

Organic Chemistry



T.W. GRAHAM SOLOMONS

University of South Florida

CRAIG B. FRYHLE

Pacific Lutheran University

SCOTT A. SNYDER

University of Chicago

12e

WILEY



Brief Contents

- 1 The Basics** Bonding and Molecular Structure 1
 - 2 Families of Carbon Compounds** Functional Groups, Intermolecular Forces, and Infrared (IR) Spectroscopy 55
 - 3 Acids and Bases** An Introduction to Organic Reactions and Their Mechanisms 104
 - 4 Nomenclature and Conformations of Alkanes and Cycloalkanes** 144
 - 5 Stereochemistry** Chiral Molecules 193
 - 6 Nucleophilic Reactions** Properties and Substitution Reactions of Alkyl Halides 240
 - 7 Alkenes and Alkynes I** Properties and Synthesis. Elimination Reactions of Alkyl Halides 282
 - 8 Alkenes and Alkynes II** Addition Reactions 337
 - 9 Nuclear Magnetic Resonance and Mass Spectrometry** Tools for Structure Determination 391
 - 10 Radical Reactions** 448
 - 11 Alcohols and Ethers** Synthesis and Reactions 489
 - 12 Alcohols from Carbonyl Compounds** Oxidation–Reduction and Organometallic Compounds 534
 - 13 Conjugated Unsaturated Systems** 572
 - 14 Aromatic Compounds** 617
 - 15 Reactions of Aromatic Compounds** 660
 - 16 Aldehydes and Ketones** Nucleophilic Addition to the Carbonyl Group 711
 - 17 Carboxylic Acids and Their Derivatives** Nucleophilic Addition–Elimination at the Acyl Carbon 761
 - 18 Reactions at the α Carbon of Carbonyl Compounds** Enols and Enolates 811
 - 19 Condensation and Conjugate Addition Reactions of Carbonyl Compounds** More Chemistry of Enolates 849
 - 20 Amines** 890
 - 21 Transition Metal Complexes** Promoters of Key Bond-Forming Reactions 938
 - 22 Carbohydrates** 965
 - 23 Lipids** 1011
 - 24 Amino Acids and Proteins** 1045
 - 25 Nucleic Acids and Protein Synthesis** 1090
- GLOSSARY** GL-1
- INDEX** I-1
- ANSWERS TO SELECTED PROBLEMS** can be found at www.wiley.com/college/solomons

Contents

1 The Basics

BONDING AND MOLECULAR STRUCTURE 1



- 1.1 Life and the Chemistry of Carbon Compounds—We Are Stardust 2
- THE CHEMISTRY OF...** Natural Products 3
- 1.2 Atomic Structure 3
- 1.3 Chemical Bonds: The Octet Rule 5
- 1.4 **HOW TO** Write Lewis Structures 7
- 1.5 Formal Charges and **HOW TO** Calculate Them 12
- 1.6 Isomers: Different Compounds that Have the Same Molecular Formula 14
- 1.7 **HOW TO** Write and Interpret Structural Formulas 15
- 1.8 Resonance Theory 22
- 1.9 Quantum Mechanics and Atomic Structure 27
- 1.10 Atomic Orbitals and Electron Configuration 28
- 1.11 Molecular Orbitals 30
- 1.12 The Structure of Methane and Ethane: sp^3 Hybridization 32
- THE CHEMISTRY OF...** Calculated Molecular Models: Electron Density Surfaces 36
- 1.13 The Structure of Ethene (Ethylene): sp^2 Hybridization 36
- 1.14 The Structure of Ethyne (Acetylene): sp Hybridization 40
- 1.15 A Summary of Important Concepts that Come from Quantum Mechanics 43
- 1.16 **HOW TO** Predict Molecular Geometry: The Valence Shell Electron Pair Repulsion Model 44
- 1.17 Applications of Basic Principles 47
- [WHY DO THESE TOPICS MATTER?]** 48

2 Families of Carbon Compounds

FUNCTIONAL GROUPS, INTERMOLECULAR FORCES, INFRARED (IR) SPECTROSCOPY 55



- 2.1 Hydrocarbons: Representative Alkanes, Alkenes, Alkynes, and Aromatic Compounds 56
- 2.2 Polar Covalent Bonds 59
- 2.3 Polar and Nonpolar Molecules 61
- 2.4 Functional Groups 64
- 2.5 Alkyl Halides or Haloalkanes 65
- 2.6 Alcohols and Phenols 67
- 2.7 Ethers 69
- THE CHEMISTRY OF...** Ethers as General Anesthetics 69
- 2.8 Amines 70
- 2.9 Aldehydes and Ketones 71
- 2.10 Carboxylic Acids, Esters, and Amides 73
- 2.11 Nitriles 75
- 2.12 Summary of Important Families of Organic Compounds 76
- 2.13 Physical Properties and Molecular Structure 77
- THE CHEMISTRY OF...** Fluorocarbons and Teflon 81
- 2.14 Summary of Attractive Electric Forces 85
- THE CHEMISTRY OF...** Organic Templates Engineered to Mimic Bone Growth 86
- 2.15 Infrared Spectroscopy: An Instrumental Method for Detecting Functional Groups 86
- 2.16 Interpreting IR Spectra 90
- 2.17 Applications of Basic Principles 97
- [WHY DO THESE TOPICS MATTER?]** 97

