

ORGANIC CHEMISTRY

THIRD EDITION

G. Marc Loudon

PURDUE UNIVERSITY



$The \ Benjamin/Cummings \ Publishing \ Company, Inc.$

A Division of Addison-Wesley Publishing Company

Redwood City, California § Menlo Park, California Reading, Massachusetts § New York § Don Mills, Ontario § Wokingham, U.K.

Amsterdam § Bonn § Paris § Milan § Sydney § Singapore § Tokyo

Seoul § Taipei § Mexico City § San Juan

Contents

Chemical Bonding and Chemical Structure 1

- 1.1 Introduction 1
 - A. What is Organic Chemistry? 1
 - B. Emergence of Organic Chemistry 1
 - C. Why Study Organic Chemistry? 2
- 1.2 Classical Theories of Chemical Bonding 3
 - A. Electrons in Atoms 3
 - B. The Ionic Bond 4
 - C. The Covalent Bond 5
 - D. The Polar Covalent Bond 10
- 1.3 Structures of Covalent Compounds 12
 - A. Methods for Determining Molecular Structure 12
 - B. Prediction of Molecular Geometry 13
- 1.4 Resonance Structures 19
- 1.5 Wave Nature of the Electron 21
- 1.6 Electronic Structure of the Hydrogen Atom 22
 - A. Orbitals, Quantum Numbers, and Energy 22
 - B. Spatial Characteristics of Orbitals 24
 - C. Summary: Atomic Orbitals of Hydrogen 27
- 1.7 Electronic Structures of More Complex Atoms 28
- 1.8 Another Look at the Covalent Bond: Molecular Orbitals 30

- A. Molecular Orbital Theory 30
- B. Molecular Orbital Theory and Lewis Structures 34
- 1.9 Hybrid Orbitals 34
 - A. Bonding in Methane 34
 - B. Bonding in Ammonia 36

Key Ideas in Chapter 1 37 Additional Problems 39



Alkanes 45

- 2.1 Hydrocarbons 45
- 2.2 Unbranched Alkanes 47
- 2.3 Conformations of Alkanes 49
 - A. Conformation of Ethane 49
 - B. Conformations of Butane 52
- 2.4 Constitutional Isomers and
 - Nomenclature 55
 - A. Isomers 55
 - B. Organic Nomenclature 56
 - C. Substitutive Nomenclature of Alkanes **56**
 - D. Highly Condensed Structures 61
 - E. Classification of Carbon Substitution **63**
- 2.5 Cycloalkanes and Skeletal Structures 64
- 2.6 Physical Properties of Alkanes 67
 - A. Boiling Points 67
 - B. Melting Points 70
 - C. Other Physical Properties 71

2.7 Combustion and Elemental Analysis 72

- A. Reactivity of Alkanes; Combustion 72
- B. Elemental Analysis by Combustion 72
- 2.8 Occurrence and Use of Alkanes 75
- 2.9 Functional Groups and the "R" Notation 78

Key Ideas In Chapter 2 80 Additional Problems 81

Acids and Bases; the Curved Arrow Formalism 87

3.1 Lewis Acid-Base Association Reactions 87

- A. Electron-Deficient Compounds 87
- B. Reactions of Electron-Deficient Compounds with Lewis Bases 88
- C The Curved-Arrow Formalism 89

3.2 Electron-Pair Displacement Reactions 90

- A. Electron-Pair Dispacement Reactions as Lewis Acid-Base Reactions **90**
- B. The Curved-Arrow Formalism 91

3.3 Review of the Curved-Arrow Formalism 94

- A. Use of the Curved-Arrow Formalism to Represent Lewis Acid-Base Reactions **94**
- B. Use of the Curved-Arrow Formalism to Derive Resonance Structures 95

3.4 Brønsted-Lowry Acids and Bases 96

- A. Definition of Brønsted Acids and Bases **96**
- B. Strengths of Brønsted Acids 98
- C. Strengths of Brønsted Bases 100
- D. Equilibria among Different Acids and Bases 101

- 3.5 Free Energy and Chemical Equilibrium 102
- 3.6 Relationship of Structure to Acidity 105
 - A. The Element Effect 105
 - B. The Polar Effect 108

Key Ideas In Chapter 3 112 Additional Problems 113



Introduction to Alkenes; Reaction Rates 121

4.1 Structure and Bonding in Alkenes 121

- A. Carbon Hybridization in Alkenes 122
- B. Cis-Trans Isomerism 126

4.2 Nomenclature of Alkenes 129

- A. IUPAC Substitutive Nomenclature 129
- B. Nomenclature of Stereoisomers: the E,Z System 132

4.3 Unsaturation Number 136

- 4.4 Physical Properties of Alkenes 138
- 4.5 Relative Stabilities of Alkene Isomers 139
 - A. Heats of Formation 139
 - B. Relative Stabilities of Alkene Isomers 141

4.6 Addition Reactions of Alkenes 144

4.7 Addition of Hydrogen Halides to Alkenes 145

- A. Regioselectivity of Hydrogen Halide Addition 145
- B. Carbocation Intermediates in Hydrogen Halide Addition 146
- C. Structure and Stability of Carbocations 148
- D. Carbocation Rearrangement in Hydrogen Halide Addition 151

