

of the National Cancer Institute according to the methods of Geran et al.¹⁴

The antifertility testing involved a serial-mating procedure similar to that employed by Jackson.⁹ Groups of four to six male Swiss albino mice were administered **2**, both ip and orally by gavage, for five consecutive days at doses of 10, 15, 22.5, and 33.8 mg/kg. After a recovery period of 2 days, each male was placed with a female for 1 week. Females were removed and new ones placed with each male at weekly intervals for 5 weeks. Females were sacrificed 19 days after first being placed with the male and determined, via laparotomy, to be nonpregnant or pregnant with live, resorbed, or dead fetuses. Compound **1** was similarly tested at 10 mg/kg, ip and po, for 3 weeks.

Acknowledgment. This work was supported in part U.S. Public Health Service Research Grant No. CA-13123 from the National Cancer Institute.

References and Notes

- (1) Presented at the Medicinal Chemistry Section, APhA Academy of Pharmaceutical Sciences, Orlando Meeting, Nov 1976.
- (2) L. A. Cates and R. L. Gallio, *J. Pharm. Sci.*, **63**, 1480 (1974).
- (3) L. A. Cates and M. B. Cramer, *J. Pharm. Sci.*, **65**, 439 (1976).
- (4) A. Leo, C. Hansch, and D. Elkins, *Chem. Rev.*, **71**, 525 (1971).
- (5) Hexamethylphosphoric triamide (+0.28) – dimethylamine (–0.19) + 2 ring closures (–0.09 each) + 1-hydroxyladamantane (+2.14) + intramolecular H bonding (+0.65) = +3.08.
- (6) **1** (+3.08) – NH₂ (–1.16) – intramolecular H bonding (+0.65) = +3.59.
- (7) G. M. Kosolapoff, "Organophosphorus Compounds", Wiley, New York, N.Y., 1950, p 238.
- (8) Ratio of mean survival time of treated animals to control animals, expressed as percent. An initial T/C value >125% is considered necessary to demonstrate activity.
- (9) H. Jackson, *Br. Med. Bull.*, **20**, 107 (1964).
- (10) G. W. Peng, V. E. Marquez, and J. S. Driscoll, *J. Med. Chem.*, **18**, 846 (1975), and references cited therein.
- (11) H. Stetter and W. D. Last, *Chem. Ber.*, **102**, 3364 (1969).
- (12) W. P. Purcell, G. E. Bass and J. M. Clayton, "Strategy of Drug Design", Wiley, New York, N.Y., 1973, p 127.
- (13) "Handbook of Chemistry and Physics", 50th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1969, p p-32.
- (14) R. I. Geran, N. H. Greenberg, M. M. MacDonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 3*, **3**, No. 2 (1972).

Book Reviews

Monoamine Oxidase and Its Inhibition. Ciba Foundation Symposium 39. Edited by G. E. W. Wolstenholme and J. Knight. Elsevier-Excerpta Medica-North Holland, Amsterdam, and American Elsevier, New York, N.Y. 1976. 24.6 × 17.5 cm. xii + 415 pp. \$29.25.

Monoamine oxidase (MAO) was first described by Mary L. C. Bernheim in 1928 (then Mary Hare of the University of Cambridge), now a youthful heptagenarian at Duke University, to whom this symposium volume is dedicated. MAO has had an exciting and useful history and has remained on center stage of biochemical, therapeutic, and psychiatric studies. For almost 4 decades it was regarded as an entity, but with the refinement of analytical, separation, and behavioral techniques its homogeneity in different organs and species was put to the question. Forty years after its discovery, J. P. Johnston found that MAO existed in two forms, A and B, with different substrate specificities and different rates of inhibition by such newer selective inhibitors as clorgyline and deprenyl. It is not at all clear, however, whether these two forms are not artifacts arising from procedures to wrench the enzyme from subcellular structures with chaotropic reagents during its solubilization. Indeed, a gradual separation of enzyme activity from "environmental" lipids may give rise, conceivably, to the baring of two unlike catalytic sites or conformationally different solubilized forms. These uncertainties are compounded by differences in the results of in vitro and in vivo inhibition studies. The best known property of MAO is its ability to deaminate biogenic amines which play a role in maintaining behavioral "normalcy" and physiological functions such as blood pressure. Clinical inhibition of MAO raises the level of such amines with spectacular effects on depressed states. It seems that inhibition of both forms of MAO is needed for antidepressant success, and yet there are arguments against that. Many measurements of MAO and its inhibition have been made in platelets and in purified preparations from liver; transposing the results of these experiments to brain mitochondria—not to speak of poorly classified affective disorders—has many pitfalls. All these questions are being aired in the present symposium, and the verbatim discussions reprinted at the end of each paper illuminate these unresolved difficulties. Twenty-five contributors and numerous discussants have given their best to make this symposium readable and authoritative. The available MAO inhibitors

have been troubled by occasional side effects, and the present symposium with its emphasis on selectivity of inhibition may be the rejuvenating catalyst for newer drugs useful in ambulatory patients.

The book is printed beautifully, an 1882 etching of an old man grieving by van Gogh gracing the jacket and putting the reader in the right mood to delve into the biochemical causes of clinical depression.

University of Virginia

Alfred Burger

Radiotracer Techniques and Applications. Volume 1. Edited by E. Anthony Evans and Mitsuo Muramatsu. Marcel Dekker, New York, N.Y., and Basel. 1977. 16 × 23.5 cm. xiii + 687 pp. \$65.00.

This is the first of a two-volume set on the radiotracer technique as applied to chemistry, biology, and medicine. Except for one chapter dealing with the determination of radioactivity in biological material, the first volume is concerned primarily with chemical subjects.

There are three introductory chapters on the design of radiotracer experiments, selection and properties of radionuclides, and safety aspects of radiotracer experiments which provide a concise summary of their subjects. Although they are a bit telegraphic for the novice reader, there is a good reference list for those who would wish to read more broadly.