3

Acids and Bases

AN INTRODUCTION TO ORGANIC REACTIONS AND THEIR MECHANISMS 104



- 3.1 Acid–Base Reactions 105
- 3.2 **HOW TO** Use Curved Arrows in Illustrating Reactions 107
- [**A MECHANISM FOR THE REACTION**] Reaction of Water with Hydrogen Chloride: The Use of Curved Arrows 107
- 3.3 Lewis Acids and Bases 109
- 3.4 Heterolysis of Bonds to Carbon: Carbocations and Carbanions 111
- 3.5 The Strength of Brønsted–Lowry Acids and Bases: K_a and pK_a 113
- 3.6 **HOW TO** Predict the Outcome of Acid–Base Reactions 118
- 3.7 Relationships between Structure and Acidity 120
- 3.8 Energy Changes 123
- 3.9 The Relationship between the Equilibrium Constant and the Standard Free-Energy Change, ΔG° 125
- 3.10 Acidity: Carboxylic Acids versus Alcohols 126
- 3.11 The Effect of the Solvent on Acidity 132
- 3.12 Organic Compounds as Bases 132
- 3.13 A Mechanism for an Organic Reaction 134
- [**A MECHANISM FOR THE REACTION**] Reaction of *tert*-Butyl Alcohol with Concentrated Aqueous HCl 134
- 3.14 Acids and Bases in Nonaqueous Solutions 135
- 3.15 Acid–Base Reactions and the Synthesis of Deuterium- and Tritium-Labeled Compounds 136
- 3.16 Applications of Basic Principles 137
- [**WHY DO THESE TOPICS MATTER?**] 138

4

Nomenclature and Conformations of Alkanes and Cycloalkanes



- 4.1 Introduction to Alkanes and Cycloalkanes 145
- THE CHEMISTRY OF...** Petroleum Refining 145
- 4.2 Shapes of Alkanes 146

- 4.3 **HOW TO** Name Alkanes, Alkyl Halides, and Alcohols: The IUPAC System 148
- 4.4 **HOW TO** Name Cycloalkanes 155
- 4.5 **HOW TO** Name Alkenes and Cycloalkenes 158
- 4.6 **HOW TO** Name Alkynes 160
- 4.7 Physical Properties of Alkanes and Cycloalkanes 161
- THE CHEMISTRY OF...** Pheromones: Communication by Means of Chemicals 163
- 4.8 Sigma Bonds and Bond Rotation 164
- 4.9 Conformational Analysis of Butane 166
- THE CHEMISTRY OF...** Muscle Action 168
- 4.10 The Relative Stabilities of Cycloalkanes: Ring Strain 168
- 4.11 Conformations of Cyclohexane: The Chair and the Boat 170
- THE CHEMISTRY OF...** Nanoscale Motors and Molecular Switches 172
- 4.12 Substituted Cyclohexanes: Axial and Equatorial Hydrogen Groups 173
- 4.13 Disubstituted Cycloalkanes: Cis–Trans Isomerism 177
- 4.14 Bicyclic and Polycyclic Alkanes 181
- 4.15 Chemical Reactions of Alkanes 182
- 4.16 Synthesis of Alkanes and Cycloalkanes 182
- 4.17 **HOW TO** Gain Structural Information from Molecular Formulas and the Index of Hydrogen Deficiency 184
- 4.18 Applications of Basic Principles 186
- [**WHY DO THESE TOPICS MATTER?**] 187

See **SPECIAL TOPIC A**, ^{13}C NMR Spectroscopy—A Practical Introduction, in **WileyPLUS**

5

Stereochemistry

CHIRAL MOLECULES 193

- 5.1 Chirality and Stereochemistry 194
- 5.2 Isomerism: Constitutional Isomers and Stereoisomers 195
- 5.3 Enantiomers and Chiral Molecules 197
- 5.4 Molecules Having One Chirality Center are Chiral 198
- 5.5 More about the Biological Importance of Chirality 201



- 5.6 **HOW TO** Test for Chirality: Planes of Symmetry 203
- 5.7 Naming Enantiomers: The *R,S*-System 204
- 5.8 Properties of Enantiomers: Optical Activity 208
- 5.9 Racemic Forms 213
- 5.10 The Synthesis of Chiral Molecules 214
- 5.11 Chiral Drugs 216
- THE CHEMISTRY OF...** Selective Binding of Drug Enantiomers to Left- and Right-Handed Coiled DNA 218
- 5.12 Molecules with More than One Chirality Center 218
- 5.13 Fischer Projection Formulas 224
- 5.14 Stereoisomerism of Cyclic Compounds 226
- 5.15 Relating Configurations through Reactions in Which No Bonds to the Chirality Center Are Broken 228
- 5.16 Separation of Enantiomers: Resolution 232
- 5.17 Compounds with Chirality Centers Other than Carbon 233
- 5.18 Chiral Molecules that Do Not Possess a Chirality Center 233

[WHY DO THESE TOPICS MATTER?] 234

6 Nucleophilic Reactions

PROPERTIES AND SUBSTITUTION REACTIONS OF ALKYL HALIDES **240**

- 6.1 Alkyl Halides 241
- 6.2 Nucleophilic Substitution Reactions 242
- 6.3 Nucleophiles 244
- 6.4 Leaving Groups 246
- 6.5 Kinetics of a Nucleophilic Substitution Reaction: An S_N2 Reaction 246
- 6.6 A Mechanism for the S_N2 Reaction 247
- [A MECHANISM FOR THE REACTION]** Mechanism for the S_N2 Reaction 248
- 6.7 Transition State Theory: Free-Energy Diagrams 249
- 6.8 The Stereochemistry of S_N2 Reactions 252
- [A MECHANISM FOR THE REACTION]** The Stereochemistry of an S_N2 Reaction 254
- 6.9 The Reaction of *tert*-Butyl Chloride with Water: An S_N1 Reaction 254
- 6.10 A Mechanism for the S_N1 Reaction 255