4.8 Reaction Rates 154

A. The Transition State 154

- B. Multistep Reactions and the Rate-Limiting Step 156
- C. Hammond's Postulate 158
- 4.9 Catalysis 161
 - A. Catalytic Hydrogenation of Alkenes 161
 - B. Hydration of Alkenes 163
 - C. Enzyme Catalysis 165

Key Ideas in Chapter 4 166 Additional Problems 167



- 5.1 Reactions of Alkenes with Halogens 175
 - A. Addition of Chlorine and Bromine 175
 - B. Halohydrins 177
- 5.2 Writing Organic Reactions 179
- 5.3 Conversion of Alkenes into Alcohols 180
 - A. Oxymercuration-Reduction of Alkenes 180
 - B. Hydroboration-Oxidation of Alkenes 183
 - C. Comparison of Methods for the Synthesis of Alcohols from Alkenes 187
- 5.4 Ozonolysis of Alkenes 188
- 5.5 Conversion of Alkenes into Glycols 192
- 5.6 Free-Radical Addition of Hydrogen Bromide to Alkenes 194
 - A. The Peroxide Effect 194
 - B. Free Radicals 196
 - C. Free-Radical Chain Reactions 197
 - D. Explanation of the Peroxide Effect **200**
 - E. Bond Dissociation Energies 204
- 5.7 Industrial Use and Preparation of Alkenes 207
 - A. Free-Radical Polymerization

of Alkenes 207

- B. Thermal Cracking of Alkanes 210
- C. Commercial Importance of Ethylene and Propene 212

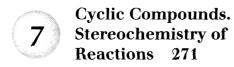
Key Ideas in Chapter 5 214 Additional Problems 215



Introduction to Stereochemistry 225

- 6.1 Enantiomers, Chirality, and Symmetry 225
 - A. Enantiomers and Chirality 225
 - B. Asymmetric Carbon and Stereocenters 228
 - C. Chirality and Symmetry 229
- 6.2 Nomenclature of Enantiomers: The *R*,*S* System 231
- 6.3 Physical Properties of Enantiomers: Optical Activity 234
 - A. Polarized Light 234
 - B. Optical Activity 235
 - C. Optical Activities of Enantiomers 238
- 6.4 Racemates 239
- 6.5 Stereochemical Correlation 240
- 6.6 Diastereomers 241
- 6.7 Meso Compounds 244
- 6.8 Enantiomeric Resolution 249
- 6.9 Chiral Molecules without Asymmetric Atoms 251
- 6.10 Conformational Stereoisomers 253
 - A. Stereoisomers Interconverted by Internal Rotations 253
 - B. Asymmetric Nitrogen: Amine Inversion 254
- 6.11 Fischer Projections 256
- 6.12 The Postulation of Tetrahedral Carbon 260

Key Ideas In Chapter 6 264 Additional Problems 265



- 7.1 Relative Stabilities of the Monocyclic Alkanes 271
- 7.2 Conformations of Cyclohexane 272
 - A. The Chair Conformation 272
 - B. Interconversion of Chair Conformations **276**
 - C. Boat and Twist-Boat Conformations 277
- 7.3 Monosubstituted Cyclohexanes and Conformational Analysis 279
- 7.4 Disubstituted Cyclohexanes 283
 - A. Cis-Trans Isomerism 283
 - B. Conformational Analysis 286
 - C. Use of Planar Structures for Cyclic Compounds 287
 - D. Stereochemical Consequences of the Chair Flip 289
- 7.5 Cyclopentane, Cyclobutane, and Cyclopropane 292
 - A. Cylopentane 292
 - B. Cyclobutane and Cyclopropane 293
- 7.6 Bicyclic and Polycyclic Compounds 294
 - A. Classification and Nomenclature 294
 - B. Cis and Trans Ring Fusion 297
 - C. *Trans*-Cycloalkenes and Bredt's Rule **299**
 - D. Steroids 300
- 7.7 Relative Reactivities of Stereoisomers 302
 - A. Relative Reactivities of Enantiomers 302
 - B. Relative Reactivities of Diastereomers **304**
- 7.8 Reactions That Form Stereoisomers 305
 - A. Reactions of Achiral Compounds That Give Enantiomeric Products 305

- B. Reactions That Give Diastereomeric Products 307
- 7.9 Stereochemistry of Chemical Reactions 310
 - A. Stereochemistry of Addition Reactions 310
 - B. Stereochemistry of Substitution Reactions 310
 - C. Stereochemistry of Bromine Addition 313
 - D. Stereochemistry of Hydroboration-Oxidation 317
 - E. Stereochemistry of Other Addition Reactions 319

Key Ideas in Chapter 7 321 Additional Problems 322



Introduction to Alkyl Halides, Alcohols, Ethers, Thiols, and Sulfides 335

- 8.1 Nomenclature 336
 - A. Nomenclature of Alkyl Halides 336
 - B. Nomenclature of Alcohols and Thiols 338
 - C. Nomenclature of Ethers and Sulfides 343
- 8.2 Structures 345
- 8.3 Effect of Molecular Polarity and Hydrogen Bonding on Physical Properties 346
 - A. Boiling Points of Ethers and Alkyl Halides 346
 - B. Boiling Points of Alcohols 348
 - C. Hydrogen Bonding 348
- 8.4 Solvents in Organic Chemistry 351
 - A. Classification of Solvents 352
 - B. Solubility 353
 - C. Cation-Binding Molecules 358
- 8.5 Acidity of Alcohols and Thiols 360
 - A. Formation of Alkoxides and Mercaptides 362

