Cinchona Alkaloids in Synthesis & Catalysis

Nature has inspired scientists for millennia, offering them the necessary tools to accomplish their goals. The field of asymmetric catalytic synthesis has greatly profited from nature's lessons. Proline, for example, is a simple natural amino acid, which has emerged as a general, highly effective catalyst. It has thus challenged the long-held notion that only complex supramolecular structures, such as enzymes, can provide high stereocontrol during catalysis. Just 10 years ago, proline catalysis initiated a new field of research, namely asymmetric organocatalysis, which now pervades a significant part of synthesis.

However, another class of naturally occurring molecules has had an even more lasting and profound impact on asymmetric synthesis, and on organic chemistry in general: the cinchona alkaloids. The role of cinchona alkaloids was firmly established with the discovery of their potential as resolving agents by Pasteur in 1853, while the first example of an asymmetric organocatalytic reaction can be traced back as early as 1912, when Bredig and Fiske reported on the quinine-catalyzed asymmetric addition of HCN to benzaldehyde. Research into the use of cinchona alkaloids in synthesis continued through the last century, including pioneering contributions by Pracejus and, later, Wynberg. These natural compounds and their derivatives have now become established as the most privileged organic inducers of chirality, efficiently catalyzing nearly all classes of organic reactions with a high degree of stereoselectivity.

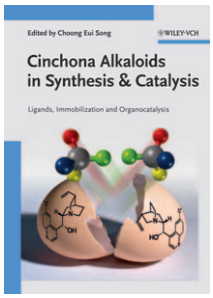
Cinchona Alkaloids in Synthesis & Catalysis, edited by Choong Eui Song, is the first text to comprehensively cover this exciting and very useful area of chemical research. It is rare for a chemistry book to be as timely and sought-after as this one, especially as there are few texts available that deal with specific applications of cinchona alkaloids in asymmetric catalysis. Despite the vast nature of the subject, the book is well organized, covering the whole spectrum of cinchona alkaloids chemistry in a systematic, concise, and clearly written way. Both as a reference source and as an introduction for beginners who wish to contribute to the extraordinary developments in the field, this monograph meets a long-standing need for an up-to-date and comprehensive survey of the subject.

The book is a collection of 13 independent chapters that can be read separately. The most important concepts and trends in the field are discussed with sufficient insight, although, in some cases, an excessively personal view is presented (as in Chapter 6). The editor has secured high-quality authors, leading to critical and insightful descriptions of the topics that are treated. However, in view of the fact that many authoritative researchers from all over the world are actively pursuing these lines of research, a greater diversity of contributors would have benefited the scientific level of the book (the editor, for example, has contributed up to six chapters).

In the introductory Chapter 1, the editor Choong Eui Song provides an interesting historical overview of the application of cinchona alkaloids in chemistry. He then illustrates the importance of conformational investigations for unraveling the "real structure" of cinchona alkaloids in solution, a factor that strongly influences the chirality-inducing and discriminating ability of these alkaloids.

The following three chapters describe the applications of cinchona alkaloids as effective ligands for a variety of metal-catalyzed asymmetric processes. Chapter 2 is an authoritative overview by Blaser of the potential and limitations of cinchona-based chiral auxiliaries for enantioselective reductions, with particular emphasis on preparative and industrial applications. Chapter 3 discusses the application of cinchona derivatives as chiral ligands in asymmetric oxidations, focusing on the famous osmium-based reactions that represent the greatest impact of cinchona alkaloids on modern synthetic chemistry. Chapter 4 illustrates how the multifunctional and easily tunable character of cinchona alkaloids makes them versatile chiral ligands or chiral co-base catalysts for many metal-promoted asymmetric carbon–carbon and carbon–heteroatom bond-forming reactions.

The main part of the book (Chapters 5–11) comprehensively charts the great progress achieved in recent years by using cinchona alkaloids in asymmetric organocatalysis. The topics are illustrated with up-to-date examples (references up to early 2009 are included). The authors distil an enormous amount of information into seven well-structured chapters, each dealing with different types of asymmetric transformations: oxidations and reductions; nucleophilic α-substitutions of carbonyl compounds; asymmetric protonation processes (with a series of critical and insightful discussions on possible developments in this recently emerging field); 1,2-addition to C=O and C=N bonds; conjugate addition to electron-deficient C=C bonds; cycloaddition reactions; and, finally, the desymmetrization of *meso* compounds and the dynamic kinetic resolution of racemic compounds. The authors nicely illustrate the impressive versatility of cinchona alkaloids as organocatalysts, which can provide disparate solutions to the same synthetic issues, attacking challenging problems by using different catalytic modes. These range from phase-transfer catalysis to Brønsted base catalysis, finishing with recently



Cinchona Alkaloids in Synthesis & Catalysis
Ligands, Immobilization and Organocatalysis. Edited by Choong Eui Song. Wiley-VCH, Weinheim 2009. 526 pp., hardcover € 149.00.—ISBN 978-3527324163

reported applications in both enamine and iminium ion activation of carbonyl compounds. The authors' approach nicely highlights the indispensable role of cinchona alkaloids in modern asymmetric catalysis, but this is at the expense of a more critical and rational discussion (in particular, concerning the principles behind the design and development of catalysts).

The last two chapters show that the chemistry of cinchona alkaloids is not limited to the field of asymmetric catalysis, but pervades different aspects of chemical sciences. Chapter 12, entitled "Organic Chemistry of Cinchona Alkaloids", discusses the chemical alterations of the alkaloids' natural scaffolds, which have made possible the direct preparation of important chiral building blocks. Chapter 13 discusses the significant progress in the field of cinchona-based enantioseparation and the use of cinchona alkaloids as enantioselective analytical tools, particularly in modern enantioselective chromatographic techniques. The monograph concludes with a useful appendix, in which the wide variety of cinchona-promoted asymmetric processes discussed throughout the text is surveyed, and provides a fast and straightforward way to visualize the contents of the book.

Cinchona Alkaloids in Synthesis & Catalysis will be warmly welcomed by many researchers, as the use of cinchona alkaloids continues to have a major impact on chemistry research. It represents the first attempt to comprehensively describe the many facets of the chemistry of this privileged compound class, which has been generously provided by nature. Song has succeeded in providing the synthesis community with a high-quality source of teaching materials as well as a useful handbook for scientists working in the exciting and fast-developing field of cinchona-based asymmetric catalysis. This book will be a valuable addition to many libraries, whether personal, academic, or industrial.

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DOI: 10.1002/anie.201000372

