

S.V. Bhat
B.A. Nagasampagi
M. Sivakumar

Chemistry of Natural Products



Narosa

Contents

<i>Preface</i>	v
<i>General Introduction</i>	1
CHAPTER 1: STEROIDS	15
1.1 Introduction	15
1.2 Nomenclature and Stereochemistry	15
1.2.A Nomenclature	15
1.2.B Configuration of Substituents	19
1.2.C Absolute Configuration in the Ring	19
1.2.D Configuration in the Side Chain	20
1.2.E Conformation	20
1.3 Biogenesis	21
1.4 Physical Methods of Characterization	24
1.4.A Melting Points	24
1.4.B Solubility	24
1.4.C Ultraviolet Spectra	24
1.4.D Infrared Spectra	26
1.4.E Nuclear Magnetic Resonance Spectra	27
1.4.F Mass Spectra	27
1.4.G Optical Rotation and Rotatory Dispersion	28
1.5 Sterols	28
1.5.A Classification of Sterols	28
1.5.B Colour Reactions	29
1.6 Cholesterol	29
1.6.A Occurrence	29
1.6.B Isolation	30
1.6.C Biogenesis	30
1.6.D Clinical Significance	30
1.6.E Commercial Significance	30
1.6.F Chemical Properties	30
1.6.G Structure Elucidation	36
1.6.H Total Synthesis of Cholesterol	41

- 1.7 Other C-27 Sterols 44
- 1.8 C-28 Sterols-Ergosterol 44
 - 1.8.A Occurrence 45
 - 1.8.B Biogenesis 45
 - 1.8.C Commercial Significance 45
 - 1.8.D Chemical Properties 45
- 1.9 C-29 Sterols 46
 - 1.9A Occurrence 47
 - 1.9B Commercial Significance 47
- 1.10 C-30 Sterols 47
 - 1.10.A Occurrence 47
 - 1.10.B Biogenesis 47
 - 1.10.C Chemical Properties 47
- 1.11 Vitamin D Group 49
 - 1.11.A Cholecalciferol 50
 - 1.11.B Occurrence 50
 - 1.11.C Colour Reactions 50
 - 1.11.D Synthesis 50
- 1.12 Bile Acids 50
 - 1.12.A Biogenesis 51
 - 1.12.B Clinical Significance 52
 - 1.12.C Colour Reactions 52
 - 1.12.D Reactions of Bile Acids 54
- 1.13 Bile Alcohols 57
- 1.14 Sex Hormones 58
- 1.15 Estrogens 58
 - 1.15.A Occurrence 59
 - 1.15.B Isolation 59
 - 1.15.C Biogenesis 59
 - 1.15.D Clinical Significance of Estrogens 59
 - 1.15.E Colour Reactions 60
- 1.16 Estrone 61
 - 1.16.A Chemical Properties 61
 - 1.16.B Partial Synthesis of Estrone 66
 - 1.16.C Total Synthesis 67
- 1.17 Estradiol 70
 - 1.17.A 17- β -Estradiol 70
 - 1.17.B 17- α -Estradiol 70
- 1.18 Estriol 71
 - 1.18.A Chemical Properties 71
 - 1.18.B Partial Synthesis of Estriol from Estrone 71

- 1.19 Equine Estrogens 72
 - 1.19.A Equilenin 72
 - 1.19.B Equilin 72
 - 1.19.C Partial Synthesis of Equilin from 19-nortestosterone Acetate 73
- 1.20 Synthetic Estrogen Analogues 73
 - 1.20.A Steroidal Analogue (17- α - ethynylestradiol) 73
 - 1.20.B Nonsteroidal Analogues 74
- 1.21 Gestogens- Progesterone 74
 - 1.21.A Occurrence 75
 - 1.21.B Isolation 75
 - 1.21.C Biogenesis 75
 - 1.21.D Clinical Significance 76
 - 1.21.E Commercial Significance 76
 - 1.21.F Colour Reactions for Pregnenediol (Metabolite of Progesterone) 76
 - 1.21.G Hydroxyprogesterone caproate 76
 - 1.21.H Chemical Properties 77
 - 1.21.I Partial Synthesis of Progesterone 78
 - 1.21.J Synthetic Analogues of Progesterone 80
- 1.22 Oral Contraceptives 81
- 1.23 Commercial Significance of 16-Dehydropregnenolone Acetate (16-DPA, 1.259), 82
- 1.24 Androgens 82
 - 1.24.A Occurrence 83
 - 1.24.B Isolation 83
 - 1.24.C Biogenesis 83
 - 1.24.D Clinical Significance 84
 - 1.24.E Colour Reactions 84
- 1.25 Testosterone 85
 - 1.25.A Physical Properties of Testosterone Heptanoate 85
 - 1.25.B Chemical Properties 85
 - 1.25.C. Partial Synthesis 87
- 1.26 Dehydroepiandrosterone 89
 - 1.26.A Partial Synthesis 89
- 1.27 Androsterone 90
 - 1.27.A Partial Synthesis 90
- 1.28 Anabolic Steroids 91
- 1.29 Adrenocortical Hormones 91
 - 1.29.A Isolation 92
 - 1.29.B Biogenesis 92
 - 1.29.C Clinical Significance 93
 - 1.29.D Determination of Adrenocortical Hormones and Metabolites 93

