

# Contents

<b>1</b>	<b>Introduction: Enzymes, Cofactors/Coenzymes, Primary and Secondary Metabolites, Natural Products and their Functions, Plant Chemical Ecology, Biosynthesis, Metabolic Pathways . . . . .</b>	<b>1</b>
1.1	Nature, Life, Cells, Molecules, Self-Replication . . . . .	1
1.2	Enzymes . . . . .	2
1.2.1	Nature of Enzymes . . . . .	2
1.2.2	Functions of Enzymes . . . . .	3
1.2.3	Enzyme Classification and Nomenclature . . . . .	3
1.3	Cofactors/Coenzymes . . . . .	5
1.4	Metabolism, The Vital Biological Processes, Primary Metabolites . . . . .	6
1.5	Metabolism, Secondary Metabolites (Natural Products) . . . . .	6
1.5.1	Natural Products . . . . .	7
1.5.2	Biomacromolecules . . . . .	7
1.6	Functions of the Natural Products: Chemical Ecology—Plant Chemical Ecology . . . . .	8
1.6.1	Chemical Ecology . . . . .	8
1.6.2	Chemical Defenses of Organisms, Plant Defenses Against Herbivores . . . . .	9
1.6.2.1	Antifeedants, Repelling Insects . . . . .	9
1.6.2.2	Wounded Plants Emitting Prussic Acid . . . . .	10
1.6.2.3	Wounded Plants Emitting Volatile Mustard Oils . . . . .	10
1.6.2.4	Plants Toxic to Animals . . . . .	11
1.6.2.5	Plants Deceiving Herbivores with False Amino Acids . . . . .	11
1.6.3	Chemical Communication with Insects and Plant–Insect interactions . . . . .	12
1.6.3.1	Formation of Courtship Pheromones . . . . .	12
1.6.3.2	Formation of Ecdysones (Molting Hormones) . . . . .	12
1.6.3.3	Pollination . . . . .	13
1.6.3.4	Plant–Insect Interactions: Another Example . . . . .	13

1.6.4	Mutualistic Interactions of Plants and Fungi: Endophytes . . . . .	14
1.6.4.1	Endophyte Fungus and Host Plant . . . . .	14
1.6.5	Plant–Plant Interactions: Allelopathy . . . . .	14
1.6.6	Plant–Microorganism Interactions: Phytoalexins . . . . .	15
1.6.7	Natural Products and Human Being . . . . .	16
1.7	Biosynthesis: Studies with Isotopically Labeled Precursors . . . . .	17
1.8	Metabolic Pathways: Mevalonic Acid Pathway, 1-Deoxy-D-xylulose Phosphate Pathway, Shikimic Acid Pathway, and Polyketide Pathway . . . . .	18
	References . . . . .	20
<b>2</b>	<b>Fundamental Stereochemical Concepts and Nomenclatures . . . . .</b>	<b>23</b>
2.1	Introduction . . . . .	23
2.2	Chirality. Symmetry Elements. Optical Rotation . . . . .	24
2.2.1	Simple or Proper Axis of Symmetry . . . . .	25
2.2.2	Plane of Symmetry . . . . .	26
2.2.3	Center of Symmetry or Inversion Center . . . . .	27
2.2.4	Alternating or Improper or Rotation-Reflection Axis ( $S_n$ ) . . . . .	27
2.2.5	Dissymmetric and Asymmetric Molecules. Chiral and Achiral Point Groups. Central Chirality . . . . .	28
2.2.6	Symmetry Number, Order of Point Groups, Achiral Point Groups . . . . .	30
2.2.7	Local Symmetry (or Site Symmetry). Desymmetrization . . . . .	34
2.2.8	Optical Isomerism. Optical Rotation . . . . .	35
2.2.8.1	Optical Activity Due to Chiral Molecular Structure . . . . .	35
2.2.8.2	Optical Activity Due to Crystalline Structure . . . . .	36
2.2.8.3	Dependence of Rotation ( $\alpha$ ) on Concentration and Cell Length. Value of $\alpha$ . . . . .	36
2.2.8.4	Dependence of Sign of $[\alpha]$ of Polar Compounds on Solvent, Concentration, and pH . . . . .	36
2.2.9	Specific Rotation. Molecular Rotation. Units . . . . .	37
2.2.10	Fischer Projection. Flying Wedge Formulas. Tetrahedral Representations of Cabcd . . . . .	38
2.3	Conformation of Simple Acyclic Molecules . . . . .	40
2.3.1	Dihedral Angle. Torsion Angle. Torsional Strength . . . . .	40
2.3.2	Klyne–Prelog Nomenclature for Torsion Angles. Conformational Chirality . . . . .	41
2.3.3	Torsional Strain Curve (Potential Energy Diagram) of Ethane . . . . .	43
2.3.4	Torsional Strain Curve of Propane . . . . .	44
2.3.5	Torsional Strain Curve of Molecules ACX <sub>2</sub> CX <sub>2</sub> B, n-Butane . . . . .	44
2.4	Configuration. Relative Configuration. Absolute Configuration . . . . .	46

2.5	Relationship Between Two Molecules of Same Molecular Formula. Homomers, Constitutional Isomers, Stereoisomers, Enantiomers, Diastereomers, Configurational/Conformational Enantiomers/Diastereomers . . . . .	48
2.6	Configurational Nomenclature . . . . .	48
2.6.1	Fischer's <b>D,L</b> Nomenclature . . . . .	48
2.6.2	<i>R,S</i> Nomenclature for Absolute Configuration . . . . .	52
2.6.2.1	<i>R,S</i> Nomenclature. Center of Chirality . . . . .	52
2.6.2.2	Specification of Center/s of Chirality . . . . .	53
2.6.2.3	Priority Sequence of the Application of the CIP Sub-rules . . . . .	56
2.6.2.4	Modification of Sub-rule 3 . . . . .	56
2.6.2.5	<b>R*</b> and <b>S*</b> Nomenclature . . . . .	59
2.6.2.6	Specification of Other Tetravalent Chiral Atoms . . . . .	60
2.6.2.7	Specification of Trivalent Chiral Compounds ( <i>with pyramidal stereocenter</i> ) . . .	61
2.6.3	Stereochemistry of Alkenes. <i>E,Z</i> Nomenclature . . . . .	61
2.7	Projection (Fischer, Newman, Sawhorse) and Perspective (Flying Wedge and Zigzag) Formulas of Molecules with Two or More Chiral Centers. Working out Stereoisomers . . . . .	63
2.7.1	Molecules with Two Unlike (Unsymmetrical) Chiral Centers (AB Type) . . . . .	63
2.7.1.1	<i>Erythro</i> and <i>Threo</i> Nomenclature . . . . .	63
2.7.1.2	" <i>Pref</i> " and " <i>Parf</i> " Nomenclature . . . . .	66
2.7.1.3	<b>Syn</b> and <b>Anti</b> System . . . . .	68
2.7.1.4	<b>Like</b> ( <i>l</i> ) and <b>Unlike</b> ( <i>u</i> ) System . . . . .	68
2.7.1.5	Brewster's System of Nomenclature . . . . .	68
2.7.2	Molecules with Two Like (Symmetrical) Chiral Centers (AA Type) . . . . .	69
2.7.3	Molecules with Three Unlike Chiral Centers (ABC Type) . . . . .	70
2.7.4	Constitutionally Symmetrical Molecules Having Three Chiral Centers (ABA Type) . . . . .	71
2.7.5	Stereogenecity and Chirotopicity . . . . .	71
2.7.6	Molecules with Four (ABCD Type) or More Unlike Chiral Centers in a Chain . . . . .	73
2.7.7	Constitutionally Symmetrical Molecules with Four or More Like Chiral Centers in a Chain (ABBA, ABCBA, etc. Types) . . . . .	74
2.7.8	Chiral Compounds with Asymmetric Carbon Atoms in Branched Chains . . . . .	75
2.8	Chirality and Dimension. One-, Two-, and Three-Dimensional Chiral Simplexes . . . . .	75

2.9	Prochirality and Prostereoisomerism. Topicity of Ligands and Faces: Homotopicity. Enantiotopicity. Diastereotopicity.	
	Nomenclature . . . . .	78
2.9.1	Introduction . . . . .	78
2.9.2	Homotopic Ligands . . . . .	79
2.9.3	Homotopic Faces . . . . .	80
2.9.4	Enantiotopic Ligands . . . . .	81
2.9.5	Nomenclature of Geminal Enantiotopic Ligands. Pro-R and Pro-S . . . . .	81
2.9.6	Enantiotopic Faces . . . . .	83
2.9.7	Nomenclature of Enantiotopic Faces . . . . .	84
2.9.8	Diastereotopic Ligands . . . . .	84
2.9.9	Nomenclature of Diastereotopic Ligands . . . . .	86
2.9.10	Diastereotopic Faces. Nomenclature . . . . .	86
2.9.11	Interesting Examples of Topicities of Homomorphic Ligands . . . . .	88
2.9.12	Interrelation of Topicity of Ligands with Isomerism . . .	89
2.9.13	Molecules with Prostereogenic but Prochirotopic Center and Multi-Prochiral Centers . . . . .	89
2.9.14	Topic Relationship of Ligands and Faces . . . . .	90
2.10	Stereoheterotopic Ligands and NMR Spectroscopy . . . . .	90
2.10.1	Anisochrony Arising out of Diastereotopic Faces . . .	91
2.11	Asymmetric Synthesis . . . . .	93
2.11.1	Introduction. Principles of Stereoselection: Enantioselection. Diastereoselection . . . . .	93
2.11.1.1	Lack of Stereoselection . . . . .	93
2.11.1.2	Enantioselection . . . . .	94
2.11.1.3	Diastereoselection . . . . .	94
2.11.2	Asymmetric Synthesis. Definition. Stereoselective and Stereospecific Reactions. Product/Substrate Stereoselectivity. Regioselectivity . . . . .	95
2.11.2.1	Enantiomeric Excess. Diastereomeric Excess. Optical Purity . . . . .	96
2.11.3	Cram's rule . . . . .	97
2.11.3.1	Cram's Open Chain Model . . . . .	97
2.11.3.2	Cram's Chelate or Cyclic Model . . . . .	98
2.11.3.3	Cram's Dipolar Model . . . . .	100
2.11.4	Felkin-Anh Models . . . . .	101
2.11.4.1	Felkin-Anh Open Chain Model . . . . .	101
2.11.4.2	Felkin-Anh Dipolar Model . . . . .	102
2.11.5	Prelog's Rule . . . . .	102
2.11.5.1	Attempted Rationalization of Prelog's Model . . . . .	104
2.11.5.2	More Examples of The Application of Prelog's Rule . . . . .	104

