Organic Chemistry

SEVENTH EDITION

Paula Yurkanis Bruice

UNIVERSITY OF CALIFORNIA SANTA BARBARA

PEARSON

Boston Columbus Indianapolis New York San Francisco Upper Saddle River Amsterdam Cape Town Dubai London Madrid Milan Munich Paris Montréal Toronto Delhi Mexico City São Paulo Sydney Hong Kong Seoul Singapore Taipei Tokyo

Brief Table of Contents

Preface xx

CHAPTER 1	Remembering General Chemistry: Electronic Structure and Bonding 2
CHAPTER 2	Acids and Bases: Central to Understanding Organic Chemistry 53
TUTORIAL	Acids and Bases 82
CHAPTER 3	An Introduction to Organic Compounds: Nomenclature, Physical Properties, and Representation of Structure 90
TUTORIAL	Using Molecular Models 146
CHAPTER 4	Isomers: The Arrangement of Atoms in Space 147
TUTORIAL	Interconverting Structural Representations 187
CHAPTER 5	Alkenes: Structure, Nomenclature, and an Introduction to Reactivity • Thermodynamics and Kinetics 190
TUTORIAL	An Exercise in Drawing Curved Arrows: Pushing Electrons 225
CHAPTER 6	The Reactions of Alkenes: The Stereochemistry of Addition Reactions 236
CHAPTER 7	The Reactions of Alkynes • An Introduction to Multistep Synthesis 299
CHAPTER 8	Delocalized Electrons and Their Effect on Stability, pK_a , and the Products of a Reaction 330
TUTORIAL	Drawing Resonance Contributors 392
CHAPTER 9	Substitution Reactions of Alkyl Halides 402
CHAPTER 10	Elimination Reactions of Alkyl Halides • Competition Between Substitution and Elimination 444
CHAPTER 11	Reactions of Alcohols, Ethers, Epoxides, Amines, and Thiols 481
CHAPTER 12	Organometallic Compounds 535
CHAPTER 13	Radicals • Reactions of Alkanes 556
TUTORIAL	Drawing Curved Arrows in Radical Systems 590
CHAPTER 14	Mass Spectrometry, Infrared Spectroscopy, and Ultraviolet/ Visible Spectroscopy 595

CHAPTER 15 NMR Spectroscopy 649

CHAPTER 16	Reactions of Carboxylic Acids and Carboxylic Derivatives	720
------------	--	-----

- **CHAPTER 17** Reactions of Aldehydes and Ketones More Reactions of Carboxylic Acid Derivatives Reactions of α, β Unsaturated Carbonyl Compounds 789
- **CHAPTER 18** Reactions at the α -Carbon of Carbonyl Compounds 853
- CHAPTER 19 Reactions of Benzene and Substituted Benzenes 907
- **TUTORIAL** Synthesis and Retrosynthetic Analysis 974
- CHAPTER 20 More About Amines Reactions of Heterocyclic Compounds 989
- **CHAPTER 21** The Organic Chemistry of Carbohydrates 1017
- **CHAPTER 22** The Organic Chemistry of Amino Acids, Peptides, and Proteins 1053
- **CHAPTER 23** Catalysis in Organic Reaction and in Enzymatic Reactions 1099
- **CHAPTER 24** The Organic Chemistry of the Coenzymes, Compounds Derived from Vitamins 1132
- **CHAPTER 25** The Organic Chemistry of the Metabolic Pathways Terpene Biosynthesis 1170
- CHAPTER 26 The Chemistry of the Nucleic Acids 1207
- **CHAPTER 27** Synthetic Polymers 1236
- CHAPTER 28 Pericyclic Reactions 1266
- **APPENDICES I** pK_a Values A-1
 - II Kinetics A-3
 - III Summary of Methods Used to Synthesize a Particular Functional Group A-8
 - IV Summary of Methods Employed to Form Carbon-Carbon Bonds A-11

Answers to Selected Problems Available in the Study Area in MasteringChemistry

Glossary G-1

Photo Credits P-1

Index I-1

Contents

New material on how to draw Lewis structures and how to predict bond angles and the orbitals used in bonding.

PART 1AN INTRODUCTION TO THE STUDY
OF ORGANIC CHEMISTRY 1

Remembering General Chemistry: Electronic Structure and Bonding 2

- 1.1 The Structure of an Atom 4
- **1.2** How the Electrons in an Atom Are Distributed 5
- **1.3** Ionic and Covalent Bonds 7
- 1.4 How the Structure of a Compound Is Represented 14 PROBLEM-SOLVING STRATEGY 17
- 1.5 Atomic Orbitals 21
- 1.6 An Introduction to Molecular Orbital Theory 23
- 1.7 How Single Bonds Are Formed in Organic Compounds 28
- **1.8** How a Double Bond Is Formed: The Bonds in Ethene 31
- **1.9** How a Triple Bond Is Formed: The Bonds in Ethyne 34
- 1.10 The Bonds in the Methyl Cation, the Methyl Radical, and the Methyl Anion 36
- 1.11 The Bonds in Ammonia and in the Ammonium Ion 37
- 1.12 The Bonds in Water 38

0

- **1.13** The Bond in a Hydrogen Halide 40
- **1.14** Hybridization and Molecular Geometry 42
- PROBLEM-SOLVING STRATEGY 42
- 1.15 Summary: Hybridization, Bond Lengths, Bond Strengths, and Bond Angles 43 **PROBLEM-SOLVING STRATEGY 47**
- **1.16** The Dipole Moments of Molecules 47

SOME IMPORTANT THINGS TO REMEMBER 48 PROBLEMS 49

New chapter on Acid/ Base Chemistry reinforces fundamental concepts.

New tutorial on Acid/ Base Chemistry provides students with opportunities to self assess and develop foundational skills needed for future topics in organic chemistry.

