

reaction mixture was diluted with water (700 mL), and the resultant precipitate was collected by suction filtration. The solid was washed with water (2 × 25 mL) and recrystallized from 2:1 hexane-CHCl<sub>3</sub> to provide 17 as white needles (5.09 g, 46%): NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 4.02 (s, 3 H, OCH<sub>3</sub>), 4.53 (s, 3 H, NCH<sub>2</sub>), 7.65 (d, 1 H, ArH), 7.73–7.78 (m, 2 H, ArH), 9.30 (s, 1 H, CHO), 13.26 (s, 1 H, COOH); IR (KBr, cm<sup>-1</sup>) 3140 (COOH), 1753, 1702, 1651 (C=O).

***N*-[(Dimethylamino)carbonyl]-*N*-[[6-methoxy-5-(trifluoromethyl)-1-naphthalenyl]carbonyl]glycine (20).** A suspension of amide 32 (20.0 g, 74.29 mmol) and sodium hydride (4.0 g, 1.12 equiv of a 50% dispersion in mineral oil) in THF (600 mL) was stirred at room temperature under a dry N<sub>2</sub> atmosphere for 45 min. A solution of *N,N*-dimethylcarbamoyl chloride (6.8 mL, 1.0 equiv) in dry THF (100 mL) was then added dropwise over a 20-min period. After an additional 45 min, saturated aqueous NH<sub>4</sub>Cl (200 mL) was added and the reaction mixture was poured into water (300 mL). This aqueous phase was acidified with 10% aqueous HCl, and the resultant precipitate was filtered. This solid was suspended in water (2 L) and basified with 10% NaOH. This suspension was filtered to remove starting amide 32. The filtrate was acidified with 10% aqueous HCl, and the resultant precipitate was collected. This white solid was washed with water and dried in vacuo to provide 33 (12.9 g, 51%): mp 169–170.5 °C.

Sodium hydride (1.90 g, 1.1 equiv, 50% dispersion in mineral oil) was added to a stirred, cold (0–10 °C) solution of 33 (11.9 g, 34.97 mmol) in dry DMF (65 mL). The solution was allowed to warm to room temperature for 20 min and then recooled to 0–10 °C. *tert*-Butyl bromoacetate (6.7 mL, 1.15 equiv) was added, and the reaction mixture was warmed to room temperature. After 45 min, the reaction mixture was added to water (1 L) and the water phase was basified (10% NaOH) and extracted with ether (7 × 400 mL). The combined ether extracts were washed with brine and dried (MgSO<sub>4</sub>). The ether was removed to provide *N*-[(dimethylamino)carbonyl]-*N*-[[6-methoxy-5-(trifluoromethyl)-1-naphthalenyl]carbonyl]glycine 1,1-dimethylethyl ester (12.2 g, 81%): mp 117.5–120 °C (hexane).

Trimethylsilyl iodide (17.6 mL, 5.3 equiv) was added to a stirred solution of this ester (10.0 g, 23.23 mmol) in CCl<sub>4</sub> (130 mL) at

room temperature under a dry N<sub>2</sub> atmosphere. After 2.5 h, the CCl<sub>4</sub> was removed and water (500 mL) was added. The reaction mixture was acidified with 10% aqueous HCl and extracted with ethyl acetate (500 mL). This extract was washed with dilute aqueous NaHSO<sub>3</sub> and dried (MgSO<sub>4</sub>). The solvent was removed and the semisolid was triturated with 2:1 benzene-hexane (450 mL) followed by benzene (2 × 100 mL) and filtered. The white solid was dried in vacuo to provide 20 (7.5 g, 77%): NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 2.62 [br s, 6 H, N(CH<sub>3</sub>)<sub>2</sub>], 4.02 (s, 3 H, OCH<sub>3</sub>), 4.37 (br s, 2 H, NCH<sub>2</sub>), 7.49 (m, 1 H, ArH), 7.66 (t, 1 H, ArH), 7.72 (d, 1 H, ArH), 8.16 (m, 1 H, ArH), 8.39 (m, 1 H, ArH), 11.1 (m, 1 H, COOH); IR (KBr, cm<sup>-1</sup>) 3650–2350 (COOH), 1750, 1690, 1650 (C=O); MS (*m/e*) 398 (3%), 309 (4%), 253 (100%).

