Preface

Since the pioneering work of Pasteur, Le Bel and van't Hoff stereochemistry has evolved to a multifaceted and interdisciplinary field that continues to grow at an exponential rate. Today, dynamic stereochemistry plays a fundamental role across the chemical sciences, ranging from asymmetric synthesis to drug discovery and nanomaterials. The immense interest and activity in these areas have led to the development of new methodologies and research directions in recent years. Chirality plays a pivotal role in efforts to control molecular motion and has paved the way for microscopic propellers, gears, switches, motors and other technomimetic devices. The concepts of Euclidian chirality have been extended to topological chirality of fascinating mechanically interlocked assemblies including rotaxanes, catenanes, and even molecular knots or pretzelanes. The impressive advance of asymmetric synthesis has been accompanied by significant progress in stereochemical analysis. Mechanistic insights into isomerization reactions and information about the conformational and configurational stability of chiral compounds are indispensable for today's chemist, and new techniques such as dynamic chromatography and stopped-flow procedures that complement chiroptical and NMR spectroscopic methods have been established. A profound understanding of the stability of chiral target compounds, intermediates and starting materials to racemization and diastereomerization is indispensable for planning an efficient synthetic route. In many cases, interconversion of stereoisomers compromises the efficacy of asymmetric synthesis and ultimately results in the loss of stereochemical purity, but it can also be advantageous. While the usefulness and scope of asymmetric transformations of the first and second kind have been known for a long time, dynamic kinetic resolution, dynamic kinetic asymmetric transformation and dynamic thermodynamic resolution have become powerful synthetic alternatives. Many strategies that afford excellent control of stereolabile substrates and reaction intermediates have been developed and are nowadays routinely employed in the synthesis of a wide range of chiral compounds including natural products. Asymmetric synthesis of complex target compounds generally entails incorporation of several chiral elements in addition to strategic carbon-carbon bond formation. Once molecular chirality has been established it is often necessary to further manipulate it. Numerous methods for selective translocation of a chiral element along an existing carbon framework or interconversion of elements of chirality without loss of stereochemical purity have been introduced and provide invaluable synthetic prospects. Both, the progress and the diversity of stereodynamic chemistry, in particular asymmetric synthesis, are unrivaled and constantly fueled by an enormous amount of new scientific contributions.

Over the last twenty years, several excellent books about asymmetric synthesis have appeared. Traditionally, asymmetric synthesis is discussed based on (1) reaction types, for example aldol reactions, hydroboration, epoxidation, dihydroxylation, hydrogenation, and so on, or (2) emerging concepts such as organocatalysis, biomimetic methods and phase-transfer catalysis. In addition, many reviews on broadly applicable asymmetric catalysts and methods can be found in the literature. While there is no need to duplicate these books and articles, I have felt that a conceptually different textbook that embraces asymmetric synthesis, interconversion of chiral compounds, analytical methods suitable for the study of racemization and diastereomerization reactions, as well as a discussion of topologically chiral assemblies and molecular propellers, switches and motors in the context of dynamic stereochemistry would be very helpful for both teaching and research. Stereoselective synthesis, analysis and stereodynamic properties and applications of chiral compounds are now combined in one text. The book is aimed at graduate students and is intended to serve as a guide for researchers with an interest in synthetic, analytical and mechanistic aspects of dynamic stereochemistry of chiral compounds.

This book is organized into three parts that contain nine chapters and a glossary of important stereochemical terms and definitions. The first chapter provides an introduction to the significance and interdisciplinary character of dynamic stereochemistry. Chapter 2 covers principles, terminology and nomenclature of stereochemistry with an emphasis on Euclidian and topological chirality. The reader is familiarized with stereodynamic properties of chiral compounds and the relative contributions of interconverting configurational and conformational isomers to selectivity, reactivity and chiral recognition. Racemization, enantiomerization and diastereomerization including mutarotation and epimerization are discussed in Chapter 3. Mathematical treatments of reversible and irreversible isomerization kinetics are presented and the wealth of racemization and diastereomerization mechanisms is reviewed separately for each class of compounds to provide a systematic overview. Numerous examples of compounds with individual energy barriers to enantioconversion are given to highlight steric and electronic effects. The principles and scope of analytical techniques that are commonly used to determine the conformational and configurational stability of chiral compounds are discussed in Chapter 4. Special emphasis is given to chiroptical methods, variable-temperature NMR spectroscopy, dynamic chromatography, and stopped-flow analysis.

The second part of this book focuses on asymmetric synthesis. Chapter 5 introduces the reader to the principles of asymmetric synthesis and outlines basic concepts of stereodifferentiation and reaction control. Chapter 6 covers asymmetric synthesis with chiral organolithium compounds and atroposelective synthesis of biaryls and nonbiaryls. This discussion leads to other strategies that are aimed at manipulation of chirality without concomitant racemization or diastereomerization, for example chirality transfer and interconversion of chiral elements during pericyclic rearrangements, S_N2' and S_E2' displacements, and self-regeneration of stereogenicity with temporary or transient chiral intermediates. Synthetic methods that utilize relays and stereodynamic catalysts for amplification of chirality and asymmetric induction link the above topics to the following chapter. Strategies that incorporate stereolabile chiral compounds and intermediates into asymmetric synthesis under thermodynamic (asymmetric transformations of the first and second kind, dynamic thermodynamic resolution) or kinetic reaction control (dynamic kinetic resolution and dynamic kinetic asymmetric transformation) are presented in Chapter 7. Because of the considerable overlap and relevance to some of the above methodologies, kinetic resolutions are also covered in detail. The scope and application spectrum of asymmetric reactions and concepts presented in Chapters 5 to 7 are highlighted with many examples and the stereochemical outcome is explained with a mechanistic rationale including transition state structures whenever possible.

The third part of this book comprises stereodynamic devices, manipulation of molecular motion, and the chemistry of topologically chiral assemblies. Chapter 8 examines the central role that chirality plays in the design of molecular propellers, bevel gears, brakes, switches, sensors, and motors. The synthesis, chirality and stereodynamics of catenanes, rotaxanes and other mechanically interlocked compounds are presented in Chapter 9.

A single monograph can not comprehensively cover the enormous scope and the many facets of dynamic stereochemistry. Topics such as switching and amplification of chirality in polymers, gels and liquid crystals had to be excluded due to limitations of space and time. In writing this book during the last two and a half years, I have tried to adhere to well-defined and established stereochemical terminology and emphasized important limitations and conflicting definitions in the text. To assist the reader, a detailed glossary of stereochemical definitions and terms is included at the end of the book, and a list of abbreviations and acronyms is provided at the beginning. All topics are extensively referenced and the principal researcher is frequently named in the text to encourage further reading and to facilitate additional literature search.

I would like to thank my colleagues, in particular Professors William H. Pirkle and the late Wilfried A. König, and my students for continuing inspiration and helpful discussions. I wish to thank Thomas J. Nguyen for the technical drawings illustrating the conceptual linkage between macroscopic mechanical devices and their molecular analogs. And I am particularly grateful to my wife Julia for her patience, encouragement and understanding during the endless hours involved in writing this book.

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This book is dedicated to
my wife Julia