

Contents

Structure and Bonding 1

- 1.1 Atomic Structure: The Nucleus 3
- 1.2 Atomic Structure: Orbitals 4
- 1.3 Atomic Structure: Electron Configurations 6
- 1.4 Development of Chemical Bonding Theory 7
- 1.5 The Nature of Chemical Bonds: Valence Bond Theory 10
- 1.6 sp^3 Hybrid Orbitals and the Structure of Methane 12
- 1.7 sp^3 Hybrid Orbitals and the Structure of Ethane 14
- 1.8 sp^2 Hybrid Orbitals and the Structure of Ethylene 15
- 1.9 sp Hybrid Orbitals and the Structure of Acetylene 17
- 1.10 Hybridization of Nitrogen, Oxygen, Phosphorus, and Sulfur 19
- 1.11 The Nature of Chemical Bonds: Molecular Orbital Theory 21
- 1.12 Drawing Chemical Structures 22
- Focus On . . . Chemicals, Toxicity, and Risk 25**
- Summary and Key Words 26 ■ Visualizing Chemistry 28
- Additional Problems 29

Polar Covalent Bonds; Acids and Bases 35

- 2.1 Polar Covalent Bonds: Electronegativity 35
- 2.2 Polar Covalent Bonds: Dipole Moments 38
- 2.3 Formal Charges 40
- 2.4 Resonance 43
- 2.5 Rules for Resonance Forms 44
- 2.6 Drawing Resonance Forms 46
- 2.7 Acids and Bases: The Brønsted–Lowry Definition 49
- 2.8 Acid and Base Strength 50
- 2.9 Predicting Acid–Base Reactions from pK_a Values 52
- 2.10 Organic Acids and Organic Bases 54
- 2.11 Acids and Bases: The Lewis Definition 57
- 2.12 Molecular Models 61
- 2.13 Noncovalent Interactions 61
- Focus On . . . Alkaloids: Naturally Occurring Bases 64**
- Summary and Key Words 65 ■ Visualizing Chemistry 66
- Additional Problems 68

Organic Compounds: Alkanes and Their Stereochemistry 73

- 3.1 Functional Groups 73
- 3.2 Alkanes and Alkane Isomers 79
- 3.3 Alkyl Groups 83
- 3.4 Naming Alkanes 86
- 3.5 Properties of Alkanes 91
- 3.6 Conformations of Ethane 93
- 3.7 Conformations of Other Alkanes 95
- Focus On . . . Gasoline 99**
- Summary and Key Words 100 ■ Visualizing Chemistry 101
- Additional Problems 102

Organic Compounds: Cycloalkanes and Their Stereochemistry 107

- 4.1 Naming Cycloalkanes 108
- 4.2 Cis–Trans Isomerism in Cycloalkanes 110
- 4.3 Stability of Cycloalkanes: Ring Strain 113
- 4.4 Conformations of Cycloalkanes 115
- 4.5 Conformations of Cyclohexane 117
- 4.6 Axial and Equatorial Bonds in Cyclohexane 119
- 4.7 Conformations of Monosubstituted Cyclohexanes 122
- 4.8 Conformations of Disubstituted Cyclohexanes 124
- 4.9 Conformations of Polycyclic Molecules 128
- Focus On . . . Molecular Mechanics 130**
- Summary and Key Words 131 ■ Visualizing Chemistry 132
- Additional Problems 133

An Overview of Organic Reactions 137

- 5.1 Kinds of Organic Reactions 137
- 5.2 How Organic Reactions Occur: Mechanisms 139
- 5.3 Radical Reactions 140
- 5.4 Polar Reactions 142
- 5.5 An Example of a Polar Reaction: Addition of HBr to Ethylene 147
- 5.6 Using Curved Arrows in Polar Reaction Mechanisms 149
- 5.7 Describing a Reaction: Equilibria, Rates, and Energy Changes 152
- 5.8 Describing a Reaction: Bond Dissociation Energies 155
- 5.9 Describing a Reaction: Energy Diagrams and Transition States 157

- 5.10 Describing a Reaction: Intermediates 160
5.11 A Comparison between Biological Reactions and Laboratory Reactions 162
Focus On . . . Where Do Drugs Come From? 164
Summary and Key Words 165 ■ Visualizing Chemistry 166
Additional Problems 168

