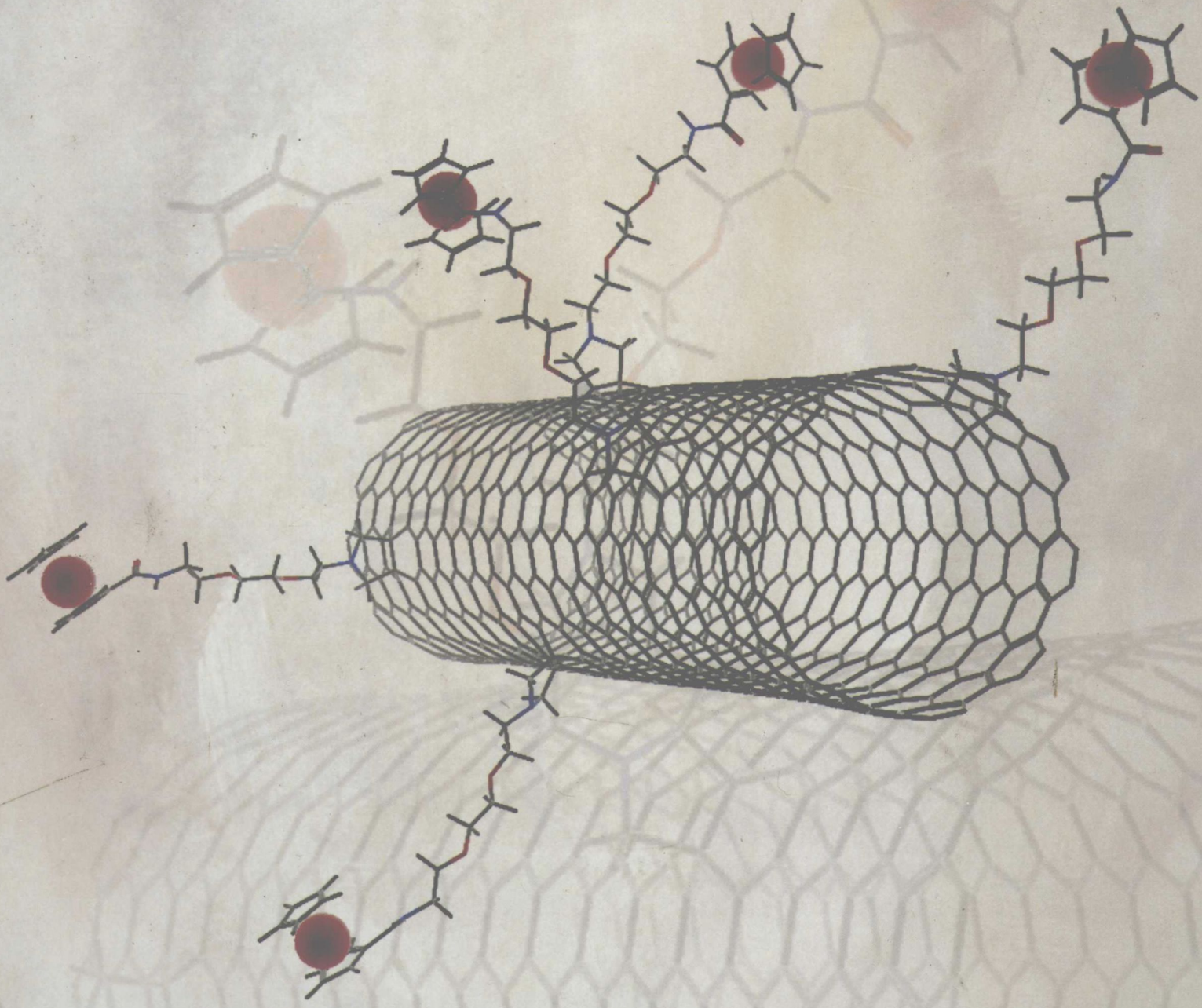
Organic Chemistry

SEVENTH EDITION



FRANCIS A. CAREY

Organic Chemistry

Seventh Edition

Francis A. Carey
University of Virginia

Mc Graw Hill Higher Education

Boston Burr Ridge, IL Dubuque, IA 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

Mc Graw Hill **Higher Education**

ORGANIC CHEMISTRY, SEVENTH EDITION

1 2 3 4 5 6 7 8 9 0 DOW/DOW 0 9 8 7 6

ISBN 978–0–07–304787–4
MHID 0–07–304787–2

Publisher: *Thomas D. Timp*
Senior Sponsoring Editor: *Tamara Good-Hodge*
Developmental Editor: *Jodi Rhomberg*
Senior Marketing Manager: *Todd Turner*
Senior Project Manager: *Gloria G. Schiesl*
Senior Production Supervisor: *Kara Kudronowicz*
Lead Media Project Manager: *Judi David*
Executive Producer: *Linda Meehan Avenarius*
Senior Designer: *David W. Hash*
Cover/Interior designer: *Elise Lansdon*
(USE) Cover Image: *Nanotube supplied by Dr. Dirk Guldi of the University of Erlangen (Germany) and Dr. Maurizio Prato of the University of Trieste (Italy)*
Senior Photo Research Coordinator: *John C. Leland*
Photo Research: *Mary Reeg*
Supplement Producer: *Tracy L. Konrardy*
Compositor: *Techbooks*
Typeface: 10.5/12 *Times*
Printer: *R. R. Donnelley Willard, OH*

