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Book Reviews

Liquid Chromatography of Polymers and Related Materials.

Edited by Jack Cazes. Marcel Dekker, New York, N.Y. 1977. viii + 180 pp. 16 × 23 cm. \$19.75.

In general, this is a good reference work for researchers working on applications of liquid chromatography to polymers and related materials. The topics and quality of the various chapters in this book are both of mixed interest and quality since this volume is reporting on the proceedings of an international symposium in this subject area. This reviewer found particularly useful the chapters on "The Gel Permeation Chromatography of Oligomers" by Ambler and Mate and the chapter on "Chromatographic Analysis of Epoxy Resins" by Crabtree and Hewitt. The latter chapter, in addition to discussing standard gel permeation chromatography (GPC), also contains an excellent presentation of the applications of high-pressure liquid chromatography (HPLC), particularly reverse-phase techniques. Some of the chapters, such as that on "Intrinsic Viscosity by Gel Permeation Chromatography: Method and Application", by M. Y. Hellman, are highly theoretical and may be of less interest to the reader primarily interested in the utilization of GPC or HPLC to the analysis of polymers. In any event, this volume should provide useful reading to most workers interested in the characterization of polymers and should certainly be in every polymer reference library.

Research Triangle Institute

Monroe E. Wall

Drug Metabolism—From Microbe to Man. Edited by D. V. Parke and R. L. Smith. Taylor and Francis, Ltd., London, and Crane, Russak & Co., New York, N.Y. 1977. xii + 460 pp. 18 × 25.5 cm. \$57.50.

In April of 1976, a group of prominent research scientists participated in a symposium which was organized in honor of Professor R. T. Williams. The proceedings of the symposium are presented in this volume which consists of 22 chapters covering a wide range of topics, followed by some brief observations by Professor Williams on future developments in the field of drug metabolism.

Book reviewers frequently feel compelled to note that the title of a given book is rather misleading. Such is not the case with this book. The topics include, among others, metabolism in fish, birds, plants, microbes, and man, as well as mechanisms of drug metabolism. The considerable emphasis given to the troublesome area of species variation is a welcome feature. The chapters are 10–25 pages in length and tend to serve as reviews of the state of various subareas of xenobiotic metabolism rather than as presentations of recent laboratory data or new hypotheses, although several authors do include data which had not been published at the time of the symposium. Most chapters are accompanied by 2–4 pages of pertinent references.

Several of the subject areas (e.g., conjugations, nitrogen oxidation, carbon oxidation, pharmacokinetics, and pharmacogenetics) are among those which have been reviewed in greater

depth by many of the same authors in other recent books, symposia proceedings, and review journals. Therefore, their presence here may not be sufficient reason for individuals to purchase the book for their personal libraries. However, the chapters on xenobiotic metabolism in plants, fish, invertebrates, and various mammalian species contain useful information which is not frequently reviewed elsewhere, rendering this volume a particularly useful reference source. It therefore deserves a place in the libraries of institutions which house active research programs in drug metabolism.

As befits a tribute to such a notable individual, the book has been carefully produced. It contains both a subject index and an author index and is marred by few typographical errors. Thanks are due the editors and publisher for providing us with the symposium proceedings within a reasonable length of time without resorting to the use of photoreproductions of the authors' typescripts. Presumably, discussions of the presentations took place at the symposium, but these are not included in the proceedings. In conclusion, it can be stated that the editors and symposium organizers have achieved their declared goal of presenting a "worthy and fitting tribute" to R. T. Williams.

University of Minnesota

Patrick E. Hanna

Advances in Chromatography. Volume 13. Edited by J. C. Giddings, E. Grushka, R. A. Keller, and J. Cazes. Marcel Dekker, New York, N.Y. 1975. xiv + 324 pp. 15 × 23.5 cm. \$28.50.

Volume 13 of this distinguished series probably will leave the reader wondering if the title of the series might be more appropriately named, "Advances in Physicochemical Chromatography". Of the six chapters contained in this volume, four pertain to the use of chromatography to generate physicochemical data, to the application of physical chemistry principles to effect molecular separations by the use of supercritical fluids, or to interpret GPC elution curves.

The initial chapter coauthored by Gouw and Jentoft represents the fifth review of the use of supercritical fluids in chromatographic separations in a 3-year period. Unfortunately, such literary attention overemphasizes the relative importance of the field which is waning due to the rapid development of high-pressure liquid chromatography. However, the principles and experimental observations set forth in this chapter may be applicable to the application of supercritical fluids in the solvent extraction of thermally labile substances and in the production of high-purity organic chemicals, such as pharmaceuticals, free from residual solvents.

The largest chapter in this volume by Altgelt and Gouw concerns itself with the chromatography of petroleum fractions. The extensive theoretical treatment of liquid-solid chromatography is probably not warranted here and violates the authors statement on p 73 of the text. The authors also attempt to give a small primer on ion exchange, in terms of experimental techniques, which probably is not germane to the title subject.

Overall their review of the chromatographic fractionation of petroleum is satisfactory and probably could have been made better if the excursions into the fundamentals of several of the applied techniques could have been avoided.

The last chapter on qualitative analysis by gas chromatography authored by D. A. Leathard probably has the most intrinsic value to medicinal chemists. Although entire books now exist on this specific subject, Leathard's keen insight into the realities of applying various detectors and the chemical reactions to identify samples, as well as schemes based on the retention behavior of organic compounds, is invaluable. Examples of this insight appear in his appraisal of the Rohrschneider stationary phase index, the use of the flame photometric detector to deduce the number of sulfur atoms in a molecule, and the indispensability of the electron capture detector for trace analysis, despite its inherent experimental complexity.

With additional chapters on the statistical mechanics of adsorption on homogeneous surfaces (Madjar et al.) and derivation of transport and kinetic parameters by GC (Suzuki and Smith), it is difficult to recommend this book to those engaged in medicinal chemistry. However, the reviews which are presented are well done and are a credit to this series.

American Can Company

Jerry W. King

Advances in Chromatography. Volume 14. Edited by J. C. Giddings, E. Grushka, J. Cazes, and P. R. Brown. Marcel Dekker, New York, N.Y. 1976. xiii + 459 pp. 15 × 23.5 cm. \$34.50.

