

The background of the cover is a photograph of a large tree trunk with rough, peeling bark. A green fern frond is visible on the right side of the trunk. In the bottom left corner, there is a ball-and-stick molecular model of a complex organic molecule, featuring a central ring system with various substituents, including hydroxyl groups (red and white spheres) and other functional groups.

ORGANIC CHEMISTRY

Structure and Function

Fifth Edition

VOLLHARDT

SCHORE

ORGANIC CHEMISTRY

Structure and Function

FIFTH EDITION

K. PETER C. VOLLHARDT

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ABOUT THE COVER

Taxol, a brand name for the generic drug paclitaxel, emerged through years of setbacks and controversy to become, by the end of the twentieth century, the best-selling anticancer drug in the world, saving and improving the quality of countless thousands of lives. The front cover shows a model of the three-dimensional structure of the molecule, superimposed on a picture of the magnificent Pacific yew tree, from the bark of which the first samples of Taxol were isolated. During the last decade, the medicinal importance of this molecule enticed several research groups to tackle its total synthesis, applying new synthetic methodologies and strategies to assemble its complicated structure. First, in what turned out to be a veritable race, were the teams of K. C. Nicolaou at The Scripps Research Institute and the University of California, San Diego (who provided the idea for the cover picture), and R. A. Holton at Florida State University (in 1994). These syntheses were followed by those of S. J. Danishefsky (Sloan-Kettering Institute for Cancer Research and Columbia University), P. A. Wender (Stanford University), T. Mukaiyama (Science University of Tokyo), and I. Kuwajima (Tokyo Institute of Technology), each featuring its own unique approach. Synthetic strategies used to construct complex molecules are discussed in Chapter 8 and subsequently throughout the text. The biological and medicinal context of organic molecules is addressed in many Chemical Highlights, in the general text (for example p. 152 for Taxol), and in numerous problems.

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PREFACE

A User's Guide to ORGANIC CHEMISTRY Structure and Function

In this edition of *Organic Chemistry: Structure and Function*, we maintain our goal of helping students organize all the information presented in the course and fit it into a logical framework for understanding contemporary organic chemistry. This framework emphasizes that the structure of an organic molecule determines how that molecule functions in a chemical reaction. By understanding the connection between structure and function, we can learn to solve practical problems in organic chemistry. In the fifth edition, we have strengthened the themes of understanding reactivity, mechanisms, and synthetic analysis to apply chemical concepts to realistic situations. We incorporated new applications of organic chemistry in the life sciences, industrial practices, and environmental monitoring and clean-up. This edition includes more than 100 new or substantially revised problems, including new problems on synthesis and green chemistry, and new “challenging” problems. For the first time, we are offering *Organic Chemistry: Structure and Function* in an online version to give students cost-effective access to all content from the text plus all student media resources. For more information, please visit our Web site at <http://ebooks.bfwpub.com>.

ACCESSIBLE FOR STUDENTS

Review and Extension of General Chemistry Concepts

The first five chapters of the book focus on the general principles of bonding, reactivity, and stereochemistry that enable students to understand the connections between structure and function. Chapter 1 reviews the fundamentals of how structure affects bonding, laying the groundwork for later study of functional groups. Chapter 2 discusses the basics of polar reactions, comparing the properties of acids and bases with those of nucleophiles and electrophiles, while also presenting initial ideas of reaction kinetics and thermodynamics.

2-1 Kinetics and Thermodynamics of Simple Chemical Processes

The simplest chemical reactions may be described as equilibration between two distinct species. Such processes are governed by two fundamental considerations:

1. **Chemical thermodynamics**, which deals with the changes in energy that take place when processes such as chemical reactions occur. Thermodynamics controls the *extent* to which a reaction goes to completion.
2. **Chemical kinetics**, which concerns the velocity or rate at which the concentrations of reactants and products change. In other words, kinetics describes the *speed* at which a reaction goes to completion.

Developing the Basic Tools for Understanding Function

An overview of the major functional groups of organic chemistry appears in Chapter 2. Chapter 2 also describes the nonreactive backbone of common organic molecules, as shown by the properties and behavior of the alkanes. Chapter 3 introduces the idea of bond-dissociation energies, illustrated by the radical halogenation of alkanes. Chapter 4 presents the first cyclic molecules—the cycloalkanes. In Chapter 5 we cover stereochemistry to prepare students for learning the mechanisms of substitution and elimination reactions of haloalkanes (Chapters 6 and 7) and the addition reactions of alkenes (Chapter 12).

