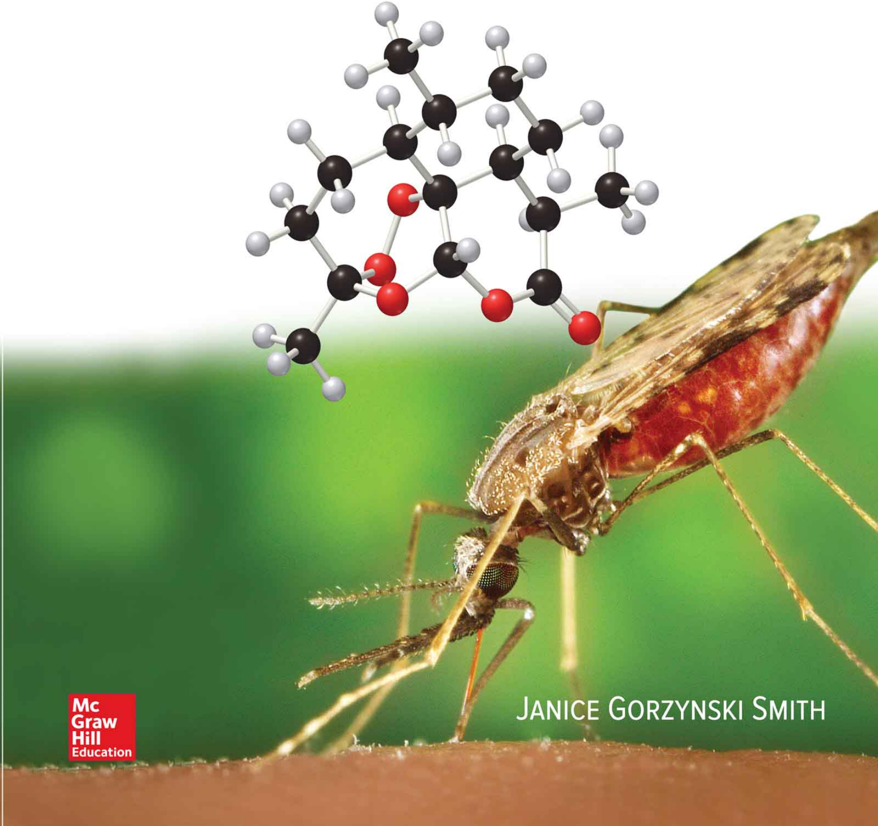
ORGANIC CHEMISTRY

Fifth Edition



JANICE GORZYNSKI SMITH

Mc Graw Hill Education

Organic Chemistry

Fifth Edition

Janice Gorzynski Smith
University of Hawai'i at Mānoa

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ORGANIC CHEMISTRY, FIFTH EDITION

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About the Author

Janice Gorzynski Smith was born in Schenectady, New York. She became interested in chemistry in high school and went on to major in chemistry at Cornell University, where she received an A.B. degree *summa cum laude*. Jan earned a Ph.D. in Organic Chemistry from Harvard University under the direction of Nobel Laureate E. J. Corey, and she also spent a year as a National Science Foundation National Needs Postdoctoral Fellow at Harvard. During her tenure with the Corey group, she completed the total synthesis of the plant growth hormone gibberellic acid.

Following her postdoctoral work, Jan joined the faculty of Mount Holyoke College, where she was employed for 21 years. During this time she was active in teaching organic chemistry lecture and lab courses, conducting a research program in organic synthesis, and serving as department chair. Her organic chemistry class was named one of Mount Holyoke's "Don't-miss courses" in a survey by *Boston* magazine. After spending two sabbaticals amidst the natural beauty and diversity in Hawai'i in the 1990s, Jan and her family moved there permanently in 2000. She is currently a faculty member at the University of Hawai'i at Mānoa, where she teaches the two-semester organic chemistry lecture and lab courses. In 2003, she received the Chancellor's Citation for Meritorious Teaching.

Jan resides in Hawai'i with her husband Dan, an emergency medicine physician, pictured with her hiking in New Zealand in 2015. She has four children and three grandchildren. When not teaching, writing, or enjoying her family, Jan bikes, hikes, snorkels, and scuba dives in sunny Hawai'i, and time permitting, enjoys travel and Hawaiian quilting.

For Megan Sarah

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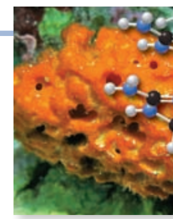

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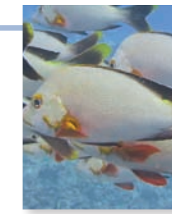
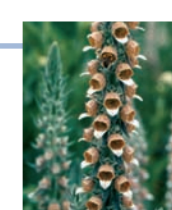





FIRST
CHECK
CHOLESTEROL
HOME TEST
1

Preface

My goal in writing *Organic Chemistry* was to create a text that showed students the beauty and logic of organic chemistry by giving them a book that they would *use.* This text is based on lecture notes and handouts that were developed in my own organic chemistry courses over my 30-year teaching career. I have followed two guiding principles: use relevant and interesting applications to illustrate chemical phenomena, and present the material in a student-friendly fashion using bulleted lists, solved problems, and extensive illustrations and summaries. *Organic Chemistry* is my attempt to simplify and clarify a course that intimidates many students—to make organic chemistry interesting, relevant, and accessible to *all* students, both chemistry majors and those interested in pursuing careers in biology, medicine, and other disciplines, without sacrificing the rigor they need to be successful in the future.

The Basic Features

- **Style** This text is different—by design. Today's students rely more heavily on visual imagery to learn than ever before. The text uses less prose and more diagrams, equations, tables, and bulleted summaries to introduce and reinforce the major concepts and themes of organic chemistry.
- **Content** *Organic Chemistry* accents basic themes in an effort to keep memorization at a minimum. Relevant examples from everyday life are used to illustrate concepts, and this material is integrated throughout the chapter rather than confined to a boxed reading. Each topic is broken down into small chunks of information that are more manageable and easily learned. Sample problems are used as a tool to illustrate stepwise problem solving. Exceptions to the rule and older, less useful reactions are omitted to focus attention on the basic themes.
- **Organization** *Organic Chemistry* uses functional groups as the framework within which chemical reactions are discussed. Thus, the emphasis is placed on the reactions that different functional groups undergo, not on the reactions that prepare them. Moreover, similar reactions are grouped together, so that parallels can be emphasized. These include acid–base reactions (Chapter 2), oxidation and reduction (Chapters 12 and 20), radical reactions (Chapter 15), and reactions of organometallic reagents (Chapter 20).

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

Organization and Presentation

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

- **Review material** Chapter 1 presents a healthy dose of review material covering Lewis structures, molecular geometry and hybridization, bond polarity, and types of bonding. While many of these topics are covered in general chemistry courses, they are presented here from an organic chemist's perspective. I have found that giving students a firm grasp of these fundamental concepts helps tremendously in their understanding of later material.

- **Acids and bases** Chapter 2 on acids and bases serves two purposes. It gives students experience with curved arrow notation using some familiar proton transfer reactions. It also illustrates how some fundamental concepts in organic structure affect a reaction, in this case an acid–base reaction. Since many mechanisms involve one or more acid–base reactions, I emphasize proton transfer reactions early and come back to this topic often throughout the text.
- **Functional groups** Chapter 3 uses the functional groups to introduce important properties of organic chemistry. Relevant examples—PCBs, vitamins, soap, and the cell membrane—illustrate fundamental solubility concepts. In this way, practical topics that are sometimes found in the last few chapters of an organic chemistry text (and thus often omitted because instructors run out of time) are introduced early, so that students can better grasp why they are studying the discipline.
- **Stereochemistry** Stereochemistry (the three-dimensional structure of molecules) is introduced early (Chapter 5) and reinforced often, so students have every opportunity to learn and understand a crucial concept in modern chemical research, drug design, and synthesis.
- **Modern reactions** While there is no shortage of new chemical reactions to present in an organic chemistry text, I have chosen to concentrate on new methods that introduce a particular three-dimensional arrangement in a molecule, so-called asymmetric or enantioselective reactions. Examples include Sharpless epoxidation (Chapter 12), CBS reduction (Chapter 20), and enantioselective synthesis of amino acids (Chapter 29).
- **Grouping reactions** Since certain types of reactions have their own unique characteristics and terminology that make them different from the basic organic reactions, I have grouped these reactions together in individual chapters. These include acid–base reactions (Chapter 2), oxidation and reduction (Chapters 12 and 20), radical reactions (Chapter 15), and reactions of organometallic reagents (Chapter 20). I have found that focusing on a group of reactions that share a common theme helps students to better see their similarities.
- **Synthesis** Synthesis, one of the most difficult topics for a beginning organic student to master, is introduced in small doses, beginning in Chapter 7 and augmented with a detailed discussion of retrosynthetic analysis in Chapter 11. In later chapters, special attention is given to the retrosynthetic analysis of compounds prepared by carbon–carbon bond-forming reactions (for example, Sections 20.11 and 21.10C).
- **Spectroscopy** Since spectroscopy is such a powerful tool for structure determination, four methods are discussed over two chapters (Chapters 13 and 14).
- **Key Concepts** End-of-chapter summaries succinctly summarize the main concepts and themes of the chapter, making them ideal for review prior to working the end-of-chapter problems or taking an exam.

New to this Edition

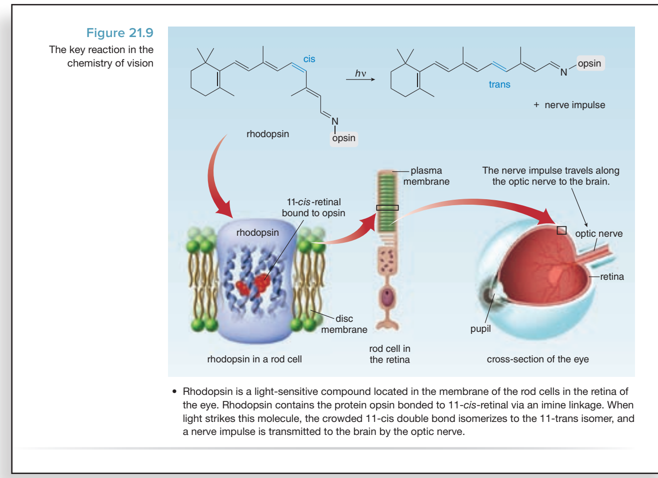
- Chemical structures were updated throughout the text for a more modern and consistent look.
- Color has also been used in many areas to help students better understand three-dimensional structure, stereochemistry, and reactions.
- All nomenclature has been updated in accord with newer IUPAC nomenclature recommendations and the 1993 nomenclature rules.
- The design of the mechanism boxes has been revised, so that students can more readily see how one intermediate is converted to another.
- In response to reviewer feedback, new material has been added to several chapters. Topics include a section on biological nucleophilic substitution with phosphorus leaving groups (Section 7.16) and a section on thiols and sulfides (Section 9.15). The section on biological oxidation was revised to include the oxidizing agent NAD^+, with new structures in the mechanism of oxidation of an alcohol, resulting in a more biological flavor to this material (Section 12.14). A new section on biological reactions with allylic diphosphates and a new mechanism on biological reactions with allylic diphosphates have been added to Section 16.2. New material on biological reduction appears in Section 20.6, and the discussion of ultraviolet spectroscopy has been expanded in Section 16.15.

