

PART I: Molecular Structure and Thermodynamics

- CHAPTER 1. Introduction to Structure and Models of Bonding 3
2. Strain and Stability 65
3. Solutions and Non-Covalent Binding Forces 145
4. Molecular Recognition and Supramolecular Chemistry 207
5. Acid-Base Chemistry 259
6. Stereochemistry 297
-

PART II: Reactivity, Kinetics, and Mechanisms

- CHAPTER 7. Energy Surfaces and Kinetic Analyses 355
8. Experiments Related to Thermodynamics and Kinetics 421
9. Catalysis 489
10. Organic Reaction Mechanisms, Part 1:
Reactions Involving Additions and/or Eliminations 537
11. Organic Reaction Mechanisms, Part 2:
Substitutions at Aliphatic Centers and Thermal
Isomerizations/Rearrangements 627
12. Organotransition Metal Reaction Mechanisms and Catalysis 705
13. Organic Polymer and Materials Chemistry 753
-

PART III: Electronic Structure: Theory and Applications

- CHAPTER 14. Advanced Concepts in Electronic Structure Theory 807
15. Thermal Pericyclic Reactions 877
16. Photochemistry 935
17. Electronic Organic Materials 1001
-

- APPENDIX 1. Conversion Factors and Other Useful Data 1047
2. Electrostatic Potential Surfaces for Representative Organic Molecules 1049
3. Group Orbitals of Common Functional Groups:
Representative Examples Using Simple Molecules 1051
4. The Organic Structures of Biology 1057
5. Pushing Electrons 1061
6. Reaction Mechanism Nomenclature 1075

INDEX 1079

List of Highlights xix
 Preface xxiii
 Acknowledgments xxv
 A Note to the Instructor xxvii

PART I
MOLECULAR STRUCTURE AND
THERMODYNAMICS

CHAPTER 1: Introduction to Structure and Models of Bonding 3

Intent and Purpose 3

1.1 A Review of Basic Bonding Concepts 4
 1.1.1 Quantum Numbers and Atomic Orbitals 4
 1.1.2 Electron Configurations and Electronic Diagrams 5
 1.1.3 Lewis Structures 6
 1.1.4 Formal Charge 6
 1.1.5 VSEPR 7
 1.1.6 Hybridization 8
 1.1.7 A Hybrid Valence Bond/Molecular Orbital Model of Bonding 10
 Creating Localized σ and π Bonds 11
 1.1.8 Polar Covalent Bonding 12
 Electronegativity 12
 Electrostatic Potential Surfaces 14
 Inductive Effects 15
 Group Electronegativities 16
 Hybridization Effects 17
 1.1.9 Bond Dipoles, Molecular Dipoles, and Quadrupoles 17
 Bond Dipoles 17
 Molecular Dipole Moments 18
 Molecular Quadrupole Moments 19
 1.1.10 Resonance 20
 1.1.11 Bond Lengths 22
 1.1.12 Polarizability 24
 1.1.13 Summary of Concepts Used for the Simplest Model of Bonding in Organic Structures 26

1.2 A More Modern Theory of Organic Bonding 26

1.2.1 Molecular Orbital Theory 27
 1.2.2 A Method for QMOT 28
 1.2.3 Methyl in Detail 29
 Planar Methyl 29
 The Walsh Diagram: Pyramidal Methyl 31
 "Group Orbitals" for Pyramidal Methyl 32
 Putting the Electrons In—The MH_3 System 33
 1.2.4 The CH_2 Group in Detail 33
 The Walsh Diagram and Group Orbitals 33
 Putting the Electrons In—The MH_2 System 33

1.3 Orbital Mixing—Building Larger Molecules 35

1.3.1 Using Group Orbitals to Make Ethane 36

1.3.2 Using Group Orbitals to Make Ethylene 38
 1.3.3 The Effects of Heteroatoms—Formaldehyde 40
 1.3.4 Making More Complex Alkanes 43
 1.3.5 Three More Examples of Building Larger Molecules from Group Orbitals 43
 Propene 43
 Methyl Chloride 45
 Butadiene 46
 1.3.6 Group Orbitals of Representative π Systems: Benzene, Benzyl, and Allyl 46
 1.3.7 Understanding Common Functional Groups as Perturbations of Allyl 49
 1.3.8 The Three Center—Two Electron Bond 50
 1.3.9 Summary of the Concepts Involved in Our Second Model of Bonding 51

1.4 Bonding and Structures of Reactive Intermediates 52

1.4.1 Carbocations 52
 Carbenium Ions 53
 Interplay with Carbonium Ions 54
 Carbonium Ions 55
 1.4.2 Carbanions 56
 1.4.3 Radicals 57
 1.4.4 Carbenes 58

1.5 A Very Quick Look at Organometallic and Inorganic Bonding 59

Summary and Outlook 61

EXERCISES 62

FURTHER READING 64

CHAPTER 2: Strain and Stability 65

Intent and Purpose 65

2.1 Thermochemistry of Stable Molecules 66

2.1.1 The Concepts of Internal Strain and Relative Stability 66
 2.1.2 Types of Energy 68
 Gibbs Free Energy 68
 Enthalpy 69
 Entropy 70
 2.1.3 Bond Dissociation Energies 70
 Using BDEs to Predict Exothermicity and Endothermicity 72
 2.1.4 An Introduction to Potential Functions and Surfaces—Bond Stretches 73
 Infrared Spectroscopy 77
 2.1.5 Heats of Formation and Combustion 77
 2.1.6 The Group Increment Method 79
 2.1.7 Strain Energy 82

2.2 Thermochemistry of Reactive Intermediates	82
2.2.1 Stability vs. Persistence	82
2.2.2 Radicals	83
<i>BDEs as a Measure of Stability</i>	83
<i>Radical Persistence</i>	84
<i>Group Increments for Radicals</i>	86
2.2.3 Carbocations	87
<i>Hydride Ion Affinities as a Measure of Stability</i>	87
<i>Lifetimes of Carbocations</i>	90
2.2.4 Carbanions	91
2.2.5 Summary	91
2.3 Relationships Between Structure and Energetics— Basic Conformational Analysis	92
2.3.1 Acyclic Systems—Torsional Potential Surfaces	92
<i>Ethane</i>	92
<i>Butane—The Gauche Interaction</i>	95
<i>Barrier Height</i>	97
<i>Barrier Foldedness</i>	97
<i>Tetraalkylethanes</i>	98
<i>The g+g—Pentane Interaction</i>	99
<i>Allylic ($A^{1,3}$) Strain</i>	100
2.3.2 Basic Cyclic Systems	100
<i>Cyclopropane</i>	100
<i>Cyclobutane</i>	100
<i>Cyclopentane</i>	101
<i>Cyclohexane</i>	102
<i>Larger Rings—Transannular Effects</i>	107
<i>Group Increment Corrections for Ring Systems</i>	109
<i>Ring Torsional Modes</i>	109
<i>Bicyclic Ring Systems</i>	110
<i>Cycloalkenes and Bredt's Rule</i>	110
<i>Summary of Conformational Analysis and Its Connection to Strain</i>	112
2.4 Electronic Effects	112
2.4.1 Interactions Involving π Systems	112
<i>Substitution on Alkenes</i>	112
<i>Conformations of Substituted Alkenes</i>	113
<i>Conjugation</i>	115
<i>Aromaticity</i>	116
<i>Antiaromaticity, An Unusual Destabilizing Effect</i>	117
<i>NMR Chemical Shifts</i>	118
<i>Polycyclic Aromatic Hydrocarbons</i>	119
<i>Large Annulenes</i>	119
2.4.2 Effects of Multiple Heteroatoms	120
<i>Bond Length Effects</i>	120
<i>Orbital Effects</i>	120
2.5 Highly-Strained Molecules	124
2.5.1 Long Bonds and Large Angles	124
2.5.2 Small Rings	125
2.5.3 Very Large Rotation Barriers	127
2.6 Molecular Mechanics	128
2.6.1 The Molecular Mechanics Model	129
<i>Bond Stretching</i>	129
<i>Angle Bending</i>	130
<i>Torsion</i>	130
<i>Nonbonded Interactions</i>	130
<i>Cross Terms</i>	131
<i>Electrostatic Interactions</i>	131
<i>Hydrogen Bonding</i>	131
<i>The Parameterization</i>	132
<i>Heat of Formation and Strain Energy</i>	132
2.6.2 General Comments on the Molecular Mechanics Method	133
2.6.3 Molecular Mechanics on Biomolecules and Unnatural Polymers—"Modeling"	135
2.6.4 Molecular Mechanics Studies of Reactions	136
Summary and Outlook	137
EXERCISES	138
FURTHER READING	143
<hr/>	
CHAPTER 3: Solutions and Non-Covalent Binding Forces	145
Intent and Purpose	145
3.1 Solvent and Solution Properties	145
3.1.1 Nature Abhors a Vacuum	146
3.1.2 Solvent Scales	146
<i>Dielectric Constant</i>	147
<i>Other Solvent Scales</i>	148
<i>Heat of Vaporization</i>	150
<i>Surface Tension and Wetting</i>	150
<i>Water</i>	151
3.1.3 Solubility	153
<i>General Overview</i>	153
<i>Shape</i>	154
<i>Using the "Like-Dissolves-Like" Paradigm</i>	154
3.1.4 Solute Mobility	155
<i>Diffusion</i>	155
<i>Fick's Law of Diffusion</i>	156
<i>Correlation Times</i>	156
3.1.5 The Thermodynamics of Solutions	157
<i>Chemical Potential</i>	158
<i>The Thermodynamics of Reactions</i>	160
<i>Calculating ΔH° and ΔS°</i>	162
3.2 Binding Forces	162
3.2.1 Ion Pairing Interactions	163
<i>Salt Bridges</i>	164
3.2.2 Electrostatic Interactions Involving Dipoles	165
<i>Ion-Dipole Interactions</i>	165
<i>A Simple Model of Ionic Solvation— The Born Equation</i>	166
<i>Dipole-Dipole Interactions</i>	168
3.2.3 Hydrogen Bonding	168
<i>Geometries</i>	169
<i>Strengths of Normal Hydrogen Bonds</i>	171
i. <i>Solvation Effects</i>	171
ii. <i>Electronegativity Effects</i>	172
iii. <i>Resonance Assisted Hydrogen Bonds</i>	173
iv. <i>Polarization Enhanced Hydrogen Bonds</i>	174
v. <i>Secondary Interactions in Hydrogen Bonding Systems</i>	175

