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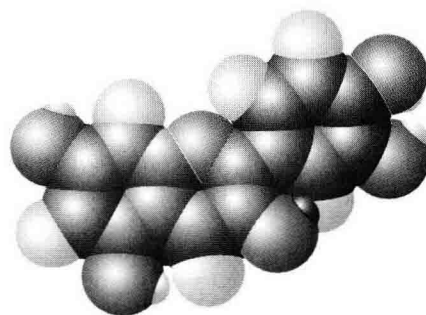
Organic Chemistry

Second Edition



*Marye Anne Fox
James K. Whitesell*

Organic Chemistry



S E C O N D E D I T I O N

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Jones and Bartlett Publishers

Sudbury, Massachusetts

Boston London Singapore

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http://www.jbpub.com

Jones and Bartlett Publishers International
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London W6 7PA UK

Acquisitions Editor: Christopher W. Hyde
Senior Production Administrator: Mary Sanger
Manufacturing Manager: Dana L. Cerrito
Design: Deborah Schneck
Editorial Production Service: Lifland et al., Bookmakers
Illustrations: JAK Graphics Ltd.
Typesetting: York Graphic Services
Cover Design: Hannus Design Associates
Printing and Binding: R.R. Donnelley & Sons Company
Cover Printing: Henry N. Sawyer Co., Inc.
Cover Photographs: © Jeff Marc, PHOTO/NATS, Inc.;
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Library of Congress Cataloging-in-Publication Data

Fox, Marye Anne, 1947–

Organic chemistry / Marye Anne Fox, James K. Whitesell. —2nd ed.
p. cm.

Includes index.

ISBN 0-7637-0178-5

1. Chemistry, Organic. I. Whitesell, James K. II. Title.

QD251.2.F69 1997

547—dc21

96-46985

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Printed in the United States of America
01 00 99 98 97 10 9 8 7 6 5 4 3 2

Preface

Each year, most of the thousands of students who finish a first course in organic chemistry clearly express their dissatisfaction with what they have learned. They convey their displeasure both vocally and, even more persuasively, by “voting with their feet”—that is, by not enrolling in other advanced science courses. Ask a typical group of such students what was wrong with their course and you will hear the same answer that this query draws from deans of medical schools, from educational psychologists who specialize in the instruction of mathematics and science, from university administrators, and even from many instructors of the courses: all say that a typical organic chemistry textbook contains too much information, much of which is excruciatingly detailed, disconnected from “real life,” irrelevant to other parts of a technical or liberal education, and just plain boring. Even the strongest students can emerge from a year of organic chemistry without a good picture of what a practicing organic chemist does.

Concentrating on Fundamentals

Adopting a “less is more” philosophy, we have tried in this book to address each of these common criticisms in an intellectually demanding year-long introductory course.

- First, the course is developed as a “story,” with each chapter containing only those topics and reactions that are needed to understand the intellectual roots of organic chemistry as it is currently practiced.
- Second, specific examples are included at each stage to illustrate familiar, concrete uses of the chemistry under discussion.
- And, third, the material is intended to enhance the student’s appreciation of the significance of chemistry in other science and preprofessional courses, in undergraduate research in a modern organic chemistry laboratory, and in industrial and biomedical research.

In attempting to accomplish these objectives, we have had to take an approach that is substantially different from that in virtually all other currently available organic texts. Like most synthetic chemists, we began by working backward. We first asked ourselves what topics a well-informed student should understand after a one-year course in organic chemistry. We

consulted extensively with health-profession faculty and with chemists of every stripe (industrial and academic, synthetic and mechanistic, material and biological), both in the United States and abroad. These conversations confirmed our initial supposition that an understanding of polymer chemistry, naturally occurring compounds, energy conversion and storage within organic molecules, molecular recognition and information transfer, modes of action of natural and artificial catalysts, and design criteria for new materials and biologically active molecules is of key importance if a student is to comprehend the contributions of organic chemistry to civilization. Most currently available texts, if they treat these topics at all, do so only as brief subsidiary applications rather than as intrinsic intellectual goals of the course.

Providing greater coverage of these topics, however, meant that something else would have to go, if we were to adhere to our first objective of concise presentation.