	2.11.5.3	Exception to and Anomalies of Prelog's Rule . . . . .	105
	2.11.6	Horeau's Rule . . . . .	106
	2.11.7	Sharpless Enantioselective Epoxidation . . . . .	107
	2.11.7.1	Kinetic Resolution of Racemate Allyl Alcohols . . . . .	108
	2.11.7.2	Mechanism of the Sharpless Reaction . . . . .	109
2.12		Conformation of Saturated Six-Membered Ring Compounds . . . . .	110
	2.12.1	Conformational Aspects of Cyclohexane . . . . .	110
	2.12.1.1	Geometry of Cyclohexane Chair. Bond Lengths. Bond Angles. Torsion Angles . . . . .	110
	2.12.1.2	Equatorial and Axial Bonds . . . . .	111
	2.12.1.3	Symmetry of Cyclohexane Conformations . . . . .	111
	2.12.1.4	Enthalpy ( <i>H</i> ) or Potential Energy ( <i>E</i> ) Difference . . . . .	112
	2.12.1.5	Cyclohexane Ring Inversion . . . . .	113
	2.12.1.6	Stable Boat or Skew-boat Conformers . . . . .	115
	2.12.2	Monosubstituted Cyclohexanes. Conformational Energy . . . . .	115
	2.12.3	1,1-Disubstituted Cyclohexanes . . . . .	117
	2.12.4	Non-geminal Disubstituted Cyclohexanes . . . . .	118
	2.12.4.1	Some Typical Disubstituted Cyclohexanes . . . . .	120
2.13		Cyclohexanone . . . . .	121
	2.13.1	Torsion Angles, Stability . . . . .	121
	2.13.2	Ring Inversion . . . . .	122
	2.13.3	Alkylketone Effects . . . . .	122
	2.13.3.1	2-Alkylketone Effect . . . . .	122
	2.13.3.2	3-Alkylketone Effect . . . . .	123
	2.13.3.3	4-Alkylketone Effect . . . . .	124
	2.13.4	Addition of Nucleophiles to Cyclohexanones. Stereochemical Aspects . . . . .	125
	2.13.4.1	PDC (PSC) and SAC (SSC) . . . . .	125
	2.13.4.2	Observations Against PSC . . . . .	126
	2.13.4.3	Torsional Strain. Role of C2 and C6 Axial Hydrogens . . . . .	126
	2.13.5	Cieplak Hypothesis . . . . .	128
	2.13.6	Highly Stereoselective Reduction of Saturated Cyclohexanones by Dissolving Metals. Birch Reduction . . . . .	131
	2.13.7	Alkylidene Cyclohexanes. Allylic <sup>(1,3)</sup> Strain . . . . .	132
	2.13.7.1	Conformational Preference . . . . .	133
	2.13.7.2	Synthetic Utility of A <sup>(1,3)</sup> Strain. Stereochemistry of Exocyclic Enolate Anion Protonation . . . . .	133

	2.13.7.3	Another Example of the Use of A <sup>(1,3)</sup> Strain Concept . . . . .	134
2.14		Cyclohexene. Conformation. A <sup>1,2</sup> Strain . . . . .	135
	2.14.1	Conformation of Cyclohexene. Torsion Angles . . . . .	135
	2.14.2	Allylic 1,2-Strain (A <sup>(1,2)</sup> -Strain) . . . . .	136
		2.14.2.1 Conformational Preference . . . . .	137
		2.14.2.2 Isomerizational Preference . . . . .	138
		2.14.2.3 Pseudoallylic 1,2-Strain in Enamines . . . . .	138
		2.14.2.4 Synthesis of Solenopsin A. Application of A <sup>1,2</sup> Strain concept . . . . .	140
2.15		Fused Ring Systems . . . . .	140
	2.15.1	Decalins . . . . .	140
		2.15.1.1 Brief History . . . . .	142
		2.15.1.2 <i>trans</i> -Decalin. Conformation. Torsion Angles. Symmetry . . . . .	142
		2.15.1.3 <i>cis</i> -Decalin. Conformations. Torsion Angles. Symmetry . . . . .	143
		2.15.1.4 Ring Inversion in <i>cis</i> -Decalin . . . . .	144
		2.15.1.5 Entropy Difference in Decalins . . . . .	145
		2.15.1.6 Enthalpy and Physical Constants. Auwers-Skita Rule . . . . .	145
		2.15.1.7 Free Energy Difference in Decalins . . . . .	146
		2.15.1.8 Effect of Introduction of Angular Methyl Group/s . . . . .	147
		2.15.1.9 <i>cis</i> -Decalones and <i>trans</i> -Decalones . . . . .	147
		2.15.1.10 <i>trans</i> -2-Decalols. Conformational Analysis . . . . .	148
		2.15.1.11 <i>cis</i> -2-Decalols. Conformational Analysis . . . . .	148
	2.15.2	Perhydrophenanthrenes (PHP's). Stability. Point Groups. Optical Activity . . . . .	149
		2.15.2.1 Stereochemistry of Some Perhydrophenanthrenes and All Perhydrodiphenic Acids (PHDPA's) . . . . .	152
	2.15.3	Perhydroanthracenes: Relative Stability. Torsion Angles. Point Group. Optical Activity . . . . .	154
2.16		Stereoisomerism: Axial Chirality, ( <i>R,S</i> ) Notations . . . . .	156
	2.16.1	Stereochemistry of Allenes. Configurational Nomenclature . . . . .	156
	2.16.2	Chiral Spiranes and Analogs. Configurational Nomenclature . . . . .	158
	2.16.3	Chiral Adamantoids. Configurational Nomenclature . . . . .	159
	2.16.4	Chiral Catenanes. Configurational Nomenclature . . . . .	160
	2.16.5	Biphenyl Derivatives and Atropisomerism . . . . .	160
		2.16.5.1 Introduction . . . . .	160
		2.16.5.2 Energy Profile Diagram . . . . .	161
		2.16.5.3 Examples of Atropisomerism . . . . .	162
		2.16.5.4 Orders of Steric Hindrance and of Buttrressing Effect . . . . .	162

	2.16.5.5	Configurational Nomenclature of Chiral Biphenyls ( <i>R,S</i> or <i>aR, aS</i> ) . . . . .	164
	2.16.5.6	Some Interesting Examples of Axially Chiral Molecules Exhibiting Atropisomerism . . . . .	164
2.17		Planar Chirality . . . . .	166
	2.17.1	Introduction . . . . .	166
	2.17.2	The ( <i>R,S</i> ) Specification of Planar Chirality . . . . .	166
2.18		Helicity and <i>P,M</i> -Designation . . . . .	167
2.19		Chiroptical Properties. Optical Rotation. ORD, CD . . . . .	168
	2.19.1	Origin of Optical Rotation. Circular Birefringence, Its Effect . . . . .	168
	2.19.2	Optical Rotatory Dispersion. Plain Curve . . . . .	170
	2.19.3	Circular Birefringence and Circular Dichroism. Cotton Effect . . . . .	171
	2.19.4	The Axial Haloketone Rule and Its Applications . . . . .	174
		2.19.4.1 Position of the Halogen Substituent . . . . .	175
		2.19.4.2 Absolute Configuration by Comparison Method . . . . .	175
		2.19.4.3 Absolute Configuration by Axial Haloketone Rule. Conformational Mobility . . . . .	176
		2.19.4.4 Boat Form of Ring A of a Steroid Bromoketone . . . . .	177
	2.19.5	The Octant Rule and Its Applications . . . . .	177
		2.19.5.1 Determination of the Preferred Conformation . . . . .	178
		2.19.5.2 Determination of Absolute Configuration of <i>trans</i> -Decalones . . . . .	180
		2.19.5.3 Tricyclic Ketones: Perhydrophenanthrenones and Perhydroanthracenones . . . . .	181
		2.19.5.4 Tetracyclic Ketones: Steroids . . . . .	182
	2.19.6	Helicity Rule or Chirality Rule . . . . .	184
		2.19.6.1 Conjugated Dienes and Enones: Steroids . . . . .	184
		2.19.6.2 Biaryl Atropisomers and Helicenes . . . . .	185
		2.19.6.3 Correlation of Optical Rotation with Ligand Polarizability: Brewster's rule . . . . .	186
		2.19.6.4 Absolute Configuration of Chiral Allenes: Lowe's Rule . . . . .	188
		2.19.6.5 The Exciton Chirality Method or The Dibenzoate Chirality Rule . . . . .	189
		2.19.6.6 Absolute Configuration of the 5 $\alpha$ -Steroid Diols by Exciton Chirality Method . . . . .	190
		2.19.6.7 Absolute Configuration of <i>trans</i> -Cyclohexane-1,2-diol Enantiomers . . . . .	191

