Brief Contents

Preface xiii
Reviewers xv
About the Authors xvii

CHAPTER 1 **Organic Mechanisms in Biological Chemistry** 1
CHAPTER 2 **Biomolecules and Their Chirality** 51
CHAPTER 3 **Lipids and Their Metabolism** 109
CHAPTER 4 **Carbohydrates and Their Metabolism** 183
CHAPTER 5 **Amino Acid Metabolism** 245
CHAPTER 6 **Nucleotide Metabolism** 333
CHAPTER 7 **Biosynthesis of Some Natural Products** 367
CHAPTER 8 **A Summary of Biological Transformations** 427
CHAPTER 9 **Chemical Principles of Enzymatic Catalysis** 449

Appendixes

A. Using PyMOL to Explore Enzyme Active Sites 467
B. Using the Kyoto Encyclopedia of Genes and Genomes (KEGG) Database 481
C. Answers to End-of-Chapter Problems 489
D. Abbreviations Used in This Book 533

Index 537

Contents

Preface xiii

Reviewers xv

About the Authors xvii

1 Organic Mechanisms in Biological Chemistry 1

1.1 Functional Groups in Biological Chemistry 3

1.2 Acids and Bases; Electrophiles and Nucleophiles 6

Brønsted–Lowry Acids and Bases 6

Lewis Acids and Bases 10

Electrophiles and Nucleophiles 11

1.3 Mechanisms: Electrophilic Alkene Additions 12

1.4 Mechanisms: Electrophilic Aromatic Substitutions 15

1.5 Mechanisms: Nucleophilic Aliphatic Substitutions 16

1.6 Mechanisms: Nucleophilic Carbonyl Additions 19

Alcohol Formation 22

Imine (Schiff Base) Formation 23

Acetal Formation 25

Conjugate (1,4) Nucleophilic Additions 27

1.7 Mechanisms: Nucleophilic Acyl Substitutions 29

1.8 Mechanisms: Carbonyl Condensations 31

1.9 Mechanisms: Eliminations 36

1.10 Mechanisms: Radical Reactions 38

1.11 Mechanisms: Pericyclic Reactions 40

1.12 Oxidations and Reductions 41

1.13 A Comparison of Biological Reactions and Laboratory Reactions 43

Problems 45

2 Biomolecules and Their Chirality 51

2.1 Chirality and Biological Chemistry 53

Enantiomers 53

Diastereomers, Epimers, and Meso Compounds 55

Prochirality 58

2.2 Biomolecules: Lipids 60

Waxes 60

Phospholipids 61
Triacylglycerols 62
Terpenoids, Steroids, and Eicosanoids 64

2.3 Biomolecules: Carbohydrates 67
Carbohydrate Stereochemistry 68
Monosaccharide Anomers 70
Disaccharides and Polysaccharides 73
Deoxy Sugars and Amino Sugars 74

2.4 Biomolecules: Amino Acids, Peptides, and Proteins 76
Amino Acids 76
Peptides and Proteins 81

2.5 Biomolecules: Nucleic Acids 84
DNA: Deoxyribonucleic Acid 87
RNA: Ribonucleic Acid 89

2.6 Biomolecules: Enzymes and Coenzymes 90
Enzymes 90
Coenzymes 93

2.7 High-Energy Compounds and Coupled Reactions 96

Problems 99

3 Lipids and Their Metabolism 109

3.1 Digestion and Transport of Triacylglycerols 110
Triacylglycerol Hydrolysis 111
A Brief Note about Visualizing Enzyme Structures 113
Triacylglycerol Resynthesis 115

3.2 Triacylglycerol Catabolism: The Fate of Glycerol 118

3.3 Triacylglycerol Catabolism: Fatty-Acid Oxidation 122

3.4 Fatty-Acid Biosynthesis 131

3.5 Terpenoid Biosynthesis 141
The Mevalonate (Mev) Pathway to Isopentenyl Diphosphate 142
The 2*C*-Methyl-D-Erithritol 4-Phosphate (MEP) Pathway to Isopentenyl Diphosphate 147
Conversion of Isopentenyl Diphosphate to Terpenoids 157