Alkenes: Structure and Reactivity 172

- 6.1 Industrial Preparation and Use of Alkenes 173
6.2 Calculating Degree of Unsaturation 174
6.3 Naming Alkenes 176
6.4 Cis-Trans Isomerism in Alkenes 178
6.5 Sequence Rules: the *E,Z* Designation 180
6.6 Stability of Alkenes 185
6.7 Electrophilic Addition Reactions of Alkenes 188
6.8 Orientation of Electrophilic Additions: Markovnikov's Rule 191
6.9 Carbocation Structure and Stability 195
6.10 The Hammond Postulate 197
6.11 Evidence for the Mechanism of Electrophilic Additions: Carbocation Rearrangements 200

Focus On . . . Terpenes: Naturally Occurring Alkenes 202

- Summary and Key Words 204 ■ Visualizing Chemistry 205
Additional Problems 206

Alkenes: Reactions and Synthesis 213

- 7.1 Preparation of Alkenes: A Preview of Elimination Reactions 214
7.2 Addition of Halogens to Alkenes 215
7.3 Addition of Hypohalous Acids to Alkenes: Halohydrin Formation 218
7.4 Addition of Water to Alkenes: Oxymercuration 220
7.5 Addition of Water to Alkenes: Hydroboration 223
7.6 Addition of Carbenes to Alkenes: Cyclopropane Synthesis 227
7.7 Reduction of Alkenes: Hydrogenation 229
7.8 Oxidation of Alkenes: Epoxidation and Hydroxylation 233
7.9 Oxidation of Alkenes: Cleavage to Carbonyl Compounds 236
7.10 Radical Additions to Alkenes: Polymers 239
7.11 Biological Additions of Radicals to Alkenes 243

Focus On . . . Natural Rubber 245

- Summary and Key Words 246 ■ Summary of Reactions 247
Visualizing Chemistry 250 ■ Additional Problems 251

Alkynes: An Introduction to Organic Synthesis 259

- 8.1 Naming Alkynes 259
- 8.2 Preparation of Alkynes: Elimination Reactions of Dihalides 261
- 8.3 Reactions of Alkynes: Addition of HX and X₂ 261
- 8.4 Hydration of Alkynes 264
- 8.5 Reduction of Alkynes 268
- 8.6 Oxidative Cleavage of Alkynes 270
- 8.7 Alkyne Acidity: Formation of Acetylide Anions 270
- 8.8 Alkylation of Acetylide Anions 272
- 8.9 An Introduction to Organic Synthesis 274

Focus On . . . The Art of Organic Synthesis 278

- Summary and Key Words 279 ■ Summary of Reactions 280
- Visualizing Chemistry 282 ■ Additional Problems 283

Stereochemistry 289

- 9.1 Enantiomers and the Tetrahedral Carbon 290
- 9.2 The Reason for Handedness in Molecules: Chirality 291
- 9.3 Optical Activity 294
- 9.4 Pasteur's Discovery of Enantiomers 296
- 9.5 Sequence Rules for Specifying Configuration 297
- 9.6 Diastereomers 302
- 9.7 Meso Compounds 305
- 9.8 Racemic Mixtures and the Resolution of Enantiomers 307
- 9.9 A Review of Isomerism 309
- 9.10 Stereochemistry of Reactions: Addition of H₂O to an Achiral Alkene 311
- 9.11 Stereochemistry of Reactions: Addition of H₂O to a Chiral Alkene 312
- 9.12 Chirality at Nitrogen, Phosphorus, and Sulfur 314
- 9.13 Prochirality 315
- 9.14 Chirality in Nature and Chiral Environments 318

Focus On . . . Chiral Drugs 320

- Summary and Key Words 322 ■ Visualizing Chemistry 323
- Additional Problems 324

Organohalides 332

- 10.1 Naming Alkyl Halides 333
- 10.2 Structure of Alkyl Halides 334
- 10.3 Preparing Alkyl Halides from Alkanes: Radical Halogenation 335

- 10.4 Preparing Alkyl Halides from Alkenes: Allylic Bromination 339
- 10.5 Stability of the Allyl Radical: Resonance Revisited 341
- 10.6 Preparing Alkyl Halides from Alcohols 344
- 10.7 Reactions of Alkyl Halides: Grignard Reagents 345
- 10.8 Organometallic Coupling Reactions 346
- 10.9 Oxidation and Reduction in Organic Chemistry 348