- 1.30 Cortisone 93
 - 1.30.A Chemical Properties 94
 - 1.30.B Total Synthesis 96
- 1.31 Cortisol 98
 - 1.31.A Chemical Properties 98
- 1.32 Aldosterone 99
 - 1.32.A Chemical Properties 100
 - 1.32.B Total Synthesis 101
- 1.33 Steroids from Plants 102
- 1.34 Cardiac Glycosides 103
- 1.35 Cardenolides 103
 - 1.35.A Isolation 104
 - 1.35.B Colour Reactions 104
 - 1.35.C Important Reaction of the Lactone Side Chain 105
- 1.36 Bufadienolides 106
 - 1.36.A Isolation 107
 - 1.36.B Differentiation of Bufadienolides from Cardenolides 108
- 1.37 Sapogenins 108
 - 1.37.A Spirostans 108
 - 1.37.B Diosgenin 109
 - 1.37.C Occurrence 110
 - 1.37.D Isolation 110
 - 1.37.E Commercial Significance 110
 - 1.37.F Identification of Spirostans 110
 - 1.37.G Chemical Properties of the Side Chain 110
- 1.38 Steroidal Alkaloids 110
 - 1.38.A Azasteroid with Nuclear Nitrogen 111
 - 1.38.B Azasteroids with Side Chain Nitrogen 111
- 1.39. Steroids from Insects 114

Exercises

Further Reading

CHAPTER 2: TERPENOIDS

115

- 2.1 Introduction 115
- 2.2 Classification 115
- 2.3 Biosynthesis 116
- 2.4 Occurrence 120
 - 2.4.A Mono- and Sesquiterpenoids 120
 - 2.4.B Diterpenoids 120

- 2.4.C Sesterterpenoids 124
- 2.4.D Triterpenoids 124
- 2.4.E Tetraterpenoids 125
- 2.5 Isolation and Separation Techniques 125
 - 2.5.A Essential Oils 125
 - 2.5.B Terpenoids 126
- 2.6 Chromatographic Methods 127
 - 2.6.A Gas Liquid Chromatography 127
 - 2.6.B Thin-Layer Chromatography 127
 - 2.6.C Column Chromatography 129
 - 2.6.D High Performance Liquid Chromatography 130
- 2.7 Structure Elucidation 131
 - 2.7.A Historical Background 131
 - 2.7.B Physical Methods 131
 - 2.7.C Spectral Methods for Structure Determination 132
 - 2.7.D Chemical Methods 134
 - 2.7.E Diels-Alder Reaction 137
 - 2.7.F Addition Reactions 137
 - 2.7.G Determination of Functional Groups Containing Oxygen 138
 - 2.7.H Determination of Number of Rings in a Molecule 139
- 2.8 Monoterpenoids 139
 - 2.8.A Myrcene 140
 - 2.8.B Geraniol 141
 - 2.8.C Citral 143
 - 2.8.D α -Pinene 144
 - 2.8.E Camphor-d 145
 - 2.8.F Menthol 149
 - 2.8.G Carvone-d 151
 - 2.8.H Stereochemistry of Monoterpenoids 154
- 2.9 Sesquiterpenoids 155
 - 2.9.A Farnesol 155
 - 2.9.B Zingiberene- α 157
 - 2.9.C β -Caryophyllene 159
 - 2.9.D Cadinenes 163
 - 2.9.E Eudesmol 167
 - 2.9.F α -Cuparenone and β -Cuparenone 169
 - 2.9.G Longifolene 170
 - 2.9.H Copaene 173
 - 2.9.I Costunolide 175
 - 2.9.J Santonin 176
 - 2.9.K Synthesis of β -vetivone 181
- 2.10 Diterpenoids 182
 - 2.10.A Hardwickic Acid 183
 - 2.10.B Abietic Acid 185

- 2.10.C Synthesis of Taxol 189
- 2.10.D Forskolin 193
- 2.11. Triterpenoids 196
 - 2.11.A β -Amyrin 196
- 2.12 Carotenes 200
 - 2.12.A β -Carotene 201

Exercises 204

Further Reading 205

CHAPTER 3 FATTY LIPIDS AND PROSTAGLANDINS

206

Section A: Fatty Lipids 206

- 3.1 Introduction 206
- 3.2 Occurrence of Triacylglycerols 206
- 3.3 Fatty Acids 207
- 3.4 Waxes 210
- 3.5 Identification and Extraction of Lipids 210
- 3.6 Reactions of Fatty Acids 211
- 3.7 Commercial uses of Oils, Fats and Waxes 212
- 3.8 Soaps and Micelle 212
- 3.9 Biosynthesis of Fatty Acids and Triglycerides 213
- 3.10 Membrane Lipids 213
 - 3.10.A Glycerophospholipids 215
 - 3.10.B Sphingophospholipids 217
 - 3.10.C Cerebrosides 218
 - 3.10.D Gangliosides 218

- 3.11 Plasma Membranes 219
- 3.12 Large Ring Lactones 220

Section B: Prostaglandins 221

- 3.13 Introduction 221
- 3.14 Occurrence 221
- 3.15 Isolation 222
- 3.16 Biogenesis and Metabolism 222
 - 3.16.A Biogenesis 222
 - 3.16.B Metabolism 222

