LANDGREBE

FOURTH EDITION

ORGANIC LABORATORY

Microscale & Standard Scale Experiments

Theory and Practice in the Organic Laboratory
with Microscale and Standard Scale Experiments

Fourth Edition

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Dedicated to the Future
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Theory and Practice in the Organic Laboratory

Preface

This text presents background material on both classical and modern laboratory techniques (microscale and macroscale) and instrumentation used in organic chemistry, as well as experiments that illustrate many of these techniques and numerous important organic reactions and concepts. The book is the laboratory portion of a one-year organic chemistry course for students entering the fields of biology, chemistry, chemical engineering, medicine, medicinal chemistry, or pharmacy. For pedagogical reasons, to provide flexibility, and so that the manual can serve as a useful reference for students doing undergraduate research, the chapters dealing with theory and techniques (Part I) remain separated from the experimental procedures (Part II). The overall emphasis is on learning fundamental techniques and procedures for handling, synthesis, separation, purification, and identification of organic compounds. While this text contains more material than can be covered in a one-year laboratory course, this fact affords the instructor flexibility and provides resource material for advanced courses. There continues to be a strong emphasis on safety and proper methods for handling and proper disposal of biohazardous materials.

Although this fourth edition retains the general philosophy and format of previous editions, it is characterized by the extensive revision of many chapters, new descriptions of modern instrumentation, reorganization of topics, and the inclusion of both microscale (<500 mg) and conventional scale experiments. Microscale procedures are compared with their conventional scale counterparts within the appropriate chapter for a particular technique, and are not tied to a specific type of glassware. In fact, many microscale operations can be performed with conventional semimicro ($ 14/20 joint) apparatus. To help guarantee a successful microscale experience, experiments are designed so that liquid products are normally obtained in quantities of about 200 μL and solid products in quantities no less than 50 mg. Although microscale experiments have the advantages of shorter procedure times, fewer hazards, decreased supply costs, and less hazardous waste generation, they fail to expose students to some important techniques and apparatus, such as the use of separatory funnels, conventional distillation procedures, and macroscale recrystallizations, that remain an important part of the everyday world of organic chemistry. It is for the latter reason that some standard scale (macroscale) experiments are included in this manual.

There have been many improvements to Part I. The "Introduction to the Organic Laboratory" has been revised to include a discussion on units, new suggestions on how to keep a scientific notebook, and sources of information on the properties of organic compounds. Chapter 1, "Emergency Procedures and Safe Laboratory Practices," now contains an up-to-date discussion of hazardous waste disposal procedures. Chapter 2 is an entirely new discussion on "General Laboratory Procedures," and presents both microscale and conventional scale examples. The chapter on "Chromatography," now much earlier in the text (Chapter 4), has been extensively revised, and includes an introduction to the polarity of molecules, reverse- and normal-phase techniques, capillary methods, new instruments such as the chromatotron, and such important research procedures as flash chromatography. An optional section on chromatographic theory has been placed at the end of the chapter. "Crystallization and Filtration" (Chapter 5) now provides detailed procedures for crystallizations on a conventional scale and microscale, the latter either with the new and convenient disposable pipet technique or with the more traditional Craig tube. The techniques both for extraction and for drying liquids are combined in Chapter 6; microscale extractions are done in small, inexpensive vials with a Teflon-lined cap. Chapter 7, "Distillation and Related Techniques," has been extensively reorganized to include comparisons of conventional and microscale procedures. Also discussed in this chapter are sublimation and steam distillation. "Introduction to Spectroscopy; Organic Structure Determination" (Chapter 8) is a new chapter with basic information on the electromagnetic spectrum, hydrogen deficiency index, and introduction to chemical methods for structure determination. From this short chapter it is possible to use any of the remaining chapters on spectroscopy in any order. Now thoroughly modernized, "Nuclear Magnetic Resonance Spectroscopy" (Chapter 9) includes the integration of proton and carbon-13 spectroscopy, an emphasis on Fourier-transform instrumentation, high-field spectra, and extensive tables of chemical shift values. Chapter 10, "Infrared Spectroscopy," has been entirely revised to include a comparison of conventional and Fourier-transform instrumentation, and numerous FT spectra. Charts of characteristic infrared frequencies have been revised and greatly expanded. "Mass Spectrometry" and "Ultraviolet-Visible Spectroscopy" are now separate chapters (Chapters 11 and 12, respectively) with the chapter on mass spectra entirely rewritten and modernized. Chapter 13, "Special Laboratory Procedures," contains such topics as drying solids and gases, addition of liquids and solids to reaction vessels, inert atmospheres and anhydrous conditions, use of compressed gas cylinders, constant temperature control, solvent purification, hydrogenation, pyrolysis, and photochemistry. This latter chapter is a valuable resource to students who will do undergraduate research or are preparing for graduate work in chemistry.