3.6 Steroid Biosynthesis 162
Conversion of Farnesyl Diphosphate to Squalene 163
Conversion of Squalene to Lanosterol 166

References 172

Problems 176

4 Carbohydrates and Their Metabolism 183

4.1 Digestion and Hydrolysis of Complex Carbohydrates 185

4.2 Glucose Catabolism: Glycolysis 188

4.3 Transformations of Pyruvate 202

Conversion of Pyruvate to Lactate 202

Conversion of Pyruvate to Ethanol 202

Conversion of Pyruvate to Acetyl-CoA 204

4.4 The Citric Acid Cycle 208

4.5 Glucose Biosynthesis: Gluconeogenesis 215

4.6 The Pentose Phosphate Pathway 224

4.7 Photosynthesis: The Reductive Pentose Phosphate (Calvin) Cycle 232

References 238

Problems 241

5 Amino Acid Metabolism 245

5.1 Deamination of Amino Acids 247

Transamination of Amino Acids 247

Oxidative Deamination of Glutamate 252

5.2 The Urea Cycle 253

5.3 Catabolism of Amino Acid Carbon Chains 257

Alanine, Serine, Glycine, Cysteine, and Threonine 259

A Brief Note about PLP Reactions 267

Asparagine and Aspartate 268

Glutamine, Glutamate, Arginine, Histidine, and Proline 269

Valine, Isoleucine, and Leucine 272

Methionine 276

Lysine 280

Phenylalanine, Tyrosine, and Tryptophan 283

A Brief Note about Oxidation States in Iron Complexes 297

5.4 Biosynthesis of Nonessential Amino Acids 298

Alanine, Aspartate, Glutamate, Asparagine, Glutamine, Arginine, and Proline 300

Serine, Cysteine, and Glycine 302

5.5 Biosynthesis of Essential Amino Acids 303

Lysine, Methionine, and Threonine 303

Isoleucine, Valine, and Leucine 310

Tryptophan, Phenylalanine, and Tyrosine 313

Histidine 321

References 323
Problems 328

6 Nucleotide Metabolism 333

6.1 Nucleotide Catabolism: Pyrimidines 336
Cytidine 336
Uridine 336
Thymidine 340

6.2 Nucleotide Catabolism: Purines 340
Adenosine 340
Guanosine 342

6.3 Biosynthesis of Pyrimidine Ribonucleotides 342
Uridine Monophosphate 342
Cytidine Triphosphate 347

6.4 Biosynthesis of Purine Ribonucleotides 348
Inosine Monophosphate 348
Adenosine Monophosphate and Guanosine Monophosphate 353

6.5 Biosynthesis of Deoxyribonucleotides 355
Deoxyadenosine, Deoxyguanosine, Deoxycytidine, and Deoxyuridine Diphosphates 355
Thymidine Monophosphate 357

References 360
Problems 362

7 Biosynthesis of Some Natural Products 367

7.1 Biosynthesis of Nonribosomal Polypeptides: Penicillins and Cephalosporins 371
Penicillins 374
Cephalosporins 379

7.2 Biosynthesis of Alkaloids: Morphine 381

7.3 Biosynthesis of Fatty-Acid-Derived Substances: Prostaglandins and Other Eicosanoids 393

7.4 Biosynthesis of Polyketides: Erythromycin 397

7.5 Biosynthesis of Enzyme Cofactors: Heme 408

References 418
Problems 420

8 A Summary of Biological Transformations 427

8.1 Hydrolyses, Esterifications, Thioesterifications, and Amidations 428
8.2 Carbonyl Condensations 430
8.3 Carboxylations and Decarboxylations 432
8.4 Aminations and Deaminations 436
8.5 One-Carbon Transfers 436
8.6 Rearrangements 438
8.7 Isomerizations and Epimerizations 439
8.8 Oxidations and Reductions of Carbonyl Compounds 441
8.9 Hydroxylations and Other Oxidations via Metal Complexes 443

9 Chemical Principles of Enzymatic Catalysis 449

9.1 Introduction to Enzyme Kinetics 450
9.2 Enzymatic Catalysis by Transition-State Stabilization 452
Mechanism of Fumarase 453
Mechanism of Mandelate Racemase 455
9.3 Enzymatic Catalysis by Changing the Reaction Mechanism 457
Mechanism of Pyruvate Decarboxylase 457
Mechanism of Alanine Racemase 460
9.4 Catalysis via Reactive High-Energy Intermediates 463
9.5 Looking Forward 465

Appendixes

A. Using PyMOL to Explore Enzyme Active Sites 467
B. Using the Kyoto Encyclopedia of Genes and Genomes (KEGG) Database 481
C. Answers to End-of-Chapter Problems 489
D. Abbreviations Used in This Book 533

Index 537