

C O N T E N T S

Preface xviii
A Guide to Using This Text xxi

CHAPTER 1 **CHEMICAL BONDING** 1

- 1.1 Atoms, Electrons, and Orbitals 1
- 1.2 Ionic Bonds 4
- 1.3 Covalent Bonds 5
- 1.4 Double Bonds and Triple Bonds 6
- 1.5 Polar Covalent Bonds and Electronegativity 7
- 1.6 Formal Charge 7
- 1.7 Structural Formulas of Organic Molecules 10
- 1.8 Isomers and Isomerism 13
- 1.9 Resonance 14
- 1.10 The Shapes of Some Simple Molecules 17
- Molecular Models** 18
- 1.11 Molecular Polarity 20
- 1.12 sp^3 Hybridization and Bonding in Methane 21
- 1.13 Bonding in Ethane 22
- 1.14 sp^2 Hybridization and Bonding in Ethylene 23
- 1.15 sp Hybridization and Bonding in Acetylene 25
- Learning Objectives** 26
- 1.16 SUMMARY 27
- Additional Problems** 29

CHAPTER 2 **ALKANES AND CYCLOALKANES** 33

- 2.1 Classes of Hydrocarbons 33
- 2.2 Reactive Sites in Hydrocarbons 34
- 2.3 The Key Functional Groups 35
- 2.4 Introduction to Alkanes: Methane, Ethane, and Propane 36
- 2.5 Conformations of Ethane and Propane 37
- Methane and the Biosphere** 38
- 2.6 Isomeric Alkanes: The Butanes 40
- 2.7 Higher Alkanes 41
- 2.8 IUPAC Nomenclature of Unbranched Alkanes 44
- 2.9 Applying the IUPAC Rules: The Names of the C_6H_{14} Isomers 45
- 2.10 Alkyl Groups 47
- 2.11 IUPAC Names of Highly Branched Alkanes 48
- 2.12 Cycloalkane Nomenclature 49
- 2.13 Conformations of Cycloalkanes 51
- 2.14 Conformations of Cyclohexane 51
- 2.15 Conformational Inversion (Ring Flipping) in Cycloalkanes 53

CONTENTS

- 2.16 Conformational Analysis of Monosubstituted Cyclohexanes 53
2.17 Disubstituted Cyclohexanes: Stereoisomers 56
2.18 Polycyclic Ring Systems 57
2.19 Physical Properties of Alkanes and Cycloalkanes 58
2.20 Chemical Properties: Combustion of Alkanes 60
Learning Objectives 60
2.21 SUMMARY 61
Additional Problems 64

CHAPTER 3**ALCOHOLS AND ALKYL HALIDES 68**

- 3.1 Nomenclature of Alcohols and Alkyl Halides 69
The Common Alcohols: Methyl, Ethyl, and Isopropyl Alcohol 70
3.2 Classes of Alcohols and Alkyl Halides 71
3.3 Bonding in Alcohols and Alkyl Halides 71
3.4 Physical Properties of Alcohols and Alkyl Halides: Intermolecular Forces 72
3.5 Acids and Bases: General Principles 75
3.6 Acid-Base Reactions: A Mechanism for Proton Transfer 78
3.7 Preparation of Alkyl Halides from Alcohols and Hydrogen Halides 79
3.8 Mechanism of the Reaction of Alcohols with Alkyl Halides 80
3.9 Structure, Bonding, and Stability of Carbocations 82
3.10 Electrophiles and Nucleophiles 83
3.11 Reaction of Primary Alcohols and Hydrogen Halides 84
Learning Objectives 84
3.12 SUMMARY 85
Additional Problems 87