Part II contains a variety of experiments to introduce and illustrate important and basic laboratory skills and techniques, some important reactions commonly encountered in the corresponding lecture course, and many fundamental mechanistic concepts. In addition to new microscale experiments, many of the experiments from the previous edition have been improved and adapted to microscale by the author, and each experiment has been carefully tested. Most experiments are offered either in microscale or conventional scale (not both), with an emphasis on the former. In addition, there is an adequate variety of experiments to provide flexibility and choices for the one-year organic course. The experiments on qualitative analysis acquaint the student with some important chemical and physical properties characteristic of many frequently encountered functional groups. However, the emphasis is on the use of spectroscopic techniques to perform the final identification.

Numerous exercises have been provided within or at the end of the chapters in Part I as well as in each experiment. Selected answers to exercises in Part I can be found in the Appendix. Students are expected to complete a formal write-up of each experiment as described in "Introduction to the Organic Laboratory."

An *Instructor's Manual* is provided with answers to exercises within the experiments and other information helpful for organizing the laboratory course and preparing for each experiment.

I should like to thank my colleagues for their encouragement and help, my teaching assistants who made many valuable suggestions, and my students for their interest and enthusiasm. Special thanks go to Professors K. Barbara Schowen and Albert W. Burgstahler for numerous insightful discussions and improvements to the experiments. I especially appreciate working with Maureen Allaire and the thoroughly professional staff at Brooks/Cole Publishing Company, and I am indebted to the expert editorial and production services of John A. Servideo. I wish to express my gratitude to Sadtler Research Laboratories, Philadelphia, Pennsylvania, and Aldrich Chemical Company, Milwaukee, Wisconsin, and Varian Associates, Palo Alto, California for permission to reproduce the nuclear magnetic resonance and infrared spectra found in Chapters 9 and 10, and to Bruker, San Jose, California, for permission to use their ^{13}C chemical shift chart in Chapter 9. Finally, to my wife Carolyn, my grateful thanks for her forbearance and love during the preparation of the manuscript.

A Word to the Instructor

The experiments in this manual represent a mix of microscale and standard or macroscale with an emphasis on the former, and provides students with a range of important laboratory experiences. The microscale experiments have been designed so that they can be done with conventional semimicro (₮ 14/20) apparatus or with commercial kits such as those distributed by Ace, Chemglass, Corning, Kontes, Reliance, or Wheaton. Depending on the exact glassware items available at a given college or university, it may be necessary for the instructor to sketch a slightly modified version of what is pictured in this text and hand that out to the students or post it in the laboratory room.

The advantage of using conventional semimicro apparatus is that many colleges and universities already have a supply of this equipment, thus decreasing the capital investment required to begin doing microscale experiments.

The heat source recommended in this text is a shielded 250-w infrared lamp connected to a Variac (or less expensive solid state or proportional control). Although many of the procedures described will work with other heat sources such as a sand bath or oil bath, the very convenient recrystallization procedure using Pasteur pipets can only be done with a heat lamp. If other sources of heat are used, instructors should do recrystallizations with the less effective and more expensive Craig-tube method outlined near the end of Chapter 5. Heat lamps are among the safest of heating sources, have rapid response, and are capable of quickly achieving temperatures in excess of 200°C when a shield is employed and foil or steam bath rings are used to confine the heat (see Figure 2.15). **It is important for safety reasons that when the shielded heat lamp is used in the vertically upward orientation (shown in Figure 2.15a), the steam bath rings shown should always be employed to protect against breakage of the bulb in the event that cold liquid is spilled.**

Following is a list of equipment recommended for doing the microscale and standard scale experiments described in this text. If the expense of supplying certain equipment for individual student drawers becomes too great, this equipment can be treated as community property, and either checked out on a daily basis as needed or marked with a laboratory station number (etched or baked enamel) and placed into a wall-mounted rack.

Individual Student Equipment

designates primarily microscale use.

1. Beakers (400 mL, 250 mL, 100 mL, 1/student)
2. Cloth strip (2 cm x 10 cm, to wrap around condensing surface of Hickman still, 1/student)
3. Condenser (West or comparable type, ST 14/20 female joint, 1/student)
4. Condenser (ST 24/40, for reflux or distillation, 1/student)
5. Cylinders, graduated (25 mL, 100 mL, 1/student)
6. Cylinder, graduated (5 mL or 10 mL, 1/student)
7. Distillation adapter (for male end of condenser, 1/student, optional)
8. Distillation column, fractional (made from a condenser with copper sponge, 1/student)
9. Distillation head (simple, for fractional distillation)
10. Distillation unit, Hickman (commercial unit or home made as in Figure 7.5,[1] 1/student)
11. Distillation unit, semimicro (1/student)[2]
12. Flask filter (250 mL, 1/student)
13. Flask, filter (125 mL, 1/student)[3]
14. Flasks, pear-shaped (ST 14/20, 2/student)
15. Flasks, Erlenmeyer (250 mL, 1/student; 125 mL, 1/student; 50 mL, 2/student; 25 mL, 2/student)
16. Flask round-bottomed, single-necked, ST 24/40 (100 mL, 250 mL, 500 mL, 1/student)
17. Funnel, Büchner (4.5 cm or 5.5 cm, 1/student)
18. Funnel, Hirsch (#5/0, with stopper or adapter for filter flask or side-armed test tube, 1/student)
19. Funnel, short stem (75 mm, 1/student)
20. Funnels, separatory, Squibb (60 or 125 mL and 250 or 500 mL, 1/student)
21. Heat lamp, 250-w red-glass infrared, with shield[4] with variable transformer (Variac) or less expensive solid-state or proportional control[5] (1/student)
22. Medicine dropper (with bulb, serves as microscale drying tube, 1/student)
23. Spatula, microscale[6] (1/student)
24. Spatula, semimicro (stainless steel or porcelain, 1/student)
25. Stirrer, magnetic (for 10 mL pear-shaped flask, 1/student)

