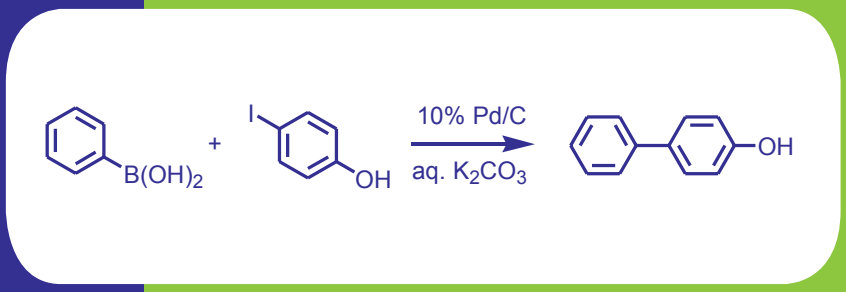
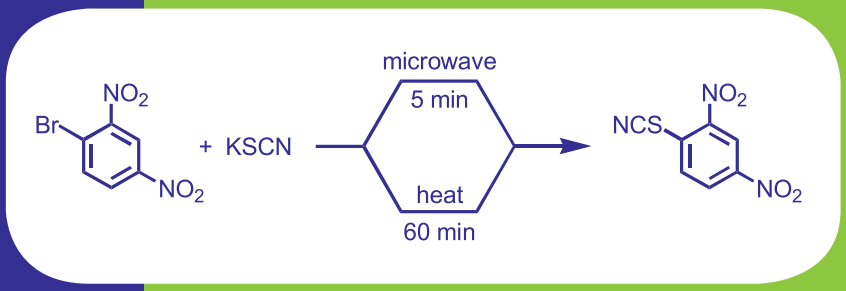
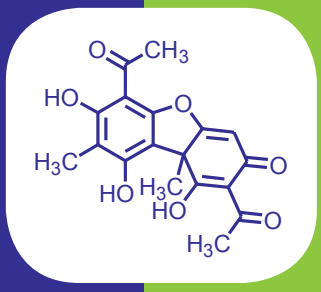


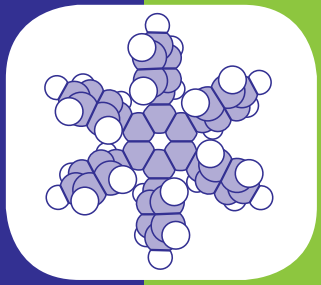


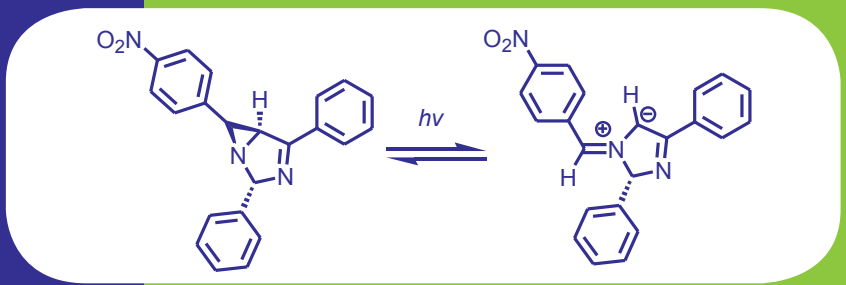


SIXTH EDITION

Microscale Organic Laboratory

With Multistep and Multiscale Syntheses





Dana Mayo
Ronald Pike
David Forbes

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Periodic Table of the Elements

