

Organic Stereochemistry: Guiding Principles and Bio-Medicinal Relevance

A General Introduction to the Series

by **Bernard Testa**^{*a)}, **John Caldwell**^{b)}, and **M. Volkan Kisakürek**^{c)}

^{a)} Department of Pharmacy, Lausanne University Hospital (CHUV), Rue du Bugnon, CH-1011 Lausanne (e-mail: btesta@vhca.ch)

^{b)} Faculty of Health and Life Sciences, University of Liverpool, Liverpool L69 7ZX, UK

^{c)} Verlag Helvetica Chimica Acta, Hofwiesenstrasse 26, Postfach, CH-8042 Zürich

*‘From asymmetry comes imbalance,
from imbalance comes change,
from change comes becoming,
the emergence of structure’ [1]*

The present issue of *Helvetica Chimica Acta* initiates a general presentation of organic stereochemistry comprising a series of eight reviews (called *Parts*) to be published in succession. The general focus of this Work is twofold:

a) First, a presentation of the guiding principles in organic stereochemistry, priority being given to didactic clarity and nomenclature issues. The first four *Parts* will introduce and illustrate the following topics:

Part 1: ‘Symmetry Elements and Operations, and Classification of Stereoisomers’

Part 2: ‘Stereoisomerism Resulting from One or Several Stereogenic Centers’

Part 3: ‘Other Stereogenic Elements: Axes of Chirality, Planes of Chirality, Helicity, and (*E,Z*)-Diastereoisomerism’

Part 4: ‘Isomerisms about Single Bonds and in Cyclic Systems’

b) These will be followed by four *Parts* focusing on the biomedical relevance of stereochemistry, with special reference to the biochemistry and pharmacology of medicinal compounds. Here, biomedical examples and applications will be discussed and illustrated based on their relevance to a given specific stereochemical aspect:

Part 5: ‘Chirality in Molecular and Clinical Pharmacology’

Part 6: ‘The Conformational Factor in Molecular Pharmacology’

Part 7: ‘The Concept of Substrate Stereoselectivity in Biochemistry and Xenobiotic Metabolism’

Part 8: ‘Prostereoisomerism and the Concept of Product Stereoselectivity in Xenobiotic Metabolism’.

In accord with our biomedical focus, examples and applications will be selected from endogenous and mainly exogenous domains of biochemistry. By endogenous, we mean *physiological chemistry*, in other words, the enzymatic reactions underpinning the normal function of living organisms. But this Work will give particular consideration to *exogenous domains of biochemistry*, namely the molecular interplay between organisms and exogenous compounds. Such compounds (known as ‘*xenobiotics*’) are defined as

the innumerable chemicals (natural and human-made) devoid of normal physiological roles to which all organisms are exposed, namely drugs, agrochemicals, pollutants, natural xenobiotics, and the like. These exogenous domains will include molecular pharmacology and toxicology, and the metabolism of drugs and other xenobiotics. Their significance in current research and technology is huge and increasing, a fact this Work will acknowledge and hopefully promote further.

To avoid misunderstanding, we also need to stress what this Work is *not* about, namely more technical aspects of stereochemistry such as asymmetric synthesis [2], stereoselective analytical and separation methods [3], and issues related to drug development [4] and patentability [5]. The few references given below are just the tip of the iceberg of the many excellent sources available.

The format and layout of these reviews are essentially identical with those of a previous series of seven reviews on the metabolism of drugs and other xenobiotics published between October 2006 and October 2009 by *B. T.* and *Stefanie D. Krämer* in *Chemistry & Biodiversity* [6], and also published in book form in 2008 (Vol. 1) and 2010 (Vol. 2) [7].

Once published in this Journal, the eight reviews will be grouped under a single cover and form the core chapters of a book enriched with additional material.

We wish our readers an enjoyable and inspiring experience!