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1. This still can be prepared from a 10 mL blank pear-shaped flask from Chemglass, Vineland, NJ (1-800-843-1794 when outside New Jersey or 1-609-696-0014) and Pyrex tubing with o.d. 10 mm, ca. 2.5 cm at the top and 3 cm at the bottom. The receiver can handle volumes from 200 μL to 1 mL.
2. The Kontes short-path still or another comparable apparatus.
3. A side-armed test tube can be substituted.
4. Swivelier shield #22093, Nanuet, NY, 10954.
5. Laboratory Craftsmen, Inc., Beloit, WI (1-608-362-2255).
6. For example, Fischer #21-401-25A or B.

26. Stirring bar (Teflon-covered, maximum length = 22–23 mm, but does not have to be the special higher-priced triangular shaped type, 1/student)
27. Syringe, plastic, 1 mL (with tight fitting plastic plunger, serves as dropping funnel, 1/student)[7]
28. Test tubes (several of assorted sizes)
29. Test tube, side-armed (20 x 150 mm, serves as vacuum oven, 1/student)
30. Tube, drying (150 mm, 1/student)
31. Tube, glass (4–5 cm x 7 mm) with rubber stopper to fit ₸ 14/20 joint (for solvent evaporation, 1/student)
32. Tweezers (1/student)
33. Vials (for extractions and recrystallizations; 1 dram, 2/student; 0.5 dram, 2/student) with screw caps (Teflon[8] or polyethylene lined)
34. Watch glass (1/student)

General Laboratory Equipment

1. Balances, top loader (1 mg readability, with shield around pan, 1/10 students)
2. Boiling chips and sticks
3. Clamps, rings, pinch clamps (an assortment in each lab)
4. Copper wire (20 gauge, 1 spool/lab)
5. Cotton (washed with hexane and methanol, several small bottles/lab)
6. Filter aid
7. Filter paper (to fit Hirsch and Büchner funnels)
8. 50 μL gas chromatography syringe (to load capillary tube for bp determination, several/lab)
9. Glass wool (Pyrex)
10. Labels
11. Melting-point capillaries
12. Microburners (1 or 2 in hood)
13. Pasteur pipets (large box/lab)
14. Pipets, automatic delivery (20 μL–200 μL, 1/10 students)
15. Pipets, automatic delivery (200 μL–1000 μL, 1/10 students)
16. Pliers (2–4 pairs/lab)
17. Ruler, plastic (several/lab)
18. Silicone oil (in dropper bottles)
19. Sponges
20. Spot plates (black and white porcelain, several/lab)
21. Stopcock grease

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7. Air-Tite Products, Vineland, NJ, 1-800-257-5318, about $0.85/ea.
8. Teflon-lined cap for 0.5 dram vial, Fischer #02-883-3AA, 8 mm size; for 1 dram vials, #02-883-3A, 13 mm size.

22. Thin-layer chromatographic equipment (wide-mouthed jars, 80 mm high, with screw cap, 3/student; microscope slides, 6/student)
23. Weighing paper (glazed, 1 box/balance)

Chemicals and Reagents for General Use[9]

1. Acetone (for drying and cleaning, in squeeze bottles)[10]
2. Calcium chloride (granular, anhydrous)
3. Decolorizing charcoal (Norite pellets, 0.8 x 3 mm, Aldrich)
4. Detergent solutions (Alkanox or Micro)
5. Hydrochloric acid (concentrated)
6. Hydrochloric acid (3*M*)
7. Magnesium sulfate (anhydrous)
8. Methylene chloride
9. Nitric acid (concentrated)
10. Salt (rock or granular, for ice-salt baths)
11. Sodium bicarbonate (satur. soln.)
12. Sodium hydroxide (3*M*)
13. Sodium sulfate (anhydrous)
14. Sulfuric acid (concentrated)

An *Instructor's Manual* can be requested from the publisher, which provides the following additional information: (1) Chemicals or special supplies required for each experiment, (2) Experiments subdivided by functional groups undergoing reaction or being produced, (3) a listing of the experimental techniques used in each experiment, (4) reaction sequences within and among various experiments, (5) answers to the exercises within each experiment, (6) experiment objectives, and (7) helpful comments.

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9. Special solvents and reagents to be supplied in appropriate quantities as needed.
10. According to OSHA (Occupational Safety and Health Administration) regulations, the maximum amount of this solvent that can be stored in glass or approved plastic containers is 1 qt and in metal or safety cans is 1 gal.

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