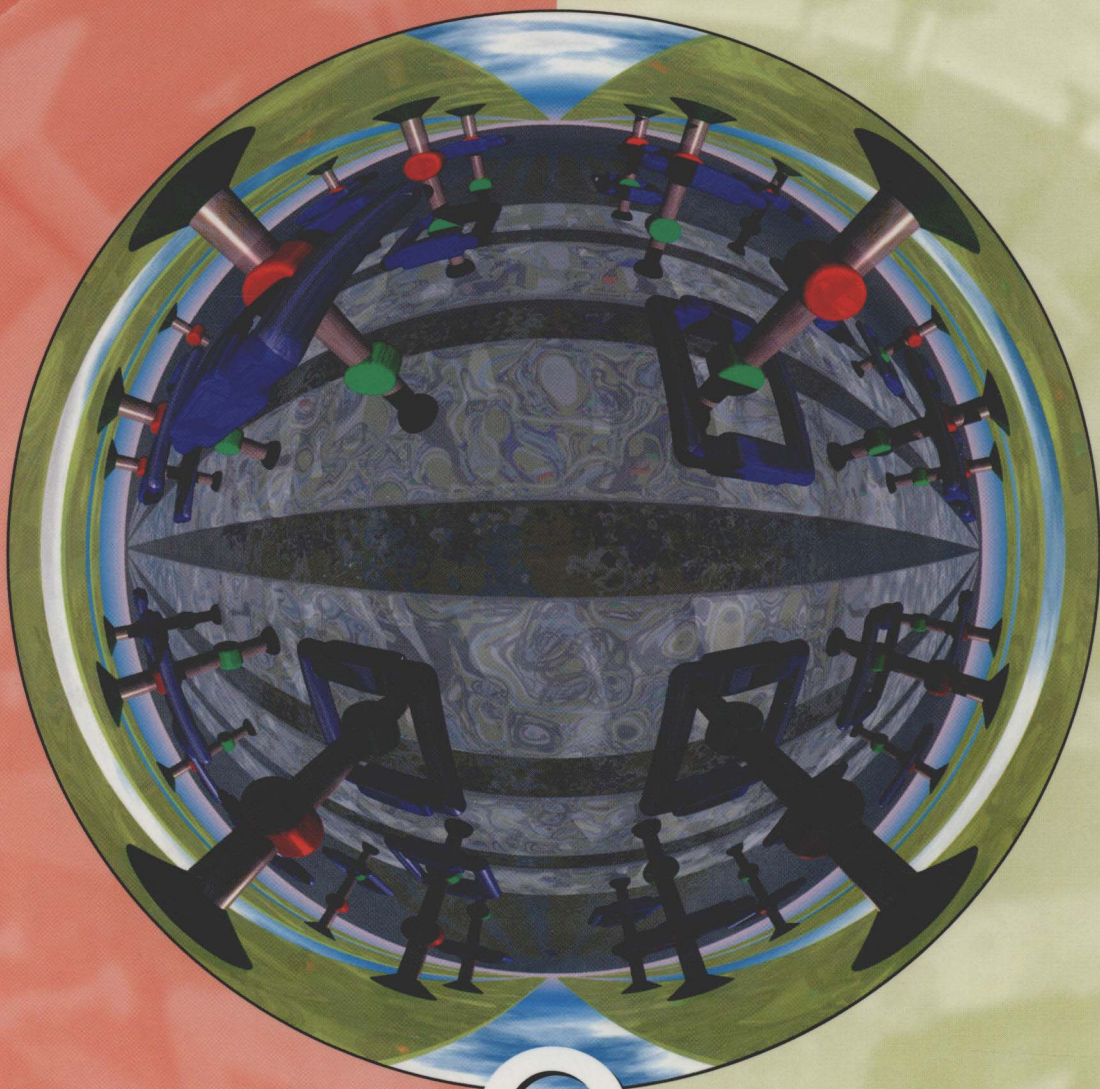




CD
Included



SOLOMONS & FRYHLE

Organic Chemistry

Eighth Edition

Organic Chemistry

Eighth Edition

T.W. Graham Solomons

University of South Florida

Craig B. Fryhle

Pacific Lutheran University



John Wiley & Sons, Inc.

***For Judith, Allen, Graham, Jennie, Guido, and Cory. TWGS
For Deanna, Lauren, and Heather. CBF***

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Cover

The cover shows a fanciful representation of nanoscale molecular switches on the surface of a droplet. Molecules such as these, called [2]rotaxanes and consisting of a cyclic molecule through which a molecular shaft is threaded (see Section 4.12), have the potential to behave like nanoscale transporters or shuttles. Changing the oxidation state of a group on the shaft leads to electrostatic forces that drive the ring along the shaft from one position to another. Research with organic molecules like these, synthesized by J. Fraser Stoddart and colleagues at UCLA, holds great promise for revolutionizing our world with new nanoscale machines and devices. Nanotechnology is indeed a burgeoning and exciting area, and it is one of the dimensions of chemistry we highlight in this edition. Image courtesy of Theresa Chang.

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This book is printed on acid-free paper. ☺

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Mechanism Review: E2 and E1 Elimination