- Material on classifying carbons, hydrogens, alcohols, alkyl halides, amines, and amides was moved from later chapters to earlier in the text (Section 3.2), so that it is included in the discussion of functional groups.
- Over 350 new problems have been added to the new edition, increasing the variety of problems for instructors and students alike.
- The chapter on lipids now appears online and is available in customizable versions of the text in McGraw-Hill Create.
- An online supplement covering imine derivatives is also available on the Online Learning Center's Instructor Resources, via the Library tab in Connect.
- New *How To*'s, Sample Problems, and micro-to-macro illustrations have also been added throughout the new edition to clarify topics and enhance the student learning experience.

Tools to Make Learning Organic Chemistry Easier

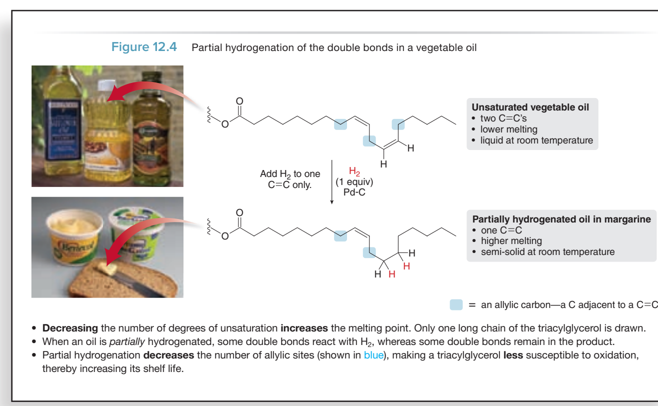
Illustrations

Organic Chemistry is supported by a well-developed illustration program. Besides traditional skeletal (line) structures and condensed formulas, there are numerous ball-and-stick molecular models and electrostatic potential maps to help students grasp the three-dimensional structure of molecules (including stereochemistry) and to better understand the distribution of electronic charge.



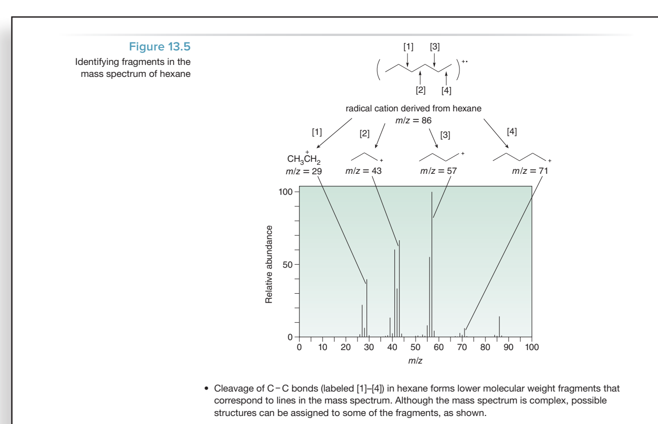
Micro-to-Macro Illustrations

Unique to *Organic Chemistry* are micro-to-macro illustrations, where line art and photos combine with chemical structures to reveal the underlying molecular structures giving rise to macroscopic properties of common phenomena. Examples include starch and cellulose (Chapter 5), adrenaline (Chapter 7), partial hydrogenation of vegetable oil (Chapter 12), and dopamine (Chapter 25).



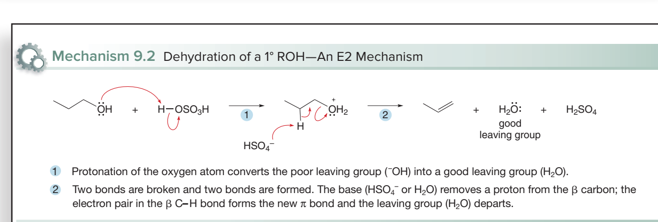
Spectra

Over 100 spectra created specifically for *Organic Chemistry* are presented throughout the text. The spectra are color-coded by type and generously labeled. Mass spectra are green; infrared spectra are red; and proton and carbon nuclear magnetic resonance spectra are blue.



Mechanisms

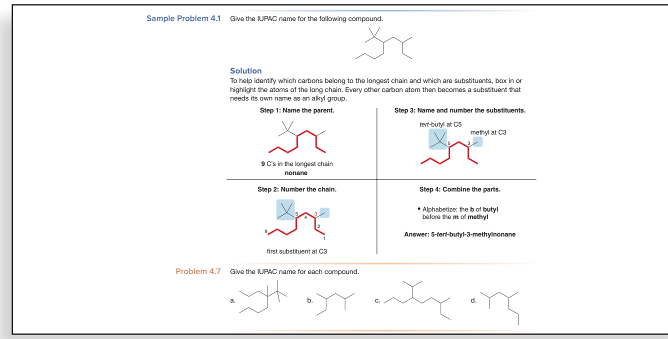
Curved arrow notation is used extensively to help students follow the movement of electrons in reactions.



Problem Solving

Sample Problems

Sample Problems show students how to solve organic chemistry problems in a logical, stepwise manner. More than 800 follow-up problems are located throughout the chapters to test whether students understand concepts covered in the Sample Problems.



Sample Problem 4.1 Give the IUPAC name for the following compound.

Solution

To help identify which carbons belong to the longest chain and which are substituents, box in or highlight the atoms of the long chain. Every other carbon atom then becomes a substituent that needs its own name as an alkyl group.

Step 1: Name the parent.

9 C's in the longest chain

nonane

Step 2: Number the chain.

first substituent at C3

Step 3: Name and number the substituents.

tert-butyl at C5

methyl at C3

Step 4: Combine the parts.

- Alphabetize: the **b** of **butyl** before the **m** of **methyl**

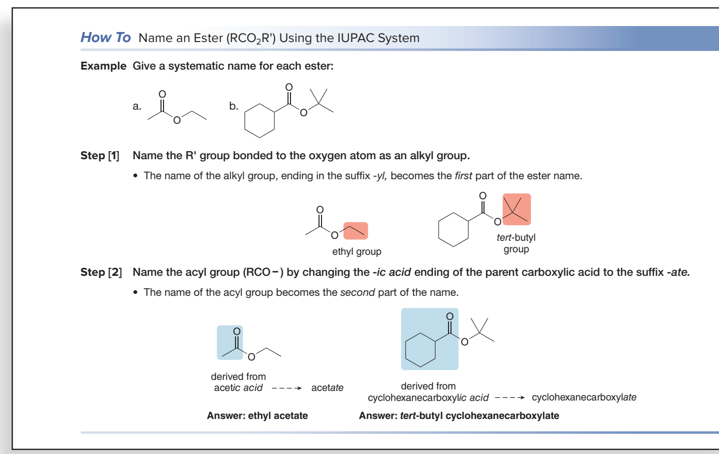
Answer: 5-*tert*-butyl-3-methylnonane

Problem 4.7 Give the IUPAC name for each compound.

a. b. c. d.

How To's

How To's provide students with detailed instructions on how to work through key processes.



How To Name an Ester (RCO_2R') Using the IUPAC System

Example Give a systematic name for each ester:

a. b.

Step [1] Name the R' group bonded to the oxygen atom as an alkyl group.

- The name of the alkyl group, ending in the suffix *-yl*, becomes the *first* part of the ester name.

ethyl group — *tert*-butyl group

Step [2] Name the acyl group (RCO–) by changing the *-ic acid* ending of the parent carboxylic acid to the suffix *-ate*.

- The name of the acyl group becomes the *second* part of the name.

derived from acetic *acid* → acet*ate*

derived from cyclohexanecarboxylic *acid* → cyclohexanecarboxyl*ate*

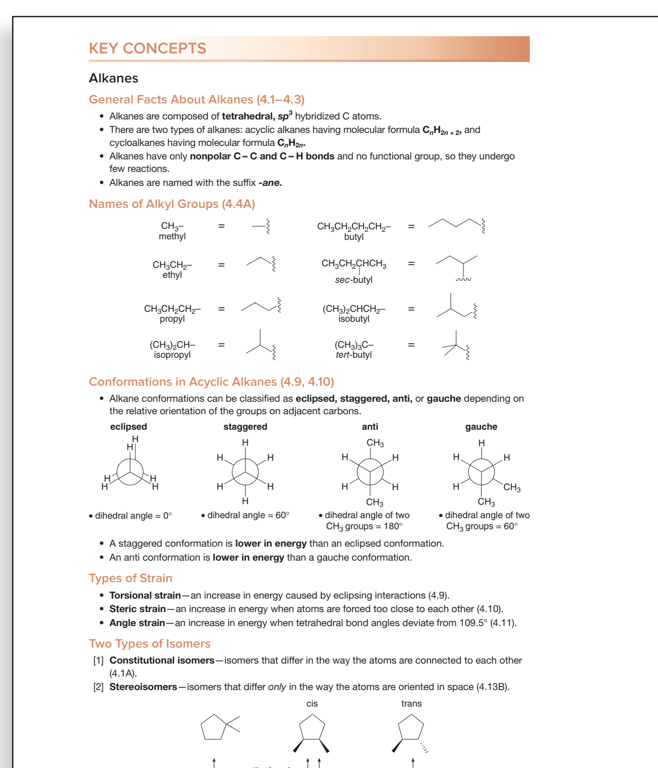
Answer: ethyl acetate

Answer: *tert*-butyl cyclohexanecarboxylate

Applications and Summaries

Key Concept Summaries

Succinct summary tables reinforcing important principles and concepts are provided at the end of each chapter.



KEY CONCEPTS

Alkanes

General Facts About Alkanes (4.1–4.3)

- Alkanes are composed of **tetrahedral, sp^3** hybridized C atoms.
- There are two types of alkanes: acyclic alkanes having molecular formula C_nH_{2n+2}, and cycloalkanes having molecular formula C_nH_{2n}.
- Alkanes have only **nonpolar C–C and C–H bonds** and no functional group, so they undergo few reactions.
- Alkanes are named with the suffix ***-ane.***

Names of Alkyl Groups (4.4A)

CH_3– methyl; CH_3CH_2– ethyl; $CH_3CH_2CH_2$– propyl; $(CH_3)_2CH$– isopropyl; $CH_3CH_2CH_2CH_2$– butyl; $CH_3CH_2CHCH_3$ *sec*-butyl; $(CH_3)_2CHCH_2$– isobutyl; $(CH_3)_3C$– *tert*-butyl

Conformations in Acyclic Alkanes (4.9, 4.10)

- Alkane conformations can be classified as **eclipsed, staggered, anti,** or **gauche** depending on the relative orientation of the groups on adjacent carbons.

eclipsed — dihedral angle = 0°; staggered — dihedral angle = 60°; anti — dihedral angle of two CH_3 groups = 180°; gauche — dihedral angle of two CH_3 groups = 60°

- A staggered conformation is **lower in energy** than an eclipsed conformation.
- An anti conformation is **lower in energy** than a gauche conformation.

Types of Strain

- **Torsional strain**—an increase in energy caused by eclipsing interactions (4.9).
- **Steric strain**—an increase in energy when atoms are forced too close to each other (4.10).
- **Angle strain**—an increase in energy when tetrahedral bond angles deviate from 109.5° (4.11).

Two Types of Isomers

[1] **Constitutional isomers**—isomers that differ in the way the atoms are connected to each other (4.1A).

[2] **Stereoisomers**—isomers that differ *only* in the way the atoms are oriented in space (4.13B).

cis — trans — **constitutional isomers** — **stereoisomers**

Margin Notes

Margin notes are placed carefully throughout the chapters, providing interesting information relating to topics covered in the text. Some margin notes are illustrated with photos to make the chemistry more relevant.

All soaps are salts of fatty acids. The main difference between soaps is the addition of other ingredients that do not alter their cleaning properties: dyes for color, scents for a pleasing odor, and oils for lubrication. Soaps that float are aerated, so that they are less dense than water.