1 IA												13 IIIA	14 IVA	15 VA	16 VIA	17 VIIA	18 VIIIA
1 H Hydrogen 1.0079	2 IIA																2 He Helium 4.0026
3 Ll Lithium 6.941	4 Be Berylium 9.0122											5 B Boron 10.811	6 C Carbon 12.011	7 N Nitrogen 14.007	8 O Oxygen 15.999	9 F Fluorine 18.998	10 Ne Neon 20.180
11 Na Sodium 22,990	12 Mg Magnesium 24.305	3 IIIB	4 IVB	5 VB	6 VIB	7 VIIB	8 VIIIB	9 VIIIB	10 VIIIB	11 IB	12 IIB	13 Al Aluminum 26.982	14 Si Silicon 28.086	15 P Phosphorus 30.974	16 S Sulfur 32.065	17 Cl Chlorine 35.453	18 Ar Argon 39.948
19 K Potassium 39.098	20 Ca Calcium 40.078	21 Sc Scandium 44.956	22 Ti Titanium 47.867	23 V Vanadium 50.942	24 Cr Chromium 51.996	25 Mn Manganese 54.938	26 Fe Iron 55.845	27 Co Cobalt 58.933	28 Ni Nickel 58.693	29 Cu Copper 63.546	30 Zn Zinc 65.409	31 Ga Gallium 69.723	32 Ge Germanium 72.64	33 As Arsenic 74.922	34 Se Selenium 78.96	35 Br Bromine 79.904	36 Kr Krypton 83.798
37 Rb Rubidium 85.468	38 Sr Strontium 87.62	39 Y Yttrium 88.906	40 Zr Zirconium 91.224	41 Nb Niobium 92.906	42 Mo Molybdenum 95.94	43 Tc Technetium (98)	44 Ru Ruthenium 101.07	45 Rh Rhodium 102.91	46 Pd Palladium 106.42	47 Ag Silver 107.87	48 Cd Cadmium 112.41	49 In Indium 114.82	50 Sn Tin 118.71	51 Sb Antimony 121.76	52 Te Tellurium 127.60	53 I Iodine 126.90	54 Xe Xenon 131.29
55 Cs Cesium 132.91	56 Ba Barium 137.33	57 *La Lanthanum 138.91	72 Hf Hafnium 178.49	73 Ta Tantalum 180.95	74 W Tungsten 183.84	75 Re Rhenium 186.21	76 Os Osmium 190.23	77 Ir Iridium 192.22	78 Pt Platinum 195.08	79 Au Gold 196.97	80 Hg Mercury 200.59	81 Tl Thallium 204.38	82 Pb Lead 207.2	83 Bi Bismuth 208.98	84 Po Polonium (209)	85 At Astatine (210)	86 Rn Radon (222)
87 Fr Francium (223)	88 Ra Radium (226)	89 #Ac Actinium (227)	104 Rf Rutherfordium (261)	105 Db Dubnium (262)	106 Sg Seaborgium (266)	107 Bh Bohrium (264)	108 Hs Hassium (277)	109 Mt Meitnerium (268)	110 Ds Darmstadtium (281)	111 Rg Roentgenium (272)	112 Cn Copernicium (285)	113 Uut (284)	114 Fl Flerovium (289)	115 Uup (288)	116 Lv Livermorium (293)	117 Uus (294)	118 Uuo (294)

Atomic number→ 6
Symbol → C
Name (IUPAC) → Carbon
Atomic mass → 12.011

IUPAC recommendations→
Chemical Abstracts Service group notation →

*Lanthanide Series	58 Ce Cerium 140.12	59 Pr Praseodymium 140.91	60 Nd Neodymium 144.24	61 Pm Promethium (145)	62 Sm Samarium 150.36	63 Eu Europium 151.96	64 Gd Gadolinium 157.25	65 Tb Terbium 158.93	66 Dy Dysprosium 162.50	67 Ho Holmium 164.93	68 Er Erbium 167.26	69 Tm Thulium 168.93	70 Yb Ytterbium 173.04	71 Lu Lutetium 174.97
# Actinide Series	90 Th Thorium 232.04	91 Pa Protactinium 231.04	92 U Uranium 238.03	93 Np Neptunium (237)	94 Pu Plutonium (244)	95 Am Americium (243)	96 Cm Curium (247)	97 Bk Berkelium (247)	98 Cf Californium (251)	99 Es Einsteinium (252)	100 Fm Fermium (257)	101 Md Mendelevium (258)	102 No Nobelium (259)	103 Lr Lawrencium (262)

