

Table II. In Vitro Effects of 3 on the Isolated Cat Atria and Papillary Muscle

Dose, $\mu\text{g/ml}$	Right atrial rate ^a	Right atrial force ^a	Left atrial force ^a	Papillary muscle force ^a
3	3 \pm 2.5 ^b	3 \pm 2.7	15 \pm 4.1	37 \pm 5.9
10	11 \pm 1.2	19 \pm 4.7	29 \pm 4.0	54 \pm 7.3
30	29 \pm 5.7	33 \pm 5.8	64 \pm 7.1	75 \pm 10.2
100	26 \pm 8.0	58 \pm 11.0	115 \pm 15.2	84 \pm 22.7

^aPercent change from control. ^bMean \pm standard error.

force accompanied by a moderate increase in right atrial rate (Table II). Pretreatment with reserpine caused a complete abolishment of the in vitro inotropic effect of 3. In vivo, pretreatment with reserpine caused a significant loss of the activity of small doses of 3 with no effect on larger doses. These experiments and others suggest that a portion of the drug's effect is mediated by endogenous catecholamine(s). The effect of dopamine on cardiac tissue has been characterized as mixed—both direct and indirect.² An explanation for the absence of an effect on heart rate at

doses which cause a significant increase in cardiac force is not apparent. Experiments designed to further elucidate the mechanism of action of the drug are continuing.

References and Notes

- (1) D. M. Gallant, M. P. Bishop, and R. Guerrero-Figueroa, *Curr. Ther. Res., Clin. Exp.*, **14**, 61 (1972).
- (2) L. I. Goldberg, *Pharmacol. Rev.*, **24**, 2 (1972).
- (3) L. L. Iversen and B. A. Callingham, "Fundamentals of Biochemical Pharmacology", Z. M. Bacq, Ed., Pergamon, New York, N.Y., pp 276-279.
- (4) H. S. Akiskal and W. T. McKinney, Jr., *Science*, **182**, 20 (1973).
- (5) N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957).
- (6) All the new compounds described in this communication gave elemental analyses (C, H, N) within 0.4% of the calculated values and were further characterized by their NMR and ir spectra.

Aram Mooradian,* Allan G. Hlavac, Paul E. Dupont
Malcolm R. Bell

Department of Chemistry

Adawia A. Alousi

Department of Pharmacology
Sterling-Winthrop Research Institute
Rensselaer, New York 12144
Received March 17, 1975

Book Reviews

Bioactive Compounds from the Sea. Edited by Harold J. Humm and Charles E. Lane. (Volume 1 of a planned series of volumes entitled Marine Science.) Marcel Dekker, New York, N.Y. 1974. xiii + 251 pp. 22.8 \times 15.2 cm. \$18.75.

This book is a collection of 13 papers presented at a symposium held in St. Petersburg, Fla., in Nov 1971 entitled "Physiologically Active Compounds from Marine Organisms". The format of most chapters follows that of journal papers: referenced introductory information, experimental results, and brief discussion of the data. The majority of the papers deal with biological and pharmacological properties of extracts of marine organisms rather than with molecular structure investigations; few of the active materials discussed have been purified to the extent that detailed structural studies are possible. Individual chapters are devoted to investigations of the toxins or venoms from each of the following sources: an Australian jellyfish, a common Indo-Pacific sea urchin, a Caribbean sponge, dinoflagellates, a variety of echinoderms, nematocysts from assorted coelenterates, and sea snakes from Southeast Asia and the Far East. A comparison of the pharmacological actions of the potent marine toxins tetrodotoxin and saxitoxin is the subject of one paper, and the fascinating and potentially economically important discovery of prostaglandins in a gorgonian is discussed in another. The remaining chapters are devoted to the ciguatoxin problem and speculations regarding its causes, an investigation of some possible exogenous sources of puffer fish toxin, the use of seaweed extracts on terrestrial plants as growth stimulators and as an inhibitor of fruit decay, and an electron microscopy study which has yielded a detailed picture of the structure of the nematocysts from the well-known stinging jellyfish, the Portuguese man-of-war.

All of the chapters are of comparable length except Chapter 3 (sea urchin toxins) which constitutes one-fourth of the entire book and contains extensive data. Most of the other chapters also contain considerable experimental detail and graphic presentations of data, and hence the book will appeal and be of benefit largely to specialists, primarily pharmacologists, physiologists, and biochemists.

The stated purpose of the planned Marine Science series of books of which this monograph is Volume 1 is to disseminate

knowledge of the ocean and its shorelines "to all the public—layman and scientists alike". Volume 1 is clearly directed to specialized scientists. In the reviewer's opinion, the title is somewhat misleading, since few discrete compounds are discussed. A shorter lapsed time between symposium date and monograph publication would be desirable if other similar symposia compilations are planned in this series.

Department of Chemistry
University of Oklahoma
Norman, Oklahoma 73069

Francis J. Schmitz

Principles of Medicinal Chemistry. Edited by William O. Foye and 37 other contributors. Lea and Febiger, Philadelphia, Pa. 1974. xviii + 857 pp. \$29.50.

The main intent of this book is to provide a text for undergraduate pharmacy students. It does, however, provide an excellent introduction to the field of medicinal chemistry for graduate students in other chemical and biological disciplines. An effort has been made to correlate information about drug action from such fields as biochemistry, pharmacology, organic chemistry, and quantum chemistry, to name a few.