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

Carey, Francis A., 1937-
Organic chemistry / Francis A. Carey.—7th ed.
p. cm.
Includes index.
ISBN 978-0-07-304787-4—ISBN 0-07-304787-2 (hard copy : alk. paper)
1. Chemistry, Organic. I. Title.
QD251.3.C37 2008
547—dc22

2006031901

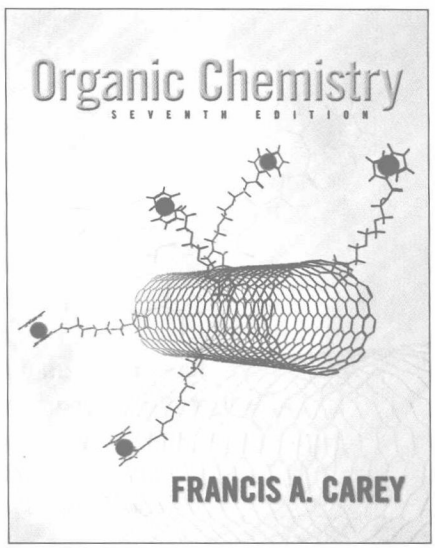
www.mhhe.com

This edition is dedicated to my colleague and friend Bob Atkins, who is not only the lead author of our *Solutions Manual* but who also has contributed generously of his time, knowledge, and common sense throughout the seven editions of this text.

About the Cover

Chemists are increasingly concerned with preparing compounds designed to have particular properties. The compound featured on the cover is the creation of Dr. Dirk Guldi of the University of Erlangen (Germany) and Dr. Maurizio Prato of the University of Trieste (Italy).

The cylindrical object is a form of carbon known as a nanotube.* About 1 percent of the carbons of this nanotube are linked to molecules of the organometallic "sandwich" compound ferrocene.† On irradiation with visible light, ferrocene transfers an electron to the nanotube, generating a charge-separated species. Thus, nanotubes that bear appropriate attached groups hold promise as materials suitable for devices, such as solar cells, that are capable of converting sunlight to electricity.



*For more about carbon nanotubes, see pages 432–433.

†For more about ferrocene, see page 600.

About the Author

Francis A. Carey, a native of Philadelphia, was educated at Drexel University (B.S. in chemistry, 1959) and Penn State (Ph.D., 1963). Following postdoctoral work at Harvard and military service, he served on the faculty of the University of Virginia from 1966 until retiring as Professor Emeritus in 2000.

In addition to this text, Professor Carey is coauthor (with Robert C. Atkins) of *Organic Chemistry: A Brief Course* and (with Richard J. Sundberg) of *Advanced Organic Chemistry*, a two-volume treatment designed for graduate students and advanced undergraduates.

Frank and his wife Jill, who is a teacher/director of a preschool and a church organist, are the parents of Andy, Bob, and Bill and the grandparents of Riyad and Ava.

List of Important Features

Mechanisms

Tables

Boxed Essays

Descriptive Passage and Interpretive Problems

Preface

What Sets This Book Apart?

The central message of chemistry is that the properties of a substance come from its structure. What is less obvious, but very powerful, is the corollary. Someone with training in chemistry can look at the structure of a substance and tell you a lot about its properties. Organic chemistry has always been, and continues to be, the branch of chemistry that best connects structure with properties.

The goal of this text, as it has been through six previous editions, is to provide students with the conceptual tools to understand and apply the relationship between the structures of organic compounds and their properties. Both the organization of the text and the presentation of individual topics were designed with this objective in mind.

A Functional Group Organization

The text is organized according to functional groups—structural units within a molecule that are most closely identified with characteristic properties. This organization offers two major advantages over alternative organizations based on mechanisms or reaction types.

1. The information content of individual chapters is more manageable when organized according to functional groups.
2. Patterns of reactivity are reinforced when a reaction used to prepare a particular functional group reappears as a characteristic reaction of a different functional group.

A Mechanistic Emphasis and Its Presentation

The text emphasizes mechanisms and encourages students to see similarities in mechanisms among different functional groups. Mechanisms are developed from observations; thus, reactions are normally presented first, followed by their mechanism.

To maintain consistency with what our students have already learned, this text presents multistep mechanisms in the same way as do most general chemistry textbooks—that is, as a series of *elementary steps*. Additionally, we provide a brief comment about how each step contributes to the overall mechanism.

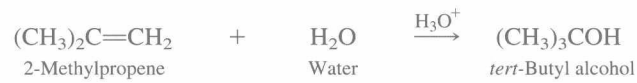
Section 1.11, "Curved Arrows and Chemical Reactions," introduces students to the notational system employed in all of the mechanistic discussions in the text.

