

According to the previously described method,<sup>14</sup> the representative compound **6** has been further characterized and it has been found that this compound potently antagonizes Et-1-induced contraction of porcine coronary arteries with a  $pA_2$  of 7.4, a value that is in accord with its  $IC_{max50}$  value for  $ET_A$  receptors (22 nM), but does not antagonize vasoconstrictions induced by ET-3, norepinephrine, or potassium chloride. Compound **6** has been also found to be highly water-soluble (>1 g/mL saline as a sodium salt).

Compound **6** (BQ-123) may therefore be an interesting tool for studying the physiological and pathophysiological roles of endothelins and their receptor subtypes, especially  $ET_A$  receptors. Extensive studies of this compound are now in progress.

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**Supplementary Material Available:** Physicochemical data including melting point, IR, high-resolution MS, NMR, and HPLC data for compounds 3–9 and NMR data on conformation analysis of compound 1 (4 pages). Ordering information is given on any current masthead page.

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## Book Reviews

**Introduction to Stereochemistry and Conformational Analysis.** By Eusebio Juaristi. John Wiley & Sons, Inc., New York. 1991. xv + 331 pp. 16 × 24 cm. ISBN 0-471-54411-6. \$49.95.

Although stereochemistry is a fundamental and integral part of organic and biological chemistry, its relevance continues to increase with the advent of stereoselective syntheses of more sophisticated molecules and the more clearly appreciated significance of stereoisomers in biology. This textbook provides highly readable descriptions of the most important principles of stereochemistry and conformational analysis. It describes a number of important topics such as chirality and prochirality, chirotopic properties, stereochemistry of organic reactions, stereochemical descriptors, determination of absolute configuration, and means for evaluating optical purity. Also presented in this book are detailed accounts of stereogenicity, asymmetric synthesis, resolution of racemates, conformational analysis of alkenes and heterocycles, comparison of theoretically calculated and experimentally determined conformational energies, and anomeric and gauche conformational effects. Each of the 18 chapters is followed with a list of pertinent references. Adequate author and subject indexes are also included.

*Introduction to Stereochemistry and Conformational Analysis* clearly describes the major concepts and principles of stereochemistry. This textbook is an excellent introduction for chemistry students. It provides a lucid description of timely principles of stereochemistry that may also benefit many practicing chemists.

### Staff

**Organic Photochemistry: A Visual Approach.** By Jan Kopecký (Long Island University). VCH, New York. 1991. ix + 285 pp. 16 × 24 cm. ISBN 0-89573-296-3. \$65.00.

Many synthetic chemists are reluctant to use photochemistry. Most texts on the subject tend to emphasize photophysics and detailed mechanistic analysis. Consequently, there is a belief that one needs to surmount a considerable learning curve before attempting photochemical reactions. This introductory text on organic photochemistry should do much to dispel that misperception. The book will be specially useful for synthetic and medicinal chemists who have no background in photochemistry, but wish to make use of it in their endeavors.

The "Visual Approach" in the title refers to the unusual format that is used. The book has no running or continuous text. Rather, it consists of a series of figures on the left half of the page with

brief captions on the right. Most of the figures/captions are self-contained. That is, they can be understood without having read the earlier material. Thus, the reader can scan the chapters, find an interesting transformation, and incorporate it into his/her work. Each caption contains extensive references to the primary and review literature. These allow the interested reader to pursue each topic in more detail. In an age where information is becoming increasingly available, the limiting factor for most scientists is time, rather than available information. Thus, useful shortcuts such as this visual presentation format should be taken seriously.

The first four chapters cover photophysics and theoretical concepts. The next nine chapters are on reaction chemistry grouped by functional groups of the reactant (e.g. alkenes, nitrogen-containing compounds, singlet oxygen). The last three chapters cover preparative photochemical techniques, factors influencing photochemical reactions, and applications of photochemistry. There is a subject index, but no author index.