The chapters on the preparation of radiotracer compounds, quality control and analyses, storage, and stability are written with great knowledge and experience. They would be read with profit by any who plan to synthesize or use organic radiotracer compounds.

The chapters on the application of radiotracers to the study of reaction kinetics, exchange processes, solution properties, diffusion, and interfacial phenomena are authoritatively written and strike a good balance between theory and practice. They demonstrate very clearly the power of the radiotracer method in elucidating these complex phenomena.

There is a final descriptive chapter on radiotracers in environmental studies that gives the flavor of this application but no great detail.

The volume is more of a handbook than textbook; it can be kept for reference and read to advantage before embarking on radiotracer experiments in the chemistry laboratory. By gathering together material found in diverse sources and by having the chapters written by authoritative figures, the editors have performed a useful service. However, for a book that is photoreproduced from a typed manuscript, it seems a bit pricey.

Harvard Medical School

S. James Adelstein

Organic Syntheses via Metal Carbonyls. Volume II. Edited by I. Wender and P. Pino. Wiley, New York, N.Y. 1977. 15.5 × 23 cm. xiii + 743 pp. \$45.00.

This book is the second volume of a two-volume series describing transition metal carbonyl chemistry. This volume follows the format of the earlier work and contains a succession of reasonably up-to-date and comprehensive reviews describing synthetic reactions of metal carbonyls. This second volume also includes short chapters on superficially related topics such as hydrocyanation, hydrosilylation, and transition metal catalyzed symmetry-restricted reactions. Most chapters are reasonably current, usually including some references into 1976.

This book appears at a time when one-carbon catalytic chemistry is enjoying a resurgence of interest. It is not a book easily read from cover to cover by a nonspecialist. However, this volume would be especially useful for a synthetic chemist who wants an introduction to one of the specific areas covered by a chapter. The types of chemistry possible with transition metal carbonyls are most applicable to industrial chemistry, and the authors of most chapters have provided a sound background with good descriptions of the limitations and advantages of these catalytic reactions. This reviewer found the inclusion of an index to be a particularly valuable feature. Many chapters contain useful tables of examples which nicely complement the discussion.

Topics reviewed include (authors): 1, Carbonylation of Saturated Oxygenated Compounds (F. Piacenti and M. Bianchi); 2, The Hydroformylation Reaction (P. Pino, F. Piacenti, and M. Bianchi); 3, Hydrocarboxylation of Olefins (P. Pino, F. Piacenti, and M. Bianchi); 4, Synthesis via Allylic Complexes of Metal Carbonyls (G. P. Chiusoli and L. Cassar); Carbon Monoxide Addition to Acetylenic Substrates (P. Pino and G. Braca); Carbonylation of Organic Halides (T. A. Weil, L. Cassar, and M. Foa); Organic Syntheses with Iron Pentacarbonyl (H. Alper); Decarbonylation Reactions (J. Tsuji); Hydrocyanation (E. S. Brown); Hydrosilylation (J. F. Harrod and A. J. Chalk); and Catalysis of Symmetry-Restricted Reactions by Transition Metal Compounds (J. Halpern).

Overall, this book has to be highly recommended for purchase as a library or reference book. The price (\$45), though not unreasonable for a technical book of this size, would seem to limit personal purchases to scientists with specialized interests in the subject area.

Texas A&M University

David E. Bergbreiter

Ion Exchange and Solvent Extraction. Volume 7. Edited by Jacob A. Marinsky and Yizhak Marcus. Marcel Dekker, New York, N.Y. 1976. 15.5 × 23.5 cm. xiv + 294 pp. \$32.50.

This volume presents five different articles on the phenomenon of ion exchange. This is the seventh volume of a series designed to explore in depth the principle and practice of ion exchange and solvent extraction. The first two chapters will appeal most directly to the synthetic chemist who must create new resins to meet specific design requirements. While few details are given which would help the practicing chemist who must apply ion exchange to his or her particular problem, it is possible that some theoretical insight into the diffusion process within the resin bead could be gained.

Chapter three contains an excellent discussion of spectroscopic studies of ion-exchange resins and zeolites. The author demonstrates the usefulness of spectroscopy in the study of both the matrix structure and the nature of the ion-exchange site itself. Chapter four deals with the ion-exchange processes found in natural water systems. A thorough and lucid discussion is

presented which should be of immense aid to the chemist studying the environmental aspects of heavy metal pollutants.

I found the last chapter on thermal regeneration of ion exchangers to be the most interesting. While such a thermal regeneration process may be useful to the analytical chemist, the authors have shown the usefulness of this process to the large-scale industrial user. Cheap and efficient softening of brackish waters and sewage treatment are two such applications which are discussed.

In my opinion, the only weakness of this book is the highly selective audience for whom it is written. While the book is definitely written for the specialist in resin design and application, the chemist who must use these resins in the laboratory should find some of the theoretical discussions to be of help in giving deeper insights into the ion-exchange process.

University of Rhode Island

Phyllis R. Brown

Psychotherapeutic Drugs. Parts I (Principles) and II (Applications). Edited by Earl Usdin and Irene Forrest. Marcel Dekker, New York, N.Y. Part I: 1976, 15.5 × 23 cm, xvi + 698 pp, \$39.50. Part II: 1977, 15.5 × 23 cm, xvi + 909 pp, \$59.50.

Less than 10 years ago there were no English language, general texts on psychopharmacology. This two-volume work adds to the growing list of books in this rapidly advancing field.

This particular contribution is part of a planned, continued series of textbooks and monographs, by Marcel Dekker, in psychopharmacology, of which Volume 1 was entitled, "Trace Elements and the Brain", edited by Earl Usdin and Merton Sandler, and additional volumes are in preparation.

Because of the multiplicity of subjects related to the field of drugs and behavior, various subspecialties have developed within the field so that a multiauthored specialist approach has become a necessity in order to obtain any related in-depth coverage of the subject matter, as Goodman and Gilman found after the second addition of their classic text on "Pharmacological Basis of Therapeutics".

It is unfortunate that such a time lapse occurred before both parts of this work appeared, because of necessary overlap of subject material and because the subject and author indexes appear only in Part II.