E2 via small base

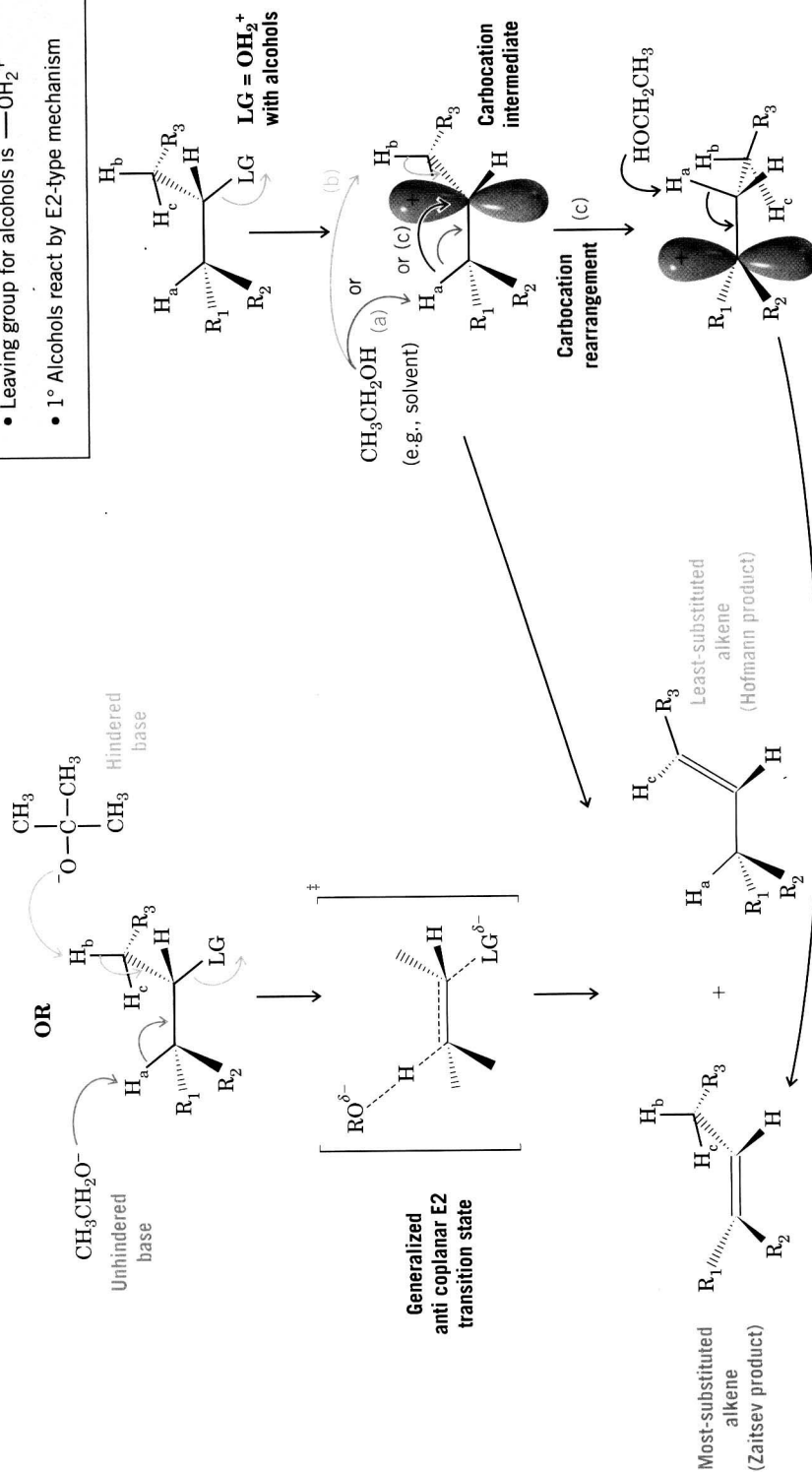
- Strong **unhindered base**,
e.g., $\text{CH}_3\text{CH}_2\text{ONa}$ (EtONa), HO^-
- Predominant formation of **most-substituted alkene** (Zaitsev product)
- Anti coplanar transition state
- Bimolecular in the rate-determining step

E2 via bulky base

- Strong **hindered** base, e.g., $(\text{CH}_3)_3\text{COK}$
- Predominant formation of **least-substituted alkene** (Hofmann product)
- Anti coplanar transition state
- Bimolecular in the rate-determining step

E1 (including Alcohol Dehydration)

- Absence of strong base (solvent is often the base)
 - Alcohols require **strong acid catalyst**
 - Carbocation formation is unimolecular rate-determining step
 - Carbocation **may rearrange**
 - Predominant formation of most substituted alkene (Zaitsev product)
 - Leaving group for alcohols is —OH_2^+
- 1° Alcohols react by E2-type mechanism



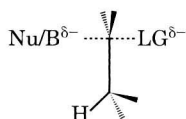
Summary and Review Tools

Mechanism Review: Substitution versus Elimination

S_N2

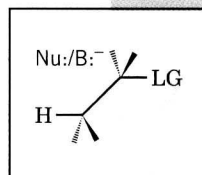
Primary substrate
Back-side attack of Nu: with respect to LG
Strong/polarizable unhindered nucleophile

Bimolecular in rate-determining step
Concerted bond forming/bond breaking
Inversion of stereochemistry
Favored by polar aprotic solvent



S_N2 and E2

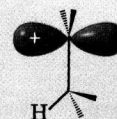
Secondary or primary substrate
Strong unhindered base/nucleophile leads to S_N2
Strong hindered base/nucleophile leads to E2
Low temperature (S_N2) / high temperature (E2)



S_N1 and E1

Tertiary substrate
Carbocation intermediate
Weak nucleophile/base (e.g., solvent)

Unimolecular in rate-determining step
Racemization if S_N1
Removal of β -hydrogen if E1
Protic solvent assists ionization of LG
Low temperature (S_N1) / high temperature (E2)



E2

Tertiary or secondary substrate
Concerted anti-coplanar TS

Bimolecular in rate-determining step
Strong hindered base
High temperature

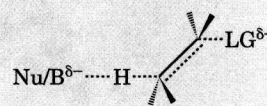
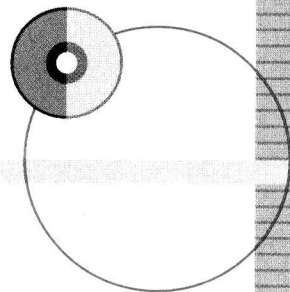


TABLE 3.1 Relative Strength of Selected Acids and Their Conjugate Bases

	Acid	Approximate pK_a	Conjugate Base	
Strongest acid	HSbF ₆	< -12	SbF ₆ ⁻	Weakest base
	HI	-10	I ⁻	
	H ₂ SO ₄	-9	HSO ₄ ⁻	
	HBr	-9	Br ⁻	
	HCl	-7	Cl ⁻	
	C ₆ H ₅ SO ₃ H	-6.5	C ₆ H ₅ SO ₃ ⁻	
	(CH ₃) ₂ OH	-3.8	(CH ₃) ₂ O	
	(CH ₃) ₂ C=OH	-2.9	(CH ₃) ₂ C=O	
	CH ₃ OH ₂ ⁺	-2.5	CH ₃ OH	
	H ₃ O ⁺	-1.74	H ₂ O	
	HNO ₃	-1.4	NO ₃ ⁻	
	CF ₃ CO ₂ H	0.18	CF ₃ CO ₂ ⁻	
	HF	3.2	F ⁻	
	CH ₃ CO ₂ H	4.75	CH ₃ CO ₂ ⁻	
	H ₂ CO ₃	6.35	HCO ₃ ⁻	
	CH ₃ COCH ₂ COCH ₃	9.0	CH ₃ COCHCOCH ₃	
	NH ₄ ⁺	9.2	NH ₃	
	C ₆ H ₅ OH	9.9	C ₆ H ₅ O ⁻	
	HCO ₃ ⁻	10.2	CO ₃ ²⁻	
	CH ₃ NH ₃ ⁺	10.6	CH ₃ NH ₂	
	H ₂ O	15.7	OH ⁻	
	CH ₃ CH ₂ OH	16	CH ₃ CH ₂ O ⁻	
	(CH ₃) ₃ COH	18	(CH ₃) ₃ CO ⁻	
	CH ₃ COCH ₃	19.2	CH ₂ COCH ₃	
	HC≡CH	25	HC≡C ⁻	
	H ₂	35	H ⁻	
	NH ₃	38	NH ₂ ⁻	
	CH ₂ =CH ₂	44	CH ₂ =CH ⁻	
Weakest acid	CH ₃ CH ₃	50	CH ₃ CH ₂ ⁻	Strongest base