Enhanced by MasteringChemistry[®]

- Acids and Bases: Equilibrium Basics
 Acids and Bases: Factors Influencing Acid Strength
- Acids and Bases: pH Influence on Acid and Base Structure

Acids and Bases: Central to Understanding Organic Chemistry 53

- 2.1 An Introduction to Acids and Bases 53 2.2 pK_ and pH 55 **PROBLEM-SOLVING STRATEGY 56** 2.3 Organic Acids and Bases 57 PROBLEM-SOLVING STRATEGY 60 24 How to Predict the Outcome of an Acid–Base Reaction 61 2.5 How to Determine the Position of Equilibrium 61 2.6 How the Structure of an Acid Affects its pK Value 63 2.7 How Substituents Affect the Strength of an Acid 66 PROBLEM-SOLVING STRATEGY 67 2.8 An Introduction to Delocalized Electrons 68 2.9 A Summary of the Factors that Determine Acid Strength 70 2.10 How pH Affects the Structure of an Organic Compound 72 PROBLEM-SOLVING STRATEGY 72 2.11 Buffer Solutions 76 2.12 Lewis Acids and Bases 77 SOME IMPORTANT THINGS TO REMEMBER 78 PROBLEMS 79
- TUTORIAL ACIDS AND BASES 82

3 An Introduction to Organic Compounds: Nomenclature, Physical Properties, and Representation of Structure 90



- 3.2 The Nomenclature of Alkanes 97
- 3.3 The Nomenclature of Cycloalkanes Skeletal Structures 101 PROBLEM-SOLVING STRATEGY 103
- 3.4 The Nomenclature of Alkyl Halides 104
- 3.5 The Nomenclature of Ethers 105
- 3.6 The Nomenclature of Alcohols 106
- 3.7 The Nomenclature of Amines 109
- 3.8 The Structures of Alkyl Halides, Alcohols, Ethers, and Amines 112
- 3.9 The Physical Properties of Alkanes, Alkyl Halides, Alcohols, Ethers, and Amines 113 PROBLEM-SOLVING STRATEGY 117

Increased content on noncovalent interactions

systems.

in chemical and biological

- 3.10 Rotation Occurs About Carbon–Carbon Single Bonds 121
- 3.11 Some Cycloalkanes Have Angle Strain 125 PROBLEM-SOLVING STRATEGY 126
- 3.12 Conformers of Cyclohexane 127
- 3.13 Conformers of Monosubstituted Cyclohexanes 130 PROBLEM-SOLVING STRATEGY 133
- 3.14 Conformers of Disubstituted Cyclohexanes 133
- **3.15** Fused Cyclohexane Rings 137

SOME IMPORTANT THINGS TO REMEMBER 139 PROBLEMS 140

PART 2 ELECTROPHILIC ADDITION REACTIONS, STEREOCHEMISTRY, AND ELECTRON DELOCALIZATION 145

TUTORIAL USING MOLECULAR MODELS 146

H Isomers: The Arrangement of Atoms in Space 147

- 4.1 Cis–Trans Isomers Result From Restricted Rotation 148
- 4.2 A Chiral Object Has a Nonsuperimposable Mirror Image 151
- 4.3 An Asymmetric Center Is a Cause of Chirality in a Molecule 152
- 4.4 Isomers with One Asymmetric Center 153
- 4.5 Asymmetric Centers and Stereocenters 154
- 4.6 How to Draw Enantiomers 154
- 4.7 Naming Enantiomers by the *R*,*S* System 155 PROBLEM-SOLVING STRATEGY 158

PROBLEM-SOLVING STRATEGY 158

- 4.8 Chiral Compounds Are Optically Active 160
- 4.9 How Specific Rotation Is Measured 161
- 4.10 Enantiomeric Excess 163
- 4.11 Compounds with More than One Asymmetric Center 164
- 4.12 Stereoisomers of Cyclic Compounds 167 PROBLEM-SOLVING STRATEGY 168
- 4.13 Meso Compounds Have Asymmetric Centers but Are Optically Inactive 169 PROBLEM-SOLVING STRATEGY 171
- 4.14 How to Name Isomers with More than One Asymmetric Center 173 **PROBLEM-SOLVING STRATEGY** 175
- 4.15 How Enantiomers Can Be Separated 178
- 4.16 Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers 180 SOME IMPORTANT THINGS TO REMEMBER 181 ■ PROBLEMS 181

Enhanced by MasteringChemistry[®]

- Using Molecular Models: Basics of Model Building
- Using Molecular Models: Interpret Chiral Models
- Using Molecular Models: Interpret Cyclic Models

The coverage of stereoisomers now precedes the coverage of the reactions of alkenes.

Two new tutorials reinforce student understanding and visualization of structure.

Enhanced by MasteringChemistry

- Interconverting Structural Representations: Interpreting Fischer Projections
- Interconverting Structural Representations: Fischer Projections with Multiple Stereocenters
- Interconverting Structural Representations: Interpreting Newman Projections

Introduces a new feature, "Organizing What We Know," which highlights how all organic compounds can be divided into families and all members of a family react in the same way. Furthermore, each family can be put into one of four groups and all the families in a group react in similar ways.

New tutorial gives students practice drawing curved arrows.

Enhanced by MasteringChemistry®

- An Exercise in Drawing Curved Arrows: Basics of Pushing Electrons
- An Exercise in Drawing Curved Arrows: Predicting Electron Movement
- An Exercise in Drawing Curved Arrows: Interpreting Electron Movement

Alkoxymercuration was removed since it is now rarely used because of toxicity concerns. Ozonolysis has been added as has using 9-BBN for hydroboration and MCPBA for epoxidation.

> **Discussion of reactivity** has been reorganized and clarified. The mechanism for keto-enol interconversion has been added.

