

ORGANIC CHEMISTRY LABORATORY

0055003

Standard and Microscale Experiments
Second Edition

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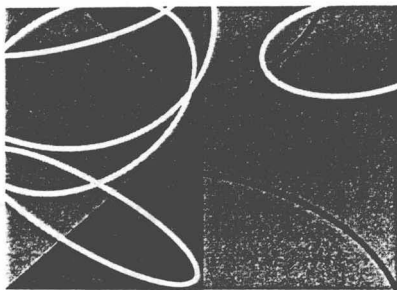
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ORGANIC CHEMISTRY LABORATORY

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P R E F A C E

The purpose of the organic laboratory course is to give students practical experience with operational organic chemistry. Our philosophy, expressed in this text, is that they will be more interested in the science, and ultimately learn more, if the work is fun to do.

At the lowest level, this means that the experiments work as written. All new experiments included have been used in the laboratory course either at Old Dominion University or at the University of Delaware. Each can be carried out in a one (or two) three-hour laboratory period. Throughout, we have tried to make the experiments practical. Rather than prepare camphor, a volatile solid, we oxidize 4-nitrobenzyl alcohol to 4-nitrobenzaldehyde. Neither the starting material nor the product is volatile, and both are crystalline. They also both have strong UV chromophores, making TLC visualization and chromatographic purification easy.

At a higher level, fun means that the experiments involve more than making a product and taking the melting point. In addition to a procedure for preparing the Grignard reagent from bromobenzene, we have included a procedure for preparing the Grignard reagent from 4-bromo-N,N-dimethylaniline. Addition of this reagent to methyl benzoate provides, after acid hydrolysis, the dye Malachite Green. Use of diethyl carbonate in place of methyl benzoate leads to the dye Crystal Violet. Another illustration of this approach occurs early in the text. In addition to a procedure for preparing acetanilide from aniline, we have included a procedure for converting anthranilic acid to the N-acetyl derivative. In the latter case, the crystals obtained are triboluminescent—they flash when ground between two watch glasses.

At the highest level, fun means that the student gets to *reason* about chemistry. We have added two chapters (12 and 13) explaining how to deduce organic structures from spectroscopic data sets. We have found that the sophomore students are able to do this, and enjoy doing it. We have included a range of problems, from simple ones early in Chapter 12, to quite challenging (but still solvable) problems at the end of Chapter 13. We anticipate that the solving of spectroscopic problems will not be limited to a single laboratory period, but rather will be a continuing activity throughout the year. As a service to instructors adopting this text, the authors will supply ten fresh spectroscopy problems each year, to use for exams.

New and Revised Experiments

The following experiments are *new* to this edition:

Experiment 3F, Preparation of Acetanilide, provides an opportunity for students to prepare a product that is easy to recrystallize using microscale methods. Students will enjoy doing Experiment 3G, Preparation of N-Acetylanthranilic Acid, which gives a triboluminescent product.

Experiment 5F, Reflux Boiling Point Method is an alternate way to do a boiling point determination while Experiment 5H, Microboiling Point Determination by the Capillary Method, gives a method for boiling determination of a very small sample.

In Experiment 7A, Separation of Ferrocene and Acetylferrocene, students can do a colorful separation of simple compounds. Experiment 7B, Isolation of Caffeine, gives students experience in separating colorless compounds using column chromatography.

In Experiment 9, High Performance Liquid Chromatography is used to analyze the caffeine in beverages.

Experiment 10E, Steam Distillation of Essential Oils, gives students an alternate choice of spices to distill.

Experiments 12 and 13 on Spectroscopy were completely rewritten and new problems and new spectra added. An integrated method for solving spectral problems is presented.

Experiment 20D, Preparation of Malachite Green, gives a colorful use of the Grignard reagent.

Experiment 21C, Oxidation of p-Nitrobenzyl alcohol has been added as a modern oxidation technique to give an easily purified product. Experiments 21E and 21F, Reduction of Benzo-phenone and Reduction of p-Nitrobenzaldehyde use sodium borohydride reduction.

Experiment 25, Carboxylic Acid Miniunknown gives students practice in applying techniques and reactions already covered in earlier experiments to solve a qualitative analysis problem.

Experiment 28B, Nitration of Toluene, gives products which are easily separated by gas chromatography to give the actual product isomer ratios.

Experiment 31C, Hydrogen Peroxide Oxidation of Lucigenin, provides an excellent colorful demonstration of the principles of chemiluminescence and energy transfer.