- We have tried to remove redundancy, believing that it is unnecessary, for example, to treat the complex metal hydride reductions of aldehydes, ketones, esters, and amides as four separate, seemingly unrelated reactions. This approach has required that we move away from the functional-group organization that has been widely used since the early 1960s as a means of tabulating reactions—an organization that has become unwieldy, owing to the ongoing development of large numbers of new reagents.
- We have tried to exercise restraint in choosing which chemical topics and reactions to include. Only those reactions that recur in the book's unfolding chemical story are retained, along with closely related ones that illustrate basic chemical principles and mechanisms for these essential reactions. We reasoned that good pedagogy does not oblige us to include every chemical topic and detail known to either of us. Rather, we sought to identify those topics absolutely required to reach our objective of giving the student sufficient information to understand the principles and practice of modern organic chemistry.

Organic Chemistry, Second Edition: A Unique Organizational Structure

These goals led to an organizational structure that begins with seven chapters that deal primarily with the three-dimensional structures of various organic functional groups (Chapters 1 through 5) and the relation between structure and reactivity, from both a thermodynamic point of view and a kinetic one (Chapters 6 and 7). As soon as the student has been exposed to the range of organic functional groups, spectroscopy is introduced (Chapter 4) to facilitate work in the laboratory. The next seven chapters (Chapters 8 through 14) deal with specific reaction types, organized by common mechanism rather than by functional group. These chapters are followed by an integrative chapter (Chapter 15) that incorporates these reactions into strategies for planning the synthesis of new compounds. Finally, Chapters 16 through 23 illustrate how the structural features considered in the first part of the book, together with the specific reactions covered in the second part, can be sources of insight into the chemical structure and function of

important naturally occurring and manufactured materials: polymers, proteins, and enzymes. We use examples to show how these materials accomplish specific chemical conversions in biological systems by molecular recognition, catalysis, and energetic coupling with cofactor conversions, and conclude by describing the function of pharmaceutical agents in the last chapter.

This textbook presupposes only the knowledge of chemistry typically attained in a high school course or in the first semester of standard college chemistry. If the curriculum requires it, the self-contained course presented in this book can be offered in the freshman year, without the quantitative development provided by a one-year general chemistry course. The topics covered here afford a solid basis for a description of common natural organic phenomena, which might effectively instill in students a greater enthusiasm for the more abstract topics of introductory physical chemistry.

Tools for Student Success

Apart from organizing the text itself in a better way, we have included a number of learning aids and motivational stimulants.

- Each chapter contains exercises for testing immediate mastery of the concepts in a section, as well as end-of-chapter problems that help to integrate the concepts in the chapter as a whole. Both the exercises and the problems range in difficulty from those that provide basic reinforcement of a concept to those that require the student to apply the concept to a new situation. We have written detailed answers for the exercises and problems, preparing the *Study Guide and Solutions Manual* ourselves to ensure that the explanations given in the manual correspond with the presentation of concepts in the text.
- Each chapter contains boxed material—short stories relating the practical utility of the reactions and materials being considered.
- Each chapter includes a summary of the principal ideas of importance in the chapter. These summaries, together with lists of important topics in the *Study Guide and Solutions Manual*, are intended to help the student recognize and learn the main concepts presented in a chapter. Most chapters contain a list of reactions that are new to the chapter, and Chapters 8 through 14 also include tables that group the reactions considered according to what they accomplish as synthetic transformations.
- The book includes a comprehensive index that allows easy access to a given topic, if reinforcement is needed when it is discussed in a new context in a later chapter.
- Finally, a glossary of key terms is included in the text, supplying a definition and a citation to the chapter and section in which a term is introduced and developed. A chapter-by-chapter glossary is provided in the *Study Guide and Solutions Manual* to assist the student in preparing for examinations; the definitions constitute an additional means of reviewing the concepts developed in each chapter.

We hope that students will enjoy and benefit from the experience of learning modern organic chemistry as it is presented in this book. We will be grateful indeed to our readers for their evaluation of our work.

What's New in This Edition?

In this second edition, we have incorporated significant revisions in response to the many positive comments we received from faculty who used the first edition. In making these changes, however, we have adhered resolutely to the intellectual objectives that originally motivated us to write an organic textbook: we maintain that the functional-group approach used in most organic texts no longer serves as an appropriate framework for teaching the fundamental concepts of organic chemistry. Instead, we believe that a thorough understanding of a small number of key principles intrinsic to the study of the structure and reactions of carbon-based compounds provides a much better basis for retaining this knowledge base and extending it to practical applications in other areas of science.