Common Organic Solvents: Table of Properties

Solvent	formula	MW	boiling point (°C)	melting point (°C)	density (g/mL)	solubility in water (g/100g)	Dielectric Constant	flash point (°C)
acetic acid	$C_2H_4O_2$	60.05	118	16.6	1.049	Miscible	6.15	39
acetone	C_3H_6O	58.08	56.2	−94.3	0.786	Miscible	20.7(25)	−18
acetonitrile	C_2H_3N	41.05	81.6	−46	0.786	Miscible	37.5	6
benzene	C_6H_6	78.11	80.1	5.5	0.879	0.18	2.28	−11
1-butanol	$C_4H_{10}O$	74.12	117.6	−89.5	0.81	6.3	17.8	35
2-butanol	$C_4H_{10}O$	74.12	98	−115	0.808	15	15.8(25)	26
2-butanone	C_4H_8O	72.11	79.6	−86.3	0.805	25.6	18.5	−7
t-butyl alcohol	$C_4H_{10}O$	74.12	82.2	25.5	0.786	Miscible	12.5	11
carbon tetrachloride	CCl_4	153.82	76.7	−22.4	1.594	0.08	2.24	—
chlorobenzene	C_6H_5Cl	112.56	131.7	−45.6	1.1066	0.05	5.69	29
chloroform	$CHCl_3$	119.38	61.7	−63.7	1.498	0.795	4.81	—
cyclohexane	C_6H_{12}	84.16	80.7	6.6	0.779	<0.1	2.02	−20
1,2-dichloroethane	$C_2H_4Cl_2$	98.96	83.5	−35.3	1.245	0.861	10.42	13
diethyl ether	$C_4H_{10}O$	74.12	34.6	−116.3	0.713	7.5	4.34	−45
diethylene glycol	$C_4H_{10}O_3$	106.12	245	−10	1.118	10	31.7	143
diglyme (diethylene glycol dimethyl ether)	$C_6H_{14}O_3$	134.17	162	−68	0.943	Miscible	7.23	67
1,2-dimethoxy-ethane (glyme, DME)	$C_4H_{10}O_2$	90.12	85	−58	0.868	Miscible	7.2	−6
dimethylether	C_2H_6O	46.07	−22	−138.5	NA	NA	NA	−41
dimethyl-formamide (DMF)	C_3H_7NO	73.09	153	−61	0.944	Miscible	36.7	58
dimethyl sulfoxide (DMSO)	C_2H_6OS	78.13	189	18.4	1.092	25.3	47	95
dioxane	$C_4H_8O_2$	88.11	101.1	11.8	1.033	Miscible	2.21(25)	12
ethanol	C_2H_6O	46.07	78.5	−114.1	0.789	Miscible	24.6	13
ethyl acetate	$C_4H_8O_2$	88.11	77	−83.6	0.895	8.7	6(25)	−4
ethylene glycol	$C_2H_6O_2$	62.07	195	−13	1.115	Miscible	37.7	111
glycerin	$C_3H_8O_3$	92.09	290	17.8	1.261	Miscible	42.5	160
heptane	C_7H_{16}	100.20	98	−90.6	0.684	0.01	1.92	−4
Hexamethylphosphoramide (HMPA)	$C_6H_{18}N_3OP$	179.20	232.5	7.2	1.03	Miscible	31.3	105
Hexamethylphosphorous triamide (HMPT)	$C_6H_{18}N_3P$	163.20	150	−44	0.898	Miscible	??	26
hexane	C_6H_{14}	86.18	69	−95	0.659	0.014	1.89	−22
methanol	CH_4O	32.04	64.6	−98	0.791	Miscible	32.6(25)	12
methyl *t*-butyl ether (MTBE)	$C_5H_{12}O$	88.15	55.2	−109	0.741	5.1	??	−28
methylene chloride	CH_2Cl_2	84.93	39.8	−96.7	1.326	1.32	9.08	1.6
N-methyl-2-pyrrolidinone (NMP)	CH_5H_9NO	99.13	202	−24	1.033	10	32	91
nitromethane	CH_3NO_2	61.04	101.2	−29	1.382	9.50	35.9	35
pentane	C_5H_{12}	72.15	36.1	−129.7	0.626	0.04	1.84	−49
Petroleum ether (ligroine)	—	—	30–60	−40	0.656	—	—	−30
1-propanol	C_3H_8O	88.15	97	−126	0.803	Miscible	20.1(25)	15
2-propanol	C_3H_8O	88.15	82.4	−88.5	0.785	Miscible	18.3(25)	12
pyridine	C_5H_5N	79.10	115.2	−41.6	0.982	Miscible	12.3(25)	17
tetrahydrofuran (THF)	C_4H_8O	72.11	66	−108.4	0.886	30	7.6	−21
toluene	C_7H_8	92.14	110.6	−93	0.867	0.05	2.38(25)	4
triethyl amine	$C_6H_{15}N$	101.19	88.9	−114.7	0.728	0.02	2.4	−11
water	H_2O	18.02	100.00	0.00	0.998	—	78.54	—
water, heavy	D_2O	20.03	101.3	4	1.107	Miscible	??	—
o-xylene	C_8H_{10}	106.17	144	−25.2	0.897	Insoluble	2.57	32
m-xylene	C_8H_{10}	106.17	139.1	−47.8	0.868	Insoluble	2.37	27
p-xylene	C_8H_{10}	106.17	138.4	13.3	0.861	Insoluble	2.27	27

T = 20 °C unless specified otherwise.
Source: http://virtual.yosemite.cc.ca.us/smurov/orgsoltab.htm

MICROSCALE ORGANIC LABORATORY

with Multistep and Multiscale Syntheses

SIXTH EDITION

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TO JEANNE D'ARC, MARILYN, AND CAROL

PREFACE

When *Microscale Organic Laboratory (MOL)* was first published in 1985 as paperback Xerox copies of an unproofed manuscript, it was the only microscale organic laboratory text available. In the February 1999 *Book Buyers Guide Supplement to the Journal of Chemical Education,* however, there were seventeen laboratory manuals (of a total of thirty-nine) containing miniaturized, fully microscale, or a mixture of micro and macro experiments. Fast forward a decade and a half and without any doubt, microscale techniques have solidly established their place in chemical education. The number of lab manuals currently in print reflects the growing number of students being introduced to organic chemistry through microscale techniques. While the conversion may not yet be quite as high as the eighty percent predicted by David Brooks back in 1985, a conservative estimate would be that a solid two-thirds majority of sophomore students now work with miniaturized experiments compared with the amounts of material employed in these laboratories in the late 1970s.