2.19.6.8	Prediction of the First CE Signs of Vicinal and Non-vicinal Dihydroxy-5 $\alpha$ -Steroid Diesters . . . . .	191
	References . . . . .	193
<b>3</b>	<b>Important Biological Events Occurring in Plants . . . . .</b>	<b>203</b>
3.1	Photosynthesis . . . . .	203
3.1.1	Light Reaction: Formation of NADPH, ATP, and O <sub>2</sub> . . .	203
3.1.2	Dark Reaction (Calvin Cycle): Formation of 3-, 4-, 5-, 6-, and 7-Carbon Sugars . . . . .	207
3.1.2.1	Some Comments and Implications Regarding Calvin Cycle Molecules . . . . .	211
3.1.3	C <sub>4</sub> -Plant Photosynthesis, C <sub>3</sub> - and C <sub>4</sub> -Plants . . . . .	212
3.1.3.1	Identification of C <sub>3</sub> and C <sub>4</sub> Metabolism Products by Mass Spectrometry . . . . .	215
3.1.3.2	Crassulacean Acid Metabolism (CAM) . . . . .	215
3.2	Biological Oxidation: Reduction (NADPH = NADP <sup>+</sup> ) . . . . .	215
3.2.1	Flavin Coenzymes . . . . .	218
3.2.2	Combined Use of NADPH and FAD . . . . .	219
3.3	Phosphorylation (ATP→ADP) and Regeneration (ADP→ATP) . . . . .	220
3.3.1	Function of ATP: Its Conversion to ADP . . . . .	220
3.3.2	Conversion of ADP to ATP . . . . .	221
3.3.3	Formation of Proteins from Amino Acids . . . . .	221
3.3.4	Biosynthesis of Starch with the Help of ATP . . . . .	222
3.4	Acetyl Coenzyme A . . . . .	223
3.4.1	Formation of Acetyl Coenzyme A from Pyruvic Acid . . .	224
3.4.2	Formation of Acetyl Coenzyme A from Coenzyme A . . .	225
3.4.3	Functions of Acetyl Coenzyme . . . . .	225
3.4.4	Enzymatic Conversion of Choline to Acetylcholine by Acetyl Coenzyme A . . . . .	226
3.5	Transamination, Isomerization, and Decarboxylation . . . . .	227
3.5.1	Transamination by Aspartate Aminotransferase . . . . .	230
3.5.2	Some Interesting Concepts of The PLP-Catalyzed Transamination Reactions . . . . .	230
3.5.2.1	Racemization and Decarboxylation . . . . .	230
3.5.2.2	C $\alpha$ Side Chain Replacement . . . . .	231
3.5.2.3	PLP-Catalyzed Reaction at $\beta$ -Carbon Atom of Amino Acids . . . . .	232
3.5.2.4	Stereochemical Concepts of the Pyridoxal Phosphate (PLP) Catalyzed Reactions . . . . .	232
3.6	Addition of C <sub>1</sub> -Unit with AdoMet (SAM) . . . . .	234
3.6.1	Methylation . . . . .	234
3.6.2	Formation of Methylenedioxy Bridge and Its Reductive Opening . . . . .	235
3.6.3	N-Methylation and Formation of a Methylene Bridge Between Nitrogen and Carbon . . . . .	236



3.7	C- and O-Alkylation . . . . .	237
3.7.1	C and O-Alkylation of Phenols . . . . .	237
3.7.2	C-Methylation and Modification of Cycloartenol Side Chain to Form Phytosterols . . . . .	239
3.8	Other Important Biological Events . . . . .	240
	References . . . . .	240
<b>4</b>	<b>Natural Products Chemistry: A General Treatment . . . . .</b>	<b>243</b>
4.1	Introduction. Isolation . . . . .	243
4.1.1	Herbarium Specimen. Voucher Specimen . . . . .	244
4.1.2	Ecological Influence on Plant Constituents. Plant Names. Plant Parts . . . . .	245
4.1.3	Literature Survey. Phytochemicals. Chemotaxonomic Significance . . . . .	246
4.1.4	Isolation of Plant Constituents: Solvent Extraction. Buffer Extraction. Thimble Extraction. Steam Distillation . . . . .	251
4.1.5	Chromatography: Different Techniques . . . . .	253
4.1.6	Column Chromatography . . . . .	255
4.1.7	Flash Chromatography . . . . .	261
4.1.8	Thin-Layer Chromatography . . . . .	263
4.1.9	Paper Chromatography . . . . .	268
4.1.10	Gas Chromatography . . . . .	268
4.1.11	High-Performance/Pressure Liquid Chromatography . . . . .	269
4.1.12	Medium Pressure Liquid Chromatography . . . . .	270
4.1.13	Reverse Phase Chromatography . . . . .	270
4.1.14	Gel Permeation Chromatography . . . . .	271
4.1.15	Bioassay-Guided Investigation . . . . .	271
4.1.16	Homogeneity and Physical Constants of the Isolated Compounds . . . . .	271
4.2	Structural Elucidation . . . . .	272
4.2.1	General Approach . . . . .	272
4.2.2	Unsaturation Number. Degradative Methods. Derivatization . . . . .	275
4.2.3	Spectral Analysis. General Discussion . . . . .	279
4.2.4	Ultraviolet Spectroscopy . . . . .	281
4.2.4.1	Different Types of Electronic Transitions . . . . .	282
4.2.5	Infrared Spectroscopy . . . . .	286
4.2.6	$^1\text{H}$ and $^{13}\text{C}$ NMR Spectroscopy . . . . .	290
4.2.7	Mass Spectral Analysis . . . . .	298
4.2.8	Electrospray Ionization Mass Spectrometry . . . . .	299
4.2.9	X-Ray Crystallography: Relative and Absolute Configuration. Conformation . . . . .	300
4.2.10	ORD and CD: Absolute Stereochemistry. Conformation . . . . .	301

4.2.11	Synthesis. Retrosynthesis. Green Chemistry. Atom Economy . . . . .	301
4.2.12	Biosynthetic Compatibility of the Proposed Structure . . .	305
4.2.13	Conclusions . . . . .	305
4.2.14	Naming of Natural Products . . . . .	306
	References . . . . .	311
<b>5</b>	<b>Biosynthesis of Terpenoids: The Oldest Natural Products . . . . .</b>	<b>317</b>
5.1	Biochemical History . . . . .	317
5.1.1	Terpenoids as the Precursor of Cholesterol . . . . .	317
5.1.2	Terpenoid Derived Diagenetic Entities . . . . .	317
5.1.3	Ruzicka's Isoprene Hypothesis . . . . .	318
5.1.4	Discovery of Isopentenyl Pyrophosphate (IPP): The Biological Isoprene Unit . . . . .	318
5.1.5	Concept of Biogenesis and Biosynthesis . . . . .	319
5.2	Mevalonic Acid Pathway . . . . .	319
5.2.1	Acetyl Coenzyme A to Isopentenyl Pyrophosphate (IPP): Stereochemical Implications . . . . .	319
5.2.2	Bioformation of ( <i>R</i> )-(+)-Mevalonic Acid . . . . .	320
5.2.3	Conversion of ( <i>R</i> )-(+)-MVA to IPP . . . . .	321
5.2.4	Isomerization of IPP to $\gamma,\gamma$ -Dimethylallyl Pyrophosphate (DMAPP): Stereochemical Implications . . . . .	322
5.2.5	Formation of Chiral Acetic Acid (7) from 2-T-MVA Pyrophosphate (1) . . . . .	323
5.2.5.1	Formation of Isotopically Substituted Chiral Farnesyl Pyrophosphate (FPP) (5) and Chiral Acetic Acid (7) . . . . .	324
5.2.5.2	The Absolute Configuration of [HDT]-Acetic Acid . . . . .	325
5.3	Non-Mevalonoid (Rohmer) Pathway { 1-Deoxy-D-Xylulose-5- Phosphate (DXP or DOXP): Mevalonate Independent . . . . .	327
5.3.1	Formation of DXP from Pyruvic Acid and D-Glyceraldehyde-3-Phosphate . . . . .	327
5.3.2	Conversion of DXP to 2-C-Methyl-D-Erythritol-4- Phosphate (MEP or ME4P) . . . . .	328
5.3.3	Conversion of MEP to IPP Via $\alpha$ Cyclic Diphosphate: Its Ring Opening, Followed by Repeated Reduction and Dehydration . . . . .	329
5.3.4	Emission of Isoprene from Some Plants . . . . .	332
5.4	Dual Origin of IPP: Labeling Patterns of IPP Derived from Labeled Glucose by Two Different Routes . . . . .	332
5.5	Chain Elongation in Terpenes (Prenyl Transfer) . . . . .	334
5.5.1	Cornforth's Concept and Its Modification by Poulter and Rilling . . . . .	335
5.5.2	Formation of C <sub>10</sub> , C <sub>15</sub> , C <sub>20</sub> , C <sub>25</sub> , C <sub>30</sub> , and C <sub>40</sub> Linear Terpenoids and Natural Rubber . . . . .	336

5.5.3	Ruzicka's Nomenclature: Terpene or Terpenoid, Head and Tail Parts of Acyclic Terpene Pyrophosphates (Diphosphates) . . . . .	337
5.5.4	Formation of Squalene (C <sub>30</sub> ) via Presqualene Pyrophosphate (Involving Cyclopropane/Cyclobutane Ring Opening) . . . . .	338
5.5.5	Different Phases of Terpenoid Biosynthesis . . . . .	341
	References . . . . .	342
<b>6</b>	<b>Monoterpenoids (C<sub>10</sub>)</b> . . . . .	<b>345</b>
6.1	Geranyl pyrophosphate, the Universal Precursor of Monoterpenoids . . . . .	345
6.1.1	Biosynthetic Formation of C <sub>10</sub> -Acyclic Terpenes . . . .	345
6.1.2	Biosynthetic Formation of Cyclic Monoterpenes . . . .	347
6.1.2.1	Monocyclic Monoterpenes. Menthane Skeleton . . . . .	347
6.1.2.2	Bicyclic Monoterpenes. Formation of Some Familiar Skeletons (Camphane/Bornane, Pinane, Fenchane, Carane, and Thujane) . . . .	350
6.1.3	Occurrence of Monoterpene Enantiomers, their Biological Responses and Biosynthesis . . . . .	351
6.1.3.1	Biosynthesis of Pinene, Limonene, and Camphor Enantiomers . . . . .	352
6.1.4	Occurrence of Monoterpenes in Plant Families . . . .	353
6.1.5	Cyclopropyl Monoterpenes (C <sub>10</sub> ): Their Biosynthesis . .	353
6.1.6	Biosynthesis of Secologanin (via Logenin), the Monoterpenoid Part of Some Indole and Quinoline Alkaloids. Iridoids . . . . .	354
6.2	Geraniol . . . . .	356
6.2.1	Occurrence, Structure Determination . . . . .	356
6.2.2	Spectral Properties . . . . .	357
6.2.3	Synthesis . . . . .	358
6.2.4	Synthesis of Chiral Geraniol-1-d . . . . .	359
6.2.5	Reactions: (i)–(x) . . . . .	360
6.2.6	Epoxidation methods of Geraniol . . . . .	363
6.2.7	Geraniol As a Synthone . . . . .	364
6.2.8	Cyclic Products from Geraniol . . . . .	367
6.2.9	Molecular Recognition (Regio- and Stereoselective) . .	369
6.2.9.1	Molecular Recognition of Carbonyl Compounds [Examples (i)–(iii)] . . . . .	369
6.2.9.2	Molecular Recognition of Prochiral Allylic Alcohols . . . . .	371
6.2.10	Microbial Hydroxylation . . . . .	371
6.2.11	Metabolism of Geraniol in Grape Berry Mesocarp . . .	372
6.2.12	Bioactivity and Uses . . . . .	372

