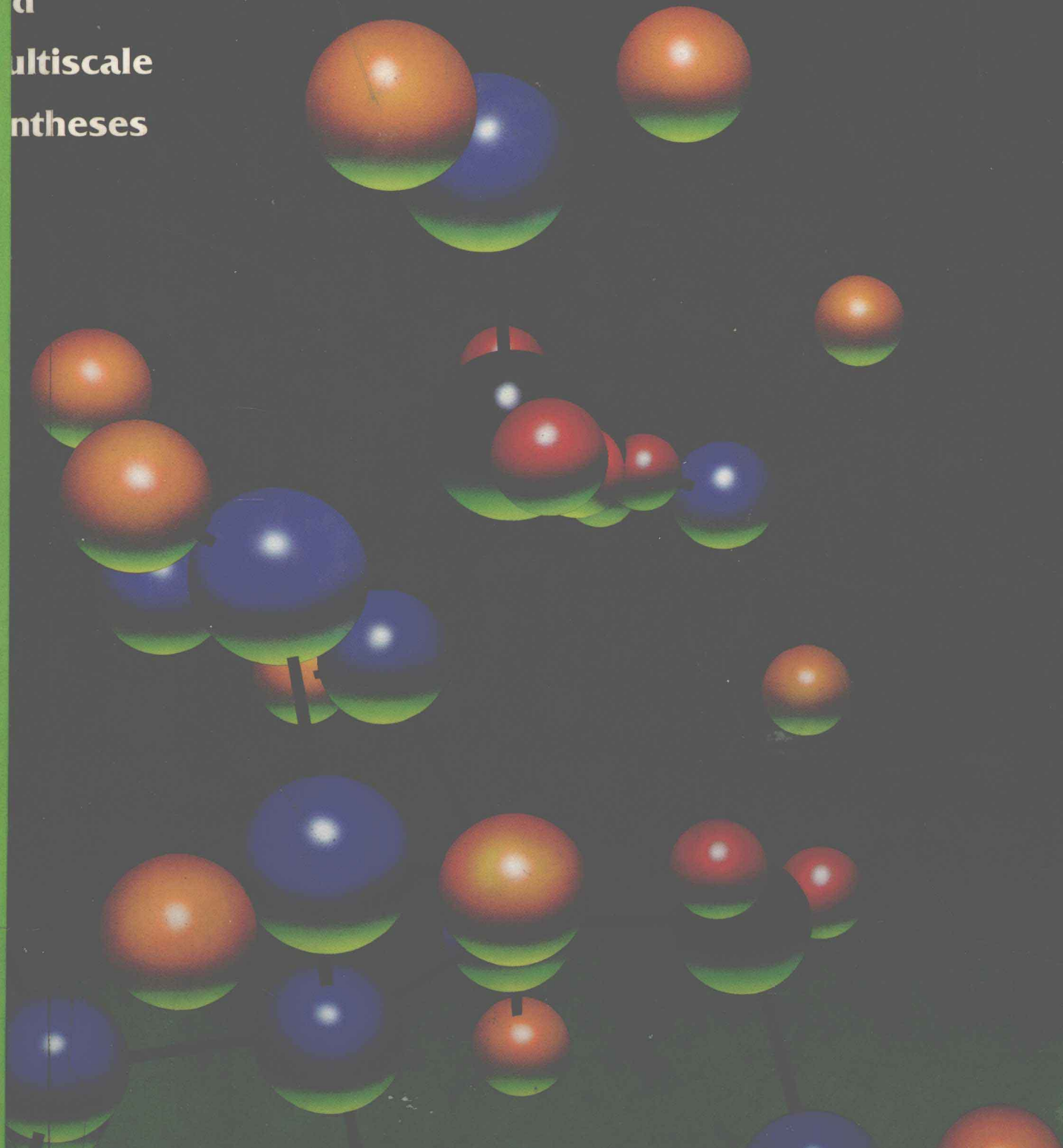
ana W. Mayo • Ronald M. Pike • Peter K. Trumper

Microscale Organic Laboratory

ith
ultistep
d
ultiscale
ntheses

Third Edition



Microscale Organic Laboratory

with Multistep and Multiscale Syntheses

THIRD EDITION

Dana W. Mayo
Charles Weston Pickard
Research Professor of Chemistry
Bowdoin College

Ronald M. Pike
Professor of Chemistry, Emeritus
Merrimack College

Peter K. Trumper
Professor of Chemistry
University of Southern Maine

John Wiley & Sons, Inc.
New York Chichester Brisbane Toronto Singapore

Acquisitions Editor Nedah Rose
Marketing Manager Catherine Faduska
Senior Production Editor Marcia Craig
Text Designer Eileen Burke
Cover Designer Karin Gerdes Kincheloe
Manufacturing Manager Andrea Price
Illustration Sigmund Malinowski
Cover Illustration: De-ethyloxodeltaline Roy Wiemann

This book was set in 10/12 Palatino by Bi-Comp, Inc. and
printed and bound by Hamilton Printing. The cover was printed by Lehigh Press.