Focus On . . . Naturally Occurring Organohalides 351

- Summary and Key Words 352 ■ Summary of Reactions 353
 Visualizing Chemistry 354 ■ Additional Problems 355

Reactions of Alkyl Halides: Nucleophilic Substitutions and Eliminations 359

- 11.1 The Discovery of Nucleophilic Substitution Reactions 359
- 11.2 The S_N2 Reaction 362
- 11.3 Characteristics of the S_N2 Reaction 365
- 11.4 The S_N1 Reaction 372
- 11.5 Characteristics of the S_N1 Reaction 376
- 11.6 Biological Substitution Reactions 381
- 11.7 Elimination Reactions of Alkyl Halides: Zaitsev's Rule 383
- 11.8 The E2 Reaction and the Deuterium Isotope Effect 386
- 11.9 The E2 Reaction and Cyclohexane Conformation 389
- 11.10 The E1 and E1cB Reactions 391
- 11.11 Biological Elimination Reactions 393
- 11.12 A Summary of Reactivity: S_N1 , S_N2 , E1, E1cB, and E2 393

Focus On . . . Green Chemistry 395

- Summary and Key Words 397 ■ Summary of Reactions 398
 Visualizing Chemistry 399 ■ Additional Problems 400

Structure Determination: Mass Spectrometry and Infrared Spectroscopy 408

- 12.1 Mass Spectrometry of Small Molecules: Magnetic-Sector Instruments 409
- 12.2 Interpreting Mass Spectra 411
- 12.3 Mass Spectrometry of Some Common Functional Groups 415
- 12.4 Mass Spectrometry in Biological Chemistry: Time-of-Flight (TOF) Instruments 417
- 12.5 Spectroscopy and the Electromagnetic Spectrum 418
- 12.6 Infrared Spectroscopy 422
- 12.7 Interpreting Infrared Spectra 423
- 12.8 Infrared Spectra of Some Common Functional Groups 426

Focus On . . . Chromatography: Purifying Organic Compounds 431

Summary and Key Words 433 ■ Visualizing Chemistry 434

Additional Problems 434

Structure Determination: Nuclear Magnetic Resonance Spectroscopy 440

13.1 Nuclear Magnetic Resonance Spectroscopy 440

13.2 The Nature of NMR Absorptions 442

13.3 Chemical Shifts 445

13.4 ^{13}C NMR Spectroscopy: Signal Averaging and FT-NMR 446

13.5 Characteristics of ^{13}C NMR Spectroscopy 448

13.6 DEPT ^{13}C NMR Spectroscopy 451

13.7 Uses of ^{13}C NMR Spectroscopy 453

13.8 ^1H NMR Spectroscopy and Proton Equivalence 454

13.9 Chemical Shifts in ^1H NMR Spectroscopy 457

13.10 Integration of ^1H NMR Absorptions: Proton Counting 459

13.11 Spin-Spin Splitting in ^1H NMR Spectra 460

13.12 More Complex Spin-Spin Splitting Patterns 465

13.13 Uses of ^1H NMR Spectroscopy 467

Focus On . . . Magnetic Resonance Imaging (MRI) 468

Summary and Key Words 469 ■ Visualizing Chemistry 470

Additional Problems 471

Conjugated Compounds and Ultraviolet Spectroscopy 482

14.1 Stability of Conjugated Dienes: Molecular Orbital Theory 483

14.2 Electrophilic Additions to Conjugated Dienes: Allylic Carbocations 487

14.3 Kinetic versus Thermodynamic Control of Reactions 490

14.4 The Diels-Alder Cycloaddition Reaction 492

14.5 Characteristics of the Diels-Alder Reaction 493

14.6 Diene Polymers: Natural and Synthetic Rubbers 498

14.7 Structure Determination in Conjugated Systems: Ultraviolet Spectroscopy 500

14.8 Interpreting Ultraviolet Spectra: The Effect of Conjugation 502

14.9 Conjugation, Color, and the Chemistry of Vision 503

Focus On . . . Photolithography 505

Summary and Key Words 507 ■ Summary of Reactions 507

Visualizing Chemistry 508 ■ Additional Problems 509

Benzene and Aromaticity 516

- 15.1 Sources and Names of Aromatic Compounds 517
- 15.2 Structure and Stability of Benzene: Molecular Orbital Theory 520
- 15.3 Aromaticity and the Hückel $4n + 2$ Rule 523
- 15.4 Aromatic Ions 525
- 15.5 Aromatic Heterocycles: Pyridine and Pyrrole 528
- 15.6 Why $4n + 2$? 530
- 15.7 Polycyclic Aromatic Compounds 531
- 15.8 Spectroscopy of Aromatic Compounds 534

