagents

Always wear appropriate protective gloves when handling corrosive reagents. Spills on the skin should be washed off immediately with copious amounts of water.

The following acids are particularly corrosive: *sulfuric, hydrochloric*, *hydrofluoric*, *hydrobromic*, *phosphoric* and *nitric acid*, as are organic acids such as *carboxylic acids* and *sulfonic acids*. *Hydrofluoric acid* is particularly corrosive and should be treated with the greatest care because of its tendency to cause extreme burns and nerve damage if spilled.

Phenol is a particularly hazardous chemical and causes severe burns, in addition to being extremely toxic and rapidly absorbed through the skin.

Alkalis such as *sodium hydroxide*, *potassium hydroxide* and, to a lesser extent, *sodium carbonate* are also extremely corrosive, as are *ammonia*, *ammonium hydroxide* and organic bases such as *triethylamine* and *pyrrolidine*.

Bromine is an extremely unpleasant chemical. It causes severe burns to the skin and eyes and must be handled in a fume hood. In addition, its high density and volatility make it almost impossible to transfer without spills when using a pipette.

Thionyl chloride, *oxalyl chloride*, *aluminium chloride* and other reagents that can generate HCl by reaction with water are also corrosive and cause severe irritation to the respiratory system.

1.2.5 Harmful and toxic reagents

The distinction between *harmful* and *toxic* is one of degree; most organic compounds can be loosely described as harmful, but many are much worse than that, and are therefore classified as toxic. Commonly encountered compounds that are particularly toxic and therefore must always be

Always handle toxic chemicals in a fume hood

handled in a fume hood include: *aniline*, *benzene*, *bromine*, *dimethyl sulfate*, *chloroform*, *hexane*, *hydrogen sulfide*, *iodomethane*, *mercury salts*, *methanol*, *nitrobenzene*, *phenol*, *phenylhydrazine*, *osmium tetraoxide*, *potassium cyanide* and *sodium cyanide*. You must always be aware of the difference between *acute* and *chronic* toxicity. The effects of acute toxicity are usually recognizable more or less immediately (for example, inhalation of ammonia) and appropriate remedial action can be taken promptly. Chronic effects are much more pernicious, exerting their influence during long periods of exposure and generally manifesting their effects only when irrecoverable long-term damage has been caused. Many compounds are classed as *cancer suspect agents*, for instance. This need not negate their use in the laboratory, but does require particularly stringent precautions to avoid exposure and these compounds must always be handled in an efficient fume hood.

When using the fume hood, make sure that the glass front (sash) is pulled well down. This ensures sufficient air flow to prevent the escape of toxic fumes. As a general rule, never start any experiment involving a highly toxic chemical until you have read and understood the instructions and safety information, fully appreciate the nature of the hazard, and know what to do in the event of an accident.

1.2.6 Suspected carcinogens

The exposure of healthy cells to certain chemicals (carcinogens) is known to result in tumour formation. The period between the exposure and the appearance of tumours in people can be several years, or even decades, and therefore the dangers are not immediately apparent. The utmost care is required when handling such chemicals. This means that the chemical is either known to cause tumours in people or in animals, or is strongly suspected of doing so.

The following compounds or compound types should be treated as suspected carcinogens: biological alkylating agents such as *iodomethane*, *epoxides* and *dimethyl sulfate*; *formaldehyde*; *hexane*; *benzene*; aromatic amines such as *2-naphthylamine* and *benzidine*; polynuclear aromatic hydrocarbons (PAHs) such as *benzpyrene*; *hydrazines* in general, *hydrazine* itself and *phenylhydrazine*; *nitrosamines*; *azo compounds*; *chromium(VI) compounds*; chlorinated hydrocarbons such as *carbon tetrachloride*; *chloroform* and *vinyl chloride*; *thiourea* and *semicarbazide hydrochloride*.

1.2.7 Irritants and lachrymators

Many organic compounds are extremely irritating to the eyes, skin and respiratory system. To minimize the chance of exposure to the reagent or its vapours, the following chemicals should always be handled in a fume hood: *benzylic* and *allylic halides*, α-halocarbonyl compounds such as *ethyl bromoacetate*, *isocyanates*, *thionyl chloride* and *acid chlorides*.

Some organic compounds, in addition to being irritants, also have a particularly penetrating or unpleasant odour. These are usually indicated by the word **stench,** and examples include *pyridine*, *phenylacetic acid*,

dimethyl sulfide and many other sulfur-containing compounds, *butanoic acid*, *skatole* and *indole*. Again, these chemicals should be confined to a well-ventilated fume hood.

1.3 Disposal of hazardous waste

Waste disposal is one of the major environmental problems of modern society and the safe disposal of potentially hazardous chemical waste places a great burden of responsibility and expense on those in charge of laboratories. It is important that everyone who works in the organic chemistry laboratory appreciates the problems and exercises their individual responsibility to their fellow citizens and to the environment by not disposing of chemical waste in a thoughtless manner. In addition to statutory legal requirements, each laboratory will have its own rules and procedures for the disposal of chemical waste; we can only offer general advice and suggest some guidelines. More information about disposal methods can be found in the texts listed the end of this Chapter.

Think before disposing of any chemical waste

1.3.1 Solid waste

Solid waste from a typical organic chemistry laboratory comprises such things as spent drying agents and chromatographic supports, used filter papers, discarded capillaries from melting-point apparatus and broken glass. Common sense is the guiding principle in deciding how to dispose of such waste. Unless the solid is toxic or finely divided (e.g. chromatographic silica; see Section 3.3.6, subsection 'Disposal of the adsorbent'), it can be placed in an appropriate container for non-hazardous waste. Filter papers can be disposed of in this way unless, of course, they are contaminated with toxic chemicals. Toxic waste should be placed in special appropriately labelled containers. It is the responsibility of your laboratory staff and your instructor to provide these containers and see that they are clearly labelled; it is *your* responsibility to use them. Some toxic chemicals need special treatment to render them less toxic before disposal. This often involves oxidation, but your instructor will advise you when this is necessary.

Broken glass, discarded capillaries and other 'sharp' items should be kept separate from general waste and should be placed in an appropriately labelled glass or sharps bin. Chromatography silica should be transferred to polythene bags in a fume hood after removal of excess solvent, moistened with water and the bags sealed for later disposal.

1.3.2 Water-soluble waste

It is very tempting to pour water-soluble laboratory waste down the sink and into the public sewer system. It then becomes a problem for someone else, namely the water authority. This is bad practice. It is best not to dispose of anything down the sink and to place any waste in an appropriate container. If in doubt, consult local health and safety rules.

Never pour solvents down the sink

1.3.3 Organic solvents

Organic solvents are the major disposal problem in the organic chemistry laboratory. They are usually immiscible in water and highly flammable, and often accumulate very quickly in a busy laboratory. Waste solvent should be poured into appropriately labelled containers, never down the sink. The containers are then removed from the laboratory for subsequent disposal by an authorized waste contractor in accordance with local legislation. There should be two waste solvent containers – one for hydrocarbons and other non-chlorinated solvents, and one for chlorinated solvents. Chlorinated solvents have to be handled differently during the combustion process since they generate hydrogen chloride. It is therefore very important that you do not mix the two types of waste solvent. If the waste container is full, ask the laboratory staff or your instructor for an empty one; do not be tempted to use the sink as an easily available receptacle. **Burning of solvents is very tightly controlled by the Environment Agency (EA) in the United Kingdom and the Environmental Protection Agency (EPA) in the United States, so the use of licensed waste routes is preferable.**

Never mix chlorinated and non-chlorinated solvents

1.4 Accident procedures

In the event of a laboratory accident, it is important that you know what to do. Prompt action is always necessary, whatever the incident. **Tell your instructor immediately** or, if you are incapacitated or otherwise occupied in dealing with the incident, ensure that someone else informs the instructor. It is the instructor's responsibility to organize and coordinate any action required.

1.4.1 Fire

For anything but the smallest fire, the laboratory should be cleared. Do not panic, but shout loudly to your colleagues to leave the laboratory. If you hear the order from someone else, do not become inquisitive: **get out**.

1.4.2 Burning chemicals

The most likely contenders for chemical fires are organic solvents. If the fire is confined to a small vessel such as a beaker, it can usually be contained by simply placing a bigger beaker over the vessel. Sand is also very useful for extinguishing small fires, and laboratories are often equipped with sand buckets for this purpose. Remove all other flammable chemicals from the vicinity, and extinguish any burners. Since most flammable solvents are less dense than water, **water must never be used in an attempt to extinguish a solvent fire**; it will have the effect of spreading the fire rather than putting it out. For larger fires, a fire extinguisher is needed; a carbon dioxide or dry

chemical type should be used. However, the use of fire extinguishers is best left to your instructor or other experienced persons; incorrect use can cause the fire to spread. If the fire cannot be quickly brought under control using extinguishers, a general fire alarm should be sounded, the fire services summoned and the building evacuated.

1.4.3 Burning clothing

If your clothes are on fire, shout for help. Lie down on the floor and roll over to attempt to extinguish the flames. Do not attempt to get to the safety shower unless it is very near.

If a colleague's clothes catch fire, your prompt action may save his or her life. Prevent the person from running towards the shower; running increases the air supply to the fire and fans the flames. Wrap the person in a fire blanket or make them roll on the floor. Knock them over if necessary; a few bruises are better than burns. If a fire blanket is not immediately to hand, use towels or wet paper towels, or douse the victim with water. **Never use a fire extinguisher on a person**. If the safety shower is nearby then use it. Once you are sure the fire is out, make the person lie still, keep them warm and **send for qualified medical assistance**. Do not attempt to remove clothing from anyone who has suffered burns unless it is obstructing airways.

1.4.4 Burns

Minor heat burns from hot flasks, steam baths and the like are fairly common events in the organic chemistry laboratory. Usually the only treatment that such minor burns require is to be held under cold running water for 10–15 minutes. Persons with more extensive heat burns need immediate medical attention.

Any chemical that is spilled on the skin should be washed off immediately with copious amounts of running water; the affected area should be flushed for at least 15 minutes. If chemicals are spilled over a large area of the body, use the safety shower. It is important to get to the shower quickly and wash yourself or the affected person with large volumes of water. Any contaminated clothing should be removed, so that the skin can be thoroughly washed. **Obtain immediate medical attention**.

1.4.5 Chemicals in the eye

If chemicals get into the eye, time is of the essence, since the sooner the chemical is washed out, the less the damage. The eye must be flushed with copious amounts of water for at least 15 minutes using an eye-wash fountain or eye-wash bottle, or by holding the injured person on the floor and pouring water into the eye. You will have to hold the eye open with your fingers to wash behind the lids. **Always obtain prompt medical attention, no matter how slight the injury might seem**.

1.4.6 Cuts

Minor cuts from broken glass are a constant potential hazard when working in the chemistry laboratory. The cut should be flushed thoroughly with running water for at least 10 minutes to ensure that any chemicals or tiny pieces of glass are removed. Minor cuts should stop bleeding very quickly and can be covered with an appropriate bandage or sticking plaster. If the bleeding does not stop, obtain medical attention.

Major cuts, that is, when blood is actually spurting from the wound, are much more serious. The injured person must be kept quiet and made to lie down with the wounded area raised slightly. A pad should be placed directly over the wound and firm pressure should be applied. **Do not apply a tourniquet.** The person should be kept warm. **Prompt medical assistance is essential**; an ambulance and doctor should be summoned immediately.

1.4.7 Poisoning

No simple general advice can be offered. **Obtain medical attention immediately**.

Further reading

There are a number of texts that deal with laboratory safety practices in general and with the specific properties of, and disposal of, hazardous chemicals. These texts are written by safety experts and give far more detail than is possible in this book. If in doubt, consult the experts.

L. Bretherick, *Bretherick's Handbook of Reactive Chemical Hazards*, 7th edn, Academic Press, Oxford, 2008.
R.J. Lewis, *Hazardous Chemicals Desk Reference*, 6th edn, John Wiley & Sons, Hoboken, NJ, 2008.
G. Lunn and E.B. Sansone, *Destruction of Hazardous Chemicals in the Laboratory*, 3rd edn, John Wiley & Sons, Hoboken, NJ, 2012.

Recommended URLs:
http://www.hse.gov.uk/coshh/basics/assessment.htm
http://www.hse.gov.uk/risk/controlling-risks.htm
http://www.unece.org/trans/danger/publi/ghs/pictograms.html

2

Glassware and equipment in the laboratory

In this Chapter, we consider some of the standard pieces of glassware and equipment that you will use in the laboratory. The emphasis will be on descriptive detail; whereas Chapter 3 is largely concerned with experimental techniques and assembly of apparatus.

Broadly speaking, equipment can be divided into two categories – that which is communal and that which is personal. Cost is usually the factor that decides the category into which an item falls, although no hard and fast rules apply and any distinction is purely arbitrary. A further arbitrary division within each category might be made by dividing equipment into that which is glassware and that which is non-glassware. Glassware is fragile, so there is much more potential for breakage – particularly with personal glassware. Communal glass apparatus, such as rotary evaporators, tend to be built fairly ruggedly.

Adhering to the procedures described in this and the next Chapter will result in safe working and should help to minimize breakages that are costly, not only in financial terms, but also in popularity.

Remember the golden rule for working in a laboratory:

If in doubt, ask.

Never plunge headlong into a new procedure without first verifying the safe and correct way of carrying it out. Breaking a piece of apparatus is bad enough; injuring yourself – or somebody else – is a far worse consequence of carrying on regardless. *Never* rely simply on the advice of your neighbour; you must always get instruction from a qualified individual. *Never* be frightened of pestering and upsetting instructors; that is the job for which they are paid. In any event, the surest way to annoy an instructor is to break an expensive piece of equipment or cause an injury!

On entering the organic chemistry laboratory for the first time, the first job, of course, is to familiarize yourself with the laboratory safety procedures and with the location of fire extinguishers, safety showers, fire exits and so on. The second job is to check out the equipment; both personal equipment

Experimental Organic Chemistry, Third Edition. Philippa B. Cranwell, Laurence M. Harwood and Christopher J. Moody.

Companion website: www.wiley.com/go/cranwell/EOC

stored in your bench or locker, and communal equipment. Personal equipment can be divided into glass and non-glass (hardware), and your locker will contain a set of such items. Obviously there is no such thing as a standard set of equipment, since each laboratory provides what is deemed necessary for the courses that are taught therein, but our set (see Figs 2.1–2.4) is fairly typical for classes dealing with standard-scale laboratory procedures.

2.1 Glass equipment

Glass equipment can be divided into that with ground-glass joints and that without. For convenience and ease of use, standard-taper ground-glass joint equipment is strongly recommended. Apparatus for a range of organic experiments can be quickly and easily assembled from relatively few basic items. Standard-taper joints are designated by numbers that refer to the diameter and length of the joint (in mm): for example, 14/20, 14/23, 19/22, 19/26 and 24/29. As the name implies, standard-taper joints are fully interchangeable with those of the same size.