- 3.17 Clinical Significance 223
- 3.18 Nomenclature and Stereochemistry 224
 - 3.18.A Nomenclature 224
 - 3.18.B Configuration in the Ring and Side Chain 225
 - 3.18.C Absolute Configuration 227
- 3.19 Structure Elucidation 227
 - 3.19.A Physical Methods of Characterization 227
 - 3.19.B Chemical Degradation Studies 227
- 3.20 Total Synthesis 229
 - 3.20.A Synthesis of PGE₁ 229
 - 3.20.B Enantioselective Synthesis 229
 - 3.20.C Total synthesis of PGE₃ 235

Exercises 235

Further Reading 236

CHAPTER 4 ALKALOIDS

237

- 4.1 Introduction 237
- 4.2 Occurrence 238
- 4.3 Function of Alkaloids in Plants 241
- 4.4 Classification 241
- 4.5 Nomenclature 242
- 4.6 Pharmaceutical Applications 242
- 4.7 Isolation 244
- 4.8 Qualitative Tests and General Properties 244
- 4.9 General Methods of Structure Determination 245
 - 4.9.A Chemical Methods 245
 - 4.9.B Degradation of Alkaloids 249
 - 4.9.C Physical Methods 252
- 4.10 Benzylisoquinoline and Related Alkaloids 252
 - 4.10.A Papaverine 253
 - 4.10.B Biosynthesis of Isoquinoline Alkaloids 255
 - 4.10.C Emetine 258
- 4.11 Morphine 258
 - 4.11.A Structure Elucidation of Morphine 260
 - 4.11.B Total Synthesis of Morphine 261
 - 4.11.C Biogenesis of Morphine 263

- 4.12 Quinoline Alkaloids 264
 - 4.12.A Quinine 264
 - 4.12.B Structure Elucidation of Quinine 265
 - 4.12.C Synthesis of Quinine 265
- 4.13 Indole Alkaloids 268
 - 4.13.A Catharanthus or Vinca (Vincristine and Vinblastine) 269
 - 4.13.B Ajmaline 269
- 4.14 Reserpine 269
 - 4.14.A Structure Elucidation of Reserpine 271
 - 4.14.B Synthesis of Reserpine 273
- 4.15 Ergot Alkaloids 276
 - 4.15.A Applications of Ergot Alkaloids 277
 - 4.15.B Ergotamine 277
 - 4.15.C Synthesis of Lysergic Acid 279
 - 4.15.D Synthesis of Peptide Portion of Ergotamine 280
 - 4.15.E Ergovine Maleate 280
- 4.16 Strychnine 281
 - 4.16.A Structure Elucidation of Strychnine 282
 - 4.16.B Synthesis of Strychnine 283
- 4.17 The Diterpene Alkaloids 284
 - 4.17.A Atisine 285
 - 4.17.B Structure Elucidation of Atisine 285
 - 4.17.C Stereochemistry of Atisine 286
 - 4.17.D Synthesis of dl-atisine 288
- 4.18 Pyridine Alkaloids of Tobacco 291
 - 4.18.A Nicotine 291
 - 4.18.B Isolation of Nicotine 292
 - 4.18.C Structure of Nicotine 292
 - 4.18.D Synthesis of Nicotine 292
- 4.19. Tropane Alkaloids 292
 - 4.19.A Atropine 293
 - 4.19.B Synthesis of Atropine 295
 - 4.19.C Cocaine 296
 - 4.19.D Structure Elucidation of Cocaine 296
 - 4.19.E Synthesis of Cocaine 298
 - 4.19.F Pomegranate Alkaloids 299
 - 4.19.G Biogenesis of Tropane Alkaloids 299
- 4.20 Alkaloid Amines (Pseudoalkaloids) 301
 - 4.20.A Ephedrine 301
 - 4.20.B Structure of Ephedrine 301
 - 4.20.C Stereochemistry of Ephedrine 302
 - 4.20.D. Total Synthesis of Ephedrine 303

- 4.21 Adrenaline (Epinephrine) 304
 - 4.21.A Extraction of Adrenaline 304
 - 4.21.B Structure Elucidation of Adrenaline 304
 - 4.21.C Synthesis of Adrenaline 305
 - 4.21.D Biosynthesis of Adrenaline 306
- 4.22 Piperine 306
 - 4.22.A Structure of Piperine 307
 - 4.22.B Synthesis of Piperine 307
- 4.23 Colchicine 308
 - 4.23.A Structure of Colchicine 309
 - 4.23.B Synthesis of Colchicine 310
- 4.24 Purine Bases 311
 - 4.24.A Caffeine 312
 - 4.24.B Isolation of Caffeine 312
 - 4.24.C Structure Elucidation of Caffeine 313
 - 4.24.D Synthesis of Caffeine 314

Exercises 315

Further Reading 316

CHAPTER 5: AMINO ACIDS, PROTEINS AND BIOCONVERSIONS

317

- 5.1 Introduction 317
- 5.2 α -Amino Acids 318
 - 5.2.A Ionization of α -Amino Acids 320
 - 5.2.B General Properties of α -Amino Acids 321
 - 5.2.C Biological Functions of Amino Acids 323
 - 5.2.D Commercial uses of α -Amino Acids 324
- 5.3 Laboratory Synthesis of α -Amino Acids 325
 - 5.3.A The Strecker's Synthesis 325
 - 5.3.B Nucleophilic Displacement of α -halo Acids 325
 - 5.3.C Modified Gabriel Synthesis 325
 - 5.3.D Malonic Ester Degradation 326
 - 5.3.E The Azalactone Synthesis (Erlenmeyer Synthesis, 1893) 326
 - 5.3.F Synthesis of Methionine 326
 - 5.3.G Hydrogenation with Modified Wilkinson Catalyst 327
- 5.4 Industrial Production of Amino Acids 327
 - 5.4.A Protein Hydrolysis 328
 - 5.4.B Chemical Synthesis 328
 - 5.4.C Microbial Production 328
- 5.5 Reactions of α -Amino Acids 330
 - 5.5.A Reactions due to the NH_2 Group 330
 - 5.5.B Reactions due to Carboxyl Group 331

