

Table of Contents

Chapter 1: Free-Radical Reactions in Carbohydrate Chemistry	1
I. The Emergence of Free-Radical Reactions	1
II. The Role of Free-Radical Reactions in Carbohydrate Synthesis.....	2
III. Chain Reaction: A Natural Pathway for Free-Radicals	2
IV. References.....	2
Chapter 2: Chain Reactions	9
I. Definitions	9
A. A Free-Radical Reaction	9
B. Free-Radical Chain Reactions	10
II. Basic Stages of a Radical Chain Reaction	10
A. The Initiation Phase	10
1. Thermal Initiation.....	10
2. Thermal Initiators.....	12
3. Photochemical Initiation	15
4. Photochemical Initiators.....	16
5. Chemical Initiation	18
B. The Propagation Phase	19
1. General Characteristics.	19
2. Examples of Propagation Sequences.....	20
3. Rate Constants and Reaction Rates	23
4. Solvent Effects	24
C. The Termination Phase.....	25
III. Reaction Efficiency	27
IV. Summary.....	29
V. References.....	30
Chapter 3: Nonchain Reactions	33
I. Introduction	33
II. Transition-Metal-Generated Radicals	34
A. Inner-Sphere and Outer-Sphere Electron Transfer	34
B. Oxidative Electron Transfer	34
1. Carbon–Cobalt Bond Homolysis	35
2. Carbon–Mercury Bond Homolysis	39

3.	Manganese(III) Acetate [Mn(OAc) ₃] Reactions	40
4.	Ammonium Cerium(IV) Nitrate [(NH ₄) ₂ Ce(NO ₃) ₆] Reactions	41
C.	Reductive Electron Transfer	42
1.	Bis(cyclopentadienyl)titanium(III) Chloride [Cp ₂ TiCl] Reactions	42
2.	Samarium(II) [SmI ₂] Iodide Reactions	45
3.	Reactions of Chromium(II) Reagents	48
III.	Photochemically Generated Radicals	48
A.	Hydrogen-Atom Abstraction	49
1.	Deciding Whether a Reaction Has a Chain or Nonchain Mechanism	50
2.	Interpretation of Quantum Yields	50
B.	Carbon–Carbon Bond Homolysis	52
C.	Oxygen–Iodine Bond Homolysis	53
D.	A Comment About Photochemical Reactions	53
IV.	Thermally Generated Radicals	54
V.	Summary	54
VI.	References	55
Chapter 4: Elementary Reactions.....		58
I.	Introduction	58
II.	Atom Abstraction.....	61
A.	Halogen-Atom Abstraction	61
B.	Hydrogen-Atom Abstraction	61
III.	Group Abstraction	63
IV.	Radical Addition	64
A.	Intermolecular Reaction	64
1.	Addition to a Multiple Bond	64
2.	Addition That Forms a Radical With a Hypervalent Atom	66
B.	Intramolecular Reaction (Radical Cyclization)	67
V.	Fragmentation Reactions	67
A.	Homolytic β-Fragmentation	67
B.	Heterolytic β-Fragmentation	69
C.	α-Fragmentation	69
D.	Bond Homolysis	70
VI.	Electron Transfer	72
A.	Reactions of Carbohydrate Radicals	72
B.	Formation of Carbohydrate Radicals.....	73
VII.	Radical Combination	75