Library of Congress Cataloging in Publication Data:

Mayo, Dana W.
Microscale organic laboratory : with multistep and multiscale syntheses / Dana W. Mayo, Ronald M. Pike, Peter K. Trumper. — 3rd ed.
p. cm.
Includes index.
ISBN 0-471-57505-4 (acid-free)
1. Chemistry, Organic—Laboratory manuals. I. Pike, Ronald M. II. Trumper, Peter K., 1955- III. Title.
QD261.M38 1994
547'.0078—dc20 93-43051
CIP

ISBN 0-471-57505-4

Printed in the United States of America

10 9 8 7 6 5 4 3 2

Preface

to the Third Edition

The Microscale Organic Laboratory, which began over a decade ago, is no longer a fledgling program. The germination of those early seeds has produced a bumper crop of conversions to this highly efficient method of laboratory instruction.

Over the eight years following the release of the *Preliminary - 1* edition, we have conducted numerous workshops and held seven, one-week, summer institutes at Bowdoin; these now continue at Merrimac College. These programs have been centered primarily on acquainting organic faculty at other institutions with the experimental techniques involved in successfully operating the microscale laboratory. In 1990 we published a separate book, *Microscale Techniques for the Organic Laboratory*, which was entirely devoted to describing the techniques required to operate an instructional program at this scale.

Based on the wide experience we have accumulated during this time, we have now undertaken a major revision of the material contained in the two earlier editions of *Microscale Organic Laboratory*. Our third edition, **MOL-3**, is a very different text.

The third edition of MOL represents a major reorganization of nearly the entire manuscript. We list here these modifications and the rationale for these changes, which significantly improve the effectiveness of the text in students' hands.

- We have moved the discussions of microscale techniques to their own chapter. No experimental exercises are to be found in this section of the text. Our approach in earlier editions placed representative experiments directly within the technique discussions. Many instructors prefer the option of employing other laboratory exercises to introduce particular techniques. As a result, students have found the unused experimental material surrounding a particular technique discussion to be confusing rather than helpful.
- To further help facilitate the student's introduction to a particular

chemists who discovered or investigated the reactions. Specific attention has been placed on those cases where the name of a reaction has become associated with a particular individual. In a few cases where fundamental mechanistic examples are introduced, we have also included historical discussions of the development of the theory surrounding these transformations and the scientists responsible for elucidating the chemistry.

- In the experimental sections we have retained the format that was used in earlier editions. Headers that identify the various stages of the experiment, margin graphics that are a guide to assembling apparatus, clear tables of physical properties and quantities of starting materials and reagents, estimated time for students to complete the experimental procedures, and convenient stopping points in those exercises expected to require more than a single laboratory period are noted. **Warnings** and **Cautions**, as well as advice regarding use of the **hood**, are in **bold type** to bring this advice to the attention of the students, teaching assistants, and instructors. References to the literature and numerous questions are given at the end of each experiment. The latter have been expanded and reorganized to correlate effectively with the experimental sections. We have dropped tables of environmental data from each experiment. While we still view this information as important data for the student, our reviewers felt that this material was readily available from other sources and was an unnecessary redundancy. We have also deleted, where possible, the physical properties of the products in order to encourage the students to locate the data in common, readily available handbooks. In a number of experiments we have retained the detailed interpretations of infrared spectra of starting materials and products. These discussions can be used as illustrative examples of how this type of spectroscopic data can be used to more deeply characterize the reaction under study.
- We have added two new sections to the experimental format:

  First, at the beginning of each exercise a description is given of the *Purpose* for which the experimental work is designed.

  Second, an assigned *Prior Reading* list follows the statement of *Purpose*. This list refers to those technique sections that apply to the experimental procedures to be utilized during the particular experiment under study.
- As in earlier editions, we continue to emphasize several very powerful experimental methods modified by us for the purification of microscale and semimicroscale quantities of liquid reaction products. A number of the experiments introduce preparative gas chromatographic (prep-GC) routines for high-resolution separation and purification of liquids. For semimicroscale liquid separations, two powerful spinning band distillation columns are introduced.
- A number of new experiments have been added and a few less attractive ones have been dropped. **Ninety-two** individual experiments are available for study.