OrganicView CD



The CD packaged with this text includes the following components to help students visualize and understand the basic concepts of organic chemistry.

1. CONCEPT UNITS The *OrganicView CD* contains some 50 animated 3D “Concept Units,” from the Science Teaching Graphics collection of Darrell J. Woodman (University of Washington). These are presentations, with audio, on key topics in organic chemistry where computer graphics and animation help to depict: 1) the particulate (microscopic) view of matter; 2) complex three-dimensional structure and relationships; 3) dynamic processes.

The CD accompanying the Eighth Edition includes several entirely new concept units on reaction mechanisms such as Electrophilic Aromatic Substitution, Acyl Substitution, Enolate Anions, and Epoxidation.

2. 3D MODELS A library of more than 400 3D molecular models is included on the *OrganicView CD*, linked to where the particular molecules are discussed in the text. These open automatically for student exploration, using either the well-known Chem3D® plugin or Rasmol® scientific visualization software (included by permission of the author, Roger Sayle). The software and the special model files allow the student to switch between various model types (wireframe, ball-stick, space-filling) with special color schemes and display options (backbone, strand, ribbon) for biomolecules. Of particular significance in this category are 3D versions of many new color molecular graphics in *Organic Chemistry, Eighth Edition*, based on quantum mechanical calculations with Chem3D® and Gaussian® software, prepared by Craig Fryhle. These new graphics feature accurate molecular orbital, electron density surface, and electrostatic potential displays, bringing a higher level of scientific sophistication to this edition.

3. ANIMATED GRAPHICS The *OrganicView CD* provides over 60 additional interactive, animated presentations of other specific text graphics and structures, including rotational or other 3D movies of many molecules of special interest, for example, the enzyme carbonic anhydrase, complexation by a crown ether, and many of the electrostatic potential maps shown in the book.

4. INTERACTIVE EXERCISES AND ASSESSMENT The new edition of *OrganicView* features 30 new types of interactive student exercises and sample multiple-choice questions, linked to the most important Concept Units. The interactive exercises provide students with feedback as they check their mastery of selected concepts in activities such as “guided drawing” (selected structures and reaction mechanisms) or “drag to assemble” complex structures. Many of the exercises utilize Shockwave® 3D, which enables students to manipulate complex chemical structures in 3D space.

5. DRILL/REVIEW AND MECHANISM PRACTICE Designed to help students practice the skills needed to be successful in this course, the Drill/Review units focus on remembering reagents for chemical transformations and applying the basic patterns of reactions either to predict the main product or to deduce the needed starting material.

6. IR TUTOR The popular IR Tutor software by Charles Abrams (Beloit College) is also included on the *OrganicView CD*. IR Tutor provides the student with animated tutorials on the theory and practice of infrared spectroscopy, as well as illustrative spectra of representative compounds. The illustrative spectra show both an animation and an assignment of the vibrational mode when the user clicks on a peak. Comparison overlays and tips help the student quickly develop the ability to analyze infrared spectra.

eGrade

Wiley's eGrade is web-based software that automates the process of assigning and grading homework, quizzes, and exams through a mathematically "smart" grading engine. eGrade provides professors and students with numerous benefits; it increases students' time-on-task while providing them with immediate feedback and scoring on their work.

WILEY eGrade Question Bank Editor

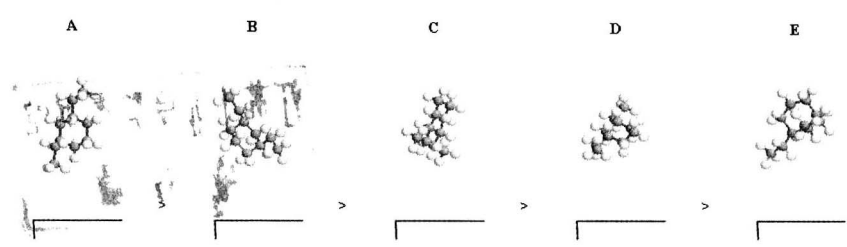
Question Bank Editor • Display Question

Back to Main Grade Edit

QUESTION NAME: 1,3-Et2cHex 3d

Within the structures below are all of the isomers of 1,3-diethylcyclohexane.
If the isomer is one of a pair of enantiomers, write "enantiomer" under it.
If the isomer is a meso compound, write "meso" under it.
If the structure is not an isomer of 1,3-diethylcyclohexane, write "na" under it.

A B C D E



1. HOMEWORK PROBLEMS Developed by K. C. Russell (Northern Kentucky University), the eGrade for Solomons/Fryhle **Organic Chemistry, Eighth Edition**, features 15–20 problems per chapter, derived from the end-of-chapter problems in the textbook. Many problems feature 3D molecules which students can manipulate as they work out answers. Each eGrade homework problem has multiple parts, each part an individual numeric response, multiple choice or fill-in-the-blank question. Most homework problems feature randomized variables, offering each student a different version of the same problem.

2. TEST BANK QUESTIONS The Solomons/Fryhle **Organic Chemistry, Eighth Edition** Test Bank material is also available in eGrade, allowing for online testing and quizzing opportunities. Instructors making use of both homework and Test Bank question files will be able to take full advantage of eGrade's robust gradebook and assignment management capabilities.

Preface

The goal of our book is to bring organic chemistry to students in the most interesting and comprehensible way possible. We believe that the Eighth Edition offers our strongest pedagogy yet for achieving these goals. The text includes many visual tools for learning, including Concept Maps, details of reaction mechanisms and thematic Mechanism Review summaries, Synthetic Connections, study tips and tool box notations, enlightening illustrations, and abundant problems. We have included chapter opening vignettes and “The Chemistry of...” boxes to help students relate organic chemistry to everyday life. The CD packaged with the text is rich with opportunities for students to review and practice the concepts of organic chemistry. Students who use the in-text learning aids, work the problems, regularly employ resources on the CD, and use the supplementary modeling kit, will be assured of success in organic chemistry.