- 5.6 Polypeptides 333
 - 5.6.A Hydrolysis of Polypeptide and Estimation of Amino Acids 333
 - 5.6.B Amino Acids Sequence of Polypeptide Chain 335
- 5.7 Functions of Peptides 335
 - 5.7.A Insulin and Glucagon 335
 - 5.7.B Mechanism of Hormone Action 337
- 5.8 Proteins 338
 - 5.8.A Colour Reactions of Proteins 339
 - 5.8.B Protein Modifications 339
- 5.9 Primary Structure of Peptides 339
 - 5.9.A N-Terminal Amino Acid Determination 340
 - 5.9.B Carboxy Terminal Amino Acid Determination 341
 - 5.9.C Partial Hydrolysis of Peptides 341
 - 5.9.D Cyclic Peptides and Proteins of Subunits 343
 - 5.9.E Isoelectric Points of Proteins 343
- 5.10 Secondary, Tertiary and Quaternary Structures of Proteins 343
 - 5.10.A Secondary Interactions 343
 - 5.10.B Secondary Structure of Peptide 344
 - 5.10.C Tertiary Structure 347
 - 5.10.D Quaternary Structure 348
- 5.11 Enzymes 348
 - 5.11.A Enzyme Classification 350
 - 5.11.B Rate Enhancement and Stereospecificity 351
 - 5.11.C Enzyme Kinetics 352
 - 5.11.D Enzymatic Reaction Mechanism 356
 - 5.11.E Regulation of Metabolism 356
 - 5.11.F Immobilization of Enzymes/Cells 358
 - 5.11.G Industrial Applications of Immobilised Enzymes and Cells 361
 - 5.11.H Commonly used Enzymatic Reactions in Organic Synthesis 362
 - 5.11.I Industrial Production of Enzymes 365
- 5.12 Immunoglobulins and Plasma Proteins 369
 - 5.12.A Immunoglobulins 369
 - 5.12.B Monoclonal Antibodies 370
 - 5.12.C Catalytic Antibodies 370
 - 5.12.D Haemoglobin 370
 - 5.12.E Plasma Proteins 371
 - 5.12.F Enzymes used in Clinical Diagnosis 372
- 5.13 Structural Proteins 372
 - 5.13.A Collagens 372
 - 5.13.B Elastin 378
- 5.14 Laboratory Synthesis of Polypeptides 379
 - 5.14.A Protection and Deprotection 381

- 5.14.B Coupling 384
 - 5.14.C Solid Phase Synthesis 385
 - 5.15 Biosynthesis
 - 5.15.A Biosynthetic Origin of Amino Acids 386
 - 5.15.B Biosynthesis of Polypeptides 386
 - 5.16 Production of Organic Chemicals Through Fermentation 389
 - 5.16.A Ethanol Production 389
 - 5.16.B Organic Acids 391
- Exercises* 392
- Further Reading* 393

CHAPTER 6: NUCLEIC ACIDS**394**

- 6.1 Introduction 394
- 6.2 Basic Structure 394
- 6.3 Deoxyribonucleic Acids (DNA) 398
 - 6.3.A The Primary Structure of DNA 399
 - 6.3.B The Secondary Structure of DNA 399
 - 6.3.C Tertiary Structure of DNA 403
 - 6.3.D Denaturation of DNA 403
- 6.4 Reactions of Nucleic Acid Bases 405
 - 6.4.A Acid Base Behaviour of Nucleic Acids 405
 - 6.4.B Electrophilic Substitution 405
 - 6.4.C Alkylations 407
- 6.5 Mutations 407
 - 6.5.A Ultraviolet Radiation 407
 - 6.5.B Chemical Reagents 408
 - 6.5.C Hydrolytic Reactions 409
- 6.6 DNA Replication 410
- 6.7 Sequence Analysis of DNA 412
- 6.8 Chromosomes and Extra-Chromosomal DNA 413
- 6.9 Genetic Code 415
- 6.10 Ribonucleic Acids 416
 - 6.10.A Transcription 417
 - 6.10.B Ribosomal RNA (rRNA) 418
 - 6.10.C Transfer RNA 419
 - 6.10.D Messenger RNA (mRNA) 421
- 6.11 Translation 423