The chief characteristic of Volume 14 of this series is the wide disparity in quality and scope of the individual review chapters. Presumably, this problem rests with the editors of the series and deserves their acute attention. The initial review, entitled "Nutrition: An Inviting Field to High-Pressure Liquid Chromatography", emphasizes nutrition more than HPLC. For example, pp 1-3 recapitulate a brief history of the field nutrition, pp 1-14 are devoted to a rather detailed discussion of hyperuricemia, and a section on the measurement of diet purines containing eight paragraphs discussed HPLC in one-half of a paragraph. Similar problems to the above occur in the section on the measurement of folic acid cofactors, while the chromatography of water- and fat-soluble vitamins rates no more than three paragraphs of discussion. Of the 86 references listed at the back of the chapter, only four are the author's work. This factor, and the limited discussion on HPLC, tends to make one wonder how expert the writer is in this particular review.

Fortunately, the tragic lead-off chapter is followed by an excellent review of polyelectrolyte effects in gel chromatography by Bengt Stenlund. Although Stenlund acknowledges that his major involvement in this technique has been the chromatography of lignosulfonates, he illustrates the importance of phenomena such as ion exclusion or inclusion, excluded volume effects, and polyelectrolyte swelling beautifully with this particular polyelectrolyte. It is Stenlund's ability to illustrate the physicochemical principles involved, without resorting to an extensive mathematical treatment, that highlights this chapter.

The treatment of chemically bonded phases in chromatography by Sebastian and Halasz is not worthy of inclusion in this series. Besides its diminutive size (9 pp), no mention is made of bonded phases for affinity chromatography or the sequestering of metal ions. The authors of this section have written better reviews; hence, this manuscript is a disappointment and one is forced to consult better and more extensive reviews of this subject which are available.

Chapter 4 of this volume is an excellent review of physicochemical measurements by chromatographic methods. It is gratifying to see the work of R. Kobayashi, a noted chemical engineer, finally being recognized by the chromatography community in this work. The extensive tables of activity coefficients are a bit of overkill, and recognition of the structure-activity relationships (Hansch) derivable from liquid chromatography experiments would have improved the chapter.

The application of gas-liquid chromatography to drug analysis is probably the highlight of the volume as far as medicinal chemistry is concerned. It is an excellent treatment by Van-

denHeuval and Zacchei, particularly with respect to sample preparation and the inclusion of actual examples of GLC analysis of drugs. The sections on detectors and data interpretation probably could have been left out, although some pertinent examples of drug analysis using specific detectors are of value. Additional topics, such as the analysis of pharmaceutical preparations, human and animal health drugs (pharmacokinetics), metabolism, and thermal conversion of drugs during analysis, make this section well worth the purchase of the entire volume.

C. L. deLigny in chapter 6 discusses complex association by chromatographic and electrophoretic methods. Although some of the subject matter discussed overlaps with the content of Locke's review, deLigny's discussion is a bit unusual in that the study of molecular association is documented using separation techniques other than GC (for example, the binding of Mn²⁺ to nucleotides by GPC). DiCorcia and Liberti's review of liquid modified for use in chromatography is well done and amply illustrates the use of liquid modified thermal carbon blacks for the analysis of a wide spectrum of organic solutes.

The contents of Volume 14 are truncated by J. K. Haken's treatise of retention indices. Although this topic has been covered in early volumes in this series (Kovats in Volume 1, Rohrschneider in Volume 4, and briefly by Leathard in Volume 13), Haken's review adequately presents new material to make the review worthwhile. In summary, the chapters by Stenlund, Locke, and VandenHeuval make this book well worth its purchase price and a value of medicinal and biochemical researchers.

American Can Company

Jerry W. King

Advances in Chromatography. Volume 15. Edited by J. C. Giddings, E. Grushka, J. Cazes, and P. R. Brown. Marcel Dekker, New York and Basel. 1977. xv + 331 pp. \$29.75.

This volume comprises chapters on detection of bacterial metabolites in media and body fluids by electron capture GLC (J. B. Brooks), signal and resolution enhancement techniques (R. Annino), analysis of water pollutants by GLC and GLC-MS (R. A. Hines), hydrodynamic and flow-induced separations (H. Small), HPLC determination of anticonvulsants (R. F. Adams), microparticulate reversed phase HPLC packings (J. A. Montgomery et al.), GC analysis of soil atmosphere (K. A. Smith), kinematics of gel permeation chromatography (A. C. Ouano), and clinical and pharmacological uses of HPLC (J. A. Nelson). It is printed by the offset process from typescript, bound in washable board, and provided with author and subject indexes and a list of the contents of the preceding volumes. Literature references in the several chapters extend into 1976.

In its entirety, the series of volumes may be a worthwhile ornament to a departmental library; however, few individual scientists are so catholic in their interests as to require or want a desk copy. This volume contains chapters that may be of direct interest to medicinal chemists, as well as others that are nevertheless stimulating. This reviewer would not purchase a series of "Advances in", but this reviewer does not believe in home encyclopedias for his children.

Warner-Lambert Research Institute

Lester Chafetz

Methods of Biochemical Analysis. Volume 23. Edited by David Glick. Wiley, New York, N.Y. 1976. vii + 435 pp. 15.5 × 23.5 cm. \$24.95.

The "Methods of Biochemical Analysis" series was conceived to help scientists keep abreast of developments in the field of biochemical analysis. It was hoped that each new volume would cover discussions of relevant, new techniques or old ones in which significant modifications had occurred and thus that the series as a whole would, in the words of editor David Glick, "comprise a self-modernizing encyclopedia of methods of biochemical analysis". Volume 23 was published in 1976 and includes discussions of five methods (calorimetry, bio- and chemiluminescence, centrifugal fast analyzers, x-ray diffraction, and affinity chromatography), an author and limited subject index for these topics, and cumulative author and subject indices for volumes 1-23.