ORGANIZATION

A central theme of our approach to organic chemistry is to emphasize the *relationship between structure and reactivity*. To accomplish this, we have chosen an organization that combines the most useful features of the traditional functional group approach with one based on reaction mechanisms. Our philosophy is to emphasize mechanisms and their common aspects as often as possible, and at the same time to use the unifying features of functional groups as the basis for most chapters. The structural aspects of our approach show students *what organic chemistry is*. Mechanistic aspects of our approach show students *how it works*. And wherever an opportunity arises, we show them *what it does* in living systems and the physical world around us.

Most important is for students to have a solid understanding of structure—of hybridization and geometry, steric hindrance, electronegativity, polarity, and formal charges—so that they can make intuitive sense of mechanisms. It is with these topics that we begin in Chapter 1. In Chapter 2 we introduce all of the important functional groups, intermolecular forces, and a key tool for identifying functional groups—infrared spectroscopy. Throughout the book we have updated our calculated models of molecular orbitals, electron density surfaces, and maps of electrostatic potential. These models enhance students’ appreciation for the role of structure in properties and reactivity.

We begin our study of mechanisms in Chapter 3 in the context of acid-base chemistry. Why? Because acid-base reactions are fundamental to organic chemistry. When looked at from the point of view of Lewis acid-base theory, the steps of most organic reaction mechanisms are acid-base reactions. Acid-base reactions, moreover, are relatively simple and they are reactions that students will find familiar. Acid-base reactions also lend themselves to an introduction of several important topics that students need to know about early in the course: (1) the curved arrow notation for illustrating mechanisms, (2) the relationship between free-energy changes and equilibrium constants, (3) how enthalpy and entropy changes affect reactions under equilibrium control, and (4) the importance of inductive and resonance effects and of solvent effects. In Chapter 3, we also begin to show students how organic chemistry works by presenting the first of many boxes called “A Mechanism for the Reaction.” All through the book, these boxes highlight and bring forth the details of important reaction mechanisms.

Throughout our study we use various opportunities to show what organic chemistry *does* in life, both in biological terms and in our physical environment, through real world applications highlighted by chapter opening vignettes and “The Chemistry of...” boxes. As students come to realize that life and much of the world around us involves organic chemistry, their fascination with the subject cannot help but increase.

KEY FEATURES OF THE EIGHTH EDITION

Some major highlights of the Eighth Edition include:

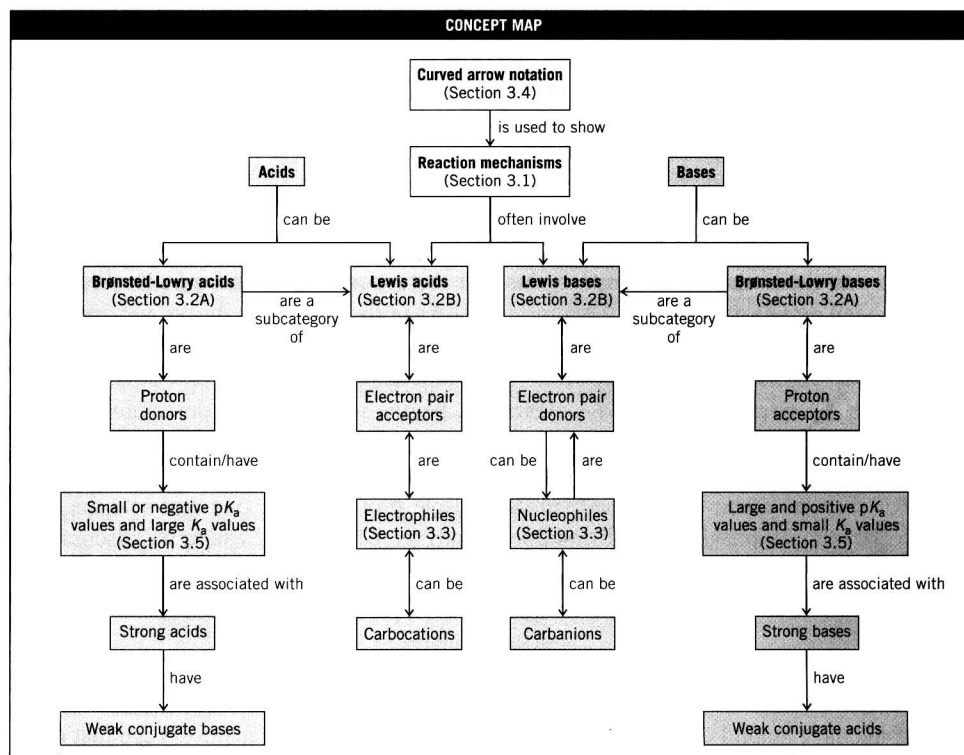
- *Concept Maps, Mechanism Reviews, and Synthetic Connections*: comprehensive new summary and review tools to enhance student learning.
- New material relating to environmentally benign (“green”) chemistry, nanotechnology, and biochemistry introduces exciting new frontiers of organic chemistry.
- All of the graphics and illustrations from the previous edition have been modernized, revised, and updated. Stylized orbital representations have been redrawn with improved shapes, and an attractive shine and color scheme permeates the presentation of models and other graphics.
- New electrostatic potential maps and electron density surfaces prepared with Gaussian software help students visualize polarity and electron distribution.
- Several new chapter-opening vignettes and boxes relate concepts to the real world.
- Highlights of Nobel Prize-winning chemistry are integrated into the text.
- Organic examples of biological and other real-world chemistry are highlighted in “The Chemistry of ...” boxes.
- Early introduction of spectroscopy gives students evidence for functional groups and structure, and supports their use of instrumentation in laboratory classes.
- Pedagogical margin notes focus attention on key tools and tips for learning.
- Learning Group Problems provide active integration of concepts and opportunities for peer-led teaching.
- New problems employ calculated molecular models created with Gaussian for viewing with the Chem3D plugin.
- OrganicView CD and web site offer technology-based learning—Woodman Concept Unit Tutorials, Shockwave® Interactive Web Exercises, Reaction Animations, and 3D models provide reinforcement of basic concepts.
- eGrade self-assessment software allows students to practice problems from the text and receive immediate feedback on their progress.