- B. Polar Effects on Alcohol Acidity 364
- C. Role of the Solvent in Acidity **365**
- 8.6 Basicity of Alcohols and Ethers 366
- 8.7 Grignard and Organolithium Reagents 367
 - A. Formation of Grignard and Organolithium Reagents 368
 - B. Protonolysis of Grignard and Organolithium Reagents 370
- 8.8 Industrial Preparation and Use of Alkyl Halides, Alcohols, and Ethers 371
 - A. Free-Radical Halogenation of Alkanes 371
 - B. Uses of Halogen-Containing Compounds *373*
 - C. Production and Use of Alcohols and Ethers 374
 - D. Safety Hazards of Ethers 377

Key Ideas in Chapter 8 378 Additional Problems 379

9 Chemistry of Alkyl Halides 385

- 9.1 An Overview of Nucleophilic Substitution and β -Elimination Reactions 385
 - A. Nucleophilic Substitution Reactions 385
 - B. β -Elimination Reactions 387
 - C. Competition between Nucleophilic Substitution and β -Elimination Reactions 388
- 9.2 Equilibrium in Nucleophilic Substitution Reactions 389
- 9.3 Reaction Rates 390
 - A. Definition of Reaction Rate 391
 - B. The Rate Law 391
 - C. Reaction Rate and the Standard Free Energy of Activation **392**

- 9.4 The S_N^2 Reaction 394
 - A. Rate Law and Mechanism of the S_N2 Reaction 394
 - B. Stereochemistry of the S_N^2 Reaction 394
 - C. Effect of Alkyl Halide Structure on the S_N2 Reaction 397
 - D. Solvent Effects on Nucleophilicity in the S_N^2 Reaction 399
 - E. Leaving-Group Effects in the $S_N 2$ Reaction 403
 - F. Summary of the S_N 2 Reaction 403
- 9.5 The E2 Reaction 404
 - A. Rate Law and Mechanism of the E2 Reaction 404
 - B. Leaving-Group Effects on the E2 Reaction 404
 - C. Deuterium Isotope Effects in the E2 Reaction 405
 - D. Stereochemistry of the E2 Reaction 407
 - E. Regioselectivity of the E2 Reaction 410
 - F. Competition between the E2 and S_N 2 Reactions: a Closer Look 411
 - G. Summary of the E2 Reaction 416
- 9.6 The S_N1 and E1 Reactions 416
 - A. Rate Law and Mechanism of the $S_N 1$ and E1 Reactions 417
 - B. Rate-Limiting and Product-Determining Steps 419
 - C. Reactivity and Product Distributions in S_N 1-E1 Reactions 421
 - D. Summary of the $S_N 1$ and E1 Reactions 423
- 9.7 Summary of Substitution and Elimination Reactions of Alkyl Halides 423
- 9.8 Carbenes and Carbenoids 427
 - A. α -Elimination Reactions 427
 - B. The Simmons–Smith Reaction 430

Key Ideas in Chapter 9 432 Additional Problems 433

10	Chemistry of Alcoho	ls,
10	Glycols, and Thiols	443

- Dehydration of Alcohols 443 10.1
- Reactions of Alcohols with 10.2 **Hydrogen Halides 447**
- **Sulfonate and Inorganic Ester** 10.3 Derivatives of Alcohols 450
 - A. Sulfonate Ester Derivatives of Alcohols 450
 - B. Alkylating Agents 454
 - C. Ester Derivatives of Strong Inorganic Acids 455
 - D. Reactions of Alcohols with Thionyl Chloride 456
- Conversion of Alcohols into Alkyl 10.4 Halides: Summary 457
- Oxidation and Reduction in Organic 10.5 Chemistry 459
 - A. Oxidation Numbers 459
 - B. Oxidizing and Reducing Agents 463
- 10.6 Oxidation of Alcohols 467
 - A. Oxidation to Aldehydes and Ketones 467
 - B. Oxidation to Carboxylic Acids 469
 - C. Oxidative Cleavage of Glycols 470
- Biological Oxidation of Ethanol 472 10.7
- 10.8 Chemical and Stereochemical Group Equivalence 475
 - A. Chemical Equivalence and Nonequivalence 476
 - B. Stereochemistry of the Alcohol Dehydrogenase Reaction 480
- Oxidation of Thiols 482
- 10.10 Synthesis of Alcohols and Glycols 485
- 10.11 Design of Organic Synthesis 486 **Key Ideas in Chapter 10** 488

Additional Problems 489

Chemistry of Ethers, 11 **Epoxides, and Sulfides 497**

- Synthesis of Ethers and Sulfides 497 11.1
 - A. Williamson Ether Synthesis 497
 - B. Alkoxymercuration-Reduction of Alkenes 499
 - C. Ethers from Alcohol Dehydration and Alkene Addition 500
- Synthesis of Epoxides 503 11.2
 - A. Oxidation of Alkenes with Peroxycarboxylic Acids 503
 - B. Cyclization of Halohydrins 505
- Cleavage of Ethers 507 11.3
- **Nucleophilic Substitution Reactions** 11.4 of Epoxides 509
 - A. Ring-Opening Reactions under Basic Conditions 509
 - B. Ring-Opening Reactions under Acidic Conditions 511
 - C. Reaction of Ethylene Oxide with Grignard Reagents 515
- Oxonium and Sulfonium Salts 516 11.5
 - A. Reactions of Oxonium and Sulfonium Salts 516
 - B. S-Adenosylmethionine: Nature's Methylating Agent 517
- **Neighboring-Group** 11.6 Participation 518
- Oxidation of Ethers and Sulfides 522 11.7
- The Three Fundamental Operations 11.8 of Organic Synthesis 523