Chapter 1, "Calorimetry as an Analytical Tool in Biochemistry and Biology", by Charles Spink and Ingemar Wadso, is the longest chapter, representing almost one-half the entire volume. It begins with a discussion of instrumentation in which the basic calorimetric theory is sketchily covered (assuming previous knowledge on the part of the reader) while the presentation of typical calorimeters is very elaborately treated with many detailed figures of calorimetric designs. However, the error discussion is very well done, as is the presentation of applications of calorimetry to biochemistry and biology. Many different types of applications are covered; usually several very interesting examples of each type are discussed and critically evaluated. This article is also very well referenced.

The second chapter is "Recent Advances in Bioluminescence and Chemiluminescence Assay" by W. Rudolph Seitz and Michael Neary. It was prepared as a supplement to a chapter by Strehler in volume 16 of this series and consequently concentrates on new developments concerning bacterial bioluminescence and chemiluminescence indicator reactions.

The third chapter, "The Use of a Centrifugal Fast Analyzer for Biochemical and Immunological Analyses" by Carl Burtis, Thomas Tiffany, and Charles Scott, contains an excellent treatment of the theory and instrumentation for centrifugal fast analysis. This discussion would be worthwhile for someone just entering the field, as well as for someone already working with the instrument. The section on applications contains a good discussion of parameters which affect the analytical performance of a fast analyzer and a limited number of examples of a wide variety of biochemical and immunological applications.

Chapter 4, "The Growth and Preliminary Investigation of Protein and Nucleic Acid Crystals for X-ray Diffraction Analysis" by Alexander McPherson, presents some very interesting and current concepts in the field, such as the use of vibrations and sound in crystallization. However, in general, the chapter seemed to be a long-winded and lengthy treatment of the material covered. For example, more than 20 pages were devoted to a tabulation of summaries of the methods used to crystallize most of the macromolecules which had been crystallized by the data of writing. However, the author cautions the reader that this lengthy list is probably not complete and that the reader should not try any method listed without first checking the references cited!

The last chapter is "The Purification of Biologically Active Compounds by Affinity Chromatography" by Meir Wilchek and Charles Hexter and provides a clear, concise introduction to the principles of affinity labeling, a brief discussion of techniques for the covalent linking of ligands to insoluble carriers, and numerous examples of affinity purifications of enzymes, enzyme inhibitors, receptors, and peptides (no immunochemical applications are discussed). Most of the examples of each type of application are presented in tables; only a few are highlighted in the text.

This volume is recommended for institutional libraries which can acquire the entire set because, as a whole, the set covers a wide spectrum of biochemical techniques. It is not recommended for personal library purchase as this individual volume contains discussions of several unrelated topics, each of which assumes a different level of prior knowledge in the field. This book is also probably not a wise investment for someone already working in one of the areas discussed because of a timeliness problem. The book was published in 1976; only two 1976 references are included, and the bibliography for chapter 3 contains no entries more recent than 1974.

Childrens Hospital Medical Center

Judy Levy

Handbook of Radioimmunoassay. Edited by Guy E. Abraham. Marcel Dekker, New York, N.Y. 1977. viii + 822 pp. 16 × 23 cm. \$75.00.

The 25 chapters in this book are divided into four groups: generalities, hormonal polypeptides, nonhormonal polypeptides, and low molecular weight compounds. The emphasis in each of the last three groups of chapters is on providing a detailed description of a specific method. Nevertheless, reasonable attention to general perspectives regarding each application is provided in most of these chapters.

There is no discussion of labels other than that of radionuclides (consistent with the title), no discussion of automation for radioimmunoassay, only one chapter on drug analysis (antibiotics), and only six pages devoted to a subject index.

Many excellent chapters by notable workers in the field are included. This makes "Handbook of Radioimmunoassay" a valuable contribution to the literature on this timely topic.

Staff Review

Pharmacological and Biochemical Properties of Drug Substances. Volume 1. Edited by Morton E. Goldberg. American Pharmaceutical Association—Academy of Pharmaceutical Sciences, Washington, D.C. 1977. xii + 411 pp. 22.4 × 15.5 cm. \$21.00.

The dust jacket, showing ball-and-stick formulas and a mouse and a female face with brightly colored portions of their brains, illustrates the need to describe all "pieces" to understand the pharmacological profile of a drug as it evolves from chemical concepts through animal studies to—hopefully—clinical utility. This first volume of a new series differs from comparable British and Swiss publications in that the editor, all members of its editorial board, and all 39 contributors are employed in the pharmaceutical industry. The high scientific level of the presentation attests to the quality of research in that industry. It also unveils a comprehensive view of the methodology, thought processes, and tribulations of industrial medicinal scientists that is quite similar all over the world.

The book contains a collection of over 16 successful drugs in eight different fields of therapeutics. There are two CNS agents (clozapine, pemoline); two cardiovascular drugs (clonidine, dobutamine); two antibiotics (amikacin, cefalozin); two nonsteroidal antiinflammatory agents (fenoprofen, tolmetin) and one steroid drug (halcinonide); three pulmonary and antiallergy compounds acting by divergent mechanisms (albuterol, cromolyn sodium, terbutaline); the exciting histamine H₂-receptor antagonists; prostaglandins with indication of clinical antisecretory, antiulcer, cytoprotective, and antifertility usefulness; and the iodinated diagnostic compound, metrizamide.

Each monograph sets forth the disease condition and the need to control it. The leads or the fortuitous or serendipitous stumbling into a promising structural series is revealed next, SAR furnishing the candidate compound for drug development. In some cases, the chemical synthesis is divulged, and in most examples biochemical detective work and *in vitro* testing are discussed.

Then comes the main body of the monograph, i.e., experimental pharmacology and toxicology. Tests for teratogenicity, carcinogenicity, blood dyscrasias, and other obstacles are listed that could, if damagingly positive, have eliminated the drug from further consideration. Clinical pharmacology and—sigh of relief and triumph—approval of the NDA conclude the story.

Since the authors of each monograph have had their own hand in the discovery and development of the respective drugs, more authoritative descriptions of these events could barely be expected. Through all of it shines the enthusiasm of the participating scientists, the pride in their achievement, and only the barest minimum of proprietary bias toward the product of their labors.