CHAPTER 4**ALKENES AND ALKYNES I: STRUCTURE AND PREPARATION 90**

- 4.1 Alkene Nomenclature 91
Ethylene 92
4.2 Structure and Bonding in Alkenes 93
4.3 Isomerism in Alkenes 95
4.4 Naming Stereoisomeric Alkenes by the *E-Z* Notational System 96
4.5 Relative Stability of Alkenes 99
4.6 Preparation of Alkenes: Elimination Reactions 101
4.7 Dehydration of Alcohols 102
4.8 The Mechanism of Acid-Catalyzed Dehydration of Alcohols 104
4.9 Dehydrohalogenation of Alkyl Halides 106
4.10 The *E2* Mechanism of Dehydrohalogenation 107
4.11 A Different Mechanism for Alkyl Halide Elimination: The *E1* Mechanism 108
4.12 Alkyne Nomenclature 111
4.13 Structure and Bonding in Alkynes: *sp* Hybridization 111
4.14 Preparation of Alkynes by Elimination Reactions 111
Natural and "Designed" Eneidyne Antibiotics 112
Learning Objectives 113
4.15 SUMMARY 113
Additional Problems 116

CHAPTER 5**ALKENES AND ALKYNES II: REACTIONS** 120

- 5.1 Hydrogenation of Alkenes 120
5.2 Electrophilic Addition of Hydrogen Halides to Alkenes 122
5.3 Regioselectivity of Hydrogen Halide Addition: Markovnikov's Rule 123
5.4 Mechanistic Basis for Markovnikov's Rule 125
5.5 Acid-Catalyzed Hydration of Alkenes 126
5.6 Addition of Halogens to Alkenes 127
5.7 Introduction to Organic Chemical Synthesis 130
Ethylene: One of the Most Important Industrial Organic Chemicals 131
5.8 Electrophilic Addition Reactions of Conjugated Dienes 132
5.9 Acidity of Acetylene and Terminal Alkynes 134
5.10 Preparation of Alkynes by Alkylation 136
5.11 Addition Reactions of Alkynes 137
Learning Objectives 140
5.12 SUMMARY 140
Additional Problems 142

CHAPTER 6**AROMATIC COMPOUNDS** 147

- 6.1 Structure and Bonding of Benzene 147
Aromatic Compounds: History and Some Applications 148
6.2 An Orbital Hybridization View of Bonding in Benzene 149
6.3 Substituted Derivatives of Benzene and Their Nomenclature 150
6.4 Polycyclic Aromatic Hydrocarbons 152
Chemical Carcinogens 153
6.5 Aromatic Side-Chain Reactions 153
6.6 Reactions of Arenes: Electrophilic Aromatic Substitution 156
6.7 Mechanism of Electrophilic Aromatic Substitution 157
6.8 Intermediates in Electrophilic Aromatic Substitution 158
6.9 Rate and Regioselectivity in Electrophilic Aromatic Substitution 163
6.10 Substituent Effects: Activating Groups 164
6.11 Substituent Effects: Strongly Deactivating Groups 168
6.12 Substituent Effects: Halogens 171
6.13 Regioselective Synthesis of Disubstituted Aromatic Compounds 172
6.14 A General View of Aromaticity: Hückel's Rule 172
6.15 Heterocyclic Aromatic Compounds 173
Learning Objectives 174
6.16 SUMMARY 175
Additional Problems 177

CHAPTER 7**STEREOCHEMISTRY** 182

- 7.1 Molecular Chirality: Enantiomers 182
7.2 The Stereogenic Center 183
7.3 Symmetry in Achiral Structures 185
7.4 Properties of Chiral Molecules 186
7.5 Absolute and Relative Configuration 188

- 7.6 The Cahn–Ingold–Prelog *R–S* Notational System 189
7.7 Fischer Projections 190
7.8 Physical Properties of Enantiomers 191
Chiral Drugs 192
7.9 Reactions That Create a Stereogenic Center 193
7.10 Chiral Molecules with Two Stereogenic Centers 195
7.11 Achiral Molecules with Two Stereogenic Centers 196
7.12 Molecules with Multiple Stereogenic Centers 197
7.13 Resolution of Enantiomers 198
Learning Objectives 199
7.14 SUMMARY 200
Additional Problems 202