6.3	Camphor . . . . .	373
6.3.1	Introduction . . . . .	373
6.3.2	Structure Determination . . . . .	374
6.3.3	Absolute Configuration and Conformation . . . . .	375
6.3.4	Meaning of Structural Representation . . . . .	376
6.3.5	Synthesis . . . . .	377
6.3.6	Industrial Preparation of Camphor . . . . .	379
6.3.7	Spectral Data of Camphor . . . . .	381
6.3.8	Biosynthesis of Camphor . . . . .	381
6.3.9	Reactions . . . . .	382
6.3.9.1	Functionalization of Camphor and Its Derivatives . . . . .	385
6.3.9.2	Ring Contraction Reaction of Camphor . . . . .	385
6.3.9.3	Ring Contraction by Photolysis . . . . .	385
6.3.10	Camphor as a Synthone and a Chiral Auxiliary . . . . .	387
6.3.11	Bioactivity and Uses . . . . .	387
6.4	Menthol . . . . .	388
6.4.1	Introduction . . . . .	388
6.4.2	Reactions, Structure, Absolute Configuration . . . . .	389
6.4.3	Spectral Data . . . . .	389
6.4.4	Synthesis of ( $\pm$ )-Menthone and ( $\pm$ )-Menthol . . . . .	390
6.4.5	Stereoisomers of Menthol, Their Conformations, and Relative Stability . . . . .	391
6.4.5.1	Relative Rates of Esterification . . . . .	392
6.4.5.2	Ionic Elimination Reactions of Menthyl Chloride and Neomenthyl Chloride . . . . .	393
6.4.6	Commercial Synthesis of (–)-Menthol (Takasago Process) . . . . .	393
6.4.6.1	Retrosynthetic Analysis and Strategy . . . . .	394
6.4.6.2	Commercial Asymmetric Synthesis of (–)-Menthol Starting from (–)- $\beta$ -Pinene . . . . .	395
6.4.7	One-Pot Conversion of ( <i>R</i> )-Citronellal to (–)-Menthol . . . . .	396
6.4.8	Applications and Uses . . . . .	396
	References . . . . .	397
7	<b>Sesquiterpenoids (C<sub>15</sub>)</b> . . . . .	403
7.1	Introduction . . . . .	403
7.2	Acyclic Sesquiterpenoids: Biosynthesis . . . . .	403
7.3	Cyclic Sesquiterpenoids . . . . .	404
7.3.1	Biosynthesis. General Mechanistic Approach . . . . .	404
7.3.2	Classification. Some Familiar Skeletal Patterns . . . . .	405
7.3.3	Monocyclic Sesquiterpenoids. Different Skeletal Patterns. Biosynthesis . . . . .	406
7.3.4	Bicyclic Sesquiterpenoids . . . . .	408
7.3.5	Tricyclic Sesquiterpenoids . . . . .	409

7.3.6	Tetracyclic Sesquiterpenoid . . . . .	410
7.4	Farnesol, The Parent Acyclic Sesquiterpene Alcohol . . . . .	411
7.4.1	Introduction and Structure . . . . .	411
7.4.2	Synthesis . . . . .	411
7.4.3	Biosynthesis . . . . .	412
7.4.4	Uses . . . . .	412
7.5	Caryophyllene and Isocaryophyllene . . . . .	413
7.5.1	Introduction . . . . .	413
7.5.2	Structure and Absolute Configuration . . . . .	413
7.5.3	<sup>1</sup> H NMR Spectral Data of Caryophyllene and Isocaryophyllene . . . . .	414
7.5.4	Synthesis of (±)-Caryophyllene . . . . .	415
7.5.4.1	Corey's Synthesis . . . . .	415
7.5.4.2	Devaprabhakara's Synthesis . . . . .	417
7.5.4.3	Suginome's Synthesis . . . . .	417
7.5.5	Rearrangements of Caryophyllene . . . . .	417
7.5.5.1	Conformations . . . . .	418
7.5.5.2	Rearrangements and Cyclizations . . . . .	419
7.5.5.3	Thermal Rearrangement of (–)-Caryophyllene to (–)-Isocaryophyllene . . . . .	421
7.5.6	Conversion of Humulene into Caryophyllene . . . . .	421
7.5.7	Apollan-11-ol: An Interesting Acid-Catalyzed Product of Humulene . . . . .	422
7.5.8	Biosynthesis of Caryophyllene . . . . .	423
7.5.9	A Caryophyllan-Type Compound in a Sea Coral . . . . .	423
7.6	Longifolene: A Tricyclic Sesquiterpene . . . . .	424
7.6.1	Occurrence . . . . .	424
7.6.2	Structure: Some Reactions of Longifolene . . . . .	424
7.6.2.1	Conversion of Longifolene to Isolongifolene . . . . .	425
7.6.3	Spectral Data of Longifolene . . . . .	427
7.6.4	Synthesis of (±)-Longifolene and (+)-Longifolene by Corey's Group . . . . .	427
7.6.5	Synthesis of (±)-Longifolene and Some of Its Relatives by Johnson Group . . . . .	429
7.6.6	Biosynthesis . . . . .	430
7.7	Longicyclene: The First Reported Tetracyclic Sesquiterpene . . . . .	430
7.7.1	Occurrence and Structure . . . . .	430
7.7.2	Spectral Properties . . . . .	431
7.7.3	Synthesis of Longicyclene . . . . .	432
7.7.4	Biosynthesis of Longicyclene . . . . .	433
7.8	Santonin . . . . .	433
7.8.1	Occurrence and Structure . . . . .	433
7.8.2	Stereocontrolled Total Synthesis of Racemic α-Santonin and β-Santonin . . . . .	435

7.8.3	Biogenetic-Type Synthesis of Santonin . . . . .	436
7.8.4	Absolute Configuration of $\alpha$ -Santonin and Related Compounds at C <sub>11</sub> . Full Stereostructures by X-ray Studies . . . . .	436
7.8.5	Molecular Conformations of $\alpha$ -Santonin and $\beta$ -Santonin . . . . .	437
7.8.6	Spectral Properties . . . . .	438
7.8.7	Conversion of Santonin to Santonic Acid . . . . .	439
7.8.8	Biosynthesis of Santonin . . . . .	440
7.8.9	Santonin as a Synthone . . . . .	441
7.8.10	Photochemical Transformations of Santonin . . . . .	442
7.9	<i>Artemisinin: A Sesquiterpene Lactone with an Endoperoxide Linkage and Profound Antimalarial Activity</i> . . . . .	444
7.9.1	Introduction. Occurrence. Structure . . . . .	444
7.9.2	Absolute Stereochemistry and Conformation . . . . .	444
7.9.3	Synthesis . . . . .	445
7.9.3.1	Semisynthesis . . . . .	447
7.9.3.2	Total Synthesis of (+)-Artemisinin by Yadav et al . . . . .	448
7.9.4	Spectral Properties . . . . .	448
7.9.5	Biosynthesis of Artemisinin (qinghaosu) . . . . .	449
7.9.6	Uses . . . . .	449
7.10	<i>Abscisic Acid: A Sesquiterpene Phytohormone</i> . . . . .	450
7.10.1	Introduction. Occurrence . . . . .	450
7.10.2	Spectral Properties . . . . .	451
7.10.3	Synthesis . . . . .	452
7.10.3.1	Cornforth's Synthesis of ( $\pm$ )-Abscisic Acid . . . . .	452
7.10.3.2	Synthesis of Optically Active Abscisic Acid . . . . .	452
7.10.4	Absolute Configuration . . . . .	453
7.10.4.1	By Chemical Correlation . . . . .	453
7.10.4.2	By CD Studies (Exciton Chirality Method) . . . . .	453
7.10.5	Molecular Conformations of (+)-ABA and (+)- <i>trans</i> -ABA . . . . .	455
7.10.6	Biosynthesis . . . . .	457
7.11	<i>Gossypol: An Interesting Dinaphthyl Bis-Sesquiterpene with Cadinane Skeletal Pattern</i> . . . . .	458
7.11.1	Introduction. Occurrence, Biological Activity . . . . .	458
7.11.2	Absolute Configuration of Gossypol . . . . .	459
7.11.3	Synthesis . . . . .	459
7.11.4	<sup>13</sup> C NMR Spectral Data of Gossypol . . . . .	460
7.11.5	Biosynthesis of Gossypol . . . . .	460

7.12	Ainsliadimer A. A Novel Sesquiterpene Lactone Dimer with a Cyclopentane Ring . . . . .	461
7.12.1	Occurrence. Structure. Biogenesis. Bioactivity . . . . .	461
7.12.2	Spectral Data . . . . .	462
7.12.3	Biogenesis . . . . .	462
7.12.4	Bioactivity . . . . .	463
	References . . . . .	463
<b>8</b>	<b>Diterpenoids (C<sub>20</sub>) . . . . .</b>	<b>469</b>
8.1	Occurrence. Biosynthesis . . . . .	469
8.1.1	Acyclic Diterpenes . . . . .	470
8.1.2	Monocyclic Diterpenes . . . . .	471
8.1.3	Bicyclic Diterpenes . . . . .	471
8.1.4	Tricyclic Diterpenes . . . . .	472
	8.1.4.1 Ring C Aromatized Diterpenes . . . . .	474
	8.1.4.2 Sandarocopimaradiene . . . . .	475
8.1.5	Tetracyclic Diterpenes . . . . .	476
8.1.6	Ginkgolide Biosynthesis . . . . .	476
8.2	Geranylgeraniol . . . . .	477
8.2.1	Introduction . . . . .	477
8.2.2	Synthesis of Geranylgeraniol . . . . .	478
8.3	Abietic Acid and Other Resin Acids . . . . .	478
8.3.1	Introduction. Occurrence . . . . .	478
8.3.2	Structure . . . . .	479
8.3.3	Synthesis . . . . .	481
8.3.4	Spectral Properties of Abietic Acid Methyl Ester . . . . .	483
8.3.5	Stereochemistry and Molecular Conformation . . . . .	484
8.3.6	A Few Interesting Reactions . . . . .	485
8.3.7	Biosyntheses of Abietic Acid . . . . .	487
8.3.8	Uses as a Synthon . . . . .	487
8.3.9	Diagenetic Products of Abietic acid . . . . .	489
8.3.10	Structure Diagrams of Some Related Resin Acids . . . . .	490
8.4	Taxol <sup>®</sup> : A Nitrogenous Diterpene Ester with Unique Antitumor Activity . . . . .	490
8.4.1	Introduction. Occurrence . . . . .	490
8.4.2	Structure . . . . .	491
8.4.3	Spectral Data . . . . .	492
8.4.4	Conformation of Taxol (1C) . . . . .	492
8.4.5	Synthesis of Taxol . . . . .	493
8.4.6	Search for Commercial Sources for Taxol . . . . .	497
	8.4.6.1 Semisynthesis . . . . .	498
	8.4.6.2 Application of Biocatalysis. Fermentation Process . . . . .	499
8.4.7	Biosynthesis of Taxol . . . . .	500
8.4.8	Uses . . . . .	501

