Book Reviews

Emerging Drugs: The Prospect for Improved Medicines. Edited by Andrew Lynch. Ashley Publications, Ltd., London. 1999. 365 pp. 21 x 28 cm. ISSN 1361-9195. $865.00.

This series is similar in concept to *Annual Reports in Medicinal Chemistry* in that it consists of reviews of drug discovery in various drug classes. In general, the book comprises authoritative discussions written by both industrial and academic experts. Unlike *Annual Reports*, the chapters are presented in random order instead of broad categories, the book is uniformly typeset rather than consisting of offset printed manuscripts, and the price of the volume is too high to put a personal copy within reach of many scientists.

The volume consists of 20 chapters that discuss TNF antagonists, hepatitis antivirals, Alzheimer's medicines, antiepileptics, tryptans, antipsychotics, melatonin agonists and antagonists, antithrombotics, antiplatelets, PARP inhibitors, aquaretics, cancer vaccines, gene therapy, narcolepsy, osteoarthritis agents, male contraceptives, antipsoriatics, antiglaucoma agents, and monoclonal antibody therapeutics. It begins with a foreword that offers a historical "perspective" so anglocentric and inaccurate as to give one concern about the reviews that follow. Ehrlich, not Hoffman and Perkin, laid "the foundations for drugs by chemical synthesis", and it was prontosil, not sulfanilamide, that Domagk found to protect rabbits and mice against coccal infections in 1932. However, the remaining chapters are generally very good.

Most of the chapters follow a standard format that begins with a useful summary, discusses the background and scientific rationale germane to the subject, and usefully considers the medical need and existing treatments of the therapeutic area. This is followed by a discussion of current research goals, a topic that is subdivided into the individual therapeutic modalities. Potential developmental issues and available animal models are further thoughtful discussions presented in many chapters. Many reviews end with a very helpful editorial analysis that considers the most important issues that have been presented. An excellently presented bibliography at the end of each chapter highlights references of special note with one asterisk (of interest) or two asterisks (of considerable interest); a one- or two-sentence summary is provided for these highlighted references.

The completeness of the best presentations can be judged from the number of references and structures in the review entitled "Emerging strategies for the treatment of Alzheimer's disease at the Millennium" by a group of authors from Parke-Davis. This chapter contains 303 references, many from 1998, and more than 60 structural formulas. Most reviews are shorter, but in general, their quality is extremely high.

The book is well-produced although one might have expected a hardcover at this price; the typographic presentation is very clear in the text, tables, and formulas. A glossary at the end of the volume decodes the "alphabet soup" of abbreviations that we all have to deal with today, and an author index, a therapeutic index, and a company/university index are provided.

This book is strongly recommended for acquisition by industrial, institutional, and academic libraries serving scientists and technology executives engaged in drug discovery.

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Principles of Process Research and Chemical Development in the Pharmaceutical Industry. Edited by David J. Ager. Marcel Dekker, Inc., New York. 1999. x + 382 pp. 16 x 24 cm. ISBN 0-8247-1058-4. $165.00.

At a time when pharmaceutical company pipelines are averaging greater than 75% chiral drug candidates, the publication of this important contribution, which focuses on the commercial-scale production of chiral compounds, is both timely and most welcome. The reality is that most of the methodologies employed for the synthesis of single enantiomers in the laboratory are not suitable for large-scale synthesis, owing to limitations based on cost, availability in bulk of the required reagents and catalysts, or specialized production equipment.

The chapters are suitably grouped by topic. After an insightful introduction framing the issues associated with the production of pure enantiomers on a commercial scale, a detailed discussion of sourcing chiral intermediates is followed by a description of successful examples taken from the top 10 list of the biggest grossing chiral drugs and agricultural products.

The ensuing set of topics describes various methodologies for the synthesis of L-phenylalanine and illustrates the use of bioprocessing and chemical resolution. This is followed by presentations of the utility of carbohydrates and terpenes as raw materials selected or derived from the "chiral pool". The next collection of chapters approaches the issues from an alternative and equally useful cross-section based on mechanism and includes substitution reactions, transition-metal-catalyzed hydrogenations, and isomerizations as well as hydroformylation, hydrosilylation, and asymmetric cyclopropanations. An intriguing chapter on powerful but underutilized classes of pericyclic reactions is valuable and may lead to important applications in the future. An excellent couplet of chapters deals sequentially with the asymmetric reduction of prochiral ketones and asymmetric oxidations such as the Sharpless asymmetric epoxidation and dihydroxylation as well as the Jacobsen epoxidation.

Of course, a book on commercial production of chiral compounds would be incomplete without a discussion of both chemical and enzymatic resolution methodolo-

gies. These topics are well-covered in a number of chapters, resulting in a comprehensive treatment. The book concludes with a salient discussion of the many important applications of the DuPHOS class of chiral ligands in asymmetric hydrogenations.

This valuable reference should be most useful to the process chemist who is facing the difficult challenges associated with devising an economic and scalable synthesis of a complex chiral molecule. In addition, the impressive collection of over 1800 references contained in the 18 chapters coupled with a comprehensive index are additional noteworthy features of this volume.

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Molecular Modeling of Nucleic Acids. Edited by Neocles B. Leontis and John SantaLucia, Jr. ACS Symposium Series 682. American Chemical Society, Washington, D.C. 1998. x + 435 pp. 15.5 x 23.5 cm. ISBN 0-8412-3541-4. $129.95.