Help in Seeing the Big Picture

Students must learn so many facts about the structures and functions of the various families of organic compounds that it is easy for them to lose sight of the most important concepts in the course. We include short **summaries** at the ends of most sections in the book, emphasizing the main ideas for students to remember. These have been revised in the new edition to better reflect the distinction between typical chemical behavior and important exceptions.

IN SUMMARY The various hydrogen atoms present in an organic molecule can be recognized by their characteristic NMR peaks at certain chemical shifts, δ . An electron-poor environment is deshielded and leads to low-field (high- δ) absorptions, whereas an electron-rich environment results in shielded or high-field peaks. The chemical shift δ is measured in parts per million by dividing the difference in hertz between the measured resonance and that of the internal standard, tetramethylsilane, $(\text{CH}_3)_4\text{Si}$, by the spectrometer frequency in megahertz. The NMR spectra for the OH groups of alcohols, the SH groups of thiols, and the NH_2 (NHR) groups of amines exhibit characteristically broad peaks with concentration- and moisture-dependent δ values.

THE BIG PICTURE

Alkanes lack functional groups, so they do not undergo the kinds of electrophile-nucleophile reactions typical of functionalized molecules. In fact, alkanes are pretty unreactive. However, under appropriate conditions, they undergo homolytic bond cleavage to form radicals, which are reactive species containing odd numbers of electrons. This is another situation in which the *structure* of a class of compounds determines their *function*. Unlike heterolytic processes, which normally proceed via movement of *pairs* of electrons to form or break bonds, homolytic chemistry utilizes the splitting of covalent bonds to give unpaired *single* electrons, as well as their combination to give new bonds.

In organic chemistry, radical reactions are not encountered as frequently as those of polar functional groups. However, radicals play prominent roles in biological, environmental, and industrial chemistry.

The halogenation of alkanes, a radical process in which hydrogen is replaced by halogen, forms the haloalkane functional group. Examination of halogenation allows us to learn about several features common to most transformations, including the way information about a reaction mechanism may be obtained from experimental observations, the relationship between thermodynamics and kinetics, and notions of reactivity and selectivity. The products of halogenation, the haloalkanes, are the starting compounds for a wide variety of reactions, as we will see in Chapters 6 through 9.

Before we examine other classes of compounds and their properties, we need to learn more about the structures and, in particular, the geometric shapes of organic molecules. In Chapter 4 we discuss compounds that contain atoms in rings and in Chapter 5 we study additional forms of isomerism. The ideas we introduce are a necessary background as we begin a systematic study in the chapters that follow of polar reactions of haloalkanes and alcohols.

themes stated in the chapter-opening introductions, which help set the context for the material in the chapter.

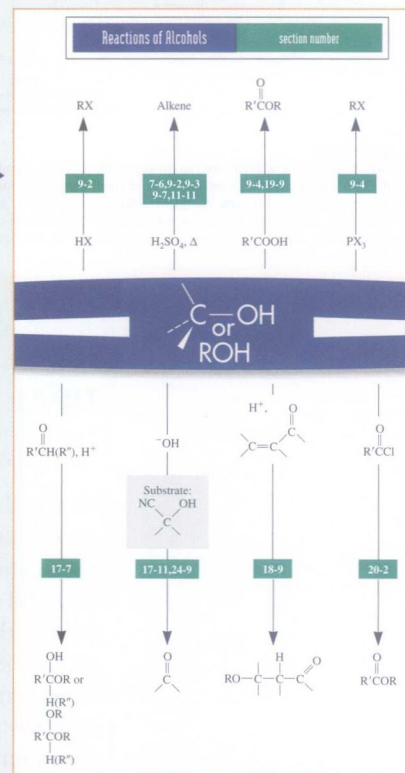
We have retained the **Reaction Summary Road Maps**, also at the ends of some chapters, which summarize the principal reactions for preparation and applications of each major functional group. The **Preparation maps** indicate the possible origins of a functionality—that is, the precursor functional groups. The **Reaction maps** show what each functional group does. In both maps, reaction arrows are labeled with particular reagents and start from or end at specific reactants or products. The reaction arrows are also labeled with new section numbers indicating where the transformation is discussed in the new edition.

