Contents

List of Contributors xi
Preface xiii

1 Principles of Molecular Chirality 1
Jean-Claude Chambron and F. Richard Keene

1.1 General Introduction 1
1.2 Geometrical Chirality 2
   1.2.1 Origins and Description of Chirality within the Rigid Model Approximation 3
   1.2.2 Dynamic and Supramolecular Chirality 18
1.3 Topological Chirality 25
   1.3.1 The Molecular Graph 25
   1.3.2 Topological Chirality 26
   1.3.3 Topologically Relevant Molecules that are not Topologically Chiral 27
   1.3.4 Topologically Chiral Milestone Molecules (Based on Covalent Bonds) 30
1.4 Conclusion 39
References 39

2 Homochirogenesis and the Emergence of Lifelike Structures 44
Pedro Cintas

2.1 Introduction and Scope 44
2.2 The Racemic State: Mirror Symmetry Breaking 45
   2.2.1 Is There a Chiral Ancestor? 47
2.3 Asymmetric Oligomerization 49
   2.3.1 Homochirality and Critical Chain Length 50
   2.3.2 Polymerization Models: Homochiral Peptides 53
   2.3.3 Lessons from Artificial Systems 55
2.4 Biochirality in Active Sites
2.5 Conclusions
Acknowledgements
References

3 Aspects of Crystallization and Chirality
Roger Bishop

3.1 Introduction
3.2 Crystal Space Groups
  3.2.1 Space Group Listing
  3.2.2 Data and Statistics
  3.2.3 Space Group Prediction
3.3 Fundamentals of Crystallization for a Racemic Mixture
  3.3.1 Racemic Compound
  3.3.2 Solid Solution
  3.3.3 Enantiopure Domains
  3.3.4 Conglomerates
3.4 More Complex Crystallization Behavior
  3.4.1 Crystallographically Independent Molecules
  3.4.2 Kryptoracemates
  3.4.3 Quasiracemates
3.5 Multiple Crystal Forms
  3.5.1 Polymorphs
  3.5.2 Solvates
  3.5.3 Hydrates
  3.5.4 Cocrystals
3.6 Conglomerates Revisited
  3.6.1 Frequency of Conglomerate Formation
  3.6.2 Enantiomer Resolution
  3.6.3 Increasing the Chiral Pool
  3.6.4 Chemical Modification
References

4 Complexity of Supramolecular Assemblies
Jonathan A. Kitchen and Philip A. Gale

4.1 Introduction
  4.1.1 Supramolecular Chirality
  4.1.2 Self-Assembly
  4.1.3 Supramolecular Chirogenesis
4.2 Generating Supramolecular Chirality through Assembly
  of Achiral Components
  4.2.1 Supramolecular Chirality – Metallo-Helicates
References
Contents

7.4 Applications of Chiral Coordination Polymers 207
  7.4.1 Enantioselective Catalysis 207
  7.4.2 Enantioselective Separations 208
7.5 Summary and Outlook 209
References 210

8 Chiral Metallosupramolecular Polyhedra 218
  Jack K. Clegg and John C. McMurtrie
  8.1 Introduction 218
  8.2 Basic Design Principles 219
  8.3 Chiral Polyhedra from Achiral Components 221
    8.3.1 Tetrahedra 222
    8.3.2 Higher Order Polyhedra 229
  8.4 Stereochemical Communication 231
    8.4.1 Stereocontrol through Ligand Modification 232
    8.4.2 Mechanisms of Interconversion between Diastereomers 234
  8.5 Resolution of Racemic Metallo-Supramolecular Polyhedra 236
  8.6 Chiral Polyhedra from Chiral Molecular Components 239
  8.7 Conclusions and Outlook 250
References 251

