

Modern Physical Organic Chemistry

Modern Physical Organic Chemistry

Eric V. Anslyn

UNIVERSITY OF TEXAS, AUSTIN

Dennis A. Dougherty

CALIFORNIA INSTITUTE OF TECHNOLOGY



University Science Books
Sausalito, California

University Science Books
www.uscibooks.com

Production Manager: *Christine Taylor*
Manuscript Editor: *John Murdzek*
Design: *Robert Ishi*
Illustrator: *Lineworks*
Compositor: *Wilsted & Taylor Publishing Services*
Printer & Binder: *Edwards Brothers, Inc.*

This book is printed on acid-free paper.

Copyright © 2005 by University Science Books

Reproduction or translation of any part of this work beyond that permitted by Section 107 or 108 of the 1976 United States Copyright Act without the permission of the copyright owner is unlawful. Requests for permission or further information should be addressed to the Permissions Department, University Science Books.

Library of Congress Cataloging-in-Publication Data

Anslyn, Eric V., 1960–
Modern physical organic chemistry / Eric V. Anslyn, Dennis A. Dougherty.
p. cm.
Includes bibliographical references and index.
ISBN 1–891389–31–9 (alk. paper)
1. Chemistry, Physical organic. I. Dougherty, Dennis A., 1952– II. Title.

QD476.A57 2004
547'.13—dc22

2004049617

Printed in the United States of America

09 08 07 06 05 10 9 8 7 6 5 4 3 2 1

Abbreviated Contents

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
Intent and Purpose 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
17. Electronic Organic Materials 1001
-

- APPENDIX 1. Conversion Factors and Other Useful Data 0000
2. Electrostatic Potential Surfaces for Representative Organic Molecules 0000
3. Group Orbitals of Common Functional Groups:
Representative Examples Using Simple Molecules 0000
4. The Organic Structures of Biology 0000
5. Pushing Electrons 0000
6. Reaction Mechanism Nomenclature 0000

List of Highlights 00
Preface 00
Acknowledgments 00
A Note to the Instructor 00

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
 Hybridization Effects
 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	160
<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
<i>ii. Electronegativity Effects</i>	172
<i>iii. Resonance Assisted Hydrogen Bonds</i>	173
<i>iv. Polarization Enhanced Hydrogen Bonds</i>	174
<i>v. 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 340

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 Kinetics 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—Brønsted 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	548
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 538
- 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 $\text{S}_{\text{RN}}1$ 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** 62811.1.1 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 63711.5.1 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 64611.5.9 Structure–Function Correlations
with the Nucleophile 64811.5.10 Structure–Function Correlations
with the Leaving Group 65111.5.11 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 65911.5.14 S_N1 Reactions Involving Non-Classical
Carbocations 661*Norbornyl Cation* 662*Cyclopropyl Carbinyl Carbocation* 66411.5.15 Summary of Carbocation Stabilization
in Various Reactions 66711.5.16 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 67011.6.5 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 67111.7.4 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 67411.8.1 Electron Pushing for the
Pinacol Rearrangement 67511.8.2 Electron Pushing in the Benzilic Acid
Rearrangement 67511.8.3 Migratory Aptitudes in the Pinacol
Rearrangement 67511.8.4 Stereoelectronic and Stereochemical Considerations
in the Pinacol Rearrangement 67611.8.5 A Few Experimental Observations for the Benzilic
Acid Rearrangement 678**11.9 Migrations to Electrophilic Heteroatoms** 67811.9.1 Electron Pushing in the Beckmann
Rearrangement 67811.9.2 Electron Pushing for the Hofmann
Rearrangement 67811.9.3 Electron Pushing for the Schmidt
Rearrangement 68011.9.4 Electron Pushing for the Baeyer–Villiger
Oxidation 68011.9.5 A Few Experimental Observations for the
Beckmann Rearrangement 68011.9.6 A Few Experimental Observations for the
Schmidt Rearrangement 68111.9.7 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 685
- 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
 - Electron Counting* 706
 - Oxidation State* 708
 - d Electron Count* 708
 - Ambiguities* 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 *d* Orbital Splitting Patterns 712
- 12.1.7 Stabilizing Reactive Ligands 713