Standard-taper ground-glass joint equipment is expensive, but with careful handling is no more fragile than any other glassware. The only problem is with the joints themselves, and when assembling the apparatus it is usually better not to use grease. The only laboratory operations that require the use of grease on the ground-glass joints of the apparatus are vacuum distillations using oil pumps for pressures lower than about 5 mmHg, and reactions involving hot sodium or potassium hydroxide solutions that will attack the glass. If grease is used, it should be applied sparingly; a very thin smear around the joint is all that is required. Hydrocarbon-based greases are easier to remove from glassware than silicone greases. The misuse of grease can cause ground-glass joints to become stuck or 'frozen'. Occasionally this happens anyway and, of course, unless the joint can be unfrozen and the pieces of apparatus separated, the equipment becomes useless. As with many things, prevention is better than cure, and the best way to prevent frozen ground-glass joints is to disassemble the apparatus as soon as the experiment is finished. Wipe the joints clean, checking that they are completely free of chemicals. Never leave assembled dirty apparatus lying around the laboratory. If, despite precautions, ground-glass joints do become tightly frozen, it may be possible to loosen them by squirting a few drops of acetone (or another solvent) around the top of the joint. Capillary action may be sufficient to suck some solvent into the joint and loosen it. If this simple trick does not work, the joint may be loosened by gentle tapping or, failing that, by heating it with a heat gun – taking care to ensure that any flammable solvent that may have been used initially to unfreeze the joint has evaporated. However, these techniques must be left to an expert. If you are unfortunate enough to break a piece of equipment that has a standard-taper ground-glass joint, do not throw all the broken glass in the glass bin, but keep the ground glass joint (the expensive bit!) since your glass-blower may be able to utilize it. Some items of equipment, such as addition and separatory funnels, possess stopcocks. These may be made of ground glass or Teflon® and should be handled carefully to prevent the stopcock 'freezing' in the barrel. The correct use of

Care! Flammable solvent

separatory funnels is discussed in more detail in Section 3.2.4, subsection 'How to use a separatory funnel'.

A typical set of standard-taper glassware is shown in Fig. 2.1, and consists of:

- *round-bottomed flasks* for reactions, distillations;
- *three-neck flasks* for more complicated reaction set-ups (two-neck flasks are also available);
- *addition funnel* for adding liquids to reaction mixtures (may be cylindrical or pear-shaped);
- *separatory funnel* for extractions and reaction work-up;
- *condenser* for heating reaction mixtures under reflux, distillations;
- *air condenser* for high-boiling liquids (can also be packed and used as a fractionating column);
- *drying tube* for filling with a drying agent and attaching to the apparatus to reduce the ingress of water;
- *stoppers;*
- *reduction/expansion adapters* for connecting equipment with different-sized joints;
- *still head* for distillation;
- *Claisen adapter* for distillation or converting a simple round-bottomed flask into a two-neck flask;
- *distillation adapter for distillation;*
- *vacuum distillation adapter* for distillation under reduced pressure;
- *take off adapter* for attaching to tubing;
- *thermometer/tubing adapter* for inserting thermometer or glass tube into apparatus.

Non-graduated standard-scale glassware and other equipment without ground glass joints is much less expensive. A typical set might contain some of the items shown in Fig. 2.2:

- *beakers* for temporary storage or transfer of materials, reactions;
- *Erlenmeyer flasks* (or *conical flasks*) for recrystallization, collecting solutions after extraction (versions with ground-glass joints are also available);
- *funnel* for transfer of liquids, filtration;
- *powder funnel* for transfer of solids;
- *stemless funnel* for hot filtration;
- *filter flask* (Büchner flask) for suction filtration;

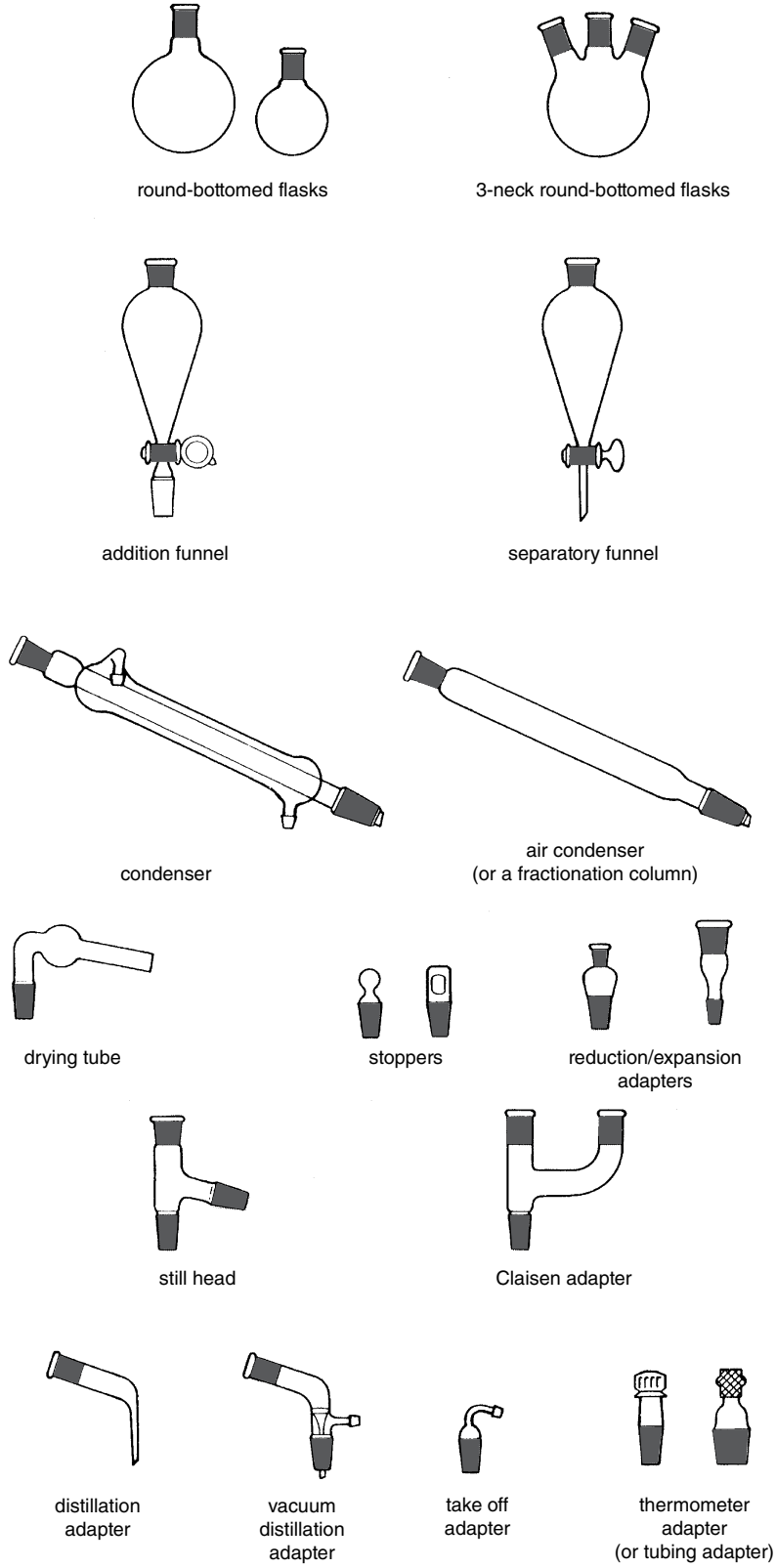

Fig. 2.1 Glass equipment with standard-taper ground-glass joints (not to scale).

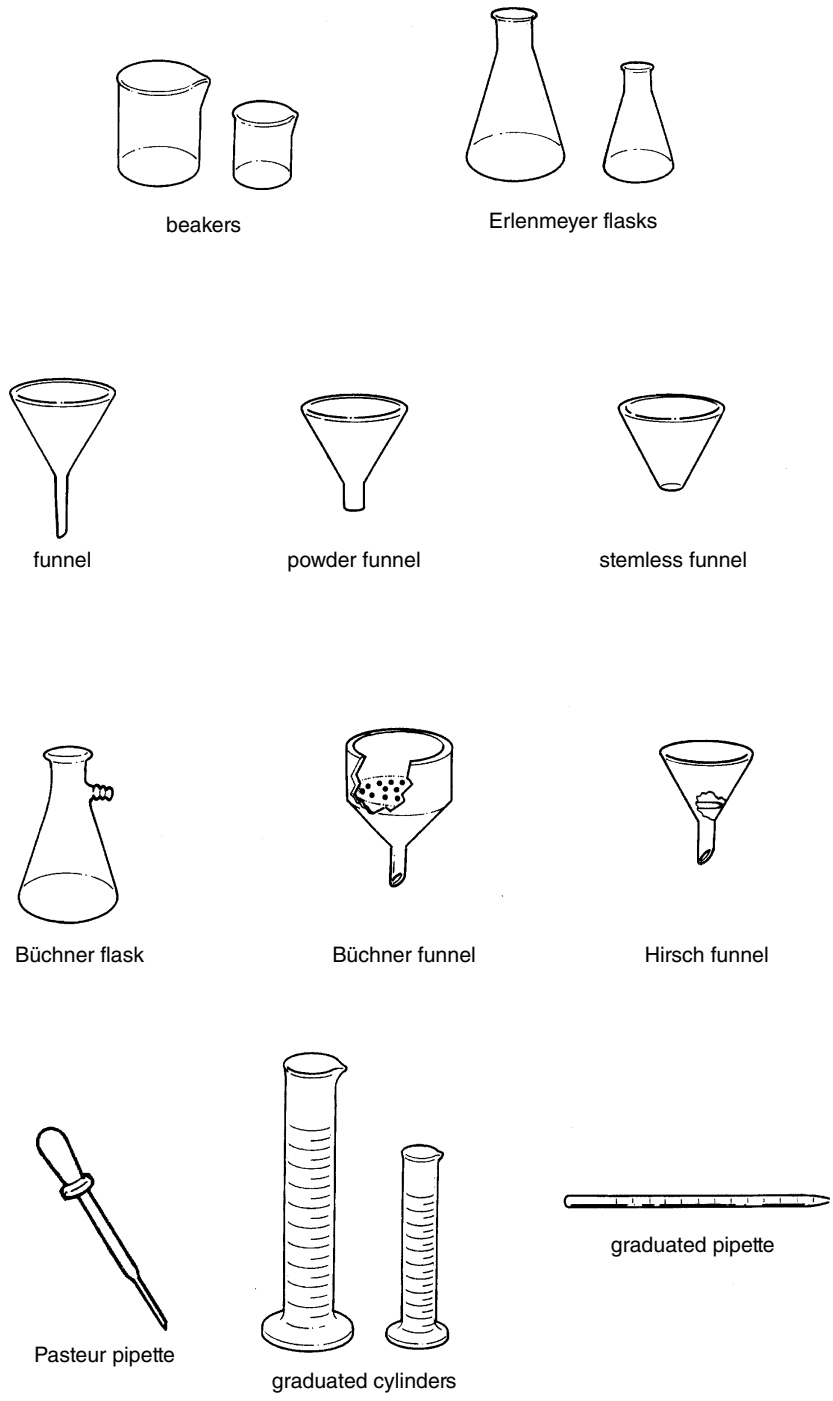

Fig. 2.2 Other standard glass equipment (not to scale).

- *Büchner funnel* for suction filtration;
- *Hirsch funnel* for suction filtration of small quantities;
- *Pasteur pipette* for transfer of smaller quantities of liquid;
- *graduated cylinders* for measuring liquids by volume;
- *graduated pipettes* for accurate measurement of liquids.

Check for cracks and or imperfections (stars)

When checking out the glassware in your bench, examine each piece carefully for imperfections such as cracks and 'star-cracks'. Star-cracks are often caused by two round-bottomed flasks impacting on each other, for example, if a drawer full of flasks is opened too rapidly, so care should be taken to ensure that round-bottomed flasks are not touching when stored. Any damaged equipment should be replaced from the stockroom. Try to get into the habit of checking glass equipment each time you use it. This is especially important for flasks; you certainly want to avoid a cracked flask breaking half way through a reaction or distillation.

2.1.1 Cleaning and drying glassware

Good laboratory practice requires that organic reactions are carried out in clean glassware. Unless the reaction is being carried out in aqueous solution, the glassware should also be dry, since many organic chemistry experiments are ruined by the presence of water.

Glassware can usually be cleaned with water and either industrial detergent or a mild scouring powder using an appropriate brush. Make sure that you clean all the inside of the piece, and that you rinse it thoroughly with water afterwards. The final rinse should be with distilled or deionized water, and the glassware should be left upside down on a drying rack or on absorbent paper to dry. The glassware can be dried more quickly by placing it in a drying oven, and this is essential if it is to be used for a reaction involving air- or moisture-sensitive reagents. For *complete* drying, glass should be left in an oven at 125 °C for at least 12 h (see also Section 3.1.4, subsection 'Drying the apparatus').

Use acetone sparingly for cleaning flasks. Acetone is flammable

The drying process can also be speeded up by rinsing the wet glassware with acetone. Acetone is freely miscible with water, and rinsing a wet flask with 5–10 mL of washing acetone (*not* reagent-grade acetone) removes the water. The acetone should be drained into the waste acetone bottle, not poured down the sink. The remaining acetone in the flask evaporates quickly in the air, but the drying can be speeded up by drawing a stream of air through the flask. To do this, connect a *clean* piece of glass tubing to the water aspirator via thick-walled tubing, turn on the suction and place the tube in the flask. Never use a compressed air line to dry equipment; the line is usually contaminated with dirt and oil from the compressor, and this will be transferred to your glassware. Alternatively, the flask can be dried with hot air using a hot-air blower of the 'hair dryer' type (see Section 2.3.4), but **remember that acetone is flammable**. Indeed, many laboratories do not permit the use of acetone for cleaning purposes because of the additional fire hazard, possible toxicity problems associated with long-term exposure and, of course, expense.

Do not use a compressed air line to dry glassware

Glassware that is heavily contaminated with 'black tars' or other polymeric deposits will not normally respond to washing with water and detergent, as the organic polymer is insoluble in water. Large amounts of tar material can often be scraped out with a spatula, but the remaining material usually has to be dissolved with an organic solvent. Acetone is usually used since it is a good solvent for most organic materials, although vigorous scrubbing and/or prolonged soaking may be necessary in stubborn cases. The dirty acetone should be poured into the waste container: many laboratories attempt to segregate washing acetone that has only been used to rinse water from a flask, and therefore can be reused, from dirty acetone that has been used to wash out tars. Always check that you are draining your acetone into the correct waste container.