It was an enormous task for the editors to provide a smoothly flowing yet comprehensive book, since different authors viewed their task in entirely different ways—from providing exhaustive reviews to brief overviews of their specialty topic. This, not to mention the extensive overlap, the Editors dealt with in clearly related subject matter. The Editors have done a more than credible job, as the result has provided fairly consistent and up-to-date coverage of most of the important aspects of basic and clinical aspects of the psychotherapeutic drugs.

However, what emerges is more in the nature of a *handbook* than a text, and although Part I deals with *Principles*, it also covers many aspects that are clinically important, such as toxicity, dosage forms, modes of drug interactions, and geriatric psychotherapy, whereas Part II, *Applications*, discusses many aspects of animal metabolism, biochemistry, and chemical structure-activity relationships. Therefore, one interested in the *clinical applications* cannot act by purchasing Part II only. Both parts must be acquired to obtain the most from the work. Therefore, the prices are beyond the reach of students, and only library usage can be recommended.

In addition, this work is not recommended for the beginner or for one casually interested but stands out as an outstanding reference addition for established workers in the field or for those serious students of the disciplines covered. For their purpose, all of the chapters are excellent in scope.

There is a bibliography at the end of each chapter, although some authors do not give titles and full pagination. At the end of Part II there is a subject and author index for both Parts—a spot-check of the latter shows an amazing lack of duplication of citations and references.

It is difficult to choose outstanding chapters among all the excellent ones, but the chapters on etiology of schizophrenia in Part I and those on the neuroleptics in Part II are about as

complete as one could find today.

*Veterans Administration Hospital
Sepulveda, California*

W. G. Clark

*Brentwood V.A. Hospital
Los Angeles, California*

Joseph del Guidice

Cannabis and Health. Edited by J. D. P. Graham. Academic Press, New York, N.Y. 1976. xvi + 481 pp. 15.5 × 23.5 cm. \$36.75.

One has to initially wonder how another new book covering the subject of marijuana could serve a useful purpose. The editor states that the book was designed "to encompass the most recent work on Cannabis which might answer the questions—1. What is Cannabis? 2. What does it do and not do? and 3. What good or bad effects may it have on the health of the individual and of the community?"

By way of an answer to these questions, 12 chapters are presented: Chapter 1, The Pharmacognosy of Cannabis; Chapter 2, The Analysis of Cannabis; Chapter 3, Chemistry of the Cannabinoids; Chapter 4, Biochemical Aspects of Cannabis; Chapter 5, A Critical Approach to Experiments on Cannabis and the Interpretation of their Results; Chapter 6, The Effect of Cannabis on A: The Mind of Man; B: Animal Behavior; Chapter 7, The Pharmacology of Cannabis and Cannabinoids; Chapter 8, Cannabis and Health; Chapter 9, Cannabis and the Psychiatric Position; Chapter 10, Social Science and Cannabis Use; Chapter 11, The Law Relating to Cannabis Use 1964–1973: How Subtle an Ass?; and Chapter 12, Cannabinoids as Therapeutic Agents. Each chapter is authored or coauthored by a scientist who has published from 1–10 papers on some phase of marijuana. All of the contributors, save one, are from English laboratories. Baroness Wootton of Abinger, Chairman of the Cannabis Subcommittee of the Advisory Committee on Drug Dependence 1967–1968, acknowledged as a contributor, prepared a one-page introduction.

The book, to some extent, reflects British experiences to a greater degree than one might expect in dealing with such an internationally important subject. It is, however, rather well written with a minimum of errors. It is disturbing to see on page 9 "Cannabinaceae" (instead of the more correct Cannabaceae); "parental" (for parenteral) on page 79, etc. Also, stating that "Cannabinol...is biologically inactive..." (page 45) seems to oversimplify the pharmacologic profile of cannabinoids. This reviewer, however, found the book to be extremely easy to read and digest, perhaps due to such humor as when Professor Fairbrain (on page 6), relating the mode of collection of Cannabis resin by workers in Afghanistan, states: "If aprons are in short supply, then they walk through naked! (Mr. P. Willey of the Anti-Slavery Society told me that he recently witnessed this taking place in Afghanistan)". If this is not enough to keep one interested, the title of Chapter 11, "The Law Relating to Cannabis Use 1964–1973: How Subtle an Ass?", should be provocative enough to keep one reading!

Whether or not the book answers all three of the questions stated as objectives is questionable. However, "Cannabis and Health", in this reviewer's opinion, should be read by everyone involved in Cannabis research: every physician, pharmacist, nurse, or other individual involved in, or concerned with, the marijuana problem. It is a book that is so fundamentally constructed, with direct attention being brought to the basic problems inherent in Cannabis use and research, that it will serve as an authoritative introduction and reference for many years. Surely every library will want to procure this book as a reference.

The editor should be complimented in being able to convince the contributors to prepare chapters that mesh so closely in content, one with another, and not to simply regurgitate isolated pieces of research data, as most reviews tend to do.

As with most scientific works now appearing on the market, the price could restrict individual purchases of such a fine scholarly work.

*University of Illinois at
the Medical Center*

Norman R. Farnsworth

The Immune System. Edited by F. Melchers and K. Rajewsky. Springer-Verlag, Berlin, Heidelberg, and New York. 1976. xiv + 299 pp. 17 × 25 cm. \$31.70.

"The Immune System" is well organized into five major sections. The first section on antibody structure reviews some basic concepts and introduces new and current research methods which are especially significant for those interested in this subject. One interesting chapter describes a random sample computer correlation of antibodies with certain amino acid positions and relates specific structure with a common idotype. Other chapters in this section discuss x-ray diffraction models which suggest some new orientations for antibody molecules. A final chapter discusses the effect of antigen-induced conformational changes in antibody structure.

The second section discusses the synthesis of antibody molecules with the view that they are coded by two distinct gene regions (V and C). Thoughts on antibody and cell-receptor diversity are also presented primarily from the viewpoint of various somatic interactions.