Key Ideas in Chapter 11 525 Additional Problems 526

Infrared Spectroscopy and Mass Spectrometry 535

- Introduction to Spectroscopy 535 12.1
 - A. Electromagnetic Radiation 535
 - B. Absorption Spectroscopy 538

12.2	Infrared	Spectroscopy	540
------	----------	---------------------	-----

- A. The Infrared Spectrum 540
- B. Physical Basis of IR Spectroscopy 541

12.3 Infrared Absorption and Chemical Structure 543

- A. Factors that Determine IR Absorption Position 544
- B. Factors that Determine IR Absorption Intensity 547

12.4 Functional-Group Infrared Absorptions 549

- A. IR Spectra of Alkanes 549
- B. IR Spectra of Alkyl Halides 550
- C. IR Spectra of Alkenes 550
- D. IR Spectra of Alcohols and Ethers 553

12.5 The Infrared Spectrometer 555

12.6 Introduction to Mass Spectrometry 556

- A. Production of the Mass Spectrum **556**
- B. Isotopic Peaks 558
- C. Fragmentation Mechanisms **561**
- D. Odd-Electron Ions and Even-Electron Ions **565**
- E. Identifying the Molecular Ion 566
- F. The Mass Spectrometer **567**

Key Ideas in Chapter 12 569 Additional Problems 570

Nuclear Magnetic Resonance Spectroscopy 579

13.1 Introduction to NMR Spectroscopy 579

- 13.2 The NMR Spectrum: Chemical Shift and Integral 582
 - A. Obtaining the NMR Spectrum 582
 - B. Chemical Shift Scales 582
 - C. The Number of Absorptions in an NMR Spectrum 584

- D. Relationship of Chemical Shift to Structure **587**
- E. Counting Protons with the Integral 591
- F. Using the Chemical Shift and Integral to Determine Unknown Structures **592**

13.3 The NMR Spectrum: Spin-Spin Splitting 594

- A. The n + 1 Splitting Rule 595
- B. Why Splitting Occurs 599
- C. Solving Unknown Structures with NMR Spectra Involving Splitting **600**

13.4 Complex NMR Spectra 603

- A. Multiplicative Splitting 603
- B. Breakdown of the n + 1 Rule **607**
- 13.5 Use of Deuterium in Proton NMR 611

13.6 Characteristic Functional-Group NMR Absorptions 611

- A. NMR Spectra of Alkenes 612
- B. NMR Spectra of Alkanes and Cycloalkanes 615
- C. NMR Spectra of Alkyl Halides and Ethers **616**
- D. NMR Spectra of Alcohols 616
- 13.7 NMR Spectroscopy of Dynamic Systems 619
- 13.8 Carbon NMR 622
- 13.9 Solving Structure Problems with Spectroscopy 628
- 13.10 The NMR Spectrometer 632
- 13.11 Other Uses of NMR 633

Key Ideas in Chapter 13 634

Additional Problems 635

14

Chemistry of Alkynes 645

- 14.1 Nomenclature of Alkynes 645
- 14.2 Structure And Bonding in Alkynes 647

14.3	Physical	Properties	of Alkynes	649

- A. Boiling Points and Solubilities 649
- B. IR Spectroscopy of Alkynes 650
- C. NMR Spectroscopy of Alkynes 650

14.4 Introduction to Addition Reaction of the Triple Bond 653

- 14.5 Conversion of Alkynes into Aldehydes and Ketones 654
 - A. Hydration of Alkynes 654
 - B. Hydroboration-Oxidation of Alkynes 657

14.6 Reduction of Alkynes 659

- A. Catalytic Hydrogenation of Alkynes **659**
- B. Reduction of Alkynes with Sodium in Liquid Ammonia **660**

14.7 Acidity of 1-Alkynes 662

- A. Acetylenic Anions 662
- B. Acetylenic Anions as Nucleophiles **665**
- 14.8 Organic Synthesis Using Alkynes 666
- 14.9 Pheromones 668
- 14.10 Occurrence and Use of Alkynes 670Key Ideas in Chapter 14 671Additional Problems 672



Dienes, Resonance, and Aromaticity 679

15.1 Structure and Stability of Dienes 680

- A. Structure and Stability of Conjugated Dienes **680**
- B. Structure and Stability of Cumulated Dienes **682**

15.2 Ultraviolet Spectroscopy 684

- A. The UV Spectrum 684
- B. Physical Basis of UV Spectroscopy **686**
- C. UV Spectroscopy of Conjugated Alkenes **688**

15.3 The Diels-Alder Reaction 690

- A. Reactions of Conjugated Dienes with Alkenes **690**
- B. Effect of Diene Conformation on the Diels-Alder Reaction **694**
- C. Stereochemistry of the Diels-Alder Reaction **696**