To help realize our objectives, we made the following changes:

- Large portions of the text have been rewritten to make them more readable for the lower-level college student. Material has been added to motivate students and to emphasize the instructor's key role in the learning process.
- Many new exercises and problems have been added to each chapter. In addition, an extensive set of supplementary problems now augments the problems at the end of each chapter. Solutions for these supplementary problems have been intentionally omitted from the *Study Guide and Solutions Manual*, so that instructors can assign them for take-home exams or graded homework sets. The added exercises, problems, and supplementary problems have a broad range of difficulties and call for skills ranging from simple algorithmic manipulations and lower-order responses through tests of higher-order cognitive skills.
- Because Chapter 8 (on nucleophilic substitution) was deemed too long by many adopters of the first edition, it has been extensively revised, with enolate chemistry moved to an entirely new Chapter 13. This latter chapter is perhaps the best example of how a mechanism-based approach can bring together related subjects that are artificially separated and disconnected in a functional-group approach.
- Chapter 23 (Molecular Basis of Drug Action) has been significantly expanded and now includes discussions of the chemistry underlying viral infections and cancer, as well as chemical treatments for these disease states.
- The number of chemical highlights (now called Chemical Perspectives) has been significantly increased. Many of our students have commented that these chemical asides helped them correlate organic chemistry with their everyday lives and motivated them to stick with their study.
- Ball-and-stick as well as space-filling models have been incorporated throughout the text to help the student appreciate the three-dimensional structures of molecules. These were created with Chem3D Pro® (Cambridge Scientific) from structures obtained by energy-minimized molecular mechanics calculations. Representations of molecular orbitals were derived from semi-empirical calculations using the AM-1 basis set with the Cache® suite of calculation programs. These models are thus state-of-the-art three-dimensional representations of the relevant structures and their molecular orbitals.

- CHEMISTRY IN MOTION™ icons throughout the book indicate a figure or illustration that comes to life in short animations created by Jim Whitesell and Mika Hase on the CHEMISTRY IN MOTION CD-ROM.
- The number of pages in the text has increased with the additional exercises and problems, the expanded Chemical Perspectives, and the extensive use of molecular representations. The chemical content, however, has remained essentially the same, consistent with what we believe can be covered realistically in a one-year course.

Customized for You

Recognizing new trends in the curriculum and the desire of some faculty and students for a more manageable text, Jones and Bartlett, the publisher of this text, now offers you choices that allow you to customize a package to meet your specific needs.

- ***Organic Chemistry, Second Edition*** (ISBN 0-7637-0178-5). As outlined on pages xxvi and xxvii.
- ***Core Organic Chemistry*** (ISBN 0-7637-0367-2). Consists of Chapters 1 through 16 from *Organic Chemistry, Second Edition*. Instructors seeking a truly “less is more” approach will be well served by this intellectually demanding introduction to organic chemistry, which is quite suitable for use in full during a year-long course.
- **Chem Modules.** If you adopt Fox and Whitesell’s *Core Organic Chemistry*, you can create a customized text that includes only the advanced topics in organic chemistry that *you* teach in *your* course. Creating a set of chem modules that match the content and sequence of your course is fast and easy. Simply choose one or more of the seven chapters (modules) that address advanced concepts in organic chemistry (Chapters 17 through 23 in *Organic Chemistry, Second Edition*). Jones and Bartlett will package these modules with the *Core Organic Chemistry* text. Your students assemble the modules into a single, easy-to-use *Chem Modules* book that serves as the perfect complement to *Core Organic Chemistry*. *Chem Modules* are the ideal solution for instructors who want to teach the core concepts of organic chemistry and only a few of the advanced topics. Available chapters cover naturally occurring compounds (Chapters 17 and 18), noncovalent interactions and molecular recognition (Chapter 19), catalyzed reactions (Chapter 20), cofactors and energy storage in biological systems (Chapters 21 and 22), and the chemical basis for drug action (Chapter 23). For details, ask your Jones and Bartlett representative, or visit the Fox and Whitesell home page at <http://www.jbpub.com>

Supplementary Material

Various supplementary materials are available to assist instructors and aid students in mastering organic chemistry:

- ***Study Guide and Solutions Manual.*** Written entirely by the authors, Marye Anne Fox and James K. Whitesell, this manual contains key con-

cepts, answers to questions, and solutions to problems. It includes the *Nucleophile/Electrophile Reaction Guide* by Dr. Donna Nelson of the University of Oklahoma, which facilitates students' recognition of patterns in these reactions. The *Study Guide and Solutions Manual* is available free to instructors; students can purchase a version of the manual for either *Organic Chemistry, Second Edition* (ISBN 0-7637-0413-X) or *Core Organic Chemistry* (ISBN 0-7637-0440-7).