- 6.12 Other Functions of Nucleotides 425
 - 6.12.A Coenzymes 425
 - 6.12.B High Energy Phosphates 426
 - 6.12.C Energy Capture in Living Organisms 427
 - 6.12.D Energy Charge in Cells 428
 - 6.12.E Medical Applications 429
 - 6.12.F Nucleoside Antibiotics 432
- 6.13 Viruses 432
 - 6.13.A Bacteriophage T₄ 432
 - 6.13.B Human Immunodeficiency Virus 432
- 6.14 Ribozymes (RNA Enzymes) 433
- 6.15 Microbial Production of Nucleosides, Nucleotides and Related Compounds 433
 - 6.15.A Production of 5'-AMP 435
 - 6.15.B Production of Adenosine and Adenine Nucleotides 436
- 6.16 Laboratory Synthesis of Nucleic Acid Bases and Nucleosides 436
 - 6.16.A Synthesis of Nucleic Acid Bases 436
 - 6.16.B Laboratory Synthesis of Nucleosides 442
 - 6.16.C Synthesis of Nucleotides 443
- 6.17 Synthesis of Nucleic Acid Sequences 444
 - 6.17.A Phosphodiester Method 444
 - 6.17.B Phosphotriester Method 445
 - 6.17.C Phosphoramidite Triester Method 445
 - 6.17.D Solid Phase Synthesis of Oligodeoxynucleotides and its Automation 445
- 6.18 Biosynthesis of Bases and Nucleosides 448
 - 6.18.A Biosynthesis of Pyrimidine Ribonucleosides 448
 - 6.18.B Biosynthesis of Deoxyribonucleotides 449
 - 6.18.C Biosynthesis of Purine Nucleotides 450
- 6.19 Recombinant DNA Technology 453
 - 6.19.A DNA Cloning 453
 - 6.19.B Applications of Genetic Engineering 454

Exercises 456

Further Reading 456

CHAPTER 7: CARBOHYDRATES

458

- 7.1 Introduction 458
- 7.2 Classification 458
- 7.3 Nomenclature 459
- 7.4 Monosaccharides 459
 - 7.4.A Aldotrioses 459
 - 7.4.B Aldotetroses 459

- 7.4.C Aldopentoses 461
- 7.4.D Aldohexoses 463
- 7.4.E Ketoses 466
- 7.4.F Ring Structures of Aldohexoses 468
- 7.4.G Structure Determination of Monosaccharides 475
- 7.4.H Oxidation 477
- 7.4.I Reactions of Monosaccharides 482
- 7.4.J Synthesis of Monosaccharides 485
- 7.4.K Glycolysis 488
- 7.4.L Sugar Analysis by Enzymatic Methods 490
- 7.4.M Some Enzymes Involved in Carbohydrates Metabolism 491
- 7.5 Carboxylic Acids 492
- 7.6 Deoxysugars 493
- 7.7 Dihydrosugars 494
- 7.8 Cyclitols 496
- 7.9 Aminosugars 496
- 7.10 Anhydrosugars 497
- 7.11 Disaccharides 498
 - 7.11.A Isolation of Disaccharides 500
 - 7.11.B Structure Elucidation of Disaccharides 500
 - 7.11.C Sucrose 501
 - 7.11.D Synthesis of Sucrose 501
 - 7.11.E Biosynthesis of Glucose, Fructose and Sucrose 502
 - 7.11.F Maltose 504
 - 7.11.G Trehalose 506
- 7.12 Trisaccharides 506
 - 7.12.A Raffinose 506
- 7.13 Polysaccharides 509
 - 7.13.A Isolation of Polysaccharides 510
 - 7.13.B Structure Determination 511
 - 7.13.C Cellulose 511
 - 7.13.D Starch 512
 - 7.13.E Glycogen 514
 - 7.13.F Chitin 514
 - 7.13.G Cleavage of Polysaccharides 515
 - 7.13.H Pectins 517
- 7.14 Mucopolysaccharides 523
 - 7.14.A Hyaluronic Acid 523
 - 7.14.B Other Mucopolysaccharides 524
- 7.15 Proteoglycans 525

- 7.16 Glycoproteins and Glycolipids 525
- 7.17 Separation of Carbohydrates 526
 - 7.17.A Chromatographic Methods 526

Exercises 534

Further Reading 535

CHAPTER 8: INSECT AND PLANT GROWTH REGULATORS

536

Section A: Insect Secretions and Control Agents 536

- 8.1 Hormones of Endocrine Organs 536
 - 8.1.A The Brain Hormones 537
 - 8.1.B The Juvenile Hormones (JH) 537
 - 8.1.C Spectral Characteristics of JHI 538
 - 8.1.D Stereospecific Synthesis 538
 - 8.1.E Insect Control with Juvenile Hormone 539
 - 8.1.F Anti-juvenile Hormones (Prococenes) 540
 - 8.1.G Ecdysones 540
- 8.2 The Exocrine Secretions 540
 - 8.2.A Pheromones 540
 - 8.2.B Pest Control with Pheromones 542
 - 8.2.C Advantages and Disadvantages of Pheromones as Pesticides 542
 - 8.2.D Total Synthesis of Pheromones 543
 - 8.2.E Defensive Secretions 547
- 8.3 Insect Control with Pyrethrins and Synthetic Analogues 548
 - 8.3.A Physical Properties of Pyrethrins I & II 549
 - 8.3.B Synthetic Analogues of Pyrethroids 550
 - 8.3.C Total Synthesis of Pyrethrins-1 551
- 8.4 Insect Control with Antifeedants 552

Section B: Plant Growth Regulators 554

- 8.5 Naturally Occurring Plant Hormones 554
 - 8.5.A Auxins 554
 - 8.5.B Occurrence 554
 - 8.5.C Isolation of Indole Acetic Acid 556
 - 8.5.D Bioassay 557
 - 8.5.E Physiological Properties 557
 - 8.5.F Biosynthesis of IAA 558
- 8.6 Gibberellins (GAs) 559
 - 8.6.A Occurrence 559
 - 8.6.B Isolation 559
 - 8.6.C Bioassay 560
 - 8.6.D Structure Activity Relationships 561

