Contents

Chapter 1 Free Energy Relationships 1

1.1 Mechanism and Structure 3
1.1.1 Interconversion of States – Reaction and Encounter Complexes 4
1.2 Universal Measure of Polarity 5
1.3 Classes of Free Energy Relationship 6
1.4 Origin of Free Energy Relationships 7
1.5 Similarity and the Leffler α-Parameter 10
1.6 Bonding in Transition Structures 12
1.7 Further Reading 13
1.8 References 15

Chapter 2 The Equations 17

2.1 The Hammett Equation (Class II) 17
2.2 The Taft Equation (Class I) 19
2.2.1 Steric Demand at Reaction Centres 23
2.3 Inductive Polar Constants σ_I 24
2.3.1 Choice of σ Value 26
2.4 The Brønsted Equation (Class I) 27
2.5 The Extended Brønsted Equation (Class II) 30
2.6 Equations for Nucleophilic Substitution 32
2.6.1 The Swain–Scott Equation (Class II) 32
2.6.2 The Ritchie Equation (Class II) 34
2.7 Solvent Equations 35
2.7.1 The Grunwald–Winstein Equation (Class II) 36
2.7.2 The Kosower Z and Reichardt E_T Scales (Class II) 39
2.7.3 The Hansch Equation (Class II) 40
2.8 Other Standard Processes 41
2.8.1 Spectroscopic Transitions 41
2.8.2 Acidity and Basicity Functions 42
2.8.3 Molar Refractivity 43
2.9 Further Reading 44
2.10 Problems 45
2.11 References 51

Chapter 3 Effective Charge **55**

3.1 Equilibria 55
3.1.1 Measuring Effective Charge in Equilibria 58
3.1.2 A Group Transfer of Biological Interest 63
3.1.3 Additivity of Effective Charge in Reactants and Products 65
3.2 Rates 65
3.2.1 Additivity of Effective Charge in Transition Structures 67
3.2.2 Effective Charge Maps for More Than Two Bond Changes 67
3.3 Further Reading 69
3.4 Problems 69
3.5 References 73

Chapter 4 Multiple Pathways to the Reaction Centre **75**

4.1 Strength of the Interaction 75
4.2 Additivity of Inductive Substituent Effects 78
4.3 Multiple Interactions 79
4.3.1 The Jaffé Relationship 80
4.3.2 Resonance Effects 83
4.3.3 The Yukawa–Tsuno Equation 86
4.3.4 Other Two-parameter Equations 88
4.3.4.1 The Dewar–Grisdale Equation 88
4.3.4.2 The Swain–Lupton Equation 89
4.3.4.3 The Edwards Equation for Nucleophilic Aliphatic Substitution 92
4.3.4.4 The Mayr Equation 93
4.4 Multi-parameter Solvent Equations 94
4.4.1 Extension of the Grunwald–Winstein Equation 94
4.4.2 The Swain Equation 94
4.4.3 Extended Hansch Equations 96
4.4.4 Solvent Equations Based on Macroscopic Quantities 96
4.5 Further Reading 97
4.6 Problems 97
4.7 References 103

Chapter 5 Coupling Between Bonds in Transition Structures of Displacement Reactions 107

5.1 Cross and Self Interaction Between Two or More Substituent Effects 107
5.1.1 Hammond and Cordes–Thornton Coefficients 109
5.2 Shapes of Energy Surfaces from Coupling Coefficients 110
5.2.1 General Acid-catalysed Addition of Thiol Anions to Acetaldehyde 115
5.2.2 Reaction of Amines with Phosphate Monoesters 116
5.2.3 Elimination Reactions of 2-Arylethylquinuclidinium Ions 117
5.3 Magnitude and Sign of Cordes–Thornton Coefficients 118
5.4 Identity Reactions 119
5.5 Further Reading 123
5.6 Problems 124
5.7 References 126

Chapter 6 Anomalies, Special Cases and Non-linearity 129

6.1 Free Energy Relationships are not Always Linear 129
6.1.1 Marcus Curvature 131
6.2 The Reactivity–Selectivity Postulate 135
6.3 Bordwell's Anomaly 138
6.4 Microscopic Medium Effects and Deviant Points 140
6.5 Statistical Treatment of Brønsted Plots 144
6.6 Are Free Energy Relationships Statistical Artifacts? 145
6.7 The *Ortho* Effect 146
6.8 Temperature Effects 147
6.9 Further Reading 148
6.10 Problems 149
6.11 References 154

Chapter 7 Applications **158**

7.1 Diagnosis of Mechanism 158
7.1.1 Mechanism by Comparison 158
7.1.2 Effective Charge Distribution of the Transition Structure 160
7.1.2.1 Effective Charge Maps and Conservation of Effective Charge 160
7.1.2.2 Charge and Bond Order Balance 161
7.2 Demonstration of Intermediates 163
7.2.1 Curvature in pH-profiles 166
7.3 Demonstration of Parallel Reactions 166
7.3.1 Concave Curvature in pH-profiles 168
7.4 Demonstration of Concerted Mechanisms 169
7.4.1 Technique of Quasi-symmetrical Reactions 169
7.4.2 Criteria for Observing the Break 173
7.4.2.1 Effective Charge Map for a Putative Stepwise Process 173
7.5 Calculation of Physico-Chemical Constants 174
7.5.1 Dissociation and Equilibrium Constants 174
7.5.2 Rate Constants 179
7.5.3 Partition Coefficients and Other Constitutive Molecular Properties 180
7.6 Resolution of Kinetically Equivalent Mechanisms 181
7.6.1 General Base versus Nucleophilic Reaction 181
7.6.2 General Acid Catalysis Versus Specific Acid–General Base Catalysis 182
7.7 Some Biological Applications 184
7.8 Further Reading 187
7.9 Problems 189
7.10 References 196

Appendix 1 Equations and the More O'Ferrall–Jencks Diagram **201**

A1.1 Summary of Equations 201
A1.1.1 The Morse Equation 201
A1.1.2 Derivation of Equation 7 (Chapter 1) 202

A1.1.3 The Effect of ΔE_o on the Leffler α Parameter 202
A1.1.4 Fitting Data to Theoretical Equations 202
A1.1.4.1 Linear Equation 203
A1.1.4.2 Bilinear Equation 203
A1.1.4.3 Global Analysis of Two Linear Equations 204
A1.1.4.4 Binomial Equation 205
A1.1.4.5 Cross-correlation 206
A1.1.5 Effective Charge from Hammett Slopes 206
A1.2 The More O'Ferrall–Jencks Diagram 207

Appendix 2 Answers to Problems 210

Appendix 3 Tables of Structure Parameters 258

Appendix 4 Some Linear Free Energy Equations 282

Subject Index 290