15.4 Addition of Hydrogen Halides to Conjugated Dienes 699

- A. 1,2- and 1,4-Additions 699
- B. Allylic Carbocations 701
- C. Kinetic and Thermodynamic Control **703**

15.5 Diene Polymers 707

- 15.6 Resonance 708
 - A. Writing Resonance Structures 709
 - B. Relative Importance of Resonance Structures **710**
 - C. Use of Resonance Structures 712

15.7 Introduction to Aromatic Compounds 715

- A. Benzene, a Puzzling "Alkene" 715
- B. Structure of Benzene 717
- C. Stability of Benzene 719
- D. Aromaticity and the Hückel 4n + 2 Rule **719**
- E. Antiaromatic Compounds 725

Key Ideas in Chapter 15 726 Additional Problems 727



Chemistry of Benzene and Its Derivatives 737

- 16.1 Nomenclature of Benzene Derivatives 737
- 16.2 Physical Properties of Benzene Derivatives 740
- 16.3 Spectroscopy of Benzene Derivatives 741
 - A. IR Spectroscopy 741
 - B. NMR Spectroscopy 742
 - C. CMR Spectroscopy 745
 - D. UV Spectroscopy 746

- 16.4 Electrophilic Aromatic Substitution Reactions of Benzene 748
 - A. Halogenation of Benzene 748
 - B. Electrophilic Aromatic Substitution 750
 - C. Nitration of Benzene 752
 - D. Sulfonation of Benzene 753
 - E. Friedel-Crafts Acylation of Benzene 754
 - F. Friedel-Crafts Alkylation of Benzene 757
- 16.5 Electrophilic Aromatic Substitution Reactions of Substituted Benzenes 760
 - A. Directing Effects of Substituents **760**
 - B. Activating and Deactivating Effects of Substituents 767
 - C. Use of Electrophilic Aromatic Substitution in Organic Synthesis 771
- 16.6 Hydrogenation of Benzene Derivatives 775
- 16.7 Source and Industrial Use of Aromatic Hydrocarbons 776

Key Ideas in Chapter 16 779 Additional Problems 780



Allylic and Benzylic Reactivity 789

- 17.1 Reactions Involving Allylic and Benzylic Carbocations 789
- 17.2 Reactions Involving Allylic and Benzylic Radicals 794
- 17.3 Reactions Involving Allylic and Benzylic Anions 799
 - A. Allylic Grignard Reagents 800
 - B. E2 Eliminations Involving Allylic or Benzylic Hydrogens **802**
- 17.4 Allylic and Benzylic S_N2 Reactions 803
- 17.5 Benzylic Oxidation of Alkylbenzenes 804

- **17.6 Terpenes 806**
 - A. The Isoprene Rule **806**
 - B. Biosynthesis of Terpenes 808

Key Ideas in Chapter 17 812 Additional Problems 813

18

Chemistry of Aryl Halides, Vinylic Halides, and Phenols 823

- $\begin{array}{cc} \textbf{18.1} & \textbf{Lack of Reactivity of Vinylic} \\ \textbf{and Aryl Halides Under } S_N \textbf{2} \\ \textbf{Conditions 824} \end{array}$
- 18.2 Elimination Reactions of Vinylic Halides 826
- $\begin{array}{cc} \text{18.3} & \text{Lack of Reactivity of Vinylic} \\ & \text{and Aryl Halides Under S}_{N} \text{1} \\ & \text{Conditions 826} \end{array}$
- 18.4 Nucleophilic Substitution Reactions of Aryl Halides 829
 - A. Nucleophilic Aromatic Substitution 829
 - B. Substitution by Elimination-Addition: Benzyne 832
 - C. Summary: Nucleophilic Substitution Reactions of Aryl Halides 835
- 18.5 Aryl and Vinylic Grignard Reagents 836
- 18.6 Acidity of Phenols 837
 - A. Resonance Effects on Acidity 837
 - B. Formation and Use of Phenoxides **840**
- 18.7 Oxidation of Phenols to Quinones 841
- 18.8 Electrophilic Aromatic Substitution Reactions of Phenols 846
- 18.9 Lack of Reactivity of the Aryl-Oxygen Bond 849
- 18.10 Industrial Preparation and Use of Phenol 851

Key Ideas in Chapter 18 852 Additional Problems 853

19

Chemistry of Aldehydes and Ketones; Carbonyl-Addition Reactions 865

- Nomenclature of Aldehydes and 19.1 **Ketones 867**
 - A. Common Nomenclature 867
 - B. Substitutive Nomenclature 869
- **Physical Properties of Aldehydes** 19.2 and Ketones 871
- Spectroscopy of Aldehydes and 19.3 Ketones 872
 - A. IR Spectroscopy 872
 - B. Proton NMR Spectroscopy 874
 - C. Carbon NMR Spectroscopy 875
 - D. UV Spectroscopy 876
 - E. Mass Spectrometry 878
- Synthesis of Aldehydes and 19.4 **Ketones 880**
- Introduction to Aldehyde and 19.5 **Ketone Reactions 880**
- **Basicity of Aldehydes and** 19.6 Ketones 881
- **Reversible Addition Reactions** 19.7 of Aldehydes and Ketones 884
 - A. Mechanisms of Carbonyl-Addition Reactions 884
 - B. Equilibria and Rates in Carbonyl-Addition Reactions 887
- Reduction of Aldehydes and 19.8 **Ketones to Alcohols 890**
- Reactions of Aldehydes and 19.9 Ketones with Grignard and Related Reagents 895
- 19.10 Acetals and Their Use as **Protecting Groups 898**
 - A. Preparation and Hydrolysis of Acetals 898
 - B. Protecting Groups 902