Numerous reaction mechanisms are accompanied by potential energy diagrams. Section 4.9, "Potential Energy Diagrams for Multistep Reactions: The S_N1 Mechanism," shows how the potential energy diagrams for three elementary steps are combined to give the diagram for the overall reaction.

MECHANISM 6.5

Acid-Catalyzed Hydration of 2-Methylpropene

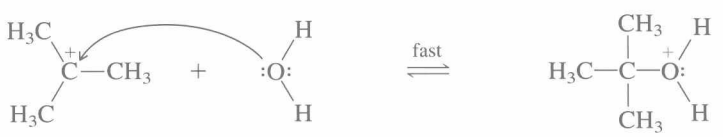
The overall reaction:



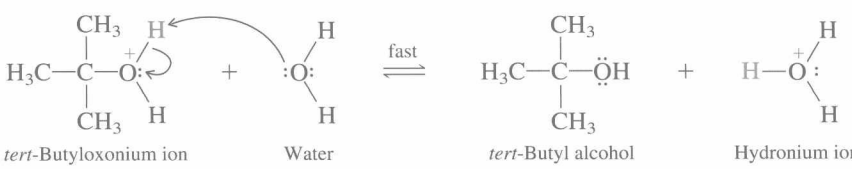
The mechanism:

STEP 1: Protonation of the carbon–carbon double bond in the direction that leads to more stable carbocation:

STEP 2: Water acts as a nucleophile to capture *tert*-butyl cation:

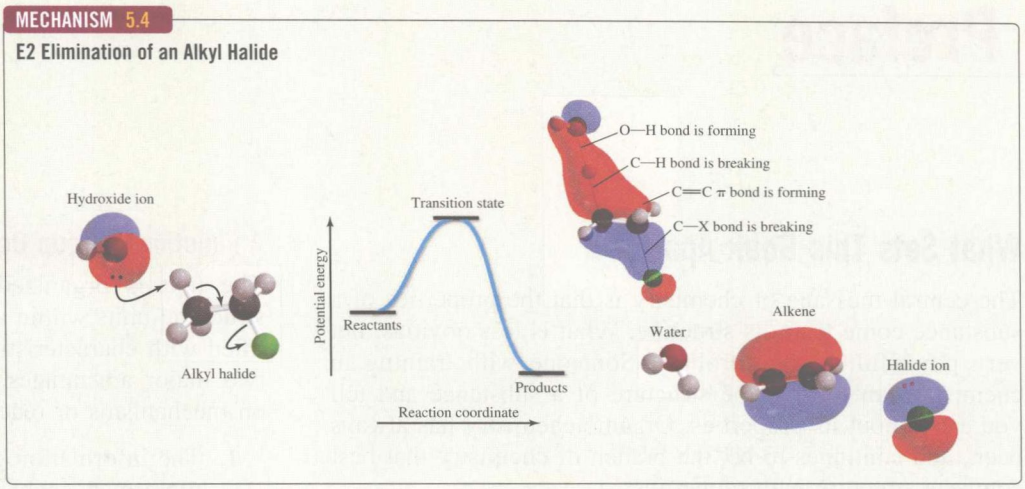


STEP 3: Deprotonation of *tert*-butyloxonium ion. Water acts as a Brønsted base:



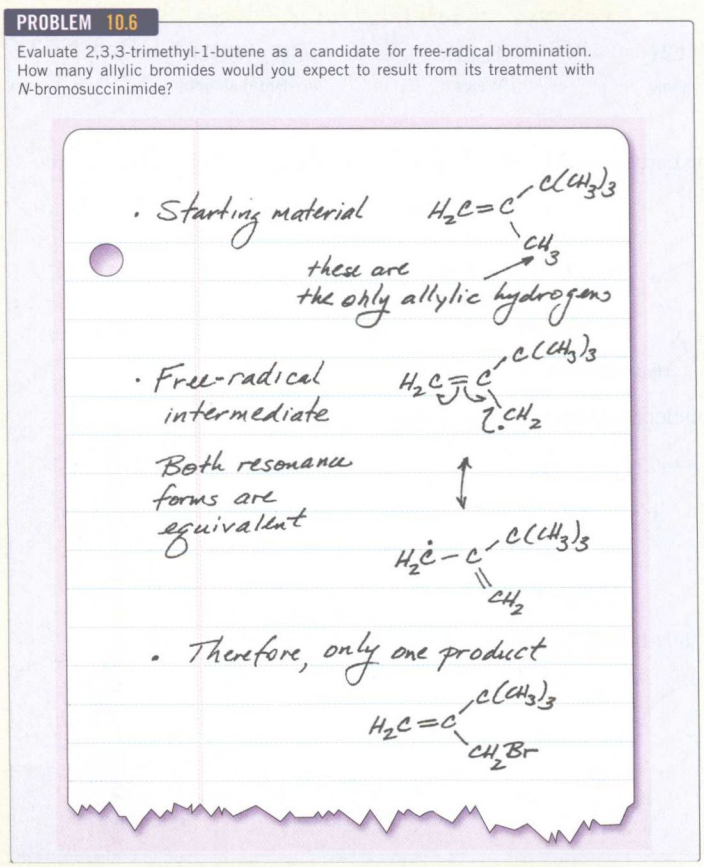
Enhanced Graphics

The teaching of organic chemistry has especially benefited as powerful modeling and graphics software have become routinely available. For example, computer-generated molecular models and electrostatic potential maps were integrated into the third edition of this text, and their number has increased with each succeeding edition. Also seeing increasing use are graphically correct representations of orbitals and the role of orbital interactions in chemical reactivity. The E2 mechanism of elimination, which involves a single elementary step, is supplemented by showing the orbital interactions that occur during that step.



Problems

Problem-solving strategies and skills are emphasized throughout. Understanding is progressively reinforced by problems that appear within topic sections. For many problems, sample solutions are given, including an increased number of examples of handwritten solutions from the author.



Generous and Effective Use of Tables

The relative reactivity of different compounds is pertinent to both the theory and practice of organic chemistry. While it is helpful—and even important—to know that one compound is more reactive than another, it is even better to know by how much. Our text provides more experimental information of this type than is customary. Chapter 8, "Nucleophilic Substitution," for example, contains seven tables of *quantitative* relative rate data, of which the following is but one example.

TABLE 8.2 Reactivity of Some Alkyl Bromides Toward Substitution by the S_N2 Mechanism*

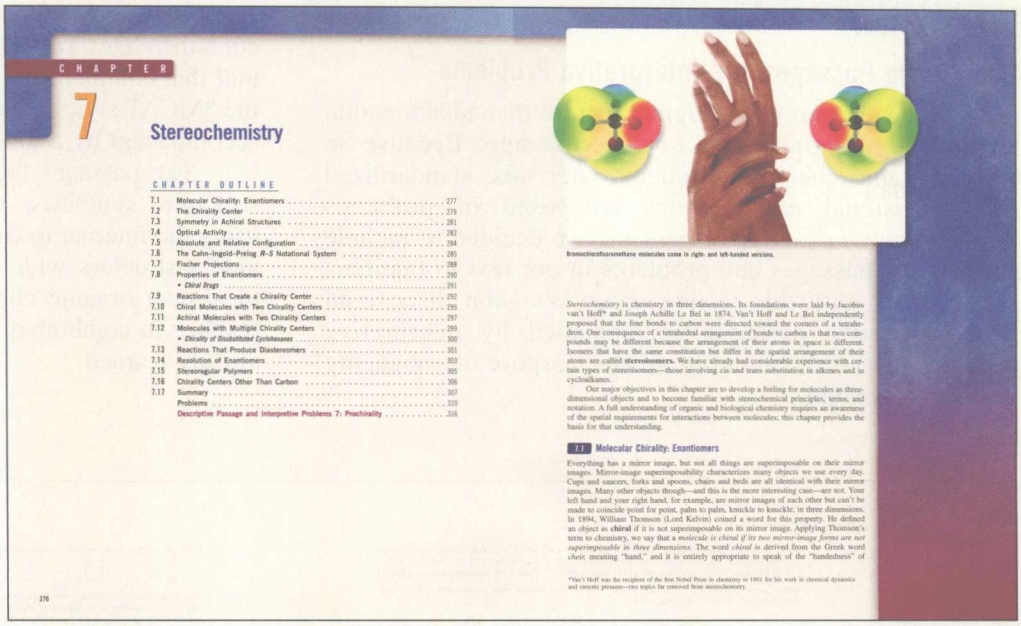
Alkyl bromide	Structure	Class	Relative rate†
Methyl bromide	CH_3Br	Unsubstituted	221,000
Ethyl bromide	CH_3CH_2Br	Primary	1,350
Isopropyl bromide	$(CH_3)_2CHBr$	Secondary	1
tert-Butyl bromide	$(CH_3)_3CBr$	Tertiary	Too small to measure

*Substitution of bromide by lithium iodide in acetone.
†Ratio of second-order rate constant k for indicated alkyl bromide to k for isopropyl bromide at 25°C.

Annotated summary tables have been a staple of *Organic Chemistry* since the first edition. Some tables review reactions from earlier chapters, others review reactions or concepts of a current chapter, and still others walk the reader step-by-step through skill builders and concepts unique to organic chemistry. Well received by students and faculty alike, these summary tables remain one of the text's strengths.

Pedagogy

- A list of mechanisms, tables, boxed essays and Descriptive Passages and Interpretive Problems is included in the front matter (page xix) as a quick reference to these important learning tools in each chapter.
- Each chapter opens with a list of section headings, boxed essays, reaction mechanisms, and Descriptive Passages and Interpretive Problems along with their corresponding page numbers.
- Summary tables allow the student easy access to a wealth of information in an easy-to-use format while reviewing information from previous chapters.
- End-of-chapter summaries highlight and consolidate all of the important concepts and reactions within a chapter.