12.2 Common Organometallic Reactions 714

- 12.2.1 Ligand Exchange Reactions 714
 - Reaction Types* 714
 - Kinetics* 716
 - Structure–Function Relationships with the Metal* 716
 - Structure–Function Relationships with the Ligand* 716
 - Substitutions of Other Ligands* 717
- 12.2.2 Oxidative Addition 717
 - Stereochemistry of the Metal Complex* 718
 - Kinetics* 718
 - Stereochemistry of the R Group* 719
 - Structure–Function Relationship for the R Group* 720
 - Structure–Function Relationships for the Ligands* 720
 - Oxidative Addition at sp^2 Centers* 721
 - Summary of the Mechanisms for Oxidative Addition* 721
- 12.2.3 Reductive Elimination 724
 - Structure–Function Relationship for the R Group and the Ligands* 724
 - Stereochemistry at the Metal Center* 725
 - Other Mechanisms* 725
 - Summary of the Mechanisms for Reductive Elimination* 726

12.2.4 α - and β -Eliminations 727

- General Trends for α - and β -Eliminations* 727
- Kinetics* 728
- Stereochemistry of β -Hydride Elimination* 729
- 12.2.5 Migratory Insertions 729
 - Kinetics* 730
 - Studies to Decipher the Mechanism of Migratory Insertion Involving CO* 730
 - Other Stereochemical Considerations* 732
- 12.2.6 Electrophilic Addition to Ligands 733
 - Reaction Types* 733
 - Common Mechanisms Deduced From Stereochemical Analyses* 734
- 12.2.7 Nucleophilic Addition to Ligands 734
 - Reaction Types* 735
 - Stereochemical and Regiochemical Analyses* 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
 - Number Average and Weight Average Molecular Weights— M_n and M_w* 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
Wave Functions* 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
 - 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

Diabatic 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

Making Highly Strained Ring Systems 973*Breaking Aromaticity* 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 N₂: Azo Compounds, Diazo Compounds, Diazirines, and Azides 981
Azoalkanes (1,2-Diazenes) 981
Diazo Compounds and Diazirines 982
Azides 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

List of Highlights

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 Superlectrophiles 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 371
- 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 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 00

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 459
- 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

CHAPTER 12

Bonding Models 709
Electrophilic Aliphatic Substitutions (S_E2 and S_E1) 715
C–H Activation, Part 1 722
C–H Activation, Part 2 723

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
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

The twentieth century saw the birth of physical organic chemistry—the study of the interrelationships between structure and reactivity in organic molecules—and the discipline matured to a brilliant and vibrant field. Some would argue that the last century also saw the near death of the field. Undeniably, physical organic chemistry has had some difficult times. There is a perception by some that chemists thoroughly understand organic reactivity and that there are no *important* problems left. This view ignores the fact that while the rigorous treatment of structure and reactivity in organic structures that is the field's hallmark continues, physical organic chemistry has expanded to encompass other disciplines.