8.5	Gibberellins . . . . .	501
8.5.1	Introduction. Biological Activity . . . . .	501
8.5.2	Structure. Synthesis . . . . .	502
8.5.3	Biosynthesis . . . . .	503
8.5.4	Uses . . . . .	503
8.6	Ginkgolides . . . . .	503
8.6.1	Introduction. Occurrence . . . . .	503
8.6.2	Chemical Constituents. Ginkgolides; Biosynthesis. Synthesis . . . . .	504
8.7	Forskolin . . . . .	504
8.7.1	Occurrence, Stereostructure . . . . .	504
8.7.2	NMR Spectral Data . . . . .	505
8.7.3	Bioactivity . . . . .	505
	References . . . . .	506
<b>9</b>	<b>Sesterterpenoids (C<sub>25</sub>) . . . . .</b>	<b>511</b>
9.1	Introduction. Occurrence. Structure . . . . .	511
9.2	Spectral Data of Ophiobolin (1) . . . . .	511
9.3	Sesterterpenoids of Plant Origin . . . . .	512
9.4	Biosynthesis of Some Sesterterpenoids . . . . .	512
9.5	Natural C <sub>25</sub> Compounds Biogenetically Not Related to Geranyl farnesyl PP . . . . .	514
	References . . . . .	514
<b>10</b>	<b>Triterpenes (C<sub>30</sub>) . . . . .</b>	<b>517</b>
10.1	Introduction. Biogenesis. Functions of Enzymes . . . . .	517
10.1.1	Monocyclic Triterpenes . . . . .	519
10.1.2	Bicyclic Triterpenes . . . . .	519
10.1.3	Tricyclic Triterpenes . . . . .	521
10.1.4	Tetracyclic Triterpenes. Substrates: (a) Oxidosqualene, (b) Squalene . . . . .	523
10.1.5	Pentacyclic Triterpenes . . . . .	524
10.1.6	Cyclization of Bis-Oxidosqualene . . . . .	526
10.1.7	Sesquiterpene–Nortriterpene Adduct (C <sub>44</sub> ) . . . . .	527
10.1.8	Triterpene Dimers (C <sub>60</sub> ) and Triterpene Trimers . . .	530
10.2	Squalene, the Universal Precursor of Triterpenoids and Steroids . . . . .	531
10.2.1	Occurrence. Biogenesis . . . . .	531
10.2.2	Synthesis of Squalene . . . . .	531
10.3	β-Amyrin . . . . .	531
10.3.1	Occurrence. Structural Elucidation . . . . .	531
10.3.2	Stereochemistry . . . . .	534
10.3.3	Spectral Data of β-Amyrin . . . . .	535
10.3.4	Synthesis of β-Amyrin . . . . .	536



10.3.5	Formal Syntheses of $\beta$ -Amyrin by Polyene Cyclization . . . . .	537
10.3.6	Johnson's Total Synthesis of $\beta$ -Amyrin by Polyene Cyclization . . . . .	537
10.3.7	3-Deoxy- $\beta$ -Amyrin by Backbone Rearrangement of $3\beta$ -Fridelanol . . . . .	540
10.3.8	Biosynthesis . . . . .	541
10.4	Analysis of Molecular Conformations of Some Common Pentacyclic Triterpenes . . . . .	542
10.4.1	Conformation of $\beta$ -Amyrin . . . . .	542
10.4.2	Molecular Conformation of $\alpha$ -Amyrin . . . . .	543
10.4.3	Conformations of Bauerenol, Isobauerenol, Multiflorenol, and Isomultiflorenol . . . . .	544
10.4.3.1	Conformation of Ring A . . . . .	544
10.4.3.2	Conformations of Rings B and C . . . . .	545
10.4.3.3	Conformations of Rings D and E . . . . .	545
10.4.4	Molecular Conformations of Eupacannol, Friedelin, and Derivatives . . . . .	547
10.4.5	Molecular Conformation of Lupeol . . . . .	548
10.5	Conclusion . . . . .	548
10.5.1	Diagenetic Product of $\beta$ -Amyrin . . . . .	548
	References . . . . .	548
<b>11</b>	<b>Steroids: Cholesterol and Other Phytosterols . . . . .</b>	<b>553</b>
11.1	Introduction . . . . .	553
11.2	Cholesterol . . . . .	553
11.2.1	Introduction: Functions in Human System . . . . .	553
11.2.1.1	Functions of LDL and HDL . . . . .	556
11.2.1.2	Occurrence in Animals and Plants . . . . .	556
11.2.2	Structural Elucidation. Relative and Absolute Stereochemistry. Conformation . . . . .	557
11.2.2.1	Location of the Double Bond . . . . .	559
11.2.2.2	Configuration at C3 . . . . .	559
11.2.2.3	A/B-, B/C-, and C/D-Ring Fusions. Absolute Configuration . . . . .	560
11.2.3	Synthesis of Cholesterol . . . . .	560
11.2.3.1	Specification of the Chiral Centers. Conformation . . . . .	564
11.2.4	NMR Spectral Data of Cholesterol . . . . .	564
11.2.5	Biosynthesis of Cholesterol in Animals, Fungi, and Plants . . . . .	565
11.2.5.1	Formation of Lanosterol in Animals and Fungi . . . . .	566
11.2.5.2	Formation of Cycloartenol in Plants . . . . .	568

	11.2.5.3	Lanosterol to Cholesterol and Cycloartenol to Cholesterol Conversions . . . . .	568
	11.2.5.4	Biosynthetic Conversion of Lanosterol to Cholesterol . . . . .	569
	11.2.5.5	Biosynthesis of Cholesterol from Cycloartenol in Plants . . . . .	571
	11.2.5.6	Biogenetic Conversion of Cycloartenol to Other Phytosterols . . . . .	571
11.3		Brassinosteroids . . . . .	574
	11.3.1	Introduction. Some Brassinosteroids . . . . .	574
	11.3.2	Biosynthesis . . . . .	576
	11.3.3	Spectral Data of Brassinolide . . . . .	576
11.4		Other Bioactive Steroidal Compounds . . . . .	577
	11.4.1	Ecdysones . . . . .	577
		11.4.1.1 Introduction. Structures . . . . .	577
		11.4.1.2 Biogenesis . . . . .	577
	11.4.2	Diosgenin: Diosgenin-Derived Steroidal Drugs . . . . .	578
		11.4.2.1 Spectral Data of Diosgenin . . . . .	580
	11.4.3	Cardioactive Glycosides . . . . .	580
		References . . . . .	581
<b>12</b>		<b>Carotenoids: GGPP-Derived Polyisoprenoid (C<sub>40</sub>) Coloring Pigments . . . . .</b>	<b>585</b>
	12.1	Introduction . . . . .	585
	12.2	Structures of Carotenoids . . . . .	586
	12.3	Spectral Properties . . . . .	586
	12.4	$\beta$ -Carotene and Lycopene . . . . .	587
	12.5	Synthesis of $\beta$ -Carotene . . . . .	588
	12.6	Conversion of Vitamin A to $\beta$ -Carotene . . . . .	589
	12.7	Synthesis of Lycopene . . . . .	591
	12.8	Biosynthesis . . . . .	591
	12.9	Uses . . . . .	592
		References . . . . .	594

## Contents for Volume 2

<b>13</b>	<b>Shikimic Acid Pathway . . . . .</b>	<b>625</b>
13.1	Introduction and Biosynthesis of C <sub>6</sub> -C <sub>3</sub> Moieties via Shikimic Acid . . . . .	625
13.1.1	(-)-Shikimic Acid . . . . .	625
13.1.1.1	Stage 1. Formation of 3-deoxy-D-arabinoheptulosonic acid 7-phosphate (DAHP) . . . . .	626
13.1.1.2	Stage 2. Formation of 3-Dehydroquinic Acid . . . . .	627
13.1.1.3	Stage 3. Formation of 3-dehydroshikimic Acid . . . . .	627
13.1.1.4	Stage 4. Formation of (-)-shikimic acid from 3-dehydroshikimic acid . . . . .	629
13.1.2	Formation of Chorismic Acid and Prephenic Acid . . . . .	629
13.1.2.1	Chorismic Acid . . . . .	629
13.1.2.2	Prephenic Acid . . . . .	630
13.1.3	Aromatic Amino Acids: Phenylalanine and Tyrosine . . . . .	631
13.1.4	Formation of <i>trans</i> -Cinnamic Acid from L-Phenylalanine . . . . .	633
13.1.5	Biosynthesis of Coumarins . . . . .	634
13.1.6	Biosynthesis of Phenylpropanoids (C <sub>6</sub> -C <sub>3</sub> ) <sub>x</sub> (Lignins) and (C <sub>6</sub> -C <sub>3</sub> -C <sub>3</sub> -C <sub>6</sub> ) (Lignans) of Different Skeletal Patterns from Cinnamyl Alcohols via Cinnamic Acids . . . . .	635
13.1.6.1	Lignins . . . . .	636
13.1.6.2	Lignans. Biosynthesis . . . . .	636
13.1.7	Biosynthesis of Some Common Phenolic Acids via Shikimic Acid and via Chorismic Acid . . . . .	636
13.1.8	(-)-Shikimic Acid As A Synthon: Synthesis of Oseltamivir Phosphate . . . . .	640