- 8.6E Physical Properties of GA₃ 561
- 8.6F Biosynthesis of GA₃ 561
- 8.6G Synthesis 563
- 8.7 Cytokinins 567
 - 8.7.A Occurrence 567
 - 8.7.B Isolation 568
 - 8.7.C Bioassay 568
 - 8.7.D Physiological Activity 569
 - 8.7.E Structure Activity Relationships 569
 - 8.7.F Biosynthesis of Zeatin 570
- 8.8 Brassinosteroids 570
 - 8.8.A Occurrence 570
 - 8.8.B Isolation 571
 - 8.8.C Bioassay 571
 - 8.8.D Physiological Activity or Plant Responses 571
 - 8.8.E Structure Activity Relationship 571
 - 8.8.F Brassinolide 571
 - 8.8.G Biosynthesis 572
 - 8.8.H Synthesis of Brassinolide 572
- 8.9 Ethylene 576
 - 8.9.A Occurrence 576
 - 8.9.B Physiological Activity or Plant Responses 577
 - 8.9.C Biosynthesis 577
- 8.10 Abscisic Acid (ABA) 577
 - 8.10.A Occurrence 577
 - 8.10.B Isolation 578
 - 8.10.C Bioassay 578
 - 8.10.D Physiological Activity/Plant Responses 578
 - 8.10.E Physical Properties of ABA 581
 - 8.10.F Structure-activity Relationship 581
 - 8.10.G Biosynthesis 581
- 8.11 Jasmonic Acid 581
 - 8.11.A Occurrence 582
 - 8.11.B Isolation 582
 - 8.11.C Thin Layer Chromatography 582
 - 8.11.D Bioassay Methods 582
 - 8.11.E Physiological Properties 582
 - 8.11.F Structure Activity Relationship 582
 - 8.11.G Biosynthesis 582

Exercises 584

Further Reading 584

CHAPTER 9: PHENOLICS, NATURAL DYES AND PIGMENTS**585****Section A: Flavonoids and Coumarins 585**

- 9.1 Classification 585
- 9.2 Biogenesis 587
- 9.3 Occurrence 591
- 9.4 Isolation and Separation 591
- 9.5 Separation Techniques 592
- 9.6 Structure Elucidation 593
 - 9.6.A Spectroscopic Methods 593
- 9.7 Total Synthesis 599
 - 9.7.A Robinson's Synthesis 599
 - 9.7.B Baker-Venkataraman Synthesis 600
 - 9.7.C Kostanecki Synthesis of Flavanone and Flavonol 600
 - 9.7.D Synthesis of Isoflavones 601
- 9.8 Anthocyanidins and Related Phenolic Molecules 602
 - 9.8.A Anthocyanidins and Anthocyanins 602
 - 9.8.B Synthesis of Anthocyanidin 604
 - 9.8.C Leucoanthocyanins and Leucoanthocyanidins 604
- 9.9 Tannins 605
 - 9.9.A Introduction 605
 - 9.9.B Classification 605
 - 9.9.C Hydrolysable Tannins 606
 - 9.9.D Condensed Tannins 608
 - 9.9.E Biosynthesis of Hydrolysable Tannins 610
 - 9.9.F Biological Activities of Tannins 610
- 9.10 Simple Phenolic Compounds 610
 - 9.10.A Naphthoquinones 610
 - 9.10.B Anthraquinones, Anthranols, Anthrones and Dianthrones 611
 - 9.10.C Simple Phenolic Compounds 612
- 9.11 Coumarins 613
 - 9.11.A Classification 613
 - 9.11.B Simple Coumarins and their Derivatives 614
 - 9.11.C Isolation of Coumarins 614
 - 9.11.D Identification 616
 - 9.11.E Chemical Methods of Degradation 617

Section B: Natural Dyes 619

- 9.12 Introduction 619
- 9.13 Classification 619

- 9.14 Flavonoids 620
 - 9.14.A Flavone Derivatives 620
- 9.15 Xanthones 622
- 9.16 Quinonoids 622
- 9.17 Polyenes 627
- 9.18 Isolation of Annatto Dye 629
- 9.19 Organic Nitrogenous Dyes 631
 - 9.19.A Porphyrins 631
 - 9.19.B Structure of Common Porphyrins 631
 - 9.19.C Hydrogenated Porphyrins 632
 - 9.19.D Oxoporphyrins 634
 - 9.19.E Isomerism 634
 - 9.19.F UV Spectral Characteristics of Porphyrins 635
 - 9.19.G Natural Occurrence 638
 - 9.19.H Biosynthesis of Porphyrins 638
- 9.20 Chlorophyll 639
 - 9.20.A Color Reactions of Chlorophyll-a and Chlorophyll-b 641
 - 9.20.B Isolation of Chlorophyll 641
 - 9.20.C Chlorophyll-a 641
 - 9.20.D Structure of Chlorophyll-a 642
- 9.21 Haemoglobin 647
 - 9.21.A Structure of Haemin 649
 - 9.21.B Metabolism of Haemoglobin in Mammals 651
- 9.22 Nitrogen Heterocyclic Organic Dyes 651
 - 9.22.A Pyrimidine 651
 - 9.22.B Alkaloids 651
- 9.23 Insect Dyes 654
- 9.24 Mineral Pigments 654
- 9.25 Application of Dyes 654
 - 9.25.A Direct Dyes 654
 - 9.25.B Mordant Dyes 654
 - 9.25.C Natural Mordants 655
- 9.26 Methods for Preparation of Some Dyes for Commercial Use 655
 - 9.26.A Direct Dyes 655
 - 9.26.B Mordant Dyes 656
 - 9.26.C Vat Dyes 656
- 9.27 Standardization of the Dyes for Improving Colour Fastness 656
 - 9.27.A Factors that Affect the Colour fastness 657
 - 9.27.B Standardization of Colour Fastness 658
 - 9.27.C Co-pigments, and Other Additives 659