The experiments are organized into three chapters, rather than all being lumped into a single massive section.

The first experimental chapter (Chapter 6), *Microscale Organic Laboratory Experiments*, contains thirty-five microscale experiments that have detailed and explicit directions.

The second experimental chapter (Chapter 7), *Advanced Microscale Organic Laboratory Experiments*, consists of seven experiments. These exercises

years 80% of all undergraduate organic students would be employing the microscale approach." With the conversions of the University of Michigan, New York University, North Carolina State, the University of North Carolina, Duke University, Purdue University, University of California at Los Angeles, the entire University of Wisconsin system (23 campuses), Rice University, the United States Military Academy, and the University of Texas to name just a few of the larger programs, it is now evident that David's vision was considerably clearer than our own. By the end of 1994 the number may not reach 80%, but certainly a majority of undergraduate organic chemistry instruction will be at the microscale level or close to it. It is no longer a question of, "Is this the best pedagogic approach?," but, "How soon will the conversion occur?" In fact, a recent advertisement for an organic chemistry laboratory instructor listed experience with microscale organic laboratory techniques as a primary job requirement.

With the introduction of *the microscale laboratory* feature column edited by Arden P. Zipp in the *Journal of Chemical Education*, the need for our *Smaller is Better Newsletter* has declined. It is now circulated only on an irregular basis. The authors are only too happy to see the journal absorb this role.

The authors wish to acknowledge a number of very helpful contributions and comments that have been incorporated into the third edition: the development of the improved separation scheme for the isomers of 4-*tert*-butylcyclohexanol by T. J. Dwyer and S. Jones of the University of California, San Diego; the development of the Sequence C experiments by S. Danishefsky of Yale University; and the Sequence F experiments by R. Marshall Wilson and D. L. Lieberman of the University of Cincinnati.

In addition, we are grateful to the colleagues listed below whose careful reviews, helpful suggestions, and thoughtful criticisms of the manuscript have been of such great value to us in developing this Third Edition.

Mark Midland
University of California, Riverside

Peggy Alley
Amarillo College

Deborah Lieberman
University of Cincinnati

Dale Ledford
University of South Alabama

Donald Slavin
Community College of Philadelphia

Doris Kimbrough
University of Colorado-Denver

Allen M. Schoffstall
University of Colorado-Colorado Springs

Warren Sherman
Chicago State University

We continue to acknowledge the outstanding contributions of the early pioneers of instructional microscale programs and techniques such as F. Emich and F. Pregl in Austria; N. D. Cheronis, L. Craig, R. C. Fuson, E. H. Huntress, T. S. Ma, A. A. Morton, F. L. Schneider, and R. L. Shriner, in the United States; and J. T. Stock in both England and the United States. Clearly, these educators laid the foundation on which we were able to fashion much of the current introductory program.

We have been very pleased to see significant reductions in the cost of the microscale glassware since the last edition and we applaud the efforts of J. Ryan and Larry Riley of the ACE Glass Company to make this educational equipment more accessible to institutions on very tight instructional budgets. Both Ryan and Riley, together with Robert Stevens of J. J. Stevens, have helped to make further significant improvements in the performance of the already powerful spinning band distillation systems that we have developed in collaboration with Robert Hinkle (Bowdoin

Preface

to the Second Edition

In the three years since 1985, when bound xerox copies of *Microscale Organic Laboratory—1 Preliminary*, the manuscript of the later *Microscale Organic Chemistry*, first became available, nearly three hundred institutions have moved to convert to this style of program. The magnitude and rapidity of adoptions really does mean that we are now in the midst of an educational revolution. Most impressive to us, however, is that of all the institutions initiating trial microscale programs, none to our knowledge has later dropped the microscale approach. Those areas in need of further refinement are being attacked by an ever-widening and skillful group of enthusiastic evangelists. Indeed, it is our view that we have just skimmed the surface of fruitful micro techniques and experiments, and we look forward in the next several years to bringing into sharper focus the direction in which this exciting approach will be heading. It is particularly gratifying to see the program being explored by a cross section of institutions ranging from small community colleges to large research-oriented universities. This variety of interest has in turn led to a wide range of useful and ingenious comments and suggestions, many of which we are pleased to be able to incorporate in this latest edition.

