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BOOK REVIEWS

Progress in the Chemistry of Organic Natural Products, Volume 87. Edited by W. Herz (The Florida State University, Tallahassee, FL), H. Falk (Johannes-Kepler-Universität, Linz, Austria), and G. W. Kirby (The University of Glasgow, Scotland). Springer-Verlag: Wien, New York. 2004. viii + 262 pp. $219. ISBN 3-211-02780-7.

Volume 87 in this continuing series contains two chapters that present interesting contrasts. Chapter 1, "Cepalostatin Analogues − Synthesis and Biological Activity" by Flessner, Jautelat, Scholz, and Winterfeldt, focuses on the chemical modifications of cephalostatin analogues as published in the literature up to early 2002. The cephalostatins are complex bis-steroids in which the two steroid units are annulated to a 1,4-pyrazine ring. Interest in this group of marine natural products, first reported in 1988, stems from the potent inhibition of the growth of tumor cells exhibited by the first member of this series, cephalostatin 1, as well as the unique spectrum of activities shown by this compound (and other cephalostains and structurally related ritterazines) in the NCI in vitro cell panel. The difficulties associated with obtaining sufficient quantities of these marine natural products from their natural sources have prompted several groups to undertake projects in both total and analogue syntheses. The Winterfeldt group has succeeded in preparing multigram quantities of cephalostatin analogues of varying compositions in pursuit of SAR data that will point the way to the preparation of clinical candidates. Although some structural features necessary for high activity are indicated from the SAR data, there still remains much to be learned. The activity patterns of these analogues in the NCI tumor panel suggest strongly that the cephalostatins and ritterazines have a unique biological mechanism of action. At the time this chapter was written, there were no published data on the mode of action of these compounds. However, research reported in late 2003 (Dirsch, V. M.; Müller, I. M.; Eichhorst, S. T.; Pettit, G. R.; Kamano, Y.; Inoue, M.; Xu, J.-P.; Ichihara, Y.; Wanner, G.; Vollmar, A. M. *Cancer Res*. **2003**, *63*, 8869−8876) showed that cephalostatin 1 indeed induces apoptosis by a novel mechanism affecting mitochondrial function. Thus, the path to further advances in drug development for the cephalostatins may now be clear.

The second chapter of the book, "Siderophores of the Pseudomonadaceae *sensu stricto* (Fluorescent and Non-Fluorescent *Pseudomonas* spp.)" by Budzikiewicz is a *tour de force*, chock-full of interesting and varied information. *Pseudomonas* bacteria are among the most important, and Budzikiewicz takes us through their many facets in an engaging and highly stimulating manner, from their roles (both good and bad) in medicine to agriculture and environmental sciences. This account takes us from late 19th century microbiology of *Pseudomonas* to present day molecular biology of the production and function of the iron transport siderophores produced by these bacteria. The focus is on the pyoverdins, polypeptide siderophores that contain an 8,9-dihydroxy-1*H*-pyrimido-[1,2-a]quinoline fluorescent chromophore. These catechol-fused heterocyclic polypeptides are produced by *Pseudomonas* under iron-limiting conditions to enable the bacteria to acquire iron from its environment. The breadth of coverage of the pyoverdins includes structural analyses (NMR and MS, but only one X-ray diffraction analysis has been reported), synthetic efforts (few thus far), metal complexation, biosynthesis, mechanisms of membrane transport, and production of other closely related siderophores by specific species of *Pseudomonas*. About one fifth of the chapter is devoted to descriptions of other siderophores produced by fluorescent *Pseudomonas*, along with general discussions of iron sequestering and *Pseudomonas* in health, agriculture, and the environment. Budzikiewicz has critically reviewed the extensive literature (∼600 references ending in September 2003) on this subject, correcting a number of errors and bringing together the vast and diverse literature in this area.