This is a multiauthor volume based on a symposium the editors organized 2 years ago at the American Chemical Society National Meeting, San Francisco, CA, April 13-17, 1997. The book appeared at the beginning of 1998, but it was not received for review until April 1999. It contains some literature citations from 1997.

Of the 399 papers and posters organized at the San Francisco meeting under the auspices of the Computers in Chemistry Division, over 60 were related to the Symposium on Molecular Modeling and Structure Determination in Nucleic Acids. Of these, 26 became chapters in the book. About half of the chapters have titles different from the talks, and many chapters have had co-authors added or dropped.

The editors brought together as wide a range of approaches to nucleic acid modeling as possible. The book is about more than just molecular modeling in the computational chemistry sense. As the editors explain in their introduction, the conception of the original DNA double helix by Watson and Crick was a molecular modeling exercise, i.e., using available experimental information to construct a three-dimensional structure. Not all modeling need be done on a computer. The editors emphasize that precision at the atomic level is not necessarily the most important element; the success of a model can be judged by how well it integrates existing experimental data and whether it suggests new experiments. The introduction puts the book in context for the expert. The reader is directed to a 1989 reference giving terminology for helical parameters. The book has a long subject index (19 pages) and an index of its 97 authors but, following standard practice in ACS books, no index of cited authors.

The book is organized into sections covering basic computational issues, crystallography, spectroscopy, secondary structure prediction, molecular dynamics simulations, and modeling with low-resolution data. It includes experimental studies in X-ray diffraction, NMR and Raman spectroscopy, thermodynamics, and kinetics. Among the specific topics are RNA folding, modeling a ribosome, fuzzy logic, a scripting language for model building, simulations in the presence of counterions, and simulating folding by genetic algorithms (an appropriate topic for a book about DNA). There is little in the book on intercalators or on molecules that regulate gene expression. Antisense drugs are briefly mentioned. Only three of the chapters have authors associated with pharmaceutical companies.

Several of the chapters serve merely as gateways to the literature and would have benefited by being more independent and giving more mathematical details. The chapters are journal-length (8-28 pages). As is typical for a book prepared from camera-ready typescripts, there is variability in how well the authors adhered to the instructions given them. Thus, a few of the chapters lack an abstract. Some of the stereodiagrams have the pairs too widely separated to be properly viewed. One chapter has a color plate, whereas a few of the other chapters could have benefited from color.

The book is a rich source of information about DNA and RNA and will help the reader appreciate the wide panorama of experimental and computational research directions. This volume should be in complete collections of books on computational chemistry or nucleic acids.

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Neuronal Nicotinic Receptors. Pharmacology and Therapeutics Opportunities. Edited by Stephen P. Arneric and Jorge D. Brioni. Wiley-Liss, Inc., New York. 1999. xii + 421 pp. 16 x 24 cm. ISBN 0-471-24743-X. $175.00.

A book that has a retail price of $175.00 had better be good. This book is good and might even be worth the exorbitant purchase price. Topics covered range between an overview of neuronal nicotinic receptors to in-depth discussions of the structure, function, and regulation of neuronal nicotinic receptors to a discussion of the chemistry of nicotinic ligands to discussions of the potential therapeutic benefit of nicotinic compounds. The book consists of a collection of 23 reviews of "things nicotinic" written by many, indeed I would argue most, of the world's leaders in this field. Nearly without exception the chapters are chock full of valuable information. Better yet, at least half of the reviews are truly critical reviews of the literature. Nearly all of the authors did a commendable job of discussing the inevitable inconsistencies in the literature, and many had the courage to take sides on controversial issues. Of greater importance, many of these authors clearly identified questions and issues that need investigation.

At least in my view, a book is worth my time and money if it educates, and if it identifies questions that must be resolved, so much the better. With respect to the former, this book is a wonderful addition. The nicotinic neophyte might be nearly overwhelmed by the volume of information that is provided, and even a grizzled veteran of the nicotinic field, such as this reviewer, will likely share my experience which could be characterized as repeated mutterings of "I didn't know that". In addition, I would be most surprised if the seeds planted by the authors did not result in an explosion of new studies. As I read this book, I continually deviated from my task of reviewer. I found myself designing new experiments or reanalyzing the results of old experiments in the light of new information. The authors did an outstanding job of summarizing the literature in a way that elicited synthesis and inspired the imagination.

The book is not without faults, however. Chief among these faults is that not even one chapter was devoted to an in-depth discussion of the toxicity of nicotine. This is not a trivial issue if the goal of this book was to produce a balanced view of the potential of nicotinics as therapeutic agents. A major roadblock to the development of nicotinics as therapeutic agents is fear of toxicity. However, one could argue that nicotine has a bad reputation because its usual delivery system is tobacco where it is associated with hundreds, if not thousands, of other chemicals, many of which are very toxic. A balanced, concise discussion of the toxicities of nicotine, not associated with tobacco, would have added immeasurably to the value of the book. Other problems include those expected of a multiauthored book. For example, many redundancies exist; more than half of the chapters include in-depth discussions of the identification and functional consequences of multiple neuronal nicotinic receptor subunits.

As noted previously, this book is expensive. I cannot state unequivocally that it is worth $175 to everyone. However, if you work in the nicotinic field or are considering getting into this field, this book is invaluable. The editors did a masterful job of recruiting a cadre of top-notch scientists who provided us with scholarly, thought-provoking synopses of most of the critical issues facing the field today.

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