The third section introduces current views on the function and specificities of B-cells, T-cells, and macrophages. These cell types are also discussed as they relate to more primitive animals.

The next section includes a superb discussion on the major histocompatibility complex and its relationship to cellular recognition and function. Chapters in this section include data which stress the exquisite specificity of the Ir gene products. Some cell surface structural models for MHC gene products are proposed in a chapter dealing with methods for cell surface component purification. It is pointed out that structural data on cell surface antigens place the present state of knowledge in a position similar to that for immunoglobulin structure in 1965.

The final section reintroduces the individual topics discussed in the previous sections with a view of the total system. Jerne discusses immune control from the point of view of idiotypic network regulation. This regulatory system is an attempt to merge his original theories on clonal selection with current discoveries on the specificities of individual cell populations. Other chapters deal with the mathematical justification for this type of regulation.

Overall this book presents an accurate research-oriented view of the immune system that would be of great value for those interested not only in current knowledge but also in future trends.

Northeastern University

James J. Gozzo

The Behavior of Blood and Its Components at Interfaces. *Annals of the New York Academy of Sciences.* Volume 283. Edited by Leo Vroman and Edward F. Leonard with 50 contributors. New York Academy of Sciences, New York, N.Y. 1977. 14.9 × 22.7 cm. 560 pp. \$41.00.

The New York Academy of Sciences has published a monograph of the proceedings of a conference held by the Academy on Feb 10, 1977. The 50 papers presented were part of a continuing program which first evaluated the bases for fabrication and testing of blood-compatible materials. The conference concerned itself principally with the series of reactions which occur following blood exposure to various surfaces: specific plasma protein absorption, adsorbate interaction with plasma, products of adsorbate interaction and their effects on platelets and white blood cells, and adhesion effects on the formation of blood aggregates. The conference was arranged to deal with the order of sequenced events in the research dealing with blood interface actions: first in stagnant blood, then flowing blood, and first in vitro and ultimately in vivo. There also is a description of efforts to improve the development and testing of biomaterials that may be tolerated in the bloodstream.

The 50 presentations are recorded under nine major headings including Part I, Overview; Part II, Adsorption and Reaction of Blood Proteins at Interfaces; Part III, Interface-Introduced Coagulation Reactions; Part IV, Platelet-Interface Reaction; Part V, Interfacial Reactions of Red and White Cells; Part VI, Transport to and from the Blood-Material Interface; Part VII, Blood and the Blood Vessel Wall; Part VIII, The Comparison and Classification of Materials; Part IX, Evaluation of Artificial Interfaces (A. In Vitro Evaluation; B. Ex Vivo and In Vivo

Evaluations); Part X, Summary; the book is preceeded by a short editors' introduction. Each part is followed by the detailed discussion that ensued with transcribed questions and answers included.

The Part I Overview provides a 36-page introduction to blood and biomaterials with an emphasis on properties of materials that affect the behavior of blood at their surfaces and consideration of the organization of blood components near interfaces. The Part X Summary considers the conference findings from the standpoint of the physical scientist, the biologist, and the clinician.

The papers represent a variety of timely reviews and scholarly research presentations dealing with the various aspects of blood component behavior under differing experimental settings. The individual papers vary in length from 2 to 30 pages and are generally well documented, and many contain detailed tables, graphs, mathematical formulas, and photographs dealing with technical, theoretical, and practical aspects of blood interface studies. The papers have been written by researchers active in their respective specialty areas but contain relatively little of general interest to the organic medicinal chemist. The more physically oriented scientist and the clinical scientists with specific interest in blood-interface behavior would find more to grasp in this comprehensive assessment of the "state of the art". Many of the papers abound with fascinating electron micrographs of blood-component interactions and provide a graphic presentation of recent research findings. Scientists with a specialized interest in biomaterials development and improved testing procedures for such agents will have considerable interest in this monograph.

The Ohio State University

Neil J. Lewis

Organic Compounds: Reactions and Methods. Volume 23.

Edited by B. A. Kazanskii, I. L. Knunyants, M. M. Shemyakin, and N. N. Mel'nikov. Translated from Russian by Brian J. Hazzard. IFI/Plenum Data Co., New York, N.Y. 1975. 16 × 23.5 cm. viii + 492 pp. \$57.50.

A time-consuming task in the performance of research involving organic synthesis is the need to review the large number of possible literature sources for material relating to the reactions or related methods of investigation. Therefore, reviews of the literature on specific types of reactions are often of enormous value to the chemist. Under the title "Reactions and Methods in the Investigation of Organic Compounds", of which this is Volume 23, the editors present reviews devoted to the most important and interesting questions of organic chemistry.

This volume begins with a review of the reactions of derivatives of acids of trivalent phosphorus with saturated electrophilic reagents by A. N. Pudovik, I. V. Konvalova, and E. A. Ishmaera. Following this is a 400-page table reviewing the literature in the reaction of derivatives of acids of trivalent phosphorus with electrophilic reagents. The table includes the reference cited, the electrophilic reagent, the compound of trivalent phosphorus, additional reagents, reaction conditions, compound obtained, and the yield as a percent of theoretical. A formula index is also included, keyed to the table, for organophosphorus compounds obtained in the reactions, from C₁ to C₃₂. The volume concludes with a list of 588 references, many of which are to Russian papers.

The authors, editors, and translator have done a commendable job in producing this highly valuable reference work. Those involved in research efforts in which these compounds might play a part will find much use for the contents of this book.

USAF Occupational and
Environmental Health
Laboratory

Donald F. Logsdon, Jr.

Alicyclic Chemistry. Volume 5. Specialist Periodical Reports. By W. Parker, Senior Reporter. Chemical Society, London. 1977. ix + 439 pp. 14 × 22.5 cm. \$56.00.