CHAPTER 8

NUCLEOPHILIC SUBSTITUTION 206

- 8.1 Functional Group Transformation by Nucleophilic Substitution 206
8.2 The S_N2 Mechanism of Nucleophilic Substitution 208
8.3 How S_N2 Reactions Occur: Stereochemistry 209
Nucleophilic Substitution and Cancer 209
8.4 Steric Effects in S_N2 Reactions 211
8.5 The S_N1 Mechanism of Nucleophilic Substitution 213
8.6 Carbocation Stability and S_N1 Reactions 214
8.7 Stereochemistry of S_N1 Reactions 216
8.8 Substitution and Elimination as Competing Reactions 217
Learning Objectives 219
8.9 SUMMARY 219
Additional Problems 219

CHAPTER 9

FREE RADICALS 224

- 9.1 Structure and Stability of Free Radicals 224
9.2 Bond Dissociation Energies 225
Free Radicals and Biology 226
9.3 Chlorination of Methane 229
9.4 Mechanism of Methane Chlorination 230
Halogenated Hydrocarbons and the Environment 231
9.5 Halogenation of Higher Alkanes 232
9.6 Chlorofluorocarbons and the Environment 233
9.7 Free-Radical Addition of Hydrogen Bromide to Alkanes 234
9.8 Polymerization of Alkenes 235
Diene Polymers 238
Learning Objectives 239
9.9 SUMMARY 239
Additional Problems 240

CHAPTER 10
ALCOHOLS, ETHERS, AND PHENOLS 242

-
- 10.1 Sources of Alcohols 242
10.2 Reactions That Yield Alcohols: A Review and a Preview 243
10.3 Preparation of Alcohols by Reduction of Aldehydes and Ketones 246
10.4 Reactions of Alcohols: A Review and a Preview 248
10.5 Oxidation of Alcohols 249
 Biological Oxidation of Alcohols 251
10.6 Thiol Nomenclature 251
10.7 Properties of Thiols 252
10.8 Introduction to Ethers 253
10.9 Ether Nomenclature 253
10.10 Preparation of Ethers 254
 Polyether Antibiotics 255
10.11 Preparation of Epoxides 257
10.12 Reactions of Epoxides 258
 Epoxides and Chemical Carcinogenesis 259
10.13 Introduction to Phenols: Nomenclature 259
10.14 Synthetic and Naturally Occurring Phenol Derivatives 260
10.15 Acidity of Phenols 261
10.16 Reactions of Phenols: Preparation of Aryl Ethers 263
10.17 Oxidation of Phenols: Quinones 263
 Agent Orange and Dioxin 264
 Learning Objectives 266
10.18 SUMMARY 266
 Additional Problems 269

CHAPTER 11
ALDEHYDES AND KETONES 274

-
- 11.1 Nomenclature 274
11.2 Structure and Bonding: The Carbonyl Group 276
11.3 Physical Properties 277
11.4 Sources of Aldehydes and Ketones 277
11.5 Reactions of Aldehydes and Ketones: A Review and a Preview 278
11.6 Principles of Nucleophilic Addition: Hydration of Aldehydes and Ketones 280
11.7 Cyanohydrin Formation 282
11.8 Acetal Formation 285
11.9 Reaction with Primary Amines: Imines 286
11.10 Reactions That Introduce New Carbon–Carbon Bonds: Organometallic Compounds 287
 Imines in Biological Chemistry 288
11.11 Grignard Reagents 290
11.12 Synthesis of Alcohols Using Grignard Reagents 292
11.13 Grignard Reagents in Synthesis 292
11.14 Oxidation of Aldehydes 295
11.15 The α -Carbon Atom and Its Hydrogens 296