University of Virginia

Alfred Burger

Annual Reports in Medicinal Chemistry. Volume 12. By Frank H. Clarke, Editor-in-chief. Academic Press, New York, N.Y. 1977. xi + 340 pp. 17 × 25 cm. \$14.00.

This is the 12th volume in the highly successful series originated by C. K. Cain. The format is by now well established and is essentially unchanged from 1965. The book is divided into six sections comprising CNS agents, pharmacodynamic agents, chemotherapeutic agents, metabolic diseases and endocrine function, topics in biology, and topics in chemistry.

The section on CNS agents contains material from fields which are sufficiently fast moving to justify annual updating. Included are chapters on antidepressant and antipsychotic agents, anti-anxiety agents, anticonvulsants and sedative hypnotics, and

narcotic analgesics and a chapter on memory and learning which was not covered last year. In the section on pharmacodynamic agents, updated areas from last year include antihypertensives and pulmonary and anti-allergy drugs, whereas areas not covered last year comprise antiarrhythmic and antianginal agents, cerebral vasodilators, antithrombotic agents, and agents affecting gastrointestinal functions.

Under *chemotherapeutic agents*, antibiotics, antineoplastic agents, and antiparasitic agents are continued from last year. Surprisingly, the chapter on antivirals is not considered appropriate for annual updating even though many such compounds were in clinical trial at the time of the review of this topic in Volume 11. On the other hand, a chapter on the biosynthesis of antibiotics is included, although it is questionable in the mind of this reviewer whether the topic is really of sufficient use, to the medicinal chemist who has read the other two chapters on antibiotics, to justify its inclusion at the expense of other areas.

The last three sections are more general in nature. The coverage of metabolic disease includes an annual update of the material on drug metabolism and disorders of lipid metabolism, as well as new sections on inflammatory disease, psoriasis, activators of adenylic cyclases, and modulation of the biosynthesis of prostaglandins. These chapters present a fascinating array of the biochemical processes underlying disease and could give rise to many new ideas in drug design. In the opinion of this reviewer, this section could easily be expanded and is far more relevant to the central problems in medicinal chemistry than are such topics as the biosynthesis of antibiotics and some of the specialized chapters in chemical synthesis toward the end of the volume.

Another thought-provoking section is entitled "Topics in Biology" and includes a chapter on cell surface receptors, a discussion of mineral metabolism, a treatment of the detection of mutagens, a discussion of neurotransmitters and neuroleptic drugs, and a chapter on muscular disorders. The material on mutagens is particularly welcome since this has been a field of constant interest, both in the scientific and lay press. It includes a discussion of the Ames test and some comments concerning the importance of metabolic processes in this area. The majority of chemical carcinogens, as the authors point out, are in fact pre-carcinogens which must be converted to the ultimate active entity by metabolic processes. The common chemical feature of electrophilicity in the ultimate carcinogenic forms is discussed. One may hope that this fundamental treatment of important problems will be extended in future years to the mechanisms and chemical entities underlying other kinds of drug toxicity, such as hepatotoxicity.

The last section, "Topics in Chemistry", seems to this reviewer to be the least pertinent to an annual report in medicinal chemistry. Two of the topics, Chapter 29 on computer-assisted organic synthetic analysis and Chapter 32 dealing with the use of stable isotopes in medicinal chemistry, are broadly based and presumably will be of general interest. The remaining four chapters, dealing with such topics as electrosynthesis, applications of metalated carboxylic acids, and biochemical procedures, seem to me better left to such publications as *Chemical Reviews* or similar treatments of purely chemical topics.

All medicinal chemists must acknowledge their gratitude to the authors and editors of this series for bringing these invaluable updates to us during the past 12 years. Having said that, however, one may also express the view that it is time to get away from the rigid six-section format and to reconsider the areas to be reviewed. The format adds nothing to the organization of the volumes and results in a confusing fragmentation of similar topics. In the current volume, for example, there are three chapters dealing with drug metabolism in three different sections, Chapter 21, "Drug Metabolism", in Section 4, Chapter 24 on mutagens in Section 5, and Chapter 32 on stable isotopes of Section 6. How much easier it would be for the reader if all of these chapters were side by side where they could be viewed as a group. Similarly, Chapters 1, 2, 18, and 25 dealing with antipsychotics and anti-anxiety agents, dopamine adenylic cyclases, and neurotransmitter receptor binding should be grouped together instead of scattered all over the volume. This is especially important since there is no subject index to the volume but only a compound name and code number index. The relevance of this outstanding series to medicinal chemistry could be enhanced if the editors would

consider reorganizing the book to emphasize the material in Sections 4 and 5, to relate these sections more closely to Sections 1, 2, and 3, and to deemphasize or eliminate the extraneous material in Section 6.

University of California, San Francisco **Manfred E. Wolff**

Rodd's Chemistry of Carbon Compounds. Second Edition. Volumes IVB and IVF. Edited by S. Coffey. Elsevier Scientific, Oxford and New York, N.Y. Volume IVB: 1977, xix + 462 pp, 16 × 23 cm, \$75.50. Volume IVF: 1976, xvii + 486 pp, 16 × 23 cm, \$75.50.

Volume IVB is in fact a continuation of Volume IVA. While volume IVA reviewed the chemistry of three-, four-, and five-membered rings containing one heteroatom, volume IVB is restricted to naturally occurring and synthetic compounds possessing the pyrrole and closely related ring systems. Therefore, as the editor points out, volume IVB will be of interest not only to organic chemists but also to "biochemists, pharmacologists, botanists and medical students".

The first chapter by J. D. Hunt and A. McKillop only briefly touched upon pyrrolidine alkaloids and offered little that was new over what was already present in the first edition.

Chapter 8, entitled "Pyrrolizidine Alkaloids", by H. C. S. Wood and R. Wrigglesworth is greatly expanded over the original edition. Besides the hydroxylated derivatives of necines, many of the necic acids, which are carboxylic acids esterified with the hydroxy groups of necines, are also described. The pyrrolizidine alkaloids are subdivided and tabulated into five groups based on the component necines and necic acids. Physical and spectroscopic data are liberally referenced.