9.28 Metallocyanins 660

Exercises 660*Further Reading* 660**CHAPTER 10: MARINE NATURAL PRODUCTS****662**

10.1 Introduction 662

10.2 Terpenoids 662

10.2.A Monoterpenoids 663

10.2.B Sesquiterpenoids 663

10.2.C Sesquiterpene Hydroquinones 667

10.2.D Sesquiterpenoid Isonitriles 668

10.2.E Diterpenoids 668

10.3 Carotenoids 669

10.3.A Carotenoids of Dinoflagellates 670

10.4 Sterols 671

10.4.A C-26-Sterols 671

10.4.B C-27-Norengosterone-type Sterols 674

10.4.C Sterols with Side Chain Modified by Addition of Extra Carbon Atoms 674

10.5 Moulting Hormones (Ecdysones) 674

10.6 Phloroglucinol Derivatives 674

10.7 Halogenated Compounds 676

10.8 Indole Derivatives 678

10.9 Adenochromes 678

10.9.A Isolation of Adenochromes 678

10.9.B Biosynthesis of Adenochromines 680

10.10 Marine Toxins 681

10.10.A Sea Anemone Toxins 681

10.10.B Dinoflagellate Toxins 681

10.11 Bioluminescence 681

10.12 Electrophysiological Studies 682

10.13 Cytokinin Activity of Seaweed Extracts 682

Exercises 682*Further Reading* 683**CHAPTER 11: ANTIBACTERIALS****684**

11.1 Introduction 684

11.2 Historical Developments 685

- 11.3 Bacterial Cell 688
 - 11.3.A Classification of Bacteria 689
 - 11.3.B Bacterial Cell Wall 689
 - 11.3.C Growth Kinetics of Microorganisms 689
- 11.4 Search for New Antibiotics 690
- 11.5 Antibiotic Assay 692
- 11.6 Modes of Antibacterial Action 692
- 11.7 Modes of Resistance 695
- 11.8 Classification of Antibacterials 696
- 11.9 β -Lactams 696
 - 11.9.A Potassium Penicillin 698
 - 11.9.B Antibiotic Assay 698
 - 11.9.C Commercial Production of Penicillin 698
 - 11.9.D Biosynthesis 701
 - 11.9.E Structure and Reactivity of Penicillin 702
 - 11.9.F Synthesis of Penicillin 703
 - 11.9.G Structure Activity Relationship of Penicillin 703
 - 11.9.H Semisynthetic Penicillins 704
 - 11.9.I Cephalosporins 707
 - 11.9.J Mechanism of Action of Penicillin and Cephalosporins 710
 - 11.9.K Clavulanic Acid (Beecham 1976) 710
 - 11.9.L Olivanic Acid 712
 - 11.9.M Thienamycin 712
 - 11.9.N Imipenem, N-Formimidoylthienamycin Monohydrate 714
 - 11.9.O Aztreonam 715
- 11.10 Tetracyclines Structure 715
 - 11.10.A Tetracyclines 716
 - 11.10.B Biosynthesis of Tetracyclines 717
 - 11.10.C Clinical Applications 718
 - 11.10.D Chlorotetracycline Hydrochloride 718
 - 11.10.E Industrial Production 719
- 11.11 Macrolide Antibiotics 719
 - 11.11.A Erythromycin A 720
 - 11.11.B Biosynthesis 721
 - 11.11.C Clarithromycin 722
- 11.12 Polyenes 723
 - 11.12.A Amphotericin B 723
 - 11.12.B Natamycin 723
- 11.13 Rifamycins (Ansamycins) 724
 - 11.13.A Rifampicin 725
 - 11.13.B Semisynthesis of Rifampicin 726

- 11.14. Griseofulvin 727
 - 11.14.A Biosynthesis 728
 - 11.14.B Total Synthesis of Griseofulvin 728
- 11.15 Chloramphenicol (Chloromycetin) 729
 - 11.15.A Synthesis of Chloramphenicol 731
 - 11.15.B Biosynthesis 731
 - 11.15.C Mode of Action 731
 - 11.15.D Thiamphenicol 732
- 11.16 Quinolone Antibacterials 733
 - 11.16.A Nalidixic Acid 733
 - 11.16.B Norfloxacin 734
 - 11.16.C Total Synthesis of Enoxacin 735
 - 11.16.D Total Synthesis of Ciprofloxacin 736
- 11.17 Sulfonamides 736
 - 11.17.A Mechanism of Action of Sulfonamides 737
 - 11.17.B Medical Applications 738
 - 11.17.C Sulfathiazole 738
 - 11.17.D Sulfamethazine 740
 - 11.17.E Sulfadoxine 741
- 11.18 Anthracyclines 742
- 11.19 Aminoglycosides 743
 - 11.19.A Streptomycin 744
 - 11.19.B Biosynthesis of Streptomycin 745
 - 11.19.C Kanamycin and Tobramycin 745
 - 11.19.D Tobramycin 746
 - 11.19.E Gentamycin 747
 - 11.19.F Neomycin 748
- 11.20 Polypeptide Antibiotics 748
 - 11.20.A Polymyxin B 749
- 11.21 Polyether Antibiotics 749
- 11.22 Miscellaneous Antibiotics 750
 - 11.22.A Cyclohexamide 750
 - 11.22.B Novobiocin 751
 - 11.22.C Mitomycin C 751
 - 11.22.D Clindamycin Hydrochloride 752
 - 11.22.E Bleomycin (BLN) 753
 - 11.22.F Glycopeptide Antibiotics (Dalbapetides) 754