The major changes that were made to *MOL* in both the fourth and fifth editions were very well received by our readers. Starting with the significant internal reorganization and rewriting with *MOL4, MOL5* witnessed modifications within the procedural sections to allow for inquiry-based experimentation and the inclusion of microwave heating as a tool. While *MOL6* on the surface will look very much like *MOL5* as it is nearing the fine-tuning stage in the evolution of this laboratory text, *MOL6* has undergone further internal reorganization and rewriting. Many helpful suggestions have been received from reviewers and from instructors who have used previous editions of this text. As a result, some major changes have been made for this new edition:

- A key change to the 6th edition is the addition of a coupling reaction, the Suzuki reaction. The inclusion of a transition metal catalyzed process brings the total number of experiments in MOL6 to 36! The discussion section accompanying this experiment provides the chemical context/background for this landmark achievement. The purpose, experimental procedure, questions and bibliography which accompany the inclusion of this experiment provides the reader with a deeper appreciation of how one can fine tune a classic C-C bond forming process and recast the experience as green.
- Also new to MOL6 are sections which highlight, have been modified, or include experimental or background information of biological relevancy. Make no mistake that when combining synthetic organic chemistry with systems of biological and medicinal importance, students are engaged. References to systems of biological importance are noted in the text by the use of the icon B and include experiments 6, 8, 11, and 36 of Chapter 6. Additional sections highlighting biological processes include Sequence C and Chapter 10W's 2adv.
- Throughout MOL6, sections have been added, revised, and expanded upon to illustrate current advances made in improving the "greenness" of an industrially important synthetic process. References to green initiatives G are noted in the text. The three examples in MOL6 are as follows: Experiment 36 highlights the use of water as solvent, experiment 15 illustrates how processes are green as a result of atom economy (and how it is not as noted in the discussion section of experiments 19 and 36), and

experiments 29D and 33 provide optional protocols involving the use of recycled materials.

- As stated in MOL5, the use of microwave heating as a tool in synthetic organic chemistry is fast-growing and is becoming an enabling technology. Optional instructions remain as part of MOL6 to allow for the integration of microwave heating as a tool for performing reactions. Since reaction times are shorter than when conventional heating methods are used, students have the opportunity to supplement these activities with traditional techniques and as stated above, engage in discussions comparing the two. Optional microwave heating instructions are part of experiments 7, 8, 15, 22, and 30. References to microwave use are noted in the text by the use of this icon M.
- The modified procedural sections allowing for question driven experimentation continues with this edition. As we highlighted in the 5th edition, this central concept is intended to develop a key skill set involving how to best monitor reactions and gauge product purity. Keeping with this format, sections have the opportunity of a more interactive experience between groups should that be the wish of the instructor. Optional inquiry-based guidelines have been added to experiments 5A, 5B, 7, 19B, 24A, and 32. Experiments 11A, 16, and 28 have been modified in a way which focuses on validation of product purity. References to inquiry-based guidelines ? and validation experiences V are noted in the text.
- A rich collection of end of chapter exercises and the addition of pre and post lab questions provides students with the valuable opportunity to test and practice their own understanding of each laboratory experiment.
- Discussion sections that appear at the beginning of each Experiment have been added, revised, and expanded upon. These discussions provide more information regarding the chemical principles involved in each experimental procedure.

Additional Resources

Text web site (http://www.wiley.com/college/mayo)

As with the previous edition, a major portion of the background theoretical discussions have been moved to the text web site, without affecting the operational part of the text. Sequences D, E, and F from Chapter 7 have been moved online to web Chapter 7W, "Advanced Laboratory Experimentation". As with the previous edition, Chapter 4W, "Refractive Index", and Chapter 10W,"Advanced Microscale Organic Laboratory Experiments"are available on the text web site. Likewise, the web site has allowed us to move a number of more advanced discussions out of the printed text. Wherever the shift of this material has occurred the move is flagged by reference call-outs using an icon www.

These **web reference discussions** include information on the following topics:

- Microscale lab equipment and techniques
- Semimicroscale distillation
- Reduced pressure distillations with microspinning band columns
- Vacuum pumps and pressure regulation
- Crystallization
- Measurement of Specific Rotation

- Introduction to Infrared Spectroscopy—Introduction to Theory
- Group Frequencies of the Hydrocarbons
- Characteristic Frequencies of the Heteroatom Functional Groups
- Instrumentation—the Infrared Interferometer
- Tables of Derivatives

The majority of the background infrared spectra and the associated discussions used to develop the use of group frequencies from these spectra are also found on the web site, while the text still contains the essential tables of characteristic frequencies that are in every day use in the laboratory. The many compound data tables, used primarily in the chapter on qualitative identification, also reside on the web site. The Classification of Experiments Based on Mechanism is also available on the web site.

