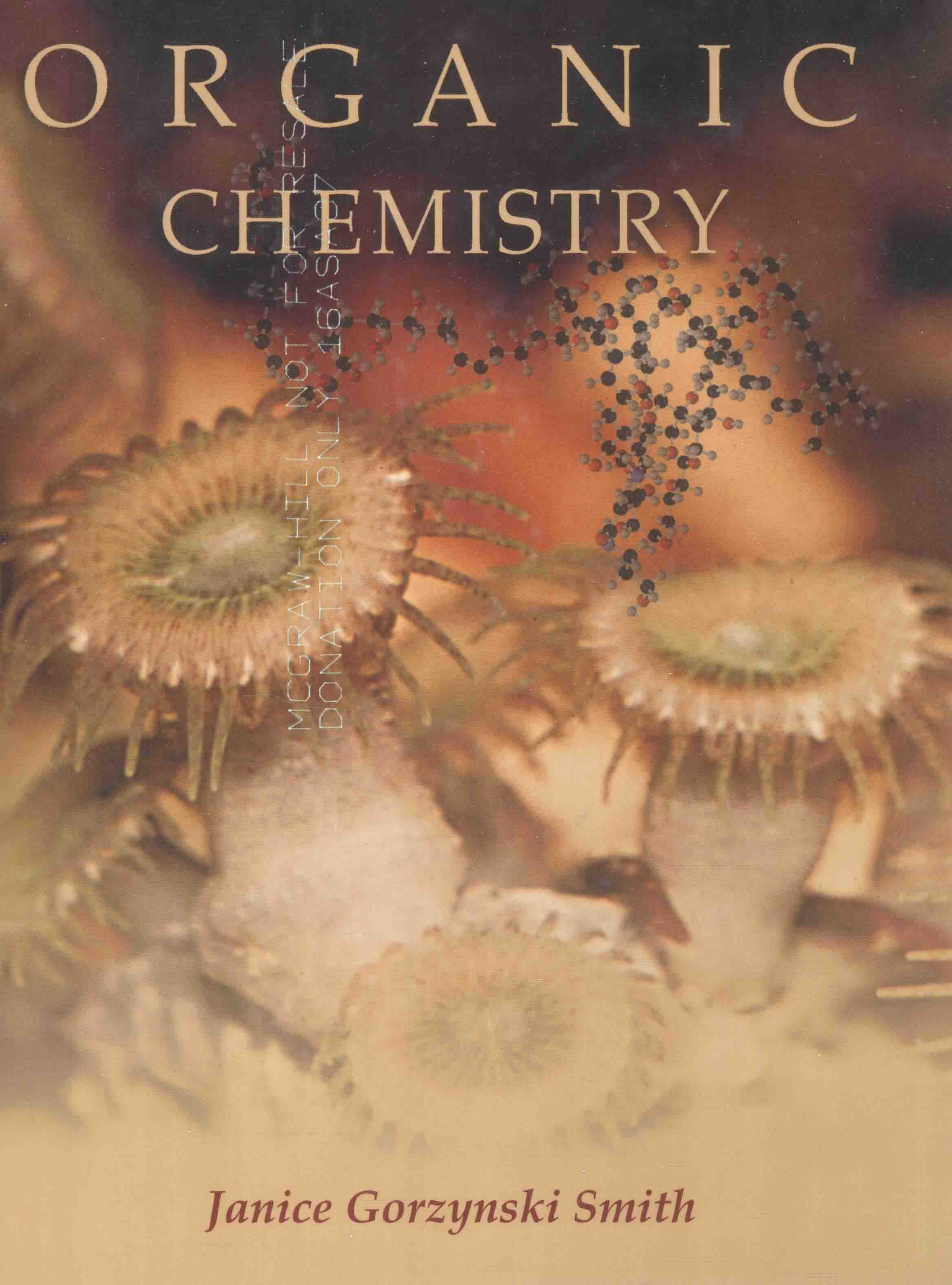
ORGANIC CHEMISTRY



Janice Gorzynski Smith

ORGANIC CHEMISTRY

Janice Gorzynski Smith
University of Hawai'i at Mānoa

McGraw-Hill Higher Education

Boston Burr Ridge, IL Dubuque, IA Madison, WI New York San Francisco St. Louis
Bangkok Bogotá Caracas Kuala Lumpur Lisbon London Madrid Mexico City
Milan Montreal New Delhi Santiago Seoul Singapore Sydney Taipei Toronto

The McGraw-Hill Companies

Higher Education

ORGANIC CHEMISTRY

Published by McGraw-Hill, a business unit of The McGraw-Hill Companies, Inc., 1221 Avenue of the Americas, New York, NY 10020.