<i>vi. Cooperativity in Hydrogen Bonds</i>	175
<i>Vibrational Properties of Hydrogen Bonds</i>	176
<i>Short–Strong Hydrogen Bonds</i>	177
3.2.4 π Effects	180
<i>Cation–π Interactions</i>	181
<i>Polar–π Interactions</i>	183
<i>Aromatic–Aromatic Interactions (π Stacking)</i>	184
<i>The Arene–Perfluoroarene Interaction</i>	184
<i>π Donor–Acceptor Interactions</i>	186
3.2.5 Induced-Dipole Interactions	186
<i>Ion–Induced-Dipole Interactions</i>	187
<i>Dipole–Induced-Dipole Interactions</i>	187
<i>Induced-Dipole–Induced-Dipole Interactions</i>	188
<i>Summarizing Monopole, Dipole, and Induced-Dipole Binding Forces</i>	188
3.2.6 The Hydrophobic Effect	189
<i>Aggregation of Organics</i>	189
<i>The Origin of the Hydrophobic Effect</i>	192
3.3 Computational Modeling of Solvation	194
3.3.1 Continuum Solvation Models	196
3.3.2 Explicit Solvation Models	197
3.3.3 Monte Carlo (MC) Methods	198
3.3.4 Molecular Dynamics (MD)	199
3.3.5 Statistical Perturbation Theory / Free Energy Perturbation	200

Summary and Outlook 201

EXERCISES 202

FURTHER READING 204

CHAPTER 4: Molecular Recognition and Supramolecular Chemistry 207

Intent and Purpose 207

4.1 Thermodynamic Analyses of Binding Phenomena 207

4.1.1 General Thermodynamics of Binding	208
<i>The Relevance of the Standard State</i>	210
<i>The Influence of a Change in Heat Capacity</i>	212
<i>Cooperativity</i>	213
<i>Enthalpy–Entropy Compensation</i>	216
4.1.2 The Binding Isotherm	216
4.1.3 Experimental Methods	219
<i>UV/Vis or Fluorescence Methods</i>	220
<i>NMR Methods</i>	220
<i>Isothermal Calorimetry</i>	221

4.2 Molecular Recognition 222

4.2.1 Complementarity and Preorganization	224
<i>Crowns, Cryptands, and Spherands—Molecular Recognition with a Large Ion–Dipole Component</i>	224
<i>Tweezers and Clefts</i>	228
4.2.2 Molecular Recognition with a Large Ion Pairing Component	228
4.2.3 Molecular Recognition with a Large Hydrogen Bonding Component	230
<i>Representative Structures</i>	230

<i>Molecular Recognition via Hydrogen Bonding in Water</i>	232
4.2.4 Molecular Recognition with a Large Hydrophobic Component	234
<i>Cyclodextrins</i>	234
<i>Cyclophanes</i>	234
<i>A Summary of the Hydrophobic Component of Molecular Recognition in Water</i>	238
4.2.5 Molecular Recognition with a Large π Component	239
<i>Cation–π Interactions</i>	239
<i>Polar–π and Related Effects</i>	241
4.2.6 Summary	241
4.3 Supramolecular Chemistry 243	
4.3.1 Supramolecular Assembly of Complex Architectures	244
<i>Self-Assembly via Coordination Compounds</i>	244
<i>Self-Assembly via Hydrogen Bonding</i>	245
4.3.2 Novel Supramolecular Architectures—Catenanes, Rotaxanes, and Knots	246
<i>Nanotechnology</i>	248
4.3.3 Container Compounds—Molecules within Molecules	249

Summary and Outlook 252

EXERCISES 253

FURTHER READING 256

CHAPTER 5: Acid–Base Chemistry 259

Intent and Purpose 259

5.1 Brønsted Acid–Base Chemistry 259

5.2 Aqueous Solutions 261

5.2.1 pK_a	261
5.2.2 pH	262
5.2.3 The Leveling Effect	264
5.2.4 Activity vs. Concentration	266
5.2.5 Acidity Functions: Acidity Scales for Highly Concentrated Acidic Solutions	266
5.2.6 Super Acids	270

5.3 Nonaqueous Systems 271

5.3.1 pK_a Shifts at Enzyme Active Sites	273
5.3.2 Solution Phase vs. Gas Phase	273

5.4 Predicting Acid Strength in Solution 276

5.4.1 Methods Used to Measure Weak Acid Strength	276
5.4.2 Two Guiding Principles for Predicting Relative Acidities	277
5.4.3 Electronegativity and Induction	278
5.4.4 Resonance	278
5.4.5 Bond Strengths	283
5.4.6 Electrostatic Effects	283
5.4.7 Hybridization	283

5.4.8	Aromaticity	284
5.4.9	Solvation	284
5.4.10	Cationic Organic Structures	285
5.5	Acids and Bases of Biological Interest	285
5.6	Lewis Acids/Bases and Electrophiles/ Nucleophiles	288
5.6.1	The Concept of Hard and Soft Acids and Bases, General Lessons for Lewis Acid-Base Interactions, and Relative Nucleophilicity and Electrophilicity	289
	Summary and Outlook	292
	EXERCISES	292
	FURTHER READING	294

CHAPTER 6: Stereochemistry 297

Intent and Purpose 297

6.1	Stereogenicity and Stereoisomerism	297
6.1.1	Basic Concepts and Terminology	298
	<i>Classic Terminology</i>	299
	<i>More Modern Terminology</i>	301
6.1.2	Stereochemical Descriptors	303
	<i>R,S System</i>	304
	<i>E,Z System</i>	304
	<i>D and L</i>	304
	<i>Erythro and Threo</i>	305
	<i>Helical Descriptors—M and P</i>	305
	<i>Ent and Epi</i>	306
	<i>Using Descriptors to Compare Structures</i>	306
6.1.3	Distinguishing Enantiomers	306
	<i>Optical Activity and Chirality</i>	309
	<i>Why is Plane Polarized Light Rotated by a Chiral Medium?</i>	309
	<i>Circular Dichroism</i>	310
	<i>X-Ray Crystallography</i>	310
6.2	Symmetry and Stereochemistry	311
6.2.1	Basic Symmetry Operations	311
6.2.2	Chirality and Symmetry	311
6.2.3	Symmetry Arguments	313
6.2.4	Focusing on Carbon	314
6.3	Topicity Relationships	315
6.3.1	Homotopic, Enantiotopic, and Diastereotopic	315
6.3.2	Topicity Descriptors—Pro-R/Pro-S and Re/Si	316
6.3.3	Chirotopicity	317
6.4	Reaction Stereochemistry: Stereoselectivity and Stereospecificity	317
6.4.1	Simple Guidelines for Reaction Stereochemistry	317
6.4.2	Stereospecific and Stereoselective Reactions	319
6.5	Symmetry and Time Scale	322
6.6	Topological and Supramolecular Stereochemistry	324
6.6.1	Loops and Knots	325
6.6.2	Topological Chirality	326

6.6.3	Nonplanar Graphs	326
6.6.4	Achievements in Topological and Supramolecular Stereochemistry	327
6.7	Stereochemical Issues in Polymer Chemistry	331
6.8	Stereochemical Issues in Chemical Biology	333
6.8.1	The Linkages of Proteins, Nucleic Acids, and Polysaccharides	333
	<i>Proteins</i>	333
	<i>Nucleic Acids</i>	334
	<i>Polysaccharides</i>	334
6.8.2	Helicity	336
	<i>Synthetic Helical Polymers</i>	337
6.8.3	The Origin of Chirality in Nature	339
6.9	Stereochemical Terminology	340
	Summary and Outlook	344
	EXERCISES	344
	FURTHER READING	350