This self-contained approach is very useful for presenting reaction chemistry where relationships between the individual topics are not critical. For example, one could understand and make use of the di- $\pi$ -methane rearrangement without necessarily knowing about the Norrish I reaction. In my opinion, the format is less successful at presenting the fundamentals of photochemistry. For example, exciplexes, electron transfer, and energy transfer are all interrelated phenomena. A conventional, unified treatment of these would be more effective. Photochemists, or those who intend to make extensive use of photochemistry, would probably want to own a traditional text in addition to this one.

In sum, this is a worthwhile book which fills an important need: presenting photochemistry to the nonspecialist. The unique format makes it possible to rapidly find relevant information.

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**Textbook of Pharmacology.** Edited by C. M. Smith and A. M. Reynard. W. B. Saunders Company, Philadelphia. 1992. xviii + 1213 pp. 22 × 28.5 cm. ISBN 0-7216-2442-1. \$45.00.

The preface to this multiauthored textbook states that "The book is designed to serve, not as a reference source, but as a readable text for the initial course in medical pharmacology [to be] used by the medical student and eventual medical practitioner." The book covers all the traditional topics of a standard pharmacology textbook, in addition to chapters on diagnostic

drugs, drug effects on sensory systems, psychiatric symptoms produced by drugs, drug-food interactions, management of acute poisoning, drug abuse, prescription writing, and information resources.

One of the most bizarre and annoying features of this book is its physical format. The book is a bulky 1213 pages measuring 22 × 28.5 cm, and weighing 2779 g. Since one-third of each page is wasted in the form of a blank margin with sophomoric annotations, the actual number of printed pages amounts to approximately 810 (or at most 850 pages if some of the rarely relevant information in the margins is incorporated into the printed text). This hardly justifies the \$45 price tag or the discomfort medical students will surely experience while lugging this book to class. By comparison, Goodman and Gilman's standard textbook of pharmacology (*The Pharmacological Basis of Therapeutics*, 8th ed., Pergamon Press, 1990, New York) boasts 1811 full pages of print, while measuring only 18 × 26 cm and weighing in at 2077 g.

There is a lack of balance and uniformity among chapters that goes beyond what can be blamed on the multiauthored nature of the book. While some chapters contain highly sophisticated molecular mechanisms of drug action and receptor structures, others emphasize highly practical clinical information.

The chasm between molecular and clinical information is vast and difficult to bridge. Furthermore, the chapter authors make no attempt at explaining how this molecular information contributes (if at all) to a better understanding of the practical mechanisms of drug action as they apply to their rational therapeutic use. There is, therefore, little justification in allotting excess space to molecular mechanisms in a clinically-oriented book for medical students and practitioners, and such information should best be relegated to specialty monographs on molecular pharmacology. As an example, it is difficult to reconcile the coexistence in the same book of highly sophisticated molecular receptor data as depicted on pp 89, 180, 232, 278, 279, and 508, with practical clinical information such as the injection technique for ulnar nerve block (p 216), case reports of phencyclidine reactions (p 387), and patient compliance problems with antianxiety medication (p 285).

There are numerous omissions and inaccuracies throughout the text that could probably have been remedied with adequate refereeing and proofing of each chapter. The following is a smorgasbord of examples:

(1) The wording of the classification of antiinflammatory agents on p 403 is confusing at best.

(2) The mechanism of action of some drugs is either incompletely described (e.g. colchicine, p 449) or totally absent (e.g. oxytocin, p 680, and GnRH analogs, p 675).

(3) The chapter on cholinomimetic drugs offers the reader three detailed pages of molecular pharmacology of muscarinic and nicotinic receptors (which has little, if any, clinical applicability) and four rather concise pages of clinically-relevant information.

(4) Other random examples of omissions include (but are not restricted to) phenytoin-induced lymphoma, adenosine and moricizine as antiarrhythmic agents, and uterine relaxants as a class.