- 19.11 Reactions of Aldehydes and Ketones with Amines 904
 - A. Reaction with Primary Amines and Other Monosubstituted Derivatives of Ammonia 904
 - B. Reaction with Secondary Amines 907
- 19.12 Reduction of Carbonyl Groups to Methylene Groups 909
- 19.13 The Wittig Alkene Synthesis 911
- 19.14 Oxidation of Aldehydes to Carboxylic Acids 915
- 19.15 Manufacture and Use of Aldehydes and Ketones 917

Key Ideas in Chapter 19 918 Additional Problems 919



Chemistry of Carboxylic Acids 929

- 20.1 Nomenclature of Carboxylic Acids 929
 - A. Common Nomenclature 929
 - B. Substitutive Nomenclature 931
- **Structure and Physical Properties** 20.2 of Carboxylic Acids 934
- **Spectroscopy of Carboxylic** 20.3 Acids 935
 - A. IR Spectroscopy 935
 - B. NMR Spectroscopy 936
- **Acid-Base Properties of Carboxylic** 20.4 Acids 937
 - A. Acidity of Carboxylic and Sulfonic Acids 937
 - B. Basicity of Carboxylic Acids 941
- Fatty Acids, Soaps, and 20.5 Detergents 942
- Synthesis of Carboxylic Acids 944 20.6
- **Introduction to Carboxylic Acid** 20.7 Reactions 945
- Conversion of Carboxylic Acids 20.8 into Esters 946

A.	Acid-Catalyzed	Esterification	946
----	----------------	----------------	-----

- B. Esterification by Alkylation 950
- 20.9 Conversion of Carboxylic Acids into Acid Chlorides and Anhydrides 952
 - A. Synthesis of Acid Chlorides 952
 - B. Synthesis of Anhydrides 954
- 20.10 Reduction of Carboxylic Acids to Primary Alcohols 956
- 20.11 Decarboxylation of Carboxylic Acids 958

Key Ideas in Chapter 20 960 Additional Problems 961

21 Chemistry of Carboxylic Acid Derivatives 971

- 21.1 Nomenclature and Classification of Carboxylic Acid Derivatives 971
 - A. Esters and Lactones 971
 - B. Acid Halides 973
 - C. Anhydrides 974
 - D. Nitriles 974
 - E. Amides, Lactams, and Imides 975
 - F. Nomenclature of Substituent Groups **976**
 - G. Carbonic Acid Derivatives 977
- 21.2 Structures of Carboxylic Acid Derivatives 978
- 21.3 Physical Properties of Carboxylic Acid Derivatives 980
 - A. Esters 980
 - B. Anhydrides and Acid Chlorides 980
 - C. Nitriles 981
 - D. Amides **981**
- 21.4 Spectroscopy of Carboxylic Acid Derivatives 982
 - A. IR Spectroscopy 982
 - B. NMR Spectroscopy 982
- 21.5 Basicity of Carboxylic Acid Derivatives 987

- 21.6 Introduction to Reactions of Carboxylic Acid Derivatives 988
- 21.7 Hydrolysis of Carboxylic Acid Derivatives 989
 - A. Hydrolysis of Esters **989**
 - B. Hydrolysis of Amides 992
 - C. Hydrolysis of Nitriles 994
 - D. Hydrolysis of Acid Chlorides and Anhydrides 995
 - E. Mechanisms and Reactivity in Nucleophilic Acyl Substitution Reactions **996**
- 21.8 Reactions of Carboxylic Acid Derivatives with Nucleophiles 1000
 - A. Reactions of Acid Chlorides with Nucleophiles 1000
 - B. Reactions of Anhydrides with Nucleophiles **1004**
 - C. Reactions of Esters with Nucleophiles 1005
- 21.9 Reactions of Carboxylic Acid Derivatives 1007
 - A. Reduction of Esters to Primary Alcohols 1007
 - B. Reduction of Amides to Amines 1008
 - C. Reduction of Nitriles to Primary Amines 1010
 - D. Reduction of Acid Chlorides to Aldehydes 1012
 - E. Relative Reactivities of Carbonyl Compounds 1014
- 21.10 Reactions of Carboxylic Acid Derivatives with Organometallic Reagents 1015
 - A. Reaction of Esters with Grignard Reagents 1015
 - B. Reaction of Acid Chlorides with Lithium Dialkylcuprates 1017
- 21.11 Synthesis of Carboxylic Acid Derivatives 1018
- 21.12 Use and Occurrence of Carboxylic Acids and Their Derivatives 1020
 - A. Nylon and Polyesters 1020
 - B. Waxes, Fats, and Phospholipids 1023