13.2	Coumarins . . . . .	642
13.2.1	General Introduction, Structure . . . . .	642
13.2.2	Spectral Properties of Some Natural Coumarins . . . .	644
13.2.3	Synthesis: Coumarin, Substituted Coumarins, 4-Hydroxycoumarins, and Dihydrocoumarins . . . . .	645
13.2.3.1	Perkin Reaction . . . . .	645
13.2.3.2	Knoevenegal Reaction . . . . .	645
13.2.3.3	Pechmann Reaction . . . . .	646
13.2.3.4	Modified Pechmann Methods . . . . .	647
13.2.3.5	Use of Nanoparticles as Catalysts . . . . .	651
13.2.3.6	A Versatile, High-Yield Coumarin Synthesis via Claisen Rearrangement . . . .	651
13.2.3.7	Some Other Methods of Coumarin Synthesis . . . . .	653
13.2.3.8	Synthesis of 4-Hydroxycoumarins . . . . .	653
13.2.3.9	Synthesis of Dihydrocoumarins (Chroman-2-Ones) . . . . .	654
13.2.4	Reactions of Coumarins . . . . .	656
13.2.5	Reactions of 4-Hydroxycoumarin with $\alpha,\beta$ -Unsaturated Carbonyls . . . . .	657
13.2.6	Photochemical Reactions of Coumarins . . . . .	659
13.2.6.1	[2 + 2]-Photodimerization in Solution . . . .	659
13.2.6.2	Photodimerization of Coumarins in the Presence of a Chiral Host . . . . .	660
13.2.6.3	Photodimerization in the Solid State . . . .	660
13.2.6.4	[2+2]-Photoaddition of Coumarin . . . . .	661
13.2.6.5	Light-induced Coumarin Cyclopentannulation . . . . .	661
13.2.7	Thermal [2+2]Cycloaddition . . . . .	661
13.2.8	Electrochemical Reduction and Reductive Dimerization of Coumarins . . . . .	662
13.2.9	As a Synthone . . . . .	663
13.2.9.1	An Efficient Synthesis of (R)-Tolterodine . . . . .	663
13.2.9.2	Synthesis of 4-Heteroaryl-substituted Coumarins . . . . .	663
13.2.9.3	Synthesis of 4-Amido- and 4-( <i>N</i> -Heteroaryl)coumarins . . . . .	664
13.2.9.4	An Efficient Synthesis of the Intrinsic Fluorescent Peptide Labels . . . . .	664
13.2.9.5	Synthesis of Warfarin by Catalytic Asymmetric Michael Reaction . . . . .	665
13.2.10	Biological Properties, Uses, and Applications . . . .	666
13.3	Marmesin . . . . .	667
13.3.1	Occurrence, Structure . . . . .	667
13.3.2	Synthesis and Absolute Configuration . . . . .	667

13.3.3	NMR Spectral Data . . . . .	668
13.3.4	Biosynthesis of Marmesin, the Obligatory Precursor of Psoralen and Other Furanocoumarins . . . . .	669
13.4	Some Interesting Natural Dimeric and Trimeric Coumarins: Structure Diagrams. Nomenclature. Some Comments . . . . .	671
	References . . . . .	674
<b>14</b>	<b>Polyketide Pathway. Biosynthesis of Diverse Classes of Aromatic Compounds . . . . .</b>	<b>679</b>
14.1	Introduction . . . . .	679
14.2	Biosynthesis of Polyketide Natural Products . . . . .	680
14.2.1	Biosynthesis of Phloroglucinol, the Simplest Polyketide Derived Aromatic Compound . . . . .	680
14.3	Fatty Acid Biosynthesis Using C <sub>2</sub> Extender . . . . .	682
14.4	Flavonoids Derived from Polyketide and Shikimic Acid Pathways . . . . .	683
14.4.1	Introduction. Various Classes . . . . .	683
14.4.2	Synthesis of Flavonoids . . . . .	686
14.4.3	Spectral Properties . . . . .	689
14.4.4	Biosynthesis of Flavonoids . . . . .	689
14.4.4.1	Biosynthesis of the Precursors of Chalcones and Flavones . . . . .	690
14.4.4.2	Biosynthesis of Chalcones and Flavones . . . . .	690
14.4.4.3	The Probable Biogenetic Relationships . . . . .	691
14.4.4.4	Biogenesis of Isoflavones from Flavanones Through Radical Formation . . . . .	692
14.4.4.5	Biosynthesis of Isoflavones from Chalcone Precursors . . . . .	692
14.4.4.6	Biosynthesis of Aurones . . . . .	693
14.4.4.7	Bioformation of Isoflavonoid Variants . . . . .	693
14.4.4.8	Biosynthesis of Resveratrol and Veniferin . . . . .	694
14.4.4.9	Flavonoids Containing C <sub>5</sub> or C <sub>10</sub> Side Chain or C <sub>5</sub> Derived Ring . . . . .	695
14.5	Catechins . . . . .	695
14.5.1	Introduction. Various Classes . . . . .	695
14.5.2	Structure Elucidation . . . . .	696
14.5.3	Relative and Absolute Configurations of Catechins . . . . .	697
14.5.3.1	Relative Configuration . . . . .	697
14.5.3.2	Absolute Configuration by Application of Prelog Rule . . . . .	698
14.5.3.3	Absolute Configuration by Chemical Correlation . . . . .	699
14.5.4	Conformations of Catechin and Epicatechin . . . . .	700
14.5.5	Synthesis of Catechins . . . . .	701
14.5.6	A Rearrangement Reaction of Catechin . . . . .	702

14.5.7	(+)-Catechin, A Potential Synthon for Representative PPAP (Polyprenylated Acylphloroglucinol) Natural Products (e.g., Garsubellin A, Hyperforin, Clusianone, etc.) . . . . .	703
14.5.8	Preparation of Some Useful Derivatives . . . . .	704
14.5.8.1	O- and C-Glycosylation of Flavonoids . . . . .	704
14.5.8.2	C-Glycosylation . . . . .	707
14.5.8.3	Preparation of Some Potential Anticancer Derivatives from (+)-Catechin and (–)-Epicatechin via Functionalization at C4 and C8 . . . . .	708
	References . . . . .	712
<b>15</b>	<b>Alkaloids. General Introduction . . . . .</b>	<b>717</b>
15.1	Classification Based on Precursor Amino Acids and Heterocyclic Rings . . . . .	719
15.2	Metabolic Engineering (Combination of Microbial and Plant Genes) . . . . .	721
15.3	Alkaloids as Chiral Auxiliaries . . . . .	722
15.4	Historical Data Concerning Some Well-known Alkaloids . . . . .	722
15.5	The Chaps . . . . .	723
	References . . . . .	723
<b>16</b>	<b>Hygrine, Hygroline, and Cuscohygrine (<i>Ornithine-Derived Alkaloids</i>) . . . . .</b>	<b>725</b>
16.1	Occurrence . . . . .	725
16.2	Structure . . . . .	725
16.3	Absolute Configuration . . . . .	725
16.4	Synthesis of (±)-Hygrine . . . . .	726
16.5	Enantioselective Synthesis of (+)-Hygrine . . . . .	727
16.6	Spectral Data of Hygrine . . . . .	728
16.7	Biosynthesis of (–)-Hygrine . . . . .	729
16.8	Hygroline and Pseudohygroline . . . . .	729
16.9	Cuscohygrine . . . . .	730
16.9.1	Stereochemistry of Cuscohygrine . . . . .	730
16.9.2	Synthesis of Cuscohygrine . . . . .	730
16.9.3	Biosynthesis of Cuscohygrine . . . . .	731
	References . . . . .	731
<b>17</b>	<b>Coniine, Conhydrine, and Pseudoconhydrine (<i>The C-Skeleton Derived from a C<sub>8</sub>-Fatty Acid and N from Transamination</i>) . . . . .</b>	<b>733</b>
17.1	Introduction. <i>Conium</i> Alkaloids . . . . .	733
17.2	Coniine . . . . .	733
17.2.1	Structure and Absolute Stereochemistry . . . . .	733
17.2.2	Conformation . . . . .	735
17.2.3	Synthesis . . . . .	735

17.2.4	Chemoenzymatic Resolution . . . . .	739
17.2.5	Spectral Data . . . . .	740
17.2.6	Biosynthesis of Coniine . . . . .	740
17.3	Conhydrine . . . . .	742
17.3.1	Stereostructure . . . . .	742
17.3.2	Synthesis of ( $\pm$ )-Conhydrine . . . . .	743
17.4	Pseudoconhydrine . . . . .	743
17.4.1	Structure. Stereochemistry. Conformation . . . . .	744
17.4.2	Synthesis of ( $\pm$ )- $\psi$ -Conhydrine . . . . .	745
17.4.3	Synthesis of Optically Active (+)- <i>N</i> -Methylpseudoconhydrine . . . . .	745
17.5	Laboratory Analogy of the Biosynthesis of Conhydrine and $\psi$ -Conhydrine . . . . .	746
	References . . . . .	747
<b>18</b>	<b>Nicotine (<i>Pyridine-Pyrrolidine Alkaloid, Derived from L-Aspartic Acid and L-Ornithine</i>) . . . . .</b>	<b>749</b>
18.1	Occurrence and Introduction . . . . .	749
18.2	Structure Determination and Absolute Configuration . . . . .	750
18.3	Absolute Configuration from Optical Rotatory Dispersion Studies . . . . .	751
18.4	Synthesis . . . . .	752
18.5	Spectral Data . . . . .	756
18.6	Biosynthesis . . . . .	757
18.7	Preferred Molecular Conformation of Natural Nicotine and Synthetic 2-Nicotine and 4-Nicotine . . . . .	758
18.8	Photochemistry of Nicotine . . . . .	759
18.9	Composition of Tobacco Smoke . . . . .	760
18.10	Racemization of Natural (–)-Nicotine. Resolution of the Racemic Variety . . . . .	761
18.11	Bioactivity, Uses, and Therapeutic Potential . . . . .	761
	References . . . . .	764
<b>19</b>	<b>Atropine [(<math>\pm</math>)-Hyoscyamine] and Cocaine (<i>Ornithine-Derived Alkaloids</i>) . . . . .</b>	<b>767</b>
19.1	Introduction . . . . .	767
19.2	Stereostructural Elucidation . . . . .	767
19.2.1	Structure, Synthesis, and Absolute Configuration of (–)-Tropic acid (a) . . . . .	768
19.2.1.1	Absolute Configuration of (–)-Tropic acid, the Hydrolyzed Product of (–)-Hyoscyamine . . . . .	768
19.2.2	Structure of Tropine . . . . .	770
19.2.3	Configuration of the Hydroxyl Group of Tropine and Pseudotropine . . . . .	771
19.2.4	Conformation of Tropine-Pseudotropine System . . . . .	771