The volume consists of 37 chapters. The first six cover broad concepts of significance to medicinal chemistry: a historical background, physical-chemical properties and biological activity, molecular orbital theory in drug design, molecular structure and pharmacological action, drug metabolism, and receptor site theory. These six chapters alone (142 double-column pages) would serve as an excellent text for a one-semester graduate course in the subject, supplemented by selected readings from the remaining 31 chapters. These cover the usual pharmacodynamic and chemotherapeutic topics, plus some not usually treated separately in a text of this kind, on antifungal agents, pesticides, and respiratory tract drugs, all of great interest to practicing pharmacists.

The general approach to the special topics includes a description of the biochemical and/or physiological systems affected, the absorption, metabolism, and excretion of the drug, methods of evaluation, structure-activity relations, and synthetic methods. The

topics are not necessarily treated in that order. Each author has utilized his own initiative to present his topic in a coherent and logical manner. Still, the various chapters are sufficiently even in treatment to provide a reasonably well-balanced text.

The format is excellent, the type readable, the text relatively free of error, remarkably so in an age when proof-reading is a vanishing profession. An occasional over-simplification may be condoned in an undergraduate text. It is to be regretted that the very useful sections offering guidance to selected readings in various monographs and reviews were included in only 15 of the 37 chapters. These references will be very valuable to more advanced students.

In browsing through this text, one cannot help reflecting on the enormous breadth of scientific disciplines in which a medicinal chemist must have some knowledge. Advances in the field will more and more be made only by specialists, but such ventures must be coordinated by scientists who are knowledgeable in all of these areas. We need to cultivate course work in the field at the graduate level in various disciplines to encourage entry into the field.

A text of this nature, consisting of a number of chapters by different authors, must inevitably be compared to the Burger Monograph (A. Burger, "Medicinal Chemistry," Wiley-Interscience). There are many similarities among which are the two-column format and the general selection of topics and subject matter. However, a conscientious effort has been made, in the present text, to introduce the student to related physiology and pharmacology, and less has been assumed regarding the readers background in biochemistry. It is appropriately much shorter and less encyclopedic in its coverage. It is a text which will undoubtedly receive acceptance by the audience for which it is intended.

Department of Chemistry
Indiana University
Bloomington, Indiana 47401

E. Campaigne

Inorganic Medicinal and Pharmaceutical Chemistry. By J. H. Block, E. B. Roche, T. O. Soine, and C. O. Wilson. Lea + Febiger, Philadelphia, Pa. 1974. ix + 472 pp. 15 × 23.5 cm. \$18.50.

The purposes stated for this textbook, designed for undergraduate pharmacy students, are to "present a review of those principles of inorganic chemistry that apply to medicinal and/or pharmaceutical chemistry", and to "present detailed discussions of those inorganic agents used as pharmaceutical aids and necessities or as therapeutic and diagnostic agents". This is the succeeding volume to "Rogers' Inorganic Pharmaceutical Chemistry", which went through eight editions, and some of the text has been taken from it. The emphasis here is to change the previous chemical classification of text material to a classification according to use. More material of pharmacological and toxicological significance also appears to have been included.

The first three chapters, covering the first 100 pp, include brief discussions of "Atomic and Molecular Structure/Complexation", "Group Properties of Elements", and "Solutions and Solubility". Although this material may be found in most textbooks on inorganic or general chemistry, a useful review is provided, and it does appear to belong in a book of this type. While the discussion is necessarily limited and leads to oversimplifications in some instances, such as the listing of only one coordination number per metal ion, it should be of value to the pharmacy student.

The remaining nine chapters are concerned with those inorganic compounds or ions of use to therapists or pharmacists. These include pharmaceutical aids and necessities (acids, bases, buffers, etc.), major intra- and extracellular electrolytes, essential and non-essential ions, gastrointestinal agents, topical agents, dental products, radiopharmaceuticals and contrast media, and some miscellaneous agents (inhalants, respiratory stimulants, expectorants and emetics, antidotes, and tableting and suspending agents). Both the theoretical basis for their use and recommended usage, including both chemical and physiological incompatibilities, are discussed. Much of this material is new and perhaps is provided with a better basis of chemical principles than is usually found in pharmacology texts.

Some discussion of metabolic schemes, such as the redox systems in the respiratory chain and metabolic pathways of copper is incorporated; future editions might well include more of this material which is of value to chemists and clinicians as well. Overall, however, the book makes a remarkably good mix and should serve

pharmacists quite well. The text is clearly written and the authors have maintained a uniform style of presentation. It fills a definite need in the pharmaceutical curriculum and should enjoy considerable use.

Massachusetts College of Pharmacy
Boston, Massachusetts 02115

William O. Foye

Marijuana: Chemistry, Pharmacology, Metabolism and Clinical Effects. Edited by R. Mechoulam. Academic Press, New York, N.Y. 1973. xiv + 409 pp. 16 × 23.5 cm. \$24.50.