9 Chirality at the Solution/Solid-State Interface 257
  Iris Destoop and Steven De Feyter
  9.1 Self-Assembly at the Solution/Solid-State Interface 257
  9.2 Chirality Expression at the Solution/Solid-State Interface 258
    9.2.1 Enantiopure Molecules at the Solution/Solid-State Interface 258
    9.2.2 Racemates at the Solution/Solid-State Interface 259
    9.2.3 Achiral Molecules at the Solution/Solid-State Interface 261
    9.2.4 Other Factors Influencing 2D Chirality 263
  9.3 Chiral Induction/Amplification at the Solution/Solid-State Interface 266
    9.3.1 Sergeants and Soldiers 266
    9.3.2 Chiral Auxiliaries 269
    9.3.3 Chiral Solvents 272
    9.3.4 Majority Rules 277
    9.3.5 Magnetic Fields 277
  9.4 Towards Applications 278
    9.4.1 Chiral Resolution at the Solution/Solid-State Interface 278
    9.4.2 Enantioselective Adsorption at the Solution/Solid-State Interface 280
  9.5 Conclusions 282
References 282
<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Nanoscale Aspects of Chiral Nucleation and Propagation</td>
<td>285</td>
</tr>
<tr>
<td></td>
<td>Edward G. Latter and Rasmita Raval</td>
<td></td>
</tr>
<tr>
<td>10.1</td>
<td>Introduction</td>
<td>285</td>
</tr>
<tr>
<td>10.1.1</td>
<td>Chirality at Surfaces</td>
<td>286</td>
</tr>
<tr>
<td>10.1.2</td>
<td>Tracking Chiral Nucleation at Surfaces</td>
<td>286</td>
</tr>
<tr>
<td>10.2</td>
<td>Systems of Discussion</td>
<td>288</td>
</tr>
<tr>
<td>10.2.1</td>
<td>System 1: Co-TPP on Cu(110) -- Chirogenesis via Intermolecular Interactions</td>
<td>288</td>
</tr>
<tr>
<td>10.2.2</td>
<td>System 2: Enantiopure and Racemic Mixtures of a Chiral Bis-lactate -- Chiral Segregation Nipped in the Bud</td>
<td>293</td>
</tr>
<tr>
<td>10.2.3</td>
<td>System 3: Tartaric Acid on Cu(110): Highly Nonlinear Chiral Crystallization</td>
<td>298</td>
</tr>
<tr>
<td>10.3</td>
<td>Conclusions</td>
<td>303</td>
</tr>
<tr>
<td></td>
<td>References</td>
<td>304</td>
</tr>
<tr>
<td>11</td>
<td>Chirality in Organic Hosts</td>
<td>307</td>
</tr>
<tr>
<td></td>
<td>Daniel Fankhauser and Christopher J. Easton</td>
<td></td>
</tr>
<tr>
<td>11.1</td>
<td>Introduction</td>
<td>307</td>
</tr>
<tr>
<td>11.2</td>
<td>Chiral Hosts in Analytical Applications</td>
<td>307</td>
</tr>
<tr>
<td>11.3</td>
<td>Chiral Hosts in Asymmetric Reactions</td>
<td>313</td>
</tr>
<tr>
<td>11.3.1</td>
<td>Native Chiral Hosts</td>
<td>315</td>
</tr>
<tr>
<td>11.3.2</td>
<td>Hosts Modified with Achiral Substituents</td>
<td>322</td>
</tr>
<tr>
<td>11.3.3</td>
<td>Hosts Modified with Chiral Substituents</td>
<td>329</td>
</tr>
<tr>
<td>11.3.4</td>
<td>Hosts Modified with Metal-Coordinating Ligands</td>
<td>332</td>
</tr>
<tr>
<td>11.4</td>
<td>Conclusion</td>
<td>337</td>
</tr>
<tr>
<td></td>
<td>Acknowledgements</td>
<td>338</td>
</tr>
<tr>
<td></td>
<td>References</td>
<td>338</td>
</tr>
<tr>
<td>12</td>
<td>Chirality Related to Biocatalysis and Enzymes in Organic Synthesis</td>
<td>343</td>
</tr>
<tr>
<td></td>
<td>Declan P. Gavin and Anita R. Maguire</td>
<td></td>
</tr>
<tr>
<td>12.1</td>
<td>Introduction</td>
<td>343</td>
</tr>
<tr>
<td>12.2</td>
<td>Biocatalysis</td>
<td>344</td>
</tr>
<tr>
<td>12.2.1</td>
<td>Historical Context</td>
<td>344</td>
</tr>
<tr>
<td>12.2.2</td>
<td>Importance of Biocatalysis</td>
<td>344</td>
</tr>
<tr>
<td>12.2.3</td>
<td>Biocatalytic Methodologies</td>
<td>345</td>
</tr>
<tr>
<td>12.2.4</td>
<td>Enzyme Classes</td>
<td>345</td>
</tr>
<tr>
<td>12.2.5</td>
<td>Advantages and Disadvantages of Biocatalysis</td>
<td>346</td>
</tr>
<tr>
<td>12.2.6</td>
<td>Whole Cells/Isolated Enzymes</td>
<td>348</td>
</tr>
<tr>
<td>12.3</td>
<td>Biocatalytic Methodologies: Kinetic/Dynamic Kinetic Resolution and Asymmetric Transformations/Chemoselective Desymmetrizations</td>
<td>348</td>
</tr>
<tr>
<td>12.3.1</td>
<td>Kinetic Resolution</td>
<td>349</td>
</tr>
<tr>
<td>12.3.2</td>
<td>Dynamic Kinetic Resolution</td>
<td>349</td>
</tr>
</tbody>
</table>
12.3.3 Asymmetric Transformations 350
12.3.4 Chemoselective Desymmetrizations 350

12.4 Optimization of Biocatalyst Performance 351
  12.4.1 Organic Solvents 351
  12.4.2 Immobilization 352
  12.4.3 Ionic Liquids 352

12.5 Protein Engineering 352
  12.5.1 Directed Evolution and Semi-Rational Design 354
  12.5.2 Rational Design 355

12.6 Hydrolysis/Reverse Hydrolysis 356
  12.6.1 Hydrolases in Biocatalysis – An Overview 356
  12.6.2 Esterification/Hydrolysis of Esters 358
  12.6.3 Epoxide Hydrolases 363
  12.6.4 Hydrolases in the Resolution of Chiral Amines 363

12.7 Redox Reactions 366
  12.7.1 Cofactors 366
  12.7.2 Reduction of Ketones 367
  12.7.3 Aldehyde Reductions 370
  12.7.4 Reductive Aminations 370
  12.7.5 Reduction of C=C Bonds 373
  12.7.6 Enantioselective Oxidation/Reduction Cascade Reactions 374
  12.7.7 Oxidases 374
  12.7.8 Other Oxidations 376

12.8 C-C and Other C-X Bond Formation 380
  12.8.1 C-C Bond Formation 380
  12.8.2 Halohydrin Dehalogenases 382
  12.8.3 Nitrile Hydratases 383
  12.8.4 Addition of H₂O/NH₃ to C=C Bonds 384

12.9 Future and Outlook 385

References 385

Index 407