19.3	Synthesis of Tropinone . . . . .	772
19.3.1	Willstätter's Synthesis . . . . .	772
19.3.2	Robinson's Synthesis . . . . .	773
19.4	Spectral Data of Atropine . . . . .	774
19.5	Biosynthesis of Tropine . . . . .	775
19.6	Biosynthesis of (–)-Tropic acid and (–)-Hyoscyamine . . . . .	776
19.7	Use of Atropine . . . . .	776
19.8	Scopolamine (6) . . . . .	776
19.9	Cocaine (7) . . . . .	776
19.9.1	Introduction . . . . .	776
19.9.2	Synthesis of Cocaine . . . . .	777
19.9.3	Biosynthesis of Cocaine . . . . .	777
19.9.4	Biological Activities and Uses . . . . .	778
	References . . . . .	779
<b>20</b>	<b>Ephedrine and Pseudoephedrine (C<sub>6</sub>–C<sub>1</sub> Part Derived from L-Phenylalanine and Nitrogen Derived by Transamination) . . . . .</b>	<b>781</b>
20.1	Introduction . . . . .	781
20.2	Structure . . . . .	781
20.3	Relative and Absolute Stereochemistry of <i>Ephedra</i> Alkaloids . . . . .	782
20.3.1	Relative Stereochemistry . . . . .	783
20.3.2	Absolute Configuration . . . . .	783
20.4	Basicity of Ephedrine and Related Compounds . . . . .	784
20.5	Synthesis of (±)-Ephedrine and (±)-ψ-Ephedrine and Their Resolution . . . . .	785
20.6	Asymmetric Synthesis of Ephedrine Derivatives via Chiral 2-Oxazolines . . . . .	786
20.7	Industrial Preparation of Optically Active Ephedrine (Combination of Biotechnology and Chemical Steps) . . . . .	787
20.8	Biosynthesis of <i>Ephedra</i> Alkaloids . . . . .	787
20.9	Conversion of Ephedrine to Methamphetamine, a Well-Known Psychostimulant Drug . . . . .	789
20.10	Bioactivity and Applications . . . . .	789
	References . . . . .	790
<b>21</b>	<b>Pilocarpine and Isopilocarpine (L-Histidine-Derived Imidazole Alkaloids) . . . . .</b>	<b>793</b>
21.1	Introduction and Structure . . . . .	793
21.2	Relative and Absolute Stereochemistry of Pilocarpine . . . . .	793
21.3	Syntheses of Pilocarpine and Isopilocarpine . . . . .	795
21.3.1	Synthesis by DeGraw . . . . .	795
21.3.2	Synthesis by Noordam et al. . . . .	795
21.3.3	Synthesis by Büchi et al. . . . .	797
21.3.4	Chirospecific Synthesis by Zhang et al. . . . .	798



21.4	Spectral Data of Pilocarpine and Isopilocarpine . . . . .	799
21.5	Biogenesis of Pilocarpidine and Pilocarpine . . . . .	799
21.6	Bioactivities and Uses . . . . .	800
	References . . . . .	801
<b>22</b>	<b>Papaverine (L-Tyrosine-Derived Alkaloid) . . . . .</b>	<b>803</b>
22.1	Occurrence . . . . .	803
22.2	Structure Determination . . . . .	803
22.3	Synthesis of Papaverine . . . . .	804
22.4	Pavine, An Interesting Rearranged Product from Papaverine . . .	805
22.5	NMR Spectral Data of Papaverine . . . . .	806
22.6	Biosynthesis of Papaverine . . . . .	806
22.7	Bioactivity and Uses in Human Health . . . . .	808
	References . . . . .	808
<b>23</b>	<b>Morphine. Codeine. Thebaine: Modified</b>	
	<b><i>Benzyltetrahydroisoquinoline Alkaloids</i> . . . . .</b>	<b>811</b>
23.1	Historical Background, Occurrence . . . . .	811
23.2	Structure Determination . . . . .	813
23.2.1	Oxygen Functions . . . . .	813
23.2.2	Nitrogen Function . . . . .	813
23.2.3	Presence of a Double Bond, Bromination . . . . .	815
23.2.4	Basic Skeleton, Oxygenation Pattern, Part Structures . . . . .	815
23.2.5	Locations of the Ether Oxygen, Double Bond, and Alcoholic OH . . . . .	817
23.2.6	Location of Ethanamine Bridge . . . . .	818
23.3	Synthesis of Morphine . . . . .	820
23.3.1	Retrosynthetic Analysis and Strategy by M. Gates et al. . . . .	820
23.3.2	Synthesis of (±)-Morphine by Gates et al. . . . .	822
23.3.3	Enantioselective Synthesis of (–)-Morphine . . . . .	823
23.3.3.1	Some Comments and Mechanistic Explanations . . . . .	825
23.3.3.2	Mechanism of Inversion in Mitsunobu Reaction . . . . .	825
23.4	Stereochemistry, Relative and Absolute Configuration, Conformation . . . . .	826
23.4.1	Determination of the Relative Stereochemistry at the Chiral Centers . . . . .	826
23.4.2	Absolute Stereochemistry . . . . .	828
23.5	Molecular Conformation of (–)-Morphine . . . . .	829
23.6	<sup>13</sup> C NMR Spectral Data . . . . .	831
23.7	Biosynthesis of Thebaine, Codeine, and Morphine . . . . .	832
23.8	Molecular Rearrangements, Mechanisms . . . . .	834

23.9	Some Bioactive Derivatives of Thebaine Synthesized Through Diels–Alder Cyclization . . . . .	838
23.9.1	Bridged Oripavine Derivatives . . . . .	838
23.9.2	Hetero Diels–Alder Reaction of Thebaine. Unexpected Cleavage of C5–C6 Bond . . . . .	838
23.10	Uses . . . . .	840
	References . . . . .	840
<b>24</b>	<b>Colchicine, A Phenylethylisoquinoline Alkaloid Derived from <i>L</i>-Tyrosine</b> . . . . .	843
24.1	Introduction, Biological Activity . . . . .	843
24.2	Structure, Stereochemistry: Absolute Configuration, Conformation, and Axial Chirality . . . . .	844
24.3	Spectral Data of Colchicine . . . . .	845
24.4	Total Synthesis . . . . .	846
24.4.1	The Pioneering Eschenmoser Synthesis . . . . .	846
24.4.2	Chiral Synthesis of (–)-Colchicine . . . . .	846
24.5	Interconversion of Colchicine, Colchicine, and Isocolchicine . . . . .	848
24.6	Biosynthesis of Colchicinoids . . . . .	848
24.7	Photochemical Reactions of Colchicine . . . . .	851
	References . . . . .	853
<b>25</b>	<b>Quinine. Cinchona Alkaloids (Tryptophan Derived Quinoline Alkaloids)</b> . . . . .	855
25.1	Introduction and Historical Background . . . . .	855
25.2	Structure of Quinine. Some Pertinent Reactions . . . . .	857
25.2.1	Formation of Quinotoxine . . . . .	858
25.2.2	Conversion of Quininone to Ethyl Quinate and Meroquinene . . . . .	858
25.2.2.1	Conversion of Quinotoxine to Quinine . . . . .	859
25.3	Relative and Absolute Stereochemistry of <i>Cinchona</i> Alkaloids . . . . .	860
25.4	Synthesis . . . . .	865
25.4.1	Woodward–Doering Synthesis of Quinine . . . . .	865
25.4.2	The First Stereoselective Total Synthesis of Quinine by Stork . . . . .	867
25.4.3	Other Syntheses of Quinine, Quinidine . . . . .	870
25.5	<sup>13</sup> C NMR and Mass Spectrometry of Cinchona Alkaloids . . . . .	870
25.6	Biosynthesis . . . . .	871
25.7	Uses . . . . .	873
	References . . . . .	873

<b>26</b>	<b>Reserpine</b> . . . . .	875
26.1	Introduction. Occurrence . . . . .	875
26.2	Gross Structure . . . . .	876
26.3	Stereochemistry. Conformation . . . . .	877
26.4	Synthesis of Reserpine . . . . .	878
26.4.1	Woodward's Total Synthesis of Reserpine . . . . .	879
26.4.2	Stork's Synthesis of ( $\pm$ )-Reserpine and (-)-Reserpine . . . . .	884
26.4.3	A Formal Synthesis of ( $\pm$ )-Reserpine by Mehta . . . . .	888
26.5	Biological Activities and Uses . . . . .	889
	References . . . . .	889
<b>27</b>	<b>Strychnine, an Alkaloid with Heptacyclic Dense Molecular Scaffold</b> . . . . .	891
27.1	Introduction. Structure . . . . .	891
27.2	Synthesis . . . . .	892
27.2.1	Enantioselective Synthesis of (-)-Strychnine . . . . .	892
27.2.2	Retrosynthetic Analysis of Kuehne's Synthesis . . . . .	893
27.2.3	Enantioselective Synthesis of (-)-Strychnine by Kuehne and Xu . . . . .	895
27.2.4	Stereoselective Synthesis by Rawal . . . . .	895
27.3	Spectral Data of Strychnine . . . . .	898
27.4	Biosynthesis. Molecular Conformation . . . . .	898
	References . . . . .	899
<b>28</b>	<b>Dimeric Indole Alkaloids. Vinblastine (Vincaleukoblastine), Vincristine (Leurocristine), and Their Derivatives</b> . . . . .	901
28.1	Introduction. Structures . . . . .	901
28.2	Semisynthetic Anticancer Drugs from Vinblastine . . . . .	901
28.3	Synthesis . . . . .	903
28.4	Shortening of Carbon Bridge Between Indole and N <sub>b</sub> . . . . .	905
28.5	Biosynthesis of the Vinblastine-Type Alkaloids . . . . .	906
	References . . . . .	907
<b>29</b>	<b>Camptothecin, A Novel Pyrrolo[3,4-b]quinoline Alkaloid: Derived by Modification of an Indole System</b> . . . . .	909
29.1	Introduction . . . . .	909
29.2	Spectral Data . . . . .	910
29.3	Synthesis of <i>dl</i> -Camptothecin . . . . .	910
29.4	Biosynthesis of Camptothecin . . . . .	911
29.5	Uses . . . . .	912
	References . . . . .	912
<b>30</b>	<b>Some More Alkaloids Having Diverse Skeletal Patterns</b> . . . . .	915
30.1	Introduction . . . . .	915
	References . . . . .	918