This book is printed on acid-free paper.

2 3 4 5 6 7 8 9 0 VNH/VNH 0 9 8 7 6

ISBN-13: 978-0-07-239746-8
ISBN-10: 0-07-239746-2

Editorial Director: *Kent A. Peterson*
Sponsoring Editor: *Thomas D. Timp*
Developmental Editor: *Joan M. Weber*
Managing Developmental Editor: *Shirley R. Oberbroeckling*
Outside Developmental Services: *John S. Murdzek*
Senior Marketing Manager: *Tamara L. Good-Hodge*
Lead Project Manager: *Joyce M. Berendes*
Senior Production Supervisor: *Laura Fuller*
Lead Media Project Manager: *Judi David*
Senior Media Technology Producer: *Jeffry Schmitt*
Designer: *Laurie B. Janssen*
Cover/Interior Designer: *Jamie E. O'Neal*
(USE) Cover Image: *Photo collection of Dr. James P. McVey, NOAA Sea Grant Program*
Lead Photo Research Coordinator: *Carrie K. Burger*
Photo Research: *Mary Reeg*
Supplement Producer: *Brenda A. Ernzen*
Compositor: *Precision Graphics*
Typeface: *10/12 Times Roman*
Printer: *Von Hoffmann Corporation*

About the Cover: Palytoxin ($C_{129}H_{223}N_3O_{54}$), a complex organic molecule, was first isolated from marine soft corals of the genus Palythoa. It is one of the most potent poisons known, historically used by ancient Hawai'ians to poison their spears. Palytoxin was isolated in pure form in 1971 at the University of Hawai'i at Mānoa, and its structure determined simultaneously by two different research groups in 1981. In 1994, Harvard chemists synthesized palytoxin in the laboratory, producing an organic compound identical to the natural product.

The credits section for this book begins on page C–1 and is considered an extension of the copyright page.

Library of Congress Cataloging-in-Publication Data

Smith, Janice G.
Organic chemistry / Janice G. Smith. — 1st ed.
p. cm.
Includes index.
ISBN 0–07–239746–2
1. Chemistry, Organic. I. Title.

QD253.2.S65 2006
547—dc22 2004057933
CIP

www.mhhe.com

List of Selected Applications

Applications make any subject seem more relevant and interesting—for nonmajors and majors alike. The following is a list of some of the biological, medicinal, and environmental applications that have been integrated throughout *Organic Chemistry.* Each chapter opener showcases an interesting and current application relating to the chapter's topic.

	Description	Reference
Prologue	The structure of palytoxin, one of the most toxic substances known, is used to illustrate the conventions for drawing skeletal (line) structures.	Figure 1
Chapter 1	The structure of capsaicin, the spicy component of hot peppers, is used to apply the most important concepts from the chapter—how to determine the hybridization and geometry around an atom, how to label all polar and nonpolar bonds, and how to compare bond length and bond strength for different C–C bonds.	Section 1.13
Chapter 2	Aspirin must be in its neutral form to cross a cell membrane, so the different properties of acids and their conjugate bases can have important physiological consequences.	Section 2.7
Chapter 3	Because of their different functional groups, vitamin A is water insoluble, whereas vitamin C is water soluble. As a result, excess vitamin A is stored in the fat cells of tissue, but excess vitamin C is excreted.	Section 3.6
Chapter 4	Lipids, water-insoluble biological compounds, contain the same structural features as alkanes, the simplest organic molecules.	Section 4.15
Chapter 5	Starch and cellulose are used to illustrate how apparently minute differences in structure can result in vastly different properties.	Section 5.1
Chapter 6	The metabolism of glucose and the combustion of gasoline are two apparently different organic reactions that share a common thread—both reactions release a great deal of useful energy.	Chapter opener, Section 6.4
Chapter 7	Nitrosamines, one potential by-product of the sodium nitrite used to preserve meats, can be converted to unstable intermediates that react with biological nucleophiles (such as DNA or an enzyme). The end result can be cancer or death of the cell.	Section 7.16
Chapter 8	Ethylene, the simplest hydrocarbon containing a carbon–carbon double bond, is a hormone that regulates plant growth and fruit ripening.	Chapter opener
Chapter 9	New asthma drugs, such as zileuton, inhibit the enzyme responsible for the synthesis of leukotriene C_4 from arachidonic acid. By blocking the synthesis of a compound responsible for the disease, zileuton treats the cause of the asthma, not just its symptoms.	Section 9.16
Chapter 10	Fats are solids at room temperature, whereas oils are liquids, because oils have more *Z* double bonds, giving rise to more kinks in their hydrocarbon chains.	Chapter opener, Section 10.6
Chapter 11	Ethynylestradiol, a synthetic compound containing a C–C triple bond, is a component of several widely used oral contraceptives.	Chapter opener
Chapter 12	Antabuse, a drug given to alcoholics to prevent them from consuming alcoholic beverages, acts by interfering with the normal oxidation of ethanol. Instead, acetaldehyde builds up in the person's system, causing them to become violently ill.	Section 12.13
Chapter 13	Vitamin E is a fat-soluble vitamin that is thought to inhibit radical reactions that cause oxidative damage to the lipids in the cell membrane.	Chapter opener, Section 13.12