PART II REACTIVITY, KINETICS, AND MECHANISMS

CHAPTER 7: Energy Surfaces and Kinetic Analyses 355

Intent and Purpose 355

7.1	Energy Surfaces and Related Concepts	356
7.1.1	Energy Surfaces	357
7.1.2	Reaction Coordinate Diagrams	359
7.1.3	What is the Nature of the Activated Complex/Transition State?	362
7.1.4	Rates and Rate Constants	363
7.1.5	Reaction Order and Rate Laws	364
7.2	Transition State Theory (TST) and Related Topics	365
7.2.1	The Mathematics of Transition State Theory	365
7.2.2	Relationship to the Arrhenius Rate Law	367
7.2.3	Boltzmann Distributions and Temperature Dependence	368
7.2.4	Revisiting "What is the Nature of the Activated Complex?" and Why Does TST Work?	369
7.2.5	Experimental Determinations of Activation Parameters and Arrhenius Parameters	370
7.2.6	Examples of Activation Parameters and Their Interpretations	372
7.2.7	Is TST Completely Correct? The Dynamic Behavior of Organic Reactive Intermediates	372
7.3	Postulates and Principles Related to Kinetic Analysis	374
7.3.1	The Hammond Postulate	374
7.3.2	The Reactivity vs. Selectivity Principle	377

7.3.3 The Curtin–Hammett Principle	378		
7.3.4 Microscopic Reversibility	379		
7.3.5 Kinetic vs. Thermodynamic Control	380		
7.4 Kinetic Experiments	382		
7.4.1 How Kinetic Experiments are Performed	382		
7.4.2 Kinetic Analyses for Simple Mechanisms	384		
<i>First Order Kinetics</i>	385		
<i>Second Order Kinetics</i>	386		
<i>Pseudo-First Order Kinetics</i>	387		
<i>Equilibrium Kinetics</i>	388		
<i>Initial-Rate Kinetics</i>	389		
<i>Tabulating a Series of Common Kinetic Scenarios</i>	389		
7.5 Complex Reactions—Deciphering Mechanisms	390		
7.5.1 Steady State Kinetics	390		
7.5.2 Using the SSA to Predict Changes in Kinetic Order	395		
7.5.3 Saturation Kinetics	396		
7.5.4 Prior Rapid Equilibria	397		
7.6 Methods for Following Kinetics	397		
7.6.1 Reactions with Half-Lives Greater than a Few Seconds	398		
7.6.2 Fast Kinetics Techniques	398		
<i>Flow Techniques</i>	399		
<i>Flash Photolysis</i>	399		
<i>Pulse Radiolysis</i>	401		
7.6.3 Relaxation Methods	401		
7.6.4 Summary of Kinetic Analyses	402		
7.7 Calculating Rate Constants	403		
7.7.1 Marcus Theory	403		
7.7.2 Marcus Theory Applied to Electron Transfer	405		
7.8 Considering Multiple Reaction Coordinates	407		
7.8.1 Variation in Transition State Structures Across a Series of Related Reactions—An Example Using Substitution Reactions	407		
7.8.2 More O’Ferrall–Jencks Plots	409		
7.8.3 Changes in Vibrational State Along the Reaction Coordinate—Relating the Third Coordinate to Entropy	412		
Summary and Outlook	413		
EXERCISES	413		
FURTHER READING	417		
<hr/>			
CHAPTER 8: Experiments Related to Thermodynamics and Kinetics	421		
Intent and Purpose	421		
8.1 Isotope Effects	421		
8.1.1 The Experiment	422		
8.1.2 The Origin of Primary Kinetic Isotope Effects	422		
<i>Reaction Coordinate Diagrams and Isotope Effects</i>	424		
			<i>Primary Kinetic Isotope Effects for Linear Transition States as a Function of Exothermicity and Endothermicity</i> 425
			<i>Isotope Effects for Linear vs. Non-Linear Transition States</i> 428
8.1.3 The Origin of Secondary Kinetic Isotope Effects	428		
<i>Hybridization Changes</i>	429		
<i>Steric Isotope Effects</i>	430		
8.1.4 Equilibrium Isotope Effects	432		
<i>Isotopic Perturbation of Equilibrium—Applications to Carbocations</i>	432		
8.1.5 Tunneling	435		
8.1.6 Solvent Isotope Effects	437		
<i>Fractionation Factors</i>	437		
<i>Proton Inventories</i>	438		
8.1.7 Heavy Atom Isotope Effects	441		
8.1.8 Summary	441		
8.2 Substituent Effects	441		
8.2.1 The Origin of Substituent Effects	443		
<i>Field Effects</i>	443		
<i>Inductive Effects</i>	443		
<i>Resonance Effects</i>	444		
<i>Polarizability Effects</i>	444		
<i>Steric Effects</i>	445		
<i>Solvation Effects</i>	445		
8.3 Hammett Plots—The Most Common LFER. A General Method for Examining Changes in Charges During a Reaction	445		
8.3.1 Sigma (σ)	445		
8.3.2 Rho (ρ)	447		
8.3.3 The Power of Hammett Plots for Deciphering Mechanisms	448		
8.3.4 Deviations from Linearity	449		
8.3.5 Separating Resonance from Induction	451		
8.4 Other Linear Free Energy Relationships	454		
8.4.1 Steric and Polar Effects—Taft Parameters	454		
8.4.2 Solvent Effects—Grunwald–Winstein Plots	455		
8.4.3 Schleyer Adaptation	457		
8.4.4 Nucleophilicity and Nucleofugality	458		
<i>Basicity/Acidity</i>	459		
<i>Solvation</i>	460		
<i>Polarizability, Basicity, and Solvation Interplay</i>	460		
<i>Shape</i>	461		
8.4.5 Swain–Scott Parameters—Nucleophilicity Parameters	461		
8.4.6 Edwards and Ritchie Correlations	463		
8.5 Acid–Base Related Effects—Bronsted Relationships	464		
8.5.1 β_{Nuc}	464		
8.5.2 β_{LG}	464		
8.5.3 Acid–Base Catalysis	466		
8.6 Why do Linear Free Energy Relationships Work?	466		
8.6.1 General Mathematics of LFERs	467		
8.6.2 Conditions to Create an LFER	468		
8.6.3 The Isokinetic or Isoequilibrium Temperature	469		

8.6.4	Why does Enthalpy–Entropy Compensation Occur?	469
	<i>Steric Effects</i>	470
	<i>Solvation</i>	470
8.7	Summary of Linear Free Energy Relationships	470
8.8	Miscellaneous Experiments for Studying Mechanisms	471
8.8.1	Product Identification	472
8.8.2	Changing the Reactant Structure to Divert or Trap a Proposed Intermediate	473
8.8.3	Trapping and Competition Experiments	474
8.8.4	Checking for a Common Intermediate	475
8.8.5	Cross-Over Experiments	476
8.8.6	Stereochemical Analysis	476
8.8.7	Isotope Scrambling	477
8.8.8	Techniques to Study Radicals: Clocks and Traps	478
8.8.9	Direct Isolation and Characterization of an Intermediate	480
8.8.10	Transient Spectroscopy	480
8.8.11	Stable Media	481
	Summary and Outlook	482
	EXERCISES	482
	FURTHER READING	487

CHAPTER 9: Catalysis 489

Intent and Purpose 489

9.1	General Principles of Catalysis	490
9.1.1	Binding the Transition State <i>Better</i> than the Ground State	491
9.1.2	A Thermodynamic Cycle Analysis	493
9.1.3	A Spatial Temporal Approach	494
9.2	Forms of Catalysis	495
9.2.1	“Binding” is Akin to Solvation	495
9.2.2	Proximity as a Binding Phenomenon	495
9.2.3	Electrophilic Catalysis	499
	<i>Electrostatic Interactions</i>	499
	<i>Metal Ion Catalysis</i>	500
9.2.4	Acid–Base Catalysis	502
9.2.5	Nucleophilic Catalysis	502
9.2.6	Covalent Catalysis	504
9.2.7	Strain and Distortion	505
9.2.8	Phase Transfer Catalysis	507
9.3	Brønsted Acid–Base Catalysis	507
9.3.1	Specific Catalysis	507
	<i>The Mathematics of Specific Catalysis</i>	507
	<i>Kinetic Plots</i>	510
9.3.2	General Catalysis	510
	<i>The Mathematics of General Catalysis</i>	511
	<i>Kinetic Plots</i>	512
9.3.3	A Kinetic Equivalency	514