- 11.16 Enols and Enolization 296
11.17 Base-Catalyzed Enolization: Enolate Ions 297
11.18 The Aldol Condensation 298
 Learning Objectives 301
11.19 SUMMARY 302
 Additional Problems 305

CHAPTER 12

CARBOXYLIC ACIDS 310

- 12.1 Carboxylic Acid Nomenclature 311
12.2 Structure and Bonding 312
12.3 Physical Properties 313
 Prostaglandins 314
12.4 Acidity of Carboxylic Acids 314
12.5 Substituents and Acid Strength 315
12.6 Ionization of Substituted Benzoic Acids 317
12.7 Salts of Carboxylic Acids 318
12.8 Sources of Carboxylic Acids 320
12.9 Synthesis of Carboxylic Acids by the Carboxylation of Grignard Reagents 322
12.10 Synthesis of Carboxylic Acids by Preparation and Hydrolysis of Nitriles 322
12.11 Reactions of Carboxylic Acids 323
 Learning Objectives 325
12.12 SUMMARY 325
 Additional Problems 328

CHAPTER 13

CARBOXYLIC ACID DERIVATIVES 331

- 13.1 Nomenclature of Carboxylic Acid Derivatives 331
13.2 Structure of Carboxylic Acid Derivatives 333
13.3 Nucleophilic Acyl Substitution: Hydrolysis 334
13.4 Natural Sources of Esters 336
 Biological Acyl Transfer 337
13.5 Preparation of Esters: Fischer Esterification 338
13.6 Preparation of Esters: Additional Methods 340
13.7 Reactions of Esters: Hydrolysis 341
 An Ester of an Inorganic Acid: Nitroglycerin 342
13.8 Preparation of Tertiary Alcohols from Esters and Grignard Reagents 345
13.9 Reduction of Esters 346
13.10 Naturally Occurring Amides 346
13.11 Preparation of Amides 347
13.12 Hydrolysis of Amides 349
 Condensation Polymers: Polyamides and Polyesters 350
 Learning Objectives 352
13.13 SUMMARY 354
 Additional Problems 357

CHAPTER 14**AMINES 361**

- 14.1 Amine Nomenclature 362
- 14.2 Structure and Bonding 363
- 14.3 Physical Properties 365
- 14.4 Basicity of Amines 365
- Amines as Natural Products 366**
- 14.5 Preparation of Amines by Alkylation of Ammonia 369
- 14.6 Preparation of Amines by Reduction 370
- 14.7 Reactions of Amines: A Review and a Preview 372
- 14.8 Reaction of Amines with Alkyl Halides 372
- 14.9 Nitrosation of Amines 374
- 14.10 Synthesis Using Aryl Diazonium Salts 375
- 14.11 Azo Coupling 379
- From Dyes to Sulfa Drugs 379**
- Learning Objectives 380**
- 14.12 SUMMARY 381
- Additional Problems 384**

CHAPTER 15**CARBOHYDRATES 388**

- 15.1 Classification of Carbohydrates 388
- 15.2 Fischer Projections and D–L Notation 389
- 15.3 Aldotetroses 390
- 15.4 Aldopentoses and Aldohexoses 392
- 15.5 Cyclic Forms of Carbohydrates: Furanose Forms 394
- 15.6 Cyclic Forms of Carbohydrates: Pyranose Forms 396
- 15.7 Hemiacetal Equilibrium 399
- 15.8 Ketoses 399
- How Sweet It Is 400**
- 15.9 Structural Variations in Carbohydrates 401
- 15.10 Glycosides 402
- 15.11 Disaccharides 404
- 15.12 Polysaccharides 405
- 15.13 Oxidation of Carbohydrates 407
- Learning Objectives 409**
- 15.14 SUMMARY 409
- Additional Problems 410**