VIII. Radical Disproportionation.....	76
IX. Group Migration	78
X. Summary.....	79
XI. References.....	79
Chapter 5: Sequential Reactions	82
I. Introduction.....	82
II. Advantages and Disadvantages of Sequential Reactions	83
III. Two-Step Sequential Reactions	85
A. Cyclization-Cyclization	85
B. Cyclization-Addition	85
C. Cyclization-Rearrangement	86
D. Fragmentation-Fragmentation	87
E. Addition-Fragmentation	87
F. Cyclization-Fragmentation	87
G. Fragmentation-Addition	89
H. Hydrogen-Atom Abstraction--Cyclization.....	89
I. Hydrogen-Atom Abstraction--Addition	90
IV. Three-Step Sequential Reactions.....	90
V. Related Reactions	91
A. Parallel Reactions	93
B. Sequences of Reactions.....	93
C. Group Migration Reactions	94
VI. Summary.....	95
VII. References.....	95
Chapter 6 Radical Structure	99
I. Introduction	99
II. Structural Formulas	100
III. Radical-Center Configuration.....	101
A. Planar and Pyramidal Structures	101
B. Configurational Determination from α - ¹³ C Hyperfine Coupling Constants	102
C. Theoretical Explanation of Observed Configurations	103
1. Frontier-Orbital Interactions	103
2. p_c/p_o Orbital Interaction	103
IV. Radical Conformation.....	104
A. Pyranos-1-yl Radicals.....	105
1. Experimentally Observed Conformations	105

2.	Radical Conformation Explained by Frontier-Orbital Interactions.....	106
3.	Radical Conformation Determined From Ab Initio Molecular-Orbital Calculations	113
4.	Influence of Steric Effects on Radical Conformation	114
5.	Effect of Hydrogen Bonding on Radical Conformation	115
B.	Pyranos-5-yl Radicals.....	117
C.	Furanosyl Radicals	118
D.	Radicals in “Locked” Conformations.....	119
V.	Quasi-Anomeric Radical Stabilization	120
VI.	Summary.....	120
VII.	References.....	121
Chapter 7 Radical Philicity		124
I.	Introduction.....	125
A.	The Evans-Polanyi Relation	125
B.	Nucleophilic and Electrophilic Radicals	125
II.	Bond Polarities, Bond Energies, and Rate Constants for Hydrogen-Atom Abstraction Reactions	126
III.	Determining Radical Philicity	128
A.	Atom Electronegativity	129
B.	Cation and Anion Stability	129
C.	Principal Component Analysis	129
D.	Ab Initio Molecular Orbital Calculations.....	130
E.	Comparing Procedures for Assigning Radical Philicity.....	130
IV.	Explaining Radical Philicity	130
A.	Valence Bond Theory.....	130
1.	Nucleophilic Radicals	131
2.	Electrophilic Radicals	132
3.	Ambiphilic Radicals	133
B.	Molecular Orbital Theory: Frontier Orbital Interactions.....	134
1.	Nucleophilic Radicals	135
2.	Electrophilic Radicals	137
C.	Balancing Polar and Enthalpy Effects	138
V.	Examples of Radical Philicity in Reactions of Carbohydrates	139
A.	Hydrogen-Atom Abstraction	139
B.	Radical Addition.....	140
C.	Polarity-Reversal Catalysis	142

VI.	Rate Constants for Hydrogen-Atom Abstraction by Carbohydrate Radicals	142
A.	Extrapolating Results from Model Radicals.....	142
B.	A Limitation on Extrapolating Alkyl Radical Reactivity to Carbohydrate Radicals	143
C.	An Explanation for Unsuccessful Extrapolation: Loss of Transition-State Stabilization	144
VII.	Summary.....	145
VIII.	References.....	145
Chapter 8: Radical Reactivity: Reaction Rate Constants.....		148
I.	Introduction.....	148
II.	Absolute and Relative Rate Constants.....	149
III.	Generation of Carbon-Centered Radicals	150
A.	Atom-Transfer Reactions	150
B.	Group-Transfer Reactions	152
C.	Fragmentation Reactions	155
D.	Electron-Transfer Reactions	156
IV.	Transformation of Carbon-Centered Radicals.....	158
A.	Hydrogen-Atom Abstraction	158
B.	Iodine-Atom Abstraction.....	159
C.	Radical Cyclization	162
D.	Radical Addition.....	165
E.	Group Migration.....	167
F.	Hydrogen-Atom Abstraction by Pyranos-1-yl Radicals.....	171
V.	Chain Collapse.....	173
A.	Collapse Due to Chain Termination	173
B.	Collapse Due to Chain Shift.....	174
VI.	Summary.....	175
VII.	References.....	175
Chapter 9 Chemoselectivity		178
I.	Introduction.....	178
II.	Formation of Carbon-Centered Radicals	178
A.	Atom Abstraction	179
1.	Halogen Atoms.....	179
2.	Hydrogen Atoms	180
B.	Group Abstraction	181
1.	The Effect on Chemoselectivity of a Reversible First Step	181