Alkenes: Structure, Nomenclature, and an Introduction to Reactivity • Thermodynamics and Kinetics 190

- Molecular Formulas and the Degree of Unsaturation 191
- 5.2 The Nomenclature of Alkenes 192
- 5.3 The Structure of Alkenes 195 5.4
 - Naming Alkenes Using the E,Z System 196
 - PROBLEM-SOLVING STRATEGY 199

PROBLEM-SOLVING STRATEGY 200

- 5.5 How an Organic Compound Reacts Depends on its Functional Group 200
- 5.6 How Alkenes React • Curved Arrows Show the Flow of Electrons 201
- 5.7 Thermodynamics and Kinetics 205
- 5.8 The Rate of a Chemical Reaction 212
- 5.9 The Difference Between the Rate of a Reaction and the Rate Constant for a Reaction 213
- 5.10 A Reaction Coordinate Diagram Describes the Energy Changes that Take Place during
 - a Reaction 216
- 5.11 Catalysis 218

5.1

5.12 Catalysis by Enzymes 219

SOME IMPORTANT THINGS TO REMEMBER 220 PROBLEMS 221

TUTORIAL AN EXERCISE IN DRAWING CURVED ARROWS: PUSHING ELECTRONS 225

The Reactions of Alkenes • D The Stereochemistry of Addition Reactions 236

- 6.1 The Addition of a Hydrogen Halide to an Alkene 237
- 6.2 Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon 238
- 6.3 What Does the Structure of the Transition State Look Like? 240
- 6.4 Electrophilic Addition Reactions Are Regioselective 242

PROBLEM-SOLVING STRATEGY 245

- 6.5 The Addition of Water to an Alkene 246
- 6.6 The Addition of an Alcohol to an Alkene 248
- 6.7 A Carbocation Will Rearrange if it Can Form a More Stable Carbocation 250
- 6.8 The Addition of Borane to an Alkene: Hydroboration–Oxidation 252
- 6.9 The Addition of a Halogen to an Alkene 256

PROBLEM-SOLVING STRATEGY 260

- 6.10 The Addition of a Peroxyacid to an Alkene 260
- 6.11 The Addition of Ozone to an Alkene: Ozonolysis 262

PROBLEM-SOLVING STRATEGY 264

- 6.12 The Addition of Hydrogen to an Alkene 266 **PROBLEM-SOLVING STRATEGY 269**
- 6.13 The Relative Stabilities of Alkenes 269
- 6.14 Regioselective, Stereoselective, and Stereospecific Reactions 271
- 6.15 The Stereochemistry of Electrophilic Addition Reactions of Alkenes 272 PROBLEM-SOLVING STRATEGY 282
- 6.16 The Stereochemistry of Enzyme-Catalyzed Reactions 284
- 6.17 Enantiomers Can Be Distinguished by Biological Molecules 286
- 6.18 Reactions and Synthesis 288

SOME IMPORTANT THINGS TO REMEMBER 290

SUMMARY OF REACTIONS 291 PROBLEMS 292

The Reactions of Alkynes An Introduction to Multistep Synthesis 299

- 7.1 The Nomenclature of Alkynes 301
- 7.2 How to Name a Compound That Has More than One Functional Group 303
- 7.3 The Physical Properties of Unsaturated Hydrocarbons 305
- 7.4 The Structure of Alkynes 305

- 7.5 Alkynes Are Less Reactive than Alkenes 306
- 7.6 The Addition of Hydrogen Halides and the Addition of Halogens to an Alkyne 308
- 7.7 The Addition of Water to an Alkyne 311
- 7.8 The Addition of Borane to an Alkyne: Hydroboration–Oxidation 313
- 7.9 The Addition of Hydrogen to an Alkyne 314
- 7.10 A Hydrogen Bonded to an *sp* Carbon Is "Acidic" 316 **PROBLEM-SOLVING STRATEGY** 317
- 7.11 Synthesis Using Acetylide Ions 318
- 7.12 An Introduction to Multistep Synthesis 319 SOME IMPORTANT THINGS TO REMEMBER 325 SUMMARY OF REACTIONS 325 PROBLEMS 326

O Delocalized Electrons and Their Effect on Stability, pK, and the Products of a Reaction 330

- 8.1 Delocalized Electrons Explain Benzene's Structure 331
- 8.2 The Bonding in Benzene 333
- 8.3 Resonance Contributors and the Resonance Hybrid 334
- 8.4 How to Draw Resonance Contributors 335
- 8.5 The Predicted Stabilities of Resonance Contributors 338
- 8.6 Delocalization Energy Is the Additional Stability Delocalized Electrons Give to a Compound 341

PROBLEM-SOLVING STRATEGY 342

- 8.7 Benzene Is an Aromatic Compound 343
- 8.8 The Two Criteria for Aromaticity 343
- 8.9 Applying the Criteria for Aromaticity 344

PROBLEM-SOLVING STRATEGY 347

- 8.10 Aromatic Heterocyclic Compounds 347
- 8.11 Antiaromaticity 349
- 8.12 A Molecular Orbital Description of Aromaticity and Antiaromaticity 350
- 8.13 More Examples that Show How Delocalized Electrons Increase Stability 351
- 8.14 A Molecular Orbital Description of Stability 356
- 8.15 How Delocalized Electrons Affect pK_a Values 360 PROBLEM-SOLVING STRATEGY 362

- 8.16 Delocalized Electrons Can Affect the Product of a Reaction 364
- 8.17 Reactions of Dienes 365
- 8.18 Thermodynamic versus Kinetic Control 369
- 8.19 The Diels–Alder Reaction Is a 1,4-Addition Reaction 374
- 8.20 Retrosynthetic Analysis of the Diels–Alder Reaction 380
- 8.21 Organizing What We Know About the Reactions of Organic Compounds 381

SOME IMPORTANT THINGS TO REMEMBER 382

SUMMARY OF REACTIONS 383 PROBLEMS 384

TUTORIAL DRAWING RESONANCE CONTRIBUTORS 392

PART 3 SUBSTITUTION AND ELIMINATION REACTIONS 401

Substitution Reactions of Alkyl Halides 402 -

- 9.1 The Mechanism for an S_N2 Reaction 404
- 9.2 Factors that Affect S_N2 Reactions 409
- **9.3** The Mechanism for an S_N 1 Reaction 417
- **9.4** Factors that Affect S_N1 Reactions 420
- 9.5 Benzylic Halides, Allylic Halides, Vinylic Halides, and Aryl Halides 421 PROBLEM-SOLVING STRATEGY 423

DESIGNING A

SIS I has been added to allow this concept to be carried

this concept to be carried throughout the text starting at an earlier point.