- [A MECHANISM FOR THE REACTION]** Mechanism for the S_N1 Reaction 256
- 6.11 Carbocations 257
- 6.12 The Stereochemistry of S_N1 Reactions 259
- [A MECHANISM FOR THE REACTION]** The Stereochemistry of an S_N1 Reaction 260
- 6.13 Factors Affecting the Rates of S_N1 and S_N2 Reactions 262
- 6.14 Organic Synthesis: Functional Group Transformations Using S_N2 Reactions 272

THE CHEMISTRY OF... Biological Methylation: A Biological Nucleophilic Substitution Reaction 273

[WHY DO THESE TOPICS MATTER?] 275

7 Alkenes and Alkynes I

PROPERTIES AND SYNTHESIS. ELIMINATION REACTIONS OF ALKYL HALIDES **282**



- 7.1 Introduction 283
- 7.2 The (*E*)-(Z) System for Designating Alkene Diastereomers 283
- 7.3 Relative Stabilities of Alkenes 284
- 7.4 Cycloalkenes 287
- 7.5 Synthesis of Alkenes: Elimination Reactions 287
- 7.6 Dehydrohalogenation 288
- 7.7 The E2 Reaction 289

[A MECHANISM FOR THE REACTION] Mechanism for the E2 Reaction 290

[A MECHANISM FOR THE REACTION] E2 Elimination Where There Are Two Axial β Hydrogens 295

[A MECHANISM FOR THE REACTION] E2 Elimination Where the Only Axial β Hydrogen Is from a Less Stable Conformer 296

7.8 The E1 Reaction 297

[A MECHANISM FOR THE REACTION] Mechanism for the E1 Reaction 298

7.9 Elimination and Substitution Reactions Compete With Each Other 299

7.10 Elimination of Alcohols: Acid-Catalyzed Dehydration 303

[A MECHANISM FOR THE REACTION] Acid-Catalyzed Dehydration of Secondary or Tertiary Alcohols: An E1 Reaction 306



[A MECHANISM FOR THE REACTION] Dehydration of a Primary Alcohol: An E2 Reaction 308

7.11 Carbocation Stability and the Occurrence of Molecular Rearrangements 308

[A MECHANISM FOR THE REACTION] Formation of a Rearranged Alkene During Dehydration of a Primary Alcohol 311

7.12 The Acidity of Terminal Alkynes 312

7.13 Synthesis of Alkynes by Elimination Reactions 313

[A MECHANISM FOR THE REACTION] Dehydrohalogenation of *vic*-Dibromides to Form Alkynes 314

7.14 Terminal Alkynes Can Be Converted to Nucleophiles for Carbon–Carbon Bond Formation 315

7.15 Hydrogenation of Alkenes 317

THE CHEMISTRY OF... Hydrogenation in the Food Industry 318

7.16 Hydrogenation: The Function of the Catalyst 319

7.17 Hydrogenation of Alkynes 320

[A MECHANISM FOR THE REACTION] The Dissolving Metal Reduction of an Alkyne 321

7.18 An Introduction to Organic Synthesis 322

THE CHEMISTRY OF... From the Inorganic to the Organic 324

[WHY DO THESE TOPICS MATTER?] 326

8 Alkenes and Alkynes II

ADDITION REACTIONS 337



8.1 Addition Reactions of Alkenes 338

8.2 Electrophilic Addition of Hydrogen Halides to Alkenes: Mechanism and Markovnikov's Rule 340

[A MECHANISM FOR THE REACTION] Addition of a Hydrogen Halide to an Alkene 341

[A MECHANISM FOR THE REACTION] Addition of HBr to 2-Methylpropene 343

8.3 Stereochemistry of the Ionic Addition to an Alkene 345

[THE STEREOCHEMISTRY OF THE REACTION] Ionic Addition to an Alkene 345

8.4 Addition of Water to Alkenes: Acid-Catalyzed Hydration 346

[A MECHANISM FOR THE REACTION] Acid-Catalyzed Hydration of an Alkene 346

8.5 Alcohols from Alkenes through Oxymercuration–Demercuration: Markovnikov Addition 349

[A MECHANISM FOR THE REACTION] Oxymercuration 351

8.6 Alcohols from Alkenes through Hydroboration–Oxidation: Anti-Markovnikov Syn Hydration 352

8.7 Hydroboration: Synthesis of Alkylboranes 353

[A MECHANISM FOR THE REACTION] Hydroboration 354

8.8 Oxidation and Hydrolysis of Alkylboranes 355

[A MECHANISM FOR THE REACTION] Oxidation of Trialkylboranes 356

8.9 Summary of Alkene Hydration Methods 358

8.10 Protonolysis of Alkylboranes 359

8.11 Electrophilic Addition of Bromine and Chlorine to Alkenes 359

[A MECHANISM FOR THE REACTION] Addition of Bromine to an Alkene 361

THE CHEMISTRY OF... The Sea: A Treasury of Biologically Active Natural Products 362

8.12 Stereospecific Reactions 363

[THE STEREOCHEMISTRY OF THE REACTION] Addition of Bromine to *cis*- and *trans*-2-Butene 364