REFERENCES

- [1] M. Gleiser, 'Tears at the Edge of Creation', Free Press, New York, 2010, p. 248.
- [2] E. M. Carreira, L. Kvaerno, 'Classics in Stereoselective Synthesis', Wiley-VCH, Weinheim, 2009, 651 pp.; 'Asymmetric Synthesis – The Essentials', Eds. M. Christmann, S. Bläse, Wiley-VCH, Weinheim, 2008, 395 pp.; 'Chiral Intermediates', Ed. C. A. Challener, Wiley-VCH, Weinheim, 2004, 828 pp.; P. Vogel, 'Recent Developments in Asymmetric Organic Synthesis: Principles and Examples', in 'Stereochemical Aspects of Drug Action and Disposition', Eds. M. Eichelbaum, B. Testa, A. Somogyi, Springer, Berlin, 2003, p. 3–44.
- [3] 'Chirality in Drug Research', Eds. E. Francotte, W. Lindner, Wiley-VCH, Weinheim, 2006, 351 pp.; S. Rudaz, J. L. Veuthey, 'Stereoselective Separations: Recent Advances in Capillary Electrophoresis and HPLC', in 'Stereochemical Aspects of Drug Action and Disposition', Eds. M. Eichelbaum, B. Testa, A. Somogyi, Springer, Berlin, 2003, p. 45–75; R. D. Shah, L. A. Nafie, 'Spectroscopic Methods for Determining Enantiomeric Purity and Absolute Configuration in Chiral Pharmaceutical Molecules', *Curr. Opin. Drug Discovery Dev.* **2001**, *4*, 764–775; A. Collet, 'Separation and Purification of Enantiomers by Crystallization Methods', *Enantiomer* **1999**, *4*, 157–172.
- [4] C. H. Gu, D. J. W. Grant, 'Physical Properties and Crystal Structures of Chiral Drugs', in 'Stereochemical Aspects of Drug Action and Disposition', Eds. M. Eichelbaum, B. Testa, A. Somogyi, Springer, Berlin, 2003, p. 113–139; M. N. Cayen, 'Racemic Mixtures and Single Stereoisomers: Industrial Concerns and Issues in Drug Development', *Chirality* **1991**, *3*, 94–98; B. Testa, W. F. Trager, 'Racemates versus Enantiomers in Drug Development: Dogmatism or Pragmatism?', *Chirality* **1990**, *2*, 129–133.
- [5] I. Agranat, S. R. Wainschein, 'The Strategy of Enantiomer Patents of Drugs', *Drug Discovery Today* **2010**, *15*, 163–170; C. P. Miller, J. W. Ullrich, 'A Consideration of the Patentability of Enantiomers in the Pharmaceutical Industry in the United States', *Chirality* **2008**, *20*, 762–770; R. R. Shah, S. K. Branch, 'Regulatory Requirements for the Development of Chirally Active Drugs', in 'Stereochemical Aspects of Drug Action and Disposition', Eds. M. Eichelbaum, B. Testa, A. Somogyi, Springer, Berlin, 2003, p. 379–399.
- [6] B. Testa, S. D. Krämer, 'The Biochemistry of Drug Metabolism – An Introduction – Part I. Principles and Overview', *Chem. Biodiversity* **2006**, *3*, 1053–1101; 'Part 2. Redox Reactions and Their

- Enzymes*', *Chem. Biodiversity* **2007**, *4*, 257–405; 'Part 3. Reactions of Hydrolysis and Their Enzymes', *Chem. Biodiversity* **2007**, *4*, 2031–2122; 'Part 4. Reactions of Conjugation and Their Enzymes', *Chem. Biodiversity* **2008**, *5*, 2171–2336; 'Part 5. Metabolism and Bioactivity', *Chem. Biodiversity* **2009**, *6*, 591–684; S. D. Krämer, B. Testa, 'Part 6. Inter-individual Factors Affecting Drug Metabolism', *Chem. Biodiversity* **2008**, *5*, 2465–2578; 'Part 7. Intra-individual Factors Affecting Drug Metabolism', *Chem. Biodiversity* **2009**, *6*, 1477–1660.
- [7] B. Testa, S. D. Krämer, 'The Biochemistry of Drug Metabolism: Principles, Redox Reactions, Hydrolyses', Verlag Helvetica Chimica Acta, Zurich, and Wiley-VCH, Weinheim, 2008, Vol. 1, 319 pp.; 'The Biochemistry of Drug Metabolism: Conjugations, Consequences of Metabolism, Influencing Factors', Vol. 2, 2010, 588 pp.

Received October 14, 2012