	Description	Reference
Chapter 14	Trace amounts of tetrahydrocannabinol (THC), the primary active constituent of marijuana, can be detected by modern instrumental methods, such as mass spectrometry and IR spectroscopy.	Chapter opener, Section 14.3
Chapter 15	Magnetic resonance imaging (MRI)—NMR spectroscopy in medicine—is a powerful diagnostic technique used routinely in hospitals today.	Section 15.12
Chapter 16	Commercial sunscreens contain conjugated compounds that absorb UV light, thus shielding your skin (for a time) from the harmful effects of UV radiation.	Section 16.15
Chapter 17	Zoloft, Viagra, and Claritin are just three of many drugs whose structures contain benzene rings.	Figure 17.5
Chapter 18	A key step in the laboratory synthesis of LSD involves carbon–carbon bond formation using electrophilic aromatic substitution.	Chapter opener, Figure 18.4
Chapter 19	Aspirin relieves pain and reduces inflammation by blocking the synthesis of prostaglandins, 20-carbon fatty acids with a five-membered ring that are responsible for pain, inflammation, and a wide variety of other biological functions.	Chapter opener, Section 19.6
Chapter 20	Juvenile hormones, the compounds that regulate the complex life cycles of some insects, are synthesized by reactions that form new carbon–carbon bonds.	Chapter opener, Figure 20.6
Chapter 21	11-*cis*-Retinal is the light-sensitive conjugated aldehyde that plays a key role in the complex chemistry of vision for all vertebrates, arthropods, and mollusks.	Chapter opener, Figure 21.9
Chapter 22	Penicillin and related β-lactams kill bacteria because they undergo a nucleophilic acyl substitution reaction that interferes with the synthesis of the bacterial cell wall.	Chapter opener, Section 22.14
Chapter 23	One method for synthesizing tamoxifen, a potent anticancer drug, forms a new carbon–carbon bond on the α carbon to a carbonyl group using an intermediate enolate.	Chapter opener, Section 23.8
Chapter 24	Gibberellic acid, a plant growth hormone, can be synthesized in the laboratory using two intramolecular aldol reactions to form two carbon–carbon bonds of the complex carbon skeleton.	Chapter opener
Chapter 25	Dopamine, a neurotransmitter, is a chemical messenger released by one nerve cell, which then binds to a receptor in a neighboring target cell. Proper dopamine levels are necessary to maintain an individual's mental and physical health. Parkinson's disease results when dopamine-producing neurons die and dopamine levels drop.	Figure 25.6
Chapter 26	Cholesterol, a lipid synthesized in the liver, is found in almost all body tissues. Even though it is a vital component for healthy cell membranes and it serves as the starting material for the synthesis of all other steroids, elevated cholesterol levels can lead to coronary artery disease.	Chapter opener, Section 26.8
Chapter 27	Lactose, a carbohydrate formed from glucose and galactose, is the principal sugar in dairy products. Individuals who lack adequate amounts of lactase, the enzyme necessary to digest and absorb lactose, suffer from a condition known as lactose intolerance.	Chapter opener, Section 27.12
Chapter 28	The two amino acids that comprise the sweetener aspartame are joined via the same peptide bond that is found in proteins and polypeptides in living organisms.	Chapter opener, Section 28.5

List of *How To*'s

How To boxes provide detailed instructions for key procedures that students need to master. Below is a list of each *How To* and where it is presented in the text.