8.13 Halohydrin Formation 364

[A MECHANISM FOR THE REACTION] Halohydrin Formation from an Alkene 365

THE CHEMISTRY OF... Citrus-Flavored Soft Drinks 366

8.14 Divalent Carbon Compounds: Carbenes 366

8.15 Oxidation of Alkenes: Syn 1,2-Dihydroxylation 368

THE CHEMISTRY OF... Catalytic Asymmetric Dihydroxylation 370

8.16 Oxidative Cleavage of Alkenes 371

[A MECHANISM FOR THE REACTION] Ozonolysis of an Alkene 373

8.17 Electrophilic Addition of Bromine and Chlorine to Alkynes 374

8.18 Addition of Hydrogen Halides to Alkynes 374

8.19 Oxidative Cleavage of Alkynes 375

8.20 HOW TO Plan a Synthesis: Some Approaches and Examples 376

[WHY DO THESE TOPICS MATTER?] 381

9 Nuclear Magnetic Resonance and Mass Spectrometry

TOOLS FOR STRUCTURE
DETERMINATION **391**



- 9.1 Introduction 392
- 9.2 Nuclear Magnetic Resonance (NMR) Spectroscopy 392
- 9.3 **HOW TO** Interpret Proton NMR Spectra 398
- 9.4 Shielding and Deshielding of Protons: More about Chemical Shift 401
- 9.5 Chemical Shift Equivalent and Nonequivalent Protons 403
- 9.6 Spin-Spin Coupling: More about Signal Splitting and Nonequivalent or Equivalent Protons 407
- 9.7 Proton NMR Spectra and Rate Processes 412
- 9.8 Carbon-13 NMR Spectroscopy 414
- 9.9 Two-Dimensional (2D) NMR Techniques 420
- THE CHEMISTRY OF...** Magnetic Resonance Imaging in Medicine 423
- 9.10 An Introduction to Mass Spectrometry 423
- 9.11 Formation of Ions: Electron Impact Ionization 424
- 9.12 Depicting the Molecular Ion 424
- 9.13 Fragmentation 425
- 9.14 Isotopes in Mass Spectra 432
- 9.15 GC/MS Analysis 435
- 9.16 Mass Spectrometry of Biomolecules 436

[**WHY DO THESE TOPICS MATTER?**] 436

See **SPECIAL TOPIC B**, NMR Theory and Instrumentation, in WileyPLUS

10 Radical Reactions

- 10.1 Introduction: How Radicals Form and How They React 449

[**A MECHANISM FOR THE REACTION**]
Hydrogen Atom Abstraction 450

[**A MECHANISM FOR THE REACTION**] Radical Addition to a π Bond 450

THE CHEMISTRY OF... Acne Medications 450



- 10.2 Homolytic Bond Dissociation Energies (DH°) 451
- 10.3 Reactions of Alkanes with Halogens 454
- 10.4 Chlorination of Methane: Mechanism of Reaction 456

[**A MECHANISM FOR THE REACTION**] Radical Chlorination of Methane 456

- 10.5 Halogenation of Higher Alkanes 459

[**A MECHANISM FOR THE REACTION**] Radical Halogenation of Ethane 459

- 10.6 The Geometry of Alkyl Radicals 462
- 10.7 Reactions that Generate Tetrahedral Chirality Centers 462

[**A MECHANISM FOR THE REACTION**] The Stereochemistry of Chlorination at C2 of Pentane 463

[**A MECHANISM FOR THE REACTION**] The Stereochemistry of Chlorination at C3 of (S)-2-Chloropentane 464

- 10.8 Allylic Substitution and Allylic Radicals 466
- 10.9 Benzylic Substitution and Benzylic Radicals 469
- 10.10 Radical Addition to Alkenes: The Anti-Markovnikov Addition of Hydrogen Bromide 472

[**A MECHANISM FOR THE REACTION**] Anti-Markovnikov Addition of HBr 472

- 10.11 Radical Polymerization of Alkenes: Chain-Growth Polymers 474

[**A MECHANISM FOR THE REACTION**] Radical Polymerization of Ethene (Ethylene) 475

- 10.12 Other Important Radical Reactions 478

THE CHEMISTRY OF... Antioxidants 480

THE CHEMISTRY OF... Ozone Depletion and Chlorofluorocarbons (CFCs) 481

[**WHY DO THESE TOPICS MATTER?**] 482

See **SPECIAL TOPIC C**, Chain-Growth Polymers, in WileyPLUS

11 Alcohols and Ethers

SYNTHESIS AND
REACTIONS **489**

- 11.1 Structure and Nomenclature 490
- 11.2 Physical Properties of Alcohols and Ethers 492
- 11.3 Important Alcohols and Ethers 494



- THE CHEMISTRY OF...** Ethanol as a Biofuel 495
- THE CHEMISTRY OF...** Cholesterol and Heart Disease 496
- 11.4 Synthesis of Alcohols from Alkenes 496
- 11.5 Reactions of Alcohols 498
- 11.6 Alcohols as Acids 500
- 11.7 Conversion of Alcohols into Alkyl Halides 501
- 11.8 Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides 501
- 11.9 Alkyl Halides from the Reaction of Alcohols with PBr_3 or SOCl_2 504
- 11.10 Tosylates, Mesylates, and Triflates: Leaving Group Derivatives of Alcohols 505
- [A MECHANISM FOR THE REACTION]** Conversion of an Alcohol into a Mesylate (an Alkyl Methanesulfonate) 507
- 11.11 Synthesis of Ethers 507
- [A MECHANISM FOR THE REACTION]** Intermolecular Dehydration of Alcohols to Form an Ether 508
- [A MECHANISM FOR THE REACTION]** The Williamson Ether Synthesis 509
- 11.12 Reactions of Ethers 513
- [A MECHANISM FOR THE REACTION]** Ether Cleavage by Strong Acids 513
- 11.13 Epoxides 514
- [A MECHANISM FOR THE REACTION]** Alkene Epoxidation 515
- THE CHEMISTRY OF...** The Sharpless Asymmetric Epoxidation 515
- 11.14 Reactions of Epoxides 516
- [A MECHANISM FOR THE REACTION]** Acid-Catalyzed Ring Opening of an Epoxide 516
- [A MECHANISM FOR THE REACTION]** Base-Catalyzed Ring Opening of an Epoxide 517
- 11.15 Anti 1,2-Dihydroxylation of Alkenes via Epoxides 519
- THE CHEMISTRY OF...** Environmentally Friendly Alkene Oxidation Methods 521
- 11.16 Crown Ethers 522
- THE CHEMISTRY OF...** Transport Antibiotics and Crown Ethers 523
- 11.17 Summary of Reactions of Alkenes, Alcohols, and Ethers 523