Focus On . . . Aspirin, NSAIDs, and COX-2 Inhibitors 537

Summary and Key Words 538 ■ Visualizing Chemistry 539

Additional Problems 541

Chemistry of Benzene: Electrophilic Aromatic Substitution 547

- 16.1 Electrophilic Aromatic Substitution Reactions: Bromination 548
- 16.2 Other Aromatic Substitutions 550
- 16.3 Alkylation and Acylation of Aromatic Rings: The Friedel–Crafts Reaction 554
- 16.4 Substituent Effects in Substituted Aromatic Rings 560
- 16.5 An Explanation of Substituent Effects 564
- 16.6 Trisubstituted Benzenes: Additivity of Effects 570
- 16.7 Nucleophilic Aromatic Substitution 572
- 16.8 Benzyne 575
- 16.9 Oxidation of Aromatic Compounds 576
- 16.10 Reduction of Aromatic Compounds 579
- 16.11 Synthesis of Trisubstituted Benzenes 581

Focus On . . . Combinatorial Chemistry 585

Summary and Key Words 587 ■ Summary of Reactions 588

Visualizing Chemistry 590 ■ Additional Problems 591

Alcohols and Phenols 599

- 17.1 Naming Alcohols and Phenols 600
- 17.2 Properties of Alcohols and Phenols 602
- 17.3 Preparation of Alcohols: A Review 607
- 17.4 Alcohols from Reduction of Carbonyl Compounds 609
- 17.5 Alcohols from Reaction of Carbonyl Compounds with Grignard Reagents 613
- 17.6 Reactions of Alcohols 617
- 17.7 Oxidation of Alcohols 623
- 17.8 Protection of Alcohols 626
- 17.9 Phenols and Their Uses 628

- 17.10 Reactions of Phenols 631
- 17.11 Spectroscopy of Alcohols and Phenols 632
- Focus On . . . Ethanol: Chemical, Drug, and Poison 636**
- Summary and Key Words 637 ■ Summary of Reactions 638
- Visualizing Chemistry 640 ■ Additional Problems 642

Ethers and Epoxides; Thiols and Sulfides 652

- 18.1 Names and Properties of Ethers 653
- 18.2 Synthesis of Ethers 654
- 18.3 Reactions of Ethers: Acidic Cleavage 657
- 18.4 Reactions of Ethers: Claisen Rearrangement 659
- 18.5 Cyclic Ethers: Epoxides 660
- 18.6 Reactions of Epoxides: Ring-Opening 662
- 18.7 Crown Ethers 666
- 18.8 Thiols and Sulfides 667
- 18.9 Spectroscopy of Ethers 671
- Focus On . . . Epoxy Resins and Adhesives 673**
- Summary and Key Words 674 ■ Summary of Reactions 675
- Visualizing Chemistry 676 ■ Additional Problems 677

A Preview of Carbonyl Compounds 686

- I Kinds of Carbonyl Compounds 686
- II Nature of the Carbonyl Group 688
- III General Reactions of Carbonyl Compounds 688
- IV Summary 694

Aldehydes and Ketones: Nucleophilic Addition Reactions 695

- 19.1 Naming Aldehydes and Ketones 696
- 19.2 Preparation of Aldehydes and Ketones 698
- 19.3 Oxidation of Aldehydes and Ketones 700
- 19.4 Nucleophilic Addition Reactions of Aldehydes and Ketones 702
- 19.5 Nucleophilic Addition of H_2O : Hydration 705
- 19.6 Nucleophilic Addition of HCN : Cyanohydrin Formation 707
- 19.7 Nucleophilic Addition of Grignard and Hydride Reagents: Alcohol Formation 708
- 19.8 Nucleophilic Addition of Amines: Imine and Enamine Formation 710
- 19.9 Nucleophilic Addition of Hydrazine: The Wolff–Kishner Reaction 715
- 19.10 Nucleophilic Addition of Alcohols: Acetal Formation 717