The Specialist Periodical Reports of the Chemical Society provide in "Alicyclic Chemistry", Volume 5, an excellent survey of the literature of 1975 on carbocyclic chemistry. The discussion is divided into five chapters entitled Three-membered Rings (reported by B. Halton), Four-membered Rings (by I. Watt), Five-

and Six-membered Rings and Related Fused Systems (by N. M. D. Brown and D. J. Cowley), Medium- and Large-ring Compounds (by E. J. Thomas), and Bridged Carbocyclics (by G. B. Gill) and has more than 2000 primary references to the literature of 1975; however, a few 1974 references crept into the review.

Inflation has nearly placed this volume out of the reach of the individual chemists' library; however, it is a volume that every organic chemist should know. It contains an excellent balance of discussion of syntheses and reactions of carbocycles mixed with a consideration of physical properties and structural studies of these systems. The volume seems to be nearly free of typographical and chemical errors; however, *Z* and *E* nomenclature is used when it is inappropriate on page 6, and *cis* and *trans* nomenclature is used instead of *Z* and *E* on page 11 and many other places.

The first chapter is filled with fascinating reactions leading to or resulting from three-membered rings. From the unusual labeling of the i-steroid, 17-(*R*)-3 α ,4 α -cycloandro-6-ene on reaction with D₃O⁺, to the system 5-cyclopropyl-6-azauracil and the description of a reagent for phosphorylating nucleosides, this chapter is rife with reactions applicable to medicinal chemistry. The cycloaddition of 1,3 dipoles of mesoionic compounds with cyclopropanones leads to a variety of interesting heterocycles.

The chapter on cyclobutanes contained many references to [2 + 2] photodimers of ethylene derivatives. For example, 220-MHz proton NMR was used to determine the structure of the photoproduct of d(TpT) in aqueous solution. The thermal dimer of 1-methyl-6-cyano-1,2-dihydropyridine is reported to be a cyclobutane apparently formed by a stepwise process. The reaction of cyclobutylimines provides a convenient synthesis 1,2,3,4-tetrahydropyridine derivatives.

Chiral syntheses from styrene and dichlorocarbene were observed by using the phase transfer catalyses PhCHOHCHN⁺(Me₂Et)Ph. The [π 2a + π 2s] cycloaddition of chiral 2,3-pentadiene and ketenes is regioselective and stereoselective to give chiral cyclobutanones.

Numerous interesting studies of conformations of cyclohexane derivatives are given in Chapter 3. For example, the use of selective complexation of equatorial and axial alcohols with metal chlorides has been used as a separation method. Conformational effects on the stereochemistry of reactions of cyclohexane derivatives received considerable attention.

X-Ray crystal structures are given for a number of natural products and the chemistry of a number of macrolides is discussed in the chapter on medium- and large-ring compounds. The last chapter on bridged bicycles contains, among other topics, the application of NMR, photoelectron spectroscopy, ORD-CD, etc., to structures.

The "Annual Reports" format provides excellent referencing of the information. There is an author index but no subject index. There is some difficulty in finding or refinding information in the volume, but browsing is always worthwhile. Every organic chemist will find something of interest.

North Texas State University

Robert E. Lyle

Introduction to the Spectroscopy of Biological Polymers.

Edited by D. W. Jones. Academic Press, New York, N.Y. 1976. 15.5 × 23.5 cm. xii + 328 pp. \$25.50.

The aim of this book, according to the editor, is "to present the principles, limitations and scope of the spectroscopic techniques that are being focused on biological molecules to undergraduates and more experienced scientists whose background is primarily in chemistry and biology". Although by no means the ideal textbook, this book fulfills its aims adequately. In eight individual chapters, it covers the important spectroscopic methods that have found wide application in the biological fields: infrared, Raman, far-infrared, electronic absorption and emission, optical rotatory dispersion and circular dichroism, nuclear magnetic resonance, electron spin resonance, and Mössbauer spectroscopy. Each chapter is written by an authority experienced in the field and includes the physical principles, experimental procedures, and some spectral interpretations of the method discussed. The technique is then illustrated in a number of applications to biopolymers, with special emphasis on peptides and proteins. The

eight chapters are tied together through an opening and a concluding chapter contributed by the editor. The first chapter serves as an introduction to the spectroscopic process, briefly surveying the methods and some of their common features. The last chapter is an outline of some combined spectroscopic applications to biological systems, followed by a very brief discussion of new spectroscopic developments.

The presentations are generally descriptive rather than mathematical and should be easily accessible to every layman. The reader who is interested in an in-depth discussion of a method is referred to more comprehensive treatises listed at the end of each chapter. The main drawback of the book is a result of its multiple-authorship format. The editor's effort to integrate all the contributed chapters into a cohesive unit is only partially successful. The discussions in each chapter are not always carried out in equal depth, some methods being presented in considerably more detail than others. While, for example, infrared spectroscopy makes up a substantial portion of the book, the chapter dealing with visible and fluorescence spectroscopy is very sketchy, with only fleeting references to the biological applications of these important techniques. The chapter on nuclear magnetic resonance is well outlined but regrettably short and does not include some of the most important applications of this method. Only a few lines are thus devoted to the widely used and very promising ^{13}C NMR. On the whole, however, this book fares well as an introductory monograph. All the chapters are written lucidly and carefully. The schematic representations are well chosen. Numerous well-reproduced representative spectra are given. Although less suitable as a textbook it compares well with what is, to the knowledge of this reviewer, already available and is reasonably up-to-date.

The book is thus recommended to the medicinal chemist, biologist, biochemist, and other bioscientist in search of a quick introduction to spectroscopic methods. It is also recommended as a text for introductory courses in spectroscopic applications in the biological sciences, provided the instructor is willing to confront his students with the steep price of this publication.

University of Connecticut

Alexandros Makriyannis

Intermolecular Interactions and Biomolecular Organization. By A. J. Hopfinger. Wiley-Interscience, New York, N.Y. 1977. x + 395 pp. 16 × 23.5 cm. \$26.00.

For many years, drug-receptor interactions were visualized in terms of small molecules interacting with specific sites on large molecules while ignoring the possibility of either or both these entities undergoing conformational changes during this process. Even more seriously, receptor molecules were tacitly assumed to be existing in a vacuum and their interactions with solvent and other biopolymers were ignored.