Some books recommend the use of powerful oxidizing mixtures, such as sulfuric/nitric acid and chromic acid, as a last-resort technique for cleaning dirty glassware. **This practice should be strongly discouraged from the safety point of view as the mixtures used are all highly corrosive and some are potentially explosive.**

Clean up as you go

Cleaning and drying glassware are an unavoidable chore in the organic chemistry laboratory, but it is part of the job. However, it can be made much easier by following one simple rule: *clean up as you go along*. By cleaning glassware as soon as you have finished with it, you know exactly what was in it and how to deal with it, and freshly dirtied glass is much easier to clean than dried-out tars and gums. There will be plenty of periods during the laboratory class when you are waiting for a reaction to warm up or cool down, for a crystallization to finish and so on. Make use of such times to clean, rinse and dry your freshly dirtied glassware. It is thoroughly bad practice to put dirty glassware back into your locker at the end of the day, and it will certainly waste a lot more of your time in the subsequent laboratory period. Deposits are much more difficult to remove once they have dried onto the glassware.

2.2 Hardware

Your locker will also contain non-glass equipment such as that shown in Fig. 2.3. Many of these items, often known as hardware, are indispensable to experimental organic chemistry. A typical set will contain:

- *metal stand* for supporting apparatus;
- *clamps and holders* for supporting apparatus (the clamp jaws should be covered with a strip of cork or with a small piece of flexible tubing to prevent metal–glass contact);
- *metal rings* for supporting separatory funnels;
- *cork rings* for round-bottomed flasks;
- *spatulas* for the transfer of solids;
- *wash bottle* for dispensing water or wash acetone;
- *Neoprene® adapters* for suction filtration;
- *pinch/screw clamps* for restricting flexible tubing.

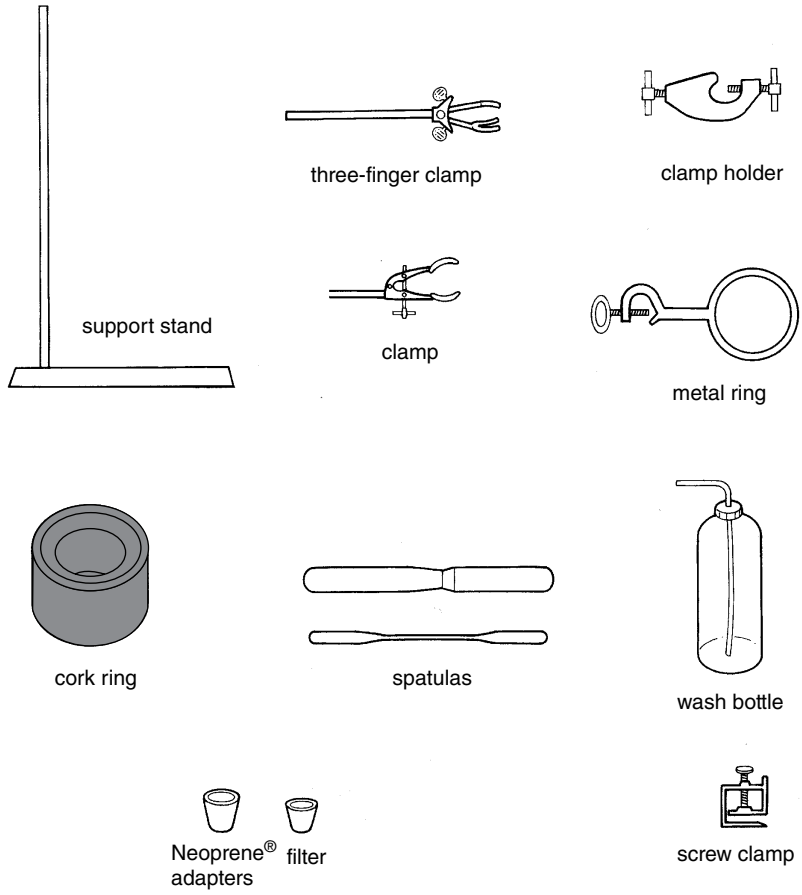

Fig. 2.3 Laboratory hardware (not to scale).

The items that require special mention are stands, clamps and clamp holders. These are essential items for supporting your glass apparatus during reactions, together with safety screens for protection during reduced pressure distillations and other potentially hazardous laboratory operations.

Chemical apparatus should always be securely clamped and fixed to a stable support.

The metal stand is the most commonly used form of stable support since it is freely movable, but its heavy base ensures that in proper use it is sufficiently stable. The only practical alternative to such stands is the purpose-built laboratory frame, a square or rectangular network of horizontal and vertical rods fixed firmly to the bench or back of the fume hood, but this is usually found only in research laboratories. The correct use of support stands requires that the clamped apparatus is always directly over the base of the stand as shown in Fig. 2.4(a). The alternative arrangement is highly unstable and potentially dangerous. Similarly, there are right and wrong ways of using clamp holders and clamps with only one movable jaw. Clamp holders should be arranged so that the open slot for the clamp faces upwards (Fig. 2.4b) and, when in the horizontal position, clamps should be fixed so that the fixed non-moving jaw is underneath (Fig. 2.4c).

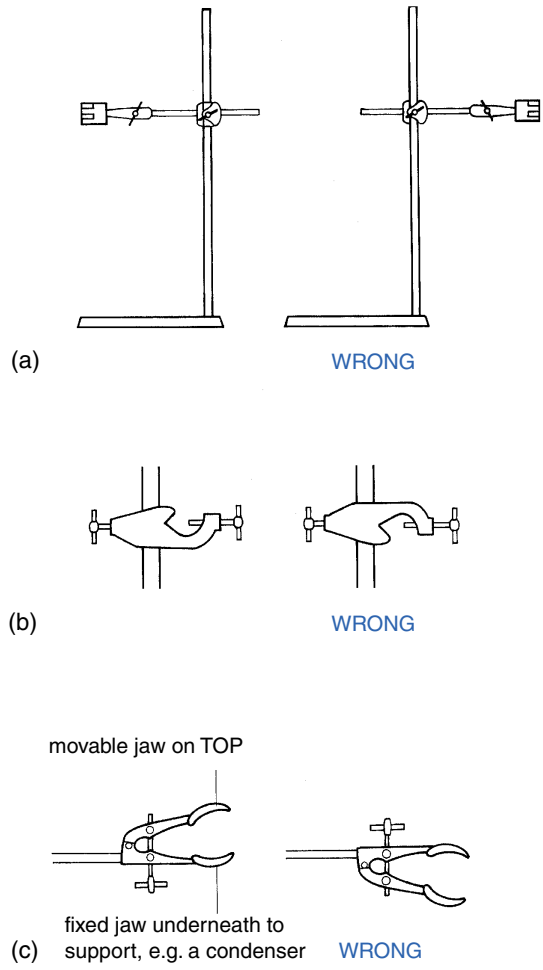

Fig. 2.4 Right and wrong ways of using support stands, clamp holders and clamps (not to scale).

Safety screens made of toughened glass or plastic should be used whenever you are carrying out reduced-pressure distillations or experiments in which there is some risk of an explosion. If in doubt, ask an instructor. In addition, any operations in a fume hood should always be carried out with the toughened glass front pulled down, leaving just sufficient space at the bottom to permit access to the apparatus. This serves the dual purpose of protecting the face and top half of the body in the event of an explosion and permitting the fume-hood extraction system to work most efficiently. The front of the fume hood should never be pushed all the way up as, in this position, it is not possible for the extractor fan to maintain the inrush of air necessary to contain noxious vapours. With the front pulled down, you will also get into the habit of not leaning over the apparatus when working. Leaning into the fume hood is very bad practice, negating all of the reasons for operating in the fume hood in the first place. It is attention to details such as these that make for good laboratory practice and characterize the good experimentalist.

Do not lean into the fume hood

2.3 Heating

Working in the laboratory, it will not be long before it will be necessary to heat a reaction mixture or distil a product. Several methods of heating are commonly encountered in the laboratory, but the ready flammability of a wide range of organic solvents, coupled with their volatility, always requires vigilance when heating. Open flames pose an obvious hazard in this respect and are almost without exception banned in the organic chemistry laboratory, but the hot metal surfaces of hotplates and the possibility of sparking with electrical apparatus can also give rise to dangerous situations. Although flames are visible, it is impossible to gauge the temperature of a metal surface simply by looking at it, so take particular care when working with hotplates.

2.3.1 Heating baths

Water and steam baths

Electrically heated water baths and steam baths are convenient means of heating liquids to up to 100 °C, although water condensing on, and running into, the vessel being heated can be a problem. This is particularly true if it is necessary to ensure anhydrous conditions within the reaction. Although the risk of fire is lowest with steam baths, you should be aware that carbon disulfide, possessing an autoignition temperature of around 100 °C, is still a potential fire hazard. In fact, carbon disulfide is so toxic and poses such a severe hazard that its use in the laboratory as a solvent should be avoided at all costs.

Heating with steam can be accomplished by suspending the vessel above the surface of a boiling water bath, or the laboratory may be equipped with a supply of superheated steam. With piped steam it will take a few minutes after turning on the steam source before the system clears itself of water and produces live steam. Set up your apparatus before turning on the system as everything will be too hot to handle afterwards.

Be careful with steam

You must always respect steam, which, owing to its high latent heat of condensation, can inflict serious burns.

Steam and water baths are the heating methods of choice for carrying out recrystallizations with volatile solvents. The baths are normally equipped with a series of overlapping concentric rings, which can be removed to give the right size of support for the particular vessel being heated. Flat-bottomed vessels should sit firmly on the bath without any wobbling (Fig. 2.5a). Round-bottomed flasks should have between one-third and half of the surface of the flask immersed in the bath with a minimal gap between the flask and the support ring (Fig. 2.5b).

Oil baths and their relatives

Electrically heated baths are frequently used in the laboratory owing to the wide temperature ranges possible with different heat-transmitting media (for example, polyethylene glycol, silicone oil. Wood's metal; see

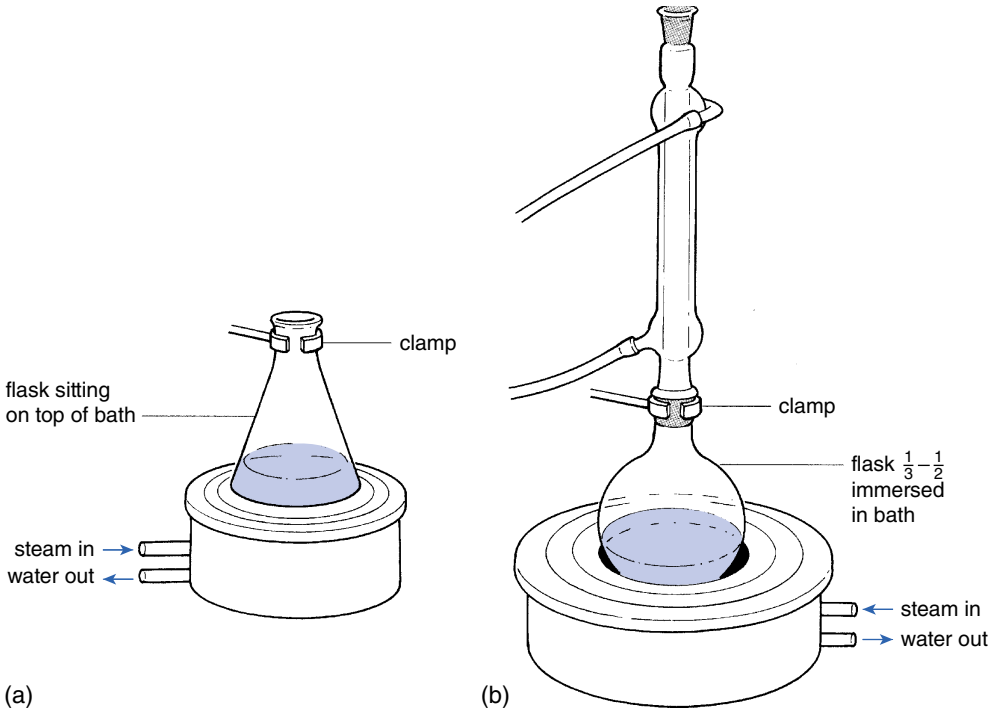

Fig. 2.5 (a) Heating an Erlenmeyer flask on a steam bath; (b) heating a reflux set-up on a steam bath.

Table 3.1). An oil bath can be heated on a hotplate (see Fig. 2.9) and determination of the bath temperature is possible using a thermometer. Alternatively, some hotplates are equipped with thermostatic temperature control.

Use an oil bath size compatible with the size of the vessel to be heated

Although particularly amenable to a wide range of heating demands in the laboratory, oil baths do possess several drawbacks. One disadvantage is the thermal inertia of the oil bath, which can cause temperature overshoot, although this can be minimized by choosing an oil bath that is not excessively large compared with the flask being heated. The container cannot be made of ferrous material if it is desired to stir the mixture magnetically, but at the same time it is advisable to avoid glass containers such as beakers or crystallizing dishes owing to the danger of breaking a glass vessel full of hot oil. Another minor irritation associated with oil baths stems from the mess and cleaning problems that result with flasks that have been suspended in silicone oil. This can be overcome by using polyethylene glycol as the heat-transmitting medium, as it is water soluble, but this has the drawback of a limited heating range before decomposition commences. Alternatively, it is possible to use sand baths or powdered graphite baths to overcome this problem, although it is less easy to control temperature gradients within the heating medium. Wood's metal baths pose their own particular problems as the alloy is solid at room temperature and thermometers and flasks must always be removed before the bath

Remove flask and thermometers from Wood's metal baths whilst hot – care!

Use oil baths in the fume hood

Never use oil that has been contaminated with water

is allowed to solidify. Heating the baths to a temperature higher than the decomposition temperature of the fluid will result in evolution of vapours that at the least are unpleasant, but are also likely to be toxic. Oil baths should always be used in a fume hood for this reason. Silicone oil has the greatest thermal stability and is preferable to paraffin-based oils although it is much more expensive. Proprietary oils used for culinary purposes must not be used in the laboratory (see Table 3.1). By far the greatest problem with an oil bath is the danger of spattering if it becomes contaminated with water and is then heated over 100 °C. This is extremely dangerous and any oil bath that is suspected to contain water should be changed immediately. Heating baths must be examined before use and the fluid should be changed regularly, disposing of the old oil in containers specifically available for such waste.

A popular alternative to using an oil bath is to use an aluminium heating block shaped to take a round-bottomed flask (Fig. 2.6). These are used more and more frequently in laboratories because they are less hazardous than a conventional oil bath (they cannot catch fire), they are also cleaner and there is no risk of spillage or breakage. Aluminium heating blocks are available in a variety of sizes and can be used from small-scale reactions up to litre-scale reactions. Usually, they are placed directly on top of a stirrer/hotplate and a thermocouple on the stirrer/hotplate can be placed in a hole in the heating block, allowing for good temperature control. In the case of small-scale reactions, or if you are using an unusual-shaped flask, it is possible to put sand in the heating block, which can help with thermal transfer. However, if you do this, bear in mind that the heat transfer is less efficient than with the aluminium metal itself, so it is often better to insert the thermocouple directly into the sand instead.