A new version of Experiment 34, Phase Transfer Catalysis, gives students the opportunity to synthesize a commercial product from the perfume industry.

The following experiments have been *revised*:

The quantities of chemicals in Experiment 41 were revised so that students can do an IR, ¹H-NMR and take a melting point on the product.

Experiment 48 was re-written and reorganized to emphasize only the wet chemical methods and not the spectral methods. With this experiment students can use the reactions learned in the lecture and solve related problems.

The appendices were expanded to include additional common substances and to give further examples of representative calculations.

Features

Another innovation in this book is the inclusion of a data report sheet with each experiment. While instructors may continue to require that the traditional laboratory notebook be submitted for grading (as we choose to do in our B.S. chemistry major course), we have found that in the larger pre-med organic laboratory course, grading of such notebooks takes an inordinate amount of the time available to the teaching assistants. We thank Professor Roger Murray of the University of Delaware for this suggestion.

We follow current practice by presenting *macroscale* and *microscale* procedures for many of the experiments. We have felt for some time that a well-rounded laboratory training course in organic chemistry should include some “macro” experiments, since some of the techniques are quite different than those used on the “micro” scale. In general, the microscale experiments were developed using the minimal practical amounts of materials. At times, the scales may be slightly larger than those described by others. Our experience has been that the slight additional savings in chemical costs realized from working on still smaller scales has not justified the increased frustration experienced by the students.

Safe laboratory practice and proper waste disposal are emphasized, both in Chapter 1, and in the **Safety Notes** associated with each experiment. To the extent possible, chemicals classified as hazardous by OSHA have been eliminated. In the few instances where they do appear, they and the associated hazards are clearly identified so that adequate safety precautions can be taken. Further advice on the safe dispensing of reagents and other general information on the experiments can be found in the accompanying Instructor's Manual.

In any laboratory course, the student's work efficiency is greatly enhanced if he or she ponders the material beforehand. To this end, we have included prelaboratory questions for almost all of the chapters. Most chapters contain two sets of prelaboratory questions A and B. Instructors can use these questions in different sections of the same course. In addition, we have included questions of variable difficulty at the ends of the chapters, which can best be answered after the experiments have been completed.

This text is appropriate for any level of the organic laboratory course, for either one or two semesters. It has been used successfully with both pre-medical students, and with chemistry majors and chemical engineers studying for a B.S. degree.

Acknowledgements

We note with sadness the untimely death of Oscar R. Rodig, senior author of our first edition. His substantial contributions and careful attention to editorial detail have been greatly missed.

The macroscale sections in this text and in our first edition are direct descendants of *Experimental Methods in Organic Chemistry, 3rd edition*, written by James A. Moore, David L. Dalrymple, and Oscar R. Rodig, and prior editions by Moore and Dalrymple. We are indebted to these colleagues, and to the many students and teaching assistants who worked with them.

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Introduction

Laboratory work is an integral and essential part of any chemistry course. Chemistry is an experimental science—the compounds and reactions that are met in lecture and classroom work have been discovered by *experimental observations*. Organic compounds exist as gases, liquids, or solids with characteristic odors and physical properties. They are synthesized, distilled, crystallized and chromatographed, and then transformed by reactions into other compounds. The purpose of laboratory work is to provide an opportunity to observe the reality of compounds and reactions and to learn something of the operations and techniques that are used in experimental organic chemistry and in other areas in which organic compounds are encountered.

A. LABORATORY SAFETY

Along with the opportunity to learn at first hand about the properties and reactions of compounds and the manipulation of laboratory equipment, there must be proper concern for safety. Most organic compounds are flammable, and they are toxic or irritating to a greater or lesser degree. Many organic reactions are potentially violent. Laboratory work in organic chemistry is not a dangerous occupation, however, nor is the laboratory a perilous place to be, provided that some simple precautions and safety rules are followed. There are some potential hazards that must be recognized and avoided; accidents can and do occur when these hazards are ignored. Throughout this book, **Safety Notes** are included for each experiment. They emphasize the specific hazards that may be encountered and must be kept in mind. In the following section, some general precautions are discussed, and a few rules are given that must be observed during any laboratory work.

Rules for Personal Safety

Avoiding injuries is largely a matter of good sense. Carelessness can lead to accidents and injuries to yourself and others. The following rules cover some important general precautions and should be observed at all times.

1. **Eye Protection.** Approved eye protection must be worn at all times in the laboratory, regardless of what is being done. In many locations, chemical safety goggles are required by law. Safety glasses (either prescription or plain) with side shields to protect from splashes also offer good eye protection.