Chapter 9 by K. S. J. Stapleford, which reviews the indole alkaloids, reflects the extensive growth of this group of natural products. Structural determinations and biosynthetic importance and interconversion are emphasized, while synthetic aspects are left to other, more specialized treatises. Selected carbazole, tryptamine, yohimbine, aspidospermine-aspidofractinine, iboga, strychnos, and bisindole alkaloids are discussed in terms of their physical and spectroscopic properties. Secondary metabolites, where known, are also described.

Chapter 10 by M. Sainsbury deals with the *Amaryllidaceae* alkaloids which covers about 100 structures. The individual subgroups are tabulated with individual members identified by melting point and specific rotation. References to their isolation are liberally provided. Because of the interest in biosynthetic origin, a considerable amount of attention is devoted to lycorine and ismine. Some syntheses are provided but most of the chemistry is confined to semisynthetic manipulations for structure proof of individual alkaloids.

Chapter 11 by H. C. S. Wood and R. Wrigglesworth is concerned with the tropane alkaloids. Most of these alkaloids have been described previously so that the literature on this group during the last two decades covers stereochemical problems, biogenesis, and synthesis. The authors provide a historical review of general synthetic methods and stereochemical aspects of the tropane ring, followed by literature citations of recent works on the individual tropane alkaloids.

Chapter 12, entitled "Pyrrole Pigments", by K. M. Smith is a subject not covered to any extent in the first edition. The author, who is an outstanding contributor in this field, introduces the uninitiated reader to the simpler open-chain pigments (pyrromethenes and bile pigments), followed by the more complex porphyrins found in metalloporphyrins, haemoglobin, chlorophylls, and vitamin B₁₂. The chapter is richly balanced with synthetic pathways, biosynthetic origins, and chemical reactions. The last few pages are devoted to the applications of spectroscopic techniques to the pyrrole pigments.

Chapter 13 by V. D. Poole is a short treatment entitled "Azaporphins, Benzoporphins, Benzoazaporphins, Phthalocyanines and Related Structures". Brief synthetic descriptions are given for this group since more extensive chemistry has been reviewed elsewhere. The tetrabenzotetraazaporphins (phthalocyanine dyes) are the most important members of this group because of their commercial applications and, therefore, are described in more detail.

Chapter 14 by M. Sainsbury deals with the time-honored indigo group of compounds. This review describes mostly the salient aspects of the subject which appeared in the older literature. The indigo analogues were not assembled as a group in the original edition, and this treatment is a logical, but brief assemblage of an important subject matter.

The last chapter, 15, by D. J. Fry is entitled "Cyanine Dyes and Related Compounds". As the author points out, a more exhaustive review of cyanine dyes is covered in other specialized compendia. The chapter is a brief overview of the synthesis, reactions, and physical properties of this important class of dyes.

Volume IVF, which is devoted to pyridine, quinoline, and isoquinoline and their derivatives, is a second edition of chapter 7 of volume IVA of the first edition. Although the subject matter now spans over twice as many pages, it hardly reflects the monumental growth that has occurred in this area of chemistry in the past 20 years. However, it is a credit to the authors of the five chapters of volume IVF to be able to condense the enormous amount of literature into 438 pages while presenting the important aspects of molecular structure, syntheses, and reactivities of these heterocyclic compounds.

The table of contents in this volume, as in volume IVB, is an excellent description of the organization of the subject as well as an invaluable aid in locating specific types of information.

In the historical development of the individual ring systems, the authors found it advantageous to include many of the references to the early literature which also appear in the first edition. This is not objectionably redundant because the reader will find this procedure necessary for a logical development and introduction of the subject to the recent contributions.

Chapter 23 by Michael H. Palmer contains a description of molecular and electronic structures of pyridine, quinoline, and isoquinoline as determined by modern instrumentation methods such as microwave, NMR (^1H , ^{13}C , ^{14}N , and ^{15}N), and ESR spectroscopy which, of course, do not appear in the first edition.

Chapter 24 by D. M. Smith is devoted to pyridine and its derivatives. After the historical treatment, 20 pages are devoted to methods of synthesis of pyridine derivatives which are followed by approximately 100 pages describing the reactions of pyridine. This section is conveniently organized into reaction type, such as electrophilic, nucleophilic, and radical substitutions. An interesting discussion of the pyridines followed by dihydropyridines concludes the chapter.

Chapter 25 by N. Campbell is a short (2.5 pages) description of "Bicyclic Compounds Containing a Pyridine Ring". This allows the author to devote chapter 26 entirely to "Quinoline and its Derivatives". It is noteworthy that Dr. Campbell is the original author of the entire subject matter covering compounds containing a six-membered ring with one nitrogen atom in the first edition. The organization of this chapter, and the next (final) chapter (27) on "Isoquinoline and its Derivatives" by S. F. Dyke follows the same format described for pyridine. Individual compounds of special biological significance, such as the aminoquinolines used in malaria chemotherapy, are given special attention by Campbell.

As a whole, chemists who have either a longstanding or casual interest in these nitrogen ring compounds will find these volumes very informative and delightful reading for a general overview of the subject, with complete references to other treatises and to the original literature. Finally, this reviewer is old fashioned enough to enjoy having the references in the text instead of searching for them at the end of chapters.

Northeastern University

Felix Granchelli

Terpenoids and Steroids. Volume 7. Edited by J. R. Hanson, Senior Reporter. The Chemical Society, Burlington House, London. 1977. x + 349 pp. 14 × 22 cm. \$50.00.

The seventh volume of this indispensable series surveys literature in the primary journals approximately between Aug 1975 and Aug 1976. Medicinal chemists will be particularly interested in four aspects of the large volume of chemistry discussed: first, the application of novel synthetic reagents to the construction of complex functional arrays among terpenoids; second, the isolation from natural sources of terpenoids and steroids having physiological activity attributable to unusual functional groups

of combinations thereof; third, a chapter reviewing steroidal properties, reactions, and partial synthesis, which will be stimulating to those involved in drug development; and fourth, a short but fascinating chapter on new developments in the total synthesis of steroids. The Reporters have, as in previous volumes, provided an excellent review of this large, diverse, and important body of literature.