9.3.4	Concerted or Sequential General-Acid–General-Base Catalysis	515
9.3.5	The Brønsted Catalysis Law and Its Ramifications	516
	<i>A Linear Free Energy Relationship</i>	516
	<i>The Meaning of α and β</i>	517
	$\alpha + \beta = 1$	518
	<i>Deviations from Linearity</i>	519
9.3.6	Predicting General-Acid or General-Base Catalysis	520
	<i>The Libido Rule</i>	520
	<i>Potential Energy Surfaces Dictate General or Specific Catalysis</i>	521
9.3.7	The Dynamics of Proton Transfers	522
	<i>Marcus Analysis</i>	522
9.4	Enzymatic Catalysis	523
9.4.1	Michaelis–Menten Kinetics	523
9.4.2	The Meaning of K_M , k_{cat} , and k_{cat}/K_M	524
9.4.3	Enzyme Active Sites	525
9.4.4	[S] vs. K_M —Reaction Coordinate Diagrams	527
9.4.5	Supramolecular Interactions	529
	Summary and Outlook	530
	EXERCISES	531
	FURTHER READING	535

CHAPTER 10: Organic Reaction Mechanisms, Part 1: Reactions Involving Additions and/or Eliminations 537

Intent and Purpose 537

10.1	Predicting Organic Reactivity	538
10.1.1	A Useful Paradigm for Polar Reactions	539
	<i>Nucleophiles and Electrophiles</i>	539
	<i>Lewis Acids and Lewis Bases</i>	540
	<i>Donor–Acceptor Orbital Interactions</i>	540
10.1.2	Predicting Radical Reactivity	541
10.1.3	In Preparation for the Following Sections	541
	—ADDITION REACTIONS—	542
10.2	Hydration of Carbonyl Structures	542
10.2.1	Acid–Base Catalysis	543
10.2.2	The Thermodynamics of the Formation of Geminal Diols and Hemiacetals	544
10.3	Electrophilic Addition of Water to Alkenes and Alkynes: Hydration	545
10.3.1	Electron Pushing	546
10.3.2	Acid-Catalyzed Aqueous Hydration	546
10.3.3	Regiochemistry	546
10.3.4	Alkyne Hydration	547
10.4	Electrophilic Addition of Hydrogen Halides to Alkenes and Alkynes	548
10.4.1	Electron Pushing	548

- 10.4.2 Experimental Observations Related to Regiochemistry and Stereochemistry 548
- 10.4.3 Addition to Alkynes 551
- 10.5 Electrophilic Addition of Halogens to Alkenes 551**
- 10.5.1 Electron Pushing 551
- 10.5.2 Stereochemistry 552
- 10.5.3 Other Evidence Supporting a σ Complex 552
- 10.5.4 Mechanistic Variants 553
- 10.5.5 Addition to Alkynes 554
- 10.6 Hydroboration 554**
- 10.6.1 Electron Pushing 555
- 10.6.2 Experimental Observations 555
- 10.7 Epoxidation 555**
- 10.7.1 Electron Pushing 556
- 10.7.2 Experimental Observations 556
- 10.8 Nucleophilic Additions to Carbonyl Compounds 556**
- 10.8.1 Electron Pushing for a Few Nucleophilic Additions 557
- 10.8.2 Experimental Observations for Cyanohydrin Formation 559
- 10.8.3 Experimental Observations for Grignard Reactions 560
- 10.8.4 Experimental Observations in LAH Reductions 561
- 10.8.5 Orbital Considerations 561
- The Bürgi–Dunitz Angle* 561
- Orbital Mixing* 562
- 10.8.6 Conformational Effects in Additions to Carbonyl Compounds 562
- 10.8.7 Stereochemistry of Nucleophilic Additions 563
- 10.9 Nucleophilic Additions to Olefins 567**
- 10.9.1 Electron Pushing 567
- 10.9.2 Experimental Observations 567
- 10.9.3 Regiochemistry of Addition 567
- 10.9.4 Baldwin's Rules 568
- 10.10 Radical Additions to Unsaturated Systems 569**
- 10.10.1 Electron Pushing for Radical Additions 569
- 10.10.2 Radical Initiators 570
- 10.10.3 Chain Transfer vs. Polymerization 571
- 10.10.4 Termination 571
- 10.10.5 Regiochemistry of Radical Additions 572
- 10.11 Carbene Additions and Insertions 572**
- 10.11.1 Electron Pushing for Carbene Reactions 574
- 10.11.2 Carbene Generation 574
- 10.11.3 Experimental Observations for Carbene Reactions 575
- ELIMINATIONS— 576
- 10.12 Eliminations to Form Carbonyls or "Carbonyl-Like" Intermediates 577**
- 10.12.1 Electron Pushing 577
- 10.12.2 Stereochemical and Isotope Labeling Evidence 577
- 10.12.3 Catalysis of the Hydrolysis of Acetals 578
- 10.12.4 Stereoelectronic Effects 579
- 10.12.5 CrO_3 Oxidation—The Jones Reagent 580
- Electron Pushing* 580
- A Few Experimental Observations* 581
- 10.13 Elimination Reactions for Aliphatic Systems—Formation of Alkenes 581**
- 10.13.1 Electron Pushing and Definitions 581
- 10.13.2 Some Experimental Observations for E2 and E1 Reactions 582
- 10.13.3 Contrasting Elimination and Substitution 583
- 10.13.4 Another Possibility—E1cB 584
- 10.13.5 Kinetics and Experimental Observations for E1cB 584
- 10.13.6 Contrasting E2, E1, and E1cB 586
- 10.13.7 Regiochemistry of Eliminations 588
- 10.13.8 Stereochemistry of Eliminations—Orbital Considerations 590
- 10.13.9 Dehydration 592
- Electron Pushing* 592
- Other Mechanistic Possibilities* 594
- 10.13.10 Thermal Eliminations 594
- 10.14 Eliminations from Radical Intermediates 596**
- COMBINING ADDITION AND ELIMINATION REACTIONS (SUBSTITUTIONS AT sp^2 CENTERS)— 596
- 10.15 The Addition of Nitrogen Nucleophiles to Carbonyl Structures, Followed by Elimination 597**
- 10.15.1 Electron Pushing 598
- 10.15.2 Acid–Base Catalysis 598
- 10.16 The Addition of Carbon Nucleophiles, Followed by Elimination—The Wittig Reaction 599**
- 10.16.1 Electron Pushing 600
- 10.17 Acyl Transfers 600**
- 10.17.1 General Electron-Pushing Schemes 600
- 10.17.2 Isotope Scrambling 601
- 10.17.3 Predicting the Site of Cleavage for Acyl Transfers from Esters 602
- 10.17.4 Catalysis 602
- 10.18 Electrophilic Aromatic Substitution 607**
- 10.18.1 Electron Pushing for Electrophilic Aromatic Substitutions 607
- 10.18.2 Kinetics and Isotope Effects 608
- 10.18.3 Intermediate Complexes 608
- 10.18.4 Regiochemistry and Relative Rates of Aromatic Substitution 609
- 10.19 Nucleophilic Aromatic Substitution 611**
- 10.19.1 Electron Pushing for Nucleophilic Aromatic Substitution 611
- 10.19.2 Experimental Observations 611

- 10.20 Reactions Involving Benzyne** 612
 10.20.1 Electron Pushing for Benzyne Reactions 612
 10.20.2 Experimental Observations 613
 10.20.3 Substituent Effects 613

- 10.21 The $S_{RN}1$ Reaction on Aromatic Rings** 615
 10.21.1 Electron Pushing 615
 10.21.2 A Few Experimental Observations 615

- 10.22 Radical Aromatic Substitutions** 615
 10.22.1 Electron Pushing 615
 10.22.2 Isotope Effects 616
 10.22.3 Regiochemistry 616

Summary and Outlook 617

EXERCISES 617

FURTHER READING 624

**CHAPTER 11: Organic Reaction Mechanisms,
 Part 2: Substitutions at Aliphatic
 Centers and Thermal Isomerizations/
 Rearrangements** 627

Intent and Purpose 627

—SUBSTITUTION α TO A CARBONYL CENTER:
 ENOL AND ENOLATE CHEMISTRY— 627

- 11.1 Tautomerization** 628
 11.1.1 Electron Pushing for Keto–Enol
 Tautomerizations 628
 11.1.2 The Thermodynamics of Enol Formation 628
 11.1.3 Catalysis of Enolizations 629
 11.1.4 Kinetic vs. Thermodynamic Control
 in Enolate and Enol Formation 629

- 11.2 α -Halogenation** 631
 11.2.1 Electron Pushing 631
 11.2.2 A Few Experimental Observations 631

- 11.3 α -Alkylations** 632
 11.3.1 Electron Pushing 632
 11.3.2 Stereochemistry: Conformational Effects 633

- 11.4 The Aldol Reaction** 634
 11.4.1 Electron Pushing 634
 11.4.2 Conformational Effects on the Aldol Reaction 634