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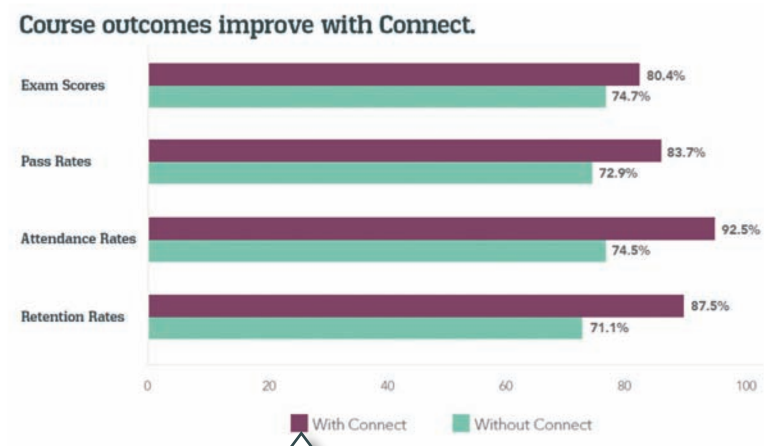

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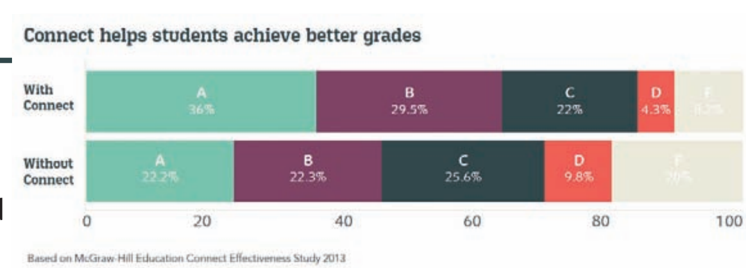

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Connect Insight is Connect's new one-of-a-kind visual analytics dashboard—now available for both instructors and students—that provides at-a-glance information regarding student performance, which is immediately actionable. By presenting assignment, assessment, and topical performance results together with a time metric that is easily visible for aggregate or individual results, Connect Insight gives the user the ability to take a just-in-time approach to teaching and learning, which was never before available. Connect Insight presents data that empowers students and helps instructors improve class performance in a way that is efficient and effective.

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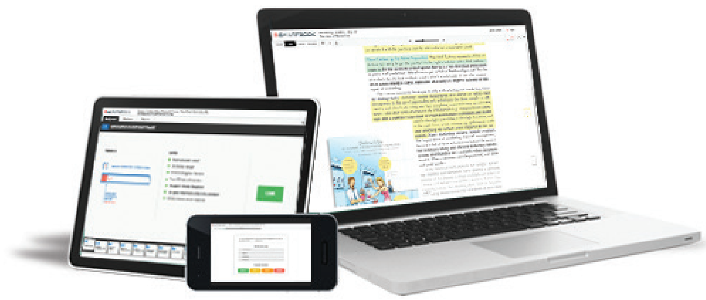

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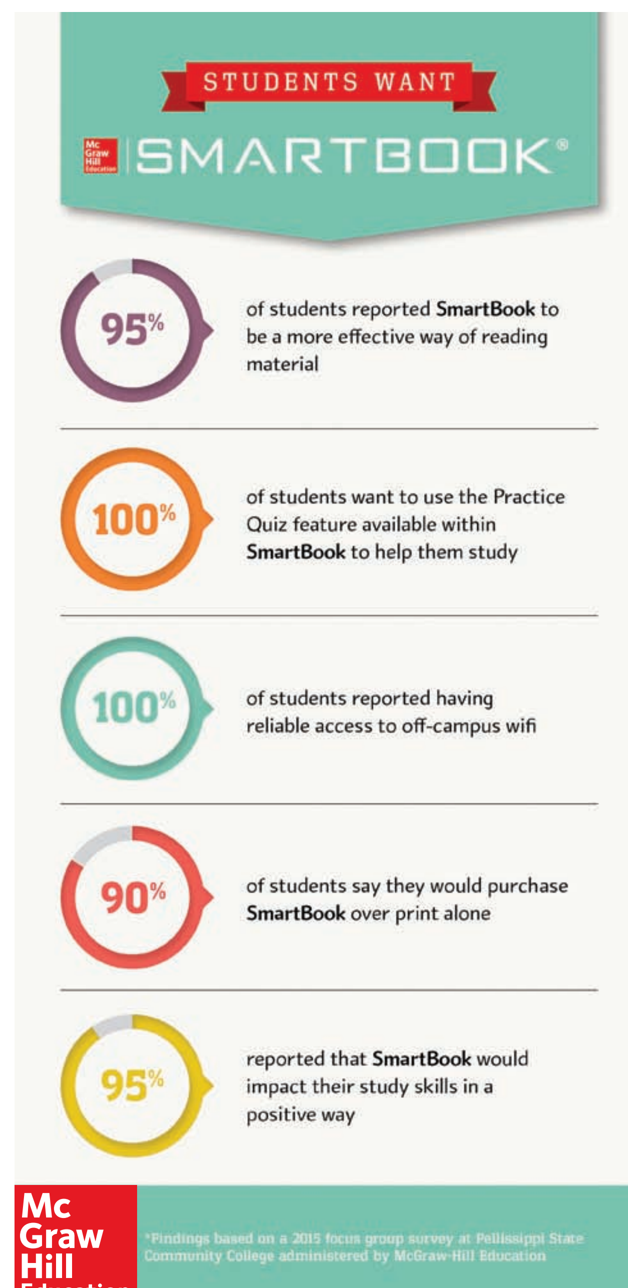

Learning Resources for Instructors and Students

The following items may accompany this text. Please consult your McGraw-Hill representative for policies, prices, and availability as some restrictions may apply.

Presentation Tools

Within the Instructor's Presentation Tools, instructors have access to editable PowerPoint lecture outlines, which appear as ready-made presentations that combine art and lecture notes for each chapter of the text. For instructors who prefer to create their lecture notes from scratch, all illustrations, photos, tables, *How To*'s, and Sample Problems are pre-inserted by chapter into a separate set of PowerPoint slides. They are also available as individual .jpg files.

An online digital library contains photos, artwork, animations, and other media types that can be used to create customized lectures, visually enhanced tests and quizzes, compelling course websites, or attractive printed support materials. All assets are copyrighted by McGraw-Hill Higher Education, but can be used by instructors for classroom purposes. The visual resources in this collection include:

- **Art** Full-color digital files of all illustrations in the book can be readily incorporated into lecture presentations, exams, or custom-made classroom materials.
- **Photos** The photo collection contains digital files of photographs from the text, which can be reproduced for multiple classroom uses.
- **Tables** Every table that appears in the text has been saved in electronic form for use in classroom presentations and/or quizzes.
- **Animations** Numerous full-color animations illustrating important processes are also provided. Harness the visual impact of concepts in motion by importing these files into classroom presentations or online course materials.

Student Study Guide/Solutions Manual

Written by Janice Gorzynski Smith and Erin R. Smith, the Student Study Guide/Solutions Manual provides step-by-step solutions to all in-chapter and end-of-chapter problems. Each chapter begins with an overview of key concepts and includes a short-answer practice test on the fundamental principles and new reactions.

Acknowledgments

When I started working on the first edition of *Organic Chemistry* in the fall of 1999, I had no sense of the magnitude of the task, or any idea of just how many people I would rely upon to complete it. Fortunately, I have had the steadfast support of a dedicated team of publishing professionals at McGraw-Hill.

I am especially thankful for the opportunity to work with Senior Product Developer Mary Hurley, who skillfully and efficiently guided me through the process of updating this fifth edition. Mary has been my rock through the many months of re-drawing chemical structures and re-designing mechanisms and art. I am grateful to once again work with Lead Content Project Manager Peggy Selle, who managed the production of this updated and re-designed text. *Organic Chemistry* has also benefited greatly from the expertise and market-based feedback provided by Marketing Manager Matthew Garcia.

Special thanks go out to Brand Manager Andrea Pellerito, who gave me the day-to-day editorial support crucial in producing a revision of *Organic Chemistry.* Thanks also to Managing Director Thomas Timp, who efficiently directed the editorial team that produced this revision. I also appreciate the work of Matt Backhaus (Designer) and Carrie Burger (Photo Researcher) who are responsible for the visually pleasing appearance of this edition. Thanks are again due to freelance Developmental Editor John Murdzek for his meticulous editing and humorous insights on my project.

My immediate family has experienced the day-to-day demands of living with a busy author. Thanks go to my husband Dan, my children Erin, Jenna, Matthew, and Zachary, and my grandchildren Max, Koa, and Alijah, all of whom keep me grounded during the time-consuming process of writing and publishing a textbook.

Among the many others that go unnamed but who have profoundly affected this work are the thousands of students I have been lucky to teach over the last 30 years. I have learned so much from my daily interactions with them, and I hope that the wider chemistry community can benefit from this experience by the way I have presented the material in this text.

This fifth edition has evolved based on the helpful feedback of many people who reviewed the fourth edition text and digital products, class-tested the book, and attended focus groups or symposiums. These many individuals have collectively provided constructive improvements to the project.

Listed below are the reviewers of the fourth edition text:

Steven Castle, *Brigham Young University*
Ihsan Erden, *San Francisco State University*
Andrew Frazer, *University of Central Florida, Orlando*
Tiffany Gierasch, *University of Maryland, Baltimore County*
Anne Gorden, *Auburn University*
Michael Lewis, *Saint Louis University*
Eugene A. Mash, Jr., *University of Arizona*
Mark McMills, *Ohio University*
Joan Mutanyatta–Comar, *Georgia State University*
Felix Ngassa, *Grand Valley State University*
Michael Rathke, *Michigan State University*
Jacob Schroeder, *Clemson University*
Keith Schwartz, *Portland State University*
John Selegue, *University of Kentucky*
Paul J. Toscano, *University at Albany, SUNY*
Jane E. Wissinger, *University of Minnesota*

The following contributed to the editorial direction of the fifth edition text by responding to our survey on the MCAT and the organic chemistry course student population:

Chris Abelt, *College of William and Mary*
Orlando Acevedo, *Auburn University*
Kim Albizati, *University of California, San Diego*
Merritt Andrus, *Brigham Young University*
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Although every effort has been made to make this text and its accompanying Student Study Guide/Solutions Manual as error-free as possible, some errors undoubtedly remain and, for them, I am solely responsible. Please feel free to email me about any inaccuracies, so that subsequent editions may be further improved.