In this extremely ambitious book Hopfinger discusses solution theory and conformational properties of some small biologically relevant molecules and provides a very short review of the numerous attempts to predict drug effectiveness on the basis of physicochemical parameters. This is followed by a review of the interaction of water, ions, and drugs with polypeptides, proteins, and nucleic acids, as well as of the interactions of DNA complexes with basic polypeptides and of polypeptides and of collagen with glycosaminoglycans and proteoglycans. The theoretical basis of predicting model solute-solvent and ligand-counterion interactions is presented, followed by a review of the problem of quaternary structure, particularly with respect to protein-protein and protein-nucleic acid interactions. The book concludes with some interesting speculations regarding the role of hydration, coulombic interactions, and van der Waals interactions in aggregate organization.

Some minor criticisms can be raised. The discussion of the relationships between drug actions, partition coefficients, and other physical parameters ignores the important Ferguson principle enunciated in 1939 which reached somewhat similar conclusions. It seems a pity that the discussion of lipid membrane models ignores the numerous studies carried out with local anesthetics using such models and it seems surprising that a discussion of antibody-antigen interactions is lacking entirely. There is also an unusually large number of typographical errors.

However, this book reviews a voluminous body of information not readily accessible and not normally considered by medicinal chemists. The writing is concise and many of the speculations are both interesting and reasonable. The book can be recommended highly.

Tufts University School of Medicine

Henry G. Mautner

Immunochemistry of Enzymes and Their Antibodies. Edited by Milton R. Satton. Wiley, New York, N.Y. 1977. ix + 230 pp. 18 × 26 cm. \$19.00.

This text contains seven chapters by ten contributors dealing with the immunochemistry of enzymes using selected enzyme model systems. The general theme of this book explores the new field of immunoenzymology and its analytic applications. Many new aspects of enzyme structure, function, immunogenicity, evolutionary relationships, and taxonomy are brought into focus by the use of immunochemistry. Each chapter is divided into a logical arrangement usually dealing with a specific enzyme as a model. For example, the first chapter deals with the immunochemistry of lysozyme, starting with a description of its antigenic structure, followed by its derivatives, fragments, synthetic analogues, and immunogenetics.

Other chapters deal with the immunochemistry of lysozyme, bacterial ATPase, relationships of fatty acid synthetases, antigenicity of cytochrome c, and enzyme analysis by quantitative immunoelectrophoresis. For example, bacterial ATPase has been purified, resulting in the ability to prepare antiserum that has been of tremendous value in establishing structure-function relationships and as a new tool for studying molecular architecture of biomembranes as outlined in chapter 4.

Chapter 6, enzyme analysis by quantitative immunoelectrophoresis, may be of particular interest to the medicinal chemist. In this chapter basic immunological methods are briefly mentioned, such as rocket immunoelectrophoresis and crossed immunoelectrophoresis. Newer immunological modifications or combinations of techniques, such as immunoaffinoelectrophoresis, and combinations of various immunochemical and immunoenzymatic techniques are also discussed. This chapter covers techniques that will have increased applications in medicinal chemistry in the future.

Each chapter is separate and some overlap is inevitable, but each chapter is highly informative and well organized and demonstrates the tremendous sensitivity and diagnostic potential of enzyme analysis coupled with immunochemistry. This text is geared toward the research-oriented medicinal chemist, microbiologist, enzymologist, or immunologist.

New England Deaconess Hospital

Anthony P. Monaco

Chemical Pharmacology of the Synapse. By D. J. Triggle and C. R. Triggle. Academic Press, London, New York, and San Francisco. 1977. 16 × 23.5 cm. viii + 654 pp. \$43.75.

This book offers a wide discussion of synaptic functions from different approaches. The first chapter presents a general view of the synapse structure and function, with a detailed discussion of the fundamental criteria for neurotransmitters: synthesis, storage, release, interaction at the receptor sites, and removal. In this chapter, the reader will find the tables and schematic presentations rather helpful. The second chapter is mainly devoted to the kinetics of ligand-receptor interactions, after a short introduction which describes the cell membrane structure, the membranal organization, and localization of receptors. This chapter offers a comprehensive review of receptor concepts and theories with regard to ligand-receptor association and response, agonists and antagonists, intrinsic activity, and efficacy. As a conclusion to the ligand-receptor interactions, other related events such as subsensitivity, supersensitivity, and desensitization processes are discussed. The third chapter describes in great length the structural requirements for the binding of neurotransmitters to the receptor sites as well as the activity changes caused by conformation changes in the neurotransmitter molecules. The structure-activity relationships are illustrated by well-selected and specific examples. The fourth chapter deals

with the electrophysiological events at the membrane of nervous and muscular tissues as mediated by neurotransmitters. The influence of ions is discussed in detail. The last chapter, which is also the shortest, describes the different approaches used for the isolation of neurotransmitter receptors, their purification, quantitation, and reconstitution.

Because of its wide scope, this book can attract the interest of the pharmacologist as well as the biochemist, physiologist, or chemist. Each chapter with the bibliography at the end is a good review by itself, the synapse as a unit being discussed from a different point of view. The reader may find some redundancy but this may very well serve the purpose of clarification. A newcomer in the field or a graduate student with little background may have some difficulties understanding this book because of the highly specialized style and the specificity of the examples discussed in every section.

It would be a good reference book for the research specialist or postgraduate students of pharmacology, biochemistry, and electrophysiology. Graduate students may find it too advanced and the price not very affordable.

Virginia Commonwealth University

Thuy Chau-Pham
Louis S. Harris

How Modern Medicines are Developed. Edited by Frank H. Clarke. Futura Publishing Company, Mount Kisco, N.Y. 1977. 15.5 × 23 cm. 144 pp. \$12.00.

This stimulating review is a sequel to "How Modern Medicines are Discovered", also edited by Dr. Clarke (Futura, 1973). The chapters, with one exception, derived from papers presented at a symposium for science writers held at Rockefeller University in May 1972.