In response to favorable reviews, we have retained the basic format of the first edition. Thus, we continue to integrate illustrative experimental examples in the techniques section; to incorporate keyed marginal illustrations of apparatus setups throughout most of the experimental section; and to describe the experiments in formal journal style prose. We have extended our energies during the last few years to refining a number of key experimental techniques and to improving the reliability, flexibility, and variety of reactions to be studied. For a number of experiments in which clarity needed to be improved, we have rewritten procedures.

We are now convinced that by the end of the coming decade the great majority of chemical educational programs in the United States will have converted to the microscale approach. The question is not whether to

tively utilized by programs looking to expand the amount of microscale chemistry involved in a particular experiment or as an alternative to instrumental characterization.

The very successful utilization of the chromatographic techniques given in the first edition has lead us to expand the coverage and application of these powerful experimental routines. Gas chromatography and thin-layer chromatography are effectively utilized in a number of new locations.

Several other areas of the text have been improved. For example, the section on acid-base extraction has been expanded and in addition includes a sequence that illustrates the separation of a three-component mixture. The variety of alternate methods to illustrate a particular reaction continues to increase. For example, an improved extraction technique for the isolation of caffeine, the Horner–Emmons modification of the Wittig reaction, and a new nitrating agent prepared from silica gel and nitric acid are now included in the reaction selections.

The authors wish to acknowledge the many helpful suggestions from Professors Charles E. Sundin, University of Wisconsin–Platteville, Chaim N. Sukenik, Case Western Reserve University, and Bruce Ronald of Idaho State University. We are also indebted to all those who have attended the Bowdoin College Microscale Summer Institutes and our workshops across the country. Your enthusiasm, interest, and insight have led to many of the improvements in procedures and techniques now incorporated into the program. The many contributors to the newsletter *Smaller Is Better* have significantly helped to sustain the momentum of the program. We especially thank Paulette Fickett and Lauren Bartlett, Laboratory Instructors at Bowdoin, for their dedication, hard work, and eternal optimism. The microscale program could not have evolved in such a successful fashion without the continued contributions of John Ryan of Ace Glass, Stephen Cantor of Pfaltz and Bauer, Robert Stevens of J. J. Stevens, and of Henry Horner and Thomas Tarrant, all of whom have given encouragement and helpful guidance at crucial stages along the way. Judy Foster again waved her magic wand and this time transformed a first-edition Apple Writer manuscript into Microsoft Word. We continue to marvel at the patience of Dennis Sawicki, our Chemistry Editor. We would like to acknowledge continued support from the Surdna Foundation in developing the microscale program. The Sloane Foundation and the National Science Foundation have supported two of the summer institutes.

We are particularly indebted to our colleague Peter Trumper for injecting his expertize in FT-NMR into the microscale program. His enthusiastic application of high-field NMR to the introductory organic program promises future exciting developments in this area.

As we stand on the threshold of the second decade of the microscale revolution, we wish to thank our students. Especially for them do we feel the program has meaning: a cleaner atmosphere in which to work, an awareness of the toxic factors associated with the chemical workplace, and a commitment to detail not hitherto fostered in the introductory laboratory. For their perseverance and eagerness to learn and adapt to new ideas, for the freshness that each new class brings, and for their willingness to grow, we are indeed most grateful.

DANA W. MAYO
RONALD M. PIKE
SAMUEL S. BUTCHER

Brunswick, Maine
October 30, 1988

Preface

to the First Edition

This introductory organic laboratory textbook is a major departure from all other modern texts dealing with this subject. For a number of very cogent reasons, we have chosen to introduce experimental organic chemistry at the microscale level. Currently, beginning students perform the large majority of their experimental work at least two orders of magnitude above that described in this manual. Although contraction from the multigram to the milligram scale is the most obvious change, there are a number of other very unique aspects to our approach.