Key Ideas in Chapter 21 1026 Additional Problems 1027

Chemistry of Enolate Ions, 22 Enols, and α,β-Unsaturated Carbonyl Compounds 1039

- 22.1 Acidity of Carbonyl Compounds 1039
 - A. Formation of Enolate Anions 1039
 - B. Introduction to Reactions of Enolate Ions 1042
- 22.2 Enolization of Carbonyl Compounds 1044
- 22.3 α-Halogenation of Carbonyl Compounds 1048
 - A. Acid-Catalyzed α -Halogenation of Aldehydes and Ketones 1048
 - B. Halogenation of Aldehydes and Ketones in Base: the Haloform Reaction 1050
 - C. α -Bromination of Carboxylic Acids 1052
 - D. Reactions of α -Halo Carbonyl Compounds 1053
- 22.4 Aldol Addition and Aldol Condensation 1055
 - A. Base-Catalyzed Aldol Reactions 1055
 - B. Acid-Catalyzed Aldol Condensation 1058
 - C. Special Types of Aldol Reactions 1060
 - D. Synthesis with the Aldol Condensation 1062
- 22.5 Condensation Reactions Involving Ester Enolate Ions 1064
 - A. Claisen Condensation 1065
 - B. Dieckmann Condensation 1068
 - C. Crossed Claisen Condensation 1069
 - D. Synthesis with the Claisen Condensation 1071

- 22.6 Alkylation of Ester Enolate Ions 1074
 - A. Malonic Ester Synthesis 1074
 - B. Direct Alkylation of Enolate Ions Derived from Simple Monoesters 1076
 - C. Acetoacetic Ester Synthesis 1079
- 22.7 Biosynthesis of Fatty Acids 1082
- 22.8 Conjugate-Addition Reactions 1085
 - A. Conjugate Addition to α,β-Unsaturated Carbonyl Compounds 1085
 - B. Conjugate Addition vs. Carbonyl-Group Reactions 1088
 - C. Conjugate Addition of Enolate Ions 1090
- **Reduction of** α , β **-Unsaturated** Carbonyl Compounds 1093
- 22.10 Reactions of α,β-Unsaturated Carbonyl Compounds with Organometallic Reagents 1094
 - A. Addition of Organolithium Reagents to the Carbonyl Group 1094
 - B. Conjugate Addition of Lithium Dialkylcuprate Reagents 1095
- 22.11 Organic Synthesis with Conjugate-Addition Reactions 1097

Key Ideas in Chapter 22 1098 Additional Problems 1099

23 Chemistry of Amines 1113

- 23.1 Nomenclature of Amines 1114
 - A. Common Nomenclature 1114
 - B. Substitutive Nomenclature 1114
- 23.2 Structure of Amines 1116
- 23.3 Physical Properties of Amines 1117
- 23.4 Spectroscopy of Amines 1118
 A. IR Spectroscopy 1118

B. NMR Spectroscopy	1119
---------------------	------

C. Mass Spectrometry 1119

23.5 Basicity and Acidity of Amines 1120

- A. Basicity of Amines 1120
- B. Substituent Effects on Amine Basicity 1121
- C. Separations Using Amine Basicity 1125
- D. Acidity of Amines 1127
- E. Summary of Acidity and Basicity 1127

23.6 Quaternary Ammonium Salts 1127

23.7 Alkylation and Acylation Reactions of Amines 1128

- A. Direct Alkylation of Amines 1128
- B. Reductive Amination 1130
- C. Acylation of Amines 1132

23.8 Hofmann Elimination of Quaternary Ammonium Hydroxides 1133

23.9 Aromatic Substitution Reactions of Aniline Derivatives 1137

23.10 Diazotization; Reactions of Diazonium Ions 1139

- A. Formation and Substitution Reactions of Diazonium Salts 1139
- B. Aromatic Substitution with Diazonium Ions 1143
- C. Reactions of Secondary and Tertiary Amines with Nitrous Acid 1144

23.11 Synthesis of Amines 1146

- A. Gabriel Synthesis of Primary Amines 1146
- B. Reduction of Nitro Compounds 1147
- C. Curtius and Hofmann Rearrangements 1148
- D. Synthesis of Amines: Summary 1153

23.12 Use and Occurrence of Amines 1153

- A. Industrial Use of Amines and Ammonia 1153
- B. Naturally Occurring Amines 1154

Key Ideas in Chapter 23 1156 Additional Problems 1157



Chemistry of Naphthalene and the Aromatic Heterocycles 1169

24.1 Chemistry of Naphthalene 1171

- A. Physical Properties and Structure 1171
- B. Nomenclature 1171
- C. Electrophilic Substitution Reactions 1173

24.2 Introduction to the Aromatic Heterocycles 1177

- A. Nomenclature 1178
- B. Structure and Aromaticity 1179
- C. Basicity and Acidity of the Nitrogen Heterocycles 1182

24.3 Chemistry of Furan, Pyrrole, and Thiophene 1184

- A. Electrophilic Aromatic Substitution 1184
- B. Addition Reactions of Furan 1187
- C. Side-Chain Reactions 1188

24.4 Synthesis of Indoles 1189

- A. Fischer Indole Synthesis 1190
- B. Reissert Indole Synthesis 1192

24.5 Chemistry of Pyridine and Quinoline 1194

- A. Electrophilic Aromatic Substitution 1194
- B. Nucleophilic Aromatic Substitution 1197
- C. Pyridinium Salts and Their Reactions 1201
- D. Side-Chain Reactions of Pyridine Derivatives 1202
- E. Skraup Synthesis of Quinolines 1204