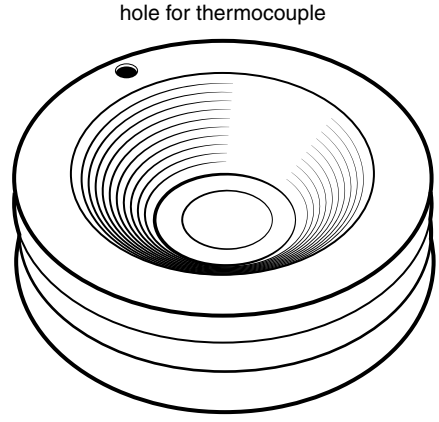

Fig 2.6 An aluminium heating block.

2.3.2 Electric heating mantles

Heating mantles provide a convenient means of heating mixtures under reflux, although their use for distillations is to be discouraged.

Mantles are designed only for heating round-bottomed flasks and must never be used for heating any other type of vessel.

Never use a mantle that is too small or too large for the flask being heated

The mantle consists of an electrical resistance wire wound within a hemispherical woven glass jacket. Each mantle is designed specifically to accept a flask of a particular size that should sit snugly in the cavity, touching the jacket at all points with no exposed heating areas. The mantle may be housed in a casing for greater protection, but all designs are particularly vulnerable to spillages of liquids. The construction of mantles can lead to the surface being abraded with constant use and this can lay bare the wires within the heating element. Any mantle suspected of having been damaged must first be verified and, if necessary, repaired by a qualified electrician before use.

Never use any mantle that you suspect to have had any liquid spilled on it or that has a frayed appearance

Most new mantles have their own heating control, but if not, the mantle should be connected to a variable heating controller and never directly to the mains power supply. Owing to their high heat capacity, mantles tend to heat up rather slowly and are particularly prone to overshoot the desired temperature substantially. Always allow for the possibility of removing the heat source quickly if it appears that a reaction is getting out of hand as a result of overheating. The best way to achieve this is to clamp the apparatus at such a height that the mantle can be brought up to it or removed from it on a laboratory jack (Fig. 2.7).

Use a laboratory jack to support the heating mantle

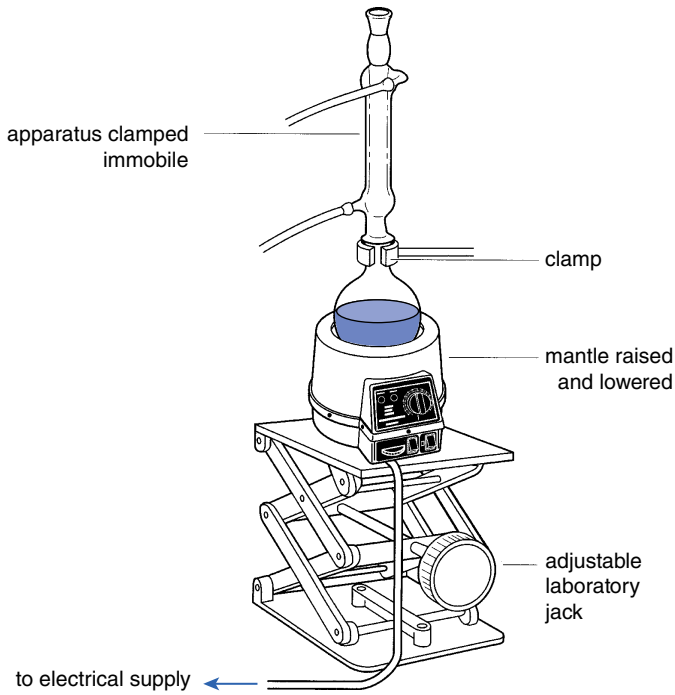

Fig. 2.7 Assembly for reflux using a heating mantle.

2.3.3 Stirrer/hotplates

Stirrer/hotplates are designed for heating flat-bottomed vessels, such as Erlenmeyer flasks or beakers, for which they are ideal provided that the liquid being heated is not flammable (Fig. 2.8). The built-in magnetic stirrer permits efficient agitation of non-viscous solvents by adding an appropriately sized magnetic stirrer bar to the liquid in the container (Fig. 2.9).

Although round-bottomed flasks cannot be heated using a hotplate alone, owing to the very small contact surface between flask and hotplate, this problem can be overcome by immersing the flask in a flat-bottomed oil bath or an aluminium heating block. Both of these are discussed earlier in the Chapter. With such an arrangement, stirrer/hotplates are very useful for heating under reflux with simultaneous stirring (Fig. 2.9).

The flat exposed surface of the hotplate, designed for transferring heat rapidly, makes it extremely dangerous when hot. It is good practice

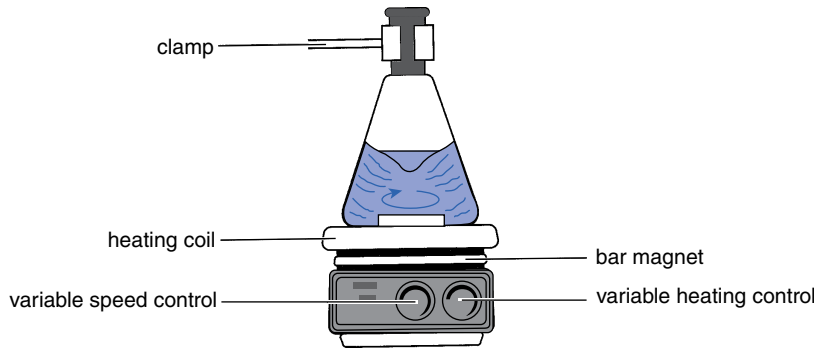

Fig. 2.8 A stirrer/hotplate.

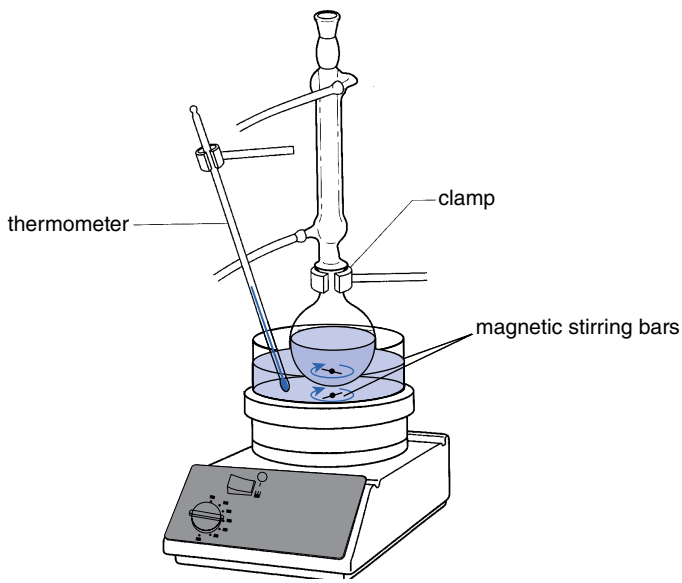

Fig. 2.9 Using a stirrer/hotplate with an oil bath to heat a round-bottomed flask.

whenever you have finished using a hotplate to place a beaker of cold water on the hot surface. This will have the dual effect of cooling the surface and alerting others to the potential danger – a hot hotplate seems very much like a cold hotplate until someone puts a hand on it.

Always check that a hotplate is cold before attempting to move it

2.3.4 Hot-air gun

Hot-air guns are particularly useful as a source of heat that can be directed fairly precisely. Commercial hot-air guns (Fig. 2.10a) are capable of achieving high temperatures near the nozzle and can be useful alternatives to Bunsen burners (now largely banned) for distillations.

The guns are able to produce a stream of heated air, usually at two rates of heat output, as well as cold air. After the gun has been used, it should not be placed directly on the bench, as the nozzle remains very hot for some period of time. It is recommended that the gun be placed in a support ring 'holster' with the cold air stream passing for a few minutes before switching it off completely (Fig. 2.10b). Do not forget that the hot nozzle can ignite solvents in addition to causing serious burns.

Heat guns are particularly useful for the rapid removal of moisture from apparatus for reactions where dry, but not absolutely anhydrous, conditions are required. Another use is for heating thin-layer chromatography (TLC) plates to visualize the components when using visualizing agents that require heat as part of the development procedure (see Section 3.3.6, subsection 'Visualizing the developed plate').

In all instances, it must be remembered that any form of hot-air gun poses the usual fire hazards associated with any piece of electrical equipment that may cause sparks on making or breaking contact.

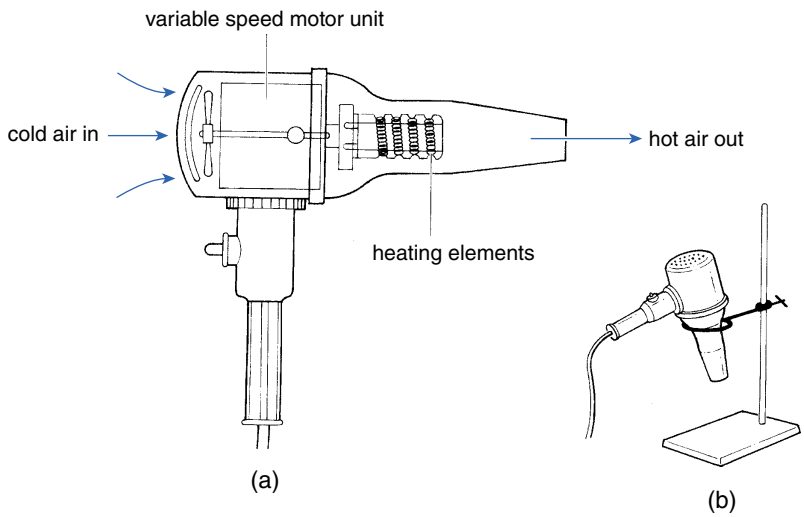

Fig. 2.10 (a) A commercial hot-air gun; (b) after use, the hot-air gun should be allowed to cool in a support ring.

2.3.5 Microwave reactors

Microwaves can also be used to heat chemical reactions and their use is becoming much more widespread within chemistry. Further information about microwaves can be found in Chapter 9.

2.4 Stirring

The methods for stirring reactions are described in Section 3.2.1, subsection 'Stirring', so here it is sufficient to describe the main types of equipment. There are three main ways in which mixtures can be agitated: by hand, with a magnetic stirrer and with a mechanical stirrer; only the last two require any particularly sophisticated equipment! Remember that homogeneous solutions do not in general require any stirring after the initial mixing. The exceptions to this rule are reactions that are carried out at low temperatures (for instance, reactions involving alkyllithium reagents or diisobutylaluminium hydride) and, in such cases, agitation is required for heat dispersal rather than for mixing of reagents.

2.4.1 Magnetic stirrers

Magnetic stirring (see Fig. 3.20a) is the method of choice if an extended period of continuous agitation is required, since it is easy to set up the apparatus, particularly for small-scale set-ups or closed systems. The main drawback to the technique is that it cannot cope with viscous solutions or reactions that contain a lot of suspended solid. In addition, volumes of liquid much greater than 1 L are not stirred efficiently throughout their whole bulk. The magnetic stirrer may also be equipped with a hotplate, and these combined stirrer/hotplates are particularly versatile pieces of apparatus. In general, the larger the volume of material to be stirred, the more powerful the motor needed and the longer the magnetic stirrer bar required.

Stirrer bars come in various designs and dimensions; a selection of bars, approximately 10, 20 and 30 mm (or 0.5 and 1 inch) long, of the variety that possess a collar around the mid-section (Fig. 2.11a), will be suitable for most occasions. For reactions in the larger volume round-bottomed flasks, heavy duty football-shaped (American or rugby - depending upon which side of the Atlantic you live!) bar magnets (Fig. 2.11b) are excellent, but these can be liable to break any delicate pieces of glassware that get in their way.

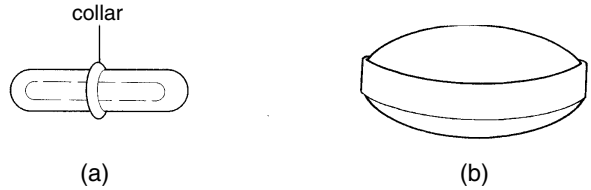

Fig. 2.11 Useful shapes of Teflon®-coated bar magnet.

Although bar magnets can be obtained with many different types of coatings, only Teflon®-coated stirrers are universally useful, and even these turn black when used for stirring reactions involving alkali metals in liquid ammonia. This discolouration does not affect the efficiency of the stirrer, at least in the short term.

2.4.2 Mechanical stirrers

Larger scale reactions or viscous mixtures require the greater power of an external motor unit turning a stirrer blade. It is highly advantageous for the motor to possess a variable speed control and a typical model is shown in Fig. 2.12. These units are rather heavy, so it is necessary to support them firmly.

Mechanical stirrers need firm support

The overhead stirrer is most simply attached to the motor by a flexible connection made from a short length of pressure tubing. However, when stirring open vessels (see Fig. 3.20b), the flexibility of this connection necessitates the use of a stirrer guide (such as a partially closed clamp) half-way down the stirrer shaft to prevent undue lateral motion ('whip'). With closed systems, such as when stirring refluxing reaction mixtures, a solvent- and air-tight adapter is required. A simple adapter, sometimes called a *Kyrides seal*, can be constructed from a tubing adapter fitted with a short length of flexible tubing that forms a sleeve around the shaft of the stirrer (Fig. 2.13a). The point of contact between the stirrer and the flexible tube is lubricated with a small amount of silicone grease, and a carefully prepared seal of this type will permit stirring under water aspirator

Use a stirrer guide

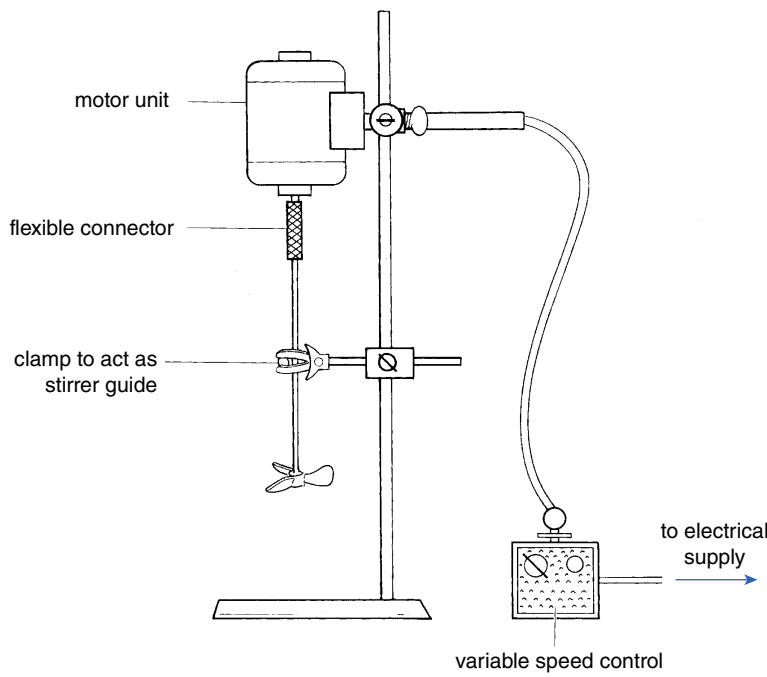

Fig. 2.12 Typical overhead mechanical stirrer.