Concept Maps, Mechanism Summaries, and Synthetic Connections

We introduce, for the first time with this edition, comprehensive visual summary and review tools for students. These tools come in three forms: Concept Maps, Mechanism Summaries, and Synthetic Connections. **Concept Maps** are hierarchical flowcharts that join one key concept to the next with a linking phrase. Our Concept Maps help students summarize, review, and organize the material in a chapter. Our new **Mechanism Summaries** tie together common themes and highlight key attributes of important mechanisms. They highlight factors influencing the type of mechanism by which a molecule will react, as well as show regiochemical and stereochemical aspects of mechanisms. **Synthetic Connections** are roadmaps that show pathways for converting molecules from one type to another. Using our Synthetic Connections, students can see how reactions they have learned are part of their growing repertoire for synthesis.

Green Chemistry, Biochemistry, and Nanotechnology

The Eighth Edition brings new material on green chemistry, biochemistry, and nanotechnology. Environmentally-benign chemical methods are increasingly important in our world, and we have highlighted examples and new directions in ‘green chemistry’ whenever possible. Students

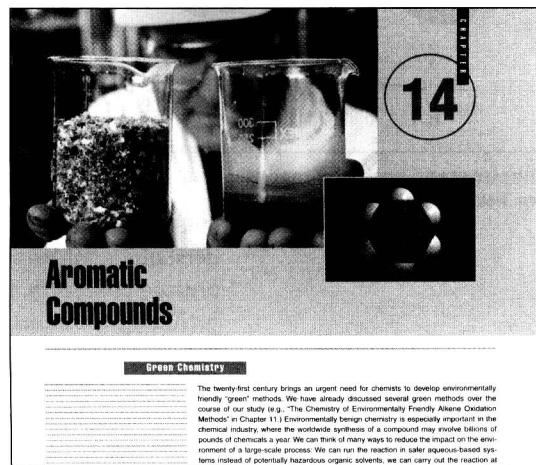


Part of the Chapter 3 Concept Map

need to know that environmentally-benign chemical methods are in use, and that opportunities exist to develop new methods. We encourage students and instructors to consult the American Chemical Society (www.chemistry.org) and the Environmental Protection Agency (www.epa.gov) web sites for further resources on green chemistry. In addition, an excellent resource is "Real World Cases in Green Chemistry," by Michael C. Cann (American Chemical Society Publications: Washington, D.C., 2000).

Biochemistry and biotechnology are always areas of high interest for students of organic chemistry, and dramatic changes are occurring in these areas. Recognizing the rapid pace of developments, we have substantially updated the biochemistry chapters in the Eighth Edition. We have included new sections on proteomics and genomics. We have updated information about key chemical tools for biotechnology, including solid-phase carbohydrate synthesis, mass spectrometry of proteins and nucleic acids, and the dideoxy method for sequencing nucleic acids. Research advances, such as the recently solved crystal structure of the ribosome, have opened many doors for revisions in our coverage. As always, we draw connections to biochemistry throughout the book in chapter-opening vignettes, "The Chemistry of..." boxes, and Special Topics.

Nanotechnology and materials science are among the most exciting areas in chemistry today. We have incorporated several new vignettes and boxes pertaining to nanotechnology, materials science, and bioengineering. Among these are the Chapter 2 opening vignette "Structure and Function: Organic Chemistry, Nanotechnology, and Bioengineering," a box in



Green chemistry opening vignette

Chapter 4 titled “The Chemistry of... Nanoscale Motors and Molecular Switches,” and a box in Chapter 23 titled “The Chemistry of... STEALTH® Liposomes for Drug Delivery.” *The cover of our book shows a spherical array of molecules like the proposed molecular switches and motors discussed in the Chapter 4 box.* Advances in nanotechnology are literally revolutionizing our lives, with pervasive influence from medicine to personal technology.

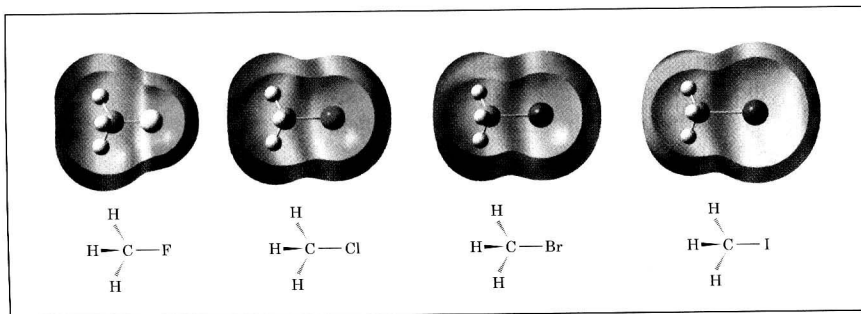
Chapter-Opening Vignettes

Students who find a subject interesting will be motivated to learn it. This idea was an innovation that made the first edition of this text the success that it became, and it is one that has been emphasized in every edition since. As in the previous edition, we open each chapter with a vignette that shows students how the chapter's subject matter relates to “real world” applications—to applications of biochemical, medical and environmental importance. Chapter 3, on acid-base chemistry, begins with an essay describing the role of the enzyme carbonic anhydrase in regulating blood acidity through the acid-base reactions involved in the mechanism of this enzyme. Opening Chapter 4 is an essay on the rotation of carbon-carbon single bonds in the muscle protein actin, one that sets the stage for the chapter's emphasis on conformational analysis. Chapter 13, where we discuss benzene in detail, begins with an essay about green chemistry and alternatives to using benzene in industrial processes. Other topics of similar engaging interest lead off each chapter in the text.

Electrostatic Potential Maps

Two of the most helpful concepts that students can apply in organic chemistry are that opposite charges attract and that delocalization of charge is a stabilizing factor. As chemists, we

know that many reactions occur because molecules with opposite charges are attracted to each other. We also know that reaction pathways are favored or disfavored partly on the basis of relative stability of charged intermediates. To fully utilize this pedagogy, we use maps of electrostatic potential at the van der Waals surface of molecules in which colors indicate the charge distribution in the various regions of a molecule or ion.