[WHY DO THESE TOPICS MATTER?] 525

12 Alcohols from Carbonyl Compounds

OXIDATION–REDUCTION AND ORGANOMETALLIC COMPOUNDS **534**

- 12.1 Structure of the Carbonyl Group 535
- 12.2 Oxidation–Reduction Reactions in Organic Chemistry 536
- 12.3 Alcohols by Reduction of Carbonyl Compounds 537

[A MECHANISM FOR THE REACTION] Reduction of Aldehydes and Ketones by Hydride Transfer 539

THE CHEMISTRY OF... Alcohol Dehydrogenase—A Biochemical Hydride Reagent 539

THE CHEMISTRY OF... Stereoselective Reductions of Carbonyl Groups 541

12.4 Oxidation of Alcohols 542

[A MECHANISM FOR THE REACTION] The Swern Oxidation 543

[A MECHANISM FOR THE REACTION] Chromic Acid Oxidation 545

12.5 Organometallic Compounds 547

12.6 Preparation of Organolithium and Organomagnesium Compounds 548

12.7 Reactions of Organolithium and Organomagnesium Compounds 549

[A MECHANISM FOR THE REACTION] The Grignard Reaction 552

12.8 Alcohols from Grignard Reagents 552

12.9 Protecting Groups 561

[WHY DO THESE TOPICS MATTER?] 562

See **FIRST REVIEW PROBLEM SET** in WileyPLUS

13 Conjugated Unsaturated Systems

- 13.1 Introduction 573
- 13.2 The Stability of the Allyl Radical 573
- 13.3 The Allyl Cation 577
- 13.4 Resonance Theory Revisited 578
- 13.5 Alkadienes and Polyunsaturated Hydrocarbons 582



- 13.6 1,3-Butadiene: Electron Delocalization 583
- 13.7 The Stability of Conjugated Dienes 586
- 13.8 Ultraviolet–Visible Spectroscopy 587
- 13.9 Electrophilic Attack on Conjugated Dienes:
1,4-Addition 595
- 13.10 The Diels–Alder Reaction: A 1,4-Cycloaddition
Reaction of Dienes 599

THE CHEMISTRY OF... Molecules with the Nobel Prize in
Their Synthetic Lineage 608

[WHY DO THESE TOPICS MATTER?] 608

14 Aromatic Compounds



- 14.1 The Discovery of Benzene 618
- 14.2 Nomenclature of Benzene Derivatives 619
- 14.3 Reactions of Benzene 621
- 14.4 The Kekulé Structure for Benzene 622
- 14.5 The Thermodynamic Stability of Benzene 623
- 14.6 Modern Theories of the Structure of Benzene 625
- 14.7 Hückel's Rule: The $4n + 2 \pi$ Electron Rule 628
- 14.8 Other Aromatic Compounds 636

THE CHEMISTRY OF... Nanotubes 639

- 14.9 Heterocyclic Aromatic Compounds 639
- 14.10 Aromatic Compounds in Biochemistry 641

THE CHEMISTRY OF... Aryl Halides: Their Uses and
Environmental Concerns 643

- 14.11 Spectroscopy of Aromatic Compounds 644

THE CHEMISTRY OF... Sunscreens (Catching the Sun's
Rays and What Happens to Them) 648

[WHY DO THESE TOPICS MATTER?] 649

See **SPECIAL TOPIC D**, Electrocyclic and Cycloaddition
Reactions, in **WileyPLUS**

15 Reactions of Aromatic Compounds



- 15.1 Electrophilic Aromatic Substitution Reactions 661
- 15.2 A General Mechanism for Electrophilic
Aromatic Substitution 662

- 15.3 Halogenation of Benzene 664

[A MECHANISM FOR THE REACTION] Electrophilic
Aromatic Bromination 664

- 15.4 Nitration of Benzene 665

[A MECHANISM FOR THE REACTION] Nitration of
Benzene 666

- 15.5 Sulfonation of Benzene 666

[A MECHANISM FOR THE REACTION] Sulfonation of
Benzene 667

- 15.6 Friedel–Crafts Reactions 668

[A MECHANISM FOR THE REACTION] Friedel–Crafts
Alkylation 668

THE CHEMISTRY OF... Industrial Styrene Synthesis 669

[A MECHANISM FOR THE REACTION] Friedel–Crafts
Acylation 671

- 15.7 Synthetic Applications of Friedel–Crafts Acylations:
The Clemmensen and
Wolff–Kishner Reductions 673

THE CHEMISTRY OF... DDT 676

- 15.8 Existing Substituents Direct the Position of
Electrophilic Aromatic Substitution 677

- 15.9 Activating and Deactivating Effects: How
Electron-Donating and Electron-Withdrawing
Groups Affect the Rate of an EAS Reaction 684