1. The laboratory environment has been made a distinct part of the experimental process. The student is given the means of easily determining his or her exposure to all volatile substances employed in the experiments. These calculations can be carried out for any laboratory by utilizing instructor-supplied ventilation rates.
2. Chemical instrumentation is given very high priority in the laboratory. The text avoids emphasizing data not directly determined by the student. Product characterization by infrared spectroscopy is routine, and detailed means for interpreting such data are provided.
3. Modern separation and purification techniques, including preparative gas chromatography, thin-layer chromatography, and column chromatography, are extensively utilized in product workups.
4. Over a third of the 82 reaction products are new to the undergraduate laboratory. Many of the reactions involve reagents or substrates that would present potential safety problems or entail exorbitant costs in a macroscale laboratory program; nevertheless, the use of these materials becomes safe and practical for experimentation at the microscale level. Reagents such as anhydrous nitric

greater importance, and a point that we have come to appreciate in retrospect, is that many reactions and operations carried out at the micro level require far less time to reach completion. Indeed, *many of the time-consuming aspects of current instructional experiments are dramatically shortened.* We believe that the concomitant advantage of the microscale approach, the substantial increase in the number of manipulations possible per laboratory period, will have a major pedagogic impact. Herein lies the significant advantage of this approach to teaching laboratory technique.

We also see the increase in use of chemical instrumentation as a further pedagogic advantage of operating at the microscale level. Routine use of gas chromatography may be avoided in macro experiments; however, if it is not employed at the microscale level, successful experimentation with liquid substances is limited. The capital investment that would allow routine use of this equipment in many undergraduate laboratories might appear to elevate the microscale program out of the reach of institutions with very limited budgets. For many institutions, however the very substantial savings in chemical costs (75–90% of current expenditures), if carefully managed, can offer a rapid payback period (2–4 years) for expanded gas chromatography capacity and for other pieces of equipment. The end result of conversion to microscale is a far more effective integration of modern instrumentation into the organic laboratory program.

Once the microscale approach is initiated, the advantages are endless. We will not dwell on them here, as many of the following points vary in importance with each institution: (1) major reduction in cost of chemicals, (2) elimination of fire or explosion danger, (3) elimination of chemical waste disposal costs, (4) expansion in variety and sophistication of experiments, (5) elimination of dependence on commercially available starting materials, and (6) more durable and less expensive glassware.

These advantages are highly compelling reasons for advocating the microscale approach. Initially, however, we had serious reservations. First, the microscale approach appeared to involve a sophisticated set of techniques and manipulations too advanced for sophomore undergraduates to master. Second, a student having experience only at the microscale level might be expected to encounter problems when larger-scale preparations were undertaken. Third, significantly less organic chemistry would be covered during the year because increased attention would have to be paid to the development of microtechniques. Fourth, certain classical procedures such as fractional distillation would have to be abandoned.

As of the completion of this text, we have conducted eight semesters of microorganic chemistry laboratory assessment. The experience with the test laboratory groups (made up of a cross section of volunteers) has been a revelation. It is clear from our observations that the entire range of the class achieves significantly better results on micro experiments. Better yields are realized and, in particular, the class appears to master experimental details and procedures more effectively. It is felt that these results arise from several causes, one of which is the increased attention to detail required in the laboratory. We also sense a synergistic influence with the analytical chemistry laboratory, which is often scheduled for the sophomore year concurrently with the organic course. Analytical chemistry is carried out at a scale not unlike that employed in the microscale organic laboratory.

At present there is no indication that the learning of micro techniques during the introduction to organic chemistry causes any adverse effects when scaleup work is introduced in advanced laboratory courses or in research areas. To the contrary, our students appear to be performing significantly better in upper-level work.

The development of the experimental section of the text, which con-

ence in the trenches and her willing contributions in any area of need at any time are most gratefully remembered. The enthusiasm of the sophomore organic students who volunteered for the initial pilot sections at Bowdoin and the field testing sections at Merrimack played a key role in encouraging us to continue these efforts.

Judy Foster's talent with a Macintosh enabled her to generate the majority of the illustrations and reaction schemes. Judy's efforts have greatly enhanced our descriptions of the techniques involved in microscale work. Her ingenuity also led to the pictorial keying of the equipment setups. The patience, understanding, and thoughtful advice of Dennis Sawicki, Chemistry Editor for Wiley, has been particularly valuable.

We thank Dean Alfred Fuchs for his constant encouragement of this program during its development. The initial exploratory work was supported by a grant from Bowdoin College and a department grant from the du Pont Company. A semester leave given to D.W.M. (spring 1984) was funded by a grant from the ARCO Corporation. A semester sabbatic leave was granted to R.M.P. by Merrimack College (spring 1985), as was an appointment as Visiting Charles Weston Pickard Professor of Chemistry at Bowdoin College (1980–1981, spring 1984). The Surdna Foundation awarded two major grants which allowed the complete development and implementation of the program at Bowdoin College and the field testing of experiments at Merrimack College. The support and faith in this educational concept by these institutions is gratefully acknowledged.