Electrostatic potential maps for the methyl halides

Electrostatic potential maps help

students visualize basic principles of structure and reactivity. For example, because an understanding of Brønsted-Lowry and Lewis acid-base reactivities is essential for success in organic chemistry, in the Seventh Edition we improved Chapter 3 (on acids and bases) by including a number of calculated electrostatic potential maps to illustrate how charge distribution influences the relative acidity of an acid and how it affects the relative stability of the conjugate base. These graphics greatly assist visualization of charge separation, localization, and dispersal. Other examples in this chapter include illustrations of the acidity of terminal alkynes, of the charge distribution in acetate anion versus that of ethoxide anion, and in the Lewis acid-base reaction of boron trifluoride and ammonia.

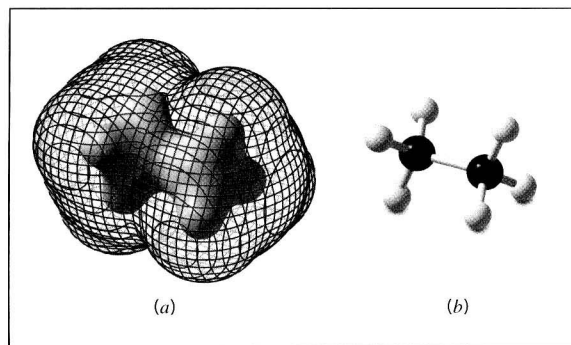
We also use electrostatic potential maps to focus attention on the complementary charges in nucleophiles and electrophiles, to show the relative charge distribution in asymmetric bromonium ions, to compare the relative stabilities of arenium ion intermediates in electrophilic aromatic substitution, and to illustrate the electrophilic nature of carbonyl groups and the β carbon in α,β -unsaturated carbonyl compounds. In one of the

early in-chapter boxes we also show how the LUMO of one reactant and the HOMO of another are important in reactions.

We generated most of the electron density surfaces and electrostatic potential maps in this book using ab initio quantum mechanical methods at the 6-31G level using Gaussian® software. Molecules that we compare within a series are depicted over the same charge range to insure that comparisons are accurate and meaningful in relative terms. Structures are energy-minimized except for those where a particular higher energy conformation is desired.

Orbital Hybridization and the Structure of Organic Molecules

Students must develop a sound understanding of the structure and shape of organic molecules. We build the foundation for their understanding of structure by introducing orbital hybridization and VSEPR theory in Chapter 1. We begin with methane for sp^3 hybridization, move directly to ethene for sp^2 hybridization, and then to ethyne for sp hybridization. We also use calculated molecular orbitals, and electron density surfaces to illustrate regions of bonding electron density and overall molecular shape. In this edition we improved our presentation of resonance in Chapter 1 by including some additional rules for drawing proper resonance structures. Students will consider these rules further when they study conjugated systems in Chapter 13.



Ethane: calculated and ball-and-stick models

Molecular Models: Hand-held and Computer-based

We emphasize the importance of three-dimensional structure by frequently encouraging students to use hand-held molecular models. We feel that the tactile experience of manipulating physical models is key to students' understanding that organic molecules have shape and occupy space. To facilitate this effort, we have arranged with the Darling Company to bundle inexpensive Molecular Visions™ model kits with the book (for those who choose that option). The model kit has been specially assembled to accompany this text.

We also emphasize structure by providing several hundred 3D computer-based molecular models on the CD accompanying the book. We use the Chem3D plugin for models that have molecular orbitals and isosurfaces (calculated using Chem3D and Gaussian), and Rasmol for models that do not have calculated properties associated with them. To reinforce students' learning through use of these models, we have included problems at the end of some chapters that call upon students to view and manipulate computer models stored on the CD or Web site.



Learning Group Problems

Active Integration of Concepts

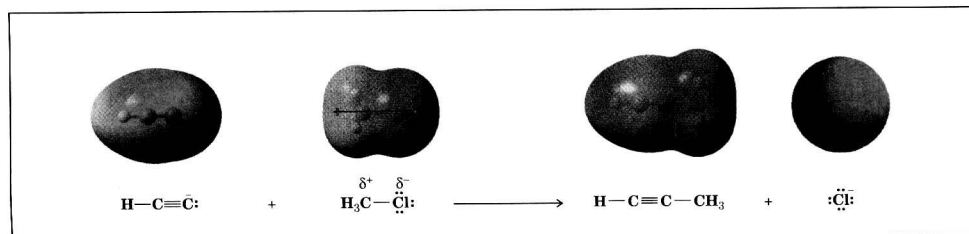
To facilitate active and collaborative student involvement in learning we have included problems at the end of each chapter that are intended to be solved by students working in small "Learning Groups." Each problem, called a Learning Group Problem (LGP), integrates concepts and requires gathering of information from the chapter for students to arrive at a complete solution. The problems can be worked inside or outside of class, with three to six students per group as a desirable size. The LGPs are a useful culminating activity to help students draw together what they have learned from each chapter, and to integrate this knowledge with ideas they have learned earlier.

Student-Led Teaching

The nature of the Learning Group Problems makes them useful as a vehicle for students to *teach* organic chemistry to their peers, as well. For example, because solutions to the problems draw out a variety of important concepts from each chapter, a group's classroom presentation of their Learning Group Problem can be the teaching mode for a given day in class. In this way, students can have the powerful experience of learning through teaching (a wonderful experience that we teachers already know first-hand). The instructor can coach the student presentations from the side of the classroom to insure that all the desired ideas are brought forth and articulated. Detailed suggestions for orchestrating a class involving Learning Group Presentations are available with information for instructors using this text.

Early Introduction to Retrosynthetic Analysis and Organic Synthesis

We use the alkylation of alkynide anions in Chapter 4 to introduce organic synthesis and retrosynthetic analysis. One advantage of using alkynide anions to introduce synthesis is that the reactivity of terminal alkynes and alkyl halides is readily understood on the basis of concepts students have learned in the beginning chapters of the book, namely acid-base chemistry and polarity. Students will use Brønsted-Lowry acid-base chemistry to outline the preparation of alkynide anions from alkynes, and they will recall Lewis acid-base concepts when they consider the reaction of an alkynide anion with an alkyl halide. They will also find reinforcement of a common theme in many organic reactions—the interaction between molecules or groups bearing opposite charges.



The alkylation of alkynide anions also gives students a method for carbon-carbon bond formation very early in their study of organic chemistry. And, it gives them a product that contains a functional group from which they can make many other compounds as their synthetic repertoire grows. Finally, because 'better' or 'worse' retrosynthetic pathways using alkynide-anion alkylation are conceivable for a given molecule, this reaction is a realistic vehicle for teaching the logic of retrosynthetic analysis.