List of Mechanisms

Mechanisms are the key to understanding the reactions of organic chemistry. For this reason, great care has been given to present mechanisms in a detailed, step-by-step fashion. The list below indicates when each mechanism in the text is presented for the first time.

Preface

When I began this project, my goal was to write a text that showed students the beauty and logic of organic chemistry by giving them a book that they would *use*. Five years and three drafts later, I present to you *Organic Chemistry,* a text based on lecture notes and handouts that have been developed in my own organic chemistry courses over the years. I have followed two guiding principles: use relevant and interesting applications to illustrate chemical phenomena, and present the material in a student-friendly fashion using bulleted lists, solved problems, and extensive illustrations and summaries. *Organic Chemistry* is my attempt to simplify and clarify a course that intimidates many students—to make organic chemistry interesting, relevant, and accessible to *all* students, both chemistry majors and those interested in pursuing careers in biology, medicine, and other disciplines, without sacrificing the rigor they need to be successful in the future.

The Basic Features

- **Style** This text is different—by design. Today's students rely more heavily on visual imagery to learn than ever before. I have therefore written a text that uses less prose and more diagrams, equations, tables, and bulleted summaries to introduce and reinforce the major concepts and themes of organic chemistry.
- **Content** *Organic Chemistry* accents basic themes in an effort to keep memorization at a minimum. Relevant materials from everyday life are used to illustrate concepts, and this material is integrated throughout the chapter rather than confined to a boxed reading. Each topic is broken down into small chunks of information that are more manageable and easily learned. Sample Problems are used as a tool to illustrate stepwise problem solving. Exceptions to the rule and older, less useful reactions are omitted to focus attention on the basic themes.
- **Organization** *Organic Chemistry* uses functional groups as the framework within which chemical reactions are discussed. Thus, the emphasis is placed on the reactions that different functional groups undergo, not on the reactions that prepare them. Moreover, similar reactions are grouped together so that parallels can be emphasized. These include acid–base reactions (Chapter 2), oxidation and reduction (Chapters 12 and 20), radical reactions (Chapter 13), and reactions of organometallic reagents (Chapter 20).

By introducing one new concept at a time, keeping the basic themes in focus, and breaking complex problems down into small pieces, I have found that many students find organic chemistry an intense but learnable subject. Many, in fact, end the yearlong course surprised that they have actually *enjoyed* their organic chemistry experience.

Illustrations

The illustration program is a key component of the visual emphasis in *Organic Chemistry.* Besides traditional skeletal (line) structures and condensed formulas, there are numerous ball-and-stick molecular models and electrostatic potential maps to help students grasp the three-dimensional structure of molecules (including stereochemistry) and to better understand the distribution of electronic charge. Unique to *Organic Chemistry* are the micro-to-macro illustrations. These pieces combine line art and photos to place molecules in a broader context. Examples include starch and cellulose (Chapter 5), adrenaline (Chapter 7), and dopamine (Chapter 25).

Organization and Presentation

For the most part, the overall order of topics in the text is consistent with the way most instructors currently teach organic chemistry. There are, however, some important differences in the way topics are presented to make the material logical and more accessible. This can especially be seen in the following areas.