CHAPTER 7

Stereochemistry

CHAPTER OUTLINE

Bromochlorofluoromethane molecules come in right- and left-handed versions.

Stereochemistry is chemistry in three dimensions. Its foundations were laid by Jacobus van't Hoff* and Joseph Achille Le Bel in 1874. Van't Hoff and Le Bel independently proposed that the four bonds to carbon were directed toward the corners of a tetrahedron. One consequence of a tetrahedral arrangement of bonds to carbon is that two compounds may be different because the arrangement of their atoms in space is different. Isomers that have the same constitution but differ in the spatial arrangement of their atoms are called **stereoisomers.** We have already had considerable experience with certain types of stereoisomers—those involving cis and trans substitution in alkenes and in cycloalkanes.

Our major objectives in this chapter are to develop a feeling for molecules as three-dimensional objects and to become familiar with stereochemical principles, terms, and notation. A full understanding of organic and biological chemistry requires an awareness of the spatial requirements for interactions between molecules; this chapter provides the basis for that understanding.

7.1 Molecular Chirality: Enantiomers

Everything has a mirror image, but not all things are superimposable on their mirror images. Mirror-image superimposability characterizes many objects we use every day. Cups and saucers, forks and spoons, chairs and beds are all identical with their mirror images. Many other objects though—and this is the more interesting case—are not. Your left hand and your right hand, for example, are mirror images of each other but can't be made to coincide point for point, palm to palm, knuckle to knuckle, in three dimensions. In 1894, William Thomson (Lord Kelvin) coined a word for this property. He defined an object as **chiral** if it is not superimposable on its mirror image. Applying Thomson's term to chemistry, we say that a *molecule is chiral if its two mirror-image forms are not superimposable in three dimensions.* The word *chiral* is derived from the Greek word *cheir,* meaning "hand," and it is entirely appropriate to speak of the "handedness" of

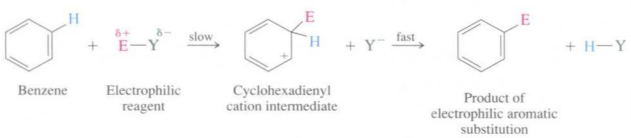
*Van't Hoff was the recipient of the first Nobel Prize in chemistry in 1901 for his work in chemical dynamics and osmotic pressure—two topics far removed from stereochemistry.

276

12.19 SUMMARY

Section 12.1 On reaction with electrophilic reagents, compounds that contain a benzene ring undergo **electrophilic aromatic substitution.** Table 12.1 in Section 12.1 and Table 12.3 in this summary give examples.

Section 12.2 The mechanism of electrophilic aromatic substitution involves two stages: bonding of the electrophile by the π electrons of the ring (slow, rate-determining), followed by rapid loss of a proton to restore the aromaticity of the ring.

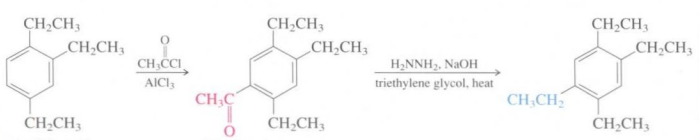


Benzene | Electrophilic reagent | Cyclohexadienyl cation intermediate | Product of electrophilic aromatic substitution

Sections 12.3–12.5 See Table 12.3

Sections 12.6–12.7 See Tables 12.3 and 12.4.

Section 12.8 Friedel–Crafts acylation, followed by Clemmensen or Wolff–Kishner reduction is a standard sequence used to introduce a primary alkyl group onto an aromatic ring.



1,2,4-Triethylbenzene | 2,4,5-Triethylacetophenone (80%) | 1,2,4,5-Tetraethylbenzene (73%)

Audience

Organic Chemistry is designed to meet the needs of the "mainstream" two-semester undergraduate organic chemistry course. From the beginning and with each new edition, we have remained grounded in some fundamental notions. These include important issues about our intended audience. Is the topic appropriate for them with respect to their interests, aspirations, and experience? Just as important is the need to present an accurate picture of the present state of organic chemistry. How do we know what we know? What makes organic chemistry worth knowing? Where are we now? Where are we headed?

Even the art that opens each chapter in this edition has been designed with the audience in mind. The electrostatic potential maps that have opened the chapters through several editions have been joined by a graphic of a familiar object that connects the map to the chapter's content. Chapter 8, for example, opens by illustrating the umbrella-in-a-windstorm analogy used by virtually everyone who has ever taught nucleophilic substitution.

This electrostatic potential map is of the transition state for the reaction of hydroxide ion with chloromethane. The tetrahedral arrangement of bonds inverts like an umbrella in a storm during the reaction.