Contact lenses should *not* be worn in the laboratory. If a splash occurs, the lens can act as a trap for corrosive materials and greatly increase the likelihood of permanent injury. Moreover, low levels of vapors that are present in the laboratory can cause severe eye irritation when trapped behind the lens.

2. Never work in a laboratory without another person being present or within calling distance. Minor accidents can become disasters if help is not available.
3. Do not carry out any reaction that is not specifically authorized by the instructor.
4. Never taste a compound; never pipet a chemical by mouth; do not eat, drink, or smoke in the laboratory.
5. Avoid contact of the skin with any chemical. If a substance is spilled on your hands, wash them thoroughly with soap and water. Do not rinse them with a solvent, since this may cause more rapid absorption.
6. Long hair should be tied back. Shoes must be worn to prevent injury from spilled chemicals or bits of glass. Avoid loose-fitting sleeves and clothing that leave expanses of skin unprotected.
7. Never heat a flask or any apparatus that is sealed or stoppered (i.e., a closed system)—make certain that there is an opening to the atmosphere.
8. When inserting glass tubing into a rubber stopper or rubber tubing, lubricate it first with a drop of glycerin and protect your hands with a towel. The same is true for inserting thermometers into stoppers. Thin-walled transfer pipets should not be used as connectors for rubber tubing or stoppers; they are fragile and very easily crushed.
9. Some experiments require the use of a well-ventilated hood. These experiments should not be attempted in the open laboratory.
10. Peroxides. A major safety concern with certain organic substances is the buildup of potentially explosive peroxides. These can form by the light-catalyzed autoxidation of ethers, alcohols, aldehydes, alkenes, and also aromatic compounds having allylic or benzylic hydrogen atoms. The danger is particularly acute when these materials are used as reaction solvents or in extractions and then are concentrated in the workup. This is one reason why liquids should never be distilled to dryness. Such commonly used substances as diethyl ether, diisopropyl ether, tetrahydrofuran, cumene, tetralin, and 2-butanol (Fig. 1.1) should be checked for peroxides if they have been stored for an extended period of time, especially in a partially empty container. Particular care should be taken with diethyl ether because of its wide use as an extraction solvent.

Peroxides can be detected with starch iodide paper or by adding 1 mL of the suspected material to 1 mL of glacial acetic acid containing 0.1 g of sodium or potassium iodide. A yellow-to-brown color indicates the presence of peroxides. A blank should be run to confirm the validity of the test.

Peroxides can be removed from ethers by shaking with a 30% solution of aqueous ferrous sulfate or by percolating through a column of alumina. The latter method also

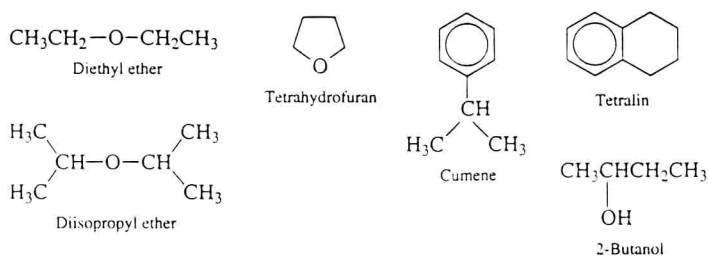


Figure 1.1 Some substances that can form peroxides by autoxidation.

removes traces of water. Additional information on peroxides can be found in the references cited at the end of the chapter.

First Aid

1. **Emergency Equipment.** Learn the location of safety showers, eyewash fountains, and fire extinguishers, and know how this equipment is used.
2. **Chemical Spills on the Skin.** Immediately flush the skin with running water for several minutes; if the eyes or face are involved, use an eyewash fountain or the nearest faucet and wash for 15 minutes. For any serious burn or splashing of chemicals in the eyes, consult a physician as soon as possible after the initial thorough water flushing.
3. **Fire.** If clothing is ignited, immediately extinguish it in a safety shower or by rolling on the floor. If necessary, cover the victim with a coat or fireblanket. Note that it is no longer recommended to wrap the victim in a fire blanket while the victim is standing. The blanket can act as a chimney and encourage the fire. These blankets can be used to cover a shock victim. Do not allow a person with burning clothing to run; such action only fans the flames. Even standing should be avoided because of the danger of inhaling superheated fumes.
4. In any severe case of chemical spill, a burn, or a cut, the affected person should be escorted to a physician or a hospital emergency room.