In our opinion, physical organic chemistry is alive and well in the early twenty-first century. New life has been breathed into the field because it has embraced newer chemical disciplines, such as bioorganic, organometallic, materials, and supramolecular chemistries. Bioorganic chemistry is, to a considerable extent, physical organic chemistry on proteins, nucleic acids, oligosaccharides, and other biomolecules. Organometallic chemistry traces its intellectual roots directly to physical organic chemistry, and the tools and conceptual framework of physical organic chemistry continue to permeate the field. Similarly, studies of polymers and other materials challenge chemists with problems that benefit directly from the techniques of physical organic chemistry. Finally, advances in supramolecular chemistry result from a deeper understanding of the physical organic chemistry of intermolecular interactions. These newer disciplines have given physical organic chemists fertile ground in which to study the interrelationships of structure and reactivity. Yet, even while these new fields have been developing, remarkable advances in our understanding of basic organic chemical reactivity have continued to appear, exploiting classical physical organic tools and developing newer experimental and computational techniques. These new techniques have allowed the investigation of reaction mechanisms with amazing time resolution, the direct characterization of classically elusive molecules such as cyclobutadiene, and highly detailed and accurate computational evaluation of problems in reactivity. Importantly, the techniques of physical organic chemistry and the intellectual approach to problems embodied by the discipline remain as relevant as ever to organic chemistry. Therefore, a course in physical organic chemistry will be essential for students for the foreseeable future.

This book is meant to capture the state of the art of physical organic chemistry in the early twenty-first century, and, within the best of our ability, to present material that will remain relevant as the field evolves in the future. For some time it has been true that if a student opens a physical organic chemistry textbook to a random page, the odds are good that he or she will see very interesting chemistry, but chemistry that does not represent an area of significant current research activity. We seek to rectify that situation with this text. A student must know the fundamentals, such as the essence of structure and bonding in organic molecules, the nature of the basic reactive intermediates, and organic reaction mechanisms. However, students should also have an appreciation of the current issues and challenges in the field, so that when they inspect the modern literature they will have the necessary background to read and understand current research efforts. Therefore, while treating the fundamentals, we have wherever possible chosen examples and highlights from modern research areas. Further, we have incorporated chapters focused upon several of the modern disciplines that benefit from a physical organic approach. From our perspective, a protein, electrically conductive polymer, or organometallic complex should be as relevant to a course in physical organic chemistry as are small rings, annulenes, or nonclassical ions.

We recognize that this is a delicate balancing act. A course in physical organic chemistry

cannot also be a course in bioorganic or materials chemistry. However, a physical organic chemistry class should not be a history course, either. We envision this text as appropriate for many different kinds of courses, depending on which topics the instructor chooses to emphasize. In addition, we hope the book will be the first source a researcher approaches when confronted with a new term or concept in the primary literature, and that the text will provide a valuable introduction to the topic. Ultimately, we hope to have produced a text that will provide the fundamental principles and techniques of physical organic chemistry, while also instilling a sense of excitement about the varied research areas impacted by this brilliant and vibrant field.

Eric V. Anslyn

Norman Hackerman Professor
University Distinguished Teaching Professor
University of Texas, Austin

Dennis A. Dougherty

George Grant Hoag Professor of Chemistry
California Institute of Technology

Acknowledgments

Many individuals have contributed to the creation of this textbook in various ways, including offering moral support, contributing artwork, and providing extensive feedback on some or all of the text. We especially thank the following for numerous and varied contributions: Bob Bergman, Wes Borden, Akin Davulcu, Francois Diederich, Samuel Gellman, Robert Hanes, Ken Houk, Anthony Kirby, John Lavigne, Charles Lieber, Shawn McCleskey, Kurt Mislow, Jeffrey Moore, Charles Perrin, Larry Scott, John Sherman, Timothy Snowden, Suzanne Tobey, Nick Turro, Grant Willson, and Sheryl Wiskur.

A very special thanks goes to Michael Sponsler, who wrote the accompanying Solutions Manual for the exercises given in each chapter. He read each chapter in detail, and made numerous valuable suggestions and contributions.

Producing this text has been extraordinarily complicated, and we thank: Bob Ishi for an inspired design; Tom Webster for dedicated efforts on the artwork; Christine Taylor for orchestrating the entire process and prodding when appropriate; John Murdzek for insightful editing; Jane Ellis for stepping up at the right times; and Bruce Armbruster for enthusiastic support throughout the project.