Rarely has so much been written on any drug of current licit or illicit use than that which has appeared in the past few years on marijuana. One is thus forced to ask oneself, do we need another book or review on this subject? This volume, however, differs from the numerous other treatises in that Professor Mechoulam has managed to bring together six other contributors of outstanding repute in their various areas of expertise and has presented a complete and up-to-date review of the chemical and pharmacological aspects of *Cannabis* without the polemics usually associated with this subject.

This volume begins with a complete and current discussion of cannabinoid chemistry: the isolation, structural elucidation, synthesis, and reactions of all known cannabinoids by R. Mechoulam, in whose laboratories many of these studies were carried out over a 10-year period. A chapter (Mechoulam and Edery) on structure-activity relationships in the cannabinoid series is also included. It is disappointing, however, that data are generally compared in laboratory animals and that the relevancy of these observations to activity in man had not been established at the time the book was published. Chapter 3 (M. D. Willinsky) reviews the analytical methods used to identify and characterize the cannabinoids, while Chapter 4 (S. H. Burstein) covers the labeling and metabolism of the tetrahydrocannabinols. The remaining three chapters deal primarily with the pharmacology of *Cannabis* in animals (W. D. Paton and R. G. Pertwee), their action in man (Paton and Pertwee), and the clinical aspects of *Cannabis*' effects (Paton, Pertwee, and E. Tylden). Each chapter contains an addendum which has enabled the authors to keep this rapidly developing field current and includes literature citations to 1972. This book is well referenced, particularly as it applies to the current chemical literature and includes an author and a subject index.

This uniformly well-written volume has remarkably few printing or other errors and has been prepared with the thoroughness characteristic of the contributors' own research on this subject. The greatest value of this volume will be to the many research workers in chemistry, pharmacology, and medicine as well as to those investigators in the forensic sciences and analytical laboratories who have an obvious special interest in this subject. As a reference book on marijuana, this book will be hard to replace for many years to come.

Department of Medicinal Chemistry
and Pharmacology
Northeastern University
Boston, Massachusetts 02115

John L. Neumeyer

Aromatic Amino Acids in the Brain. Ciba Foundation Symposium 22 (New Series). Edited by G. E. W. Wolstenholme and D. W. Fitzsimons. Elsevier-North-Holland Publishing Co., Amsterdam. 1974. 396 pp. \$19.60.

This book contains a series of papers presented at an international symposium sponsored by the Ciba Foundation and held on May 15-17, 1973. It provides an excellent review of the biochemistry of three amino acids: phenylalanine, tyrosine, and tryptophan. These compounds, like other amino acids, participate in protein metabolism and transamination reactions. However, these amino acids are unique because they are precursors to monoamine neurotransmitters in the brain as well as to other "minor" amines whose role in brain function is not clear.

A major theme of the book is whether the availability of the aromatic amino acids to brain cells controls the rate of cellular reactions. In this context, the various factors that influence the brain concentration of the aromatic amino acids are thoroughly discussed. Perhaps the best documented case in which the concentration of an aromatic amino acid can control the rate of a cellular

reaction is the control of 5-HT synthesis by the neuronal concentration of tryptophan. The type of diet as well as a variety of drugs affects tryptophan distribution in plasma, the metabolism of tryptophan by the liver, and its rate of transport into brain. The resultant change in brain tryptophan levels exerts profound effects on the rate of serotonin synthesis.

On the other hand, the availability of aromatic amino acids does not appear to control the rate of brain catecholamine or protein synthesis under normal conditions. Thus, the regulation of protein synthesis in the brain may differ from that of liver, where the rate appears to be influenced by the availability of tryptophan. Presumably, in brain, the enzymes of these reactions are saturated with aromatic amino acid substrate. This concept is consistent with the evidence that suggests that, under normal conditions, catecholamine synthesis is limited by the activity of tyrosine hydroxylase, which may be affected allosterically by a variety of factors. However, during certain pathological conditions or states of malnutrition, it is possible that the rate of synthesis of catecholamines as well as protein may decrease due to a deficient supply of aromatic amino acids.

The latter section of the book contains articles on the effects of L-Dopa and synthetic analogs of the aromatic amino acids, α -methyl-Dopa, α -methyltryptophan, and *p*-chlorophenylalanine, on the various biochemical reactions in which the aromatic amino acids participate. These compounds appear to affect all facets of aromatic amino acid metabolism. They can alter the brain concentration of aromatic amino acids and affect the rates of synthesis of both the monoamine transmitters and proteins.

The objective of this symposium was to integrate the research of scientists working on different aspects of the metabolism of aromatic amino acids. These are the control of brain aromatic amino acid concentrations, the role of these amino acids in neurotransmitter synthesis, and the relationship between the concentration of the aromatic amino acids and protein synthesis in the brain. This purpose has been achieved, and a coherent picture of the biochemistry of the aromatic amino acids is presented. Particularly helpful in this regard are the sections at the end of each paper, where the data are discussed by the participants and critically evaluated. All of the papers, as well as the discussions, are well written and documented. This book will be of considerable value to anyone interested in the biochemistry of amino acids and neurotransmitters and, in particular, the emerging field of the effects of nutrition on brain biochemistry.

Department of Neurology
Harvard Medical School
Children's Hospital Medical Center
Boston, Massachusetts 02115

Norman J. Uretsky

Total Synthesis of Steroids. Volume 30 (Organic Chemistry Monographs, Alfred T. Blomquist and Harry Wasserman, Ed.). By Robert T. Blickenstaff, Anil C. Ghosh, and Gordon C. Wolf. Academic Press, New York, N.Y. 1974. xiii + 328 pp. 16 × 23 cm. \$29.50.