**Registry No.** 5, 121731-07-5; 5 (methyl ester), 121731-38-2; 6, 121731-08-6; 7, 121731-09-7; 7 (methyl ester), 121731-39-3; 8, 121731-10-0; 8 (methyl ester), 121731-40-6; 9, 121731-11-1; 9 (methyl ester), 121731-41-7; 10, 121731-12-2; 10 (*tert*-butyl ester), 121731-48-4; 11, 121731-13-3; 11 (*tert*-butyl ester), 121731-42-8; 12, 121731-14-4; 12 (*tert*-butyl ester), 121731-43-9; 13, 121731-15-5; 13 (*tert*-butyl ester), 121731-44-0; 14, 121731-16-6; 14 (*tert*-butyl ester), 121731-45-1; 15, 121731-17-7; 15 (*tert*-butyl ester), 121731-46-2; 16, 121731-18-8; 16 (*tert*-butyl ester), 121731-47-3; 17, 121731-19-9; 17 (*tert*-butyl ester), 121731-49-5; 18, 121731-20-2; 18 (*tert*-butyl ester), 121731-50-8; 19, 121731-21-3; 19 (*tert*-butyl ester), 121731-51-9; 20, 121731-22-4; 20 (*tert*-butyl ester), 121731-52-0; 21, 90162-13-3; 22, 121731-23-5; 23, 121731-24-6; 24, 121731-25-7; 24 (R = Me), 121731-37-1; 25, 121731-26-8; 26, 84533-04-0; 27, 121731-28-0; 28, 92121-27-2; 29 (R = Me), 121731-29-1; 29 (R = Pr), 121731-54-2; 29 (R = *i*-Pr), 121731-55-3; 29 (R = CH<sub>2</sub>Bu-*t*), 121731-56-4; 29 (R = CH<sub>2</sub>Ph), 121731-57-5; 30, 121731-30-4; 30 (thioamide analogue), 121731-53-1; 31 (R = H), 121731-31-5; 31 (R = Me), 121731-58-6; 31 (R = Ph), 121731-59-7; 32, 121731-32-6; 33, 121731-33-7; BrCH<sub>2</sub>COOBu-*t*, 5292-43-3; H-Gly-OBu-*t*, 6456-74-2; H-Sar-OMe-HCl, 13515-93-0; aldose reductase, 9028-31-3; 6-[(*N,N*-dimethylthiocarbamoyl)-oxy]-1-naphthalenecarboxylic acid methyl ester, 121731-34-8; 6-[(*N,N*-dimethylcarbamoyl)thio]-1-naphthalenecarboxylic acid methyl ester, 121731-35-9; 6-mercaptop-1-naphthalenecarboxylic acid, 121731-36-0.

## Book Reviews

**The Chemistry of Antitumor Antibiotics. Volume 2.** By William A. Remers. John Wiley and Sons, New York, 1988. viii and 290 pp. 16 × 23.5 cm. ISBN 0471-08180-9. \$49.95.

This volume consists of a brief, unsigned introduction and seven chapters covering antitumor antibiotics under the following headings: Streptozocin; Pyrrolo[1,4]benzodiazepines; Saframycins, Renieramycins and Safracins; Naphthyridomycin, Cyanocyclines and Quinocarcin; CC-1065; Nogalomycin and Related Compounds; and Streptonigrin and Lavendamycin.

The title of this book is far too modest since a great deal more than the chemistry of these antibiotics is included. Each chapter is subdivided into the following headings: Discovery, Isolation and Characterization; Structure Elucidation and Chemical Transformations, Mode of Action; Synthesis; Biosynthesis; Structure-Activity Relationships and References. As the author points out, with the exception of streptozocin, the rest of the antibiotics discussed are no longer of clinical interest. However, there has been a renewal of interest in analogues of CC-1065, a very potent antitumor agent which manifested delayed toxicity. Some of the more recent compounds do not suffer from this disadvantage while still possessing antitumor activity in the microgram per kilogram range.

On the whole this is a very good book which can be useful to investigators and others interested in cancer chemotherapy. However, there are a few shortcomings which detract from the

overall excellence of the book.