- 15.10 Directing Effects in Disubstituted Benzenes 685

- 15.11 Reactions of Benzene Ring Carbon Side
Chains 686

- 15.12 Synthetic Strategies 689

- 15.13 The S_NAr Mechanism: Nucleophilic Aromatic
Substitution by Addition–Elimination 691

[A MECHANISM FOR THE REACTION] The S_NAr
Mechanism 692

THE CHEMISTRY OF... Bacterial Dehalogenation of a PCB
Derivative 693

- 15.14 Benzyne: Nucleophilic Aromatic Substitution
by Elimination–Addition 694

[A MECHANISM FOR THE REACTION] The Benzyne
Elimination–Addition Mechanism 694

THE CHEMISTRY OF... Host–Guest Trapping of
Benzyne 697

- 15.15 Reduction of Aromatic Compounds 697

[A MECHANISM FOR THE REACTION] Birch
Reduction 698

[WHY DO THESE TOPICS MATTER?] 699

16

Aldehydes and Ketones

NUCLEOPHILIC
ADDITION TO THE CARBONYL
GROUP 711



16.1 Introduction 712

16.2 Nomenclature of Aldehydes and Ketones 712

16.3 Physical Properties 714

THE CHEMISTRY OF... Aldehydes and Ketones in
Perfumes 715

16.4 Synthesis of Aldehydes 715

[A MECHANISM FOR THE REACTION] Reduction of
an Acyl Chloride to an Aldehyde 718

[A MECHANISM FOR THE REACTION] Reduction of an
Ester to an Aldehyde 719

[A MECHANISM FOR THE REACTION] Reduction
of a Nitrile to an Aldehyde 719

16.5 Synthesis of Ketones 720

16.6 Nucleophilic Addition to the Carbon–Oxygen
Double Bond: Mechanistic Themes 723

[A MECHANISM FOR THE REACTION] Addition of a
Strong Nucleophile to an Aldehyde or Ketone 724

[A MECHANISM FOR THE REACTION] Acid-Catalyzed
Nucleophilic Addition to an Aldehyde or Ketone 724

16.7 The Addition of Alcohols: Hemiacetals and
Acetals 726

[A MECHANISM FOR THE REACTION] Acid-Catalyzed
Hemiacetal Formation 726

[A MECHANISM FOR THE REACTION] Acid-Catalyzed
Acetal Formation 728

16.8 The Addition of Primary and Secondary
Amines 731

[A MECHANISM FOR THE REACTION] Imine
Formation 732

[A MECHANISM FOR THE REACTION]
The Wolff–Kishner Reduction 733

[A MECHANISM FOR THE REACTION] Enamine
Formation 734

THE CHEMISTRY OF... A Very Versatile Vitamin, Pyridoxine
(Vitamin B₆) 735

16.9 The Addition of Hydrogen Cyanide:
Cyanohydrins 736

[A MECHANISM FOR THE REACTION] Cyanohydrin
Formation 736

16.10 The Addition of Ylides: The Wittig Reaction 737

[A MECHANISM FOR THE REACTION] The Wittig
Reaction 739

16.11 Oxidation of Aldehydes 741

16.12 The Baeyer–Villiger Oxidation 741

[A MECHANISM FOR THE REACTION] The Baeyer–
Villiger Oxidation 742

16.13 Chemical Analyses for Aldehydes and
Ketones 743

16.14 Spectroscopic Properties of Aldehydes and
Ketones 743

16.15 Summary of Aldehyde and Ketone Addition
Reactions 746

[WHY DO THESE TOPICS MATTER?] 747

17

Carboxylic Acids and Their Derivatives

NUCLEOPHILIC ADDITION–
ELIMINATION AT THE ACYL CARBON 761



17.1 Introduction 762

17.2 Nomenclature and Physical Properties 762

17.3 Preparation of Carboxylic Acids 770

17.4 Acyl Substitution: Nucleophilic
Addition–Elimination at the Acyl Carbon 773

[A MECHANISM FOR THE REACTION] Acyl
Substitution by Nucleophilic Addition–Elimination 773

17.5 Acyl Chlorides 775

[A MECHANISM FOR THE REACTION] Synthesis of
Acyl Chlorides Using Thionyl Chloride 776

17.6 Carboxylic Acid Anhydrides 777

17.7 Esters 778

[A MECHANISM FOR THE REACTION] Acid-Catalyzed
Esterification 779

[A MECHANISM FOR THE REACTION] Base-Promoted
Hydrolysis of an Ester 782

17.8 Amides 784

[A MECHANISM FOR THE REACTION] DCC-Promoted
Amide Synthesis 787

THE CHEMISTRY OF... Some Hot Topics Related to
Structure and Activity 787

[A MECHANISM FOR THE REACTION] Acidic
Hydrolysis of an Amide 789

[A MECHANISM FOR THE REACTION] Basic Hydrolysis of an Amide 789

[A MECHANISM FOR THE REACTION] Acidic Hydrolysis of a Nitrile 791

[A MECHANISM FOR THE REACTION] Basic Hydrolysis of a Nitrile 791

THE CHEMISTRY OF... Penicillins 792

17.9 Derivatives of Carbonic Acid 792

17.10 Decarboxylation of Carboxylic Acids 795

17.11 Polyesters and Polyamides: Step-Growth Polymers 797

17.12 Summary of the Reactions of Carboxylic Acids and Their Derivatives 798

[WHY DO THESE TOPICS MATTER?] 802

See **SPECIAL TOPIC E**, Step-Growth Polymers, in WileyPLUS

18 Reactions at the α Carbon of Carbonyl Compounds



ENOLS AND ENOLATES 811

18.1 The Acidity of the α Hydrogens of Carbonyl Compounds: Enolate Anions 812

18.2 Keto and Enol Tautomers 813

18.3 Reactions via Enols and Enolates 815

[A MECHANISM FOR THE REACTION] Base-Catalyzed Enolization 815

[A MECHANISM FOR THE REACTION] Acid-Catalyzed Enolization 816

[A MECHANISM FOR THE REACTION] Base-Promoted Halogenation of Aldehydes and Ketones 817