Exercises 754

Further Reading 755

CHAPTER 12: VITAMINS

- 12.1 Introduction 756
- 12.2 Vitamin A 756
 - 12.2.A Physical Properties 756
 - 12.2.B Occurrence 757
 - 12.2.C Isolation 757
 - 12.2.D Structure Elucidation 757
 - 12.2.E Biogenesis 758
 - 12.2.F Biochemical Function and Biological Activity 759
 - 12.2.G Detection 759
 - 12.2.H Synthesis 759
 - 12.2.I Other Vitamin A Factors 761
- 12.3 Vitamin D 761
- 12.4 Vitamin E 761
 - 12.4.A Physical Properties 762
 - 12.4.B Occurrence 762
 - 12.4.C Isolation 762
 - 12.4.D Structure Elucidation 762
 - 12.4.E Biogenesis 764
 - 12.4.F Biochemical Function and Clinical Significances 764
 - 12.4.G Detection 764
 - 12.4.H Synthesis 764
- 12.5 Vitamin K 764
 - 12.5.A Physical Properties 765
 - 12.5.B Occurrence 765
 - 12.5.C Isolation 765
 - 12.5.D Structure Elucidation 765
 - 12.5.E Biogenesis 767
 - 12.5.F Biochemical Function and Clinical Significance 767
 - 12.5.G Detection 767
 - 12.5.H Synthesis 767
 - 12.5.I Vitamin K Antagonists 767
- 12.6 Vitamin B Complex 768
- 12.7 Vitamin B₁ 768
 - 12.7.A Physical Properties 768
 - 12.7.B Occurrence 769
 - 12.7.C Isolation 769
 - 12.7.D Structure Elucidation 769
 - 12.7.E Biogenesis 770
 - 12.7.F Clinical Significance 771
 - 12.7.G Detection 771
 - 12.7.H Synthesis of Thiamine 771
 - 12.7.I Cocarboxylase (Thiamine Pyrophosphate) 771

- 12.8 Vitamin B₂ 772
 - 12.8.A Physical Properties 773
 - 12.8.B Occurrence 773
 - 12.8.C Isolation 773
 - 12.8.D Structure Elucidation 773
 - 12.8.E Biogenesis 775
 - 12.8.F Biochemical Function and Biological Activity 775
 - 12.8.G Detection 776
 - 12.8.H Synthesis of Riboflavin 776
- 12.9 Vitamin B₆ (Pyridoxine, Adermine) 777
 - 12.9.A Physical Properties 777
 - 12.9.B Occurrence 777
 - 12.9.C Isolation 777
 - 12.9.D Structure Elucidation 777
 - 12.9.E Biogenesis 779
 - 12.9.F Biochemical Function and Biological Activity 779
 - 12.9.G Detection 780
 - 12.9.H Synthesis 780
- 12.10 Vitamin B₁₂ 781
 - 12.10.A Physical Properties 781
 - 12.10.B Occurrence 783
 - 12.10.C Isolation 783
 - 12.10.D Biochemical Function and Clinical Significance 783
- 12.11 Niacin 783
 - 12.11.A Physical Properties-784
 - 12.11.B Occurrence 784
 - 12.11.C Isolation 784
 - 12.11.D Biogenesis 784
 - 12.11.E Biochemical Function and Clinical Significance 784
 - 12.11.F Detection 785
 - 12.11.G Synthesis 785
- 12.12. Pantothenic Acid 785
 - 12.12.A Occurrence 786
 - 12.12.B Isolation 786
 - 12.12.C Biogenesis 786
 - 12.12.D Biochemical Function and Clinical Significance 786
 - 12.12.E Detection 786
 - 12.12.F Synthesis 786
- 12.13 Folic Acid 787
- 12.14 Vitamin C 788
 - 12.14.A Physical Properties 788
 - 12.14.B Occurrence 788
 - 12.14.C Isolation 788

- 12.14.D Structure Elucidation 789
- 12.14.E Biogenesis 790
- 12.14.F Biochemical Function and Clinical Significance 790
- 12.14.G Estimation 790
- 12.14.H Synthesis 791

- 12.15 Vitamin H 792
 - 12.15.A Occurrence 792
 - 12.15.B Isolation 793
 - 12.15.C Structure Elucidation 793
 - 12.15.D Biochemical Function of Biotin 794
 - 12.15.E Estimation of Biotin 794
 - 12.15.F Synthesis of Biotin 794

Exercises 796

Further Reading 796

Appendix 797

Subject Index 823