STRONGER PEDAGOGY FOR SOLVING PROBLEMS

Examples of Problem-Solving Approaches

We include worked-out solutions to in-chapter exercises, called **Working with the Concepts**. These solutions emphasize the reasoning students need to apply in attacking problems, arranging the steps logically and carefully so students can see potential pitfalls and avoid

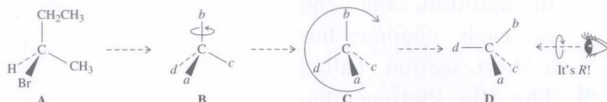
In addition, the end of each chapter has a short section, called **The Big Picture**, that reinforces the connections between topics within chapters and between chapters, and fits the material into the overall presentation of the course. These sections are not summaries, but serve to indicate where we've been and where we're going. They have been revised in this edition to better reinforce the



EXERCISE 5-9

Assign the absolute configuration of the molecules depicted in Table 5-1.

WORKING WITH THE CONCEPTS Let us look at (–)-2-bromobutane, reproduced in the arrangement (labeled A) in which it appears in Table 5-1. Remember that the fact that this enantiomer is levorotatory does not tell you its absolute configuration; it could be *R* or *S*. To establish which one it is, we focus on the stereocenter and arrange the molecule in space in such a way that the substituent with the lowest priority is pointing away from the observer. Therefore, the first task is to assign priorities: Br is *a*, CH₂CH₃ is *b*, CH₃ is *c*, and H is *d*, as depicted in structure B. The second task, arranging the molecule in space as required, is more difficult at first, but becomes easier with practice. A safe approach is that described in Figure 5-6, in which we move the tetrahedral frame such as to place the C–*d* bond in the plane of the page pointing to the left and imagine us looking down this axis from the right, as in D. For structure B, this procedure means rotating the carbon atom (to move the C–*d* bond into the plane of the page) to reach C and then the entire molecule (clockwise) to reach D. Looking at D from the right as shown reveals the absolute configuration: *R*. As you do more of these assignments, you will become increasingly adept at “seeing” the molecule in three dimensions and placing your “eye” appropriately such that the trio *a*, *b*, *c* is pointing toward you, group *d* away from you.



them. The exercises chosen for solution are typical homework or test problems, enabling students to acquire a feel for solving complex problems, rather than artificially simplified situations. In response to strong positive feedback on this feature, we have increased the number of these solutions by about 50 percent in the book overall.

A Wide Variety of Problem Types

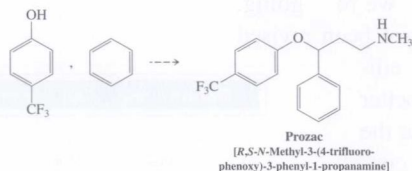
Users and reviewers of past editions have often cited the end-of-chapter problems as a major strength of the book, both for the range of difficulty levels and the variety of practical applications. In this edition, we have highlighted those end-of-chapter problems that are more

difficult with a special **CHALLENGE** icon.

- The **Chapter Integration Problems** include worked-out step-by-step solutions to problems involving several concepts from within chapters and from among several chapters. These solutions place particular emphasis on problem analysis, deductive reasoning, and logical conclusions.

Chapter Integration Problems

21-22. On the basis of the synthetic methods for amines provided in this chapter, carry out retrosynthetic analyses of Prozac, with 4-trifluoromethylphenol and benzene as your starting materials.



SOLUTION:

As for any synthetic problem, you can envisage many possible solutions. However, the constraints of given starting materials, convergence, and practicality rapidly narrow the number of available options. Thus, it is clear that the 4-trifluoromethylphenoxy group is best introduced by Williamson ether synthesis (Section 9-6) with an appropriate benzylic halide, compound A (Section 22-1), with the use of our first starting compound, 4-trifluoromethylphenol.

(continued)

- **Team Problems** encourage discussion and collaborative learning among students. They can be assigned as regular homework or as projects for groups of students to work on.
- For students planning careers in medicine or related fields, **Preprofessional Problems** offer a multiple-choice format typical of problems on the MCAT®, GRE, and DAT. In addition, a selection of actual test passages and questions from past MCAT® exams appears in an appendix.