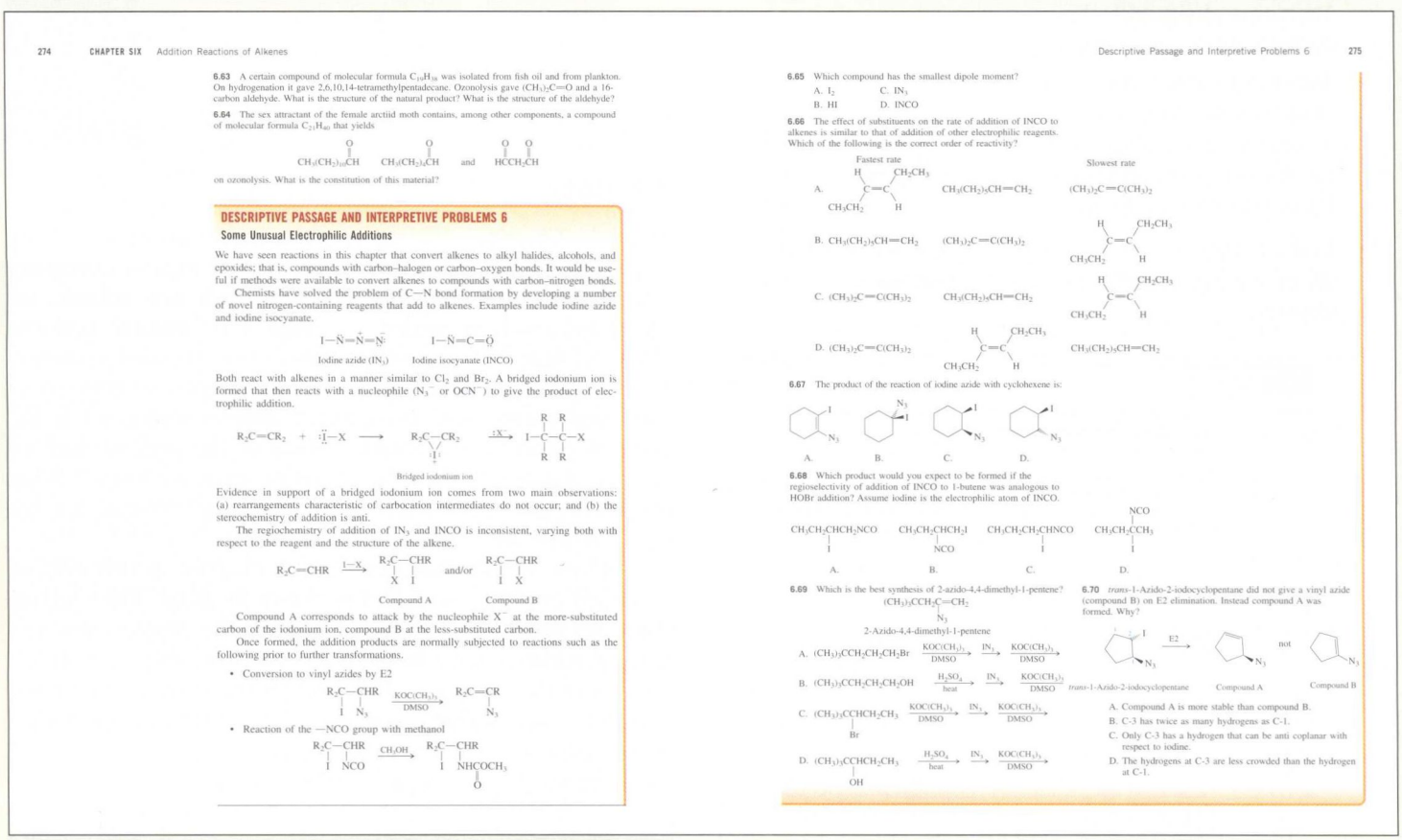
What's New?

Descriptive Passages and Interpretive Problems

New to this edition is an original feature that adds breadth, flexibility, and timeliness to our coverage. Because so many organic chemistry students later take standardized pre-professional examinations composed of problems derived from a descriptive passage, we decided to include comparable passages and problems in our text to familiarize students with this testing style. We soon discovered that descriptive passages accompanied by interpretive problems can serve the even greater purpose of enhancing this text's content.

Thus, *every* chapter now concludes with a self-contained *Descriptive Passage and Interpretive Problems* unit that complements the chapter's content while emulating the "MCAT style." These 29 passages (listed on p. xxiii) are accompanied by a total of 179 multiple-choice problems.

The passages focus on a wide range of topics—from structure, synthesis, mechanism, and natural products to using the Internet to calculate ^{13}C chemical shifts. They provide instructors with numerous opportunities to customize their own organic chemistry course while giving students practice in combining new information with what they have already learned.



274 CHAPTER SIX Addition Reactions of Alkenes

6.63 A certain compound of molecular formula $C_{19}H_{38}$ was isolated from fish oil and from plankton. On hydrogenation it gave 2,6,10,14-tetramethylpentadecane. Ozonolysis gave $(CH_3)_2C{=}O$ and a 16-carbon aldehyde. What is the structure of the natural product? What is the structure of the aldehyde?