2. <i>O</i> -Thiocarbonyl Compounds.....	182
C. Radical Addition.....	183
1. Reversible Reaction.....	183
2. Preventing Reversible Addition and Polymerization	183
D. Unreactive Groups and Atoms	187
III. Carbon-Centered Radicals.....	187
IV. Summary.....	189
V. References.....	189
Chapter 10 Regioselectivity	191
I. Introduction.....	192
A. Definitions of Regiospecific and Regioselective Reactions.....	192
B. Regioselectivity in Radical Reactions of Carbohydrates	192
II. Intermolecular Addition Reactions.....	193
A. General Reaction Equation.....	193
B. Reaction at the Less-Substituted Carbon Atom.....	194
C. Transition State Structure	195
D. Factors Controlling Regioselectivity	195
1. Bond Strengths	196
2. Steric Effects	196
3. Polar Effects	198
4. Frontier-Orbital Interactions	201
5. Adduct-Radical Stabilization.....	202
III. Intramolecular Addition (Cyclization) Reactions.....	204
A. Five- and Six-Membered Rings.....	204
1. Factors Determining Ring Size	204
2. Transition-State Structure	205
3. Altering Normal Regioselectivity	206
B. Three- and Four-Membered Rings	210
C. Larger Rings	211
D. A Terminology for Describing Cyclization Reactions.....	213
IV. β -Fragmentation Reactions.....	213
A. Ring-Opening Reactions	213
1. Oxygen-Centered Radicals.....	213
2. Carbon-Centered Radicals.....	213
B. Radical Expulsion.....	216
V. Site-Selective Reactions	218
A. Atom Replacement Reactions	218

1. Intermolecular Hydrogen-Atom Abstraction	218
2. Intramolecular Hydrogen-Atom Abstraction	224
3. Halogen-Atom Abstraction Reactions.....	227
B. Group Replacement Reactions	228
1. <i>O</i> -Thiocarbonyl Compounds.....	228
2. Isonitriles.....	229
VI. Summary.....	230
VII. References.....	231
Chapter 11 Stereoselectivity	234
I. Introduction.....	235
A. Definitions	235
B. Factors Affecting Stereoselectivity	235
II. Minimizing Steric Interaction: The Least Hindered Pathway	236
A. Shielding of Radical Centers	237
1. Groups on Opposite Faces of a Cyclic Radical	238
2. Groups on the Same Face of a Cyclic Radical	239
3. Fused and Bridged Ring Systems.....	239
4. Groups not Adjacent to the Radical Center.....	241
B. Steric Effects in Reactant Molecules.....	241
1. Radical Addition Reactions.....	241
2. Hydrogen-Atom Abstraction Reactions	242
C. Torsional Effects	244
III. Maximizing Transition-State Stabilization by Orbital Interaction:	
The Kinetic Anomeric Effect	246
A. Radical Formation	246
B. Radical Reaction.....	248
1. The Role of Radical Conformation	248
2. Effect of Temperature on Stereoselectivity.....	265
IV. Maximizing Transition-State Stability During Ring Formation.....	266
A. Five-Membered Ring Formation	267
1. Chair-like Transition State	267
2. Boat-like Transition State.....	268
3. Factors Affecting Transition-State Stability	270
B. Six-Membered Ring Formation.....	272
V. Stereoselectivity in Synthesis	273
A. β -Glycoside Synthesis	273
B. Reaction at Remote Radical Centers (Carbohydrates as Chiral Auxiliaries)....	275

1. Substrate-Controlled Reactions.....	275
2. Complex-Controlled Reactions.....	276
C. Enantioselective Reactions.....	277
VI. Summary.....	279
VII. References	280
Index	283