DANA W. MAYO
RONALD M. PIKE
SAMUEL S. BUTCHER

March 1985
Brunswick, Maine

About the Authors

Dana W. Mayo holds the Charles Weston Pickard Research Professor of Chemistry Chair at Bowdoin College. A former Fellow of the School for Advanced Study at MIT and a Special Fellow of the National Institute of Health at the University of Maryland, he received his Ph.D. in Chemistry from Indiana University. Professor Mayo is Director of the Bowdoin College Summer Course in Infrared Spectroscopy. His research interests include the application of vibrational spectroscopy to molecular structure determination, natural products chemistry, and environmental studies of oil pollution.

Ronald M. Pike is Professor Emeritus of Chemistry at Merrimack College and is currently Director of the National Microscale Chemistry Center (NMC^2) at that institution. He received his Ph.D. from Massachusetts Institute of Technology. He is the author of numerous papers and patents in the area of silicone chemistry, is coauthor (with Szafran and Singh) of *Microscale Inorganic Chemistry: A Comprehensive Laboratory Experience* and (with Szafran and Foster) of *Microscale General Chemistry With Selected Macroscale Experiments*. He was previously associated with Union Carbide Corporation and the Lowell Technological Institute. He has been a Visiting Charles Weston Pickard Professor of Chemistry at Bowdoin College and a Visiting Professor at the U.S. Military Academy, West Point, NY.

Peter K. Trumper is an Assistant Professor of Chemistry at the University of Southern Maine. He received his B.A. from St. Olaf College and his Ph.D. from the University of Minnesota. He held an NIH postdoctoral fellowship at the University of Pennsylvania.

Dana Mayo and **Ronald Pike** jointly received the James Flack Norris Award (1988) for outstanding achievement in the teaching of chemistry, and the

John A. Timm Award (1987) for their work in developing the microscale instructional program. They also received (DM, 1989; RP, 1990) the Catalyst National Award of the Chemical Manufacturers Association for excellence in chemistry teaching. Together with Samuel Butcher, they were corecipients of the first Charles A. Dana Foundation Award (1986) for pioneering Achievement in Health and Higher Education and the American Chemical Society Division of Chemical Health and Safety Award (1987). They are also the coauthors together with Samuel Butcher and Peter Trumper of *Microscale Techniques For The Organic Laboratory*.

tains eighty reactions, has been a major effort. The conditions for a large proportion of these reactions have been optimized to maximize yields at the micro level. We have chosen to describe the experimental work in language similar to formal journal style. At first, this impersonal construction would appear to be "user unfriendly" and to make the text a bit boring and difficult to read. On field testing with students, however, we have found that they quickly adapt to the style and soon come to appreciate the use of precise routine terminology. This introduction to formal style pays substantial dividends in upper-level courses where students are expected to consult the original literature.

The philosophy of this text is to focus the student, to a very large extent, on the *experimental* aspects of organic chemistry. We have purposely attempted to keep to a minumum the theoretical discussions, supplying only sufficient background material to cover potential discontinuities between lecture and laboratory. We want the student to become comfortable, and to develop a substantial degree of independence with the use of chemical instrumentation. To meet this objective, we have centered attention specifically on infrared spectroscopy and gas chromatography. We do this because we feel that these basic instrumental techniques can be utilized to a much larger extent by sophomores than the more expensive techniques.

We recognize the dominant role of nuclear magnetic resonance in modern organic chemistry. The current real-life situation is, however, that only in a very limited number of cases do second-year students ever have the opportunity to generate their own data with this instrumentation. Because we are concerned primarily with focusing student excitement and interest on gathering actual laboratory data, we feel that artificially incorporating material from outside the laboratory as a means of including the nuclear magnetic resonance or mass spectroscopy experiment may not enhance but divert attention away from the laboratory experience. We are seriously exploring ways to overcome this particular problem and hope to address this issue successfully in future editions.

The six-year road to completion of this text has been a long, but rewarding one. Many individuals have made vital contributions. Arnold Brossi, David Brooks, Miles Pickering, Lea Clapp, Eugene Cordes, and Henry Horner provided encouragement and sound advice at crucial points along the way.

We gratefully acknowledge that the large majority of the infrared and nuclear magnetic resonance spectra not recorded at Bowdoin College were obtained from the Aldrich Libraries of FT-IR and NMR Spectra through the courtesy of Dr. Charles Pouchert and the Aldrich Chemical Company.