Staff Review

Chromenes, Chromanones, and Chromones. Edited by G. P. Ellis. Wiley, New York, N.Y. 1977. xiii + 1196 pp. 16 × 23.5 cm. \$100.00.

This 31st volume in the continuing series of monographs on heterocyclic compounds is the first of a two-part survey on 1-benzopyrans and their condensed derivatives. The literature on chromenes, chromanones, and chromones is surveyed through 1973.

As stated by volume editor G. P. Ellis, many compounds in this family have biological activity and are therefore of potential interest to medicinal chemists. A few examples will suffice to underscore this point. A number of simple alkylchromones (e.g., the 3-methyl compound) have been found to have muscle relaxant, coronary vasodilating, and bronchodilating activity. Alkoxy-substituted analogues also exhibit these properties, and one of them, the natural product khellin, is actually used as a standard reference compound in the preclinical and clinical evaluation of synthetic antispasmodic agents. In other areas, 3-hydroxy-methyl-8-methoxychromone is an inhibitor of anaphylaxis, a number of 8-(*N,N*-dialkylamino)-7-methoxy-2,3-dimethylchromones are CNS stimulants and have been tested as potential barbiturate antagonists, and 2-(tetrazol-5-yl)chromone and related compounds have been evaluated as antihistaminic agents. Chromone-2-carboxylic acid *N,N*-diethylamide elicits similar effects but, in addition, shows some sedative and hypnotic activity. Best known, perhaps, among the members of the chromone family is the bifunctional antiallergic drug, 1,3-di(2-carboxy-4-oxochroman-5-yl)propan-2-ol (disodium cromoglycate).

The organization of this volume follows the traditional style of its predecessors, in that chapters are arranged hierarchically according to the "principal functional group" rule. Thus, coverage of the chromones includes first the unsubstituted parent compound and its benzo derivatives and, then consecutively, compounds that contain alkyl, hydroxy, alkoxy, halogen, nitro, amino, ketone, nitrile, aldehyde, and carboxyl substituents. Separate chapters deal with the naturally occurring chromones and the analytical chemistry of chromones, respectively. Altogether the book contains 21 chapters, and no fewer than 15 of them (60% of the total pages of text) are written by G. P. Ellis himself. One chapter by E. E. Schweizer and D. Meeder-Nycz is devoted to 1-benzopyrans, and four by I. M. Lockhart deal with chromanols and chromanones (the 3- as well as the 4-substituted types). In addition, there is an introductory chapter by Ellis setting forth the overall plan of the volume and discussing nomenclature, which frequently is a cause of confusion to inexperienced readers of the heterocyclic chemical literature. Each chapter includes an exhaustive discussion of physical properties, methods of synthesis, chemical reactions, and commercial use. A vast number of references are provided, as well as author and subject indexes.

Consistently with the practice in other volumes of the Weissberger-Taylor series, ample use is made of structural formulas. There is also a massive amount of tabulated information on physical constants, some of which is unfortunately printed in very small type and may be difficult to read without a magnifying glass. Apart from this minor inconvenience the typography is excellent, and the paper and binding are of high quality.

Since Ellis and his intrepid coauthors deliberately omitted flavones and coumarins from this review in order to expedite its publication, it would be quite unfair to criticize them for this "weak spot" in an otherwise monumental achievement. One can only hope that a companion volume on flavones and coumarins—these immense and extraordinarily diverse families of heterocyclic natural products—will follow without undue delay. As a pair, these volumes would surely represent the definitive work on 1-benzopyran ring systems for many years to come.

Sidney Farber Cancer Institute

Andre Rosowsky

Cyclic Nucleotides in the Nervous System. Volume II. By John Daly. Plenum Press, New York, N.Y. 1977. xiv + 399 pp. 16 × 23.5 cm. \$32.50.

The area of cyclic nucleotide research has virtually exploded within the past few years and should make the appearance of a specialized volume such as this one a very welcome addition to the personal library of researchers in this area. This book is designed primarily for workers specializing specifically in research involving cyclic nucleotides in the nervous system. The specific coverage is best described by the chapter titles and subheadings as follows: Chapter 1, a short "Introduction"; Chapter 2, "Enzymatic Formation, Degradation, and Action of Cyclic Nucleotides", with the subheadings of 2.1 Adenylate Cyclases, 2.2 Guanylate Cyclases, 2.3 Phosphodiesterases, 2.4 Protein Kinases, and 2.5 Phosphoprotein Phosphatases; Chapter 3, "Accumulation of Cyclic Nucleotides", with the subheadings of 3.1 Accumulation of Cyclic Nucleotides, 3.2 Cyclic GMP in Brain Slices, 3.3 Cyclic AMP in Ganglia and Peripheral Neurons, 3.4 Cyclic GMP in Ganglia and Peripheral Neurons, and 3.5 Cyclic Nucleotides in Cells of Neuronal or Glial Origin; Chapter 4, "Functional Role of Cyclic Nucleotides", with subheadings of 4.1 Enzymatic Processes, 4.2 Cell Morphology, Differentiation and Growth, 4.3 Membrane Phenomena, 4.4 Levels of Cyclic Nucleotides in the Brain, and 4.5 Central Behavioral and Vegetative Functions, followed by a short conclusion (p 301).

The subheadings are also divided into more specific areas, e.g., in Chapter 2 the subheadings 2.3 Phosphodiesterases is further divided into 2.3.1 Regional Distribution in Brain, 2.3.2 Morphological Localization in Brain, 2.3.3 Subcellular Distribution in Brain, 2.3.4 Multiplicity of Brain Phosphodiesterases, 2.3.5 Activation, 2.3.6 Inhibitors, 2.3.7 Analogs of Cyclic AMP and Cyclic GMP, 2.3.8 Developmental Changes in Brain Phosphodiesterases, 2.3.9 Strain Differences in Brain Phosphodiesterases, 2.3.10 Ganglia and Peripheral Neurons, and 2.3.11 Cultured Cells. There is an excellent list of references (pp 303-362) and an adequate index. The structures of cyclic nucleotides and agonists and antagonists used for studies on cyclic nucleotide-generating systems in the nervous system are included in an appendix (pp 363-379). This volume is relatively free of errors (although, as with any volume, there are a few minor typos and mistakes in structures). In summary, this volume provides an excellent review and can be used as a source book for research on cyclic nucleotides in the nervous system. This volume should be in the personal library of researchers already in this specific area of research or researchers that may be contemplating the initiation of research in this area.