—SUBSTITUTIONS ON ALIPHATIC CENTERS— 637

- 11.5 Nucleophilic Aliphatic Substitution Reactions** 637
 11.5.1 S_N2 and S_N1 Electron-Pushing Examples 637
 11.5.2 Kinetics 638
 11.5.3 Competition Experiments and Product Analyses 639
 11.5.4 Stereochemistry 640
 11.5.5 Orbital Considerations 643
 11.5.6 Solvent Effects 643
 11.5.7 Isotope Effect Data 646
 11.5.8 An Overall Picture of S_N2 and S_N1 Reactions 646

- 11.5.9 Structure–Function Correlations
 with the Nucleophile 648
 11.5.10 Structure–Function Correlations
 with the Leaving Group 651
 11.5.11 Structure–Function Correlations
 with the R Group 651
Effect of the R Group Structure on S_N2 Reactions 651
Effect of the R Group Structure on S_N1 Reactions 653
 11.5.12 Carbocation Rearrangements 656
 11.5.13 Anchimeric Assistance in S_N1 Reactions 659
 11.5.14 S_N1 Reactions Involving Non-Classical
 Carbocations 661
Norbornyl Cation 662
Cyclopropyl Carbinyl Carbocation 664
 11.5.15 Summary of Carbocation Stabilization
 in Various Reactions 667
 11.5.16 The Interplay Between Substitution
 and Elimination 667

- 11.6 Substitution, Radical, Nucleophilic** 668
 11.6.1 The SET Reaction—Electron Pushing 668
 11.6.2 The Nature of the Intermediate
 in an SET Mechanism 669
 11.6.3 Radical Rearrangements as Evidence 669
 11.6.4 Structure–Function Correlations
 with the Leaving Group 670
 11.6.5 The $S_{RN}1$ Reaction—Electron Pushing 670

- 11.7 Radical Aliphatic Substitutions** 671
 11.7.1 Electron Pushing 671
 11.7.2 Heats of Reaction 671
 11.7.3 Regiochemistry of Free Radical
 Halogenation 671
 11.7.4 Autoxidation: Addition of O_2
 into C–H Bonds 673
Electron Pushing for Autoxidation 673

—ISOMERIZATIONS AND REARRANGEMENTS— 674

- 11.8 Migrations to Electrophilic Carbons** 674
 11.8.1 Electron Pushing for the
 Pinacol Rearrangement 675
 11.8.2 Electron Pushing in the Benzilic Acid
 Rearrangement 675
 11.8.3 Migratory Aptitudes in the Pinacol
 Rearrangement 675
 11.8.4 Stereoelectronic and Stereochemical Considerations
 in the Pinacol Rearrangement 676
 11.8.5 A Few Experimental Observations for the Benzilic
 Acid Rearrangement 678

- 11.9 Migrations to Electrophilic Heteroatoms** 678
 11.9.1 Electron Pushing in the Beckmann
 Rearrangement 678
 11.9.2 Electron Pushing for the Hofmann
 Rearrangement 679
 11.9.3 Electron Pushing for the Schmidt
 Rearrangement 680
 11.9.4 Electron Pushing for the Baeyer–Villiger
 Oxidation 680
 11.9.5 A Few Experimental Observations for the
 Beckmann Rearrangement 680

11.9.6	A Few Experimental Observations for the Schmidt Rearrangement	681
11.9.7	A Few Experimental Observations for the Baeyer–Villiger Oxidation	681
11.10	The Favorskii Rearrangement and Other Carbanion Rearrangements	682
11.10.1	Electron Pushing	682
11.10.2	Other Carbanion Rearrangements	683
11.11	Rearrangements Involving Radicals	683
11.11.1	Hydrogen Shifts	683
11.11.2	Aryl and Vinyl Shifts	684
11.11.3	Ring-Opening Reactions	685
11.12	Rearrangements and Isomerizations Involving Biradicals	685
11.12.1	Electron Pushing Involving Biradicals	686
11.12.2	Tetramethylene	687
11.12.3	Trimethylene	689
11.12.4	Trimethylenemethane	693
	Summary and Outlook	695
	EXERCISES	695
	FURTHER READING	703

CHAPTER 12: Organotransition Metal Reaction Mechanisms and Catalysis 705

Intent and Purpose 705

12.1	The Basics of Organometallic Complexes	705
12.1.1	Electron Counting and Oxidation State	706
	<i>Electron Counting</i>	706
	<i>Oxidation State</i>	708
	<i>d Electron Count</i>	708
	<i>Ambiguities</i>	708
12.1.2	The 18-Electron Rule	710
12.1.3	Standard Geometries	710
12.1.4	Terminology	711
12.1.5	Electron Pushing with Organometallic Structures	711
12.1.6	<i>d</i> Orbital Splitting Patterns	712
12.1.7	Stabilizing Reactive Ligands	713
12.2	Common Organometallic Reactions	714
12.2.1	Ligand Exchange Reactions	714
	<i>Reaction Types</i>	714
	<i>Kinetics</i>	716
	<i>Structure–Function Relationships with the Metal</i>	716
	<i>Structure–Function Relationships with the Ligand</i>	716
	<i>Substitutions of Other Ligands</i>	717
12.2.2	Oxidative Addition	717
	<i>Stereochemistry of the Metal Complex</i>	718
	<i>Kinetics</i>	718
	<i>Stereochemistry of the R Group</i>	719
	<i>Structure–Function Relationship for the R Group</i>	720

	<i>Structure–Function Relationships for the Ligands</i>	720
	<i>Oxidative Addition at sp^2 Centers</i>	721
	<i>Summary of the Mechanisms for Oxidative Addition</i>	721
12.2.3	Reductive Elimination	724
	<i>Structure–Function Relationship for the R Group and the Ligands</i>	724
	<i>Stereochemistry at the Metal Center</i>	725
	<i>Other Mechanisms</i>	725
	<i>Summary of the Mechanisms for Reductive Elimination</i>	726
12.2.4	α - and β -Eliminations	727
	<i>General Trends for α- and β-Eliminations</i>	727
	<i>Kinetics</i>	728
	<i>Stereochemistry of β-Hydride Elimination</i>	729
12.2.5	Migratory Insertions	729
	<i>Kinetics</i>	730
	<i>Studies to Decipher the Mechanism of Migratory Insertion Involving CO</i>	730
	<i>Other Stereochemical Considerations</i>	732
12.2.6	Electrophilic Addition to Ligands	733
	<i>Reaction Types</i>	733
	<i>Common Mechanisms Deduced from Stereochemical Analyses</i>	734
12.2.7	Nucleophilic Addition to Ligands	734
	<i>Reaction Types</i>	735
	<i>Stereochemical and Regiochemical Analyses</i>	735

12.3 Combining the Individual Reactions into Overall Transformations and Cycles 737

12.3.1	The Nature of Organometallic Catalysis—Change in Mechanism	738
12.3.2	The Monsanto Acetic Acid Synthesis	738
12.3.3	Hydroformylation	739
12.3.4	The Water–Gas Shift Reaction	740
12.3.5	Olefin Oxidation—The Wacker Process	741
12.3.6	Palladium Coupling Reactions	742
12.3.7	Allylic Alkylation	743
12.3.8	Olefin Metathesis	744

Summary and Outlook 747

EXERCISES	748
FURTHER READING	750

CHAPTER 13: Organic Polymer and Materials Chemistry 753

Intent and Purpose 753

13.1	Structural Issues in Materials Chemistry	754
13.1.1	Molecular Weight Analysis of Polymers	754
	<i>Number Average and Weight Average Molecular Weights—M_n and M_w</i>	754
13.1.2	Thermal Transitions—Thermoplastics and Elastomers	757
13.1.3	Basic Polymer Topologies	759

- 13.1.4 Polymer-Polymer Phase Behavior 760
 13.1.5 Polymer Processing 762
 13.1.6 Novel Topologies—Dendrimers and Hyperbranched Polymers 763
 Dendrimers 763
 Hyperbranched Polymers 768
 13.1.7 Liquid Crystals 769
 13.1.8 Fullerenes and Carbon Nanotubes 775
- 13.2 Common Polymerization Mechanisms 779**
 13.2.1 General Issues 779
 13.2.2 Polymerization Kinetics 782
 Step-Growth Kinetics 782
 Free-Radical Chain Polymerization 783
 Living Polymerizations 785
 Thermodynamics of Polymerizations 787
 13.2.3 Condensation Polymerization 788
 13.2.4 Radical Polymerization 791
 13.2.5 Anionic Polymerization 793
 13.2.6 Cationic Polymerization 794
 13.2.7 Ziegler-Natta and Related Polymerizations 794
 Single-Site Catalysts 796
 13.2.8 Ring-Opening Polymerization 797
 13.2.9 Group Transfer Polymerization (GTP) 799