Discussion of aromaticity

New tutorial gives students practice drawing resonance contributors.

Enhanced by MasteringChemistry*

- Drawing Resonance Contributors: Moving *π* Electrons
- Drawing Resonance Contributors: Predicting Contributor Structure
- Drawing Resonance Contributors: Substituted Benzene Compounds

Rewritten to incorporate the new finding that secondary alkyl halides do not undergo S_w1 reactions.

9.7 The Role of the Solvent in S₁1 and S₂2 Reactions 428 9.8 Intermolecular versus Intramolecular Reactions 433 PROBLEM-SOLVING STRATEGY 435 9.9 Methylating Agents Used by Chemists versus Those Used by Cells 436 SOME IMPORTANT THINGS TO REMEMBER 438 SUMMARY OF REACTIONS 439 PROBLEMS 439 Elimination Reactions of Alkyl Halides • **Competition Between Substitution and Elimination** 444 10.1 The E2 Reaction 445 10.2 An E2 Reaction Is Regioselective 446 10.3 The E1 Reaction 452 **PROBLEM-SOLVING STRATEGY 455** 10.4 Benzylic and Allylic Halides 455 10.5 Competition Between E2 and E1 Reactions 456 10.6 E2 and E1 Reactions Are Stereoselective 457 PROBLEM-SOLVING STRATEGY 460 10.7 Elimination from Substituted Cyclohexanes 462 10.8 A Kinetic Isotope Effect Can Help Determine a Mechanism 465 10.9 Competition Between Substitution and Elimination 466 **10.10** Substitution and Elimination Reactions in Synthesis 471 **10.11** Approaching the Problem 474 Hypochlorous acid SOME IMPORTANT THINGS TO REMEMBER 476 introduced as an alternative SUMMARY OF REACTIONS 477 PROBLEMS 477 to toxic-chromuium-**Reactions of Alcohols, Ethers, Epoxides,** Amines, and Thiols 481 11.1 Nucleophilic Substitution Reactions of Alcohols: Forming Alkyl Halides 482 11.2 Other Methods Used to Convert Alcohols into Alkyl Halides 487 11.3 Converting an Alcohol Into a Sulfonate Ester 488 11.4 Elimination Reactions of Alcohols: Dehydration 492

Competition Between S_N2 and S_N1 Reactions 424

PROBLEM-SOLVING STRATEGY 426

- **PROBLEM-SOLVING STRATEGY 495** Oxidation of Alcohols 499
- 11.5
- 11.6 Nucleophilic Substitution Reactions of Ethers 502
- 11.7 Nucleophilic Substitution Reactions of Epoxides 505
- 11.8 Arene Oxides 512
- Amines Do Not Undergo Substitution or Elimination Reactions 516 11.9
- 11.10 Quaternary Ammonium Hydroxides Undergo Elimination Reactions 519
- 11.11 Thiols, Sulfides, and Sulfonium Salts 521
- 11.12 Organizing What We Know About the Reactions of Organic Compounds 524 SOME IMPORTANT THINGS TO REMEMBER 525

SUMMARY OF REACTIONS 526 PROBLEMS 528

Organometallic Compounds 535

- 12.1 Organolithium and Organomagnesium Compounds 536
- 12.2 Transmetallation 538
- 12.3 Organocuprates 538
- 12.4 Palladium-Catalyzed Coupling Reactions 541 **PROBLEM-SOLVING STRATEGY 546**
- 12.5 Alkene Metathesis 548

SOME IMPORTANT THINGS TO REMEMBER 551 SUMMARY OF REACTIONS 552 PROBLEMS 553

Rewritten to incorporate the new finding that secondary alkyl halides do not undergo E1 reactions.

9.6

containing compounds.

Discussion of palladiumcatalyzed coupling reactions and their mechanisms has been expanded. Solved problems and problemsolving strategies were added to facilitate understanding.

13	Radicals • Reactions of Alkanes 556	Now includes the mechanism for the oxidation of fats and oils by oxygen.
13.1 13.2 13.3	Alkanes Are Unreactive Compounds 556 The Chlorination and Bromination of Alkanes 558 Radical Stability Depends On the Number of Alkyl Groups Attached to the Carbon the Unpaired Electron 560	with
13.4 13.5 13.6 13.7 13.8 13.9	The Distribution of Products Depends On Probability and Reactivity 561 The Reactivity–Selectivity Principle 564 PROBLEM-SOLVING STRATEGY 566 Formation of Explosive Peroxides 567 The Addition of Radicals to an Alkene 568 The Stereochemistry of Radical Substitution and Radical Addition Reactions 577 Radical Substitution of Benzylic and Allylic Hydrogens 573	1
13.10 13.11 13.12	more ridence man manager synthesis 570	IGNING A THESIS III

TUTORIAL DRAWING CURVED ARROWS IN RADICAL SYSTEMS 590

PART 4 **IDENTIFICATION OF ORGANIC** COMPOUNDS 594

Mass Spectrometry, Infrared Spectroscopy, and Ultraviolet/ Visible Spectroscopy 595