University of Utah

Leroy B. Townsend

Hormone Chemistry. Second Edition. Volume 2. By W. R. Butt. Halsted Press, a division of Wiley, New York, N.Y. 1977. 272 pp. 16 × 23.5 cm. \$37.50.

This monograph consists of eight chapters. They are entitled "The Steroid Hormones", "Progesterone", "Oestrogens", "Androgens", "Corticosteroids", "Thyroid Hormones", "Catecholamines and Related Compounds", and "Prostaglandins". Each chapter is concisely written and contains a wealth of information, particularly relating to methodology.

The weakest chapter is the one on prostaglandins. There are several erroneous statements and numerous errors in nomenclature and structures. As an example, in referring to the primary prostaglandins, the PGE's and PGF's, the author writes, "The six parent compounds are derived from prostanic acid, a C₂₀ unsaturated hydroxy fatty acid with a cyclopentane ring at C-8 to C-12". C-8 and C-12 are part of the cyclopentane ring in prostanic acid. This is a saturated fatty acid, and it does not contain any hydroxyl group. The parent compounds are not PGE's and PGF's. They are PGG's and PGH's, the endoperoxides. In one place, the author refers to the endoperoxides as endoperoxidases and in another he speaks of hydroxyperoxidase when in fact he means hydroperoxide.

In discussing the total synthesis of the prostaglandins, the author indicates "that each compound can potentially form sixty-four stereoisomers". This statement is patently incorrect

as the maximum number of stereoisomers formed in the synthesis of PGE₁ is less than sixty-four, while with PGF₃ it is more than sixty-four.

Other obvious errors include 5,8,12,14-eicosatetraenoic acid, 7-oxa-13-prostanic acid, and 2-(3-methoxyphenyl)-5,6-dihydro-s-triazolo(5,1a)isoquiniline. Clearly structure II in Figure 8.5 cannot possibly lead to the PGE's or the PGF's. In other structures, bonds are either missing or misplaced (e.g., Figures 8.4 and 8.8). This is evident in other chapters as well. Thus, the 7,8 double bond is missing in equilin (Figure 1.13). An extra bond is found in diethylstilboestrol (Figure 3.7), adrenochrome, and the enol form of adrenolutine (Figure 7.9). In other structures, a substituent is missing as, for example, in structures II and V in Figure 6.6. Other glaring structural errors are found in Figures 2.5 and 6.4.

On p 32, 11 α -hydroxylation is said to lead to 11 β -hydroxy-5 β -pregnenedione. On p 98, reference is made to "an active C₍₁₃₎ methylene group" in oestrone and equilenin. On p 130, the Zimmermann reaction is said to be produced by compounds "with a carboxyl group adjacent to an active methylene group". On p 150, the author speaks of the "configuration around C₍₁₈₎ and C₍₂₀₎"—and the oxy configuration at C₍₂₀₎". The compounds he is referring to are 20-keto steroids. On p 179, amphenone B is said to have a β -aminophenyl group in its structure. On p 170, oxidation of 18-hydroxycorticosteroids is reported to lead to the production of 18,10-lactones. On p 177, the author speaks of the Δ^1 -dihydro derivatives. On p 193, Chaikoff's name is misspelled. On p 252, carboxyl groups are said to be protected by the formation of the trimethylsilyl ethers.

These mistakes tend to detract from the usefulness of this book, which is intended primarily for clinical chemists, chemical pathologists, and related research workers. This book can be read profitably, but the reader must be cognizant and wary of these errors.

G. D. Searle & Co.

Leland J. Chinn

Prostaglandin Research. Volume 36. Organic Chemistry Series. Edited by P. Crabbé. Academic Press, New York, N.Y. 1977. xv + 341 pp. 16 × 23.5 cm. \$26.00.

This volume is a collection of articles intended to describe "the present status of prostaglandin research". Although the book makes an attempt to stress cross-discipline contributions, emphasis is clearly on chemistry with more than half of the book devoted to the synthesis of prostaglandins and their analogues. Chapter 1 is a brief introduction to nomenclature, origin, and biological properties of prostaglandins (Crabbé) and is followed by a chapter devoted almost entirely to a synopsis of current research on prostaglandin endoperoxides and thromboxanes (Samuelson). In keeping with the other chapters, a general introduction to prostaglandin biosynthesis would have been helpful. The chapter on biology and ecology of Gorgonian *Plexaura homomalla* (V. L. Theodor) makes interesting reading but provides no reference to techniques of extraction or the chemistry of prostaglandins from marine sources. This is followed by an excellent chapter on the pharmacology of prostaglandins (R. L. Jones), which will serve as a useful introduction for chemists and biologists interested in the field.

Chapter 5, dealing with physical methods in prostaglandin research, describes extraction and purification procedures, along with a brief section on qualitative and quantitative analysis (Hensby). Readers interested in the application of physical methods to prostaglandin research, however, will need to supplement their reading with Crabbé's excellent review on the subject published elsewhere [*Tetrahedron*, 30, 1979 (1974)].

The chapters on total synthesis and syntheses of modified prostaglandins (Garcia, Maldonado, and Crabbé) provide a valuable summary of work done during the past decade and are the strongest part of the book. Unfortunately, absence of reaction yields and frequent recourse to multiple formulas make rapid screening of flow charts and evaluation of relative merits of the various approaches rather difficult.

Overall, the book contains a wealth of information primarily for chemists interested in prostaglandin research, and it should be a worthwhile addition to their libraries.

Pfizer Inc.

Jasjit S. Bindra

Prostaglandin Synthesis. By Jasjit S. Bindra and Ranjna Bindra. Academic Press, New York, San Francisco, and London. 1977. xiii + 522 pp. 15.5 × 23 cm. \$24.00.

This book provides a critical, comprehensive review of prostaglandin synthesis and reactions. The chemical literature is covered through about the first half of 1976 with later references added in proof. Patent literature, a valuable source of information often neglected in reviews of this type, is also covered.