[A MECHANISM FOR THE REACTION] Acid-Catalyzed Halogenation of Aldehydes and Ketones 818

[A MECHANISM FOR THE REACTION] The Haloform Reaction 819

THE CHEMISTRY OF... Chloroform in Drinking Water 819

18.4 Lithium Enolates 821

18.5 Enolates of β -Dicarbonyl Compounds 824

18.6 Synthesis of Methyl Ketones: The Acetoacetic Ester Synthesis 825

18.7 Synthesis of Substituted Acetic Acids: The Malonic Ester Synthesis 830

[A MECHANISM FOR THE REACTION] The Malonic Ester Synthesis of Substituted Acetic Acids 830

18.8 Further Reactions of Active Hydrogen Compounds 833

18.9 Synthesis of Enamines: Stork Enamine Reactions 834

18.10 Summary of Enolate Chemistry 837

[WHY DO THESE TOPICS MATTER?] 838

19 Condensation and Conjugate Addition Reactions of Carbonyl Compounds



MORE CHEMISTRY OF ENOLATES 849

19.1 Introduction 850

19.2 The Claisen Condensation: A Synthesis of β -Keto Esters 850

[A MECHANISM FOR THE REACTION] The Claisen Condensation 851

[A MECHANISM FOR THE REACTION] The Dieckmann Condensation 853

19.3 β -Dicarbonyl Compounds by Acylation of Ketone Enolates 855

19.4 Aldol Reactions: Addition of Enolates and Enols to Aldehydes and Ketones 856

[A MECHANISM FOR THE REACTION] The Aldol Addition 857

[A MECHANISM FOR THE REACTION] Dehydration of the Aldol Addition Product 858

[A MECHANISM FOR THE REACTION] An Acid-Catalyzed Aldol Condensation 858

THE CHEMISTRY OF... A Retro-Aldol Reaction in Glycolysis—Dividing Assets to Double the ATP Yield 860

19.5 Crossed Aldol Condensations 861

[A MECHANISM FOR THE REACTION] A Directed Aldol Synthesis Using a Lithium Enolate 865

19.6 Cyclizations via Aldol Condensations 867

[**A MECHANISM FOR THE REACTION**] The Aldol Cyclization 867

THE CHEMISTRY OF... Polyketide Anticancer Antibiotic Biosynthesis 868

19.7 Additions to α,β -Unsaturated Aldehydes and Ketones 869

[**A MECHANISM FOR THE REACTION**] The Conjugate Addition of HCN 870

[**A MECHANISM FOR THE REACTION**] The Conjugate Addition of an Amine 871

[**A MECHANISM FOR THE REACTION**] The Michael Addition 871

THE CHEMISTRY OF... Conjugate Additions to Activate Drugs 873

19.8 The Mannich Reaction 874

[**A MECHANISM FOR THE REACTION**] The Mannich Reaction 874

THE CHEMISTRY OF... A Suicide Enzyme Substrate 875

19.9 Summary of Important Reactions 876

[**WHY DO THESE TOPICS MATTER?**] 877

See **SPECIAL TOPICS F**, Thiols, Sulfur Ylides, and Disulfides, **AND G**, Thiol Esters and Lipid Biosynthesis, in **WileyPLUS**

20 Amines



20.1 Nomenclature 891

20.2 Physical Properties and Structure of Amines 892

20.3 Basicity of Amines: Amine Salts 894

THE CHEMISTRY OF... Biologically Important Amines 899

20.4 Preparation of Amines 901

[**A MECHANISM FOR THE REACTION**] Reductive Amination 904

[**A MECHANISM FOR THE REACTION**] The Hofmann Rearrangement 908

20.5 Reactions of Amines 909

20.6 Reactions of Amines with Nitrous Acid 911

[**A MECHANISM FOR THE REACTION**] Diazotization 912

THE CHEMISTRY OF... *N*-Nitrosoamines 912

20.7 Replacement Reactions of Arenediazonium Salts 913

20.8 Coupling Reactions of Arenediazonium Salts 917

20.9 Reactions of Amines with Sulfonyl Chlorides 919

THE CHEMISTRY OF... Essential Nutrients and Antimetabolites 920

20.10 Synthesis of Sulfa Drugs 921

20.11 Analysis of Amines 921

20.12 Eliminations Involving Ammonium Compounds 923

20.13 Summary of Preparations and Reactions of Amines 924

[**WHY DO THESE TOPICS MATTER?**] 927

See **SPECIAL TOPIC H**, Alkaloids, in **WileyPLUS**

21 Transition Metal Complexes



PROMOTERS OF KEY BOND-FORMING REACTIONS 938

21.1 Organometallic Compounds in Previous Chapters 939

21.2 Transition Metal Elements and Complexes 939

21.3 **HOW TO** Count Electrons in a Metal Complex 940

21.4 Mechanistic Steps in the Reactions of Some Transition Metal Complexes 942

21.5 Homogeneous Hydrogenation: Wilkinson's Catalyst 944

[**A MECHANISM FOR THE REACTION**] Homogeneous Hydrogenation Using Wilkinson's Catalyst 945