With much aloha,

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List of *How To's*

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

List of Mechanisms

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

List of Selected Applications

Applications make any subject seem more relevant and interesting—for nonmajors and majors alike. The following is a list of the biological, medicinal, and environmental applications that have been integrated throughout *Organic Chemistry.* Each chapter opener showcases an interesting and current application relating to the chapter's topic. (Code: G = general; M = medicinal; B = biological; E = environmental)

Prologue

G Methane, the main component of natural gas
G Ethanol, the alcohol in beverages
E Trichlorofluoromethane, a CFC responsible for destroying the stratospheric ozone layer
M Amoxicillin, a widely used antibiotic
M Fluoxetine, the antidepressant Prozac
M AZT, a drug used to treat HIV
M Capsaicin, a compound found in topical pain relief creams
E DDT, a nonspecific pesticide that persists in the environment
M The antimalarial drugs quinine, chloroquine, and artemisinin

Chapter 1 Structure and Bonding

M L-Dopa, a drug used to treat Parkinson's disease (Chapter opener and Section 1.14)
M Alendronic acid (Fosamax), a drug used to prevent osteoporosis (Section 1.5)
B Enanthotoxin, a poisonous compound isolated from hemlock water dropwort (Section 1.7)
G Vanillin, the principal component in the extract of the vanilla bean (Section 1.8B)
M Structures of active ingredients in common sunscreens (Section 1.8B)
G Ethane, a component of natural gas (Section 1.10A)
G Ethylene, a hydrocarbon used to make the plastic polyethylene (Section 1.10B)
G Acetylene, a gas used in welding torches (Section 1.10C)
G Cucumber aldehyde, the compound responsible for the odor of freshly cut cucumbers (Section 1.10C)
M Sinemet, a drug used to treat Parkinson's disease that combines L-dopa and carbidopa (Section 1.14)
B Vitamin B_6 (Section 1.14)

Chapter 2 Acids and Bases

M Aspirin, a common analgesic and antipyretic (Chapter opener and Section 2.7)
M The acid–base chemistry of morphine (Section 2.1)
M The nasal decongestant pseudoephedrine (Section 2.5, Problem 2.17)
M Glycolic acid, an α-hydroxy acid used in skin care products (Section 2.5, Problem 2.20)
E Sulfuric acid, a major contributor to acid rain (Section 2.6)
M Salicin, an analgesic found in willow bark

Chapter 3 Introduction to Organic Molecules and Functional Groups

B Vitamin C, a water-soluble vitamin that is important in the formation of collagen (Chapter opener and Section 3.5B)
M The local anesthetic chloroethane (Section 3.2B)
E Hemibrevetoxin B, a neurotoxin produced by algal blooms ("red tides") (Section 3.2B)
M Diethyl ether, the first common general anesthetic (Section 3.2B)
B Bilobalide, a compound isolated from the *Ginkgo biloba* extracts used in Chinese medicine (Section 3.2B, Problem 3.3)
M Dexamethasone, a synthetic steroid (Section 3.2B, Problem 3.5)
B Spermine, isolated from semen, and meperidine, the narcotic Demerol (Section 3.2B, Problem 3.6)
M Atenolol, a β blocker used to treat high blood pressure, and donepezil, used to treat Alzheimer's disease (Section 3.2C)
M Dolastatin, an anticancer compound isolated from the seahare *Dolabella auricularia* (Section 3.2C, Problem 3.8)
M Tamiflu, an antiviral drug used to treat influenza (Section 3.2C, Problem 3.9)
G How geckos use van der Waals forces to stick to walls (Section 3.3B)
G MTBE, a high-octane additive in unleaded gasoline, and 4,4'-dichlorobiphenyl, a PCB (Section 3.4C)
B Norethindrone, an oral contraceptive, and arachidonic acid, a fatty acid (Section 3.4C, Problem 3.18)
B Vitamin A (retinol), a fat-soluble vitamin found in the vision receptors of the eyes (Section 3.5A)
B β-Carotene, a precursor to vitamin A (Section 3.5A)
B Vitamin B_3 and vitamin K_1 (Section 3.5B, Problem 3.19)
B Avocados as a source of pantothenic acid, vitamin B_5 (Section 3.5B, Problem 3.20)

M Morphine and heroin (Section 3.7A, Problem 3.23)
M The antibiotics nonactin and valinomycin (Section 3.7B)
B Biomolecules, such as glucose, oleic acid, alanine, and dAMP (Section 3.9)
B The artificial sweetener aspartame (Section 3.9, Problem 3.28)

Chapter 4 Alkanes

E Oil slicks that result from crude petroleum being spilled into the ocean from oil tankers or oil wells (Chapter opener)
B The cockroach pheromone undecane (Section 4.1)
B Cyclohexane, one component of mangoes (Section 4.1)
B Allicin, a compound responsible for the odor of garlic (Section 4.3)
M Systematic names, generic names, and trade names in over-the-counter drugs like Motrin (Section 4.3)
G Fossil fuels such as natural gas and petroleum (Section 4.7)
E The combustion of alkanes and how it contributes to global warming (Section 4.14B)
B Lipids such as fat-soluble vitamins, phospholipids, waxes, prostaglandins, and steroids (Section 4.15)
B Pristane, a high molecular weight alkane found in shark liver oil (Section 4.15, Problem 4.33)
B End-of-chapter problems: 4.66 and 4.69

Chapter 5 Stereochemistry

M, B Paclitaxel (Taxol), a drug used to treat ovarian, breast, and other cancers (Chapter opener)
B How differences in the three-dimensional structure of starch and cellulose affect their shape and function (Section 5.1)
M, B Identifying stereogenic centers in Darvon (an analgesic), ephedrine (a decongestant), and fructose (a simple sugar) (Section 5.4A)
M The three-dimensional structure of thalidomide, an anti-nausea drug that caused catastrophic birth defects (Section 5.5)
M, B Identifying stereogenic centers in paclitaxel (anticancer agent) and sucrose (Section 5.5)
M Identifying stereogenic centers in gabapentin (a drug used to treat seizures and chronic pain), gabapentin enacarbil, cholesterol, and Zocor (cholesterol-lowering drug) (Section 5.5, Problems 5.9 and 5.10)
M Assigning *R* and *S* configurations in the drugs Plavix and Zestril (Section 5.6, Problems 5.14 and 5.15)
B The sweetener sorbitol (Section 5.9, Problem 5.24)
B The specific rotation of MSG, a common flavor enhancer (Section 5.12D, Problem 5.32)
M Chiral drugs and how mirror image isomers can have drastically different properties—the analgesic ibuprofen, the antidepressant fluoxetine, and the anti-inflammatory agent naproxen (Section 5.13A)
B The sense of smell and how mirror image isomers (e.g., carvone and celery ketone) can smell differently (Section 5.13B and Problem 5.35)
M, B End-of-chapter problems: 5.36, 5.43, 5.49, 5.50, 5.53, 5.55, 5.60, and 5.65–5.71

Chapter 6 Understanding Organic Reactions

B Entropy changes in the metabolism of glucose (Chapter opener and Section 6.4)
B The synthesis of capsaicin by a substitution reaction (Section 6.2)
B Precursors to the female sex hormone estrone (Section 6.2C, Problem 6.2)
G The reaction of gasoline with O_2 (Section 6.9A)
G Refrigeration and spoilage (Section 6.9A)
B Enzymes, biological catalysts (Section 6.11)
B End-of-chapter problems: 6.33, 6.55, and 6.59

Chapter 7 Alkyl Halides and Nucleophilic Substitution

M Flonase, a synthetic steroid used to treat seasonal allergies (Chapter opener)
B, M Telfairine (insecticide) and halomon (antitumor agent), halogenated compounds isolated from red algae (Section 7.1, Problem 7.1)
B, M Simple alkyl halides—chloromethane (found in emissions from volcanoes), dichloromethane (once used to decaffeinate coffee), and halothane (a general anesthetic) (Section 7.4)
E CFCs and DDT, two polyhalogenated compounds once widely used, now discontinued because of adverse environmental effects (Section 7.4)
B, M Maʻilione and plocoralide B, halogenated compounds isolated from red algae (Section 7.4)
B Chondrocole A, a marine natural product isolated from red seaweed (Section 7.4, Problem 7.5)
M The antiseptic CPC (Section 7.6)
M Nucleophilic substitutions in the syntheses of Myambutol (used to treat tuberculosis) and Prozac (an antidepressant) (Section 7.11)
M The synthesis of imatinib, an anticancer drug, by a nucleophilic substitution reaction (Section 7.11, Problem 7.22)
B, M Biological nucleophilic substitution reactions: phosphate leaving groups and *S*-adenosylmethionine (SAM) (Section 7.16)

B The biological synthesis of adrenaline using SAM (Section 7.16)
B The synthesis of nicotine using SAM (Section 7.16, Problem 7.36)
M The importance of organic synthesis in preparing useful drugs such as aspirin (Section 7.18)
B, M End-of-chapter problems: 7.64–7.66, 7.70, 7.76

Chapter 8 Alkyl Halides and Elimination Reactions

E DDE, a degradation product of the pesticide DDT (Chapter opener and Section 8.1)
B Ethylene, a hormone that regulates plant growth and fruit ripening (Section 8.2)
B Classifying alkenes using vitamins A and D (Section 8.2, Problem 8.2)
B Identifying stereoisomerism in alkenes using (*E*)-ocimene, found in lilacs (Section 8.2, Problem 8.4)
B, M Elimination reactions in the syntheses of a prostaglandin, quinine, and estradiol (Section 8.4)
B, M End-of-chapter problems: 8.29 and 8.66

Chapter 9 Alcohols, Ethers, and Related Compounds

B Linalool, an alcohol used in scented soaps and lotions and as an insecticide for controlling fleas and cockroaches (Chapter opener)
B Classifying alcohols using cortisol (Section 9.1)
B Classifying ethers and alcohols using brevenal, a marine natural product formed in red tides (Section 9.1, Problem 9.1)
G, E Ethanol, a gasoline additive and renewable fuel source that can be produced from the fermentation of carbohydrates in grains (Section 9.5A)
G Useful simple alcohols: methanol (wood alcohol), isopropanol (rubbing alcohol), and ethylene glycol (antifreeze) (Section 9.5A)
M Diethyl ether, a general anesthetic (Section 9.5B)
M Sevoflurane, a halogenated ether currently used as a general anesthetic (Section 9.5B)
M Medicinal epoxides: eplerenone (a drug that reduces cardiovascular risk in patients who have already had a heart attack) and tiotropium bromide (a bronchodilator) (Section 9.5C)
M A Williamson ether synthesis in the preparation of paroxetine (antidepressant) (Section 9.6, Problem 9.9)
G The syntheses of vitamin A and patchouli alcohol (used in perfumery) using a dehydration reaction (Section 9.10)
G, B The unpleasant odors related to skunks, onions, and human sweat (Section 9.15A)
B The oxidation of a thiol to a disulfide using grapefruit mercaptan (Section 9.15A, Problem 9.31)
B The synthesis of SAM from methionine and ATP by an S_N2 reaction (Section 9.15B)
M The syntheses of salmeterol and albuterol (two bronchodilators) by the opening of an epoxide ring (Section 9.16)
M The design of asthma drugs that block the synthesis of leukotrienes, highly potent molecules that contribute to the asthmatic response (Section 9.17)
B The metabolism of polycyclic aromatic hydrocarbons (PAHs) to carcinogens that disrupt normal cell function, resulting in cancer or cell death (Section 9.18)
M End-of-chapter problems: 9.49, 9.73, and 9.81

Chapter 10 Alkenes

B The unsaturated fatty acids found in kukui nuts (Chapter opener)
M Degrees of unsaturation in the drugs Ambien and mefloquine (Section 10.2, Problem 10.3)
B 11-*cis*-Retinal, the light-sensitive aldehyde involved in the vision of all vertebrates, arthropods, and mollusks (Section 10.3B, Problem 10.7)
B The sex pheromone of the codling moth (Section 10.3B, Problem 10.9)
G Ethylene, the starting material for preparing polyethylene and a variety of other polymers (Section 10.5)
B The naturally occurring alkenes β-carotene, zingiberene, (*R*)-limonene, and α-farnesene (Section 10.5)
B Triacylglycerols, fatty acids, fats, and oils (Section 10.6)
B Omega-3 fatty acids (Section 10.6, Problem 10.11)
B The synthesis of the female sex hormone estrone (Section 10.15B)
M The synthesis of artemisinin, an antimalarial drug, by a hydroboration–oxidation step (Section 10.16B)
B, M End-of-chapter problems: 10.37, 10.43, 10.44, 10.45, 10.69, and 10.71