6.64 The sex attractant of the female arctiid moth contains, among other components, a compound of molecular formula $C_{21}H_{40}$ that yields

$CH_3(CH_2)_{10}CH$ $CH_3(CH_2)_{13}CH$ and $HCCH_2CH$

on ozonolysis. What is the constitution of this material?

DESCRIPTIVE PASSAGE AND INTERPRETIVE PROBLEMS 6

Some Unusual Electrophilic Additions

We have seen reactions in this chapter that convert alkenes to alkyl halides, alcohols, and epoxides; that is, compounds with carbon–halogen or carbon–oxygen bonds. It would be useful if methods were available to convert alkenes to compounds with carbon–nitrogen bonds.

Chemists have solved the problem of C—N bond formation by developing a number of novel nitrogen-containing reagents that add to alkenes. Examples include iodine azide and iodine isocyanate.

Iodine azide (IN_3) Iodine isocyanate (INCO)

Both react with alkenes in a manner similar to Cl_2 and Br_2. A bridged iodonium ion is formed that then reacts with a nucleophile (N_3^- or OCN^-) to give the product of electrophilic addition.

Bridged iodonium ion

Evidence in support of a bridged iodonium ion comes from two main observations: (a) rearrangements characteristic of carbocation intermediates do not occur; and (b) the stereochemistry of addition is anti.

The regiochemistry of addition of IN_3 and INCO is inconsistent, varying both with respect to the reagent and the structure of the alkene.

Compound A Compound B

Compound A corresponds to attack by the nucleophile X^- at the more-substituted carbon of the iodonium ion, compound B at the less-substituted carbon.

Once formed, the addition products are normally subjected to reactions such as the following prior to further transformations.

- Conversion to vinyl azides by E2
- Reaction of the —NCO group with methanol

Descriptive Passage and Interpretive Problems 6 275

6.65 Which compound has the smallest dipole moment?

A. I_2 C. IN_3
B. HI D. INCO

6.66 The effect of substituents on the rate of addition of INCO to alkenes is similar to that of addition of other electrophilic reagents. Which of the following is the correct order of reactivity?

Fastest rate Slowest rate

A. $CH_3(CH_2)_5CH{=}CH_2$ $(CH_3)_2C{=}C(CH_3)_2$

B. $CH_3(CH_2)_5CH{=}CH_2$ $(CH_3)_2C{=}C(CH_3)_2$

C. $(CH_3)_2C{=}C(CH_3)_2$ $CH_3(CH_2)_5CH{=}CH_2$

D. $(CH_3)_2C{=}C(CH_3)_2$ $CH_3(CH_2)_5CH{=}CH_2$

6.67 The product of the reaction of iodine azide with cyclohexene is:

A. B. C. D.

6.68 Which product would you expect to be formed if the regioselectivity of addition of INCO to 1-butene was analogous to HOBr addition? Assume iodine is the electrophilic atom of INCO.

A. B. C. D.

6.69 Which is the best synthesis of 2-azido-4,4-dimethyl-1-pentene?

2-Azido-4,4-dimethyl-1-pentene

6.70 *trans*-1-Azido-2-iodocyclopentane did not give a vinyl azide (compound B) on E2 elimination. Instead compound A was formed. Why?

trans-1-Azido-2-iodocyclopentane Compound A Compound B

A. Compound A is more stable than compound B.
B. C-3 has twice as many hydrogens as C-1.
C. Only C-3 has a hydrogen that can be anti coplanar with respect to iodine.
D. The hydrogens at C-3 are less crowded than the hydrogen at C-1.

Boxed Essays: Revised and New

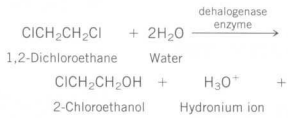
- *What's in a Name? Organic Nomenclature* describes the evolution of organic nomenclature and compares the 1979, 1993, and 2004 IUPAC recommendations for naming organic compounds.
- *β-Lactam Antibiotics* expands the familiar penicillin story beyond its discovery to include its large-scale development as a lifesaving drug during World War II and its mode of action.
- *Peptide Mapping and MALDI Mass Spectrometry* illustrates the application of a cutting-edge mass spectrometric technique to peptide sequencing.

New Topics

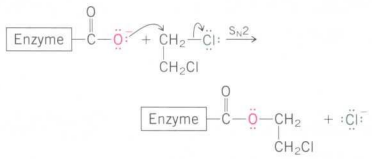
- Section 10.4: "S_N2 Reactions of Allylic Halides"
- Section 10.7: "Allylic Anions"
- Section 11.14: "S_N1 Reactions of Benzylic Halides"
- Section 11.15: "S_N2 Reactions of Benzylic Halides"

Enzyme-Catalyzed Nucleophilic Substitutions of Alkyl Halides

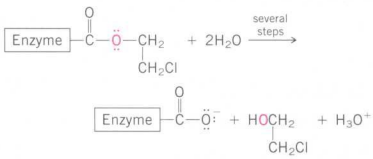
Nucleophilic substitution is one of a variety of mechanisms by which living systems detoxify halogenated organic compounds introduced into the environment. Enzymes that catalyze these reactions are known as *haloalkane dehalogenases*. The hydrolysis of 1,2-dichloroethane to 2-chloroethanol, for example, is a biological nucleophilic substitution catalyzed by the dehalogenase shown in Figure 8.4.