REAL CHEMISTRY BY PRACTICING CHEMISTS

An Emphasis on Practical Applications

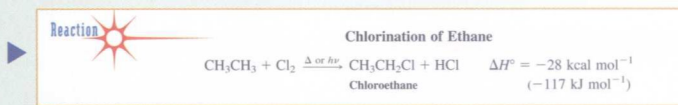
Every chapter of this text features discussions of biological, medical, and industrial applications of organic chemistry, many of them new to this edition. Some of these applications are found in the text discussion, others in the exercises and problems, and still others in the **Chemical Highlight** boxes. Topics range from the chemistry behind the effects on human health of “compounds in the news” (cholesterol, trans fatty acids, grape seed extracts, green tea), to the role played by chemistry in the development of the fields of modern biology and medicine, to DNA fingerprinting and how it works. Updated applications include advances in the development of “green,” environmentally friendly methods in the chemical industry, new chemically-based

methods of disease diagnosis and treatment, and uses of transition metals and enzymes to catalyze reactions in pharmaceutical and medicinal chemistry, including brief introductions to alkene metathesis and metal-catalyzed coupling reactions (Heck, Stille, Suzuki, and Sonogashira).

A major application of organic chemistry, stressed throughout the text, is the synthesis of new products and materials. We emphasize the development of good synthetic strategies and the avoidance of pitfalls, illustrating these ideas with many Working with the Concepts and Integration Problems. Many chapters contain specific syntheses of biological and medicinal importance.

Early Introduction of Reactions

The payoff for learning how structure affects function comes in understanding organic reactions. In Chapter 2 we emphasize how structure affects function in polar reactions, stressing their importance throughout the course. However, as in previous editions, the first reaction we discuss in detail is the radical halogenation of methane, presented in Chapter 3. This order enables us to introduce the concepts of bond-dissociation energy and the stability of radicals in the context of the simplest organic bonds, C—H and C—C. Because the halogenation of methane does not include ionic species, we can analyze the overall process, as well as the individual steps, from the point of view of thermodynamics and potential energy diagrams, giving students new tools for judging the feasibility of all future transformations. Finally, our choice of the lead reaction permits us to generalize to issues of reactivity and selectivity, providing students with a model for how to deal with molecules containing several equally reactive sites. Icons in the page margins highlight the location of most major reactions discussed in the text.



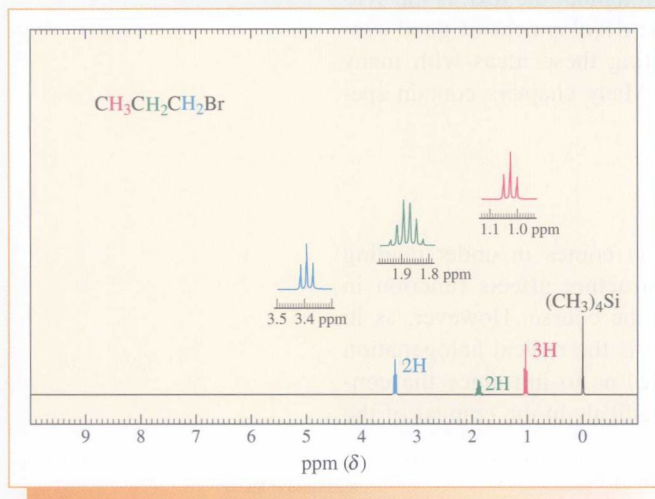
A Uniform Chapter Organization Based on Structure and Function

The structures of haloalkanes and how they determine haloalkane behavior in nucleophilic substitution and elimination reactions are the main topics of Chapters 6 and 7. Subsequent chapters present material on functional-group compounds according to the same scheme introduced for haloalkanes: nomenclature, structure, spectroscopy, preparations, reactions, and biological and other applications. The emphasis on structure and function allows us to discuss the mechanisms of all new important reactions concurrently, rather than scattered throughout the text. We believe this unified presentation of mechanisms benefits students enormously.

We treat alcohols early (Chapters 8 and 9) because understanding their chemistry leads to appreciating their central role in synthesis. Similarly, we present carbocations (and their rearrangements; see Section 9-3) before the Markovnikov rule (Chapter 12); alkenes (Chapter 12) before conjugated polyenes (Chapter 14); and conjugated polyenes before aromatic systems (Chapter 15). The coverage of spectroscopy in the first half of the text (Chapters 10 and 11), after students have learned some of the basic functional groups, continues the theme of how structure affects function. This organization allows students to apply spectroscopic techniques in the context of later functional groups.