Chapter 11 Alkynes

M Oral contraceptives (Chapter opener and Section 11.4)
B Nepheliosyne B, a novel acetylenic fatty acid (Section 11.1, Problem 11.1)
M Synthetic hormones mifepristone and Plan B, drugs that prevent pregnancy (Section 11.4)
B Histrionicotoxin, a diyne isolated from the skin of a frog, used as a poison on arrow tips by the Choco tribe of South America (Section 11.4)
B Acetylide anion reactions in the synthesis of two marine natural products (Section 11.11)
M, B End-of-chapter problems: 11.25 and 11.43

Chapter 12 Oxidation and Reduction

B The metabolism of ethanol, the alcohol in alcoholic beverages (Chapter opener and Section 12.14)
B The partial hydrogenation of vegetable oils and the formation of "trans fats" (Section 12.4)
B The reduction of an alkyne to form *cis*-jasmone, a component of perfume (Section 12.5B, Problem 12.10)
B The use of disparlure, a sex hormone, in controlling the spread of gypsy moths (Section 12.8B)
G The production of ozone from O_2 during electrical storms (Section 12.10)
G Blood alcohol screening (Section 12.12)
E Green chemistry—environmentally benign oxidation reactions (Section 12.13)
B Biological oxidations (Section 12.14)
B The synthesis of insect pheromones using asymmetric epoxidation (Section 12.15)
B, M End-of-chapter problems: 12.37, 12.41, 12.51, 12.53, 12.55, 12.56, 12.60, and 12.61

Chapter 13 Mass Spectrometry and Infrared Spectroscopy

M Infrared spectroscopy and the structure determination of penicillin (Chapter opener and Section 13.8)
M Applying the nitrogen rule to 3-methylfentanyl and MPPP, two drugs that mimic the effects of heroin (Section 13.1)
B Determining the molecular formula of nootkatone (found in grapefruit) (Section 13.1, Problem 13.3)
M Using instrumental analysis to detect THC, the active compound in marijuana, and other drugs (Section 13.4B)
B Mass spectrometry and high molecular weight biomolecules (Section 13.4C)
B End-of-chapter problems: 13.29, 13.30, 13.44, and 13.62

Chapter 14 Nuclear Magnetic Resonance Spectroscopy

B Modern spectroscopic methods and the structure of palau'amine, a complex natural product isolated from a sea sponge (Chapter opener and Problem 14.23)
E The high-octane gasoline additive MTBE, which has contaminated water supplies (Section 14.1B)
B Esters of chrysanthemic acid (from chrysanthemum flowers) as insecticides (Section 14.11, Problem 14.29)
M Magnetic resonance imaging (Section 14.12)
B End-of-chapter problem: 14.37

Chapter 15 Radical Reactions

G Polystyrene, a common synthetic polymer used in packaging materials and beverage cups (Chapter opener)
E Ozone destruction and CFCs (Section 15.9)
B The oxidation of unsaturated lipids by radical reactions (Section 15.11)
M, B Two antioxidants—naturally occurring vitamin E and synthetic BHT (Section 15.12)
B The antioxidant rosmarinic acid (Section 15.12)
G The formation of useful polymers from monomers by radical reactions (Section 15.14)
B, G, M End-of-chapter problems: 15.63, 15.66–15.70, and 15.79

Chapter 16 Conjugation, Resonance, and Dienes

M The laboratory synthesis of morphine by a Diels–Alder reaction (Chapter opener)
B Allylic carbocations in biological reactions, such as the formation of geranyl diphosphate (Section 16.2B)
B Isoprene, a conjugated compound that helps plants tolerate heat stress (Section 16.7)
M The antioxidant lycopene (Sections 16.7 and 16.15A)
M Simvastatin (Zocor) and calcitriol (Rocaltrol), two drugs with conjugated double bonds (Section 16.7)
B The synthesis of tetrodotoxin (found in Japanese puffer fish) by a Diels–Alder reaction (Section 16.12)
B The trienes zingiberene and β-sesquiphellandrene found in ginger root (Section 16.13A, Problem 16.21)
B The Diels–Alder reaction in the synthesis of steroids (Section 16.14C)
G Why lycopene and other highly conjugated compounds are colored (Section 16.15A)
G How sunscreens work (Section 16.15B)
B, M End-of-chapter problems: 16.54, 16.61, 16.69, 16.73, and 16.75

Chapter 17 Benzene and Aromatic Compounds

B, M Capsaicin, the spicy component of hot peppers and the active ingredient in topical creams for the treatment of chronic pain (Chapter opener)
G Polycyclic aromatic hydrocarbons (PAHs), constituents of cigarette smoke and diesel exhaust (Section 17.5)
M Examples of common drugs that contain an aromatic ring—Zoloft, Valium, Novocain, Viracept, Viagra, and Claritin (Section 17.5)
B Histamine and scombroid fish poisoning (Section 17.8)
M Quinine, an antimalarial drug (Section 17.8, Problem 17.13)
M Januvia, a drug used to treat type 2 diabetes (Section 17.8, Problem 17.14)
G Diamond, graphite, and buckminsterfullerene (Section 17.11)
M, B End-of-chapter problems: 17.37, 17.57, 17.60–17.63, and 17.67

Chapter 18 Reactions of Aromatic Compounds

B Vitamin K_1, a fat-soluble vitamin that regulates the synthesis of proteins needed for blood to clot (Chapter opener and Section 18.5E)
M, E Biologically active aryl chlorides: the drugs bupropion and chlorpheniramine, and 2,4-D and 2,4,5-T, herbicide components of the defoliant Agent Orange (Section 18.3)
M Intramolecular Friedel–Crafts acylation in the synthesis of LSD (Section 18.5D)
M The synthesis of sertraline (Zoloft), an SSRI antidepressant (Section 18.5D, Problem 18.10)
B A biological Friedel–Crafts reaction (Section 18.5E)
M Nucleophilic aromatic substitution by addition–elimination in the synthesis of Prozac (Section 18.13A, Problem 18.25)
M Benzocaine, the active ingredient in the over-the-counter topical anesthetic Orajel (Section 18.15C)
M, G, B End-of-chapter problems: 18.42–18.44, 18.61, 18.63, 18.67, 18.68, 18.70, 18.73, and 18.77

Chapter 19 Carboxylic Acids and the Acidity of the O–H Bond

B The essential amino acid lysine (Chapter opener)
B Hexanoic acid, the foul-smelling carboxylic acid in ginkgo seeds (Section 19.2B)
B Biologically significant diacids: oxalic acid, malonic acid, and succinic acid (Section 19.2C)
M Depakote (used to treat seizures) (Section 19.2C, Problem 19.5)
B Biologically significant carboxylic acids: formic acid (ant stings), acetic acid (vinegar), butanoic acid (body odor), oxalic acid (spinach), and lactic acid (sour milk) (Section 19.5)
B GHB (4-hydroxybutanoic acid), an illegal recreational intoxicant used as a “date rape” drug (Section 19.5)
M Isotretinoin, a fatty acid used to treat severe acne (Section 19.5, Problem 19.8)
M, B How NSAIDs block the synthesis of prostaglandins to prevent inflammation (Section 19.6)
B Mandelic acid, a naturally occurring carboxylic acid in plums and peaches (Section 19.9, Problem 19.15)
M The irritant urushiol in poison ivy (Section 19.11, Problem 19.19)
B An introduction to amino acids, the building blocks of proteins; why vegetarians must have a balanced diet (Section 19.14)
B, M End-of-chapter problems: 19.31, 19.41, 19.52, 19.62–19.68, 19.71, and 19.72

Chapter 20 Introduction to Carbonyl Chemistry; Organometallic Reagents; Oxidation and Reduction

B The use of a reduction reaction to synthesize the marine neurotoxin ciguatoxin CTX3C (Chapter opener and Section 20.7A)
B The aldehyde α-sinensal, a component of mandarin oil (Section 20.1, Problem 20.1)
M The anticancer drug Taxol and nucleophilic substitution (Section 20.2, Problem 20.2)
B, M Reduction reactions in the synthesis of the analgesic ibuprofen and the perfume component muscone (Section 20.4)
M The synthesis of the long-acting bronchodilator salmeterol (Section 20.6A)
M The use of CBS reagents in the synthesis of cholesterol-lowering drugs (Section 20.6A, Problem 20.9)
B Biological oxidation–reduction reactions with the coenzymes NADH and NAD^+ (Section 20.6B)
B The synthesis of NAD^+ from the vitamin niacin (Section 20.6B)
M The use of organometallic reagents to synthesize the oral contraceptive ethynylestradiol (Section 20.10C)
B The use of Grignard reagents in the synthesis of C_{18} juvenile hormones and the use of juvenile hormone mimics to regulate the life cycle of insects (Section 21.10C)
B The use of organolithium reagents in the synthesis of two components of lavender oil (Section 20.11, Problem 20.24)
M The use of protecting groups in the conversion of estrone to ethynylestradiol (Section 20.12, Problem 20.26)
M, B End-of-chapter problems: 20.50, 20.56, 20.61, 20.68, 20.75, and 20.78

Chapter 21 Aldehydes and Ketones—Nucleophilic Addition

M Digitoxin, a naturally occurring drug isolated from the woolly foxglove plant and used to treat congestive heart failure (Chapter opener and Problem 21.37)
B Determining the IUPAC names of neral (from lemon grass) and cucumber aldehyde (Section 21.2E, Problem 21.7)
G Formaldehyde and acetone, an industrially useful aldehyde and ketone (Section 21.5)
B Examples of naturally occurring compounds that contain aldehydes or ketones—vanillin, citronellal, cinnamaldehyde, and geranial (Section 21.5)
M Cortisone and prednisone, steroids that contain ketones (Section 21.5)
B Naturally occurring cyanohydrin derivatives: linamarin, from cassava root; and amygdalin, from apricot, peach, and wild cherry pits (Section 21.9B)
B The use of the Wittig reaction in the synthesis of β-carotene, the orange pigment in carrots (Section 21.10B)
B The role of rhodopsin in the chemistry of vision (Section 21.11B)

B The acid-catalyzed hydrolysis of safrole, a carcinogen once used in root beer (Section 21.14B, Problem 21.33)
B, M The acid-catalyzed hydrolysis of the acetal in oleandrin (Section 21.14B, Problem 21.34)
B The carbohydrates glucose and lactose (Section 21.17)
M The role of carbohydrates in diabetes (Section 21.17)
B The carbohydrate galactose (Section 21.17, Problem 21.39)
M, B End-of-chapter problems: 21.52, 21.65, 21.69–21.71, 21.79, 21.80, 21.82, and 21.84–21.86