The **Instructor's Manual**, also available on the web site, provides a list of chemicals for each experiment, setup suggestions, and anticipated outcomes. The Instructor's Manual has a separate listing for each experiment developed in the text, which often includes tips for avoiding potential trouble spots and adds considerable information and important references.

Wiley Custom Select

Wiley's custom publishing program, "Wiley Custom Select" (http://customselect.wiley.com/) gives you the freedom to build your course materials exactly the way you want them. Through a simple, on-line three step process, Wiley Custom Select allows instructors to select content from a vast database of experiments to create a customized laboratory text that meets the needs of their particular course. Each book can be fully customized—instructors can select their own output method, create a cover, arrange the sequence of content, and upload their own materials. At any time, instructors can preview a full version of what the customized book will look like, before the final order is placed.

Acknowledgements

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 (who first defined 100 mg of starting substrate in an organic reaction as a microscale transformation), 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. These educators laid the foundation on which we were able to fashion much of the current introductory program.

In addition, we are grateful to the colleagues listed below whose careful reviews, helpful suggestions, comments, and thoughtful criticisms of the manuscript have been of such great value to us in developing the final version of this sixth edition of *MOL*.

Andrew Frazer, *University of Central Florida*
Rick Heldrich, *College of Charleston*
Deborah Lieberman, *University of Cincinnati, Main Campus*
Kevin Minbiole, *Villanova University*
Evonne Rezler, *Florida Atlantic University, Boca Raton*
Kirk Voska, *Rogers State University*

We appreciate the support from Wiley which allowed us to revisit each exeriment in MOL5 so that we could properly identify which experiments were best served to be modified. Much of modifications in MOL6 were a result of the hard work of many who contributed to MOL5, and we are happy to acknowledge them: Stephen Arnold, Sampada Bettigeri, Amanda Brewton, Sarah Dolbear, and Brian Finnigan. And finally, we would like to extend our gratitude to Petra Recter, Jennifer Yee, and Jolene Ling who shepherded this projected from conception to press.

We continue to applaud the widespread development of affordable glassware for use in microscale instructional laboratories. We are particularly pleased to note that the particular style of equipment (cap-seal connectors) that we developed for this program at Bowdoin College has accomplished an outstanding record of survival on the battleground of the sophomore laboratory bench. Much of the credit for the granitelike character of this equipment goes to J. Ryan and Larry Riley of the ACE Glass Company. Several contributors have played long-term roles in the successful evolution of the microscale organic laboratory program, and we are happy to acknowledge them: Peter Trumper, Janet Hotham, Judy Foster, Henry Horner, Lauren Bartlett, Robert Stevens, and Samuel Butcher have all made vital contributions along the way.

We are particularly indebted to our colleagues Andrew Dicks, Nicholas Leadbeater, Cynthia McGowan, and Elizabeth Stemmler. Their willingness to contribute to this project is gratefully appreciated. Cynthia and Nicholas provided in its entirety the microwave contribution, which was introduced in MOL5 and is a key component of MOL6. The addition of a brand new experiment, Experiment 36, is because of Andrew. The discussion section, experimentation, and safety contribution truly adds to the wealth of this edition and the excitement of a comprehensive introductory laboratory experience. As it was with MOL4, Elizabeth's contribution of an introductory discussion on the *Application of Mass Spectrometry to Organic Chemistry* continues to offer the reader a diverse experience using this powerful technique to the introductory laboratory experience.

The development of our kinetics experiment fell on the strong shoulders of Paulette Messier, Laboratory Instructor, and adds just one more accomplishment to her unending contributions to the development of the microscale program at Bowdoin College. Paulette is rapidly closing in on three and a half decades of continuous laboratory instruction at the microscale level, a unique record of experience in microscale anywhere in the world of chemical education. Paulette, more than any other person, has made this program a success in the trenches between the lab benches where it really counts. The thousands of students who have dealt directly with her and gained her respect are a tribute to Paulette's quiet, confident way of instilling enthusiasm and excitement into the microscale experience. Paulette Messier is indelibly linked to the Microscale Organic Laboratory at Bowdoin College.

With the publication of the Sixth Edition, *Microscale Organic Laboratory* might be considered to have reached a mature state. In our opinion, however, chemical education is as dynamic as the subject itself. For on our drawing boards are thoughts almost as outrageous as the idea that occurred in the early winter of 1980 to 1981— to run an introductory organic laboratory program on a milligram scale!