John Ryan, Larry Reilly, Don Sellars, and Hugh Bowie of Ace Glass are primarily responsible for the development of the novel microglassware. They exhibited considerable patience throughout the ordeal. Ed Hollenbach and Lyle Phifer of Chem Services saw the advantage of making available small quantities of high-purity reagents and starting materials as a way of ensuring success at the microscale level.

The vast amount of experimental development was shared by Teaching Research Fellows Janet Hotham, David Butcher, Paulette Fickett, and Caroline Foote, plus a number of Bowdoin students—Mark Bowie, Sandy Hebert, Rob Hinkle, Marcia Meredith, and Gregory Merklin. The experimental ground covered by this group, much of which required ingenious solutions, is remarkable. The breadth of experiments available is a tribute to their dedication. Janet deserves a special thanks. A Merrimack College graduate adopted by Bowdoin College, she has been with the program almost from the beginning. Her thoughtful suggestions based on experi-

acid, diborane, chloroplatinic acid, "instant ylids," silver persulfate, chromium trioxide resin, tetrabutylammonium bromide, and triflic acid are representative of the materials that the student will encounter during the year.

Why are we committed to the goal of attempting to reduce significantly the scale of starting materials in the introductory organic laboratory? The academic community has become increasingly aware of the necessity of improving air quality in instructional laboratories. The standard solution to this problem, a costly upgrading of the ventilation system, has generally been considered the most reasonable answer.

Our study of the problem led us to the following conclusions. First, although current organic laboratory texts are filled with details of product characterization employing the latest spectroscopic methods, the descriptions of the techniques of preparing compounds have changed very little from those of a century ago. In particular, the scale of synthesis has changed very little over this period. (Indeed, the quantities of materials employed have only decreased modestly, and in some cases have actually increased!) Clearly, the strategy of introducing the student to organic chemical laboratory techniques, originally and still today, is centered on the multigram level (see Table 1).

TABLE 1 Starting Materials Employed in Classical Organic Laboratory Syntheses, 1902–1980

		Acetanilide	4-Bromoacetanilide	Benzoin
		Starting Materials Required (grams)		
Date	Author	Aniline	Acetanilide	Benzaldehyde
1902	Levy, 4th ed.	46.2	—	50.0
1915	Cohen, 3rd ed.	25.0	5.0	25.0
1933	Adkins	25.0	13.5	10.0
1941	Fieser, 2nd ed.	18.2	13.5	25.0
1963	Adams	20.0	13.5	16.0
1980	Durst	10.0	5.2	10.0

We seriously question the wisdom of maintaining the introduction of laboratory work at conventional levels. Is this approach relevant when one considers the quantities of materials commonly used in natural products, pharmaceutics, biochemistry, and other fields of modern research in which costly substances are employed?

Second, it is now fully recognized that there has been a very serious decrease in undergraduate laboratory contact time over the past two decades. It seems to us that an increasingly important question should be asked in evaluating the introductory organic program: At what scale of introductory laboratory work can the student gain the maximum ability to handle organic materials within the shortest period of time?

We now firmly believe that the microscale laboratory approach resolves both these concerns and, in addition, affords a number of significant bonuses. The immediate result of "going micro" is that there is a change in the laboratory air quality that can be described only as spectacular! Of

miniaturize but how best to go about the job. We feel that *flexibility* in program design is vitally important in order to accommodate the wide variety of local educational environments. In our first edition we sent the message "Smaller is better," and all the experiments utilized approximately 150 mg or less of starting material. In this second edition we feel that it is now appropriate to build more flexibility of scale into the experimental design. We have, therefore spent a good deal of time modifying ten experiments and three of our four Sequential Sequences to include *Optional Scaleup* procedures. These range from twofold to two hundredfold above the microscale level. We have two reasons for this change in content. First, although many students have the opportunity to experience multigram reaction scales in upper-level laboratories or independent study, a significant number depend on a single year of experimental organic chemistry to gain acquaintance with the field. We agree that this second category of students, and indeed perhaps many of the first, should experience the excitement of undertaking a set of sequential steps (starting with multigram quantities) that clearly emulates a research laboratory synthesis. These experiments form a fitting conclusion to the end of the microscale laboratory. Second, for programs that are interested in "going micro," but need time and equipment to effect the transition, these optional experiments offer a temporary bridge to begin moving in the micro direction. In this regard we should emphasize that for programs that have reached the microscale level, the recommended time for incorporation of the Optional Upscale procedures is late in the second semester.