The format is a series of eight chapters written by widely experienced and successful research directors, each of whom draws on a wealth of personal lore to illustrate the importance of developmental science in transforming a scientific observation into a useful therapeutic agent.

The developmental aspects of the drug-producing industry have been largely neglected in the literature, although they are often determining factors in making new therapies available. Examples described by the chapter authors include anecdotal accounts of the development of prostaglandins, ethambutol, narcotic antagonists, clinically useful dosage forms, tranquilizers, and antigout and uricosuric agents. Each example is a brief but accurate vignette of developmental problems and opportunities. An introductory chapter recounts the role of technology in the developmental process and a concluding chapter gives predictions on developmental research and the future.

On balance, the book is a very readable and interesting account of drug development, even to one with 30-odd years of experience in the field. The examples used, although limited by necessity, are good ones and are representative of hundreds of others which were not included. The book should be recommended reading for everyone in the drug field and should be interesting and informative to the informed layman who wishes to know more about this process.

Format, binding, and typography are excellent. The few typographical errors are not misleading and will certainly be corrected at the next printing.

The Upjohn Company

E. L. Schumann

Topics in Enzyme and Fermentation Biotechnology. Volume 1. Edited by Alan Wiseman. Halsted Press, New York, N.Y. 1977. 16 × 24 cm. 191 pp. \$25.00.

This book is described as the foundation volume of a new "open ended" series which will attempt to offer balanced, up-to-date, and thorough presentations of enzyme and fermentation biotechnology. The series hopes to target a broad array of research disciplines for potential readership including medicinal chemists, biochemists, chemists, microbiologists, and others. The first volume consists of 8 chapters including a brief introduction by the editor.

The reviews in Volume 1 are thorough and authoritative although they are all somewhat dated. Most of the literature cited is 1975 or earlier, with some chapters containing references largely from the 1960's.

J. Melling provides an excellent discussion on the regulation of enzyme synthesis in continuous culture. The chapter dealing with foam separations of biological materials (A. Thomas and M. A. Winkler) is devoted to the application of this procedure to the separation of enzymes from other proteins. The important problem of aeration in mold and Streptomyces culture media is covered in chapter 3 by G. T. Banks. Aspects of this problem have been reviewed in detail elsewhere although the present work pays specific attention to mold and Actinomycete fermentations. M. O. Moss reviewed the enzymic alteration of penicillins and cephalosporins. Although most references are earlier than 1975, the review is well written, and some experimental details are included for the β -lactamases and penicillin acylases. An unusual part of this volume is chapter 6 which is concerned with patenting developments with microorganisms and their products. Although no references are given, F. S. M. Grylls gives us a good introduction to the roots of patent laws and the problems associated with patenting microbial processes. The uses of industrial glucose isomerases are covered by C. Bucke. Attention is given to microbial sources of the enzymes and to the immobilization of whole cells or soluble enzymes and their applications. Chapter 8 is written by the editor to describe microbial cytochrome P-450 with specific emphasis on drug applications. The review is good, but most references are from 1975 or earlier in this rapidly developing field.

A major problem with this new series is that it will have to compete with existing series which address similar topics. It remains to be seen how the quality and timeliness of future volumes will compare with these. On the whole, ownership of this volume would be valuable to people working with enzymes and/or fermentation processes.

The University of Iowa

John P. Rosazza

Fluorescent Protein Tracing. Fourth Edition. Edited by R. C. Nairn. Churchill Livingstone, Edinburgh, London, and New York. 1976. 14 × 22 cm. xvii + 648 pp. \$45.00.

The book is devoted mainly to fluorescent antibody techniques in immunological tracing of bacteria, protozoa, fungi (chapter 7); virus and rickettsias (chapter 8); direct protein tracing in experimental physiology and pathology (chapter 8); tissue antigens and antibody (chapter 9); and properties of conjugated protein (chapter 3). R. C. Nairn has demonstrated his expertise in the field of fluorescent protein tracing by writing 5 out of the 10 chapters in the book. The volume will be useful for workers involved in practical application of fluorescent antibody techniques which in recent years have found widespread application. This is clear by the more than 3000 references cited alone in this volume.

Bacteriologists, virologists, pathologists, physiologists, and clinicians could find this book very useful if they are prepared to read 368 pages of very informative literature and then 18 pages of appendix items as a reference to the commonly used reagents and routine methods. Investigators in the field of cell biology, cytochemistry and bacteriology, virology, and clinical pathology would find it a valuable source of information.

Sidney Farber Cancer Institute

Sisir K. Sengupta

Nonstriatal Dopaminergic Neurons. Edited by E. Costa and G. L. Gessa. Raven Press, New York, N.Y. 1977. 16 × 24 cm. xx + 708 pp. \$47.50.

In some fields of science publication of the proceedings of a major symposium heralds the death of the area, as "everything has been discovered" and only the small details remain to be elucidated. This is by no means the case of the neurotransmitter dopamine and the present volume. Dopamine is best known as the neurotransmitter of a neuronal pathway with cell bodies in the substantia nigra of the brain stem and terminals in the corpus striatum. This nigrostriatal dopamine pathway degenerates in

the brains of patients with Parkinson's disease, and replacement of the "missing" dopamine by treatment with L-Dopa dramatically alleviates symptoms. Many symposia have been devoted to the role of dopamine in the corpus striatum.

Quite recently several laboratories have identified new dopamine pathways with neuronal projections to parts of the cerebral cortex implicated in emotional behavior. It is speculated that these dopamine pathways might be involved in the actions of the antischizophrenic neuroleptic drugs whose therapeutic effects are presumed to be mediated by blockade of dopamine receptors. This volume summarizes the proceedings of a meeting held in Sardinia and devoted to dopamine systems outside the corpus striatum. The first section focuses upon the newly discovered "mesocortical" dopamine system. Nobel Laureate Julius Axelrod introduces this section and speakers from the laboratories of Glowinski, Bjorklund, and Hökfelt, all involved in the discovery of the mesocortical dopamine pathway, describe its diverse aspects.