- **Review material**—Chapter 1 presents a healthy dose of review material covering Lewis structures, molecular geometry and hybridization, bond polarity, and types of bonding. While many of these topics are covered in general chemistry courses, they are presented here from an organic chemist's perspective. I have found that giving students a firm grasp of these fundamental concepts helps tremendously in their understanding of later material.
- **Acids and bases**—Chapter 2 on acids and bases serves two purposes. It gives students experience with curved arrow notation using some familiar proton transfer reactions. It also illustrates how some fundamental concepts in organic structure affect a reaction, in this case an acid–base reaction. Since many mechanisms involve one or more acid–base reactions, I emphasize proton transfer reactions early and come back to this topic often throughout the text.
- **Functional groups**—Chapter 3 uses the functional groups to introduce important properties of organic chemistry. Relevant examples—PCBs, vitamins, soap, and the cell membrane—illustrate basic solubility concepts. In this way, practical topics that are sometimes found in the last few chapters of an organic chemistry text (and thus often omitted because instructors run out of time) are introduced early so that students can better grasp why they are studying the discipline.
- **Stereochemistry**—Stereochemistry (the three-dimensional structure of molecules) is introduced early (Chapter 5) and reinforced often, so students have every opportunity to learn and understand a crucial concept in modern chemical research, drug design, and synthesis.
- **Modern reactions**—While there is no shortage of new chemical reactions to present in an organic chemistry text, I have chosen to concentrate on new methods that introduce a particular three-dimensional arrangement in a molecule, so-called asymmetric or enantioselective reactions. Examples include Sharpless epoxidation (Chapter 12), CBS reduction (Chapter 20), and enantioselective synthesis of amino acids (Chapter 28).
- **Grouping reactions**—Since certain types of reactions have their own unique characteristics and terminology that make them different from the basic organic reactions, I have grouped these reactions together in individual chapters. These include acid–base reactions (Chapter 2), oxidation and reduction (Chapters 12 and 20), radical reactions (Chapter 13), and reactions of organometallic reagents (Chapter 20). I have found that focusing on a group of reactions that share a common theme helps students to better see their similarities.
- **Synthesis**—Synthesis, one of the most difficult topics for a beginning organic student to master, is introduced in small doses, beginning in Chapter 7 and augmented with a detailed discussion of retrosynthetic analysis in Chapter 11. In later chapters, special attention is given to the retrosynthetic analysis of compounds prepared by carbon–carbon bond forming reactions (for example, Sections 20.11 and 21.10C).
- **Spectroscopy**—Since spectroscopy is such a powerful tool for structure determination, four methods are discussed over two chapters (Chapters 14 and 15).
- **Key concepts**—End-of-chapter summaries succinctly summarize the main concepts and themes of the chapter, making them ideal for review prior to working the end-of-chapter problems or taking an exam.

Acknowledgments

When I started working on this project in the fall of 1999, I had no sense of the magnitude of the task nor any idea of just how many people I would rely upon to complete it. Although mine is the only name that appears on the cover, this text is truly the result of extensive contributions from a number of individuals.

I must first thank two chemist–friends, Spencer Knapp and John Murdzek, for the roles they have played in seeing this project to its completion. I never imagined that Spencer Knapp, a former classmate from Cornell and co-worker from Harvard, would one day serve as my "right-hand person" for a number of aspects for this text. In addition to his excellent work in reviewing the manuscript and illustrations and overseeing the creation of the spectra, along with his colleagues Patrick J. O'Connor and Richard A. Huhn, his steady encouragement and keen insight throughout the writing process have been of enormous value.

John Murdzek helped develop every aspect of this project with uncanny attention to detail. He took a wordy and rambling first draft and helped me polish it into a cleaner and well-organized final manuscript. His thoughtful feedback has significantly improved the quality of this book. He is a true professional and I have been most fortunate to have had his assistance from first to final draft. I hope our collaboration continues for many future editions.

I have also benefited greatly from a team of advisors who have helped guide me through the many intricate aspects of the text and also provided great moral support. They include:

Robert S. Coleman *The Ohio State University*
Malcolm D.E. Forbes *University of North Carolina—Chapel Hill*
Susan M. King *University of California—Irvine*
Spencer Knapp *Rutgers University*
C. Peter Lillya *University of Massachusetts—Amherst*
Robert E. Maleczka, Jr. *Michigan State University*
Keith T. Mead *Mississippi State University*
Richard Pagni *University of Tennessee*
Michael Rathke *Michigan State University*
Ieva L. Reich *University of Wisconsin—Madison*
John W. Taylor *Rutgers University*
Laren M. Tolbert *Georgia Institute of Technology*
Jane E. Wissinger *University of Minnesota*

Having served as an accuracy checker for professional publications in the past, I know how important and challenging this can be for an organic chemistry text. I have had the good fortune to be supported by a great group of instructors who have helped insure that this text is as "error-free" as possible. They include:

Daniel A. Adsmond *Ferris State University*
Kay M. Brummond *University of Pittsburgh*
Donnie N. Byers *Johnson County Community College*
Todd S. Deal *Georgia Southern University*
Susan M. King *University of California—Irvine*
Kathleen V. Nolta *University of Michigan—Ann Arbor*
Catherine Woytowicz *The George Washington University*

Throughout the development of this first edition I have been impressed with the quality of the feedback I have received on how the manuscript could be improved. Some individuals have provided in-depth reviews, while others have agreed to class test sections of the manuscript. Still others have provided very candid feedback to me or my editors at focus groups and symposiums. Collectively, these individuals have made the most significant contributions to this project.

Reviewers

Christopher J. Abelt, *College of William & Mary*
Madeline Adamczeski, *San Jose City College*
Jennifer Adamski, *Old Dominion University*
Ruquia Ahmed-Schofield, *Xavier University of Louisiana*
Yu Mi Ahn, *Deciphera Pharmaceuticals LLC*
Igor Alabugin, *Florida State University*
Angela J. Allen, *University of Michigan—Dearborn*
Neil T. Allison, *University of Arkansas*
Eric Anslyn, *University of Texas—Austin*
Jon C. Antilla, *University of Mississippi*
Mark Arant, *University of Louisiana—Monroe*
Paramjit Arora, *New York University*
Arthur J. Ashe III, *University of Michigan—Ann Arbor*
Donald H. Aue, *University of California—Santa Barbara*
George C. Bandik, *University of Pittsburgh*
John Barbaro, *University of Florida*
Debra L. Bautista, *Eastern Kentucky University*
Byron L. Bennett, *University of Nevada—Las Vegas*
Stuart R. Berryhill, *California State University—Long Beach*
Steve Bertman, *Western Michigan University*
Robert S. Bly, *University of South Carolina*
Debra J. Boehmler, *University of Maryland—College Park*
Ned B. Bowden, *University of Iowa*
Stephen E. Branz, *San Jose State University*
Phil A. Brown, *North Carolina State University*
Kay M. Brummond, *University of Pittsburgh*
Christine Brzezowski, *University of Alberta*
Patrick E. Buick, *Florida Atlantic University—Boca Raton*
Arthur W. Bull, *Oakland University*
Paul Buonora, *California State University—Long Beach*
Kevin Burgess, *Texas A&M University—College Station*
Rachel L. Burroughs, *Columbus State Community College*
Donald J. Burton, *University of Iowa*
Sylvester Burton, *Southern University*
Donnie N. Byers, *Johnson County Community College*
Kevin C. Cannon, *Penn State Abington College*
Neal Castagnoli, *Virginia Tech*
Young-Tae Chang, *New York University*
Dana Chatellier, *University of Delaware*
Michelle Chatellier, *University of Delaware*
Clair J. Cheer, *San Jose State University*
Barry A. Coddens, *Northwestern University*
Randolph A. Coleman, *College of William & Mary*
David M. Collard, *Georgia Institute of Technology*
Gregory R. Cook, *North Dakota State University*
Scott W. Cowley, *Colorado School of Mines*
Sonja E. Davison, *Tarrant County College—North East Campus*
Todd S. Deal, *Georgia Southern University*
Mark R. DeCamp, *University of Michigan—Dearborn*
Roman Dembinski, *Oakland University*
Michael R. Detty, *SUNY—Buffalo*
Mark Distefano, *University of Minnesota*
Lisa M. Dollinger, *University of Arizona*
William A. Donaldson, *Marquette University*
Ralph Dougherty, *Florida State University*
Liangcheng Du, *University of Nebraska—Lincoln*
Norma Dunlap, *Middle Tennessee State University*
Ihsan Erden, *San Francisco State University*
Ken Feldman, *Penn State University*
Martin Feldman, *Howard University*
Gary B. Fisher, *De Anza College*
Steven A. Fleming, *Brigham Young University*
Paul Floreancig, *University of Pittsburgh*
David C. Forbes, *University of South Alabama*
Maryam Foroozesh, *Xavier University of Louisiana*
John W. Francis, *Columbus State Community College*
Natia L. Frank, *University of Washington*
Andreas H. Franz, *University of the Pacific*
Kevin P. Gable, *Oregon State University*

Contents


ALEVE