Unified Presentation of Spectroscopy

In this edition we have consolidated the presentation of NMR, IR, and mass spectroscopy into two chapters (10 and 11) toward the end of the first half of the book. At this point, students have attained some familiarity with the functional groups used to illustrate spectroscopic methods and can then learn the spectroscopic characteristics of all other types of compounds as they are introduced. As in earlier editions, we cover UV and visible spectroscopy in the context of delocalized pi systems (Chapter 14). Several discussions and problems in the second half of the book unify the application of spectroscopic techniques in structure determination.

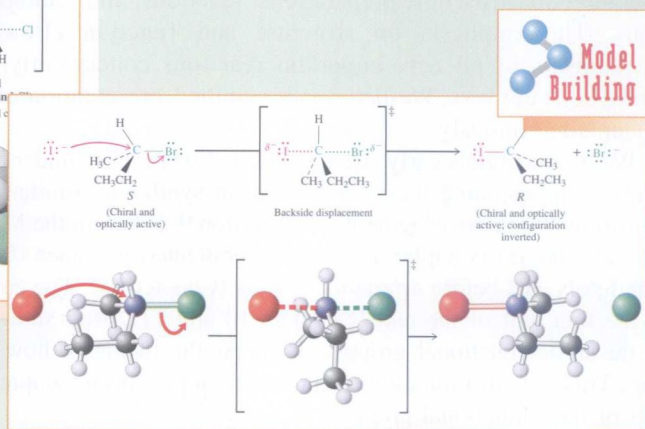
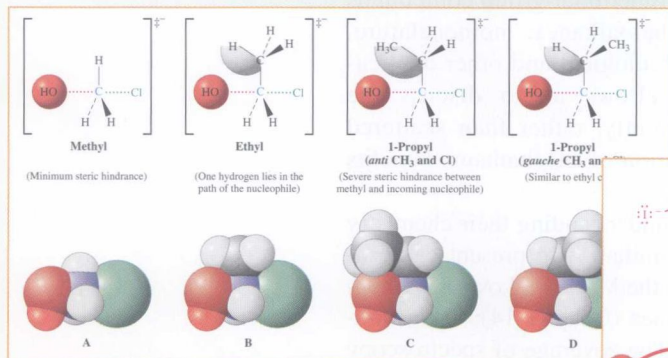
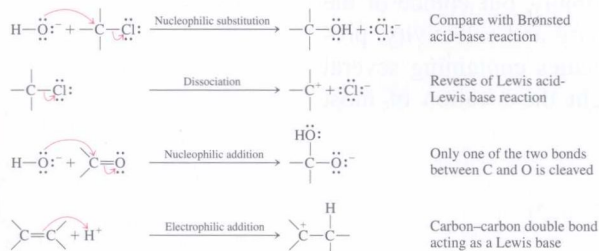


VISUALIZING ORGANIC CHEMISTRY

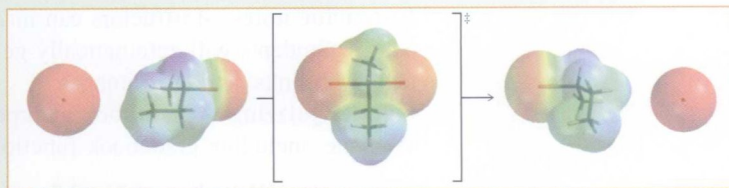
We have continued in this edition to emphasize mechanisms as a way of understanding why and how reactions occur.

- The use of electron-pushing arrows, introduced in Section 2-2, is reinforced in Section 6-3 and applied extensively in all subsequent chapters.
- Computer-generated ball-and-stick and space-filling models help students visualize steric factors in many kinds of reactions. Icons in the page margins indicate where model building by students would be especially helpful for visualizing three-dimensional structures and dynamics.

Curved-Arrow Representations of Several Common Types of Mechanisms



- Electrostatic potential maps of many species help students see how electron distributions affect the behavior of species in various interactions. Once again, we emphasize that structure determines function.



- Icons in the page margins highlight the locations of important mechanisms.



- In this edition we have included approximately 50 animated mechanisms on the W. H. Freeman Web site. All mechanisms are indicated by Media Link icons in the page margins.