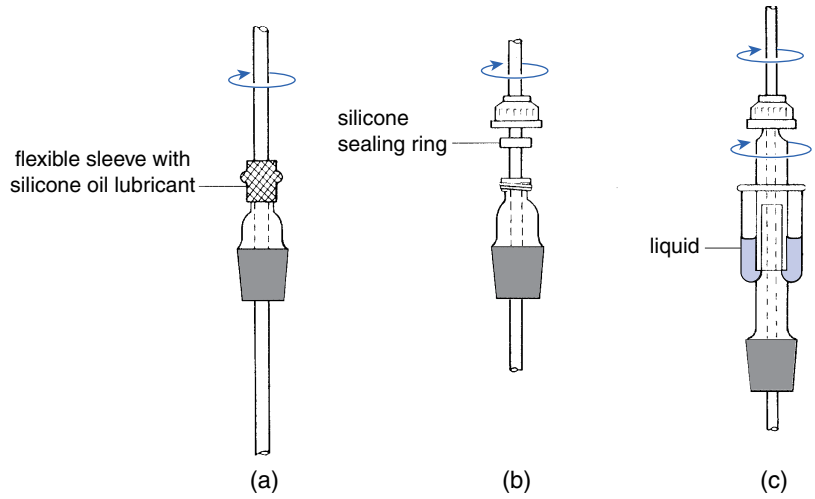

Fig. 2.13 Stirrer guides for closed systems: (a) Kyrides seal; (b) screw-cap adapter (exploded view); (c) fluid-sealed stirrer.

vacuum (*ca*. 20 mm). A screw-cap adapter, commonly used to hold thermometers, can also be used to good effect if slight lubrication is applied to the silicone sealing ring and the plastic screw-cap is not tightened to its fullest extent (Fig. 2.13b). Mercury-sealed stirrer guides (Fig. 2.13c) have lost favour owing to their tendency to splash highly toxic mercury metal everywhere when used at high speeds. In addition, although the arrangement does permit a good air-tight seal, it cannot be used with systems under vacuum. If such an adapter is used, it is preferable to use silicone oil in place of mercury.

The stirrer rods may be made of glass, metal or Teflon® and the paddle or blade arrangements come in a bewildering array of forms. Teflon® is the material of choice for construction of the whole stirrer as it will not break when placed under stress (when dropped on the floor, for instance), nor is it likely to break the flask in which it is being used. Normally, however, the propeller-type stirrer (Fig. 2.14a), which is useful for stirring open containers with wide mouths, is commercially available constructed from metal. A glass or Teflon® stirrer, possessing a movable Teflon® blade (Fig. 2.14b), is a very simple and robust design that is suitable for use with vessels possessing restricted openings. In addition, the Teflon® blade possesses a curved edge, making it ideal for efficient stirring in round-bottomed flasks.

2.5 Vacuum pumps

The common procedures that call for reduced pressure in the organic chemistry laboratory are filtration with suction (see Section 3.1.3, subsection 'Suction filtration') and reduced-pressure distillation (see Section 3.3.5, subsection 'Distillation under reduced pressure'). The former technique simply requires a source of suction and is adequately served by use of a

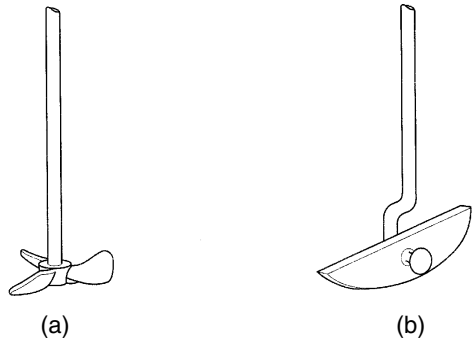

Fig. 2.14 Two useful types of stirrer: (a) propeller design for use in open vessels; (b) movable Teflon® blade for use with tapered-joint glassware.

water aspirator, although the reduced pressures that can be achieved with this simple apparatus (*ca*. 10–20 mmHg) are frequently sufficient for use also with reduced-pressure distillations. Alternatively, reduced pressures of this magnitude can be attained using a diaphragm pump. However, very high-boiling materials, or purifications involving sublimations, require recourse to a vacuum of 0.1–1.0 mmHg that is provided by an oil immersion rotary vacuum pump. An even higher vacuum is achieved by using a mercury vapour diffusion pump in series with a double-action rotary oil pump, but such conditions are required only rarely in the laboratory and will not be discussed here. It should not be forgotten, however, that mass spectrometric analysis would be impossible without the ability to achieve reduced pressures in the region of 10^{-6} mmHg; however, specialized pumping systems are available to achieve this.

2.5.1 Water aspirators

Water aspirators are made of glass, metal or plastic (Fig. 2.15) and operate on the Venturi effect in which the pressure in a rapidly moving gas is lower than that in a stationary gas. The aspirator is designed such that the water rushing through the aspirator drags air along with it and thus generates the region of low pressure.

The theoretical maximum vacuum attainable with such an apparatus is equal to the vapour pressure of the water passing through it and is therefore dependent on the temperature of the water source. In practice, the working pressure is usually *ca*. 5–10 mmHg higher than the minimum owing to leaks. Anything lower than about 30 mmHg should be acceptable in a teaching laboratory. Unfortunately, water aspirators do not work efficiently at high altitudes and alternative methods have to be found in these circumstances.

The major disadvantage with a water aspirator is that the pressure generated depends on the speed with which the water passes through it and that, in turn, is directly affected by the water pressure. In a busy teaching laboratory, the use of a large number of water aspirators at the same time places great demands on the water supply and may be too much for it to cope with efficiently. The result is that the pressure generated by

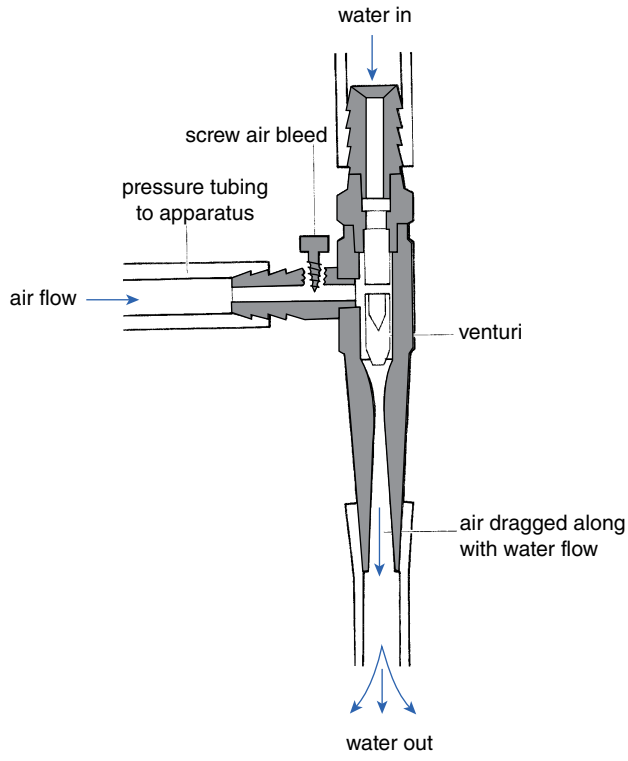

Fig. 2.15 Schematic diagram of a water aspirator.

aspirators around the laboratory is liable to be variable depending on their position in the line. The tendency for the vacuum generated by any individual aspirator to vary over a period of time as the water pressure changes can have deleterious effects in reduced-pressure distillations where boiling points are very sensitive to pressure variations within the system. The worst situation occurs with an abrupt drop in the water pressure (for instance, when your neighbour turns on their aspirator) as this leads to 'suck-back'. In this case, the vacuum generated by the aspirator suddenly cannot cope and water floods into the apparatus – a very sad sight indeed, but one that can be avoided by interposing a trap between the aspirator and apparatus (see Fig. 2.16). The use of water aspirators is not particularly environmentally friendly owing to the sheer volume of water used, hence many laboratories have moved towards the use of diaphragm pumps instead (see Section 2.5.2).

Using a water aspirator

Always use aspirators with the water full on

Whereas the flow of water passing through a condenser does not need to be more than a gentle trickle, *water aspirators must never be used with the water at less than full blast*. With the water turned on full, check that the air bleed screw on the side arm is open (as these little screws have a tendency to become stuck or become lost from communal apparatus; some aspirators do not have them, but an additional stopcock attached to the

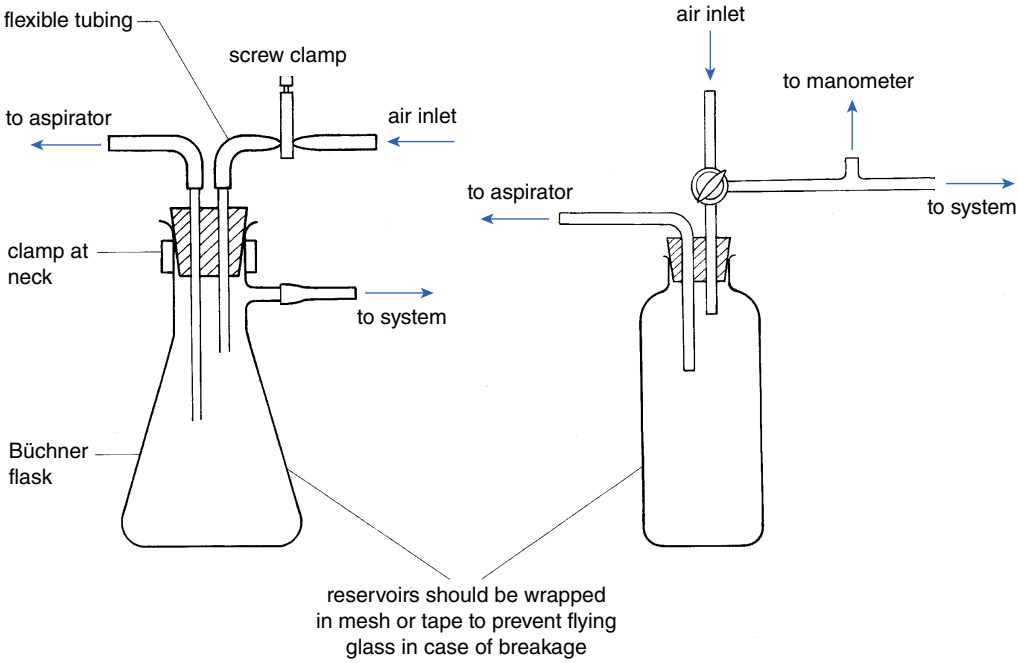

Fig. 2.16 Typical examples of water traps suitable for use with water aspirators.

water trap will serve the same purpose) and then attach the pressure tubing to the apparatus to be evacuated. Close the air bleed (or stopcock on the water trap) and observe the pressure drop on the manometer. For vacuum filtrations, the actual quality of the vacuum is largely unimportant but, of course, it will be necessary to note and regulate this pressure if you are carrying out a vacuum distillation.

Never turn off the water aspirator before releasing the vacuum

The critical stage in working with water aspirators comes when the vacuum is to be released. It is imperative that the water supply to the aspirator *remains on until the pressure within the system has been allowed to return to that of the atmosphere*. If you do not observe this simple procedure, the inevitable result will be a suck-back of water into the apparatus.

With suction filtration, it is frequently sufficient simply to remove the pressure tubing from the side arm of the receiving vessel before turning off the tap, although this lazy practice runs the risk of spillage when the tubing is suddenly removed and air rushes into the receiver. The correct procedure for both reduced-pressure filtration and distillation involves the unscrewing of the air bleed on the side arm of the aspirator (or opening the stopcock on the water trap) until the manometer registers a steady increase in pressure within the system, or the tone of the water rushing through the aspirator changes abruptly. Do not continue to unscrew the air bleed, otherwise the screw will drop out and be lost forever down the sink. It is always good practice when carrying out reduced-pressure distillations to allow the residue in the distilling flask to cool to near room temperature before admitting air, particularly if the flask has been healed strongly during distillation.

Water traps

Always use a water trap between the aspirator and your apparatus

The danger of water sucking back into the apparatus when a sudden drop in water pressure occurs is a constant problem when working with water aspirators. To safeguard against this, a water trap must always be included between the aspirator and the apparatus. Two simple examples are shown in Fig. 2.16; the optional modifications might include the attachment of a manometer or a means of introducing air into the system. The latter is necessary when the aspirator does not possess an air bleed, but even when one is present, using the stopcock on the water trap avoids leaning over the bench to the sink or losing the air bleed screw. As the trap simply acts as a dead space between the apparatus and the aspirator, which fills up with water on suck-back, it must be large enough to cope with this and should be no less than 1 L in volume.

2.5.2 Diaphragm pumps

Diaphragm pumps (or membrane pumps) are commonly used in research and undergraduate laboratories. These pumps use a combination of the pulsation of a rubber, thermoplastic or Teflon® diaphragm and suitable valves on either side of the diaphragm to generate a vacuum. Diaphragm pumps are often connected to rotary evaporators in place of a water aspirator. Diaphragm pumps are good at providing a continuous vacuum, and can provide reduced pressures of between 50 and 0.5 mmHg, depending on the model. An important advantage of using a diaphragm pump rather than a water aspirator on a rotary evaporator is that the pressure can be set. This is of great use if a volatile solvent is being removed as it allows most of the solvent to be collected, or for removal of a solvent that regularly bumps, such as dichloromethane. It is important when using a diaphragm pump that there is a trap between the pump and the equipment under vacuum to prevent solvent entering the system and causing corrosion of the parts. Although diaphragm pumps are effective, oil immersion vacuum pumps are more commonly used when an extremely high vacuum is required.

2.5.3 Oil immersion rotary vacuum pumps

Frequently, vacuum distillations demand a better vacuum than can be achieved using a water aspirator, either because a lower pressure is needed, or because that produced by the aspirator is too erratic. In these instances, an oil immersion rotary pump is ideal. Unfortunately, with the lower pressures comes increased complexity of operation of the pump and there are several extremely important rules that must be observed when using such equipment. Although the instructions given here should be generally applicable, always check the precise operation of your particular piece of apparatus with an instructor before use.