Summary and Outlook 800

EXERCISES 801

FURTHER READING 803

PART III

**ELECTRONIC STRUCTURE:
THEORY AND APPLICATIONS**

**CHAPTER 14: Advanced Concepts in Electronic
Structure Theory 807**

Intent and Purpose 807

14.1 Introductory Quantum Mechanics 808

- 14.1.1 The Nature of Wavefunctions 808
 14.1.2 The Schrödinger Equation 809
 14.1.3 The Hamiltonian 809
 14.1.4 The Nature of the ∇^2 Operator 811
 14.1.5 Why do Bonds Form? 812

**14.2 Computational Methods—Solving the Schrödinger
Equation for Complex Systems 815**

- 14.2.1 *Ab Initio* Molecular Orbital Theory 815
 Born-Oppenheimer Approximation 815
 The Orbital Approximation 815
 Spin 816
 The Pauli Principle and Determinantal
Wavefunctions 816
 The Hartree-Fock Equation and
the Variational Theorem 818

SCF Theory 821

- Linear Combination of Atomic Orbitals—
Molecular Orbitals (LCAO-MO) 821
 Common Basis Sets—Modeling Atomic Orbitals 822
 Extension Beyond HF—Correlation Energy 824
 Solvation 825
 General Considerations 825
 Summary 826

- 14.2.2 Secular Determinants—A Bridge Between *Ab Initio*,
Semi-Empirical/ Approximate, and Perturbational
Molecular Orbital Theory Methods 828
 The “Two-Orbital Mixing Problem” 829
 Writing the Secular Equations and Determinant
for Any Molecule 832

- 14.2.3 Semi-Empirical and Approximate Methods 833
 Neglect of Differential Overlap
(NDO) Methods 833
 i. CNDO, INDO, PNDO (C = Complete,
I = Intermediate, P = Partial) 834
 ii. The Semi-Empirical Methods:
MNDO, AM1, and PM3 834
 Extended Hückel Theory (EHT) 834
 Hückel Molecular Orbital Theory (HMOT) 835

- 14.2.4 Some General Comments on Computational
Quantum Mechanics 835

- 14.2.5 An Alternative: Density Functional
Theory (DFT) 836

**14.3 A Brief Overview of the Implementation
and Results of HMOT 837**

- 14.3.1 Implementing Hückel Theory 838
 14.3.2 HMOT of Cyclic π Systems 840
 14.3.3 HMOT of Linear π Systems 841
 14.3.4 Alternate Hydrocarbons 842

14.4 Perturbation Theory—Orbital Mixing Rules 844

- 14.4.1 Mixing of Degenerate Orbitals—
First-Order Perturbations 845
 14.4.2 Mixing of Non-Degenerate Orbitals—
Second-Order Perturbations 845

**14.5 Some Topics in Organic Chemistry for
Which Molecular Orbital Theory Lends
Important Insights 846**

- 14.5.1 Arenes: Aromaticity and Antiaromaticity 846
 14.5.2 Cyclopropane and Cyclopropylcarbinyl—
Walsh Orbitals 848
 The Cyclic Three-Orbital Mixing Problem 849
 The MOs of Cyclopropane 850
 14.5.3 Planar Methane 853
 14.5.4 Through-Bond Coupling 854
 14.5.5 Unique Bonding Capabilities of Carbocations—
Non-Classical Ions and Hypervalent Carbon 855
 Transition State Structure Calculations 856
 Application of These Methods to Carbocations 857
 NMR Effects in Carbocations 857
 The Norbornyl Cation 858
 14.5.6 Spin Preferences 859
 Two Weakly Interacting Electrons:
H₂ vs. Atomic C 859

- 14.6 Organometallic Complexes 862
 14.6.1 Group Orbitals for Metals 863
 14.6.2 The Isolobal Analogy 866
 14.6.3 Using the Group Orbitals to Construct Organometallic Complexes 867

Summary and Outlook 868

EXERCISES 868

FURTHER READING 875

CHAPTER 15: Thermal Pericyclic Reactions 877

Intent and Purpose 877

15.1 Background 878

15.2 A Detailed Analysis of Two Simple Cycloadditions 878

15.2.1 Orbital Symmetry Diagrams 879

[2+2] 879

[4+2] 881

15.2.2 State Correlation Diagrams 883

[2+2] 883

[4+2] 886

15.2.3 Frontier Molecular Orbital (FMO) Theory 888

Contrasting the [2+2] and [4+2] 888

15.2.4 Aromatic Transition State Theory/Topology 889

15.2.5 The Generalized Orbital Symmetry Rule 890

15.2.6 Some Comments on "Forbidden" and "Allowed" Reactions 892

15.2.7 Photochemical Pericyclic Reactions 892

15.2.8 Summary of the Various Methods 893

15.3 Cycloadditions 893

15.3.1 An Allowed Geometry for [2+2] Cycloadditions 894

15.3.2 Summarizing Cycloadditions 895

15.3.3 General Experimental Observations 895

15.3.4 Stereochemistry and Regiochemistry of the Diels–Alder Reaction 896

An Orbital Approach to Predicting Regiochemistry 896

The Endo Effect 899

15.3.5 Experimental Observations for [2+2] Cycloadditions 901

15.3.6 Experimental Observations for 1,3-Dipolar Cycloadditions 901

15.3.7 Retrocycloadditions 902

15.4 Electrocyclic Reactions 903

15.4.1 Terminology 903

15.4.2 Theoretical Analyses 904

15.4.3 Experimental Observations: Stereochemistry 906

15.4.4 Torquoselectivity 908

15.5 Sigmatropic Rearrangements 910

15.5.1 Theory 911

15.5.2 Experimental Observations: A Focus on Stereochemistry 913

15.5.3 The Mechanism of the Cope Rearrangement 916

15.5.4 The Claisen Rearrangement 921
Uses in Synthesis 921

Mechanistic Studies 923

15.5.5 The Ene Reaction 924

15.6 Cheletropic Reactions 924

15.6.1 Theoretical Analyses 926

15.6.2 Carbene Additions 927

15.7 In Summary—Applying the Rules 928

Summary and Outlook 928

EXERCISES 929

FURTHER READING 933

CHAPTER 16: Photochemistry 935

Intent and Purpose 935

16.1 Photophysical Processes—The Jablonski Diagram 936

16.1.1 Electromagnetic Radiation 936

Multiple Energy Surfaces Exist 937

16.1.2 Absorption 939

16.1.3 Radiationless Vibrational Relaxation 944

16.1.4 Fluorescence 945

16.1.5 Internal Conversion (IC) 949

16.1.6 Intersystem Crossing (ISC) 950

16.1.7 Phosphorescence 951

16.1.8 Quantum Yield 952

16.1.9 Summary of Photophysical Processes 952

16.2 Bimolecular Photophysical Processes 953

16.2.1 General Considerations 953

16.2.2 Quenching, Excimers, and Exciplexes 953
Quenching 954

Excimers and Exciplexes 954

Photoinduced Electron Transfer 955

16.2.3 Energy Transfer I. The Dexter Mechanism—Sensitization 956

16.2.4 Energy Transfer II. The Förster Mechanism 958

16.2.5 FRET 960

16.2.6 Energy Pooling 962

16.2.7 An Overview of Bimolecular Photophysical Processes 962

16.3 Photochemical Reactions 962

16.3.1 Theoretical Considerations—Funnels 962
Adiabatic Photoreactions 963

Other Mechanisms 964

16.3.2 Acid–Base Chemistry 965

16.3.3 Olefin Isomerization	965
16.3.4 Reversal of Pericyclic Selection Rules	968
16.3.5 Photocycloaddition Reactions	970
<i>Making Highly Strained Ring Systems</i>	973
<i>Breaking Aromaticity</i>	974
16.3.6 The Di- π -Methane Rearrangement	974
16.3.7 Carbonyls Part I: The Norrish I Reaction	976
16.3.8 Carbonyls Part II: Photoreduction and the Norrish II Reaction	978
16.3.9 Nitrobenzyl Photochemistry: "Caged" Compounds	980
16.3.10 Elimination of N ₂ : Azo Compounds, Diazo Compounds, Diazirines, and Azides	981
<i>Azoalkanes (1,2-Diazenes)</i>	981
<i>Diazo Compounds and Diazirines</i>	982
<i>Azides</i>	983
16.4 Chemiluminescence	985
16.4.1 Potential Energy Surface for a Chemiluminescent Reaction	985
16.4.2 Typical Chemiluminescent Reactions	986
16.4.3 Dioxetane Thermolysis	987
16.5 Singlet Oxygen	989
Summary and Outlook	993
EXERCISES	993
FURTHER READING	999
CHAPTER 17: Electronic Organic Materials	1001
Intent and Purpose	1001
17.1 Theory	1001
17.1.1 Infinite π Systems—An Introduction to Band Structures	1002
17.1.2 The Peierls Distortion	1009
17.1.3 Doping	1011
17.2 Conducting Polymers	1016
17.2.1 Conductivity	1016
17.2.2 Polyacetylene	1017
17.2.3 Polyarenes and Polyarenevinylenes	1018
17.2.4 Polyaniline	1021
17.3 Organic Magnetic Materials	1022
17.3.1 Magnetism	1023
17.3.2 The Molecular Approach to Organic Magnetic Materials	1024
17.3.3 The Polymer Approach to Organic Magnetic Materials—Very High-Spin Organic Molecules	1027