Chapter 22 Carboxylic Acids and Their Derivatives—Nucleophilic Acyl Substitution

B, M Ginkgolide B, a major constituent of the extracts of the ginkgo tree, *Ginkgo biloba* (Chapter opener and Problem 22.21)
B The esters responsible for the odors of banana, mango, and pineapple (Section 22.6A)
M, B Compounds that contain an ester: vitamin C, cocaine, and the immunosuppressant FK506 (Section 22.6A)
M, B Useful amides: proteins, met-enkephalin, the anticancer drug Gleevec, the penicillin antibiotics, and the cephalosporin antibiotics (Section 22.6B)
G The synthesis of the insect repellant DEET (Section 22.8)
B Mechanism for the synthesis of blattellaquinone, the sex pheromone of the female German cockroach (Section 22.8, Problem 22.13)
M Acylation in the syntheses of aspirin, acetaminophen, and heroin (Section 22.9)
M The cholesterol-lowering drug fenofibrate (Section 22.11B, Problem 22.20)
B The hydrolysis of triacylglycerols in the metabolism of lipids (Section 22.12A)
G Olestra, a fake fat (Section 22.12A)
G The synthesis of soap (Section 22.12B)
M The mechanism of action of β-lactam antibiotics like penicillin (Section 22.14)
G Natural and synthetic fibers: nylon and polyesters (Section 22.16)
B Biological acylation reactions (Section 22.17)
M Cholesteryl esters in plaque, the deposits that form on the inside walls of arteries (Section 22.17)
B The acylation of glucosamine to form NAG, the monomer in chitin (Section 22.17, Problem 22.30)
B, M End-of-chapter problems: 22.48, 22.52, 22.53, 22.56–22.61, 22.67, 22.68, 22.72, 22.77, and 22.83–22.85

Chapter 23 Substitution Reactions of Carbonyl Compounds at the α Carbon

M The synthesis of the anticancer drug tamoxifen (Chapter opener and Section 23.8C)
B Keto–enol tautomerizations in glycolysis (Section 23.2A, Problem 23.2)
M The synthesis of the antimalarial drug quinine by an intramolecular substitution reaction (Section 23.7C)
M The heterocyclic ring system in some antitumor agents (Section 23.8C, Problem 23.19)
M The use of the acetoacetic ester synthesis in the synthesis of illudin-S, an antitumor agent (Section 23.10, Problem 23.27)
M Retrosynthesis of the pain reliever nabumetone (Section 23.10, Problem 23.28)
B, M End-of-chapter problems: 23.38, 23.40, 23.45, 23.53, 23.54, 23.61, 23.64, 23.68, 23.72, and 23.74

Chapter 24 Carbonyl Condensation Reactions

M The synthesis of ibuprofen (Chapter opener and Problem 24.20)
B The perfume component flosal, an α,β-unsaturated aldehyde (Section 24.2B, Problem 24.6)
B The synthesis of periplanone B, sex pheromone of the female American cockroach (Section 24.3)
B The synthesis of *ar*-turmerone, a component of turmeric, a principal ingredient in curry powder (Section 24.3)
B The conversion of zingerone to gingerol, components of ginger, using a directed aldol reaction (Section 24.3, Problem 24.11)
M A directed aldol reaction in the synthesis of the drug donepezil (for treating dementia) (Section 24.3, Problem 24.12)
B The synthesis of the steroid progesterone by an intramolecular aldol reaction (Section 24.4)
M Avobenzone, a common ingredient in commercial sunscreens (Section 24.6A, Problem 24.18)
B The synthesis of the female sex hormone estrone by a Michael reaction (Section 24.8)
M, B End-of-chapter problems: 24.34, 24.44, 24.50, 24.53–24.56, 24.58, 24.66, 24.72, and 24.73

Chapter 25 Amines

M Scopolamine, an alkaloid used to treat the nausea and vomiting associated with motion sickness (Chapter opener)
M The stereogenic centers in dobutamine, an amine used in stress tests (Section 25.2, Problem 25.1)
B Poisonous diamines with putrid odors: putrescine and cadaverine (Section 25.6A)
B Naturally occurring alkaloids: atropine, nicotine, and coniine (Section 25.6A)
M Histamine, antihistamines, and antiulcer drugs like Tagamet (cimetidine) (Section 25.6B)
B, M Biologically active derivatives of 2-phenylethanamine: adrenaline, noradrenaline, methamphetamine, mescaline, and dopamine (Section 25.6C)
B, M The neurotransmitter serotonin and SSRI antidepressants (Section 25.6C)
B Bufotenin and psilocin (hallucinogens) (Section 25.6C)

M The synthesis of methamphetamine (Section 25.7C)
M The synthesis of enalapril, an antihypertensive, by reductive amination (Section 25.7C, Problem 25.14)
M The synthesis of the drugs rimantadine and pseudoephedrine by reductive amination (Section 25.7C, Problem 25.15)
M The systematic name of a component of the diet drug fen–phen (Section 25.7C, Problem 25.16)
M Drugs, such as the antihistamine diphenhydramine, sold as water-soluble ammonium salts (Section 25.9)
M Hybridization effects on the basicity of nicotine (Section 25.10E, Problem 25.22)
M Acid–base properties of the drugs chloroquine, matrine, tacrine, and quinine (Section 25.10F and Problem 25.23)
G Azo dyes (Section 25.15)
G Perkin's mauveine and synthetic dyes (Section 25.16A)
M Sulfa drugs (Section 25.16B)
M End-of-chapter problems: 25.37, 25.42, 25.44, 25.54, 25.57, 25.58, 25.68, 25.70, 25.77, and 25.78

Chapter 26 Carbon–Carbon Bond-Forming Reactions in Organic Synthesis

M Ingenol mebutate, used to treat the skin condition actinic keratosis (Chapter opener and Section 26.6, Problem 26.16)
B The synthesis of C_{18} juvenile hormone (Section 26.1A, Problem 26.2)
B, E Use of the Suzuki reaction to prepare bombykol, the sex pheromone of the female silkworm moth, and humulene, a lipid isolated from hops (Section 26.2B)
E Pyrethin I, a biodegradable insecticide isolated from chrysanthemums, and decamethrin, a synthetic analogue (Section 26.4)
M Ring-closing metathesis and the synthesis of epothilone A, an anticancer drug, and Sch38516, an antiviral agent (Section 26.6)
M, B, G End-of-chapter problems: 26.25, 26.26, 26.33, 26.37, 26.38, 26.50

Chapter 27 Pericyclic Reactions

B One synthesis of periplanone B (sex pheromone of the female American cockroach) using pericyclic reactions (Chapter opener and Section 27.5B, Problem 27.22)
B The role of photochemical electrocyclic ring opening and sigmatropic rearrangements in the formation of vitamin D_3 from 7-dehydrocholesterol (Section 27.3C, Problem 27.9)
M The synthesis of the alkaloid reserpine by a [4 + 2] cycloaddition reaction (Section 27.4B, Problem 27.15)
M Garsubellin A and the synthesis of the neurotransmitter acetylcholine (Section 27.5B, Problem 27.25)
B End-of-chapter problems: 27.43, 27.48, and 27.62

Chapter 28 Carbohydrates

B Solanine, the defensive toxin found in the leaves, stems, and green spots of potatoes (Chapter opener and Section 28.7C)
B The use of fructose in "lite" foods (Section 28.2)
B Dihydroxyacetone, the active ingredient in many artificial tanning agents (Section 28.2)
B Glucose, the most common simple sugar (Section 28.6)
G Honey, a mixture of D-fructose and D-glucose (Section 28.6D)
B, M The naturally occurring glycosides salicin and solanine (Section 28.7C)
G Rebaudioside A, a sweet glycoside from the stevia plant (Section 28.7C, Problem 28.19)
B Glucitol (sorbitol), a sucrose substitute (Section 28.9A)
B The common disaccharides maltose, lactose, and sucrose (Section 28.11)
M Lactose intolerance (Section 28.11B)
G Artificial sweeteners (Section 28.11C)
B The common polysaccharides cellulose, starch, and glycogen (Section 28.12)
B, M Glucosamine, an over-the-counter remedy for osteoarthritis, and chitin, the carbohydrate that gives rigidity to crab shells (Section 28.13A)
B *N*-Glycosides and the structure of DNA (Section 28.14B)
B, M End-of-chapter problems: 28.66 and 28.69

Chapter 29 Amino Acids and Proteins

B Myoglobin, the protein that stores oxygen in tissues (Chapter opener and Section 29.10C)
B The naturally occurring amino acids (Section 29.1)
M L-Thyroxine, used to treat thyroid hormone deficiency (Section 29.1B, Problem 29.4)
B The structures of the hormones bradykinin, oxytocin, and vasopressin (Section 29.5C)
B The artificial sweetener aspartame (Section 29.5C)
B The amino acid sequence of leu-enkephalin, an analgesic and opiate (Section 29.5C, Problem 29.17)
B The structure of glutathione, a powerful antioxidant in cells (Section 29.5C, Problem 29.18)
B The Merrifield method of automated protein synthesis (Section 29.8)
B The structures of lysozyme and spider silk (Section 29.9B)

M The structure of insulin (Section 29.9C)
B α-Keratin, the protein in hair, hooves, nails, skin, and wool (Section 29.10A)
B Collagen, the protein in connective tissue (Section 29.10B)
B, M Hemoglobin and the structure of sickle cell hemoglobin (Section 29.10C)
M, B End-of-chapter problems: 29.32, 29.46, 29.48, 29.50, 29.54, 29.56, 29.67, and 29.70

Chapter 30 Synthetic Polymers

G Polyethylene terephthalate, an easily recycled synthetic polymer used in transparent soft drink containers (Chapter opener and Sections 30.6B and 30.9A)
G Consumer products made from Lexan, nylon 6,6, rubber, and polyethylene (Section 30.1)
G Polyethylene, the plastic in milk jugs and plastic bags, and other chain-growth polymers (Section 30.2)
G ABS, a copolymer used in crash helmets, small appliances, and toys (Section 30.3, Problem 30.11)
G Using Ziegler–Natta catalysts to make high-density polyethylene (Section 30.4)
G Dyneema, a strong fiber made of ultra high-density polyethylene (Section 30.4)
B Natural and synthetic rubber (Section 30.5)
G The synthesis of the step-growth polymers nylon, Kevlar, Dacron, spandex, and Lexan (Section 30.6)
M Dissolving sutures (Section 30.6B)
E Polyethylene furanoate, a polymer synthesized from renewable resources (Section 30.6B, Problem 30.16)
G Spandex for active wear (Section 30.6C)
G Lexan for bike helmets, goggles, catcher's masks, and bulletproof glass (Section 30.6D)
G Epoxy resins (Section 30.6E)
G Bakelite for bowling balls (Section 30.7)
E Green polymer synthesis: environmentally benign methods for preparing polymers (Section 30.8)
E Polymer recycling (Section 30.9A)
E Biodegradable polymers (Section 30.9B)
G, E, M End-of-chapter problems: 30.34, 30.35, 30.50, 30.52, and 30.56–30.58

Chapter 31 Lipids (Available online)

B Cholesterol, the most prominent steroid (Chapter opener and Section 31.8B)
B Structure of spermaceti wax (Section 31.2)
B Waxes obtained from jojoba seeds that are used in cosmetics and personal care products (Section 31.2, Problem 31.1)
B Triacylglycerols, the components of fats and oils (Section 31.3)
B Essential fatty acids (Section 31.3)
B The saturated versus unsaturated fatty acid content of fats and oils (Section 31.3)
B Energy storage and the metabolism of fats (Section 31.3)
B The phospholipids in cell membranes (Section 31.4)
B Fat-soluble vitamins: A, D, E, and K (Section 31.5)
B The eicosanoids, a group of biologically active lipids that includes the prostaglandins and leukotrienes (Section 31.6)
M Misoprostol, an analogue of PGE_1 used to prevent gastric ulcers, and unoprostone isopropyl, a prostaglandin analogue used to treat glaucoma (Section 31.6)
M NSAIDs like aspirin and ibuprofen and the COX-1 and COX-2 enzymes (Section 31.6)
M The anti-inflammatory drugs Vioxx, Bextra, and Celebrex (Section 31.6)
B Essential oils that are terpenes and terpenoids (Section 31.7)
B Locating isoprene units in geraniol, vitamin A, grandisol (pheromone), and camphor (Section 31.7, Problem 31.10)
B Biformene, a terpenoid from amber (Section 31.7, Problem 31.11)
B, M The structures of steroids: cholesterol, sex hormones (female and male), adrenal cortical steroids, anabolic steroids, and oral contraceptives (Section 31.8)
M Cholesterol and the cholesterol-lowering drugs Lipitor and Zocor (Section 31.8B)
B, M Anabolic steroids (Section 31.8C)
B, M End-of-chapter problems: 31.20, 31.26–31.28, 31.30, 31.31, 31.35, 31.36, and 31.39

Prologue

What is organic chemistry?
Some representative organic molecules
Organic chemistry and malaria

Organic chemistry. You might wonder how a discipline that conjures up images of eccentric old scientists working in basement laboratories is relevant to you, a student in the twenty-first century.