- 19.11 Nucleophilic Addition of Phosphorus Ylides: The Wittig Reaction 720
- 19.12 Biological Reductions 723
- 19.13 Conjugate Nucleophilic Addition to α,β -Unsaturated Aldehydes and Ketones 725
- 19.14 Spectroscopy of Aldehydes and Ketones 730

Focus On . . . Enantioselective Synthesis 734

Summary and Key Words 736 ■ Summary of Reactions 736
Visualizing Chemistry 739 ■ Additional Problems 740

Carboxylic Acids and Nitriles 751

- 20.1 Naming Carboxylic Acids and Nitriles 752
- 20.2 Structure and Properties of Carboxylic Acids 754
- 20.3 Biological Acids and the Henderson–Hasselbalch Equation 758
- 20.4 Substituent Effects on Acidity 759
- 20.5 Preparation of Carboxylic Acids 762
- 20.6 Reactions of Carboxylic Acids: An Overview 764
- 20.7 Chemistry of Nitriles 765
- 20.8 Spectroscopy of Carboxylic Acids and Nitriles 770

Focus On . . . Vitamin C 772

Summary and Key Words 774 ■ Summary of Reactions 775
Visualizing Chemistry 776 ■ Additional Problems 777

Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution Reactions 785

- 21.1 Naming Carboxylic Acid Derivatives 786
- 21.2 Nucleophilic Acyl Substitution Reactions 789
- 21.3 Nucleophilic Acyl Substitution Reactions of Carboxylic Acids 794
- 21.4 Chemistry of Acid Halides 800
- 21.5 Chemistry of Acid Anhydrides 806
- 21.6 Chemistry of Esters 808
- 21.7 Chemistry of Amides 813
- 21.8 Chemistry of Thioesters and Acyl Phosphates: Biological Carboxylic Acid Derivatives 816
- 21.9 Polyamides and Polyesters: Step-Growth Polymers 818
- 21.10 Spectroscopy of Carboxylic Acid Derivatives 822

Focus On . . . β -Lactam Antibiotics 824

Summary and Key Words 825 ■ Summary of Reactions 826
Visualizing Chemistry 829 ■ Additional Problems 830

Contents

- © Erich Lessing/Art Resource, NY

[illegible]

- 24.5 Biological Amines and the Henderson–Hasselbalch Equation 925
- 24.6 Synthesis of Amines 927
- 24.7 Reactions of Amines 936
- 24.8 Reactions of Arylamines 939
- 24.9 Heterocycles 945
- 24.10 Spectroscopy of Amines 952

Focus On ... Green Chemistry II: Ionic Liquids 956

- Summary and Key Words 958 ■ Summary of Reactions 959
- Visualizing Chemistry 961 ■ Additional Problems 963

Biomolecules: Carbohydrates 973

- 25.1 Classification of Carbohydrates 974
- 25.2 Depicting Carbohydrate Stereochemistry: Fischer Projections 975
- 25.3 D,L Sugars 980
- 25.4 Configurations of the Aldoses 981
- 25.5 Cyclic Structures of Monosaccharides: Anomers 984
- 25.6 Reactions of Monosaccharides 987
- 25.7 The Eight Essential Monosaccharides 996
- 25.8 Disaccharides 997
- 25.9 Polysaccharides and Their Synthesis 1000
- 25.10 Some Other Important Carbohydrates 1002
- 25.11 Cell-Surface Carbohydrates and Carbohydrate Vaccines 1003

Focus On ... Sweetness 1005

- Summary and Key Words 1006 ■ Summary of Reactions 1007
- Visualizing Chemistry 1008 ■ Additional Problems 1009

Biomolecules: Amino Acids, Peptides, and Proteins 1016

- 26.1 Structures of Amino Acids 1017
- 26.2 Amino Acids, the Henderson–Hasselbalch Equation, and Isoelectric Points 1022
- 26.3 Synthesis of Amino Acids 1025
- 26.4 Peptides and Proteins 1027
- 26.5 Amino Acid Analysis of Peptides 1030
- 26.6 Peptide Sequencing: The Edman Degradation 1031
- 26.7 Peptide Synthesis 1033
- 26.8 Automated Peptide Synthesis: The Merrifield Solid-Phase Method 1036
- 26.9 Protein Structure 1038
- 26.10 Enzymes and Coenzymes 1040
- 26.11 How Do Enzymes Work? Citrate Synthase 1043