17.4 Superconductivity	1030
17.4.1 Organic Metals/Synthetic Metals	1032
17.5 Non-Linear Optics (NLO)	1033

17.6 Photoresists	1036
17.6.1 Photolithography	1036
17.6.2 Negative Photoresists	1037
17.6.3 Positive Photoresists	1038

Summary and Outlook 1041

EXERCISES	1042
FURTHER READING	1044

APPENDIX 1: Conversion Factors and Other Useful Data	1047
APPENDIX 2: Electrostatic Potential Surfaces for Representative Organic Molecules	1049
APPENDIX 3: Group Orbitals of Common Functional Groups: Representative Examples Using Simple Molecules	1051
APPENDIX 4: The Organic Structures of Biology	1057
APPENDIX 5: Pushing Electrons	1061
A5.1 The Rudiments of Pushing Electrons	1061
A5.2 Electron Sources and Sinks for Two-Electron Flow	1062
A5.3 How to Denote Resonance	1064
A5.4 Common Electron-Pushing Errors	1065
Backwards Arrow Pushing	1065
Not Enough Arrows	1065
Losing Track of the Octet Rule	1066
Losing Track of Hydrogens and Lone Pairs	1066
Not Using the Proper Source	1067
Mixed Media Mistakes	1067
Too Many Arrows—Short Cuts	1067
A5.5 Complex Reactions—Drawing a Chemically Reasonable Mechanism	1068
A5.6 Two Case Studies of Predicting Reaction Mechanisms	1069
A5.7 Pushing Electrons for Radical Reactions	1071
Practice Problems for Pushing Electrons	1073
APPENDIX 6: Reaction Mechanism Nomenclature	1075
Index	1079

CHAPTER 1

- How Realistic are Formal Charges? 7
- NMR Coupling Constants 10
- Scaling Electrostatic Surface Potentials 15
- 1-Fluorobutane 16
- Particle in a Box 21
- Resonance in the Peptide Amide Bond? 23
- A Brief Look at Symmetry and Symmetry Operations 29
- CH₅⁺—Not Really a Well-Defined Structure 55
- Pyramidal Inversion: NH₃ vs. PH₃ 57
- Stable Carbenes 59

CHAPTER 2

- Entropy Changes During Cyclization Reactions 71
- A Consequence of High Bond Strength:
 - The Hydroxyl Radical in Biology 73
- The Half-Life for Homolysis of Ethane at Room Temperature 73
- The Probability of Finding Atoms at Particular Separations 75
- How do We Know That $n = 0$ is Most Relevant for Bond Stretches at $T = 298$ K? 76
- Potential Surfaces for Bond Bending Motions 78
- How Big is 3 kcal/mol? 93
- Shouldn't Torsional Motions be Quantized? 94
- The Geometry of Radicals 96
- Differing Magnitudes of Energy Values in Thermodynamics and Kinetics 100
- "Sugar Pucker" in Nucleic Acids 102
- Alternative Measurements of Steric Size 104
- The Use of A Values in a Conformational Analysis Study for the Determination of Intramolecular Hydrogen Bond Strength 105
- The NMR Time Scale 106
- Ring Fusion—Steroids 108
- A Conformational Effect on the Material Properties of Poly(3-Alkylthiophenes) 116
- Cyclopropenyl Cation 117
- Cyclopropenyl Anion 118
- Porphyrins 119
- Protein Disulfide Linkages 123
- From Strained Molecules to Molecular Rods 126
- Cubane Explosives? 126
- Molecular Gears 128

CHAPTER 3

- The Use of Solvent Scales to Direct Diels–Alder Reactions 149
- The Use of Wetting and the Capillary Action Force to Drive the Self-Assembly of Macroscopic Objects 151
- The Solvent Packing Coefficient and the 55% Solution 152
- Solvation Can Affect Equilibria 155
- A van't Hoff Analysis of the Formation of a Stable Carbene 163

- The Strength of a Buried Salt Bridge 165
- The Angular Dependence of Dipole–Dipole Interactions—The "Magic Angle" 168
- An Unusual Hydrogen Bond Acceptor 169
- Evidence for Weak Directionality Considerations 170
- Intramolecular Hydrogen Bonds are Best for Nine-Membered Rings 170
- Solvent Scales and Hydrogen Bonds 172
- The Extent of Resonance can be Correlated with Hydrogen Bond Length 174
- Cooperative Hydrogen Bonding in Saccharides 175
- How Much is a Hydrogen Bond in an α -Helix Worth? 176
- Proton Sponges 179
- The Relevance of Low-Barrier Hydrogen Bonds to Enzymatic Catalysis 179
- β -Peptide Foldamers 180
- A Cation– π Interaction at the Nicotine Receptor 183
- The Polar Nature of Benzene Affects Acidities in a Predictable Manner 184
- Use of the Arene–Perfluorarene Interaction in the Design of Solid State Structures 185
- Donor–Acceptor Driven Folding 187
- The Hydrophobic Effect and Protein Folding 194
- More Foldamers: Folding Driven by Solvophobic Effects 195
- Calculating Drug Binding Energies by SPT 201

CHAPTER 4

- The Units of Binding Constants 209
- Cooperativity in Drug Receptor Interactions 215
- The Hill Equation and Cooperativity in Protein–Ligand Interactions 219
- The Benesi–Hildebrand Plot 221
- How are Heat Changes Related to Enthalpy? 223
- Using the Helical Structure of Peptides and the Complexation Power of Crowns to Create an Artificial Transmembrane Channel 226
- Preorganization and the Salt Bridge 229
- A Clear Case of Entropy Driven Electrostatic Complexation 229
- Salt Bridges Evaluated by Non-Biological Systems 230
- Does Hydrogen Bonding *Really* Play a Role in DNA Strand Recognition? 233
- Calixarenes—Important Building Blocks for Molecular Recognition and Supramolecular Chemistry 238
- Aromatics at Biological Binding Sites 239
- Combining the Cation– π Effect and Crown Ethers 240
- A Thermodynamic Cycle to Determine the Strength of a Polar– π Interaction 242
- Molecular Mechanics/Modeling and Molecular Recognition 243
- Biotin/Avidin: A Molecular Recognition/Self-Assembly Tool from Nature 249
- Taming Cyclobutadiene—A Remarkable Use of Supramolecular Chemistry 251

CHAPTER 5

- Using a pH Indicator to Sense Species Other Than the Hydronium Ion 264
- Realistic Titrations in Water 265
- An Extremely Acidic Medium is Formed During Photo-Initiated Cationic Polymerization in Photolithography 269
- Super Acids Used to Activate Hydrocarbons 270
- The Intrinsic Acidity Increase of a Carbon Acid by Coordination of BF_3 276
- Direct Observation of Cytosine Protonation During Triple Helix Formation 287
- A Shift of the Acidity of an N-H Bond in Water Due to the Proximity of an Ammonium or Metal Cation 288
- The Notion of Superelectrophiles Produced by Super Acids 289

CHAPTER 6

- Stereoisomerism and Connectivity 300
- Total Synthesis of an Antibiotic with a Staggering Number of Stereocenters 303
- The Descriptors for the Amino Acids Can Lead to Confusion 307
- Chiral Shift Reagents 308
- C_2 Ligands in Asymmetric Synthesis 313
- Enzymatic Reactions, Molecular Imprints, and Enantiotopic Discrimination 320
- Biological Knots—DNA and Proteins 325
- Polypropylene Structure and the Mass of the Universe 331
- Controlling Polymer Tacticity—The Metallocenes 332
- CD Used to Distinguish α -Helices from β -Sheets 335
- Creating Chiral Phosphates for Use as Mechanistic Probes 335
- A Molecular Helix Created from Highly Twisted Building Blocks 338

CHAPTER 7

- Single-Molecule Kinetics 360
- Using the Arrhenius Equation to Determine Differences in Activation Parameters for Two Competing Pathways 370
- Curvature in an Eyring Plot is Used as Evidence for an Enzyme Conformational Change in the Catalysis of the Cleavage of the Co-C Bond of Vitamin B_{12} 371
- Where TST May be Insufficient 374
- The Transition States for $\text{S}_{\text{N}}1$ Reactions 377
- Comparing Reactivity to Selectivity in Free Radical Halogenation 378
- Using the Curtin-Hammett Principle to Predict the Stereochemistry of an Addition Reaction 379
- Applying the Principle of Microscopic Reversibility to Phosphate Ester Chemistry 380
- Kinetic vs. Thermodynamic Enolates 382
- Molecularity vs. Mechanism. Cyclization Reactions and Effective Molarity 384
- First Order Kinetics: Delineating Between a Unimolecular and a Bimolecular Reaction of Cyclopentyne and Dienes 386
- The Observation of Second Order Kinetics to Support a Multistep Displacement Mechanism for a Vitamin Analog 387

