Modern Drug Synthesis

The discovery and development of a new drug is today a long process whose cost is increasing exponentially with its progress and has recently been estimated to vary from US$ 800 million to nearly US $2 billion. It is also a high-risk activity with still growing failure rates in clinical phase II and III, as a consequence of lack of efficacy or safety issues. Obtaining the approval for a drug is therefore a challenge in which medicinal chemists play a crucial role at each stage. This role, however, has evolved within the last decades and the conception of a drug candidate now requires several skills that are beyond a strong background in organic chemistry. In order to identify lead structures likely to reach the market, the chemists must now have a broad knowledge of biology and pharmacology with respect to the therapeutic targets, and pay careful attention to pharmacokinetic properties as well as to toxicology.

The book *Modern Drug Synthesis*, edited by Jie Jack Li and Douglas S. Johnson, perfectly mirrors this evolving role and the necessity for medicinal chemists to encompass these domains. It covers in details 21 successful stories written by experts from several industrial R&D laboratories and academia. The drugs in question have generally been launched in the 2000s with, as an evidence for the latest developments reported therein, the story of Vernakalant approved in September 2010 in Europe for the treatment of atrial fibrillation. This book also focuses on hot topics in medicinal chemistry such as the development of kinase inhibitors against cancer or the search of dipeptidyl peptidase IV inhibitors for the treatment of type 2 diabetes, whereas the review of either first-in-class drugs or second-generation therapeutics allows a broad survey of the drug discovery phase. However, should the authors plan to publish a fourth edition of the book, the coverage of stories emphasizing more explicitly the significance of natural products as a source of marketed drugs, for example, with the recently approved Halaven or Yondelis, is suggested.

Compared to the previous monographs by the same editors—*Contemporary Drug Synthesis* and *The Art of Drug Synthesis*—this book is more organized, being divided in five sections each devoted to a major type of diseases, i.e. infectious diseases (exclusively HIV/AIDS), cancer (particularly through the overview of three kinase inhibitors), cardiovascular and metabolic diseases, CNS diseases, and others.

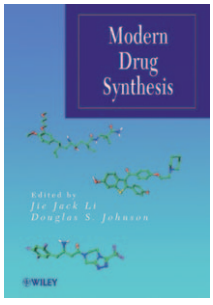
With the exception of one or two chapters, all of them follow a common outline. A first paragraph provides general information such as some facts and figures about the disease in question, the relevant biological targets of therapeutic interest and the molecules already on the market. These are helpful to clarify the context in which the present drug has been approved. The following parts then introduce key aspects of medicinal chemistry, that are, successively, the mechanism of action of the drug, the optimization through SAR studies which has culminated in the structure of the lead compound, and the issues of absorption, distribution, metabolism, and excretion. Once again, in order to improve the *Drug Synthesis Series*, it could be more educational to illustrate the mechanisms of action with schemes, whereas it would be worth briefly explaining specific key terms with which organic chemists are not familiar. This can also apply to the paragraph where efficacy and safety, both evaluated in clinical phases II and III, are discussed.

The final sections, generally the largest part of each chapter, then focus on the syntheses. The latter are described with ample experimental details and include several cautionary notes on the procedures underscoring the issues encountered and the solutions found to circumvent them. These paragraphs are therefore crammed with invaluable information for chemists. Moreover, a relevant choice of the drugs discussed therein showcases the impact of catalytic asymmetric synthesis in drug synthesis. But more significantly, these surveys provide, in many cases, the presentation of either discovery or first-generation syntheses followed by a discussion of the advantages and shortcomings that have been taken into consideration for the development of the manufacturing method. The parallel drawn between these approaches gives insights into the hurdles that need to be overcome during the scale-up of a laboratory synthesis. Each chapter ends with an updated list of references, generally up to 2009.

In conclusion, *Modern Drug Synthesis* is definitely an improved version of the previous monographs edited by the same authors, with an educational presentation that provides a good snapshot of modern medicinal chemistry. As such, it will be a very useful book to lecturers who could illustrate, with recent successful stories, all the stages through which a molecule must pass before turning into a drug. The unique analytical overview of the evolution of a drug synthesis according to the phase of development also makes this book highly valuable not only for students but also for research scientists in academia or industry, involved in drug discovery or process chemistry.

Philippe Dauban
Institut de Chimie des Substances Naturelles
CNRS, Gif-sur-Yvette (France)

DOI: 10.1002/anie.201101165



Modern Drug Synthesis
Edited by Jie Jack Li and Douglas S. Johnson. John Wiley & Sons, Hoboken 2010. 356 pp., hardcover, € 95.90.—ISBN 978-0470525838