- **Test Bank.** This evaluation tool, prepared by the authors, contains more than 600 questions, with at least twenty-five questions per chapter. Available free to instructors.
- **Electronic Test Bank.** An electronic version of the test bank that instructors can use to prepare customized tests is available for Windows and Macintosh operating systems.
- **Lecture Success CD-ROM.** The Lecture Success CD-ROM is an easy-to-use instructional device that contains many figures from the text, including their full captions. Images are arranged by chapter, topic, and figure number. It is designed as a lecture demonstration aid that replaces traditional transparency masters.
- **CHEMISTRY IN MOTION™ CD-ROM.** Included on the inside front cover of the text, this CD is an invaluable tool that helps students better visualize challenging concepts. CHEMISTRY IN MOTION icons throughout the text indicate figures and illustrations that come alive in short animations on this CD. In addition to the animations, more than 500 practice problems are provided.
- **CHEM TV®.** This visualization aid, by Dr. Betty Luceigh of the University of California at Los Angeles, and MECHANISMS IN MOTION, by Dr. Bruce Lipschitz of the University of California at Santa Barbara, may be available through your college or university's chemistry department. CHEM TV icons are placed throughout the text to match discussion with animation appearing on the CD that can be used effectively both in lecture and by the individual student. If your department does not already own copies of this visualization tool, consider acquiring a copy to aid students.
- **Reaction Flash Cards.** This set of preprinted flash cards has the reactants and reagents on the front of a card and the products on the back for all of the reactions covered in Chapters 8–14. A convenient way for students to learn reactions as they are encountered and to test their knowledge as they study.

Acknowledgments

Preparing an organic chemistry text that departs so markedly from the traditional pedagogical approach of the past three decades has been a fascinating experience that has been significantly aided by the very useful and detailed criticisms of a number of reviewers, whose names are given below. We are indeed grateful to each of them. Their comments were universally helpful; any errors or deviations from their advice are our own responsibility.

Shelby R. Anderson, *Trinity College*
 Eric Anslyn, *University of Texas, Austin*
 Steven W. Baldwin, *Duke University*
 Tadgh Begley, *Cornell University*
 Eric Block, *State University of New York, Albany*
 Erich C. Blosssey, *Rollins College*
 William T. Brady, *University of North Texas*
 John I. Brauman, *Stanford University*
 Keith Brown, *University of Saskatchewan*
 Jared A. Butcher, Jr., *Ohio University*
 William D. Closson, *State University of New York, Albany*
 Imre Cszimadia, *University of Toronto*
 Dennis P. Curran, *University of Pittsburgh*
 William P. Dailey, *University of Pennsylvania*
 Kurt Deshayes, *Bowling Green State University*
 Vera Dragisich, *University of Chicago*
 Graham W. L. Ellis, *Bellarmine College*
 Jacqueline Gervay, *University of Arizona*
 Warren Giering, *Boston University*
 Rainer Glaser, *University of Missouri*
 Joseph J. Grabowski, *University of Pittsburgh*
 Roland Gustafsson, *Umeå Universitet, Sweden*
 Martha A. Hass, *Albany College of Pharmacy*
 Henk Hiemstra, *University of Amsterdam*
 Robert Hoffman, *New Mexico State University*
 Jack Isidor, *Montclair State University*
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 Paul J. Kropp, *University of North Carolina, Chapel Hill*
 David M. Lemal, *Dartmouth College*
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 Marshall W. Logue, *Michigan Technological University*
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 Daniel J. Pasto, *University of Notre Dame, Indiana*
 C. Dale Poulter, *University of Utah*
 Suzanne Purrington, *North Carolina State University*
 Harold R. Rogers, *California State University, Fullerton*
 David A. Shultz, *North Carolina State University*
 William M. Scovell, *Bowling Green State University*
 Donald Slavin, *Community College of Philadelphia*
 Richard T. Taylor, *Miami University, Ohio*
 William P. Todd, *State University of New York, Brockport*
 Guy Tourigny, *University of Saskatchewan*
 Christopher T. Walsh, *Harvard Medical School*
 Walter W. Zajac Jr., *Villanova University*
 Charles K. Zercher, *University of New Hampshire*