- Pseudo-First Order Kinetics: Revisiting the Cyclopentyne Example 388
- Zero Order Kinetics 393
- An Organometallic Example of Using the SSA to Delineate Mechanisms 395
- Saturation Kinetics That We Take for Granted— $\text{S}_{\text{N}}1$ Reactions 397
- Prior Equilibrium in an $\text{S}_{\text{N}}1$ Reaction 398
- Femtochemistry: Direct Characterization of Transition States, Part I 400
- “Seeing” Transition States, Part II: The Role of Computation 401
- The Use of Pulse Radiolysis to Measure the pK_{a} s of Protonated Ketyl Anions 402
- Discovery of the Marcus Inverted Region 406
- Using a More O’Ferrall-Jencks Plot in Catalysis 410

CHAPTER 8

- The Use of Primary Kinetic Isotope Effects to Probe the Mechanism of Aliphatic Hydroxylation by Iron(III) Porphyrins 425
- An Example of Changes in the Isotope Effect with Varying Reaction Free Energies 428
- The Use of an Inverse Isotope Effect to Delineate an Enzyme Mechanism 431
- An Ingenious Method for Measuring Very Small Isotope Effects 432
- An Example of Tunneling in a Common Synthetic Organic Reaction 436
- Using Fractionation Factors to Characterize Very Strong Hydrogen Bonds 439
- The Use of a Proton Inventory to Explore the Mechanism of Ribonuclease Catalysis 440
- A Substituent Effect Study to Decipher the Reason for the High Stability of Collagen 444
- Using a Hammett Plot to Explore the Behavior of a Catalytic Antibody 450
- An Example of a Change in Mechanism in a Solvolysis Reaction Studied Using σ^+ 452
- A Swain-Lupton Correlation for Tungsten-Bipyridine-Catalyzed Allylic Alkylation 453
- Using Taft Parameters to Understand the Structures of Cobaloximes; Vitamin B_{12} Mimics 455
- The Use of the Schleyer Method to Determine the Extent of Nucleophilic Assistance in the Solvolysis of Arylvinyl Tosylates 459
- The Use of Swain-Scott Parameters to Determine the Mechanism of Some Acetal Substitution Reactions 462
- ATP Hydrolysis—How β_{LG} and β_{Nuc} Values Have Given Insight into Transition State Structures 465
- How Can Some Groups be Both Good Nucleophiles and Good Leaving Groups? 466
- An Example of an Unexpected Product 472
- Designing a Method to Divert the Intermediate 473
- Trapping a Phosphorane Legitimizes Its Existence 474
- Checking for a Common Intermediate in Rhodium-Catalyzed Allylic Alkylations 475
- Pyranoside Hydrolysis by Lysozyme 476
- Using Isotopic Scrambling to Distinguish Exocyclic vs. Endocyclic Cleavage Pathways for a Pyranoside 478

- Determination of 1,4-Biradical Lifetimes Using
a Radical Clock 480
- The Identification of Intermediates from a Catalytic Cycle
Needs to be Interpreted with Care 481

CHAPTER 9

- The Application of Figure 9.4 to Enzymes 494
- High Proximity Leads to the Isolation of a Tetrahedral
Intermediate 498
- The Notion of "Near Attack Conformations" 499
- Toward an Artificial Acetylcholinesterase 501
- Metal and Hydrogen Bonding Promoted Hydrolysis
of 2',3'-cAMP 502
- Nucleophilic Catalysis of Electrophilic Reactions 503
- Organocatalysis 505
- Lysozyme 506
- A Model for General-Acid-General-Base Catalysis 514
- Anomalous Brønsted Values 519
- Artificial Enzymes: Cyclodextrins Lead the Way 530

CHAPTER 10

- Cyclic Forms of Saccharides and Concerted Proton
Transfers 545
- Squalene to Lanosterol 550
- Mechanisms of Asymmetric Epoxidation Reactions 558
- Nature's Hydride Reducing Agent 566
- The Captodative Effect 573
- Stereoelectronics in an Acyl Transfer Model 579
- The Swern Oxidation 580
- Gas Phase Eliminations 588
- Using the Curtin-Hammett Principle 593
- Aconitase—An Enzyme that Catalyzes Dehydration
and Rehydration 595
- Enzymatic Acyl Transfers I: The Catalytic Triad 604
- Enzymatic Acyl Transfers II: Zn(II) Catalysis 605
- Enzyme Mimics for Acyl Transfers 606
- Peptide Synthesis—Optimizing Acyl Transfer 606

CHAPTER 11

- Enolate Aggregation 631
- Control of Stereochemistry in Enolate Reactions 636
- Gas Phase S_N2 Reactions—A Stark Difference in Mechanism
from Solution 641
- A Potential Kinetic Quandary 642
- Contact Ion Pairs vs. Solvent-Separated Ion Pairs 647
- An Enzymatic S_N2 Reaction: Haloalkane
Dehydrogenase 649
- The Meaning of β_{LG} Values 651
- Carbocation Rearrangements in Rings 658
- Anchimeric Assistance in War 660
- Further Examples of Hypervalent Carbon 666
- Brominations Using *N*-Bromosuccinimide 673
- An Enzymatic Analog to the Benzilic Acid Rearrangement:
Acetohydroxy-Acid Isomeroreductase 677
- Femtochemistry and Singlet Biradicals 693

CHAPTER 12

- Bonding Models 709
- Electrophilic Aliphatic Substitutions (S_E2 and S_E1) 715
- C-H Activation, Part I 722

- C-H Activation, Part II 723
- The Sandmeyer Reaction 726
- Olefin Slippage During Nucleophilic Addition to
Alkenes 737
- Pd(0) Coupling Reactions in Organic Synthesis 742
- Stereocontrol at Every Step in Asymmetric Allylic
Alkylations 745
- Cyclic Rings Possessing Over 100,000 Carbons! 747

CHAPTER 13

- Monodisperse Materials Prepared Biosynthetically 756
- An Analysis of Dispersity and Molecular Weight 757
- A Melting Analysis 759
- Protein Folding Modeled by a Two-State Polymer
Phase Transition 762
- Dendrimers, Fractals, Neurons, and Trees 769
- Lyotropic Liquid Crystals: From Soap Scum to
Biological Membranes 774
- Organic Surfaces: Self-Assembling Monolayers and
Langmuir-Blodgett Films 778
- Free-Radical Living Polymerizations 787
- Lycra/Spandex 790
- Radical Copolymerization—Not as Random
as You Might Think 792
- PMMA—One Polymer with a Remarkable Range
of Uses 793
- Living Polymers for Better Running Shoes 795
- Using ^{13}C NMR Spectroscopy to Evaluate Polymer
Stereochemistry 797

CHAPTER 14

- The Hydrogen Atom 811
- Methane—Molecular Orbitals or Discrete Single
Bonds with sp^3 Hybrids? 827
- Koopmans' Theorem—A Connection Between *Ab Initio*
Calculations and Experiment 828
- A Matrix Approach to Setting Up the LCAO Method 832
- Through-Bond Coupling and Spin Preferences 861
- Cyclobutadiene at the Two-Electron Level of Theory 862

CHAPTER 15

- Symmetry Does Matter 887
- Allowed Organometallic [2+2] Cycloadditions 895
- Semi-Empirical vs. *Ab Initio* Treatments of Pericyclic
Transition States 900
- Electrocyclization in Cancer Therapeutics 910
- Fluxional Molecules 913
- A Remarkable Substituent Effect: The Oxy-Cope
Rearrangement 921
- A Biological Claisen Rearrangement—The Chorismate
Mutase Reaction 922
- Hydrophobic Effects in Pericyclic Reactions 923
- Pericyclic Reactions of Radical Cations 925

CHAPTER 16

- Excited State Wavefunctions 937
- Physical Properties of Excited States 944
- The Sensitivity of Fluorescence—Good News and
Bad News 946
- GFP, Part I: Nature's Fluorophore 947

HIGHLIGHTS

Isosbestic Points—Hallmarks of One-to-One Stoichiometric Conversions 949
The “Free Rotor” or “Loose Bolt” Effect on Quantum Yields 953
Single-Molecule FRET 961
Trans-Cyclohexene? 967
Retinal and Rhodopsin—The Photochemistry of Vision 968
Photochromism 969
UV Damage of DNA—A [2+2] Photoreaction 971
Using Photochemistry to Generate Reactive Intermediates: Strategies Fast and Slow 983

Photoaffinity Labeling—A Powerful Tool for Chemical Biology 984
Light Sticks 987
GFP, Part II: Aequorin 989
Photodynamic Therapy 991

CHAPTER 17

Solitons in Polyacetylene 1015
Scanning Probe Microscopy 1040
Soft Lithography 1041