14.1 Mass Spectrometry 597

- 14.2 The Mass Spectrum • Fragmentation 598
- 14.3 Using the m/z Value of the Molecular Ion to Calculate the Molecular Formula 600 PROBLEM-SOLVING STRATEGY 601
- 14.4 Isotopes in Mass Spectrometry 602
- 14.5 High-Resolution Mass Spectrometry Can Reveal Molecular Formulas 603
- 14.6 The Fragmentation Patterns of Functional Groups 604
- 14.7 Other Ionization Methods 611
- 14.8 Gas Chromatography–Mass Spectrometry 611
- 14.9 Spectroscopy and the Electromagnetic Spectrum 611
- 14.10 Infrared Spectroscopy 614
- 14.11 Characteristic Infrared Absorption Bands 616
- 14.12 The Intensity of Absorption Bands 617
- **14.13** The Position of Absorption Bands 618
- **14.14** The Position and Shape of an Absorption Band Is Affected By Electron Delocalization, Electron Donation and Withdrawal, and Hydrogen Bonding 619

PROBLEM-SOLVING STRATEGY 622

- 14.15 The Absence of Absorption Bands 626
- 14.16 Some Vibrations Are Infrared Inactive 627
- 14.17 How to Interpret an Infrared Spectrum 629
- 14.18 Ultraviolet and Visible Spectroscopy 631
- 14.19 The Beer–Lambert Law 633
- **14.20** The Effect of Conjugation on λ_{max} 634
- 14.21 The Visible Spectrum and Color 635
- 14.22 Some Uses of UV/ VIS Spectroscopy 637

SOME IMPORTANT THINGS TO REMEMBER 639 PROBLEMS 640

Added the "rule of 13".

Interpreting Electron Movement

Enhanced by MasteringChemistry

xiii

- · Curved Arrows in Radical Systems: Curved Arrows in Radical Systems:
- Predicting Electron Movement
- Curved Arrows in Radical Systems: Resonance

spectroscopy problems in the Study Guide and Solutions Manual.

NMR Spectroscopy 649

- 15.1 An Introduction to NMR Spectroscopy 649
- **15.2** Fourier Transform NMR 652
- 15.3 Shielding Causes Different Hydrogens to Show Signals at Different Frequencies 653
- 15.4 The Number of Signals in an ¹H NMR Spectrum 654 PROBLEM-SOLVING STRATEGY 655
- 15.5 The Chemical Shift Tells How Far the Signal Is from the Reference Signal 656
- **15.6** The Relative Positions of ¹H NMR Signals 658
- 15.7 The Characteristic Values of Chemical Shifts 659
- 15.8 Diamagnetic Anisotropy 661
- **15.9** The Integration of NMR Signals Reveals the Relative Number of Protons Causing Each Signal 663
- **15.10** The Splitting of Signals Is Described by the N + 1 Rule 665
- 15.11 What Causes Splitting? 668
- **15.12** More Examples of ¹H NMR Spectra 670
- **15.13** Coupling Constants Identify Coupled Protons 675

PROBLEM-SOLVING STRATEGY 677

- 15.14 Splitting Diagrams Explain the Multiplicity of a Signal 679
- 15.15 Diastereotopic Hydrogens are Not Chemically Equivalent 681
- **15.16** The Time Dependence of NMR Spectroscopy 683
- 15.17 Protons Bonded To Oxygen and Nitrogen 684
- 15.18 The Use of Deuterium in ¹H NMR Spectroscopy 686
- 15.19 The Resolution of ¹H NMR Spectra 687
- 15.20 ¹³C NMR Spectroscopy 689

PROBLEM-SOLVING STRATEGY 692

- 15.21 Dept ¹³C NMR Spectra 694
- **15.22** Two-Dimensional NMR Spectroscopy 695
- 15.23 NMR Used in Medicine Is Called Magnetic Resonance Imaging 698
- 15.24 X-Ray Crystallography 699

SOME IMPORTANT THINGS TO REMEMBER 701 PROBLEMS 701

PART 5 CARBONYL COMPOUNDS 719

16 Reactions of Carboxylic Acids and Carboxylic Derivatives 720

- 16.1 The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives 722
- 16.2 The Structures of Carboxylic Acids and Carboxylic Acid Derivatives 726
- **16.3** The Physical Properties of Carbonyl Compounds 728
- 16.4 Fatty Acids Are Long-Chain Carboxylic Acids 729
- 16.5 How Carboxylic Acids and Carboxylic Acid Derivatives React 731 PROBLEM-SOLVING STRATEGY 733
- **16.6** The Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives 733
- 16.7 The General Mechanism for Nucleophilic Addition–Elimination Reactions 736
- 16.8 The Reactions of Acyl Chlorides 737
- 16.9 The Reactions of Esters 739
- 16.10 Acid-Catalyzed Ester Hydrolysis and Transesterification 741
- 16.11 Hydroxide-Ion-Promoted Ester Hydrolysis 746
- 16.12 How the Mechanism for Nucleophilic Addition–Elimination Was Confirmed 749
- **16.13** Fats and Oils Are Triglycerides 751
- 16.14 Reactions of Carboxylic Acids 755

PROBLEM-SOLVING STRATEGY 756

- 16.15 Reactions of Amides 757
- 16.16 Acid–Catalyzed Amide Hydrolysis and Alcoholysis 760
- 16.17 Hydroxide-Ion Promoted Hydrolysis of Amides 762
- 16.18 The Hydrolysis of an Imide: A Way to Synthesize Primary Amines 763
- 16.19 Nitriles 764

Acid anhydrides are carboxylic acid derivatives but they don't look like carboxylic acids. Anhydrides, therefore, were moved to the end of the chapter to allow students to focus on the similarities between carboxylic acids, acyl chlorides, esters, and amides. Acid anhydrides are now better placed since they come just before phosphoric acid anhydrides.

