Contents

List of Symbols and Abbreviations XV Introduction XVII

1	General Concepts of Stereoselective Synthesis 1
1.1	Principles of Differentiating Molecules 1
1.2	Characterization of Stereoisomers. Conformation and Configuration
1.3	Intramolecular Symmetry. Topicity and Prochirality 7
1.4	Selectivity in Chemistry 11
1.4.1	Substrate Selectivity 11
1.4.1.1	Substrate Diastereoselectivity (Diastereomer Selectivity) 12
1.4.1.2	Substrate Enantioselectivity (Enantiomer Selectivity). Kinetic Resolution 13
1.4.2	Product Selectivity 17
1.4.2.1	Formation of Stereoisomers 18
1.4.2.2	Conditions Necessary for Stereoselectivity 23
1.4.2.3	Concept of Stereodifferentiation 27
1.4.2.4	Methods for Inducing Stereoselectivity 27
1.4.3	Stereoselective Synthetic Strategies 36
1.4.3.1	Enantioconvergent Synthesis 36
1.4.3.2	Selective Preparation of Both Enantiomers from a Single Substrate 39
1.5	Kinetics and Thermodynamics of Stereoselective Reactions 41
2	Stereoselective Catalytic Reductions 45
2.1	Stereoselective Homogeneous Hydrogenations with Rhodium-,
	Ruthenium- and Iridium-Phosphine Catalysts 45
2.1.1	Hydrogenation of Olefinic Bonds 48
2.1.1.1	Chiral Phosphorus Containing Ligands 48
2.1.2	Enantioselective Catalytic Hydrogenation of Ketones and Imines 66
2.1.3	Diastereoselective Hydrogenations in Homogeneous Phase 68
2.2	Catalytic Hydrosilylation 70



XII	Contents
2.3 2.3.1 2.3.2	Heterogeneous Stereoselective Catalytic Hydrogenations 76 Enantioselective Heterogeneous Catalytic Hydrogenations 77 Diastereoselective Heterogeneous Catalytic Hydrogenations 78
3	Stereoselective Non-Catalytic Reductions 81
3.1 3.1.1 3.1.1.1 3.1.2 3.1.2 3.1.3 3.1.4 3.1.4.1 3.1.4.2 3.1.4.3 3.1.4.4 3.1.5 3.2 3.2.1 3.2.2	Enantioselective Reductions 81 Chiral Lithium Aluminum Hydrides 81 Reduction of Carbonyl Groups 81 Reduction of C=N and C≡C Bonds 88 Chirally Modified Hydridoborates 88 Chiral Boranes and Boronates 90 Enantioselective Reductions with Hydride Transfer from Carbon 92 Chiral Trialkylboranes 92 Chiral Metal Alkyls 94 Chiral Metal Alkoxides 95 Chiral 1,4-Dihydropyridines 95 Correlation of Substrate Constitution and Enantioselectivity 96 Diastereoselective Reductions of Carbonyl Groups 100 Stereochemistry of Diastereoselective Ketone Reductions 101 Practical Aspects of Diastereoselective Ketone Reductions 110
1	Stereoselective Oxidations 123
4.1 4.1.1 4.1.2 4.2 4.2.1 4.2.2	Enantioselective Oxidations 123 Epoxidation with Chiral Oxidants 123 Oxidations in the Presence of Chiral Catalysts 124 Diastereoselective Oxidations 130 Diastereoselective Epoxidation 130 Various Diastereoselective Oxidations 133
5	Stereoselective Carbon-Carbon Bond Forming Reactions by Nucleophilic Addition to Carbonyl Groups 135
5.1 5.1.1 5.1.2 5.1.3 5.2 5.2.1	Addition of Simple Nucleophiles to Carbonyl Compounds 136 Enantioselective Additions 136 Diastereoselective Additions 139 Additions to C=N Bonds 154 Additions Involving Allylmetal and Allylboron Compounds 157 General Aspects of Allylboron Compounds 162

5.2.3	Addition of Allyltitanium Compounds 167
5.2.4	Addition of Allylsilanes 170
5.2.5	Addition of Allylstannanes 173
5.2.6	Addition of Other Allylmetals 175
5.3	Stereoselective Aldol Reactions 177
5.3.1	Stereochemistry and Mechanism of the Aldol Reaction 178
5.3.2	Generation of Enolates and their Addition to Achiral Aldehydes and
	Ketones 184
5.3.3	Addition of Enolates to Ketones (the Cross-Aldol Reaction) 197
5.3.4	Addition of Achiral Enolates to Achiral Aldehydes Under Chiral
	Catalysis 198
5.3.5	Addition of Chiral Enolates to Achiral Aldehydes 200
5.3.6	Addition of Achiral Enolates to Chiral Aldehydes 205
5.3.7	Stereoselective Aldol Condensations 209
5.4	Catalytic Addition of Isonitriles to Aldehydes 210
_	
6	Stereoselective Carbon-Carbon Bond Forming Reactions 213
6. 1	Carbon-Carbon Bond Formation Involving Olefins 213
6.1.1	Addition of Carbanions to Activated Olefins 213
6.1.1.1	The Michael Addition 213
6.1.1.2	Addition of Metalorganics to α,β -Unsaturated Ketones and Esters 218
6.1.1.3	Addition of Metalorganics to α,β -Unsaturated Azomethines and
	2-Vinyloxazolines 224
6.1.2	Allylic Alkylation 226
6.1.3	Stereoselective Hydrocarbonylation 229
6.2	Stereoselective Alkylations 230
6.2.1	Alkylation of Enolates 230
6.2.1.1	Alkylation of Enolates with a Removable Chiral Auxiliary Group 231
6.2.1.2	Diastereoselective Alkylation of Enolates 240
6.2.2	Alkylation of Stabilized Carbanions 241
6.2.3	Alkylation of Enamines and Metallated Azomethines 244
6.2.4	Alkylation of Metallated Hydrazones and Amidines 246
6.3	Enantioselective Grignard Cross-Coupling and Other Stereoselective
	Catalytic Carbon-Carbon Bond Forming Reactions 249
6.3.1	Grignard Cross-Coupling 249
6.3.2	Stereoselective Codimerization of Olefins 251
6.4	Miscellaneous Stereoselective Carbon-Carbon Bond Forming

Reactions 252

XIV	Contents
7	Stereoselective Carbon-Carbon Bond Formation by Pericyclic Reactions 257
7.1	Asymmetric Induction in Cycloadditions 257
7.1.1	Asymmetric Induction in the Diels-Alder Reaction 258
7.1.2	Asymmetric Induction in [3+2] Cycloadditions 268
7.1.3	Asymmetric Induction in [2+2] Cycloadditions 269
7.1.4	Stereoselective Carbene Additions 273
7.2	Chirality Transfer in Sigmatropic Rearrangements 277
7.2.1	[3,3] Sigmatropic Rearrangements 278
7.2.2	[2,3] Sigmatropic Rearrangements 283
7.2.3	Ene Reactions 287
8	Stereoselective Formation of Carbon-Heteroatom Bonds 293
8.1	Stereoselective Formation of Carbon-Nitrogen Bonds 293
8.2	Stereoselective Formation of Carbon-Phosphorus Bonds 296
8.3	Stereoselective Formation of Carbon-Oxygen Bonds 297
8.4	Stereoselective Formation of Carbon-Sulfur Bonds 303
8.5	Stereoselective Formation of Carbon-Halogen Bonds 305
8.6	Stereoselective Protonation and Hydrogen Migration 306

Appendix 311
References 315
General References 357
Subject Index 359