In addition to the pump itself, the set-up will have a series of important pieces of ancillary equipment essential for the protection of the pump, achievement of the highest vacuum possible and measurement of the

pressure within the system. All of these accessories will be connected by a rather complicated set of glass and flexible tubing, but the general arrangement will look something like that depicted in Fig. 2.17.

The pump is mounted firmly on its base on the bench top or, more conveniently, on a trolley that can be moved to wherever it is desired to carry out the distillation (such as in a fume hood). It is supplied with two connecting tubes made of thick-walled tubing. One (the 'downstream' side) is the exhaust tube and should always be led into a fume hood, while the 'upstream' tube leads eventually to the apparatus to be evacuated. It is what occurs on the upstream side of the pump that is crucially important.

The basic construction of the pump involves a rotor that is concentric with the motor drive shaft but is mounted eccentrically within a cylinder (Fig. 2.18). In the commonly encountered 'internal vane' design, the rotor is fitted with one ('single-action') or two ('double-action') pairs of blades that bear tightly against the walls of the cylinder. Double-action pumps are capable of attaining a higher vacuum and the internal vane design is preferred because of its quiet operation.

On turning, the rotor blades cut off pockets of gas and sweep them through the pump to be exhausted via an oil-sealed non-return valve. A thin film of oil within the cylinder maintains a seal between the blades and the cylinder wall. The very close tolerances between the rotor blades and the cylinder mean that the pumps are very susceptible to damage by solid particles or corrosive gases.

Never draw air through a rotary vacuum pump

Under normal circumstances, the pump must never be allowed to work whilst open to the atmosphere for two very important reasons. First, drawing air continuously through the oil in the pump will cause water vapour to be trapped in the oil. This reduces the vacuum that can be achieved due to the vapour pressure of the contaminating water and might cause the pump to seize. Abuse of the pump in this way will necessitate frequent oil changes and other more extensive repairs. However, a second, more important,

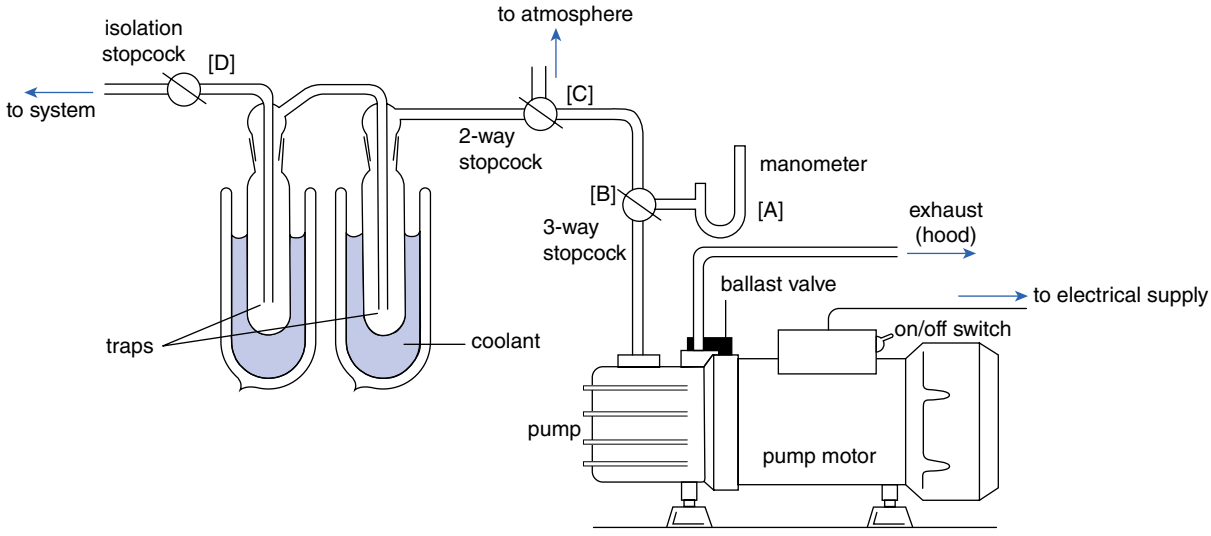

Fig. 2.17 Schematic diagram representing the typical arrangement of a rotary vacuum pump.

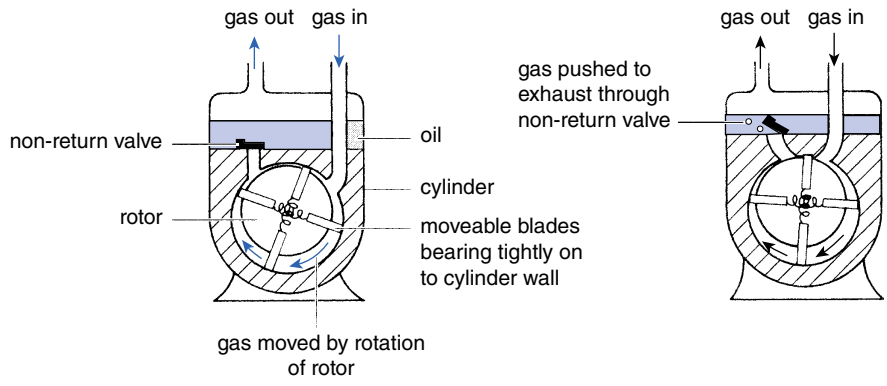

Fig. 2.18 The 'internal vane' double-action oil immersion rotary pump.

reason is the possibility of condensation of liquid oxygen in the cold traps if liquid nitrogen is being used as the coolant.

The potentially lethal consequences of combining liquid oxygen and organic material cannot be overemphasized and this situation must be avoided at all costs.

One of the authors (LMH) clearly remembers the sensation he experienced when, after carrying out a reduced-pressure distillation in his first week of postgraduate research, he succeeded in half filling a cold trap with liquid oxygen by forgetting to remove the nitrogen Dewar flask for 25 minutes after opening up the apparatus to the atmosphere. Do not learn this particular lesson the hard way. Unlike the author, you may never get a second chance to get things right.

Pressure measurement

Although the order of attachment of the accessories may vary, in Fig. 2.17 the nearest attachment to the pump is the manometer A, attached by a three-way stopcock B. One design of manometer usually found on most rotary vacuum pumps is a compact variant of a McLeod gauge that allows accurate measurement of pressures between 0.05 and 10 mmHg. It must always be kept in the horizontal position when not being used to measure pressure. The three-way stopcock is designed to permit isolation of either the pump, the manometer or the distillation apparatus at any one time, or to allow all three to be interconnected. One design of such a stopcock is shown in Fig. 2.19.

Air-leak stopcocks

The next attachment, that should be found between the pump and the cold traps, is a two-way stopcock (Fig. 2.17, C). This allows for both isolation of the pump from the apparatus and also entry of air. Its positioning here is important for safety reasons, as the system must never be arranged such that the pump can draw air through the cold traps if it is left switched on with this stop cock open to the atmosphere. A typical design uses a double-bored key as shown in Fig. 2.20.

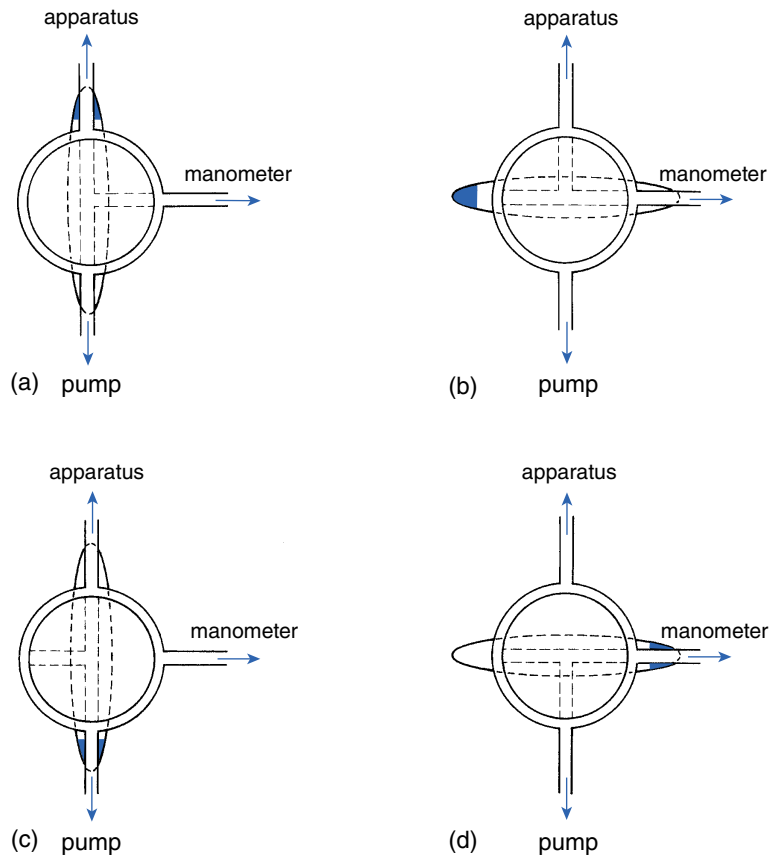

Fig. 2.19 Positions of the three-way stopcock: (a) pump, manometer and apparatus connected; (b) pump isolated; (c) manometer isolated; (d) apparatus isolated.

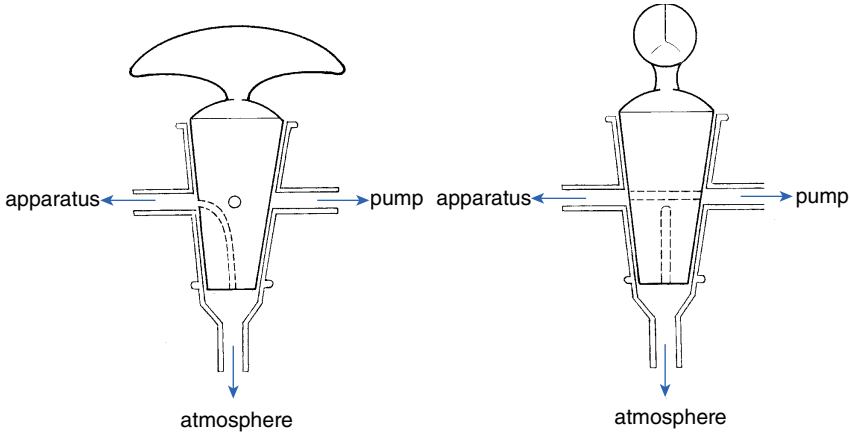

Fig. 2.20 A double-bored key two-way stopcock.

Cold traps

Cold traps must always be used to protect the pimp

Organic vapours must not be allowed to pass through the oil of the pump as they will be trapped in the oil and will very rapidly reduce the capacity of the pump to produce a vacuum. To protect the pump, it is necessary to place two cold traps between the distillation apparatus and the pump to condense out any vapours that pass through the receiver flask. Two forms of trap are commonly found on such systems and are used for cooling with a solid CO_2–acetone slush bath (*ca.* –78 °C) or liquid nitrogen (–196 °C). However, neither cooling system is really ideal and care must be taken when using either of them to avoid splashes on the skin as unpleasant cold burns can result. The apparatus shown in Fig. 2.21(a) is particularly suited for use with a slush bath as fresh pieces of solid CO_2 can be added easily. That shown in Fig. 2.21(b) is better used with liquid nitrogen, as the Dewar flask containing the coolant can be removed before permitting air into the system at the completion of distillation. The drawback to the use of the slush bath is its relatively low condensing efficiency compared with liquid nitrogen. Nonetheless, its use is recommended, at least for the type of pump found in the teaching laboratory, as there is a very significant hazard associated with the use of liquid nitrogen that will cause liquid oxygen (bp –183 °C) to condense in the cold traps if air is allowed into them.

Never, never draw air through a liquid nitrogen cold trap!

All mixtures of liquid oxygen and organic materials are dangerously explosive. If using liquid nitrogen as the coolant in the cold traps, NEVER permit air to enter the system. The Dewar vessel containing the liquid nitrogen must not be placed around the trap until immediately before turning on the pump and must be removed before releasing the vacuum in the system. Always wear insulating gloves when handling liquid nitrogen.

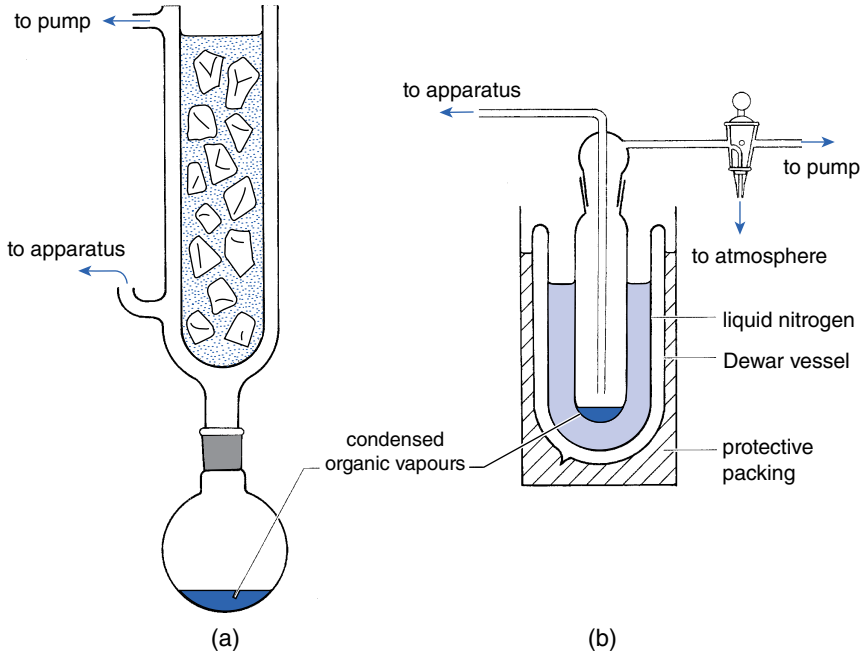

Fig. 2.21 (a) Solid CO_2–acetone trap; (b) liquid nitrogen trap.

Isolation stopcocks

The system should be equipped with a standard stopcock at its extremity in order to isolate the pump unit from either the atmosphere or the distillation apparatus.

Operation of the rotary vacuum pump

The procedures detailed here attempt to cover the general points and potential hazards associated with the use of rotary vacuum pumps. Nonetheless, it is imperative to consult an instructor before commencing to use the apparatus, particularly for the first time. It is possible that accepted procedures in your laboratory may differ from those outlined here, which are for general guidance only. In such circumstances, you must always follow the rules laid down by your laboratory.

Evacuating the system

Before using a rotary pump to evacuate the distillation apparatus, it is essential to have ensured that only minimal quantities of volatiles are present in the sample by connecting the system to a water aspirator for several minutes. The cold traps on the rotary pump will condense out small amounts of volatile materials, but it is unsafe to permit quantities of material to accumulate as there is a potential risk of explosion when reintroducing air into the traps at the end of the distillation.