Steroids have been intensively synthesized for decades and several excellent reviews on total synthesis have been published during the last 4 years. "Total Synthesis of Steroids" has chapters on each of the general synthetic approaches to the steroid ABCD ring system, e.g., AB → ABC → ABCD and CD → BCD → ABCD, and reviews the literature through late 1973. A brief chapter on biogenetic-like steroid syntheses is also included.

A very useful summary of recent reviews on steroid total synthesis is included in the first three pages, so more detailed reviews on particular kinds of steroids can be consulted. While the chapters are organized on an "approach" basis (e.g., A + D → AD → ABCD), an excellent subject index is included so that routes to particular compounds (e.g., 19-nortestosterone) or to particular classes of steroids (e.g., 11,14-diazasteroids) may be found irrespective of the "approach" used. An extensive author index is also included. The first chapter has a nice discussion of steroid total synthesis "strategy" and common reactions. As a result, this book would be very useful as a graduate text or as a general reference.

Compound numbers in the text appear with bold-faced type, making discussion related to particular diagrams easy to find and easy to distinguish from reference numbers. Diagrams of synthetic schemes are drawn well and clearly arranged, although some readers may find the small type size in the diagrams an inconvenience. All diagrams clearly show the stereochemistry and substitution at

each asymmetric carbon. Although percent yields are not included in the diagrams, they are given in the text—often with information on the relevance of the percent given.

As the title implies, only total syntheses are discussed in the book and not partial syntheses nor interconversion of one class of steroids to another.

In summary, this is a useful book which will be invaluable to many steroid chemists—especially those who do not have an adequate collection of previously published reviews on total synthesis of steroids.

Department of Medicinal Chemistry
University of Minnesota
Minneapolis, Minnesota 55455

Dwight S. Fullerton

Biosynthesis. Volume 2 (Specialist Periodical Reports). By T. A. Geissman, Senior Reporter. The Chemical Society, London. 1973. xi + 308 pp. 14 × 22 cm. £ 8.00.

This volume comprises a review of the increments to our knowledge of the biosynthesis of several classes of naturally occurring compounds which appeared in the literature in 1972. While the major portion of the work deals with metabolic pathways in plants, sections on sterol transformations in both vertebrate and invertebrate animals are included, along with a very useful review of the special techniques in NMR and mass spectrometry which are being increasingly applied to the solutions of complex biosynthetic problems.

In my opinion a few trends in research on biosynthetic mechanisms are worth particular mention. Increasing attention is being devoted to the identification of and studies on the enzymes actually involved in many biotransformations which, in earlier publications, were assumed or indicated as probable or reasonable on the basis of less direct evidence. It is gratifying to learn, too, that alkaloids can no longer be dismissed as end products of plant metabolism; evidence is beginning to accumulate to show that many of these compounds are rapidly transformed, by the plants, to other alkaloids or to nonalkaloidal constituents during specific phases of the growth cycle.

The inclusion of reports on the advances in the biosynthesis of gibberellins, of steroid intermediates in the metabolism of cholesterol, and of sterol metabolism in insects should make this compact volume, with its 950 literature citations, of value to the plant physiologist, the entomologist, and the vertebrate physiologist—as well, of course, to the organic chemist—whose interests are based on biosynthetic pathways.

Department of Medicinal Chemistry
and Pharmacology
College of Pharmacy and Applied
Health Professions
Northeastern University
Boston, Massachusetts 02115

Robert F. Raffa

Synthetic Production and Utilization of Amino Acids. Edited by T. Kaneko, Y. Izumi, I. Chibata, and T. Itoh with four other contributors. Translated from Japanese (Kodansha Ltd., Tokyo). Halsted Press, Wiley, New York, N.Y. 1974. 312 pp. \$22.50.

In 1955 the price for a kilogram of L-alanine, calculated from the gram amounts then offered, was about \$5000; today it is \$50/kg for the 50-kg lot. The dramatic development in amino acid production (ca. 250,000 tons in 1974) was pioneered mainly in Japan in the 1950's and 1960's. During that period of time the traditional extraction of protein hydrolysates as a source for L-amino acids has almost completely been replaced by microbial fermentation and by chemical synthesis. Following a book on "The Microbial Production of Amino Acids" (K. Yamada et al., Ed., Kodansha and Wiley, 1972), this volume focuses on chemical methods. Edited and written by four highly reputed authorities along with several other experts in the field, the book is organized into two parts, entitled (1) Synthetic Production of Amino Acids, and (2) Amino Acid Utilization.

Part 1 opens with a clearly and concisely written brief survey of synthetic procedures by Y. Izumi which is appealing due to the well-arranged structural formulas. Chibata's chapter on "Optical Resolution of DL-Amino Acids" deals with physicochemical, chem-

ical, enzymatic, and biological techniques and with procedures for efficient racemization, a prerequisite for utilization of undesired enantiomers. A brief chapter on asymmetric synthesis by Y. Izumi is then followed by the multi-authored description of synthetic preparative methods for individual amino acids which occupies more than half of the book. Emphasis is given to yield- and cost-efficient procedures which are used for industrial production or hold promise to be developed for commercial application. References to patents amount to 21% of literature quotations.