- We have retained the **Interlude** following Chapter 14 for students that summarizes the relatively few types of mechanisms that drive the majority of organic reactions.

INTERLUDE

A Summary of Organic Reaction Mechanisms

Although we are only just past the halfway point in our survey of organic chemistry, with the completion of Chapter 14 we have in fact now seen examples of each of the three major classes of organic transformations: radical, polar, and pericyclic processes. This section summarizes all of the individual mechanism types that we have so far encountered in each of these reaction classes.

SUPPLEMENTS

NEW! eBook

This online version of *Organic Chemistry*, Fifth Edition, combines the text, all existing student media resources, along with additional eBook features. The eBook includes:

- Intuitive navigation** to any section or subsection, as well as any printed book page number.
- Integration of all student **animated mechanisms** and **animations**.
- In-text **self-quiz questions**.
- In-text links to all glossary **term definitions**.
- Interactive chapter **summary exercises**.
- Bookmarking, Highlighting, and Notes** features, with all activity automatically saved that allows students or instructors to add notes to any page.
- A full **glossary** and **index**, and **full-text search**, including an option to also search the glossary and/or index.

***For instructors**, the eBook also offers unparalleled flexibility and customization options including **Custom chapter selection**—students will see only chapters the instructor selects.

Instructor notes—Instructors can incorporate notes into the eBook used for their course. Students will automatically get the customized version. Notes can include text, Web links, and even images.

Online Quizzing—The eBook incorporates the online quizzing from the student Web site, including gradebook functions.

Companion Web site: www.whfreeman.com/vollhardtschore5e

Student Web site includes:

- New animations—Web-based animations allow students to view motion, three-dimensions, atomic and molecular interactions, and chemical reactions at a microscopic level. Topics focus on orbitals and hybridization.
- Animated mechanisms—Includes 13 new animated mechanisms! These animations allow students to view molecular interactions as structural formulas and as ball-and-stick models. Topics include chemical reactivity and structures and bonding.
- Nomenclature exercises—19 drag and drop exercises designed for rote memorization.
- Reaction exercises—16 drag and drop exercises designed for memorization.
- Online quizzes—Self-study quizzing helps students master organic chemistry.
- Molecule structure database—120 CHIME Molecular Models sorted by molecule type: structures mentioned in the book and depicted as three-dimensional animations with multiple-display options.
- A Tools section features electronic calculators, a graph plotter, and a dynamic Periodic Table.
- An MCAT preparation quiz.
- Interactive Periodic Table.

Instructor Web site includes:

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- Instructor Quiz Gradebook
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- Video lectures by Peter Vollhardt

Additional Instructor Supplements:

Test Bank, Kay Brummond, University of Pittsburgh

Printed 0-7167-2565-7 or CD-ROM 0-7167-6193-9

The test bank includes hundreds of multiple-choice questions. The CD version is compatible with both Windows and Mac operating systems, and allows instructors to add, edit, and resequence questions.

Enhanced Instructor's Resource CD-ROM, 0-7167-6171-8

To help instructors create lecture presentations, Web sites, and other resources, this CD-ROM allows instructors to **search** and **export** all the resources contained below by key term or chapter:

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- Animations, Animated Mechanisms, Flashcards and more
- Instructor's Manual
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Overhead Transparencies, 0-7167-6195-5

A thoroughly updated set of key figures with optimized labels for better classroom projection.

Online Course Materials (WebCT, Blackboard)

As a service for adopters, we will provide content files in the appropriate online course format, including the instructor and student resources for this text.

Additional Student Supplements:

Free Self-Study Page, 0-7167-7600-6

The laminated self-study page summarizes key points in the text. It includes concise descriptions of relevant terms and concepts, and presents reactions and mechanisms using both text and equations. Related topics are grouped together with section references to clarify difficult-to-understand ideas and to help students organize their studying.

Molecular Model Set, 0-7167-4822-3

This inexpensive kit, the best of its kind, lets students construct representations of lone pairs of electrons, radicals, double bonds, and triple bonds.

Study Guide and Solutions Manual, Neil Schore, University of California, Davis, 0-7167-6172-6

The guide includes chapter introductions that highlight new material, chapter outlines, detailed comments for each chapter section, a glossary, and solutions to the end-of-chapter problems, presented in a way that shows students how to reason their way to the answer.

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