Isolate the pump from the distilling apparatus by closing stopcock **D**, from the atmosphere by closing stopcock **C** and from the manometer by closing stopcock **B**, with the stopcock positions such as to allow the cold traps to be evacuated (see Fig. 2.17). Do not add any coolant at this stage, but if using solid CO_2–acetone, the traps may be one-third filled with acetone (Fig. 2.21a). Turn on the pump and immediately add the solid CO_2 or liquid nitrogen to the trap, being careful to avoid splashing the coolant onto yourself. The few seconds of pumping without coolant in the isolated traps will do the pump no harm, but will ensure that the air-filled traps are not surrounded by liquid nitrogen. (Although this is irrelevant with solid CO_2–acetone, it is a good idea to develop the habit of doing things in this way whatever the coolant.) After about 1 minute, check the quality of the vacuum using the manometer. If the pump is pulling a satisfactory vacuum (at least l.0 mmHg and probably better), *slowly* open stopcock **D** to evacuate the apparatus (**safety screen!**). Allow several minutes for residual volatile solvents in the sample to be removed and for the system to stabilize, then recheck the vacuum with the manometer. When satisfied that an acceptable stable vacuum has been established, the distillation may be commenced. Remember to check the pressure periodically during the distillation and make sure that the traps do not need additional coolant (generally unnecessary unless the distillation is protracted).

Wear insulating gloves when handling liquid nitrogen or solid CO_2

Always use a safety screen when carrying out reduced-pressure distillations

Releasing the vacuum

At the end of the distillation, close stopcock **D** to isolate the apparatus from the pump and wait until the distilling flask has cooled. If using a McLeod gauge, ensure that the manometer is in its horizontal position and then turn

stopcock **C** such that the traps are isolated but the pump is open to the atmosphere. You will hear the air rushing in through the outlet. Turn off the pump without delay, as drawing air through the oil in the pump for extended periods of time will cause a degradation of its performance. However, you must never switch off the pump when the line is still under vacuum, as oil from the pump will be sucked back into the line, ruining the whole unit. If liquid nitrogen is being used as the coolant, the Dewar flasks should be removed without delay. Turn the two-way tap to allow air into the traps and dismantle them carefully (**they are very cold – wear thermal gloves**). Place the collecting tubes or flasks in a fume hood ready for disposal of any condensed material (some may be toxic – consult an instructor) at a later stage. Finally, *slowly* open stopcock **D** to allow air to enter the apparatus. Always make sure that the traps have been cleaned and dried and that any coolant has been removed after use.

Do not switch off the pump while it is still connected to the vacuum

Ballasting the pump

Report poor pump performance immediately to the person responsible

A common cause of poor performance with rotary vacuum pumps is the presence of occluded gases and solvent vapour within the sealant oil. Even with careful use, this cannot be totally avoided and it is usually necessary to carry out an oil change at regular intervals of 6 months to 1 year depending on the treatment the pump has had. The life of the oil and the performance of the pump can be increased by degassing the oil at regular periods, a process referred to as *gas ballasting*. The ballast valve is designed to protect the oil from condensation of liquids by allowing a small amount of air to bleed continuously into the pump. This obviously reduces the performance of the pump, and it is more common practice to use the pump with the ballast valve closed and to compensate for this by ballasting for an equivalent period of time after the experiment. In the laboratory, it is a good rule of thumb to ballast for 12 h for every 8 h of use.

To ballast a pump, isolate the vacuum side of the pump from the atmosphere and open the ballast valve fully – no cold traps are necessary. Lead the exhaust pipe into the fume hood to remove any potentially toxic fumes and turn on the pump. If this procedure is carried out regularly, the pump will continue to operate satisfactorily for long periods, perhaps requiring topping up occasionally with a small amount of fresh oil.

2.6 The rotary evaporator

This piece of apparatus, usually communal in the teaching laboratory, is designed for the rapid removal of large quantities of volatile solvent at reduced pressure from solutions, leaving behind a relatively involatile component. Rotary evaporation finds greatest use for removing extraction and chromatography solvents used in the isolation and purification of reaction products. The principle of operation that distinguishes the apparatus from that used for ordinary reduced-pressure distillation is the fact that the distillation flask is rotated during the removal of solvent. This performs the two important functions of reducing the risk of bumping (which accompanies all reduced-pressure distillations), and increasing the rate of removal of

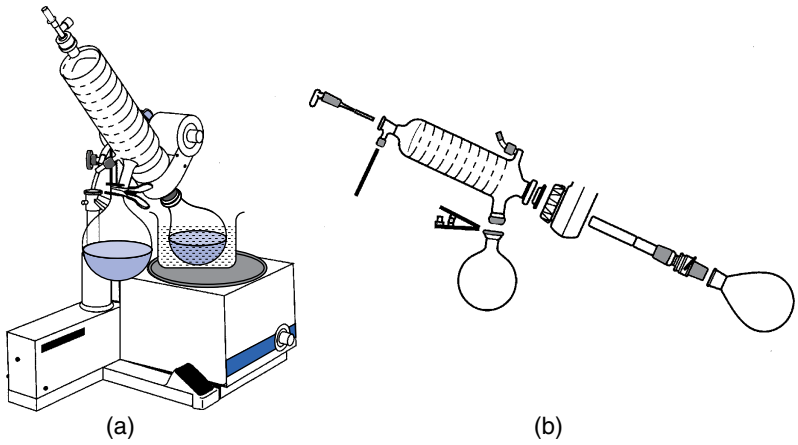

Fig. 2.22 (a) Typical example of a rotary evaporator; (b) exploded view of glassware showing vapour duct.

solvent by spreading the contents around the walls of the flask in a thin film, with a consequent increase in the ratio of surface area to volume of solution.

A wide range of designs is available commercially for a variety of specific uses, but a basic model most commonly encountered in the teaching laboratory is depicted in Fig. 2.22(a).

2.6.1 The apparatus

The *evaporating flask*, which may be pear-shaped or any round-bottomed flask possessing a standard-taper joint, is connected to a glass sleeve (*vapour duct*) that passes through a seal permitting a vacuum to be maintained, but at the same time allowing rotation. The vapour duct leads solvent vapour from the flask onto a spiral condenser and the condensed solvent is collected in a round-bottomed *receiver flask*, connected by means of a hemispherical glass joint. The motor unit for rotating the flask is housed above the point of the seal and the rate of rotation may be varied. The water aspirator is attached through the condenser outer jacket and the application and removal of the vacuum are controlled by using the stopcock at the end of the condenser. This stopcock may be fitted with a long, flexible tube that passes the length of the condenser into the evaporating flask to permit introduction of additional solution without releasing the vacuum and interrupting the evaporation.

The whole unit is mounted on a stand, of which several models exist, all designed to permit easy vertical movement of the rotary evaporator for introduction of the evaporating flask into a heating bath. The clamping system also provides for adjustment of the inclination of the rotary evaporator. The most convenient angle is around 45° from the vertical, but this should not normally require adjustment.

Regular maintenance of the rotating seal is necessary to produce a reliable vacuum. Failure of this seal will result in poor and variable pressures, but any

Report poor rotary evaporator pressures immediately to the person responsible

corrective work should be left to others after first ensuring that it is the seal and not the water aspirator that is the cause of the trouble. To do this, isolate the rotary evaporator and examine the pressure developed by the water aspirator. The only components that you will need to remove in the ordinary course of events are the evaporating and receiving flasks, for filling and emptying.

Always use the clips to hold flasks on the rotary evaporator

During evaporation, the reduced pressure within the system will tend to hold the evaporating flask firmly in place. However, **never rely on a combination of friction and vacuum to hold the evaporating flask on the rotary evaporator** – the additional precaution of using a clip for the flask must be followed (the hemispherical joint on the receiver flask makes such a clip an absolute necessity). The sight of a flask bobbing upside-down in a hot water bath is only too common in the teaching laboratory where water pressure fluctuations (and hence the quality of the water aspirator vacuum) are liable to occur.

Splash traps reduce the risk of contamination

If a standard round-bottomed flask is being used as the evaporating flask, it is likely that an expansion adapter will be necessary to attach the flask to the cone of the vapour duct. A very useful piece of apparatus for use with rotary evaporators, particularly communal ones, is a splash adapter that is placed between the evaporating flask and the vapour duct (Fig. 2.23). This acts as an expansion adapter, and at the same time prevents your sample from contaminating the vapour duct by bumping up into it and also stops refluxing solvent or a bumping solution washing down somebody else's prior contamination into your sample. You should get into the habit of cleaning the splash trap before and after use with acetone from a wash bottle.

2.6.2 Correct use of the rotary evaporator

Ensure that the receiving flask is empty of solvent and that water is passing through the condenser coils at a slow but steady rate. Turn on the water aspirator to its fullest extent and then attach the evaporating flask (with adapter if required) to the vapour duct, using a clip to ensure that the flask stays in place. Support the flask lightly with the hand, commence slow

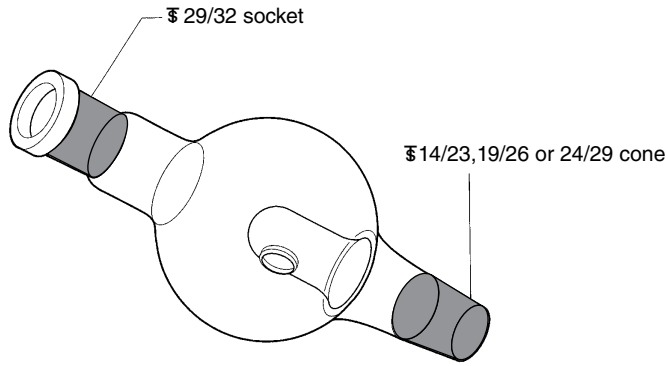

Fig. 2.23 A typical splash trap for use with a rotary evaporator.

rotation and then close the stopcock at the end of the condenser. When the manometer indicates a significant reduction in pressure within the system (if no manometer is attached to the apparatus, listen for a marked change in tone of the sound made by the water rushing from the aspirator), it is safe to remove your hand and regulate the speed of rotation to spread the solvent out around the flask without causing it to splash. If the mixture commences to boil uncontrollably, *temporarily* open the stopcock at the top of the condenser to allow entry of air and then reclose the stopcock. Once the evaporation from the solution has stabilized, the evaporating flask may be introduced into a bath of warm water if desired. However, be ready to remove the flask immediately if there is any indication that the mixture is beginning to boil too vigorously. The majority of common solvents such as ether or light petroleum have boiling points well below room temperature at the reduced pressures possible using this system, so you must exercise great care when heating the evaporating flask. With the more volatile solvents it is advisable to place the flask in a cold water bath at the outset and then allow the bath to warm up slowly during the course of solvent removal. The last traces of solvent are difficult to remove from samples, particularly the kinds of gummy materials that are often isolated from reactions, so it is necessary to leave the residue on the rotary evaporator for at least 5 minutes after the last of any solvent has been seen running into the receiver.

Keep the flask supported until the system is under vacuum

Heat cautiously

If the volume of solvent you wish to remove is inconveniently large for the size of the evaporating flask you are using (which should never be filled to more than about one-quarter of its volume), it is possible to introduce additional solution if the stopcock at the top of the condenser is fitted with a length of tubing that reaches into the evaporating flask. Simply attach a length of glass tubing to the external connector on the stopcock and dip this into the extra solution you wish to add (Fig. 2.24). Opening the stopcock carefully will cause solution to be drawn into the evaporating flask by the reduced pressure within the rotary evaporator and the solvent removal can continue after closure of the stopcock.

Continuous evaporation of large quantities of solution

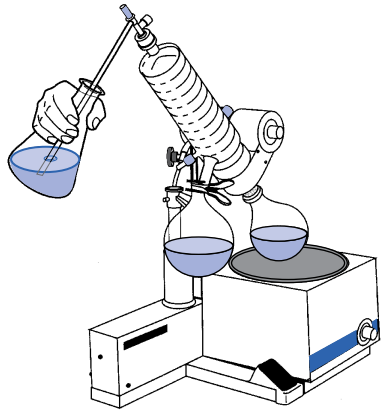

Fig. 2.24 The procedure for continuous solvent removal using a rotary evaporator.

Do not leave your solvent in the receiver flask and check that the vapour duct is clean

When you are satisfied that all of the solvent has been removed from your sample, stop the rotation of the flask and raise it from the heating bath. If you reverse the order of these operations, you will get wet with spray from the flask! Open the stopcock to allow air into the system, **supporting the flask with your hand**, remove the flask and turn off the aspirator and condenser water. Empty the contents of the receiver flask into the container designated for used solvents (**not down the sink!**) and check that you have left no material adhering to the inside of the vapour duct as this will not only reduce your yield, but also contaminate the next user's sample.

2.7 Catalytic hydrogenation

Catalytic hydrogenation is a particularly useful means of reducing alkenes and alkynes (see Experiments 27 and 28). It is frequently necessary to avoid over-reduction, for instance in the Lindlar-catalysed reduction of alkynes to alkenes, or if it is desired to reduce selectively only one unsaturated site within the molecule as in Experiment 28. In such instances, it is necessary to use a gas burette system that enables the volume of gas taken up to be measured at atmospheric pressure and at the same time permits a certain amount of overpressure (up to about 0.5 atm) to be applied to the reaction mixture. An example of such an arrangement is shown schematically in Fig. 2.25. However, increasingly it is less common to use this system so it will not be discussed further. Usually a balloon filled with hydrogen is used.

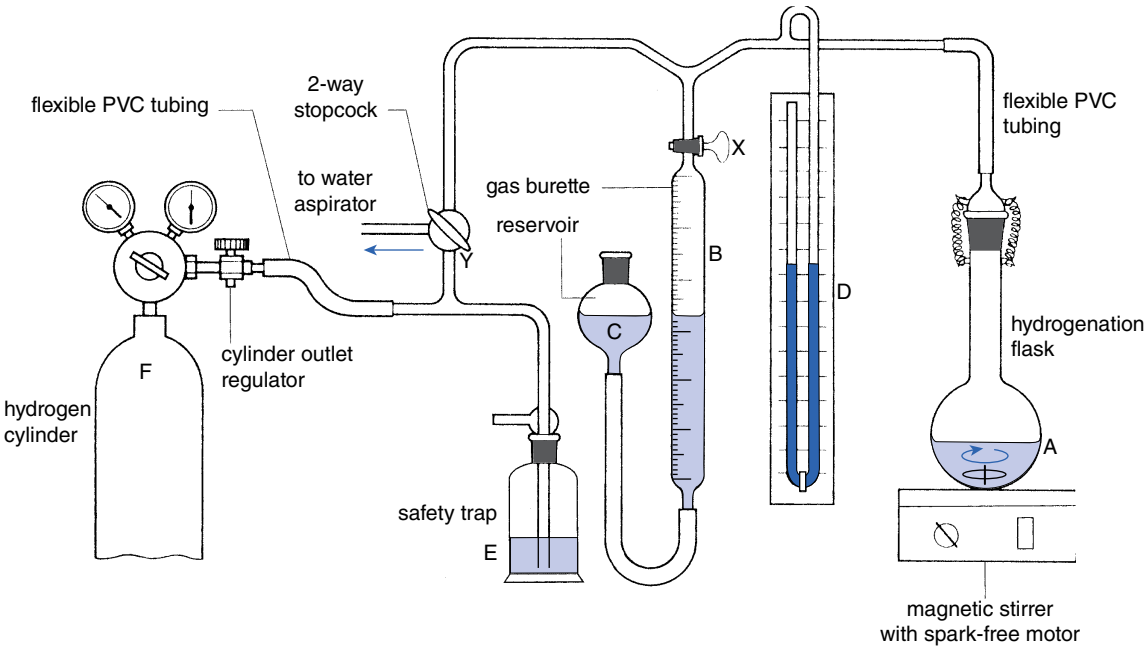

Fig. 2.25 Schematic of low-pressure hydrogenation apparatus.

