Book Reviews

The Organic Chemistry of Drug Design and Drug Action. Second Edition. By Richard B. Silverman. Elsevier Academic Press, London. 2004. xix + 617 pp. 19 × 27 cm. ISBN 0-12-643732-7. $80.00.

The second edition of "The Organic Chemistry of Drug Design and Drug Action" is an updated and expanded version of the original edition. While the intent of the first edition was to provide a textbook for advanced undergraduate students or graduate students, the scope of the second edition has been expanded so that it not only serves the original purpose but also serves as an excellent reference book for practicing medicinal chemists. As the title indicates, this book is written from the perspective of organic chemistry, which is the foundation underlying drug discovery, so it will nicely complement other organic chemistry courses taken by students.

While the book is built on organic chemistry, it is primarily organized around molecular targets (receptors, enzymes, DNA). There are also chapters on lead identification, drug metabolism, and drug delivery. Most concepts are illustrated with examples of marketed drugs, which adds a practical dimension to the discussions. The book is not meant to be an exhaustive review of any given area, but numerous references are provided so that additional details can readily be found. Detailed case studies are used in many of the chapters to summarize the concepts introduced earlier. Some specific examples of topics in the book are discussed below.

The section on combinatorial chemistry in Chapter 2 is of historical interest but does not really reflect the current practice in most pharmaceutical companies, which have shifted to smaller arrays prepared by parallel synthesis. The lead modification strategies in Chapter 2, in particular the table of bioisosteres and the Topliss decision tree, should serve as a valuable reference for practicing medicinal chemists. In Chapter 3, the cimetidine case study brings together many of the concepts introduced earlier and illustrates the importance of physical organic chemistry principals for lead optimization. Chapter 5 includes numerous examples of the design and optimization of enzyme inhibitors. The case study on ritonavir also introduces the importance of ADME properties in lead optimization. Finally, the section on bioprecursor drugs in Chapter 8 is a useful reminder that it is not always necessary to block metabolism in order to develop a useful drug.

In summary, this book is a thorough overview of drug discovery and development from an organic chemistry perspective. It is not only an excellent textbook for students but also a valuable resource for those already practicing medicinal chemistry.

John W. Ellingboe

Wyeth Research
401 North Middletown Road
Pearl River, New York 10965

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