<b>31</b>	<b>Important Outcomes of Chemical Studies on Natural Products . . .</b>	<b>923</b>
31.1	Introduction . . . . .	923
31.2	Chromatography . . . . .	925
31.3	Instrumental Analysis . . . . .	925
31.4	Synthesis. Asymmetric (Stereoselective and Stereospecific) Synthesis . . . . .	926
31.4.1	Chemical Phenomena Like Some Reactions, Rules, Degradations, Rearrangements Methodologies, Etc., Emerged from Studies of Natural Products . . . . .	926
31.5	From Studies on Camphor or Related Compounds . . . . .	927
31.5.1	Bredt's Rule (K. Julius Bredt, 1855–1937) . . . . .	927
31.5.2	Wagner (George Wagner, 1849–1903)—Meerwein (Hans Lebrecht Meerwein, 1879–1965) Rearrangement . . . . .	928
31.5.3	Nametkin Rearrangement . . . . .	929
31.5.4	Chiral Auxiliary . . . . .	931
31.6	From Studies on Menthone . . . . .	931
31.6.1	Baeyer–Villiger Oxidation . . . . .	931
31.6.2	Enantioselective Metal-Catalyzed Version of B–V Oxidation . . . . .	933
31.6.3	Microbial Baeyer–Villiger Oxidation . . . . .	933
31.7	From Studies on Quinine . . . . .	934
31.7.1	Skraup Reaction . . . . .	934
31.7.2	A Precursor of Meerwein–Pondorff–Verley (MPV) Reduction . . . . .	935
31.7.3	Some Other Outcomes . . . . .	935
31.8	From Studies on Santonin . . . . .	936
31.8.1	Dienone–Phenol Rearrangement . . . . .	936
31.8.2	Intramolecular Michael Addition . . . . .	937
31.9	From Studies on Coniine . . . . .	937
31.9.1	Hofmann Degradation/Hofmann Elimination . . . . .	937
31.9.2	The Hofmann–Löffler–Freitag (H–L–F) Reaction (Reactions at Nonactivated Carbon Atom Involving Intramolecular H Abstraction by N Radical From $\delta$ - (or 4-) Position) . . . . .	938
31.10	From Studies on Morphine . . . . .	940
31.10.1	Morphine, A Miraculous Pain Killer . . . . .	940
31.10.2	Phenanthrene Chemistry and Pschorr's Synthesis of Phenanthrene . . . . .	940
31.11	From Studies on Colchicine . . . . .	941

31.11.1	Zeisel's Gravimetric Method for Methoxyl Group Estimation and Its Subsequent Modification to a Volumetric Method . . . . .	941
31.11.2	Tropolone Chemistry. Tropylium Ion . . . . .	942
31.12	From Studies on Coumarins . . . . .	943
31.12.1	Perkin Reaction . . . . .	943
31.12.2	Pechmann Reaction . . . . .	943
31.13	From Studies on Steroids . . . . .	944
31.13.1	Diels Hydrocarbon. Se Dehydrogenation . . . . .	944
31.13.2	Barton Reaction (A New Photochemical Reaction for Remote Functionalization) . . . . .	945
31.14	From Studies on Abietic Acid . . . . .	946
31.14.1	Conformational Analysis . . . . .	946
31.15	Biomimetic Synthesis . . . . .	946
31.15.1	Biomimetic Synthesis of Tropolones . . . . .	946
31.15.2	Biomimetic Oxidative Coupling of Phenols . . . . .	947
31.16	From Studies on $\beta$ -Carotene . . . . .	948
31.16.1	Kuhn-Roth Oxidation: Methyl Side-Chain Determination (1931) . . . . .	948
31.17	Woodward-Fieser-Scott Empirical Rules . . . . .	948
31.17.1	Conjugated Polyene Absorptions . . . . .	948
31.17.2	Conjugated Ketone/Aldehyde Absorptions . . . . .	948
	References . . . . .	949
<b>32</b>	<b>Chiral Recognition in Biological Systems and Natural Chiral Auxiliaries . . . . .</b>	<b>953</b>
32.1	Introduction . . . . .	953
32.2	Chiral Discrimination. Enantiomeric Stereospecificity . . . . .	954
32.3	Asymmetric Synthesis In Vivo and In Vitro . . . . .	959
32.4	Resolution by Chiral Ligands. Chiral Recognition . . . . .	960
32.5	Natural Products and Natural Products-Derived Chiral Auxiliaries . . . . .	961
32.5.1	<i>Cinchona</i> Alkaloids as Chiral Auxiliaries. Phase Transfer Catalysis . . . . .	962
32.6	Chiral Organoboranes . . . . .	967
32.6.1	Another Useful Application of (+)-di-3-Pinanylborane . . . . .	968
32.7	Camphor-Derived Chiral Auxiliaries . . . . .	969
32.8	A Few Proline-Derived Chiral Auxilliaries . . . . .	972
32.9	Concluding Remarks . . . . .	972
	References . . . . .	973
<b>33</b>	<b>Natural Products in the Parlor of Pharmaceuticals . . . . .</b>	<b>977</b>
33.1	Introduction. Historical Background . . . . .	977
33.2	Modern Drugs. Ethnotherapeutics. Bioactivity . . . . .	979
33.2.1	Drug Discovery Process . . . . .	985

	33.2.2	Drug Administration and Its Journey to Receptor . . .	986
	33.2.3	Prodrugs . . . . .	987
33.3		Important Terminologies in the Study of Drugs . . . . .	987
	33.3.1	Pharmacophore. Pharmacophoric Pattern, Auxophore, Receptor Map . . . . .	987
	33.3.2	Pharmacokinetics . . . . .	988
	33.3.2.1	Therapeutic Window . . . . .	988
	33.3.3	Pharmacodynamic Phase . . . . .	989
	33.3.4	Toxicology. LD <sub>50</sub> . IC <sub>50</sub> . ID <sub>50</sub> . ED <sub>50</sub> . . . . .	989
	33.3.5	Pharmacogenetics . . . . .	989
	33.3.6	Bioavailability and Bioequivalence . . . . .	989
33.4		Anti-inflammatory, Antipyretic, and Pain Reliever. <u>Aspirin</u> , the Miracle Drug (Baeyer, 1897) . . . . .	990
33.5		Antimalarials . . . . .	991
	33.5.1	Introduction . . . . .	991
	33.5.2	Quinine . . . . .	992
	33.5.3	Artemisinin . . . . .	993
	33.5.4	Probable Modes of Action of Antimalarials . . . . .	995
	33.5.5	Flinderoles A–C . . . . .	995
33.6		Anticancer Drugs . . . . .	996
	33.6.1	Vinblastine, Vincristine, and Semisynthetic Analogues . . . . .	997
	33.6.2	Mechanism of Action of Anticancer Drugs . . . . .	997
	33.6.3	Taxol and Other Taxoids. Their Bioactivity . . . . .	998
	33.6.4	Camptothecins . . . . .	1000
	33.6.5	Colchicine, A Tubulin-Interacting Potential Anticancer Drug . . . . .	1000
33.7		Reserpine . . . . .	1001
33.8		Opioid Analgesic Drugs. Morphine, the Active Principle of Opium, and its Analogues . . . . .	1001
33.9		Huperzine A . . . . .	1003
33.10		Curcumin . . . . .	1003
33.11		Natural Products Affecting the Production of Nitric Oxide . . .	1004
33.12		Natural Products as NF- $\kappa$ B Inhibitors . . . . .	1004
33.13		<i>Aloe vera</i> (Liliaceae) . . . . .	1004
33.14		Flavanoids as Antioxidants . . . . .	1005
33.15		Pharmaceutical Applications of Some Other Drugs . . . . .	1005
33.16		Concluding Remarks . . . . .	1005
		References . . . . .	1005
<b>34</b>		<b>Organic Phytonutrients, Vitamins, and Antioxidants . . . . .</b>	<b>1111</b>
	34.1	Introduction . . . . .	1111
	34.2	Flavors of Some Fruits, Nuts, Beans, and Vegetables . . . . .	1112

34.3	Classes of Common Phytochemicals in Food and Drinks. Their Beneficial Effects . . . . .	1114
34.4	Some Phytochemicals as Radical Scavengers (Antioxidants) . . .	1115
34.5	Resveratrol, an Important Antioxidant Present in Red Wine and Blueberries. Constituents of Red Wine and Other Drinks: Polyhydroxystilbene Derivatives and Flavonoids . . . . .	1116
34.6	Tea, The Most Popular and Wonder Drink of the World. Its Rival Coffee . . . . .	1118
34.7	Vitamins and Related Compounds . . . . .	1120
34.7.1	Vitamin A <sub>1</sub> Formation. The Stereochemistry of Vision . . . . .	1122
34.7.2	Lycopene . . . . .	1124
34.7.3	Vitamin K <sub>1</sub> . Vitamin B <sub>3</sub> . Vitamin B <sub>6</sub> . Folic Acid (Vitamin B <sub>9</sub> ). Vitamin C . . . . .	1125
34.8	Long Chain Polyunsaturated Fatty Acids (LCPUFA): Omega-3- and Omega-6 Fatty Acids . . . . .	1125
34.9	Nitrogen Heterocycles (Indole Derivatives) . . . . .	1126
34.10	Some Constituents (Sulfur Compounds) of Garlic and Onion . . . . .	1127
34.11	Some Active Principles of Several Commonly Used Spices . . .	1128
34.12	Edible Sources of Some Beneficial Phytonutrients . . . . .	1031
34.13	Nutraceuticals . . . . .	1031
34.14	Some Natural Toxins . . . . .	1032
34.15	Some Useful Remarks . . . . .	1034
	References . . . . .	1035
	<b>Erratum to: Chemistry of Plant Natural Products . . . . .</b>	<b>E1</b>
	<b>Appendix A: Brief Life Sketches of Some Pioneers Who Significantly Contributed, Directly or Indirectly, to Natural Products Chemistry . . . . .</b>	<b>1039</b>
	<b>Appendix B: A Chronology of Landmark Inventions/Discoveries Leading Directly or Indirectly to the Development of Natural Products Chemistry . . . . .</b>	<b>1121</b>
	<b>Appendix C: Miscellaneous Helpful Information for Students . . . . .</b>	<b>1141</b>
	<b>Plant Index . . . . .</b>	<b>1151</b>
	<b>Subject Index . . . . .</b>	<b>1157</b>





Chemistry of Plant Natural Products  
Stereochemistry, Conformation, Synthesis, Biology, and  
Medicine

Talapatra, S.K.; Talapatra, B.

2015, LXIII, 1180 p. 1015 illus., 21 illus. in color. In 2  
volumes, not available separately., Hardcover

ISBN: 978-3-642-45409-7