Part 2 features an interesting chapter on "Quality of Amino Acids" by T. Itoh which contains an up-to-date table of physical and analytical data. A multi-authored chapter deals with "Utilization of Amino Acids" for foods, animal feeds, medicines, and cosmetics and as starting materials for the manufacture of surface-active agents, polyamino acids, and peptides. "Future Prospects for the Amino Acid Industry" are briefly outlined by Y. Izumi in the closing pages of the book.

The subject matters have been handled authoritatively by researchers active in their respective areas. The value of this volume would have gained much if more nonproteinogenic amino acids than β -alanine, Dopa, and sarcosine were included. The main chapter on "Synthetic Methods for Individual Amino Acids" is essentially an abbreviated version of the voluminous encyclopedic Greenstein-Winitz (1961) treatise. It is well done and has value as such, but it could have been enhanced by including more on recent developments. Nevertheless, this book as a whole represents an attractive and useful compendium.

In general, the writing is concise and clear with only rare instances where the translation affected syntax or wording. Structural formulas and graphic representations are all good. There is no author index but an adequate subject index.

Chemical Research Department
Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Johannes Meienhofer

Progress in Drug Research. Volume 18. Tropical Diseases. I.

Edited by E. Jucker. Birkhäuser Verlag, Basel and Stuttgart. 1974. 498 pp. 17 × 24.5 cm. \$73.50; Swiss Fr., 184.

The traditional format of this series is a collection of reviews of interest in medicinal sciences, occasionally interspersed with legal and sociological implications of drug research and development. The present volume contains two chapters in this established sense, one on the toxicity of aerosol propellants—a bone of contention between the FDA and the chemical industry—and a 74-page review of applications of mass spectrometry in pharmaceutical research. The latter chapter affords a good exercise in mass spectrometric analysis of natural products and drug metabolites. The main thrust of this volume, however, is publication of one-half of a symposium on tropical medicine held at the Haffkine Institute in Bombay in January 1974. The second half will be printed in Volume 19.

A wide-ranging review of tropical diseases, their prevention and therapy, addressed to medically oriented readers, comes at a very opportune time. Drug development, being the primary activity of the pharmaceutical industry rather than of academic medicinal science, has regarded research in tropical medicine as a stepchild to whom one cannot accord one's full measure of devotion. The reason is not lack of scientific or humanitarian interest but entails economic necessity. Industrial drug development leading to the introduction of new drugs into medicine is centralized in laboratories of nontropical developed nations. Such R and D has to be paid for and must render a justifiable return on the tremendous gamble and risk involved in such studies. The nations with severe problems of tropical diseases are, almost without exception, underdeveloped, unable to mount significant R and D of their own, and restricted in their ability to pay for drugs developed in medically advanced regions. Besides, the developed countries have overwhelming problems of their own in many urgent areas of medicine and must invest their talents, know-how, scientific enthusiasm, and rapidly dwindling economic resources in domestic tasks above all.

Only a handful of American, British, and continental European companies and research institutes can claim ongoing studies in tropical medicine. Yet, the potential applications are limitless. It takes no market research to ascertain that the incidence of micro-

bial and parasitic diseases encountered primarily in the tropics and subtropics is staggering. Ascariasis affects 10^9 people, *Trichuris* and *Enterobius* combined are harbored by 10^9 humans, and *Hymenolepis nana* by 5×10^7 persons. Schistosomiasis has been diagnosed in 12×10^7 patients. Leprosy occurs in 3.1×10^6 persons in India alone, and the crowded and unsanitary living conditions coupled with the unchecked population explosion allow extrapolation to 6.2 million cases in India by 1995. *Trichinella spiralis* occurs in 5×10^7 individuals, and lung worm in 10^8 cases. Between 189 and 250×10^6 people harbor filarial nematodes. Amebiasis, although most rampant in hot humid climates, affects 10% of all North Americans and has therefore been studied more thoroughly. The enormity of the task of suppressing and curing these diseases by chemotherapy should be an invitation to mount massive industrial research programs. The present volume may be a catalyst for increased activity in these areas.

Since the symposium was held in India and many contributors live in that country, many of the research papers on the diseases, their distribution, vectors, and chemotherapy are concerned with conditions on that subcontinent. Several American and European contributors have taken a broader geographic view. Among the best examples are the reviews by E. F. Elslager on his own extensive work, and that of others, on antimalarials and drugs for filariasis and leprosy and by E. A. Steck on the leishmaniasis. Twenty-one well-documented and sometimes beautifully illustrated chapters on such chemotherapeutic problems form the main body of the volume. No physician who reads these pages should miss the essay by K. M. Cahill on the teaching of tropical medicine and that by M. J. Colbourne on the implementation of disease control in Asia and Africa. These chapters outline the base that will have to be established if chemotherapeutic research is to be translated into clinical reality.

The book extends from structure-activity relationships, pharmacology, clinical manifestations, and treatment schedules to the biochemical causation of many tropical diseases. It will appeal to readers all the way from organic chemistry to those in epidemiological field work and should stimulate innumerable questions about these topics that anxiously await investigation.