Consider for a moment the activities that occupied your past 24 hours. You likely showered with soap, drank a caffeinated beverage, ate at least one form of starch, took some medication, listened to a CD, and traveled in a vehicle that had rubber tires and was powered by fossil fuels. If you did any *one* of these, your life was touched by organic chemistry.

What Is Organic Chemistry?

- Organic chemistry is the chemistry of compounds that contain the element carbon.

It is one branch in the entire field of chemistry, which encompasses many classical subdisciplines including inorganic, physical, and analytical chemistry, and newer fields such as bioinorganic chemistry, physical biochemistry, polymer chemistry, and materials science.

Some compounds that contain the element carbon are *not* organic compounds. Examples include carbon dioxide (CO_2), sodium carbonate (Na_2CO_3), and sodium bicarbonate ($NaHCO_3$).

Organic chemistry was singled out as a separate discipline for historical reasons. Originally, it was thought that compounds in living things, termed ***organic compounds,*** were fundamentally different from those in nonliving things, called ***inorganic compounds.*** Although we have known for more than 150 years that this distinction is artificial, the name *organic* persists. Today the term refers to the study of the compounds that contain carbon, many of which, incidentally, are found in living organisms.

It may seem odd that a whole discipline is devoted to the study of a single element in the periodic table, when more than 100 elements exist. It turns out, though, that there are far more organic compounds than any other type. **Organic chemicals affect virtually every facet of our lives, and for this reason, it is important and useful to know something about them.**

Clothes, foods, medicines, gasoline, refrigerants, and soaps are composed almost solely of organic compounds. Some, like cotton, wool, or silk are naturally occurring; that is, they can be isolated directly from natural sources. Others, such as nylon and polyester, are synthetic, meaning they are produced by chemists in the laboratory. By studying the principles and concepts of organic chemistry, you can learn more about compounds such as these and how they affect the world around you.

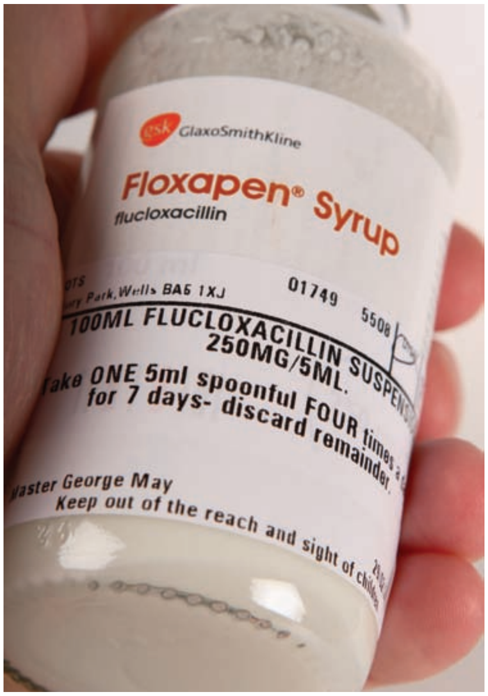
Realize, too, what organic chemistry has done for us. Organic chemistry has made available both comforts and necessities that were previously nonexistent, or reserved for only the wealthy. We have seen an enormous increase in life span, from 47 years in 1900 to over 70 years currently. To a large extent this is due to the isolation and synthesis of new drugs to fight infections and the availability of vaccines for childhood diseases. Chemistry has also given us the tools to control insect populations that spread disease, and there is more food for all because of fertilizers, pesticides, and herbicides. Our lives would be vastly different today without the many products that result from organic chemistry (Figure 1).

Figure 1
Products of organic chemistry used in medicine

a. Oral contraceptives

b. Plastic syringes

c. Antibiotics

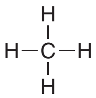


d. Synthetic heart valves

- Organic chemistry has given us contraceptives, plastics, antibiotics, and the knitted material used in synthetic heart valves.

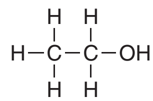
Some Representative Organic Molecules

Perhaps the best way to appreciate the variety of organic molecules is to look at a few. Three simple organic compounds are **methane, ethanol,** and **trichlorofluoromethane.**

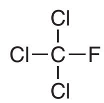


methane

- **Methane,** the simplest of all organic compounds, contains one carbon atom. Methane—the main component of natural gas—occurs widely in nature. Like other **hydrocarbons**—organic compounds that contain only carbon and hydrogen—methane is combustible; that is, it burns in the presence of oxygen. Methane is the product of the anaerobic (without air) decomposition of organic matter by bacteria. The natural gas we use today was formed by the decomposition of organic material millions of years ago. Hydrocarbons such as methane are discussed in Chapter 4.



ethanol



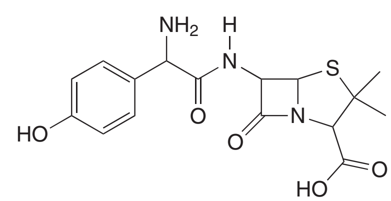
trichlorofluoromethane

- **Ethanol,** the alcohol present in beer, wine, and other alcoholic beverages, is formed by the fermentation of sugar, quite possibly the oldest example of organic synthesis. Ethanol can also be made in the lab by a totally different process, but **the ethanol produced in the lab is *identical* to the ethanol produced by fermentation.** Alcohols including ethanol are discussed in Chapter 9.
- **Trichlorofluoromethane** is a member of a class of molecules called **c**hloro**f**luoro**c**arbons or **CFCs,** which contain one or two carbon atoms and several halogens. Trichlorofluoromethane is an unusual organic molecule in that **it contains no hydrogen atoms.** Because it has a low molecular weight and is easily vaporized, trichlorofluoromethane has been used as an aerosol propellant and refrigerant. It and other CFCs have been implicated in the destruction of the stratospheric ozone layer, a topic discussed in Chapter 15.

Three complex organic molecules that are important medications are **amoxicillin, fluoxetine,** and **AZT.**

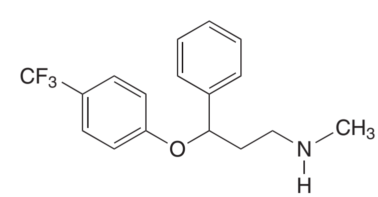
- **Amoxicillin** is one of the most widely used antibiotics in the penicillin family. The discovery and synthesis of such antibiotics in the twentieth century have made routine the treatment of infections that were formerly fatal. You were likely given some amoxicillin to treat an ear infection when you were a child. The penicillin antibiotics are discussed in Chapter 22.

Complex organic structures are drawn with shorthand conventions described in Chapter 1.



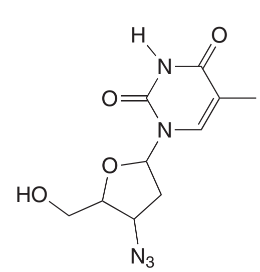
amoxicillin

- **Fluoxetine** is the generic name for the antidepressant **Prozac.** Prozac was designed and synthesized by chemists in the laboratory, and is now produced on a large scale in chemical factories. Because it is safe and highly effective in treating depression, Prozac is widely prescribed. Over 40 million individuals worldwide have used Prozac since 1986.



fluoxetine

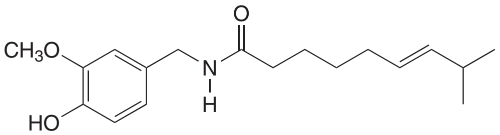
- **AZT, az**idodeoxy**t**hymidine, is a drug that treats human immunodeficiency virus (HIV), the virus that causes acquired immune deficiency syndrome (AIDS). Also known by its generic name **zidovudine,** AZT represents a chemical success to a different challenge: synthesizing agents that combat viral infections.



AZT

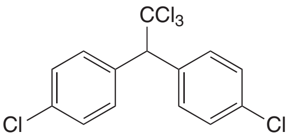
Other complex organic compounds having interesting properties are **capsaicin** and **DDT.**

- **Capsaicin,** one member of a group of compounds called *vanilloids,* is responsible for the characteristic spiciness of hot peppers. It is the active ingredient in pepper sprays used for personal defense and topical creams used for pain relief.



capsaicin

- **DDT, d**ichloro**d**iphenyl**t**richloroethane, is a pesticide once called "miraculous" by Winston Churchill because of the many lives it saved by killing disease-carrying mosquitoes. DDT use is now banned in the United States and many developed countries because it is a non-specific insecticide that persists in the environment.



DDT

What are the common features of these organic compounds?

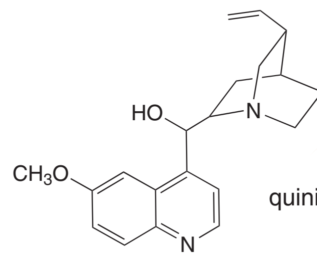
- All organic compounds contain carbon atoms and most contain hydrogen atoms.
- All the carbon atoms have four bonds. A stable carbon atom is said to be *tetravalent*.
- Other elements may also be present. Any atom that is not carbon or hydrogen is called a *heteroatom*. Common heteroatoms include N, O, S, P, and the halogens.
- Some compounds have chains of atoms and some compounds have rings.

These features explain why there are so many organic compounds: **Carbon forms four strong bonds with itself and other elements. Carbon atoms combine together to form rings and chains.**

Organic Chemistry and Malaria

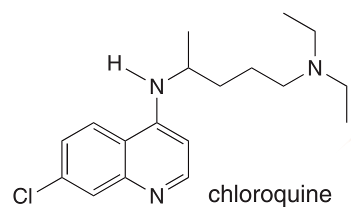
A vast array of organic compounds is now available to fight malaria, a mosquito-borne infectious disease that affects an estimated 200 million people worldwide. Antimalarial medications include organic compounds isolated from natural sources or those synthesized by chemists in the laboratory. Two common antimalarial drugs shown in Figure 2 are **quinine,** a centuries-old remedy obtained from the bark of the cinchona tree native to the Andes Mountains, and **chloroquine,** a synthetic drug introduced in the late 1940s.

Figure 2
Antimalarial drugs



quinine

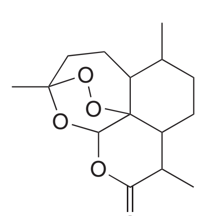
buds and leaves of *Cinchona pubescens*



chloroquine

Because malaria is caused by a variety of closely related parasitic microorganisms and drug-resistant strains have developed, currently recommended therapy consists of a combination of drugs that includes **artemisinin** or a related compound. Artemisinin is a complex compound isolated from sweet wormwood, *Artemisia annua,* a plant used for hundreds of years in traditional Chinese medicine. Although artemisinin can be obtained by extracting the active drug from the dried leaves of *Artemisia annua,* this process does not meet the worldwide demand. As a result, artemisinin can now be obtained using genetic engineering and fermentation processes.