It would have been quite helpful if the sections on the mode of action of these antibiotics immediately preceded the sections on structure-activity and relationships since in many instances the mode of action was invoked to clarify the SAR. In this reviewer's opinion experimental details of the isolation procedures, although brief, and the reproductions of the IR, UV, and NMR spectra should have been omitted. This information could best be obtained by referring to the original literature. The stereo drawing of the CC-1065/DNA adduct is so poorly reproduced that it is almost impossible to discern the structural details.

In the discussion of the mode of action of streptozocin the author states "The first step involves decomposition of the drug into the corresponding isocyanate and methyl diazohydroxide. The latter species decomposes further to methyl carbonium ion, nitrogen and hydroxide ion." Methyl diazohydroxide, if it is formed at all, would decompose to diazomethane and water and not to a primary carbonium ion.

There are some grammatical and typographical errors which are more annoying than serious. In Scheme 4.3 (p 134), which illustrates Evans' synthesis of cyanocycline A, a key nitrogen atom is missing from two intermediates. In the synthesis of U-71184 (Scheme 5.5, p 161) an oxygen atom is missing from the last intermediate shown. These are just two examples of many such errors. Finally, it would have been easier to follow the discussions of the many synthetic schemes if the formulas were numbered

and in certain cases if the syntheses and their relevant discussions were in closer proximity in the text.

Chemistry Department  
Rensselaer Polytechnic Institute  
Troy, New York 12180-3590

Sydney Archer

developments in this area, a periodic updating will undoubtedly be needed.

Department of Chemistry  
The Wichita State University  
Wichita, Kansas 67208-1595

William C. Groutas

**The Software Encyclopedia 1989. A Comprehensive Guide to Software Packages for Business Professional or Personal Use.** Compiled by R. R. Bowker. New York. 1989. 2 105 pp. 21.5 × 28 cm. Volume 1. Titles/Publishers: ISBN 0-8352-2650-6. Volume 2. System Compatibility/Applications: ISBN 0-8352-2651-4. Set: ISBN 0-8352-2649-2. \$179.95.

*The Software Encyclopedia* consists of two volumes that provide comprehensive and detailed information on microcomputer software of all kinds. This two-volume set contains entries from over 20 000 microcomputer software packages from about 4000 publishers. It has been organized for easy access through four indexes: Title Index, Guide to Systems, Guide to Applications, and System Compatibility/Applications Index. Volume 1 contains titles and publishers. Each entry includes a description of the software, number of disks, version, series, author(s), release date, compatible hardware, microprocessor type(s), requisite operating systems, language, necessary memory capacity, price, ISBN identification number, publisher name and address. The remaining indexes are in Volume 2.

The encyclopedia references virtually every software package known. It will find use in all libraries.

Staff

**Mechanism-Based Enzyme Inactivation: Chemistry and Enzymology. Volumes I & II.** By Richard B. Silverman. CRC Press, Boca Raton, FL. 210 pp (Vol. I). 265 pp (Vol. II). 18.5 × 26 cm. 1988. \$125.00 each volume.

These two volumes provide the first comprehensive treatment of mechanism-based inactivation by a premier investigator in this field. The material is superbly organized, well-balanced, and presented with clarity. The crisp style of presentation of the material made it a pleasure to read these two volumes.

Volume 1 begins with a lucid and thorough coverage of the fundamentals of mechanism-based inactivation that also includes a section on standard experimental protocols. This is followed by a comprehensive coverage of a diversity of mechanism-based inactivators reported through mid-1987. A strong and highly appealing feature of these two volumes is the mechanistic classification of the various inhibitors under such headings as protonation and deprotonation reactions (Chapter 2), phosphorylation reactions (Chapter 3), acylation reactions (Chapter 4), and elimination reactions (Chapter 5). Volume 2 covers isomerization, decarboxylation, oxidation, deoxygenation, and polymerization reactions.

The two volumes are remarkably free of typographical errors. The intimate relationship between the chemistry and enzymology of mechanism-based inactivators is clearly presented and easy to follow. The same is true for the synthesis of the various inhibitors. The synthetic schemes and illustrations are superbly drawn and the style of presentation is such that the two volumes can be of great value and benefit not only to researchers in the areas of enzyme inhibition and drug design, but also to graduate students taking a course in bioorganic chemistry, enzymatic reaction mechanisms, drug design, and even organic synthesis.