Hydrogenations at higher pressures (2–400 atm) require very specialized apparatus to enable safe working owing to the highly explosive nature of hydrogen, especially when under pressure. These are beyond the scope of this book but, whatever the pressure and whatever the quantity of hydrogen being used, all naked flames must be extinguished.

Whenever working with hydrogen, there must be no naked flames in the laboratory. Any electrical apparatus in the vicinity must be spark-proof.

The warning about flames and hydrogen cannot be repeated too often and is particularly important if the experiment is being carried out in a busy teaching laboratory with many people all doing different things. It is far better for the apparatus to be kept in a separate room specifically designed for hydrogenations.

2.7.1 Hydrogenation procedure

When undertaking a hydrogenation using a balloon, it is important that hydrogen and oxygen **NEVER** meet in the presence of the catalyst because this can lead to a fire. It is therefore essential that the correct care is taken to set-up the reaction. In order to do this, a manifold that can provide both vacuum and nitrogen or argon is extremely helpful.

When setting up the reaction using a manifold, place the starting material then the solvent in a two-neck round-bottomed flask, followed by the catalyst. Seal the flask with a rubber septum, then connect the flask to the manifold, usually with a needle or an adapter. Next, remove any air in the flask by placing the flask under vacuum. When the air has mostly been removed, the solvent will start to bubble. At this point, **carefully** back-fill the flask with nitrogen or argon, taking care to ensure that the manifold does not suffer from 'suck-back'. Repeat this purging process at least three times, to ensure that all oxygen has been removed. After the final purge, remove the gas from the flask, close the tap on the manifold, then **carefully** refill the flask with hydrogen from the balloon through the other neck.

If a vacuum manifold is not present, it is possible to prepare the hydrogenation reaction using an inert gas to displace any air in the reaction vessel. In this case, place the starting material then solvent in a two-neck round-bottomed flask, followed by the catalyst. Seal the flask with a rubber septum at both necks, then connect the flask either to the manifold or to a balloon filled with an inert gas, usually nitrogen or argon, through one septum. Place an exit needle in the other septum, thus ensuring that the air inside the flask is displaced by the inert gas. Leave the mixture purging for a suitable length of time; the time taken and volume of inert gas required will depend upon the scale of the reaction. When the reaction has been thoroughly purged, replace the nitrogen or argon balloon with a hydrogen balloon. Now the inert gas inside the balloon needs to be replaced with hydrogen, therefore the purging process needs to be repeated. Again, the length of time required to refill the flask with hydrogen will depend upon the scale of the reaction.

In both cases, when the hydrogenation is complete the hydrogen must be removed, either by vacuum or displacement with another inert gas using

the procedure already described before permitting re-entry of air. This is to avoid spontaneous combustion of the air–hydrogen mixture on the catalyst surface. After assiduously setting up the reaction, many people forget this part of the procedure, with dangerously spectacular results. The reaction mixture may then be filtered with suction to remove the catalyst and the catalyst placed in the residues bottle for recycling. This filtration must always be carried out using a glass sinter funnel and care should be taken not to draw air through the dry catalyst, as many are pyrophoric.

2.7.2 Flow Hydrogenation

For more information about flow chemistry, see Chapter 9

It is also possible to undertake hydrogenation using flow chemistry. This provides an alternative procedure in which the solid hydrogenation catalyst, such as palladium on charcoal, is inside a prepacked cartridge. The hydrogen gas required for the hydrogenation can be prepared *in situ* by electrolysis of water and there is no need for a hydrogen gas cylinder, greatly reducing the hazards. Using this method, a solution of the substrate is passed through the cartridge directly into a collection vial; there is no need to remove the reducing agent. Usually the systems can be pressurized and heated, hence a wide range of substrates can be reduced using this method.

Further reading

H.C. Brown and C.A. Brown, *J. Am. Chem. Soc.*, 1962, **84**, 1495.
P.N. Rylander, *Hydrogenation Methods*, Academic Press, New York, 1992.

2.8 Ozonolysis

The cleavage of double bonds using ozone, followed by either a reductive or oxidative work-up to yield carbonyl-containing fragments, is an important procedure in synthesis (see Experiment 91), and also in structure-determination studies when characterization of the fragments may be easier than for the original alkene. The great advantage of ozone is its selectivity; hydroxyl groups, for instance, remain untouched by this reagent.

Ozone (O_3) is obtained by passing oxygen between two electrodes that have a high-voltage electrical discharge between them. Commercial ozonizers can provide oxygen enriched with up to about 10% ozone by regulation of the operating voltage and the oxygen throughput, and yield around 0.1 mol h^{-1} of ozone. It is possible to estimate the production rate of the ozonizer by passing the ozone stream through a solution of potassium iodide in 50% aqueous acetic acid for a measured period and then determining the liberated iodine titrimetrically. However, many commercial instruments have reliable calibration charts and, in any case, it is usually sufficient to monitor the progress of the reaction by TLC and adjust the ozone production rate accordingly.

The operation simply involves passing dry oxygen over the charged plates at a predetermined rate, although the exact procedural details vary with each instrument and you must consult an instructor before attempting to use the ozonizer.

Remember that the instrument contains a very high voltage (7000–10 000 V) when in operation. Ozone is highly toxic and experiments must always be carried out in a fume hood. In addition, the intermediate ozonides must never be isolated as they are potentially explosive compounds. An appropriate work-up must always be carried out before attempting to isolate the product.

2.8.1 The apparatus

A typical arrangement is shown in Fig. 2.26 and essentially consists of an oxygen supply, the ozonizer, a trap and the reaction vessel. Some means of testing the effluent gas for the presence of ozone may also be used to check for completion of reaction. The oxygen supply comes from a cylinder, and that part of the apparatus that delivers or contains ozone (from the ozonizer outlet onwards) must be contained in an efficient fume hood.

Ozone is toxic – FUME HOOD!

2.8.2 Ozonolysis procedure

The substrate is dissolved in an inert solvent, commonly dichloromethane or cyclohexane, in a flask arranged for stirring at reduced temperature (Fig. 2.26) and fitted with a sintered inlet tube and a means of venting the ozone. The sintered inlet tube disperses the incoming stream of gas, increasing its surface area and hence the rate of absorption of the ozone.

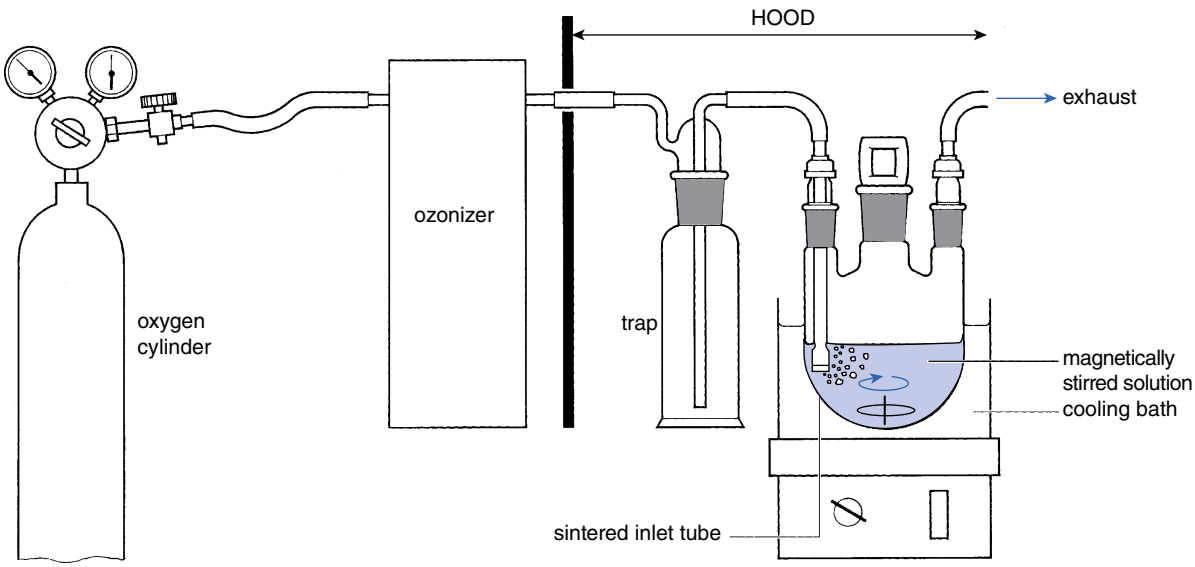

Fig. 2.26 Typical arrangement of apparatus for ozonolysis (not to scale).

The ozonolysis is carried out with external cooling of the reaction mixture using an ice bath or a solid CO_2–acetone bath (–78 °C). The progress of the reaction may be monitored by TLC, observing the disappearance of starting material, or the effluent gas may be checked for ozone using moist starch–iodide paper that turns blue–black if ozone is present in the effluent gas. Simple observation of the reaction mixture should give a good indication of when excess ozone is present, as solutions of ozone are pale blue. If the passage of gas is too rapid for all of the ozone to be absorbed, a positive blue–black colouration may be obtained with the starch–iodide paper before the reaction is complete, so it is always a good idea to check by TLC before moving to the next stage of the experiment.

Ozone is highly toxic and irritates the lungs and eyes. Extreme care must be exercised when removing samples from the reaction flask for TLC analysis.

The ozonide contained in solution must be decomposed by either reduction or oxidation before any isolation work can be carried out.

Ozonides are potentially explosive and must never be isolated.

A particularly convenient reductive work-up procedure involves treating the reaction mixture with excess dimethyl sulfide, which is immediately oxidized to dimethyl sulfoxide. However, dimethyl sulfide possesses a repulsive odour of rotten cabbage and its use in a crowded teaching laboratory might not be very popular! Reduction with zinc in acetic acid or triphenylphosphine present slightly more involved, but much more socially acceptable, alternatives. Use of sodium borohydride permits reductive decomposition of the ozonide with further reduction of the carbonyl fragments to alcohols. Alternatively, the ozonide may be hydrolysed, but in this instance the hydrogen peroxide produced oxidizes aldehyde groups to carboxylic acids. To ensure complete oxidation, excess hydrogen peroxide should be added to the reaction mixture in such instances. Details of these procedures may be found in the following publications.

Further reading

For a procedure for reductive work-up of ozonolysis reactions using catalytic hydrogenation, see: B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A.R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th edn, Longman, London, 1989, p. 106.

V.N. Odinokov and G.A. Tolstikov, Ozonolysis – a modern method in the chemistry of olefins, *Russ. Chem. Rev. (Engl. trans.)*, 1981, **50**, 636, and references cited therein.

M.B. Smith, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 7th edn, John Wiley & Sons, Hoboken, NJ, 2013.

2.9 Irradiation

The commonest way of increasing the rate of chemical reactions is to supply additional energy in the form of heat. Electromagnetic radiation in the ultraviolet (UV) region is also useful in synthetic organic chemistry, and not only

serves as an energy source, but may also alter the course of the chemical reaction ('thermally forbidden–photochemically allowed' processes). The only requirement is for the incident light to possess a wavelength that can be absorbed either by the substrate (*direct photolysis*) or by an added molecule that can transfer its energy to the substrate molecule (*sensitized photolysis*).

In favourable climates, sunlight is a convenient source of radiant energy, with wavelengths down to 320 nm suitable for carrying out a wide range of chemical reactions. However, this option is not open to all laboratories and, additionally, many photochemical transformations require higher energy light with wavelengths down to 220 nm. Mercury arc lamps are the most convenient sources of radiant energy in the organic chemistry laboratory. There are three types available, *low-*, *medium-* and *high-pressure* mercury are lamps, which differ in the range of wavelengths and intensity of the light that they produce. The low- and medium-pressure types are those most commonly used in photochemical synthetic work. Commonly, low-pressure lamps, operating at roughly 10^{-3} mmHg, emit light particularly rich in the 254 nm wavelength, together with some at 184 nm that can be filtered out. However, other low-pressure lamps are available that emit at 300 and 350 nm. Medium-pressure lamps, with internal vapour pressures of 1–10 atm, produce a range of wavelengths between 200 and 1400 nm with intensity maxima at 313, 366, 436 and 546 nm. High-pressure lamps effectively give an intense continuum between 220 and 1400 nm, being particularly rich in the visible region. Both medium- and high-pressure lamps produce a great deal of heat during use, necessitating relatively elaborate cooling arrangements.

Low-pressure lamps give out minimal heat and the main requirement of the apparatus is containment and focusing of the light onto the sample. Attention must be paid to the container in which the sample is held, as Pyrex® glass – the usual medium for laboratory glassware – is opaque to light below 300 nm. Reactions requiring light of shorter wavelengths must be carried out in quartz vessels, which are very expensive. Great care must be taken when using them, not only against breakage, but also against touching with the hands as this leaves UV-opaque deposits.

The light may come from an external source shining onto the reaction vessel or the apparatus may be designed such that the lamp is totally surrounded by solution. A photochemical reactor is frequently used with low-pressure lamps for external irradiation. The silvered interior, together with rotation of the reaction vessels on a 'carousel', permits efficient and even irradiation of samples, and the low level of heat generated is removed by a fan. Medium-pressure lamps are usually used as internal irradiation sources. In this arrangement, efficient heat removal is ensured by enclosing the light source in a water jacket.

Both the intensity and the wavelengths of the emissions from all mercury vapour lamps make the light produced intensely hazardous to the eyesight in addition to having deleterious effects on the skin. Special eye protection against UV light and gloves must be worn at all times when working with mercury lamps. All photochemical reactors must be thoroughly covered in order not to permit the escape of light and, wherever possible, experiments should be carried out in a specifically designated blacked-out fume hood. Never commence a photochemical reaction in the teaching laboratory without first consulting an instructor to check the apparatus.