Substitution and Elimination Reactions

Substitution and elimination reactions provide an opportunity for students to encounter one of the important realities of organic chemistry. Reactions almost never follow exclusively one path, much as we would like them to. As chemists, we know very well how frequently one kind of reaction competes with another to complicate our synthetic plans. Therefore, bringing students to the point where they can propose reasonable syntheses using substitutions or eliminations requires a careful orchestration of topics. In this edition, as in the last, Chapter 6 focuses on substitution, but it also briefly introduces elimination reactions. We have done this because the two reactions nearly always occur together, and it is vitally important that students gain a chemically accurate understanding of this. Chapter 7, then, rounds out the discussion by giving detailed treatment of E2 and E1 reactions, including stereochemistry, regiochemistry, and overall product distribution. The Eighth Edition includes new Mechanism

Review tools for summarizing the factors that favor substitution or elimination and unimolecular or bimolecular reaction. Due to the importance of these reaction types, we have placed a copy of this Mechanism Review inside the front cover of the book.

Synthesis Updates

The 2001 Nobel Prize in Chemistry was awarded to K. Barry Sharpless, William Knowles, and Ryoji Noyori for their work on catalytic asymmetric methods for oxidation and reduction. We have highlighted these powerful synthesis tools in several new or revised boxes in the Eighth Edition, including mention of their relevance to well-known compounds such as Naproxen™ and L-DOPA. The Sharpless asymmetric epoxidation was already a boxed topic in Chapter 11 of the Seventh Edition, and we have now included the Sharpless asymmetric dihydroxylation. We have also included information on “green” catalytic methods such as the oxidation of alkenes using catalytic rather than stoichiometric amounts of osmium, and oxidation using Jacobsen’s catalyst.



In the previous edition we updated a number of sections so that other important tools for synthesis were illustrated. These prior updates included sections on the use of lithium enolates, silyl ether protecting groups, and silyl enol ethers in Chapter 17. We also added enantioselective carbonyl reduction methods to Chapter 12, including the use of enzymes in organic synthesis (e.g., use of extremozymes from thermophilic bacteria for reduction reactions), and we substantially updated discussion of the Diels-Alder reaction in Chapter 13. In addition, we mentioned development of catalytic antibodies for aldol condensations (in relation to the Robinson annulation, Diels-Alder reactions, and ester hydrolyses). The latter are found in Chapter 24 regarding proteins.

In this edition we moved oxymercuration-demercuration and hydroboration-oxidation from Chapter 11 to Chapter 8 because these reactions belong with other addition reactions of alkenes. This change also groups these reactions with acid-catalyzed hydration of alkenes as a collection of methods for alcohol synthesis from alkenes. Then, when alcohols and ethers are discussed in Chapter 11, we briefly review the ensemble of methods given in Chapter 8 for synthesis of alcohols from alkenes.

We have also deleted some sections that, although dear to us as chemists, provided reasonable opportunities to trim material from the book. We removed our coverage of the Hell-Vollhard-Zelinski reaction, the Wolff-Kishner reduction, and the debromination of vicinal dibromides, and we moved the Special Topic on Reactions and Synthesis of Heterocyclic Amines to the CD as an electronic rather than a print resource. Though we were tempted to delete it due to our emphasis on IR, we retained the Hinsberg classification test for amines. We welcome your suggestions for other topics that could be shortened or removed.

Advantages of Introducing Spectroscopy Early

Our book gives instructors the opportunity, if they desire, to use spectroscopy as an early and integral part of their course. We present infrared (IR) spectroscopy in Chapter 2, immediately after the introduction of functional groups. Placement of IR here shows students one of the important ways chemists obtain evidence about functional groups. It also supports early experiences students may have using IR in their laboratory experiments. Thus, as students study functional groups for the first time in Chapter 2, they also learn about the best method for detecting the presence of functional groups in a molecule. In addition, IR gives evidence for intermolecular forces, such as hydrogen bonding, which is also discussed in Chapter 2.

*The CD that accompanies the book also includes **IR Tutor**, a widely acclaimed computerized tutorial on IR spectroscopy created at Columbia University. It has been said that students cannot help but learn IR spectroscopy if they use the IR Tutor program.*

We also give nuclear magnetic resonance (NMR) and mass spectrometry (MS) prominence by placing them together in Chapter 9, relatively early in the book. These two methods are among the most powerful structure elucidation tools in organic chemistry and biochemistry, and for this reason they deserve early and substantial coverage. We also use spectroscopy with problems in almost every chapter after the introduction of each spectroscopic method, and we give details about the spectroscopic characteristics of each functional group as we study them in later chapters. To enhance students' appreciation for ultraviolet-visible (UV-Vis) spectroscopy, we place it in the context of conjugated unsaturated systems (Chapter 13).

We also briefly introduce gas chromatography (GC) before mass spectrometry so that we can describe GCMS as a tool for obtaining structural information on compounds in mixtures. In Chapter 9 and again in Chapter 24 we discuss electrospray ionization mass spectrometry (ESI-MS) because it is key to the analysis of biomolecules.

The essence of our rationale for making all of these changes is that modern instrumental methods are central to the way chemists and biochemists elucidate molecular structures. Early introduction of spectroscopic methods provides important support for the laboratory experiences of organic chemistry students, where instrumental methods play an increasing and early role in their training, and NMR and mass spectrometry, together with IR, complete the typical analytical ensemble used by many of today's organic chemists.

User-friendly Spectra and Interpretation Tools

All of the ^1H and ^{13}C NMR spectra in the book are 300 MHz Fourier transform NMR spectra. NMR spectra used to teach spectral interpretation are clearly annotated to show which atoms are responsible for producing each signal in the spectrum. Offset zoom expansions of many ^1H spectra are provided for clarity, and integral curves are shown. ^{13}C NMR data is given with DEPT information to indicate the number of hydrogen atoms bonded to each unique carbon atom. Two-dimensional NMR spectroscopy (COSY and HETCOR) is discussed in Chapter 9, as well.

In this edition we have included new graphical chemical shift correlation charts for ^1H and ^{13}C NMR spectra. (There is also a new IR frequency chart.) These figures are found inside the covers of the book for easy reference.

All of the 1D NMR data files are provided on the World-Wide Web via a link from the book's website in both JCAMP format and NUTS format (an NMR software program from Acorn NMR, Inc.). The JCAMP format allows direct viewing of the NMR spectra using a Web browser (but does not provide for extensive data manipulation). The NUTS format allows users to manipulate the data and prepare it for presentation in whatever manner they desire.