The rapid, almost breathtaking speed of technique innovation taking place in the microscale laboratory program is best exemplified by the changes found in the completely rewritten section on fractional distillation. The development of bottom-driven, low-cost micro spinning band distillation columns in the authors' laboratories over the past three years has resulted in a major breakthrough in the technique for illustrating classic fractional distillation. These systems are unquestionably the most powerful stills ever to become available as instructional equipment at the introductory level. In particular, the Hinkle modification of the classic Hickman still will clearly have a major impact on the entire field of micro distillation, including the advanced research laboratory.

Developments in chemical instrumentation also continue to accelerate. The availability of low-cost Fourier transform-infrared systems has broken the jam of making infrared data available to students in real time and has provoked us into adding new detailed interpretations of the FT–IR spectra of reactants and products in fourteen experiments. We hope that these discussions can be used as a means of leading the student into a deeper appreciation of the value of these spectroscopic data. Fourier transform–nuclear magnetic resonance (^{1}H, ^{13}C) and ultraviolet–visible data have been introduced for the first time in modest fashion where they are appropriate for the characterization of reaction products. It is clear that the instrumental and cost barriers to the utilization of experimentally derived NMR data in the introductory organic laboratory are finally beginning to be bridged. Although earlier we had significant reservations about incorporating NMR data in the microscale experiments, we now expect their use in these programs to expand. The ability of the student to collect and interpret spectroscopic data is an essential aspect of "characterization science," which is one of the most vital elements of the modern-day academic and industrial laboratory.

To further the flexibility of the approach, we have added keyed references in each experiment to the appropriate qualitative identification tests and derivative preparations in Chapter 7. These operations can be effec-

1986, Ph.D., University of Utah 1993). We are greatly indebted to the efforts of Robert Mathieu of GOW-MAC in providing information that will assist institutions to obtain funding for instructional gas chromatographic instrumentation. We wish to add our deep appreciation of the patience, understanding, and support that our editor at Wiley, Nedah Rose, has given us over the past three years. This major revision could not have materialized without her thoughtful advice and counsel.

The development of Chapter 8 is largely the work of a collection of outstanding Bowdoin students: Marlene L. Castro, Jodie K. Chin, Helen E. Counts, Jonathan M. Dugan, Patricia A. Ernst, Lenore R. Menger-Anderson, Joanne M. Holland, and Jessica B. Radin. We are particularly grateful for the tenacity with which Joanne attacked the chemistry leading to the photosensitive azomethine ylide in Sequence F. A number of our close associates continue to play vital roles in the evolution of the microscale program and we are pleased to acknowledge them: Lauren Bartlett (now in the Department of Environmental Engineering, Duke University), Judith Foster, Henry Horner, and Samuel Butcher. Sam, as our resident expert on air chemistry and laboratory atmosphere contamination, has retired from active participation in the further evolution of the microscale instructional program.

We wish to thank both the National Science Foundation and the PEW Charitable Trusts for continued support of our Microscale Summer Institutes. We are further indebted to the PEW Charitable Trusts for major support that has allowed us to develop and construct a new microscale organic laboratory at Bowdoin College. This new laboratory, which is now in operation, has the potential to become the prototype laboratory design for new instructional facilities at other institutions. We also acknowledge the PEW Charitable Trusts for support of the development of our second generation video programs and add our thanks to Barbara J. Kaster, Harrison King McCann Professor Emerita of Oral Communication, and her assistant, biochemistry major Anthony Gosselin, for their time, effort, enthusiasm, and dedication to detail, which have made these Technique Tapes such a success.

We are more than pleased to acknowledge the unparalleled contributions of Paulette Fickett, Laboratory Instructor, to the microscale program. Paulette lead us through a three-year conversion period in the early 1980s when the program was in its infancy, and she remains in charge of making the microscale program function effectively on the day-to-day basis at Bowdoin in the early 1990s. Without exaggeration, Paulette has had more experience at operating microscale instructional laboratories than any person in history. Her dedication to this program, her friendly advice to hundreds of calls for help from students in Brunswick and faculty halfway around the world, her starring role in the videotapes, and her organization of the laboratory program for the summer institutes, have all been vital to the success of Microscale Organic Laboratory. For all of these endless contributions we are most grateful.

The revolution is over. The microscale era has arrived! We are confident that future students now will be assured the opportunity to experience the thrill of coaxing one complex molecular structure into another and to bring about these transformations on quantities of material that are just visible to the human eye!

DANA W. MAYO
RONALD M. PIKE
PETER K. TRUMPER

Brunswick, Maine
March 22, 1993