The book is designed for the organic or medicinal chemist either doing research or about to begin a research project in the prostaglandin area. Its organization is such that it could also be interesting to a nonprostaglandin expert or to a student in organic chemistry. The text could form the basis for part of the type of course usually titled "Natural Products Synthesis" or "Advanced Undergraduate Seminar in..."

Chapters 2 and 3 discuss the original isolation and structure determination and nomenclature of prostaglandins. Chapter 4 explains how the various synthetic approaches are presented. It explains the table of contents and, along with the preface, should be read in the interest of efficiency. The remaining chapters, 5–21, comprising 473 pages, are devoted to the presentation and discussion of prostaglandin chemistry. Chapter 21, entitled "Prostaglandin Analogs", should interest both the practicing medicinal chemist and student.

The flow diagrams are large, clear, and easy to follow. Reagents are listed for each step and are conveniently located to the pertinent diagrams. These characteristics make this review easy to read or browse through. Another valuable feature is the inclusion of complete experimental details for what the authors term "core" reactions. When appropriate, the individual chapters are concluded by a discussion of biological results and there is an appendix listing selected reviews according to pharmacological area.

The book has no comprehensive author index. Although not a major problem to someone familiar with the area, since there are many cross-references in the text, such an index would be valuable to the nonexpert. I found few mistakes in the text and those were minor, e.g., structure 4, p 101.

I do not hesitate to recommend this book. In fact, I feel it to be a bargain in this day of \$40 and \$100 volumes "for the expert".

G. D. Searle & Co.

Richard A. Mueller

Biosynthesis. Volume 5. Specialist Periodical Reports. J. D. Bu'Lock, Senior Reporter. The Chemical Society, Burlington House, London. 1977. ix + 318 pp. 14 × 22 cm. \$45.00.

This volume covers the literature of 1975–1976 in the same style and format as its predecessors. Dr. T. J. Simpson replaces Dr. Money as reporter on the biosynthesis of polyketides; the major review article, now standard for each volume of the series, is a 65-page account of the biosynthesis of naturally occurring oligopeptides by Drs. Vining and Wright.

It is embarrassing to have to report that at least some of the subscribers to this volume will get parts of Chapter 5 (Non-protein Amino Acids) and Chapter 6 (Alkaloids) bound in the volume upside down and backward!

Staff Review

Serotonin in Health and Disease. Volume IV. Clinical Correlates. Edited by W. B. Essman. Spectrum Publications, New York, N.Y. 1977. 444 pp. 16 × 23.5 cm. \$37.50.

This book provides an assessment of current issues relevant to the functional position of serotonin as a correlate of clinically important processes and systems, excluding those aspects of central nervous system pathophysiology which are found in Volumes III and V. However, the distinctions are not absolute

and the reader should consult Volumes III–V to ensure adequate coverage of "clinical correlates".

An elucidation of serotonin to human disease processes has been severely hampered by the lack of selective serotonin agonists and antagonists. In this difficult area, the present volume provides in six chapters a series of specialized aspects of serotonin in disease processes. The chapters are concerned with serotonin and collagen metabolism, the kidney, joint disease, platelet uptake and storage, the alimentary system, and tumors. In their respective areas the authors have satisfactorily reviewed the literature and in many cases have included original data. While inevitably the correlation of an altered serotonin function to a precise clinical symptomatology is often speculative, the value of the book is to provide the reader with both an authoritative and stimulating basis for further work. The book is well organized and presented and, when understood as a component in a series, has undoubted value both to the clinician and researcher.

University of Bradford

Robert J. Naylor

Books of Interest

Chemie der Pflanzenschutz- und Schädlings-Bekämpfungsmittel. By R. Wegler. Springer-Verlag, Berlin, Heidelberg, and New York. 1976. xiii + 322 pp. 17 × 25.5 cm. \$55.80.

Principles of Colloid and Surface Chemistry. By Paul C. Hiemenz. Marcel Dekker, New York, N.Y. 1977. xi + 516 pp. 16 × 23 cm. \$19.50.

Environmental Cancer. Advances in Modern Toxicology. Volume 3. By H. F. Kraybill and Myron A. Mehlman. Halsted Press, New York, N.Y. 1977. xii + 388 pp. 16 × 23.5 cm. \$24.50.

Methods in Enzymology. Volume XXXIV. Affinity Techniques and Enzyme Purification. Part B. By William B. Jakoby and Meir Wilchek. Academic Press, New York, N.Y. 1977. xxxiii + 810 pp. 16 × 23.5 cm. \$39.50.

Writing a Scientific Paper. Fourth Edition. By Vernon Booth. The Biochemical Society, London (Published by permission of Koch-Light Laboratories Ltd.). 1977. 32 pp. 15.5 × 24 cm. \$2.00.

Encyclopedia of PVC. Volume 3. By Leonard I. Nass. Marcel Dekker, New York, N.Y. 1977. xiii + 610 pp. 18 × 26 cm. \$Fr 240.00.

Advances in General and Cellular Pharmacology. Volume 1. By T. Narahashi and C. P. Bianchi. Plenum Press, New York, N.Y. 1976. \$24.50.

Infrared and Raman Spectroscopy. Part C. By Edward G. Brame, Jr., and Jeanette G. Grasselli. Marcel Dekker, New York, N.Y. 1977. \$36.50.

Interfacial Synthesis. Volume 2. Polymer Applications and Technology. By Frank Millich and Charles E. Carraher, Jr. Marcel Dekker, New York, N.Y. 1977. \$59.50.

Anionic Surfactants—Chemical Analysis. Surfactant Science Series. Volume 8. By John Cross. Marcel Dekker, New York, N.Y. 1977. \$29.75.

Clinical Neuropharmacology. Volume 2. By Harald L. Klawans. Raven Press, New York, N.Y. 1977. \$18.75.

Hazards in the Chemical Laboratory. Second Edition. By G. D. Muir. The Chemical Society, Burlington House, London. 1977. \$14.00.

Please note: from time to time we will list a series of books, not really of sufficient interest for a thorough review, but yet readers of the *Journal of Medicinal Chemistry* may wish to be alerted to their existence.