Dana W. Mayo
Ronald M. Pike
David C. Forbes
January 2014

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Chapter 7

SEQUENTIAL SYNTHESES: THE TRANSITION FROM MACRO TO MICRO 428

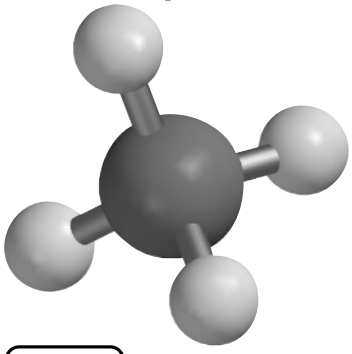
Chapter 9

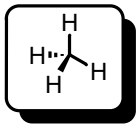
Chapter 9W

Chapter 10W

CH$_4$apter 1

INTRODUCTION





You are about to embark on a challenging adventure—the microscale organic chemistry laboratory!

Your course is going to be quite different from the conventional manner in which this laboratory has been taught in past decades. You will be learning the experimental side of organic chemistry from the microscale level. Although you will be working with very small amounts of materials, you will be able to observe and learn more organic chemistry in one year than many of your predecessors did in nearly two years of laboratory work. You will find this laboratory an exciting and interesting place to be. While we cannot guarantee it for you individually, the majority of students who went through the program during its development found the microscale organic laboratory to be a surprisingly pleasant adventure.

This textbook is centered on helping you develop skills in microscale organic laboratory techniques. Its focus is twofold. For those of you in the academic environment and involved with the introductory organic laboratory, it allows the flexibility of developing your own scaling sequence without being tied to a prescribed set of quantities. For those of you working in a research environment at the advanced undergraduate or graduate level or in the industrial area, this text will provide the foundation from which you can develop a solid expertise in microscale techniques directly applicable to your work. Working at the microscale level is substantially different from using conventional operations in the organic laboratory with multigram quantities of materials.

During the last two decades, the experimental side of organic chemistry has moved ever closer to the microscale level. This conversion started in earnest nearly thirty years ago and has been spurred on by the rapidly accelerating cost of chemical waste disposal. As we have said, you will be working with very small amounts of materials, but the techniques that you will learn, and experience you will gain, will allow you to accomplish more organic chemistry in the long run than many of your predecessors.

First, we want to acquaint you with the organization and contents of the text. ***With the sixth edition, a continued effort has been made to streamline the basic reference material from the text using our accompanying website (www.wiley.com/college/MOL6). Accordingly, Chapter 10W (formerly Chapter 7 of the fourth edition) and Chapter 7W (selected experiments from the fifth edition) have been placed online. Throughout this edition, content is identified with a "W" (e.g., Chapter 10W), indicating its location online. Furthermore, an icon will be used in the margin to indicate website material that will be of interest to the user. We hope this treatment of the laboratory will make the more important aspects of the basic text easier to access and will speed your laboratory work along.*** We then give you a few words of advice, which, if they are heeded, will allow you to avoid many of the sand traps you will find as you develop microscale laboratory techniques. Finally, we wax philosophical and attempt to describe what we think you should derive from this experience.

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Chapter 1: CH_4, Methane
a substance of natural origin, known as Marsh Gas to the alchemists.

After this brief introduction, the second chapter is concerned with safety in the laboratory. This chapter supplies information that will allow you to estimate your maximum possible exposure to volatile chemicals used in the microscale laboratory. Chapter 2 also discusses general safety protocol for the laboratory. It is vitally important that you become familiar with the details of the material contained in this chapter; your health and safety depend on this knowledge.

The next three chapters are concerned primarily with the development of experimental techniques. Chapter 3 describes in detail the glassware employed in microscale organic chemistry: the logic behind its construction, tips on its usage, the common arrangements of equipment, and various other laboratory manipulations, including techniques for transferring microquantities of materials. Suggestions for the organization of your laboratory notebook are presented at the end of this chapter.

Chapter 4 deals with equipment and techniques for determining a number of physical properties of microscale samples. Chapter 5 is divided into nine technique sections. Detailed discussions develop the major areas of experimental technique that are used in the microscale organic laboratory.

Chapters 6, 7, 7W, and 10W contain the main experimental sections of this text. Chapter 6 is focused primarily on preparative organic chemistry at the microscale level and consists of 36 experiments. Six experiments (Experiments 5A, 5B, 7, 19B, 24A, and 32) in Chapter 6 have been modified in a way which replaces the posting of a reaction time with the task of monitoring the reaction by TLC until complete. The TLC technique is asked of the experimentalist in three more experiments (Experiments 11A, 16, and 28) in order to provide additional evidence of reaction purity upon recrystallization of the crude reaction mixture. And finally, five experiments (Experiments 7, 8, 15, 22, and 30) in Chapter 6 now have optional exercises which utilize microwave technologies. Additional selections of individual experiments can be drawn from those experiments presented in Chapter 7. Chapter 10W, which is now located online, contains a series of seven experiments of a more sophisticated nature. A number of the experiments contained in Chapters 6 and 10W are of optional scale so that you may also have the opportunity to gain some experience with experimentation at larger scales. Chapter 7 consists of a set of six sequential experiments that are essentially identical to the type of problems tackled by research chemists involved in synthetic organic chemistry. A number of these multistep procedures begin the first step in the experiment with large-scale, multigram quantities of starting material, but require microscale techniques to complete the final step or two. The use of this chapter is most appropriate in the final stages of the course—for example, the latter part of the second semester of a two-semester sequence.