16.20 16.21 16.22 16.23	Acid Anhydrides 766 Dicarboxylic Acids 769 How Chemists Activate Carboxylic Acids 771 How Cells Activate Carboxylic Acids 773 SOME IMPORTANT THINGS TO REMEMBER 776
17	SUMMARY OF REACTIONS 777 = PROBLEMS 780 Reactions of Aldehydes and Ketones • More Reactions of Carboxylic Acid Derivatives • Reactions of α,β -Unsaturated Carbonyl Compounds 789
17.11	The Nomenclature of Aldehydes and Ketones 790 The Relative Reactivities of Carbonyl Compounds 793 How Aldehydes and Ketones React 795 The Reactions of Carbonyl Compounds with Gringard Reagents 796 PROBLEM-SOLVING STRATEGY 800 The Reactions of Carbonyl Compounds with Acetylide Ions 801 The Reactions of Aldehydes and Ketones with Cyanide Ion 801 The Reactions of Carbonyl Compounds with Hydride Ion 803 More About Reduction Reactions 808 Chemoselective Reactions 810 The Reactions of Aldehydes and Ketones with Amines 811 The Reactions of Aldehydes and Ketones with Water 817 The Reactions of Aldehydes and Ketones with Alcohols 820
17.15	PROBLEM-SOLVING STRATEGY 822 Protecting Groups 823 The Addition of Sulfur Nucleophiles 825 The Reactions of Aldehydes and Ketones with a Peroxyacid 826 The Wittig Reaction Forms an Alkene 827 Disconnections, Synthons, and Synthetic Equivalents 829 Nucleophilic Addition to α , β -Unsaturated Aldehydes and Ketones 832 Nucleophilic Addition to α , β -Unsaturated Carboxylic Acid Derivatives 837

SOME IMPORTANT THINGS TO REMEMBER 838

SUMMARY OF REACTIONS 839 PROBLEMS 843

18 Reactions at the α -Carbon of Carbonyl Compounds 853

- 18.1 The Acidity of an α -Hydrogen 854 PROBLEM-SOLVING STRATEGY 856
- 18.2 Keto–Enol Tautomers 857
- 18.3 Keto–Enol Interconversion 858
- 18.4 Halogenation of the α -Carbon of Aldehydes and Ketones 859
- 18.5 Halogenation of the α -Carbon of Carboxylic Acids: The Hell–Volhard–Zelinski Reaction 861
- 18.6 Forming an Enolate Ion 862
- 18.7 Alkylating the α -Carbon of Carbonyl Compounds 863 PROBLEM-SOLVING STRATEGY 865
- 18.8 Alkylating and Acylating the α -Carbon Using an Enamine Intermediate 866
- 18.9 Alkylating the β -Carbon: The Michael Reaction 867
- **18.10** An Aldol Addition Forms β -Hydroxyaldehydes or β -Hydroxyketones 869
- **18.11** The Dehydration of Aldol Addition Products Forms α,β -Unsaturated Aldehydes and Ketones 871
- **18.12** A Crossed Aldol Addition 872
- **18.13** A Claisen Condensation Forms a β -Keto Ester 875
- 18.14 Other Crossed Condensations 878
- 18.15 Intramolecular Condensations and Intramolecular Aldol Additions 879
- 18.16 The Robinson Annulation 881 PROBLEM-SOLVING STRATEGY 882

Streamlined the discussion of both the reactions of enolate ions and crossed aldol additions and condensations. Added new examples of retrosynthetic analysis.

XV

- 18.17 Carboxylic Acids with a Carbonyl Group at the 3-Position Can Be Decarboxylated 883
- **18.18** The Malonic Ester Synthesis: A Way to Synthesize a Carboxylic Acid 885
- 18.19 The Acetoacetic Ester Synthesis: A Way to Synthesize a Methyl Ketone 887
- 18.20 Making New Carbon–Carbon Bonds 888

18.21 Reactions at the α -Carbon in Living Systems 890

18.22 Organizing What We Know About the Reactions of

Organic Compounds 894

SOME IMPORTANT THINGS TO REMEMBER 894

SUMMARY OF REACTIONS 895 PROBLEMS 898

PART 6 AROMATIC COMPOUNDS 906

19 Reactions of Benzene and Substituted Benzenes 907

- 19.1 The Nomenclature of Monosubstituted Benzenes 909
- 19.2 How Benzene Reacts 910
- 19.3 The General Mechanism for Electrophilic Aromatic Substitution Reactions 912
- 19.4 The Halogenation of Benzene 913
- **19.5** The Nitration of Benzene 916
- 19.6 The Sulfonation of Benzene 917
- **19.7** The Friedel–Crafts Acylation of Benzene 918
- 19.8 The Friedel–Crafts Alkylation of Benzene 920
- 19.9 The Alkylation of Benzene by Acylation–Reduction 922
- **19.10** Using Coupling Reactions to Alkylate Benzene 924
- 19.11 It Is Important to Have More than One Way to Carry Out a Reaction 924
- 19.12 How Some Substituents on a Benzene Ring Can Be Chemically Changed 925
- 19.13 The Nomenclature of Disubstituted and Polysubstituted Benzenes 927
- **19.14** The Effect of Substituents on Reactivity 929
- 19.15 The Effect of Substituents on Orientation 935
- **19.16** The Effect of Substituents on pK, 939
- PROBLEM-SOLVING STRATEGY 940
- **19.17** The Ortho–Para Ratio 941
- 19.18 Additional Considerations Regarding Substituent Effects 941
- 19.19 The Synthesis of Monosubstituted and Disubstituted Benzenes 943
- 19.20 The Synthesis of Trisubstituted Benzenes 945
- 19.21 The Synthesis of Substituted Benzenes Using Arenediazonium Salts 947
- **19.22** The Arenediazonium Ion as an Electrophile 950
- **19.23** The Mechanism for the Reaction of Amines with Nitrous Acid 953

SUMMARY OF REACTIONS 960 PROBLEMS 962

SOME IMPORTANT THINGS TO REMEMBER 959

- 19.24 Nucleophilic Aromatic Substitution: An Addition–Elimination Reaction 955
- **19.25** The Synthesis of Cyclic Compounds 957

DESIGNING A SYNTHESIS VII

DESIGNING A

SYNTHESIS V

including two examples of a multistep synthesis from the literature.