CHAPTER 16**LIPIDS 413**

- 16.1 Classification of Lipids 413
- 16.2 Fats, Oils, and Fatty Acids 413
- 16.3 Phospholipids 416
- 16.4 Waxes 417
- 16.5 Steroids: Cholesterol 418
- 16.6 Vitamin D 418
- “Good” Cholesterol? “Bad” Cholesterol? What’s the Difference? 419**

- 16.7 Bile Acids 420
- 16.8 Corticosteroids 420
- 16.9 Sex Hormones 421
- 16.10 Carotenoids 421
 - Anabolic Steroids 422**
- 16.11 Biosynthesis: Acetyl Coenzyme A 423
- 16.12 Terpene Biosynthesis: The Isoprene Rule 424
- 16.13 Isopentyl Pyrophosphate: The Biological Isoprene Unit 428
- 16.14 Carbon–Carbon Bond Formation in Terpene Biosynthesis 428
 - Learning Objectives 429**
- 16.15 SUMMARY 429
 - Additional Problems 431**

CHAPTER 17

AMINO ACIDS, PEPTIDES, AND PROTEINS 434

- 17.1 Structure of Amino Acids 434
- 17.2 Stereochemistry of Amino Acids 438
- 17.3 Acid–Base Behaviors of Amino Acids 439
- 17.4 Synthesis of Amino Acids 440
 - Electrophoresis 441**
- 17.5 Peptides 442
- 17.6 Peptide Structure Determination: Amino Acid Analysis 445
- 17.7 Peptide Structure Determination: Principles of Sequence Analysis 446
- 17.8 Partial Hydrolysis of Peptides 447
- 17.9 End Group Analysis 448
- 17.10 The Strategy of Peptide Synthesis 449
- 17.11 Protecting Groups and Peptide Bond Formation 450
- 17.12 Secondary Structures of Peptides and Proteins 451
- 17.13 Tertiary Structure of Peptides and Proteins 452
 - Solid-Phase Peptide Synthesis: The Merrifield Method 452**
- 17.14 Coenzymes 456
- 17.15 Protein Quaternary Structure: Hemoglobin 456
 - Learning Objectives 457**
- 17.16 SUMMARY 458
 - Additional Problems 460**

CHAPTER 18

NUCLEIC ACIDS 463

- 18.1 Pyrimidines and Purines 463
- 18.2 Nucleosides 464
- 18.3 Nucleotides 465
- 18.4 Nucleic Acids 467
- 18.5 Structure and Replication of DNA: The Double Helix 468
- 18.6 DNA-Directed Protein Biosynthesis 470
 - Cancer Chemotherapy 471**
 - AIDS 473**
 - Learning Objectives 474**
- 18.7 SUMMARY 475
 - Additional Problems 475**

CHAPTER 19
SPECTROSCOPY 477

- 19.1 Principles of Molecular Spectroscopy 478
- 19.2 Nuclear Magnetic Resonance Spectroscopy 479
- 19.3 Nuclear Shielding and ^1H Chemical Shifts 480
- 19.4 Effects of Molecular Structure on ^1H Chemical Shifts 482
- 19.5 Interpreting Proton NMR Spectra 484
- 19.6 Spin–Spin Splitting in NMR Spectroscopy 485
- 19.7 Patterns of Spin–Spin Splitting 487
- 19.8 ^{13}C NMR Spectroscopy 488
- 19.9 ^{13}C Chemical Shifts 490
- 19.10 Infrared Spectroscopy 491
 - Magnetic Resonance Imaging 492**
- 19.11 Ultraviolet–Visible Spectroscopy 495
- 19.12 Connecting Spectroscopy and Structural Type 497
- 19.13 Mass Spectrometry 502
 - Gas Chromatography, GC/MS, and MS/MS 504**
- 19.14 Molecular Formula as a Clue to Structure 505
 - Learning Objectives 506**
- 19.15 SUMMARY 507
 - Additional Problems 508**

ANSWERS TO IN-TEXT PROBLEMS A-1**GLOSSARY G-1****INDEX I-1**