The 2015 Nobel Prize in Physiology or Medicine was awarded to Youyou Tu for her discovery of artemisinin as an antimalarial drug.



artemisinin

Artemisia annua, sweet wormwood

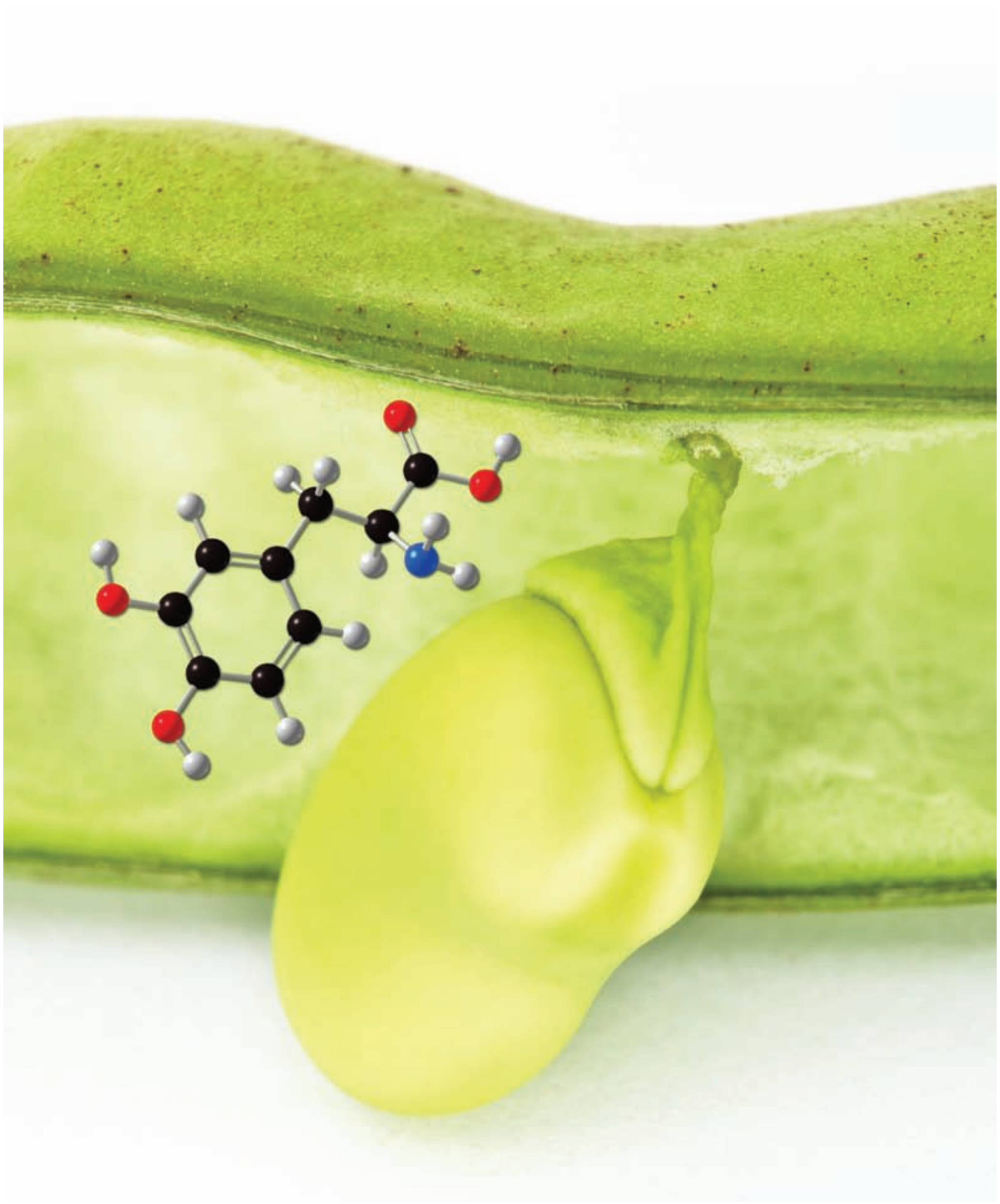
Malaria continues to present a major public health challenge for chemists, health professionals, and biologists. Despite extensive efforts to prevent and control the disease in the equatorial regions of Asia, Africa, and Latin America, it is estimated that malaria was responisble for over 450,000 deaths in 2012.

In this introduction, we have seen a variety of molecules that have diverse structures. They represent a miniscule fraction of the organic compounds currently known and the many thousands that are newly discovered or synthesized each year. The principles you learn in organic chemistry will apply to all of these molecules, from simple ones like methane and ethanol, to complex ones like capsaicin and artemisinin. It is these beautiful molecules, their properties, and their reactions that we will study in organic chemistry.

WELCOME TO THE WORLD OF ORGANIC CHEMISTRY!

Structure and Bonding

1



L-Dopa, also called levodopa, was first isolated from seeds of the broad bean plant *Vicia faba* in 1913. Since 1967 it has been the drug of choice for the treatment of Parkinson's disease, a debilitating illness that results from the degeneration of neurons that produce the neurotransmitter dopamine in the brain. L-Dopa is an oral medication that is transported to the brain by the bloodstream, where it is converted to dopamine. Since L-dopa must be taken in large doses with some serious side effects, today it is often given with other drugs that lessen its negative impact. In Chapter 1, we learn about the structure, bonding, and properties of organic molecules like L-dopa.

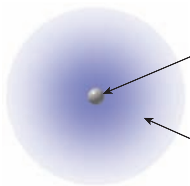
Before examining organic molecules in detail, we must review topics about structure and bonding learned in previous chemistry courses. We will discuss these concepts primarily from an organic chemist's perspective, and spend time on only the particulars needed to understand organic compounds.

Important topics in Chapter 1 include drawing Lewis structures, predicting the shape of molecules, determining what orbitals are used to form bonds, and how electronegativity affects bond polarity. Equally important is Section 1.8 on drawing organic molecules, both shorthand methods routinely used for simple and complex compounds, as well as three-dimensional representations that allow us to more clearly visualize them.

1.1 The Periodic Table

All matter is composed of the same building blocks called **atoms.** There are two main components of an atom.

- The **nucleus** contains positively charged **protons** and uncharged **neutrons.** Most of the mass of the atom is contained in the nucleus.
- The **electron cloud** is composed of negatively charged **electrons.** The electron cloud comprises most of the volume of the atom.



The charge on a proton is equal in magnitude but opposite in sign to the charge on an electron. In a neutral atom, the **number of protons in the nucleus equals the number of electrons.** This quantity, called the **atomic number,** is unique to a particular element. For example, every neutral carbon atom has an atomic number of six, meaning it has six protons in its nucleus and six electrons surrounding the nucleus.

In addition to neutral atoms, we will also encounter **charged ions.**

- A *cation* is positively charged and has fewer electrons than protons.
- An *anion* is negatively charged and has more electrons than protons.

The number of neutrons in the nucleus of a particular element can vary. **Isotopes** are two atoms of the same element having a different number of neutrons. The **mass number** of an atom is the total number of protons and neutrons in the nucleus. Isotopes have different mass numbers. The **atomic weight** of a particular element is the weighted average of the mass of all its isotopes, reported in atomic mass units (amu).

Isotopes of carbon and hydrogen are sometimes used in organic chemistry. The most common isotope of hydrogen has one proton and no neutrons in the nucleus, but 0.02% of hydrogen atoms have one proton and one neutron. This isotope of hydrogen is called **deuterium,** and is sometimes symbolized by the letter **D.**

Each atom is identified by a one- or two-letter abbreviation that is the characteristic symbol for that element. Carbon is identified by the single letter **C.** Sometimes the atomic number is indicated as a subscript to the left of the element symbol, and the mass number is indicated as a superscript. Using this convention, the most common isotope of carbon, which contains six protons and six neutrons, is designated as ${}^{12}_{6}C$.

A **row** in the periodic table is also called a ***period,*** and a **column** is also called a ***group.*** A periodic table is located on the inside front cover for your reference.

Long ago it was realized that groups of elements have similar properties, and that these atoms could be arranged in a schematic way called the **periodic table.** There are more than 100 known elements, arranged in the periodic table in order of increasing atomic number. The periodic table is composed of rows and columns.

- **Elements in the same row are similar in *size.***
- **Elements in the same column have similar *electronic and chemical properties.***

Each column in the periodic table is identified by a **group number,** an Arabic (1 to 8) or Roman (I to VIII) numeral followed by the letter A or B. Carbon is located in group **4A** in the periodic table in this text.

Although more than 100 elements exist, most are not common in organic compounds. Figure 1.1 contains a truncated periodic table, indicating the handful of elements that are routinely seen in this text. **Most of these elements are located in the first and second rows of the periodic table.**

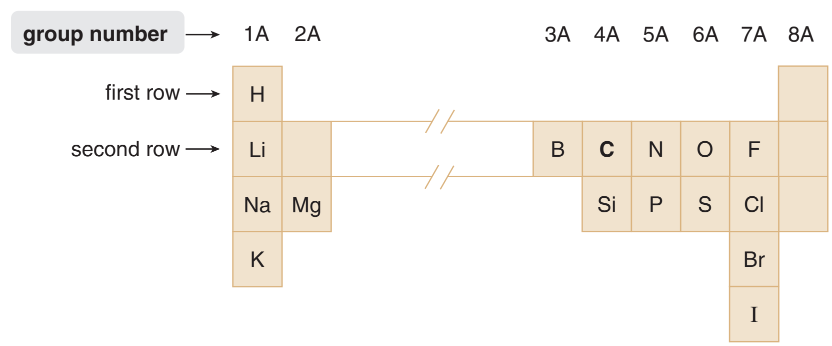
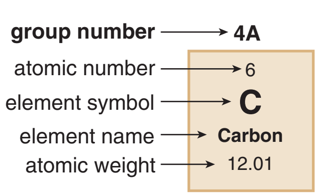


Figure 1.1
A periodic table of the common elements seen in organic chemistry

- Carbon is located in the second row, group 4A.

Carbon's entry in the periodic table:

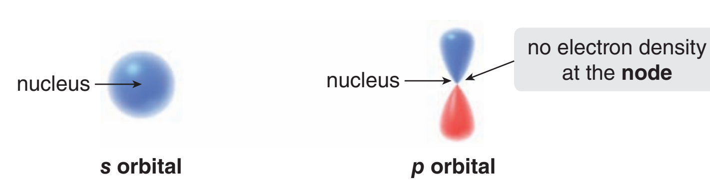


Across each row of the periodic table, electrons are added to a particular shell of orbitals around the nucleus. The shells are numbered 1, 2, 3, and so on. Adding electrons to the first shell forms the first row. Adding electrons to the second shell forms the second row. **Electrons are first added to the shells closest to the nucleus.**

Each shell contains a certain number of **orbitals.** An orbital is a region of space that is high in electron density. There are four different kinds of orbitals, called ***s, p, d,*** and ***f.*** The first shell has only one orbital, called an *s* orbital. The second shell has two kinds of orbitals, *s* and ***p,*** and so on. Each type of orbital has a particular shape.

For the first- and second-row elements, we must consider only ***s*** **orbitals** and ***p*** **orbitals.**

- **An *s* orbital has a sphere of electron density. It is *lower in energy* than other orbitals of the same shell, because electrons are kept closer to the positively charged nucleus.**
- **A *p* orbital has a dumbbell shape. It contains a node of electron density at the nucleus. A node means there is *no* electron density in this region. A *p* orbital is *higher in energy* than an *s* orbital (in the same shell) because its electron density is farther away from the nucleus.**



An *s* orbital is filled with electrons before a *p* orbital in the same shell.