(5) The statement on p 609 that "Beta blockers antagonize both the cardiac ( $\beta_1$ ) and noncardiac ( $\beta_2$ ) receptors" is misleading, since there is no indication that the author is referring to the nonselective  $\beta$  blockers or to high doses of the selective blockers. Numerous such inappropriately-worded phrases occur throughout the book.

(6) Statements such as "pronethalol had some unusual toxicity" (p 609) do not enlighten the reader. Pronethalol carcinogenicity would have been a more informative choice of words. Many such vague statements appear throughout the book.

(7) Although five antiandrogens (some of which are obsolete) are described on pp 692-694, the more important long-acting GnRH analogs (leuprolide, goserelin, nafarelin, histrelin) are not included in this discussion (although GnRH is described, albeit poorly, in another chapter on p 675, with no discussion of the different mechanisms by which it both stimulates and inhibits gonadotropin secretion). Similar omissions occur elsewhere.

(8) In a book of such massive (albeit artificial) size, a lack of discussion of AIDS in the chapter on antiviral drugs is disconcerting.

(9) In one glib paragraph on p 943 of the antineoplastics chapter, the author dismisses as inappropriate for discussion the important issue of immunostimulation in cancer therapy, where a number of lymphokines and cytokines are now available for therapy. Another author makes the same omission in the chapter on immunopharmacology, despite the fact that immunostimulation represents an example of one of the most exciting areas of pharmacotherapeutics in recent years. These (and other) chapters were clearly outdated at the time of publication.

Excluding the closing chapter (which deals with information resources), only 7 of the 67 chapters of the book list references from the 1991 literature. A small number of chapters list an aggregate total of 91 references from 1990. Most chapters provide a reference list predating the 1990 literature, and four chapters do not include any references. In one chapter, a reference cites a less-than-recent edition of Goodman and Gilman's textbook. It is evident that many chapters were written prior to 1990.

Some chapters are very well written and illustrated, although not necessarily up-to-date (e.g., Antiarrhythmic Agents, Substance Abuse Treatment, Treatment of Congestive Heart Failure), others lack focus and tend toward the verbose (e.g. Nonsteroidal Anti-inflammatory Drugs, Antianxiety Drugs), and still others read like compendiums of facts (e.g., Antiviral Drugs, Treatment of Headache).

Overall, this book embodies too many detracting elements that diminish its usefulness to medical students or other health professionals. To the discriminating reader, this book is not likely to be considered a serious alternative or competitor to such readable texts as Katzung's *Basic and Clinical Pharmacology* (Appleton and Lange, Norwalk, Connecticut, 1992) or Rang and Dale's *Pharmacology* (Churchill Livingstone Inc., London, 1991).

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**Neuromethods. 20. Intracellular Messengers.** Edited by Alan A. Boulton, Glen B. Baker, and Colin W. Taylor. Humana Press, Totowa, NJ. 1992. xix + 580 pp. 16 × 23.5 cm. ISBN 0-89603-207-8. \$99.50.

This latest volume in the *Neuromethods* series details the major advances in understanding the signaling mechanisms of nerve tissues. As with earlier volumes, the treatment of each subject is comprehensive and methods and techniques are described in a manner that will be useful for neuroscientists. Specific topics addressed are identification and analysis of function of heterotrimeric guanine-nucleotide-binding proteins; methods for analysis of phosphoinositides and inositol phosphates, inositol triphosphate receptors, and intracellular calcium; measurement of intracellular calcium with fluorescent calcium indicators; single-cell imaging technology; analysis of protein kinase C function, synthetic analogues of intracellular messengers; methods in cyclic nucleotide research; caged intracellular messengers and the inositol signaling pathway; protein phosphorylation; investigation of intracellular regulators and components of the exocytotic pathway; intracellular messengers in vertebrate photoreceptors; and intracellular messengers in invertebrate photoreceptors studied in mutant flies. Each section is accompanied by a list of pertinent and up-to-date references. A subject index is also included.

This volume describes many aspects of neural function; it is a useful source of clearly described, easily understood methodologies that will be of interest to specialists in neuroscience.