Chemical Toxicity and Carcinogens

It has long been recognized that certain chemicals—for example, phosgene or the nerve gas isopropyl methylfluorophosphonate—are highly toxic substances that are lethal in extremely small amounts. In recent years there has been a considerable increase in awareness and concern about the toxicity of all chemicals encountered in laboratory and manufacturing environments. Major efforts are now being made to identify toxic chemicals and avoid exposure to them.

The National Institute of Occupational Safety and Health (NIOSH) has prepared a registry of a large number of compounds for which some data on toxic effects are available. Another government agency, the Occupational Safety and Health Administration (OSHA), issues regulations governing permissible limits of exposure to chemicals, with particular attention being placed on compounds that are commonly encountered as air contaminants. Many of the compounds for which limits have been set, such as diethyl ether and ethanol, have relatively low toxicity, but limits are nevertheless placed on prolonged exposure. On the other hand, compounds that may have high acute toxicity can be transferred and used in a laboratory experiment with simple precautions to avoid contact.

A major concern in recent years has been the carcinogenicity of organic compounds, that is, their ability to induce cancer. For certain compounds that were used industrially for many

years, there is a clear link between exposure to the compound and the incidence of certain types of cancer in the workers who handled them. More recently, evidence has been found for the occurrence of tumors in experimental animals exposed to very large doses of a wide variety of other organic compounds. A much-publicized example is the artificial sweetener saccharin, which was used for many years in low-calorie beverages.

Government agencies, such as the Carcinogen Assessment Group (CAG) of the Environmental Protection Agency (EPA) and NIOSH, have compiled lists of suspected carcinogens, and laboratory chemical catalogs often identify these as "cancer suspect agents." The National Institutes of Health has published guidelines for the laboratory use of certain chemical carcinogens, and OSHA, in turn, has issued regulations on exposure to a number of carcinogenic substances, most of which are in commercial use.

A brief list of carcinogenic compounds that are sometimes encountered in laboratory work is given in Table 1.1. It should be pointed out that this list contains only a very small fraction of the compounds for which data on carcinogenic properties are known. Remember that carcinogenic activity is usually based on tests in animals at high doses for prolonged duration, and the risk from occasional brief exposure is unknown. The chief concern with carcinogens, as with other toxic substances, is with permissible levels for continuous exposure, not occasional use. The important consideration for laboratory work is to avoid any unnecessary exposure and to use these compounds only when essential, with due care and protection. In particular, benzene, chloroform, and carbon tetrachloride should not be used as solvents for extraction or column chromatography.

Table 1.1 Partial List of Chemical Carcinogens

acetamide	CH_3CONH_2	dioxane	$\text{O}(\text{CH}_2\text{CH}_2)_2\text{O}$
acrylonitrile	$\text{CH}_2=\text{CHCN}$	ethyl carbamate	$\text{NH}_2\text{CO}_2\text{C}_2\text{H}_5$
aminobiphenyl	$\text{NH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_5$	hydrazine	NH_2NH_2
benzene	C_6H_6	methyl iodide	CH_3I
benzidine	$\text{NH}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{NH}_2$	1-naphthylamine	$1\text{-C}_{10}\text{H}_7\text{NH}_2$
benzpyrene	$\text{C}_{20}\text{H}_{12}$	2-naphthylamine	$2\text{-C}_{10}\text{H}_7\text{NH}_2$
<i>n</i> -butyl chloride	$(\text{CH}_3)_3\text{CCl}$	4-nitrobiphenyl	$\text{NO}_2\text{C}_6\text{H}_4\text{C}_6\text{H}_5$
carbon tetrachloride	CCl_4	nitrosomethylurea	$\text{NH}_2\text{CON}(\text{CH}_3)\text{NO}$
chloroform	CHCl_3	phenylhydrazine	$\text{C}_6\text{H}_5\text{NHNH}_2$
chromic anhydride	CrO_3	thiourea	NH_2CSNH_2
diazomethane	CH_2N_2	<i>o</i> -toluidine	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}_2$
dibromoethane	$\text{BrCH}_2\text{CH}_2\text{Br}$	trichloroethylene	$\text{CHCl}=\text{CCl}_2$
dimethyl sulfate	$(\text{CH}_3)_2\text{SO}_4$		

In the experiments in this book, all compounds that have been implicated as carcinogens have been eliminated wherever possible; in the remaining few cases they have been identified as such. It must be emphasized that, with present knowledge, these compounds should *not* be considered as deserving any more concern than many others. Careless handling of simple acids or solvents normally presents a much greater safety hazard.