Chapter 8 develops the characterization of organic materials at the microscale level by spectroscopic techniques. The chapter starts with a brief discussion of the interpretation of infrared (IR) group frequencies and is followed by a more detailed treatment of nuclear magnetic resonance (NMR) spectral data, a brief discussion of ultraviolet-visible (UV–vis) spectroscopy, and a brief introduction to the theory, experimental techniques, and applications of mass spectrometry to organic chemistry. A more detailed introduction to the theoretical basis for these spectroscopic techniques is also presented on the accompanying website.

Chapter 9 develops the characterization of organic materials at the microscale level by the use of classical organic reactions to form solid derivatives. Tables of derivative data for use in compound identification by these techniques are discussed and are included on the website as Appendix A.

A list of all the experiments grouped by reaction mechanism is given on the website as Appendix B.

The organization of the experimental procedures given in Chapters 6, 7, 7W, and 10W is arranged in the following fashion. A short opening statement describing the reaction to be studied is followed by the reaction scheme. www

Generally, a brief discussion of the reaction follows, including a mechanistic interpretation. In a few cases of particularly important reactions, or where the experiment is likely to precede presentation of the topic in the classroom, a more detailed description is given. The estimated time needed to complete the work, along with a table of reactant data, comes next. For ease in organizing your laboratory time, the experimental section is divided into four subsections: *reagents and equipment, reaction conditions, isolation of product, and purification and characterization.*

We then introduce a series of questions and problems designed to enhance and focus your understanding of the chemistry and the experimental procedures involved in a particular laboratory exercise. Finally, a bibliography offering a list of literature references is given. Although this list comes at the end of the experimental section, we view it as a very important part of the text. The discussion of the chemistry involved in each experiment is necessarily brief. We hope that you will take time to read and expand your knowledge about the particular experiment that you are conducting. You may, in fact, find that some of these references become assigned reading.

A prompt (➡) in the text indicates that experimental apparatus involved with that stage of the experiment are shown in the margin. Important comments are italicized in the text, and **Warnings** and **Cautions** are given in boxes and also indicated in the margins.

In an effort to streamline our treatment of the laboratory we have moved a considerable quantity of material from the previous editions, MOL3, MOL4, and MOL5 and placed it in easily accessible form on our website (www.wiley.com/college/MOL6). An icon lets you know that supplemental material is available on the website. New to this edition is a detailed listing within the table of contents of all materials available online. We hope this format will make the more important aspects of the basic text easier to access and speed your laboratory work along. www

GENERAL RULES FOR THE MICROSCALE LABORATORY

1. Study the experiment before you come to lab. This rule is a historical plea from all laboratory instructors. In the microscale laboratory it takes on a more important meaning. You will not survive if you do not prepare ahead of time. In microscale experiments, operations happen much more quickly than in the macroscale laboratory. Your laboratory time will be overflowing with many more events. If you are not familiar with the sequences you are to follow, you will be in deep trouble. Although the techniques employed at the microscale level are not particularly difficult to acquire, they do demand a significant amount of attention. For you to reach a successful and happy conclusion, you cannot afford to have the focus of your concentration broken by having to constantly refer to the text during the experiment. Disaster is ever present for the unprepared.

2. ALWAYS work with clean equipment. You must take the time to scrupulously clean your equipment before you start any experiment. Contaminated glassware will ultimately cost you additional time, and you will

experience the frustration of inconsistent results and lower yields. Dirty equipment is the primary cause of reaction failure at the microscale level.

3. CAREFULLY measure the quantities of materials to be used in the experiments. A little extra time at the beginning of the laboratory can speed you on your way at the end of the session. A great deal of time has been spent optimizing the conditions employed in these experiments in order to maximize yields. Many organic reactions are very sensitive to the relative quantities of substrate (the material on which the reaction is taking place) and reagent (the reactive substance or substances that bring about the change in the substrate). After equipment contamination, the second-largest cause of failed reactions is attempting to run a reaction with incorrect quantities of the reactants present. Do not be hurried or careless at the balance.