Staff

**Progress in Drug Research. Volume 37.** Edited by Ernst Jucker. Birkhäuser Verlag, Basel. 1991. 419 pp. 17 × 24 cm. ISBN 0-8176-2626-3. \$239.00.

This is the 37th volume in this well-known series to be edited by its founder Ernst Jucker since its inception in 1959. As in previous volumes, topics of current interest to medicinal chemists and others involved in drug research are reviewed in depth. The present volume of *Progress in Drug Research* is comprised of seven articles dealing with topical aspects of drug research. Topics reviewed include leukotriene antagonists and inhibitors of leu-

kotriene biosynthesis as potential therapeutic agents; bacterial resistance to antibiotics: the role of biofilms; pharmacological properties of the natural polyamines and their depletion by biosynthesis inhibitors as a therapeutic approach; potassium channel openers; airway pharmacology and clinical possibilities in asthma; antifungal chemotherapy; the hopanoids, bacterial triterpenoids, and the biosynthesis of isoprenic units in prokaryotes; and isosterism and bioisosterism in drug design. All of the reviews present an informative introduction to the topic which will be helpful to nonspecialists in obtaining an overview of the particular field in a relatively short time. Specialists will benefit from the details of the up-to-date reviews and the comprehensive bibliographies. The contribution by Alfred Burger on "isosterism and bioisosterism in drug design" will particularly benefit those who wish to apply these principles to provide direction for derivation of novel therapeutic agents. The book includes a thorough index for the present volume, indexes of titles for volumes 1-37, and an author and paper index for volumes 1-37.

This volume is recommended for specialists and nonspecialists in medicinal chemistry. It is especially recommended for institutional libraries. The 37 volumes of *Progress in Drug Research* provide a superb encyclopedic source of information for researchers in the drug-discovery field.

#### Staff

#### Books of Interest

**Computational Advances in Organic Chemistry: Molecular Structure and Reactivity.** Edited by Cemil Ogretir and Imre G. Csizmadia. Kluwer Academic Publishers, The Netherlands. 1990. vii + 421 pp. 17 × 24.5 cm. ISBN 0-7923-1064-0. \$137.00.

**Oligonucleotides and Analogues. A Practical Approach.** Edited by Fritz Eckstein. Oxford University Press, New York. 1992. xxiv + 313 pp. 18 × 24.5 cm. ISBN 0-19-963280-4. \$65.00.

**Annual Review of Neuroscience. Volume 15. 1992.** Edited by W. Cowan, E. Shooter, C. Stevens, and R. Thompson. Annual Reviews, Inc., Palo Alto, CA. 1992. vii + 454 pp. 15.5 × 23 cm. ISBN 0-8243-2415-3. \$44.00.

**General and Synthetic Methods. Volume 13. A Specialist Periodical Report. A Review of the Literature Published in 1988.** Senior Reporter G. Pattenden. Royal Society of Chemistry, Cambridge, U.K. 1992. xii + 500 pp. 14.5 × 22 cm. ISBN 0-85186-944-0. £140.00.

**Theoretical Aspects of Physical Organic Chemistry. The SN2 Mechanism.** By Sason S. Shaik, H. Bernard Schlegel, and Saul Wolfe. John Wiley & Sons, Inc., New York. 1992. xv + 285 pp. 16.5 × 24.5 cm. ISBN 0-471-84041-6. \$59.95.

**Molecular Neurovirology. Pathogenesis of Viral CNS Infections.** Edited by Raymond P. Roos. The Humana Press, Clifton, NJ. 1992. xx + 597 pp. 16 × 23.5 cm. ISBN 0-89603-222-1. \$99.50.

**Biological Asymmetry and Handedness. Ciba Foundation Symposium 162.** Edited by Gregory R. Bock and Jean Marsh. John Wiley & Sons, Inc., New York. 1991. ix + 327 pp. 16 × 23.5 cm. ISBN 0-471-92961-1. \$69.50.