This haloalkane dehalogenase is believed to act by using one of its side-chain carboxylates to displace chloride by an S_N2 mechanism. (Recall the reaction of carboxylate ions with alkyl halides from Table 8.1.)

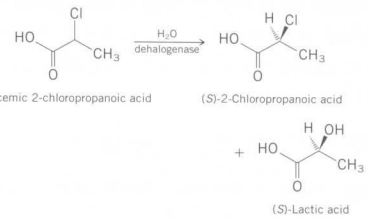


The product of nucleophilic substitution then reacts with water, restoring the enzyme to its original state and giving the observed products of the reaction.



This stage of the reaction proceeds by a mechanism that will be discussed in Chapter 20. Both stages are faster than the reaction of 1,2-dichloroethane with water in the absence of the enzyme.

Enzyme-catalyzed hydrolysis of racemic 2-chloropropanoic acid is a key step in the large-scale preparation of (*S*)-2-chloropropanoic acid used for the preparation of agricultural chemicals.



In this enzymatic resolution (Section 7.14), the dehalogenase enzyme catalyzes the hydrolysis of the *R*-enantiomer of 2-chloropropanoic acid to (*S*)-lactic acid. The desired (*S*)-2-chloropropanoic acid is unaffected and recovered in a nearly enantiomerically pure state.

Some of the most common biological S_N2 reactions involve attack at methyl groups, especially a methyl group of *S-adenosylmethionine*. Examples of these will be given in Chapter 16.

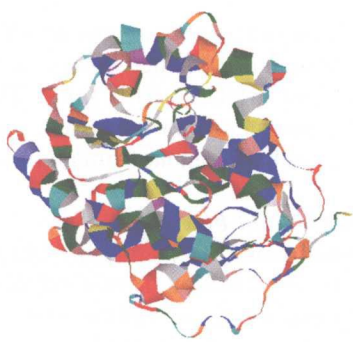
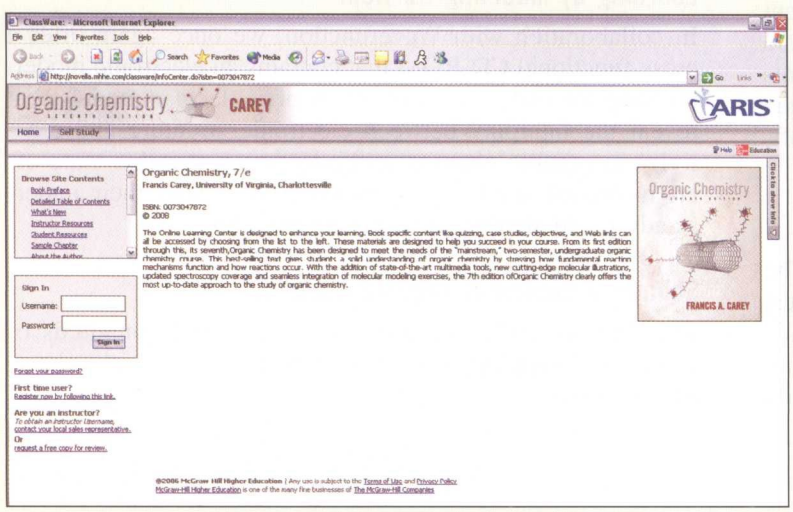


FIGURE 8.4
A ribbon diagram of the dehalogenase enzyme that catalyzes the hydrolysis of 1,2-dichloroethane. The progression of amino acids along the chain is indicated by a color change. The nucleophilic carboxylate group is near the center of the diagram.

Major Revisions

- Sections 13.20–13.22 are a complete rewrite of infrared (IR) spectroscopy. All of the IR spectra displayed in the text are new and were recorded by Thomas Gallaher of James Madison University using the attenuated total reflectance (ATR) method.
- Section 25.8 "Mutarotation and the Anomeric Effect" revises the previous discussion of mutarotation to include the now-generally accepted molecular orbital explanation for the anomeric effect.



Instructor Resources

McGraw-Hill's ARIS

The Assessment, Review, and Instruction System for *Organic Chemistry* is a complete online tutorial, electronic homework, and course management system. Instructors can create and share course materials and assignments with colleagues with a few clicks of the mouse. All PowerPoint® images, PowerPoint lecture outlines, mechanism animations, assignments, quizzes, and tutorials are directly tied to text-specific materials in *Organic Chemistry*. Instructors can also edit questions and algorithms, import their own content, and create announcements and due dates for assignments. ARIS has automatic grading and reporting of easy-to-assign algorithmically generated homework, quizzing, and