Enhanced by MasteringChemistry[®]

New tutorial on synthesis

and retrosynthetic analysis

- Synthesis and Retrosynthetic Analysis: Functional Groups
- Synthesis and Retrosynthetic Analysis: Carbon Chain
- Synthesis and Retrosynthetic Analysis: Retrosynthesis of 2-Pentanone Using Reactions of Carbonyl Compounds
- TUTORIAL SYNTHESIS AND RETROSYNTHETIC ANALYSIS 974

20 More About Amines • Reactions of Heterocyclic Compounds 989

- 20.1 More About Amine Nomenclature 990
- 20.2 More About the Acid–Base Properties of Amines 991
- 20.3 Amines React as Bases and as Nucleophiles 993
- 20.4 The Synthesis of Amines 994
- 20.5 Aromatic Five-Membered-Ring Heterocycles 994
- **20.6** Aromatic Six-Membered-Ring Heterocycles 999

PROBLEM-SOLVING STRATEGY 999

DESIGNING A SYNTHESIS V

- **20.7** Some Amine Heterocycles Have Important Roles in Nature 1005
- **20.8** Organizing What We Know About the Reactions of Organic Compounds 1010

SOME IMPORTANT THINGS TO REMEMBER 1010 SUMMARY OF REACTIONS 1011 PROBLEMS 1012

PART 7 BIOORGANIC COMPOUNDS 1016

The Organic Chemistry of Carbohydrates 1017

- 21.1 The Classification of Carbohydrates 1018
- **21.2** The D and L Notation 1019
- **21.3** The Configurations of the Aldoses 1020
- **21.4** The Configurations of the Ketoses 1022
- 21.5 The Reactions of Monosaccharides in Basic Solutions 1023
- **21.6** The Oxidation–Reduction Reactions of Monosaccharides 1024
- 21.7 Lengthening the Chain: The Kiliani–Fischer Synthesis 1026
- **21.8** Shortening the Chain: The Wohl Degradation 1026
- 21.9 The Stereochemistry of Glucose: The Fischer Proof 1027
- 21.10 Monosaccharides Form Cyclic Hemiacetals 1030
- 21.11 Glucose Is the Most Stable Aldohexose 1032
- 21.12 Formation of Glycosides 1034
- 21.13 The Anomeric Effect 1036
- 21.14 Reducing and Nonreducing Sugars 1036
- 21.15 Disaccharides 1037
- 21.16 Polysaccharides 1040
- 21.17 Some Naturally Occurring Compounds Derived from Carbohydrates 1043
- 21.18 Carbohydrates on Cell Surfaces 1045
- 21.19 Artificial Sweeteners 1047

SOME IMPORTANT THINGS TO REMEMBER 1048

SUMMARY OF REACTIONS 1049 PROBLEMS 1050

22 The Organic Chemistry of Amino Acids, Peptides, and Proteins 1053

- 22.1 The Nomenclature of Amino Acids 1054
- 22.2 The Configuration of Amino Acids 1058
- **22.3** The Acid–Base Properties of Amino Acids 1060
- 22.4 The Isoelectric Point 1062
- 22.5 Separating Amino Acids 1064
- 22.6 The Synthesis of Amino Acids 1068
- 22.7 The Resolution of Racemic Mixtures of Amino Acids 1070
- 22.8 Peptide Bonds and Disulfide Bonds 1071
- **22.9** Some Interesting Peptides 1075
- 22.10 The Strategy of Peptide Bond Synthesis: N-Protection and C-Activation 1076
- 22.11 Automated Peptide Synthesis 1079
- **22.12** An Introduction to Protein Structure 1081
- **22.13** How to Determine the Primary Structure of a Polypeptide or Protein 1082
- PROBLEM-SOLVING STRATEGY 1084
- 22.14 Secondary Structure 1088
- 22.15 Tertiary Structure 1091
- 22.16 Quaternary Structure 1093
- 22.17 Protein Denaturation 1094

SOME IMPORTANT THINGS TO REMEMBER 1094 PROBLEMS 1095

A new discussion on diseases caused by protein misfolding.

The reactions of aromatic heterocycles now follows the reactions of other aromatic compounds. Revised to emphasize the connection between the organic reactions that occur in test tubes with the organic reactions that occur in cells. Catalysis in Organic Reactions and in Enzymatic Reactions 1099

- 23.1 Catalysis in Organic Reactions 1101
- 23.2 Acid Catalysis 1101
- 23.3 Base Catalysis 1105
- 23.4 Nucleophilic Catalysis 1106
- 23.5 Metal-Ion Catalysis 1107
- 23.6 Intramolecular Reactions 1109
- 23.7 Intramolecular Catalysis 1111
- 23.8 Catalysis in Biological Reactions 1113
- 23.9 The Mechanisms for Two Enzyme-Catalyzed Reactions that are Reminiscent of Acid-Catalyzed Amide Hydrolysis 1115
- **23.10** The Mechanism for an Enzyme-Catalyzed Reaction that Involves Two Sequential S_{N2} Reactions 1121
- 23.11 The Mechanism for an Enzyme-Catalyzed Reaction that Is Reminiscent of the Base-Catalyzed Enediol Rearrangement 1125
- 23.12 The Mechanism for an Enzyme-Catalyzed Reaction that Is Reminiscent of an Aldol Addition 1126

