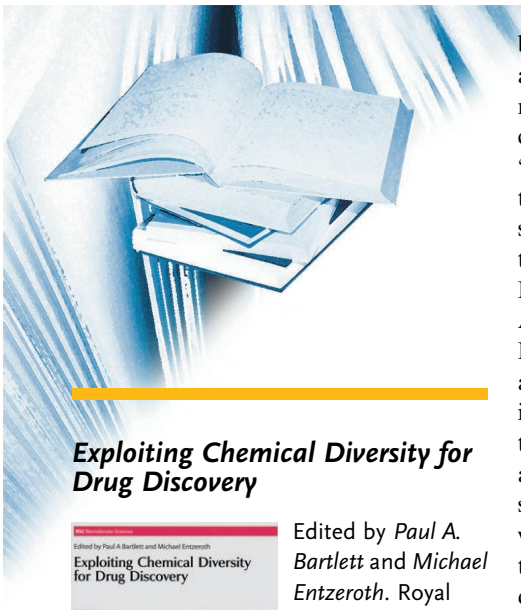

Exploiting Chemical Diversity for Drug Discovery

Edited by *Paul A. Bartlett* and *Michael Entzeroth*. Royal Society of Chemistry, Cambridge 2006. 402 pp., hardcover £119.95.—ISBN 0-85404-842-1

The task of distinguishing between significant innovations and trendy novelties at an early stage is a difficult one that is of practical concern in medicinal chemistry. It is especially important for scientists who have to make tactical decisions about the integration of new developments into their toolkit to overcome the various bottlenecks in the way of drug discovery. Reading *Exploiting Chemical Diversity for Drug Discovery* might help them to come to the right decisions faster. This book provides a timely and comprehensive overview of state-of-the-art developments in the diverse scientific and engineering disciplines that contribute to the identification of biologically active compounds.

The thoughtful preface to the book discusses the difference between conceptual and operational inventions, and emphasizes the value of information-rich high-content screening as opposed to mere data acquisition in the context of high-throughput screening.

The 17 chapters that follow, written by well-known experts from academia and industry cover the many components of the drug discovery process. The chapters are organized in five sections: "Operational Developments in Chemistry"; "Conceptual Advances in Synthesis"; "Prospecting and Mining"; "Operational Developments in Screening and High Throughput Assays"; "Conceptual Advances in Lead Evaluation: Screen Early and Often". The topics thus addressed include the design of chemical libraries and methods for optimizing their diversity, automated and accelerated chemistry such as polymer-assisted solution-phase synthesis and microwave-enhanced fluorous-phase chemistry, high-throughput assay design and detection techniques, and strategies for data analysis and property optimization, including prediction of properties. This clear organization by the editors is the key to effective reporting of the material and achieving a balanced proportion of the individual topics.

Does the book succeed in describing a standard operational procedure to discover blockbuster drugs? Because therapeutic products on the market are either atrociously complex in structure or look incredibly simple, with everything in-between (as discussed by A. Ganesan in his chapter), there is little hope of finding a single blueprint for this challenging endeavor. But the novel arsenal of tools described in this book, such as combinatorial chemistry, or aspects of structure-based design (use of crystallography or NMR spectroscopy for structure-based drug design, molecular modeling, fragment screening) might result in synergistic improvements if used wisely. Ways of achieving that are discussed in the chapters of the book, on the basis of recent examples and the authors' own rich experiences. These include iterative structure-based screening of virtual chemical libraries and the application of isoform specificity in the design of selective receptor modulators. These are also combined with personal thoughts, viewpoints, and comments that the authors may have given as a communication at a congress banquet, but are hardly to be found in a research paper. This is often helpful and refreshing. In Chapter 4.5, A. Ganesan asks the stimulating and entertaining question: "Are certain scaffolds privileged because they are heavily explored, or do they inherently possess favorable characteristics for the discovery of new drugs?" From his point of view, he concludes that both explanations appear equally likely, and that one of the greatest achievements of combinatorial chemistry is the testing of this hypothesis by the exploration of relatively uncharted chemical space.

The book is an excellent and astonishingly complete compilation on this broad and demanding topic for current practitioners. Researchers in organic and medicinal chemistry, and in biological and pharmacological sciences, as well as those interested in allied computational and engineering disciplines, will benefit from the up-to-date coverage, which is illustrated in full color. Many details, for example, a list of providers of compound collections in Chapter 5, make this publication suitable as a handbook, a unique source of information even for beginners in the field. The book includes literature references (sometimes with too many typographical errors) and an insufficient index, but it might be too rich in information content for students in the early phase of their education. Some minor mistakes, such as the occasional wrong use of retrosynthetic arrows, and inconsistencies in the quality of structural figures (e.g., incorrect bond angles) may be attributed to the general weaknesses of multi-author books. In this case, however, the high quality of the individual chapters definitely outweighs those deficiencies.

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