Another section of the book includes chapters on the supra-infundibular dopamine neurons. These have nerve terminals in the median eminence of the hypothalamus where they presumably regulate the synthesis and release of pituitary hormones, especially prolactin.

Besides the mesocortical system, a neuronal pathway projecting to parts of the limbic system of the brain may also be involved in dopamine actions in emotional regulation. A series of nine chapters deals with this system. A less clear role for dopamine exists in a group of "small intensely fluorescent" (SIF) cells which are localized to nervous ganglia primarily. Considerable interest in these cells, evidenced by the eight chapters dealing with them, may relate to their possible regulation of sympathetic ganglia function and blood pressure modulation.

Other sections of the book deal with more general properties of dopamine neurons. For instance, numerous chapters focus upon metabolic effects of dopamine which may be related to influence at dopamine receptor sites. Indeed, the continual rebirth of "dopamine field" is evident from the fact that, about the time of this meeting, it became possible to label dopamine receptors, defined as the recognition site for dopamine at postsynaptic membranes. Though this rapidly expanding area of interest is not included in the present volume, it will no doubt serve as a focus of much future work.

The authors of the various chapters of this book represent the leading laboratories dealing with dopamine research. The book is well edited and reasonably up-to-date. A unique feature of the meeting is that, coincident with the meeting, honorary degrees were presented by the University of Cagliari to Arvid Carlsson and Oleh Hornykiewicz whose research sparked most of the present interest in dopamine. Professor Carlsson is responsible for developing a sensitive and specific fluorimetric assay for dopamine and then showing that dopamine in the brain was highly localized to the corpus striatum. Soon thereafter Professor Hornykiewicz demonstrated the depletion of striatal dopamine in the brains of patients with Parkinson's disease and showed that intravenous L-Dopa rapidly improved the symptoms of the patients. Tributes to both of these outstanding scientists constitute the final chapter of a well-designed and presented book which will be a *sine qua non* for researchers in brain chemistry and pharmacology.

The John Hopkins University

Solomon H. Snyder

Mass Spectrometry. Volume 4. Specialist Periodical Reports. R. A. W. Johnstone, Senior Reporter. The Chemical Society, Burlington House, London. 1977. 14.5 × 22 cm. xii + 337 pp. \$45.00.

This volume represents the fourth in the series of biennial literature surveys in the field of mass spectrometry. To the credit of the editor and the contributors, it is not a mere compilation of references but indeed a comprehensive coverage of developments in the field over the period 1974-1976. Moreover, continuing the trend set with volume 3 in the series, new advances in mass spectrometry are covered somewhat critically and in

greater detail in the condensed review chapters. In this specific case, the topics covered are "Trends in Instrumentation" (by A. McCormick), "Field Ionization and Field Desorption" (by P. J. Derrick), and "Negative Chemical Ionization Mass Spectrometry" (by K. R. Jennings). In addition to the review chapters, the literature survey covers the areas of "Theory and Energetics in Mass Spectrometry" (by B. N. McMasters), "Structure and Mechanism in Mass Spectrometry" (by T. W. Bentley), "Computerized Data Acquisition and Interpretation" (by F. A. Mellon), "Alternative Methods of Ionization and Analysis" (by J. M. Wilson), "Gas Chromatography-Mass Spectrometry" (by C. J. W. Brooks and B. S. Middleditch), "Drug Metabolism" (by B. J. Millard), "Reactions of Organic Functional Groups" (by J. H. Bowie), "Natural Products" (by D. E. Games), and "Organometallic, Co-ordination, and Inorganic Compounds" (by T. R. Spalding).

As with the previous volumes, this latest edition should be of significant value to those actively involved in the field of mass spectrometry. It is unfortunate, however, that the high price of this book may deter many individuals from acquiring this or subsequent volumes in the series.

Northeastern University

Paul Vouros

Analytical Profiles of Drug Substances. Volume 6. Edited by K. Florey. Academic Press, New York, N.Y. 1977. 15.5 × 22 cm. ix + 600 pp. \$27.50.

The sixth volume of this series includes the usual detailed description of the physical and chemical properties of the following drugs: amphotericin B, betamethasone dipropionate, clonazepam, cyclizine, dipiperodon, ergotamine tartrate, fenopropfen calcium, isoniazid, kanamycin sulfate, ketamine, minocycline, nystatin, proparacaine hydrochloride, propylthiouracil, sodium nitroprusside, sulfamerazine, and triamcinolone hexacetonide. A few addenda and corrigenda are given for items in earlier volumes and a cumulative index to the series is included.

In addition to its value as a reference work, teachers of drug or pharmaceutical analysis will find it an excellent source of practical, relevant, and challenging problems for their students.

Staff Review

Medicinal Chemistry. V. Proceedings of the 5th International Symposium on Medicinal Chemistry. Edited by J. Mathieu. Elsevier, Amsterdam and New York, N.Y. 1977. 17 × 25 cm. vii + 456 pp. \$52.95.

The 5th International Symposium on Medicinal Chemistry was organized by the Société de Chimie Thérapeutique, under the auspices of the International Union of Pure and Applied Chemistry, the Fédération Internationale Pharmaceutique, and the European Federation for Medicinal Chemistry.

This volume, containing 37 contributions divided among eight major topics, provides a record of the plenary lectures of the symposium. The papers may be classified into two types: contributions by academic lectures devoted to fundamental research and papers by industrial contributors dealing with applications. All the papers are in English except for one in French.

The main themes of the meeting reported in these proceedings are as follows: peptides, transmitters and medications of the central nervous system, the contribution of immunology to medicinal chemistry, the prevention of aging, and new methods of synthesis of potential interest in medicinal chemistry. In addition, papers from the two sessions on the themes of cardiovascular medications and prodrugs are included.

This volume provides up-to-date coverage of the trends and advances in the medicinal chemistry of the central nervous system and cardiovascular system, as well as information on the prospects of such new fields as peptides, immunology, and aging.

Staff Review