Finally, it takes a pair of very understanding wives to put up with a six-year writing process. We thank Roxanna Anslyn and Ellen Dougherty for their remarkable patience and endless support.

A Note to the Instructor

Our intent has been to produce a textbook that could be covered in a one-year course in physical organic chemistry. The order of chapters reflects what we feel is a sensible order of material for a one-year course, although other sequences would also be quite viable. In addition, we recognize that at many institutions only one semester, or one to two quarters, is devoted to this topic. In these cases, the instructor will need to pick and choose among the chapters and even sections within chapters. There are many possible variations, and each instructor will likely have a different preferred sequence, but we make a few suggestions here.

In our experience, covering Chapters 1–2, 5–8, selected portions of 9–11, and then 14–16, creates a course that is doable in one extremely fast-moving semester. Alternatively, if organic reaction mechanisms are covered in another class, dropping Chapters 10 and 11 from this order makes a very manageable one-semester course. Either alternative gives a fairly classical approach to the field, but instills the excitement of modern research areas through our use of “highlights” (see below). We have designed Chapters 9, 10, 11, 12, and 15 for an exhaustive, one-semester course on thermal chemical reaction mechanisms. In any sequence, mixing in Chapters 3, 4, 12, 13, and 17 whenever possible, based upon the interest and expertise of the instructor, should enhance the course considerably. A course that emphasizes structure and theory more than reactivity could involve Chapters 1–6, 13, 14, and 17 (presumably not in that order). Finally, several opportunities for special topics courses or parts of courses are available: computational chemistry, Chapters 2 and 14; supramolecular chemistry, Chapters 3, 4, and parts of 6; materials chemistry, Chapters 13, 17, and perhaps parts of 4; theoretical organic chemistry, Chapters 1, 14–17; and so on.

One of the ways we bring modern topics to the forefront in this book is through providing two kinds of highlights: “Going Deeper” and “Connections.” *These are integral parts of the textbook that the students should not skip when reading the chapters* (it is probably important to tell the students this). The Going Deeper highlights often expand upon an area, or point out what we feel is a particularly interesting sidelight on the topic at hand. The Connections highlights are used to tie the topic at hand to a modern discipline, or to show how the topic being discussed can be put into practice. We also note that many of the highlights make excellent starting points for a five- to ten-page paper for the student to write.

As noted in the Preface, one goal of this text is to serve as a reference when a student or professor is reading the primary literature and comes across unfamiliar terms, such as “dendrimer” or “photoresist.” However, given the breadth of topics addressed, we fully recognize that at some points the book reads like a “topics” book, without a truly in-depth analysis of a given subject. Further, many topics in a more classical physical organic text have been given less coverage herein. Therefore, many instructors may want to consult the primary literature and go into more detail on selected topics of special interest to them. We believe we have given enough references at the end of each chapter to enable the instructor to expand any topic. Given the remarkable literature-searching capabilities now available to most students, we have chosen to emphasize review articles in the references, rather than exhaustively citing the primary literature.

We view this book as a “living” text, since we know that physical organic chemistry will continue to evolve and extend into new disciplines as chemistry tackles new and varied problems. We intend to keep the text current by adding new highlights as appropriate, and perhaps additional chapters as new fields come to benefit from physical organic chemistry. We would appreciate instructors sending us suggestions for future topics to cover, along with particularly informative examples we can use as highlights. We cannot promise that

they will all be incorporated, but this literature will help us to keep a broad perspective on where the field is moving.

Given the magnitude and scope of this project, we are sure that some unclear presentations, misrepresentations, and even outright errors have crept in. We welcome corrections and comments on these issues from our colleagues around the world. Many difficult choices had to be made over the six years it took to create this text, and no doubt the selection of topics is biased by our own perceptions and interests. We apologize in advance to any of our colleagues who feel their work is not properly represented, and again welcome suggestions.

We wish you the best of luck in using this textbook.

Modern Physical Organic Chemistry