University of Virginia
Charlottesville, Virginia 22901

Alfred Burger

Antimicrobial Agents in Medicine. By Brian M. Barker and Frederick Prescott. J. B. Lippincott Company, Philadelphia, Pa. 1974. xi + 296 pp. 15.5 × 23.5 cm. Paperback. \$18.50.

The book is divided into ten chapters, three of which cover Properties, Toxicity, Action and Uses; Applications; and Side Effects, Toxicity, and Contraindications of Antimicrobials.

The second chapter consists of a brief discussion of source, activity, mode of actions, absorption, uses, dose, and side effects for each antibiotic. In addition, each paragraph contains a number of references to the current literature. The chapter on Applications covers clinical conditions in the same thorough fashion. Subtopics include clinical features of the condition, infecting organisms, agent of choice, alternative agent, and other therapy.

The latter half of the book contains tables covering topics including blood parameters, excretion characteristics, tissue levels, allergic reactions, side effects involving the blood, cardiovascular system, and nervous system, miscellaneous side effects, contraindications, minimum inhibitory concentrations, and interactions with other drugs.

The book contains a cross index of names of antimicrobial agents including all generic and proprietary names in addition to a subject index.

The format of this book allows for rapid and easy access to a great deal of information about antimicrobial agents and their use. It should prove to be primarily useful to clinicians, educators, clinical pharmacists, and others involved in the clinical application of antimicrobial agents.

Department of Medicinal Chemistry
and Pharmacology
Northeastern University
College of Pharmacy and Allied
Health Professions
Boston, Massachusetts 02115

Victor D. Warner

Advances in Chromatography. Volume 11. Edited by J. Calvin Giddings and R. A. Keller. Marcel Dekker, New York, N.Y. 1974. xi + 196 pp. \$19.75.

This book, which is the eleventh volume in "The Advances in Chromatography" series has four separate and diverse articles. The first by Josef Novak is a highly theoretical discussion of "Quantitative Analysis by Gas Chromatography". It is an excellent review with over 110 references. Included in the article are definitions of fundamental terms and classification of detectors. The relation between peak areas and the amount in a chromatographic band as well as with other peak parameters is well covered, and the possibility of predicting molar response is discussed. In the last section, the problems in quantitation and various working techniques are described. The discussions are all based on mathematical expressions; however, the descriptive material is clear and can be read by those without a rigorous mathematical background.

The second article by Wang, Lin, and Wang is a practical account of polyamide layer chromatography. The sorption mechanism is discussed and the techniques for preparing the layers are described in detail. The technique has been used in separating phenols, amino acid derivatives, heterocyclic compounds, acids, esters, and lactones. The R_f values and solvent systems used in separating some of these compounds are given. The bibliography has 177 references.

The third article by Bartels and Prijs is on an interesting chromatographic phenomenon: the induction in silica gel of a specific adsorption capacity to only one substance. These specifically absorbing silica gels can be used in the batch method, thin-layer, or column chromatography. They have been utilized to isolate compounds which are not readily resolved by other chromatographic techniques, to separate optical isomers, to determine the relative configuration of organic molecules, and to find bioisomeric compounds. In addition, the specifically absorbing gels may be used as models for biological specificity phenomenon.

The last article is an excellent practical review of the nondestructive methods available for detecting compounds in paper and thin-layer chromatography. The limitations as well as the virtues and applications of the methods are discussed and the bibliography includes 348 references.

This book will not have universal appeal but will be useful to anyone working in these areas. It is an excellent addition to the library of the analytical chemist or the chromatographer.

Department of Chemistry
University of Rhode Island
Kingston, Rhode Island 02881

Phyllis R. Brown

Using the Chemical Literature. A Practical Guide (Books in Library and Information Science Series. Volume 11). By Henry M. Woodburn. Marcel Dekker, New York, N.Y. 1974. viii + 302 pp. 15 × 21.5 cm. \$14.50.

There is a rumor to the effect that, after 25 years of reliance on personal contact as the most important method for transmitting information, our chemists and chemical engineers are finding it necessary to go to fewer conferences and to spend more time in the library. If they received their formal training since 1950 they probably never took a course in the use of the literature of chemistry and chemical engineering and therefore should welcome Professor Woodburn's book, written after 50 years of experience teaching chemistry at what is now SUNY—Buffalo. The book is equally applicable as a text in what is hoped will be a revival of formal instruction in the use of chemical literature.

The author chose to make the book a practical guide to the use of those periodicals and reference works that present unusual difficulties to the uninitiated. Because no comprehensive text on the literature of chemistry and chemical engineering has been published since the days of Crane, Patterson, and Marr (1957) and Mellon (1958), we hope that the acceptance of Professor Woodburn's current book encourages him to expand it to a more comprehensive type in a future edition.

The book includes succinct "how to use" instructions for U.S. government publications, monographs, review serials, reference books, Chemical Abstracts (and other abstracting services), the Wiswesser line-formula notation, Landolt-Bornstein (and other similar collections of data), collections of spectra, Beilstein, Houben-Weyl, Theilheimer, Gmelin, the Science Citation Index, alerting services (both wide and narrow coverage), microform reproduc-

tion, translation services, the patent literature, and computer-readable data bases. Also included are a glossary of acronyms and a chapter on nomenclature. The literature of medicinal chemistry is not treated specifically. Each chapter includes references to more extensive descriptions of the topics covered.

