

**Chirality in Drug Research**, by E. Francotte and W. Lindner, Wiley-VCH: Weinheim, **2006**, hardcover, 370 pp, £95/€142.50, ISBN 978-3-527-31076-0

*Chirality In Drug Research* (Volume 33 of the *Methods and Principles in Medicinal Chemistry* series) brings together a range of industrial and academic experts to discuss many aspects of chirality in drug research and development. The book begins with a very nice introduction entitled 'Chiral Drugs from a Historical Point of View.' This gives a whirlwind tour of the history of chiral drugs over the last 5000 years, from natural remedies used thousands of years ago (e.g., februgine, ephedrine, morphine) to more recent homochiral drugs (e.g., fluoxetine, sotalol), touching upon the recognition of chirality, and its importance in drug action and metabolism. The rest of the book is divided into two sections, the first (chapters 2–4) discussing 'Synthesis' and the second, larger section (chapters 5–10) covering 'Separations'.

Chapter 2 gives a fascinating account of the stereoselective synthesis of drugs from an industrial perspective, and is most informative and very well written. It is interesting to note that despite the abundance of homochiral drugs on the market, only a handful of chemocatalyzed enantioselective processes (<20) are known to be operated commercially. As one might expect, asymmetric hydrogenation dominates this area, with the largest commercial application producing more than 10,000 tonnes per annum of product. Chapter 3 seems a little disjointed in comparison, covering various aspects of chirality in natural products chemistry, including methods of determining relative and absolute stereochemistry, mechanisms of stereochemical control in biosynthesis, and the effect of stereochemistry on biological activity. Chapter 4 is another fascinating contribution, discussing the established applications of biocatalysts in the preparation of chiral drugs and intermediates, and later covering recent developments in the area.

The remainder of the book is mainly dedicated to separations of chiral compounds. As a synthetic chemist, I had reservations that this would be less interesting than the synthetic portion of the book, but in general I was mistaken. Resolution via crystallization is discussed in Chapter 5, with the authors drawing on their personal experience in this area, giving a lot of information about the physical aspects of crystallizing enantiomeric compounds. The chapter also includes a very useful table, with examples of diastereomeric salt based resolutions performed in the pharmaceutical industry. The standout chapters in the Separations section detail the 'Isolation and Production of Optically Pure Drugs by Enantioselective Chromatography' (Chapter 6), and 'Stereoselective Chromatographic Methods for Drug Analysis' (Chapter 7). The former be-

gins with a history of the use of chiral stationary phases (CSPs) for enantioseparation, which started in 1904 with attempts to use the optically active polymers wool and silk for separations. It discusses in detail the development and application of CSPs for preparative separations and also includes a table of reported preparative resolutions of racemic drugs and drug intermediates showing the technique employed (e.g., HPLC, MPLC, SMB) and the CSP selected. Pilot-, process-, and manufacturing-scale separations are also discussed, although given the importance of simulating moving bed (SMB) chromatography to this area I would have liked to have seen more detail on this powerful technique. Chapter 7 compliments its predecessor nicely, giving a very well written and in-depth look at chiral analysis, focusing mainly on HPLC. This begins with some discussion of the mechanisms and thermodynamic principles of enantiomeric separations. There is then a large section which describes the different available CSPs, type by type, from the commonly used cellulose- and amylose-based CSPs to more recent developments such as glycopeptide CSPs based on vancomycin and teicoplanin. The scope and limitations of the various CSPs are discussed and the trade names and manufacturers of the various columns are usually given, too.

Unfortunately, the later chapters are a little weaker. Chapter 8 focuses on the relatively recent development of chiral CEMS (capillary electrophoresis mass spectrometry), giving the background, challenges and successes of efforts to couple together these two technologies. Chapter 9 is basically a review focusing on the author's work on the derivatization of racemic alcohols using their own chiral acids, separating the diastereomers and obtaining the absolute configuration using either X-ray diffraction or proton NMR anisotropy. The theory behind these techniques is well presented, but I feel that a more general review of chiral derivatizing agents would have been more valuable than a focused, personal review. The final chapter briefly discusses molecular modeling. It includes some discussion on the different software packages available, although I was surprised that the outdated Chemdraw 6.0 was referenced, given that the latest version is 11.0.

Overall, the strong sections in the book make this a solid text but the weaker sections do let it down a little. Generally the book is written in an engaging way, and the information in the book is well referenced. The price of US\$ 190 means this book will mainly be on the shelves of libraries, where it will provide a useful reference point, with some excellent sections covering certain key areas.

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