THE CHEMISTRY OF... Homogeneous Asymmetric Catalytic Hydrogenation: Examples Involving *L*-DOPA, (*S*)-Naproxen, and Aspartame 946

21.6 Cross-Coupling Reactions 947

[**A MECHANISM FOR THE REACTION**] The Heck–Mizoroki Reaction Using an Aryl Halide Substrate 948

THE CHEMISTRY OF... The Wacker Oxidation 950

THE CHEMISTRY OF... Complex Cross Couplings 952

21.7 Olefin Metathesis 955

[**A MECHANISM FOR THE REACTION**] The Olefin Metathesis Reaction 955

THE CHEMISTRY OF... Organic Chemistry Alchemy: Turning Simple Alkenes into “Gold” 957

21.8 Transition Metals in Nature: Vitamin B₁₂ and Vanadium Haloperoxidases 958

[WHY DO THESE TOPICS MATTER?] 959

See **SECOND REVIEW PROBLEM SET** in WileyPLUS

22 Carbohydrates

22.1 Introduction 966

22.2 Monosaccharides 968

22.3 Mutarotation 973

22.4 Glycoside Formation 974

[A MECHANISM FOR THE REACTION] Formation of a Glycoside 974

[A MECHANISM FOR THE REACTION] Hydrolysis of a Glycoside 975

22.5 Other Reactions of Monosaccharides 976

22.6 Oxidation Reactions of Monosaccharides 979

22.7 Reduction of Monosaccharides: Alditols 984

22.8 Reactions of Monosaccharides with Phenylhydrazine: Osazones 984

[A MECHANISM FOR THE REACTION] Phenyllosazone Formation 985

22.9 Synthesis and Degradation of Monosaccharides 986

22.10 The D Family of Aldoses 988

22.11 Fischer's Proof of the Configuration of D-(+)-Glucose 988

22.12 Disaccharides 990

THE CHEMISTRY OF... Artificial Sweeteners (How Sweet It Is) 993

22.13 Polysaccharides 994

22.14 Other Biologically Important Sugars 998

22.15 Sugars that Contain Nitrogen 999

22.16 Glycolipids and Glycoproteins of the Cell Surface: Cell Recognition and the Immune System 1001

THE CHEMISTRY OF... Patrolling Leukocytes and Sialyl Lewis^x Acids 1002

22.17 Carbohydrate Antibiotics 1003

22.18 Summary of Reactions of Carbohydrates 1004

[WHY DO THESE TOPICS MATTER?] 1004



23 Lipids

23.1 Introduction 1012

23.2 Fatty Acids and Triacylglycerols 1012

THE CHEMISTRY OF... Olestra and Other Fat Substitutes 1016

THE CHEMISTRY OF... Poison Ivy 1019

THE CHEMISTRY OF... Self-Assembled Monolayers—Lipids in Materials Science and Bioengineering 1020

23.3 Terpenes and Terpenoids 1021

THE CHEMISTRY OF... The Bombardier Beetle's Noxious Spray 1025

23.4 Steroids 1026

THE CHEMISTRY OF... The Enzyme Aromatase 1031

23.5 Prostaglandins 1035

23.6 Phospholipids and Cell Membranes 1036

THE CHEMISTRY OF... STEALTH[®] Liposomes for Drug Delivery 1039

23.7 Waxes 1040

[WHY DO THESE TOPICS MATTER?] 1040

24 Amino Acids and Proteins

24.1 Introduction 1046

24.2 Amino Acids 1047

24.3 Synthesis of α -Amino Acids 1053

[A MECHANISM FOR THE REACTION] Formation of an α -Aminonitrile during the Strecker Synthesis 1054

24.4 Polypeptides and Proteins 1055

24.5 Primary Structure of Polypeptides and Proteins 1058

24.6 Examples of Polypeptide and Protein Primary Structure 1062

THE CHEMISTRY OF... Sickle-Cell Anemia 1064

24.7 Polypeptide and Protein Synthesis 1065



- 24.8 Secondary, Tertiary, and Quaternary Structures of Proteins 1071
- 24.9 Introduction to Enzymes 1075
- 24.10 Lysozyme: Mode of Action of an Enzyme 1077
- THE CHEMISTRY OF...** Carbonic Anhydrase: Shuttling the Protons 1079
- 24.11 Serine Proteases 1079
- 24.12 Hemoglobin: A Conjugated Protein 1081
- THE CHEMISTRY OF...** Some Catalytic Antibodies 1081
- 24.13 Purification and Analysis of Polypeptides and Proteins 1083
- 24.14 Proteomics 1085
- [WHY DO THESE TOPICS MATTER?]** 1087

25 Nucleic Acids and Protein Synthesis



- 25.1 Introduction 1091
- 25.2 Nucleotides and Nucleosides 1092
- 25.3 Laboratory Synthesis of Nucleosides and Nucleotides 1095

- 25.4 Deoxyribonucleic Acid: DNA 1098
- 25.5 RNA and Protein Synthesis 1105
- 25.6 Determining the Base Sequence of DNA: The Chain-Terminating (Dideoxynucleotide) Method 1113
- 25.7 Laboratory Synthesis of Oligonucleotides 1116
- 25.8 Polymerase Chain Reaction 1118
- 25.9 Sequencing of the Human Genome: An Instruction Book for the Molecules of Life 1120
- [WHY DO THESE TOPICS MATTER?]** 1121

GLOSSARY GL-1

INDEX I-1

ANSWERS TO SELECTED PROBLEMS can be found at www.wiley.com/college/solomons

EULA