SOME IMPORTANT THINGS TO REMEMBER 1128 PROBLEMS 1129

The Organic Chemistry of the Coenzymes, Compounds Derived from Vitamins 1132

- 24.1 Niacin: The Vitamin Needed for Many Redox Reactions 1134
- **24.2** Riboflavin: Another Vitamin Used in Redox Reactions 1140
- **24.3** Vitamin B₁: The Vitamin Needed for Acyl Group Transfer 1144
- **24.4** Vitamin H: The Vitamin Needed for Carboxylation of an α -Carbon 1149
- **24.5** Vitamin B₆: The Vitamin Needed for Amino Acid Transformations 1151
 - **24.6** Vitamin B₁₂: The Vitamin Needed for Certain Isomerizations 1156
 - **24.7** Folic Acid: The Vitamin Needed for One-Carbon Transfer 1159
 - **24.8** Vitamin K: The Vitamin Needed for Carboxylation of Glutamate 1164

SOME IMPORTANT THINGS TO REMEMBER 1166 PROBLEMS 1167

25 The Organic Chemistry of the Metabolic Pathways • Terpene Biosynthesis 1170

- 25.1 ATP Is Used for Phosphoryl Transfer Reactions 1171
- 25.2 ATP Activates a Compound by Giving it a Good Leaving Group 1172
- **25.3** Why ATP Is Kinetically Stable in a Cell 1174
- 25.4 The "High-Energy" Character of Phosphoanhydride Bonds 1174
- 25.5 The Four Stages of Catabolism 1176
- 25.6 The Catabolism of Fats 1177
- 25.7 The Catabolism of Carbohydrates 1180

PROBLEM -SOLVING STRATEGY 1183

- 25.8 The Fate of Pyruvate 1184
- 25.9 The Catabolism of Proteins 1185
- 25.10 The Citric Acid Cycle 1187
- **25.11** Oxidative Phosphorylation 1191
- 25.12 Anabolism 1192
- 25.13 Gluconeogenesis 1192
- 25.14 Regulating Metabolic Pathways 1194
- 25.15 Amino Acid Biosynthesis 1195
- 25.16 Terpenes Contain Carbon Atoms in Multiples of Five 1195
- **25.17** How Terpenes are Biosynthesized 1197

PROBLEM-SOLVING STRATEGY 1200

25.18 How Nature Synthesizes Cholesterol 1202

SOME IMPORTANT THINGS TO REMEMBER 1203 PROBLEMS 1204

Added the mechanism for the conversion of succinate to fumarate.

New coverage of organic reactions that occur in gluconeogenesis and discussions of thermodynamic control and the regulation of metabolic pathways. Revised to emphasize the connection between the organic reactions that occur in test tubes with those that occur in cells. New section on terpene biosynthesis.

26 The Chemistry of the Nucleic Acids 1207

- **26.1** Nucleosides and Nucleotides 1207
- 26.2 Other Important Nucleotides 1211
- 26.3 Nucleic Acids Are Composed of Nucleotide Subunits 1211
- **26.4** Why DNA Does Not Have A 2' –OH Group 1215
- 26.5 The Biosynthesis of DNA Is Called Replication 1215
- 26.6 DNA and Heredity 1216
- **26.7** The Biosynthesis of RNA Is Called Transcription 1217
- 26.8 The RNAs Used for Protein Biosynthesis 1219
- 26.9 The Biosynthesis of Proteins Is Called Translation 1221
- **26.10** Why DNA Contains Thymine Instead of Uracil 1225
- 26.11 Antiviral Drugs 1227
- 26.12 How the Base Sequence of DNA Is Determined 1228
- **26.13** The Polymerase Chain Reaction (PCR) 1230
- 26.14 Genetic Engineering 1231

SOME IMPORTANT THINGS TO REMEMBER 1232 PROBLEMS 1233

PART 8 SPECIAL TOPICS IN ORGANIC CHEMISTRY 1235

Synthetic Polymers 1236

- 27.1 There Are Two Major Classes of Synthetic Polymers 1237
- 27.2 Chain-Growth Polymers 1238
- 27.3 Stereochemistry of Polymerization Ziegler–Natta Catalysts 1249
- 27.4 Polymerization of Dienes The Manufacture of Rubber 1250
- 27.5 Copolymers 1252
- 27.6 Step-Growth Polymers 1253
- 27.7 Classes of Step-Growth Polymers 1254
- 27.8 Physical Properties of Polymers 1258
- 27.9 Recycling Polymers 1261
- 27.10 Biodegradable Polymers 1261

SOME IMPORTANT THINGS TO REMEMBER 1262 PROBLEMS 1263

28 Pericyclic Reactions 1266

- 28.1 There Are Three Kinds of Pericyclic Reactions 1267
- 28.2 Molecular Orbitals and Orbital Symmetry 1269
- **28.3** Electrocyclic Reactions 1272
- 28.4 Cycloaddition Reactions 1278
- **28.5** Sigmatropic Rearrangements 1281
- **28.6** Pericyclic Reactions in Biological Systems 1286
- 28.7 Summary of the Selection Rules for Pericyclic Reactions 1289

SOME IMPORTANT THINGS TO REMEMBER 1289 PROBLEMS 1290

APPENDICES A-1

- I pK Values A-1
- II Kinetics A-3
- III Summary of Methods Used to Synthesize a Particular Functional Group A-8
- IV Summary of Methods Employed to Form Carbon-Carbon Bonds A-11

Answers to Selected Problems Available in the Study Area in MasteringChemistry Glossary G-1 Photo Credits P-1 Index I-1