24.6 Occurrence of Heterocyclic Compounds 1206

Key Ideas in Chapter 24 1208 Additional Problems 1209



Pericyclic Reactions 1219

- 25.1 Molecular Orbitals of Conjugated π-Electron Systems 1222
 - A. Molecular Orbitals of Conjugated Alkenes 1222
 - B. Molecular Orbitals of Conjugated Ions and Radicals 1226
 - C. Excited States 1227
- 25.2 Electrocyclic Reactions 1229
 - A. Thermal Electrocyclic Reactions 1229
 - B. Excited-State (Photochemical) Electrocyclic Reactions 1231
 - C. Selection Rules and Microscopic Reversibility 1232
- 25.3 Cycloaddition Reactions 1235
- 25.4 Sigmatropic Reactions 1239
 - A. Classification and Stereochemistry 1239
 - B. [3,3] Sigmatropic Rearrangements 1246
 - C. Summary: Selection Rules for Sigmatropic Reactions 1248
- 25.5 Summary of The Pericyclic Selection Rules 1250
- 25.6 Fluxional Molecules 1251
- 25.7 Formation of Vitamin D 1252

Key Ideas in Chapter 25 1254

Additional Problems 1255



Amino Acids, Peptides, and Proteins 1263

- 26.1 Nomenclature of Amino Acids and Peptides 1264
 - A. Nomenclature of Amino Acids 1264
 - B. Nomenclature of Peptides 1265
- 26.2 Stereochemistry of the α-Amino Acids 1268
- 26.3 Acid-Base Properties of Amino Acids and Peptides 1269

- A. Zwitterionic Structures of Amino Acids and Peptides 1269
- B. Isoelectric Points of Amino Acids and Peptides 1271
- C. Separations of Amino Acids and Peptides Using Acid-Base Properties 1275
- 26.4 Synthesis and Enantiomeric Resolution of α -Amino Acids 1278
 - A. Alkylation of Ammonia 1278
 - B. Alkylation of Aminomalonate Derivatives 1278
 - C. Strecker Synthesis 1279
 - D. Enantiomeric Resolution of α -Amino Acids 1280
- 26.5 Acylation and Esterfication Reactions of α -Amino Acids 1281
- 26.6 Determination of Peptide Structure 1282
 - A. Hydrolysis of Peptides; Amino Acid Analysis 1282
 - B. Sequential Degradation of Peptides 1284
 - C. Specific Cleavage of Peptides 1286
- 26.7 Solid-Phase Peptide Synthesis 1291
- 26.8 Structures of Peptides and Proteins 1299
 - A. Primary Structure 1299
 - B. Secondary Structure 1301
 - C. Tertiary and Quaternary Structures 1303
- 26.9 Enzymes: Biological Catalysts 1308
- 26.10 Occurrence of Peptides and Proteins 1311

Key Ideas in Chapter 26 1313 Additional Problems 1315



Carbohydrates and Nucleic Acids 1325

27.1 Classification and Properties of Carbohydrates 1326

- 27.2 Structures of the Monosaccharides 1327
 - A. Stereochemistry and Configuration 1327
 - B. Cyclic Structures of the Monosaccharides 1331
- 27.3 Mutarotation of Carbohydrates 1337
- 27.4 Base-Catalyzed Isomerization of Aldoses and Ketoses 1341
- 27.5 Glycosides 1343
- 27.6 Ether and Ester Derivatives of Carbohydrates 1346
- 27.7 Oxidation and Reduction Reactions of Carbohydrates 1348
 - A. Oxidation to Aldonic Acids 1349
 - B. Oxidation to Aldaric Acids 1350
 - C. Periodate Oxidation 1352
 - D. Reduction to Alditols 1353
- 27.8 Kiliani-Fischer Synthesis 1353
- 27.9 Proof of Glucose Stereochemistry 1355
 - A. Which Diastereomer? The Fischer Proof 1355
 - B. Which Enantiomer?
 The Absolute Configuration of D-(+)-Glucose 1359
- 27.10 Disaccharides and Polysaccharides 1361
 - A. Disaccharides 1361
 - B. Polysaccharides 1364
- 27.11 Nucleosides, Nucleotides, and Nucleic Acids 1367
 - A. Nucleosides and Nucleotides 1367
 - B. Structures of DNA and RNA 1370
- 27.12 DNA, RNA, and the Genetic Code 1375
 - A. Role of DNA and RNA in Protein Synthesis 1375
 - B. DNA Modification and Chemical Carcinogenesis 1378

Key Ideas in Chapter 27 1380 Additional Problems 1382



Appendices A-1

- I. Substitutive Nomenclature of Organic Compounds A-1
- II. Important Infrared Absorptions A-2
- III. Important Proton NMR Chemical Shifts A-4
 - A. Protons within Functional Groups A-4
 - B. Alkyl Protons Adjacent to Functional Groups A-4
- IV. Summary of Synthetic Methods A-5
- V. Reactions Used to Form Carbon-Carbon Bonds A-11
- VI. Typical Acidities and Basicities of Organic Functional Groups A-12
 - A. Acidities of Groups That Ionize to Give Anionic Conjugate
 Bases A-12
 - B. Basicities of Groups That Ionize to Give Cationic Conjugate Bases A-13

Credits c-1

Index 1-13