We are also deeply grateful for the highly professional developmental editing of Philippa Solomon and copyediting of Leona Greenhill. Chris Hyde's tireless promotion of the first edition and efforts as editor for the second edition are also appreciated. The production team, directed by Mary Sanger at Jones and Bartlett and Jane Hoover at Lifland et al., Bookmakers, has been extraordinarily helpful in transforming crude copy into a visually appealing textbook. The moral support and direction of Dave Phanco will always be deeply appreciated.

Special recognition goes to Hal Rogers of the California State University at Fullerton for his important work as an accuracy reviewer of both the text and the *Study Guide and Solutions Manual*. Finally, we wish to thank all our colleagues who adopted the first edition and to acknowledge those who provided extensive reviews of the first and second editions, offering invaluable suggestions and comments.

Tricks of the Trade—A Special Message to the Student

Mastering organic chemistry is likely to be among the most stimulating learning experiences you will have at an undergraduate level. Being able to understand the structures and functions of new synthetic molecules, as well as naturally occurring ones, will enable you to appreciate the excitement of this fascinating science. Yet, because of its reputation as a difficult course, organic chemistry is sometimes regarded with apprehension. You can take several steps, however, to help ensure success:

- Prepare adequately for lectures. This means reading the material in the text before it is presented in a lecture. This is crucial if you are to ask intelligent questions about a topic.
- Attend lectures regularly. You should set out to extract as much information as possible from your instructor. After difficult lectures, review your notes carefully; you may find it helpful to consult with classmates.
- Do the in-chapter exercises conscientiously while proceeding through each chapter. You should work the exercises on your own and then consult the *Study Guide and Solutions Manual* to confirm your answers.
- Work the end-of-chapter problems promptly after finishing each chapter. This activity, together with diligence in working the in-chapter exercises, will help assure that you integrate the concepts in the chapter as a whole.
- Use the Review of Reactions, Summary, and tables of synthetic reactions to review what you have learned in each chapter.
- Design your own learning aids. Everyone has a personal learning style and techniques. You should develop learning aids that suit your style—perhaps using molecular models to visualize structures or compiling a set of index cards to review important reactions.
- Seek additional assistance. You should take advantage of your instructor's or teaching assistant's office hours, participate in recitation or help sessions, seek supporting materials (such as handouts, sample tests, and computer programs), review audio or video tapes, and form regularly scheduled discussion groups.
- Make the most of laboratory experiences. Actually working with organic compounds when you have prepared sufficiently for the experiments reinforces the utility of the reactions learned.

Marye Anne Fox
James K. Whitesell

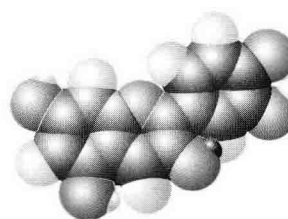
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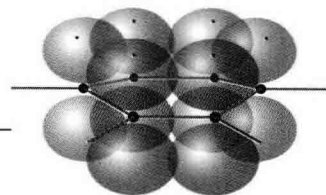
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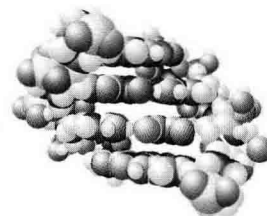
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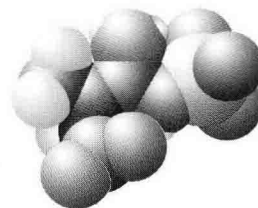
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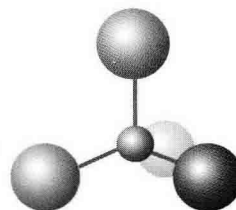
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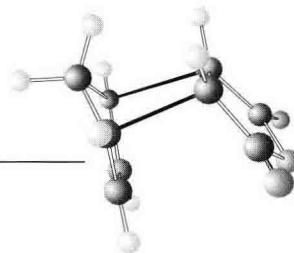
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