Armed with this book, and with Fletcher, Dermer, and Fox, "Nomenclature of Organic Compounds" (*Adv. Chem. Ser.*, No. 126) at his elbow, no chemist, young or old, should fear to tackle the problems that the so-called "literature explosion" of the past 30 years seems to pose. As Howard Nutting pointed out years ago, the techniques for carrying out retrospective and current-awareness searches are well established. If one does not want to take the time to learn them, perhaps he should march to the beat of a different drummer and take in a few more conferences.

Arthur D. Little, Inc.
Cambridge, Massachusetts 02140

Edward R. Atkinson

Phenothiazines and Structurally Related Drugs. Advances in Biochemical Psychopharmacology. Volume 9. Edited by Irene S. Forrest, C. Jelleff Carr, and Earl Usdin. Raven Press, New York, N.Y. 1974. xxii + 818 pp. \$40.00.

The phenothiazines and analogs with the same pharmacologic properties are without a doubt the most important drugs in the history of psychiatry and among the most important of drugs in all medical practice. Since their introduction into clinical use about 20 years ago, vast research efforts and comparable numbers of publications have been devoted to an evaluation of their clinical activities, their chemistry, and, most intriguingly, their mechanism of action. There is now general agreement that these drugs do exert a selective antischizophrenic action. Thus, if one were to understand at a biochemical level exactly how they elicit their therapeutic benefit, one might be exceedingly close to an understanding of the fundamental brain abnormalities in schizophrenia. Sadly, progress toward this goal has been greatly hindered by the failure of researchers at one level of inquiry to be fully cognizant of the significance of investigators studying the same drugs but with different techniques and from another perspective. For instance, numerous biochemists have described interesting effects of the parent phenothiazine, chlorpromazine, upon one or another biochemical process and clamored that they now possessed a clue to schizophrenia. Unfortunately, certain of these investigators, lacking knowledge of the varying pharmacology of phenothiazines, have been unaware that there were available phenothiazine drugs closely related in structure to chlorpromazine but which have no antischizophrenic activity. Only much later would other investigators then show that the much heralded effects were produced just as effectively by closely related phenothiazines that lack antischizophrenic efficacy.

Because of these considerations, the present volume is a welcome addition to the literature on phenothiazines. In the symposium, of which this book represents the published proceedings, the organizers brought together a remarkable array of workers representing widely disparate fields. There are many papers on the chemistry of the phenothiazines, with considerable focus on crystallographic and molecular orbital approaches. At the other end of the spectrum are numerous papers on the clinical actions of the drugs. An entire series of papers is devoted to the thioxanthenes, a new class of phenothiazine-related antischizophrenic agents. Though individuals from markedly divergent disciplines are represented, the papers are not "toned down" for the amateur. They are all written at the most sophisticated level for the given discipline and explore subtle though often important nuances. For instance, there are entire papers devoted exclusively to the side effects in clinical practice from certain drugs.

One of the most important contributions of the volume lies in the efforts in several chapters to elucidate clinical differences among various drugs. Early studies had suggested that all the drugs were equivalent. They were either antischizophrenic or not, and none seemed to have differential influences upon particular subtypes of the disease. Some papers in this book suggest that there might be specificity among different drugs. This would be a virtue for the treating physician and would take advantage of the fact that there exists such a large number of commercially available phenothiazines.

The only area of phenothiazine-related research which is not covered in detail relates to the selective effects of the drugs upon dopamine receptors in the brain, much of which was uncovered only after the organization of this symposium. Another minor but

irksome defect of a book with so many contributors is the lack of an author index.

In sum, this book represents one of the most exhaustive and penetrating inquiries into the phenothiazines and other drugs of therapeutic value in schizophrenia. Because its scope is so widespread, the book will be an indispensable volume for most pharmacologists, medicinal chemists, biochemists, and even clinicians with an interest in psychopharmacology.

*Departments of Pharmacology and
Experimental Therapeutics and
Psychiatry and Behavioral Sciences
The Johns Hopkins University School of Medicine
Baltimore, Maryland 21205*

Solomon H. Snyder

Molluscicides in Schistosomiasis Control. Edited by T. C. Cheng. Academic Press, New York, N.Y. 1974. xiv + 266 pp. \$12.50.

The concept of symposia as means for interchange of ideas and summarizing of results may not be highly productive when limited to a group present at sessions. This volume represents a meaningful, and successful, effort in retaining the tempo which led to a practical symposium. Bases for continuing advances are very apparent in the present volume, which was issued only 10 months after the symposium was held. Some credit may be due the rapid manuscript reproduction approach; however, the cooperation of authors with the symposium chairman was crucial.

The symposium was opened with a well-honed appraisal of circumstances which have made schistosomiasis (bilharziasis) a continuing world health problem. There followed 12 units relating to molluscicides in control of transmission of that disease and other, lesser snail-borne infections. A well-balanced assessment of problems, principles, and policies in snail control resulted from the presentations and discussions. Included were matters relating to cost-effectiveness, persistence, toxicity to various species, and ecological effects in general. The practical aspects on presently available molluscicides were complimented by discussions of approaches to more nearly ideal substances through laboratory and other microenvironmental testing. Most contributors supplied numerous references for their presentations.

