Book Reviews

Handbook of Pharmaceutical Salts: Properties, Selection, and Use. Edited by P. Heinrich Stahl and Camile G. Wermuth. VHCA, Verlag Helvetica Chimica Acta, Zürich, Switzerland, and Wiley-VCH, Weinheim, Germany. 2002. vix + 374 pp. 17.5 × 24.5 cm. ISBN 3-906390-26-8. $130.00

Most drug molecules employed in medicinal therapy are administered as salts. When organic chemists choose a particular salt form, the decision is often made on the basis of ease of handling. However, as this text emphasizes, medicinal chemists must consider numerous other properties when selecting a particular salt for use as the active pharmaceutical ingredient. Solubility, stability, bioavailability, the common ion effect (particularly for hydrochloride salts), formation of solvates or polymorphs, potential for ion-pairing, toxicity, local irritation, and sensitization as well as potential for corrosion of manufacturing equipment must all be taken into consideration. Prior to publication of this handbook, there was no one text the novice medicinal chemist could consult for information about the critical decisions that are involved in the selection of appropriate salts for development. Here, one can find a systematic strategy for selection of the optimal salt forms for acidic and basic drugs. Very useful specific case histories are provided that illustrate the decision process involved in salt selection. In some instances, as the authors point out, salt formation is not feasible, e.g., if the pK_a of the conjugate acid is larger than the pK_a value of the conjugate base. When proton transfer cannot occur from the acidic to the basic species, it is futile to attempt salt formation.

A chapter written by the editors contains many useful hints on practical aspects of preparing salts and cites examples from the patent literature. Experienced chemists know that in preparing hydrochloride salts employing ethereal hydrogen chloride, it is often observed that the hydrochloride initially formed redissolves. This is due to the fact that the reagent produces the very polar ethyloxonium chloride that solubilizes the initially precipitated hydrochloride. Where else can one find this kind of information?

The editors also contributed a chapter that provides monographs on the acids and bases used to prepare salts. It includes information such as pK_a values, properties, safety and toxicology, and specific examples of salts and their applications. There are also useful chapters on the evaluation of solid-state properties, large-scale processing, and patent and regulatory aspects.

This handbook includes both a subject index and a substance index. The emphasis is on the practical. For those interested in a more theoretical approach, I would recommend Butler and Cogley's text, "Ionic Equilibrium: Solubility and pH Calculations". Some readers will find the syntax to be rather awkward in places. The majority of the authors and the editors are European. However, this in no way detracts from the overall value of the text. It makes interesting reading and I recommend it highly.

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Drug Design. Cutting Edge Approaches. Edited by Darren R. Flower. Royal Society of Chemistry, Cambridge, U.K. 2002. x + 192 pp. 16 × 24 cm. ISBN 0-85404-816-2. £59.50

It is one of life's pleasures to return to a field that you once knew intimately and to note what astonishing progress has been made in your absence. This compact little book from the Royal Society of Chemistry packs a lot into its 192 pages, not the least of which is an insightful preface by the editor Darren Flower. It is the fruit of the first of a series of one-day meetings inaugurated in March 2001 by the Royal Society of Chemistry to address molecular informatics in drug design, which involved several renowned speakers from both British academia and the international pharmaceutical industry. Some of them were unfortunately unable to contribute to the book, but their lecture topics are reviewed by other contributors including three by the editor. There are only eight chapters, covering an introduction to molecular informatics, high-throughput X-ray crystallography, virtual techniques for lead generation and optimization, identification and modeling of G-protein receptors, physical organic chemistry in drug design, and computational vaccine design. The book is liberally illustrated, with many black and white drawings and photographs as well as numerous chemical structures. There is a brief but adequate subject index. Despite excellent references from 1833 through 2002, there is no author index.

The stated aim of the proceedings from these Royal Society of Chemistry meetings is to balance technical accuracy with accessibility and readability for the nonspecialist. However, while most chapters are less than 20 pages, the balance of the book is uneven; one chapter is as short as 7 pages and others are around 50 pages, leaving one with a strange sense of being alternately under- and overwhelmed. Thus, Darren Flower's long introduction to molecular informatics is delightfully easy to read and is full of useful tips and historical anecdotes, but his concluding and only marginally shorter contribution on computational vaccine design is hard-going. The shortest chapter, by Tom Blundell on high-throughput X-ray crystallography, cries out for a longer discussion of an important topic for drug discovery. Nevertheless, the book represents a highly educative and informative trawl through many of the latest techniques to be used for lead finding and

drug design. A nice touch is the constant use of actual examples to demonstrate the utility and limitations of the various methods. Focused diversity and virtual libraries may now be replacing the earlier utopian vision of potentially endless structural variations that combinatorial chemistry appeared to offer (10^{30} "druglike" molecules have been suggested), while virtual screening is supplementing high-throughput screening. The book is useful reading for all involved in drug discovery, be they medicinal chemists or biologists, and is an ideal primer for busy research directors. It is cheap, although the declining dollar makes it less so by the day. The second Royal Society of Chemistry meeting on this topic has already been held, and another is planned. One of the good things is the availability of all information at the Royal Society of Chemistry's Web site.

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