4. Clean means DRY. Water or cleaning solution can be as detrimental to the success of a reaction as dirt or sludge in the system. You often will be working with very small quantities of moisture-sensitive reagents. The glass surface areas with which these reagents come in contact, however, are relatively large. A slightly damp piece of glassware can rapidly deactivate a critical reagent and result in reaction failure. *This rule must be strictly followed.*

5. ALWAYS work on a clean laboratory bench surface, preferably glass!

6. ALWAYS protect the reaction product that you are working with from a disastrous spill by carrying out all solution or solvent transfers over a crystallizing dish.

7. ALWAYS place reaction vials or flasks in a clean beaker when standing them on the laboratory bench. Then, when a spill occurs the material is more likely to be contained in the beaker and less likely to be found on the laboratory bench or floor.

8. NEVER use cork rings to support round-bottom flasks, particularly if they contain liquids. If you do, you are inviting disaster to be a guest at your laboratory bench.

9. ALWAYS think through the next step you are going to perform *before* starting it. Once you have added the wrong reagent, it is back to square one.

10. ALWAYS save everything you have generated in an experiment until it is successfully completed. You can retrieve a mislabeled chromatographic fraction from your locker, but not from the waste container!

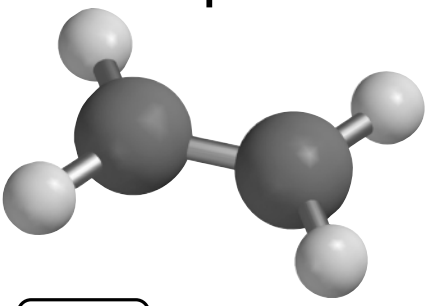
THE ORGANIC CHEMISTRY LABORATORY

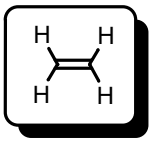
The confidence gained by mastering the microscale techniques described here will pay big dividends as you progress into modern-day experimental chemistry. The organic laboratory has had a reputation of being smelly, long, tedious, and pockmarked with fires and explosions; but present-day organic chemistry is undergoing a revolution at the laboratory bench. New techniques are sweeping away many of the old complaints, as an increasing fraction of industrial and academic research is being carried out at the microscale level.

This book allows the interested participant to rapidly develop the skills needed to slice more deeply into organic chemistry than ever before. The attendant benefits are greater confidence and independence in acquired laboratory techniques. The happy result is that in a microscale-based organic chemistry laboratory, you are more likely to have a satisfying encounter with the experimental side of this fascinating field of knowledge.

C_2H_4apter 2

SAFETY





Research laboratories vary widely with respect to facilities and support given to safety. Large laboratories may have several hundred chemists and an extensive network of co-workers, supervisors, safety officers, and hazardous-waste managers. They also, pursuant to government regulations, have an extensive set of safety procedures and detailed practices for the storage and disposal of hazardous wastes. In small laboratories, the individual chemist may have to take care of all these aspects of safety. Some laboratories may routinely deal with very hazardous materials and may run all reactions in hoods. Others may deal mainly with relatively innocuous compounds and have very limited hood facilities.

Our approach is to raise some questions to think about and to suggest places to look for further information. In this chapter, we do not present a large list of safety precautions for use in all situations; rather, we present a list of very basic precautionary measures. A bibliography at the end of the chapter offers a list of selected references. *We urge you to consult these references concerning specific safety regulations.* Many laboratories may have safety guidelines that will supercede this very cursory treatment. This chapter is no more than a starting point.

MAKING THE LABORATORY A SAFER PLACE

Murphy's law states in brief, "If anything can go wrong, it will." Although it is often taken to be a silly law, it is not. Murphy's law means that if sparking switches are present in areas that contain flammable vapors, sooner or later there will be a fire. If the glass container can move to the edge of the shelf as items are moved around or because the building vibrates, at some time it will come crashing to the floor. If the pipet can become contaminated, then the mouth pipetter will eventually ingest a contaminant.

We cannot nullify Murphy's law, but we can do a lot to minimize the damage. We can reduce the incidence of sparks and flames and flammable vapors. We can make sure that if the accident does occur, we have the means to contain the damage and to take care of any injuries that result. All of this means thinking about the laboratory environment. Does your laboratory have or enforce regulations related to important items such as eye, face, and foot protection, safety clothing, respiratory equipment, first aid supplies, fire equipment, spill kits, hoods, and compliance regulations? *Think ahead* about what could go wrong and then *plan* and *prepare* to minimize the chance of an accident and be prepared to respond when one does occur.

NATURE OF HAZARDS

The chemistry laboratory presents a wide assortment of risks. These risks are outlined briefly here so that you can begin to think about the steps necessary to make the laboratory safer:

1. **Physical hazards.** Injuries resulting from flames, explosions, and equipment (cuts from glass, electrical shock from faulty instrumentation, or improper use of instruments).

Chapter 2: C_2H_4, Ethylene
a substance of natural origin, released by ripening fruit.