The pedagogical features of these two volumes are particularly appealing and their adoption for classroom use in one of the aforementioned courses or as a strongly recommended supplementary text should be seriously considered.

In summary, these two volumes fill a critical need in this area of research and should be a valuable addition to any academic or industrial library as well as the shelf of any investigator working in this area or other professionals and students wishing to acquire a fundamental understanding and appreciation of the concepts involved in mechanism-based inactivation. Considering the rapid

**Anthracycline and Anthracenedione-Based Anticancer Agents. Bioactive Molecules, Volume 6.** Edited by J. William Low. Elsevier, Amsterdam. 1988. xx + 753 pp. 17 × 25 cm. ISBN 0-444-87275-2. \$231.50.

Since its introduction to the clinic in the early 1970s, doxorubicin (adriamycin) has become one of the most useful and widely prescribed anticancer agents: 1988 world-wide sales approached US\$300 million. Not surprisingly, interest in doxorubicin, other anthracyclines, and their kin continues high.

The present volume contains 20 chapters, many written by leading authorities in individual areas, and provides broad coverage of recent developments. Chapters are grouped under three headings: "Isolation, Synthesis and Properties", "Biophysical and Biochemical Studies Related to Mechanisms of Action", and "Pharmacology, Toxicity and Clinical Aspects". Those headings accurately represent the scope of the contents.

Individual chapters generally concentrate on work from 1980 onwards, with occasional references to papers appearing (or in press) as recently as early 1987. Most of the chapters are extensively referenced, with citation of upwards of 50 references being the rule; commendably, all references include the title of the article cited.

The subject index is only fair and is devoid of cross referencing; fortunately, the Table of Contents is relatively detailed and individual Chapters are preceded by their own Tables of Contents, so subjects of interest can usually be tracked down with a bit of persistence. There is no author index.

The book has been produced by photoreduction of double-spaced typed copy. Consequently, the density of information per page is less than one might expect, although that is compensated for by the number of pages.

For those working in the areas of anthracycline and/or anthracenedione-based anticancer research, access to this book seems indispensable. Given the price, however, there is much to be said for interlibrary loan.

Boston College  
Department of Chemistry  
Chestnut Hill, Massachusetts 02167

T. Ross Kelly

**Prostaglandins in Clinical Practice.** Edited by W. D. Watkins, M. B. Peterson, and J. R. Fletcher. Raven Press, New York. 1989. xii + 263 pp. 15.5 × 24 cm. ISBN 0-88167-489-3. \$98.00.

The editors' stated purpose for this book is to place eicosanoid biology in the framework of current clinical concepts. For the most part, they have succeeded admirably. Following a concise and well-written review of basic biosynthetic and metabolic pathways of the eicosanoid family, the subsequent chapters discuss the physiological, pathological, pharmacological, and therapeutic aspects of eicosanoids in individual organ systems as well as specific clinical disciplines. In addition to the expected chapters on gynecology and cardiovascular, inflammatory, pulmonary, and gastrointestinal diseases, there are excellent and informative treatments of eicosanoids in oncology, nutrition, wound healing, critical care, renal disease, neonatology, and endocrinology. The book is adequately referenced, indexed, and, with a few obvious exceptions (for example on pages 136 and 138,  $\mu$  is omitted from g/min and g/mL, respectively), remarkably free of errors.

The book has some shortcomings. In many instances, the discussions are too brief to adequately cover a topic, yet the references provided are not current. An example is the cursory treatment of prostaglandins in tumor metastasis with no reference after 1983. Additionally, the chapter on cardiovascular diseases fails to mention any of the newer, more stable analogues of prostacyclin while the gastroenterology chapter omits any reference to the NSAID ulcer preventive studies which led to the recent FDA approval of misoprostol.

The book would be very useful to anyone interested in a broad perspective of eicosanoid physiology, pathology, and clinical applications, but experts in a particular field may find the information limited and not sufficiently current.

*Gastrointestinal Diseases Research*      **Paul W. Collins**  
G. D. Searle & Co., Inc.  
Skokie, Illinois 60077

**Handbook of Stereoisomers: Therapeutic Drugs.** Edited by Donald F. Smith. CRC Press, Boca Raton, Florida. 1989. vi + 405 pp. 17.5 × 25.5 cm. ISBN 0-8493-3421-7. \$145.00.