Focus On ... The Protein Data Bank 1048

- Summary and Key Words 1049 ■ Summary of Reactions 1050
- Visualizing Chemistry 1052 ■ Additional Problems 1053

Biomolecules: Lipids 1060

- 27.1 Waxes, Fats, and Oils 1061
- 27.2 Soap 1064
- 27.3 Phospholipids 1066
- 27.4 Prostaglandins and Other Eicosanoids 1067
- 27.5 Terpenoids 1070
- 27.6 Steroids 1079
- 27.7 Biosynthesis of Steroids 1084

Focus On . . . Saturated Fats, Cholesterol, and Heart Disease 1090

Summary and Key Words 1091 ■ Visualizing Chemistry 1092
Additional Problems 1093

Biomolecules: Nucleic Acids 1100

- 28.1 Nucleotides and Nucleic Acids 1100
- 28.2 Base Pairing in DNA: The Watson–Crick Model 1103
- 28.3 Replication of DNA 1106
- 28.4 Transcription of DNA 1107
- 28.5 Translation of RNA: Protein Biosynthesis 1109
- 28.6 DNA Sequencing 1112
- 28.7 DNA Synthesis 1114
- 28.8 The Polymerase Chain Reaction 1117

Focus On . . . DNA Fingerprinting 1118

Summary and Key Words 1119 ■ Visualizing Chemistry 1120
Additional Problems 1121

The Organic Chemistry of Metabolic Pathways 1125

- 29.1 An Overview of Metabolism and Biochemical Energy 1126
- 29.2 Catabolism of Triacylglycerols: The Fate of Glycerol 1130
- 29.3 Catabolism of Triacylglycerols: β -Oxidation 1133
- 29.4 Biosynthesis of Fatty Acids 1138
- 29.5 Catabolism of Carbohydrates: Glycolysis 1143
- 29.6 Conversion of Pyruvate to Acetyl CoA 1150
- 29.7 The Citric Acid Cycle 1154
- 29.8 Carbohydrate Biosynthesis: Gluconeogenesis 1159
- 29.9 Catabolism of Proteins: Transamination 1165
- 29.10 Some Conclusions about Biological Chemistry 1169

Focus On . . . Basal Metabolism 1169

Summary and Key Words 1170 ■ Visualizing Chemistry 1171
Additional Problems 1172

Orbitals and Organic Chemistry: Pericyclic Reactions 1178

- 30.1 Molecular Orbitals and Pericyclic Reactions of Conjugated Pi Systems 1178
- 30.2 Electrocyclic Reactions 1181
- 30.3 Stereochemistry of Thermal Electrocyclic Reactions 1183
- 30.4 Photochemical Electrocyclic Reactions 1185
- 30.5 Cycloaddition Reactions 1186
- 30.6 Stereochemistry of Cycloadditions 1188
- 30.7 Sigmatropic Rearrangements 1191
- 30.8 Some Examples of Sigmatropic Rearrangements 1192
- 30.9 A Summary of Rules for Pericyclic Reactions 1196

Focus On . . . Vitamin D, the Sunshine Vitamin 1197

Summary and Key Words 1198 ■ Visualizing Chemistry 1199
Additional Problems 1200

Synthetic Polymers 1206

- 31.1 Chain-Growth Polymers 1207
- 31.2 Stereochemistry of Polymerization: Ziegler–Natta Catalysts 1209
- 31.3 Copolymers 1210
- 31.4 Step-Growth Polymers 1212
- 31.5 Polymer Structure and Physical Properties 1215

Focus On . . . Biodegradable Polymers 1218

Summary and Key Words 1220 ■ Visualizing Chemistry 1221
Additional Problems 1221

Appendix A Nomenclature of Polyfunctional Organic Compounds A-1

Appendix B Acidity Constants for Some Organic Compounds A-8

Appendix C Glossary A-10

Appendix D Answers to In-Text Problems A-30

Index I-1