As may be anticipated from rapid compilation of material covered at a symposium, this volume lacks indexes. That lack will be the less critical through clear definition of topics covered. That deficiency will be decreasingly apparent with justified frequent use (which the book withstands well). The editor and his cohorts have done a thorough job of reporting and assessing this aspect of schistosomiasis control.

*Division of Medicinal Chemistry
Walter Reed Army Institute of Research
Walter Reed Army Medical Center
Washington, D.C. 20012*

E. A. Steck

Beta-Adrenergic Blocking Agents in the Management of Hypertension and Angina Pectoris. Edited by Bruno Magnani. Raven Press, New York, N.Y. 1974. xi + 190 pp. 16 × 24 cm. \$10.00.

β -Adrenergic blocking agents are one of the most recent classes of drugs added to the therapeutic armament. They are mostly used for treatment of cardiovascular disorders although they might also be effective in the treatment of anxiety. Only one of the β -adrenergic blocking agents, propranolol, is currently available in the U.S. Several agents, however, are used or undergoing clinical investigation in England and other countries.

The book is a collection of papers presented at a symposium during the IX International Congress of Angiology, held in Florence, Italy, in April 1974. Ten out of 15 papers contain results of clinical experiments in which effects of a new β -adrenergic blocking agent, timolol, were investigated in the treatment of hypertension and angina pectoris. The symposium is introduced by Ahlquist's paper describing the history and concept of β -adrenergic blockade, and in the next paper Kincaid-Smith presents an overview of the use of β -adrenergic blocking agents in the treatment of hypertension.

The second part of the book, devoted to treatment of angina pectoris, is introduced by two papers describing the design of a protocol for the medical treatment and the criteria for measurement of effectiveness of β blockers. The symposium is concluded by Dalla-Volta's paper discussing medical vs. surgical treatment of angina pectoris.

The book documents exhaustively the effectiveness of β -adrenergic blocking agents in the treatment of hypertension and makes one wonder why propranolol is still not approved in the U.S. for this indication. Several papers, and especially the results of a multicenter, multinational, cooperative trial presented by Brailovsky, indicate that β -adrenergic blocking agents are effective also in treatment of angina pectoris.

Results presented in the book indicate that various β -adrenergic blocking agents, when used in an optimal dosage, are similar in their clinical effectiveness. Comparison of various blockers might help to elucidate the mechanism of their clinical effects. Thus timolol is as effective as propranolol even though it does not decrease the cardiac output. Both blockers decrease the blood level of renin but there is a poor correlation between renin changes and the antihypertensive effect. More experiments are clearly needed to elucidate mechanisms by which β blockers produce their therapeutic effects.

The book suffers from lack of editing. The casual reader might be misled by the fact that some papers mention timolol only by a code name (MK-950) and some use a trade name (Blocadren) in the title. The book provides detailed information about the clinical use of β -adrenergic blocking agents and would be most useful for clinicians and clinical investigators.

*Department of Pharmacology and
Experimental Therapeutics
Boston University School of Medicine
Boston, Massachusetts 02118*

Ladislav Volicer

Terpenoids and Steroids. Volume 4 (Specialist Periodical Reports). K. H. Overton, Senior Reporter. The Chemical Society, Burlington House, London. x + 602 pp. 14 × 22 cm. £18.50.

The enormous volume of literature related to terpenoids and steroids published annually throughout the world makes it almost impossible to follow for the individual investigator. Therefore the series of Specialist Periodical Reports covering these topics is a useful and important summary of publications which should find its way into the hands of every practitioner of the art. The newly published report of "Terpenoids and Steroids. Volume 4", which covers the literature from September 1972 through August 1973, provides an exhaustive source of information of the developments which occurred within that span of time. Professor K. H. Overton, the Senior Reporter, and his colleagues should be congratulated for the very excellent job of compiling the literature and its rapid publication. As usual, the paper and printing are of good quality and the summaries are succinct and to the point.

The volume is divided into two major sections. Part I reviews terpenoids and has chapters covering (1) Monoterpenoids, (2) Sesquiterpenoids, (3) Diterpenoids, (4) Sesterterpenoids, (5) Triterpenoids, (6) Carotenoids and Polyterpenoids, and (7) Biosynthesis of Terpenoids and Steroids. Part II deals with steroids and has chapters covering (1) Steroid Properties and Reactions, (2) Microbiological Reactions with Steroids, and (3) Steroid Conformations from X-Ray Analysis Data. Of particular relevance are the reviews of microbiological reactions and the summary of X-Ray studies of steroids which cover also the literature prior to 1972.

It is somewhat paradoxical that the work of this referee on the biosynthesis of sterols from methionine was misinterpreted (p 282).

This is a most useful and recommended reference book. However, its high price (£18.50) when computed at the official rate of exchange (\$2.40 per £) which amounts to \$44.40 may place it out of reach of the individual investigator who is in daily need of it and for whom it was written. It also came to our attention that the Special Issues Sales Division of the American Chemical Society distributes "Specialist Periodical Reports" and charges \$51.50 for Volume 4.

*Worcester Foundation for Experimental Biology
Shrewsbury, Massachusetts 01545*

Eliahu Caspi