Overall, the quality of this book is good, although the first chapter has many typographical errors that should have been corrected by English-speaking editors. As is often the case, the price of the book will probably put it out of the range of most, but certainly it should be found on the shelves of all chemistry libraries.

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Advances in Antiviral Drug Design, Volume 4. Edited by E. De Clercq (Katholieke Universiteit Leuven). Elsevier B. V.: Amsterdam. 2004. xii + 218 pp. $119.95. ISBN 0-444-50602-0.

Research on antiviral drugs is a rapidly evolving field. Beginning with the first publication in 1993, the four volumes in this series cover most of the key topics in this critical area of modern medicinal chemistry. All six chapters in the current volume are up-to-date, interesting reading, and written by experts on each subject. Specialists will find some chapters more interesting than others, because the chapters vary considerably in principal focus, comprising synthetic chemistry, medicinal chemistry, pharmacology, or clinical drug development.

The first chapter on "New Anti-HIV Agents in Preclinical or Clinical Development" is written by the editor, who is a recognized authority in this area. It is an excellent overview of current advances in the clinic and the laboratory. Not only does this review thoroughly cover drugs acting by conventional mechanisms, such as reverse transcriptase and protease inhibition, it also details agents operating by novel mechanisms. There is very little overlap with the brief second chapter by Hazuda and Young entitled "Inhibitors of Human Immunodeficiency Virus Integration", which covers only one class of such agents, the 4-aryl-2,4-diketobutanoic acids. Only seven of the 230 references in the previous chapter cite publications on these

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integrase inhibitors. Similarly, the chapter by Mayers, Curry, Kohlbrenner, and McCallister on "Non-peptidic Protease Inhibitors (NPPIs): Tipranavir" deals only with the title compound and details formulation, pharmacodynamics, pharmacokinetic profile, viral resistance, and results of clinical trials.

A highlight of the volume is the chapter by Gilead co-workers Jin and Kim entitled "Design of Neuraminidase Inhibitors as Anti-Influenza Virus Agents". This is an excellent description of the medicinal chemistry of an important new class of antiviral drugs based on enzyme X-ray structures and structure−activity relationships. It minimizes overlap with other recent reviews on this subject by tracing the development of new neuraminidase inhibitors containing cyclopentane and pyrrolidine rings. The fifth chapter on "Six-Membered Carbocyclic Nucleosides" by Wang, Froeyen, and Herdewijn will be primarily of interest to organic chemists, because it details the syntheses of experimental drugs in 20 schemes and describes biological activities of only a few agents. The final, lengthy chapter by Meier entitled "*cyclo*Sal-pronucleotides - Design of the Concept, Chemistry and Antiviral Activity" details the unique approach to nucleoside monophosphate prodrugs involving masking phosphate anions as neutral *cyclo*-saligenyl esters, which are hydrolyzed nonenzymatically at the site of action.

While this book does not comprehensively cover all current developments in antiviral drug studies, it provides very useful information and it is thorough in some areas. Though brief, the three-page index enhances the utility of this work. The volume will prove a valuable addition to the personal collections of many medicinal and some organic chemists, and it should be an essential acquisition for complete libraries in academic institutions and pharmaceutical companies.

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100 Years of Physical Chemistry: A Collection of Landmark Papers. Royal Society of Chemistry: Cambridge. 2003. viii + 376 pp. $159.00. ISBN 0-85404-987-8.

This book celebrates the centennial of the founding of the Faraday Society in 1903 and consists of 23 memorable papers that have been published over the past 100 years from Faraday journals: *Transactions*, *General Discussions*, and *Symposia*. Each paper was selected by an expert in the general area of the topic covered and is preceded by a brief commentary by that expert describing how the paper influenced the development of the field as well as his or her own work. For example, Buckingham comments on "The general theory of molecular forces" by London; Phillips comments on "Picosecond-jet spectroscopy and photochemistry" by Zewail; and Luckhurst comments on "On the theory of liquid crystals" by Frank. The book does not include a subject or author index.

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