"The Chemistry of ..." Boxes

In most chapters, we use one or more boxes called "The Chemistry of ..." to provide enhanced coverage of a chapter topic, to supply a relevant biological, environmental, or materials science example, or to expand upon concepts from the opening vignettes. Some examples are:

- The Chemistry of ... The Bombardier Beetle's Noxious Spray
- The Chemistry of ... Organic Templates Engineered to Mimic Bone Growth
- The Chemistry of ... Nanoscale Motors and Molecular Switches
- The Chemistry of ... Radicals in Biology, Medicine, and Industry
- The Chemistry of ... The Sharpless Asymmetric Epoxidation
- The Chemistry of ... Epoxides, Carcinogens, and Biological Oxidation
- The Chemistry of ... Sunscreens (Catching the Sun's Rays and What Happens to Them)

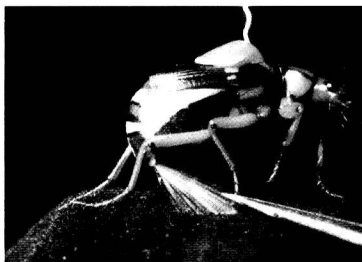
The Chemistry of...

The Bombardier Beetle's Noxious Spray

The bombardier beetle defends itself by spraying a jet stream of hot (100°C), noxious *p*-benzoquinones at an attacker. The beetle mixes *p*-hydroquinones and hydrogen peroxide from one abdominal reservoir with enzymes from another reservoir. The enzymes convert hydrogen peroxide to oxygen, which in

turn oxidizes the *p*-hydroquinones to *p*-benzoquinones and explosively propels the irritating spray at the attacker. Photos by T. Eisner and D. Aneshansley (Cornell University) have shown that the amazing bombardier beetle can direct its spray in virtually any direction, even parallel over its back, to ward off a predator.

Bombardier beetle in the process of spraying. From Eisner, T.; Aneshansley, D. J. *Proc. Natl. Acad. Sci. USA* 1999, 96, 9705–9709.



- The Chemistry of ... Vaccines Against Cancer
- The Chemistry of ... Antibody-Catalyzed Aldol Condensations
- The Chemistry of ... A Suicide Enzyme Substrate
- The Chemistry of ... Artificial Sweeteners

These and other boxes within the text show students the many ways in which organic chemistry is central to life and the world around us.

Relating Organic Chemistry to Biosynthesis

When an aspect of organic chemistry arises that has a biosynthetic counterpart we have juxtaposed that topic with coverage of the relevant fundamental organic chemistry. An example is the biosynthesis of lanosterol from 2,3-oxidosqualene, a step along the pathway to cholesterol. Because this biosynthetic transformation is such a beautiful example of enzyme-mediated epoxide ring opening, alkene addition steps, and skeletal migrations, we placed “The Chemistry of ... Cholesterol Biosynthesis” in Chapter 8, directly in relation to alkene addition reactions and shortly after students’ acquaintance with hydride and methanide migrations. Another example of this approach is placement of “The Chemistry of ... Polyketide Antibiotic Biosynthesis” in Chapter 19, directly in relation to the malonic ester synthesis and the Claisen condensation. We believe that a student’s appreciation of organic chemistry can be enhanced tremendously by showing the elegance of organic chemical reactions that take place in nature. Some other examples are:

- The Chemistry of ... Biochemical Nucleophilic Substitution
- The Chemistry of ... Pyridoxal Phosphate (Vitamin B₆)
- The Chemistry of ... Thiamine Pyrophosphate (Vitamin B₁)
- The Chemistry of ... Biological Methylation

Other Pedagogical Features

We use the margins of the wide-format pages to note the central importance of certain topics, to provide study aids or practical tips for students where appropriate, and to add brief notes of a practical or historical nature where appropriate.

Concept Maps, Mechanism Reviews, and Synthetic Connections These new features for the Eighth Edition appear at the ends of chapters as summary and review tools.



Study Tip Icons We have used “Study Tip” icons to highlight places in the text where a point is made that can be particularly helpful for a student learning organic chemistry. An example is the Study Tip icon in Section 1.7A regarding formal charges, pointing out that it will be necessary for students to keep track of formal charges later when they learn organic reactions. Another example is the Study Tip icon used to emphasize conventions used by chemists when we draw reaction and electron movement arrows (Section 1.8). Study Tip icons occur throughout the book.



Tool Box Icons We have used “Tool Box” icons in the margin to emphasize concepts that are fundamental “tools” in organic chemistry. Some examples where the Tool Box icon is used are in Chapter 1, when we introduce the hybridization states of carbon and when we introduce VSEPR theory. These concepts are among the many essential “tools” for success in learning organic chemistry. We also use the Tool Box icon when a key process or reaction is described, such as the Robinson annulation for synthesis of carbocyclic rings. Tool Box icons occur throughout the book.

“A Mechanism for the Reaction” These specially designed mechanism presentations give detailed explanations for every key mechanism in the book. Curved arrows show precisely and unambiguously how electrons flow in each step of a mechanism. Steps are identified and annotated in the mechanisms to further explain each transformation.

Solved Problems Sample problems with solutions are included at key points to show students how to approach problems in organic chemistry.

In-Chapter Problems Numbered problems appear at the end of sections to reinforce students’ learning immediately after each topic is introduced.

Key Terms and Concepts A list of key terms and concepts with section references at the end of each chapter allows students to test their memory regarding key ideas and if necessary to easily refer back to a full presentation of the concept in the chapter. The key terms and concepts listed are also defined in the glossary.

Library of 3D Computer Models All ball-and-stick, space filling, and many other molecules in the book are included in a library of 3D molecules in Chem3D or Rasmol format on the CD. Downloadable JPEG files for all illustrations and selected photographs are available at the Web site.

Use of Color in Mechanisms Consistent color schemes are used in presentation of reaction mechanisms. Changes in the bonding of atoms from reactants to products are highlighted on the basis of the color used for atoms and bonds.

Molecular Modeling Exercises Probe Structure and Properties Problems at the end of some chapters call upon students to answer questions where viewing is required of molecules from the CD or Web site in Chem3D or Rasmol format.

SUPPLEMENTS

OrganicView CD and Web Site

The CD included with the text includes “Chemistry Teaching Graphics for Organic Chemistry” by Darrell Woodman (University of Washington). The Woodman graphics use multimedia and animation to amplify many concepts in the text with compelling interactive tutorials and problems. The CD also features:

- A full multimedia approach that includes Shockwave animations and Interactive Exercises
- Concept Units comprised of animations and simulations accompanied by audio explanations