Book reviews

Methods and Principles in Medicinal Chemistry (Volume 2): Chemometric Methods in Molecular Design
edited by Han van der Waterbeemd, VCH, 1995. DM 198 (xix + 359 pages) ISBN 3 527 30044 9

There are very few books on chemometrics directed at the QSAR practitioner, so it was with great anticipation that I picked up this volume for review and I was not disappointed. The editor has done an excellent job in identifying the key practical tools required by the modern QSAR expert and in assembling an impressive team of authors to explain their use. Four major topics are covered: derivation of descriptors suitable for SAR studies; exploration of a series with experimental design; series optimization and finally statistical validation.

The book is probably at its weakest in the discussion of the derivation of descriptors. Certain relevant areas are covered well, such as whole molecule and substituent parameters and topological descriptors; but no attempt is made to cover the more interesting topic of 3D spatial parameters, such as those used for comparative molecular field analysis (CoMFA). This omission is excusable as this topic has recently been covered fully elsewhere[1].

The chapters on experimental design are well written and informative, and some very good practical guides for the synthetic chemist are provided. However, it becomes evident on reading that we are still at an early stage in our understanding of how to design the best set of compounds for synthesis. The importance of such designs is explained, as are the statistical techniques to be used. However, the selection of the best parameters to employ in designing a set of compounds is still not fully understood. This is a big problem, but the reader is left with the impression that it is one that cannot be ignored by the drug designer.

The book is very strong in its treatment of series exploration and optimization, covering not only the derivation of a quantitative model, but also the search in data for patterns that may be useful to guide drug design. Hansch analysis is given superficial coverage (this area is reviewed fully in the first volume of the series[2]), and the book concentrates instead on the more recent advances of principal components and factor analysis, partial least squares (PLS), non-linear mapping, cluster analysis, discriminant analysis and pattern recognition. Most of these chapters explain each topic simply, although a statistical knowledge is required, and are exemplified with practical examples.

Finally, the section on statistical validation, which is written by the recognized leading experts in the field, is a fitting crescendo for the book and should be required reading for any scientist embarking on QSAR.

This book is a healthy mix of theory and practical examples and is almost a QSAR practitioner's manual. It should be widely read by computer-aided drug designers and the more mathematically minded medicinal chemists; it is highly recommended.

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REFERENCES

1 Kubinyi, H. (1993) *3D QSAR in Drug Design, Theory, Methods and Applications*, ESCOM
2 Kubinyi, H. (1996) *Methods and Principles in Medicinal Chemistry: QSAR: Hansch Analysis and Related Approaches* (Vol. 1), VCH

Classics in Total Synthesis: Targets, Strategies, Methods
edited by K.C. Nicolaou and E.J. Sorensen, VCH, 1996. DM 78 (xxii + 798 pages) ISBN 3 527 29231 4

Classics in Total Synthesis is a thorough compilation and an in-depth discussion of some of the pioneering achievements in natural products synthesis of the past four decades. Natural products synthesis is a multifaceted discipline that integrates synthetic organic methodology with transition-metal and inorganic chemistry. The daunting task of covering such a topic is successfully executed by Nicolaou and Sorensen. They provide a historical perspective underpinning the text and highlight advances in synthetic methods that are coupled with parallel leaps in synthetic strategy.

The book offers a detailed and scholarly description of the construction of 36 important natural products commencing with the 1954 strychnine synthesis by Woodward and closing with the 1995 synthesis of brevetoxin by Nicolaou. For each of the targets, the authors delineate the biological and structural features that define each molecule as an important candidate for total synthesis. Following these introductory comments, a retrosynthetic analysis is presented that provides intellectual grounding for the ensuing detailed description of the synthetic scheme. A discussion of methodology that defines the successful synthetic strategy is included within each chapter. This particular aspect of the book is noteworthy and highly informative. In addition, the individual syntheses have been selected as case studies that serve to highlight revolutionary advances in synthetic methodology, including cyclic, acyclic and macrocyclic stereocontrol as well as asymmetric catalysis,