This book closely follows the format of its predecessor *Handbook of Stereoisomers: Drugs in Psychopharmacology*. In the present handbook experts in various branches of medicine consider in moderate depth the three-dimensional features of drugs utilized in various therapeutic areas. After an introductory chapter by the editor describing briefly the fundamental concepts, principles, and problems encountered in studying the effects of stereoisomeric drugs follow chapters dealing with the chirality of agents in producing effects in various therapeutic areas. Areas addressed in detail are  $\alpha$ -adrenergic, antiarrhythmic, antihypertensive, anticoagulant, anti-inflammatory, antihistaminic, anti-allergic, antibiotic and antimicrobial, antimalarial, antineoplastic, opioid analgesic, and psychotropic drugs. These chapters review our present knowledge of stereocomplementarity and the action of these drugs in a fashion that is easily comprehended by the reader. As such it serves as an excellent introduction of medicinal chemists to the various therapeutic areas that are considered. Somewhat disappointingly the stereochemical details vary considerably among the topics treated and relatively little speculation is advanced to address the role of stereocomplementarity to deduce ideas about the nature of the drug binding sites from a knowledge of the stereochemistry of the drug. Perhaps this is attributable to the varying importance of stereochemistry in the different therapeutic classes. Also, recent references are very few. The only citations as recent as 1987 are personal communications.

In summary, this book will probably be of interest to most medicinal chemists; however, the price of the book coupled with the depth in which each of the topics is treated will likely limit its appeal to general library access.

Staff

**The Calcium Channel: Structure, Function and Implications.** Edited by M. Morad, W. Nayler, S. Kazda, and M. Schramm. Springer-Verlag, New York. 1988. xxiv + 643 pp. 16.5 × 24.5 cm. ISBN 0-387-50061-8. \$84.40.

This book is based on research presented at the Bayer AG Centenary Symposium held in Stesa, Italy, May 11-14, 1988. The symposium attracted many of the leading researchers in the areas

of calcium channel structure and function and as a consequence the resulting book provides a scientifically thorough treatment of these subjects. The book, which is composed of 49 manuscripts preceded by two introductory papers, is divided into seven sections. The first describes the history of Bayer pharmaceutical research, together with a reconstruction of Sydney Ringer's remarkable presentation to the Physiological Society December 9, 1882 and a paper regarding the homology of calcium-modulated proteins. The second section is concerned with the function of the calcium channel and deals with the modulation of calcium channels by a variety of physiological and pharmacological interventions. The next considers the structure, molecular characterization, and reconstitution of the calcium channel. The role played by the calcium channel under physiological and pathological conditions in the cardiovascular and endocrine systems is examined in the fourth section. The neuropharmacology of the calcium channel and endogenous ligands for the channel are considered in the next two sections. A brief exploration into calcium and aging is found in the last section.

In general a book of this type quickly becomes outdated by the rapid progress with which science develops. However, the diversity of the tissue systems included, combined with the comprehensive nature of this book, makes this a useful volume.

*Wyeth-Ayerst Research*      **Dennis M. Ackerman**  
CN 8000  
Princeton, New Jersey 08543-8000

**Medical and Health Care Books and Serials in Print 1989.**

**An Index to Literature in the Health Sciences. 18th Edition.** Compiled by R. R. Bowker. New York. 1989. 21 507 pp. 22 × 29 cm. Volume 1. Subjects/Authors: ISBN 0-8352-2615-8. Volume 2. Titles/Serials/Publishers: ISBN 0-8352-2616-6. Set: ISBN 0-8352-2613-1. \$149.95.

This two-volume set provides information relative to 61 268 books from 4008 publishers in the medical and health care field. In the first volume books are indexed by author, title, and 5936 specialized subject categories plus 6837 cross references to ensure facile location. Each entry gives information relative to author, coauthor, editor, translator, title, number of volumes, edition, Library of Congress Number, series, whether or not illustrated, page count, publication data, price, binding, publisher, publisher's order number, and ISBN. In Volume 2 are listed 12 561 international journals. Each entry provides complete ordering and subscription details plus an assortment of other information about the journal. This volume also provides an index to all publishers and distributors including full contact and ordering information plus telephone numbers for U.S. and Canadian organizations.

These volumes provide an excellent reference source for all medical and health care libraries.

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