acid (30%, 450 V, 4 h); $[\alpha]^{22}_D$ −42° (c 0.5, 1 M acetic acid). Anal. ($C_{51}H_{73}N_{13}O_{11}S_2 \cdot 3CH_2COOH \cdot 5H_2O$) C, H, N. Amino acid analysis gave Tyr, 0.95; Phe, 0.98; Val, 0.98; Asp, 0.98; $^1/_2$Cys, 0.40; Pro, 1.01; Arg, 0.86; Gly, 1.00; $NH_3$, 1.83. Analysis following performic acid oxidation[22] gave a Cys($O_3$H):Gly ratio of 1.03:1.00.

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## References and Notes

(1) M. Manning, J. Lowbridge, C. T. Stier, Jr., J. Haldar, and W. H. Sawyer, *J. Med. Chem.*, **20**, 1228 (1977).
(2) M. Manning, L. Balaspiri, M. Acosta, and W. H. Sawyer, *J. Med. Chem.*, **16**, 975 (1973).
(3) W. H. Sawyer, M. Acosta, L. Balaspiri, J. Judd, and M. Manning, *Endocrinology*, **94**, 1106 (1974).
(4) W. H. Sawyer, M. Acosta, and M. Manning, *Endocrinology*, **95**, 140 (1974).
(5) H. Schulz and V. du Vigneaud, *J. Med. Chem.*, **9**, 647 (1966).
(6) R. J. Vavrek, M. F. Ferger, G. A. Allen, D. H. Rich, A. T. Blomquist, and V. du Vigneaud, *J. Med. Chem.*, **15**, 123 (1972).
(7) J. J. Nestor, Jr., M. F. Ferger, and V. du Vigneaud, *J. Med. Chem.*, **18**, 284 (1975).
(8) D. F. Dyckes, J. J. Nestor, Jr., M. F. Ferger, and V. du Vigneaud, *J. Med. Chem.*, **17**, 250 (1974).
(9) R. B. Merrifield, *J. Am. Chem. Soc.*, **85**, 2149 (1963).
(10) R. B. Merrifield, *Biochemistry*, **3**, 1385 (1964).
(11) M. Manning, *J. Am. Chem. Soc.*, **90**, 1348 (1968).
(12) M. Manning, J. Lowbridge, J. Haldar, and W. H. Sawyer, *J. Med. Chem.*, **19**, 376 (1976).
(13) J. Lowbridge, M. Manning, J. Haldar, and W. H. Sawyer, *J. Med. Chem.*, **20**, 1173 (1977).
(14) W. König and R. Geiger, *Chem. Ber.*, **103**, 788 (1970).
(15) M. F. Ferger and W. Y. Chan, *J. Med. Chem.*, **18**, 1020 (1975).
(16) V. du Vigneaud, C. Ressler, J. M. Swan, P. Katsoyannis, and C. W. Roberts, *J. Am. Chem. Soc.*, **76**, 3115 (1954).
(17) D. B. Hope, V. V. S. Murti, and V. du Vigneaud, *J. Biol. Chem.*, **237**, 1563 (1962).
(18) M. Manning, T. C. Wuu, and J. W. M. Baxter, *J. Chromatogr.*, **38**, 396 (1968).
(19) H. O. Schild, *Br. J. Pharmacol.*, **2**, 189 (1947).
(20) D. H. Spackman, W. H. Stein, and S. Moore, *Anal. Chem.*, **30**, 1190 (1958).
(21) M. Bodanszky, M. Konda, C. Y. Lin, and G. F. Sigler, *J. Org. Chem.*, **39**, 444 (1974).
(22) S. Moore, *J. Biol. Chem.*, **238**, 235 (1963).

# *Book Reviews*

**Annual Review of Pharmacology and Toxicology. Volume 17.** Edited by H. W. Elliott, R. George, and R. Okun. Annual Reviews, Palo Alto, Calif. 1977. 750 pp. 15 × 22 cm. $17.00.

This latest volume of "Annual Reviews" is dedicated to Professor Henry W. Elliott who helped to establish this series and guided the "Annual Reviews" to become an important reference in pharmacology.

The prefactory chapter of this volume is an autobiographical sketch of Karl H. Beyer, Jr., who has retired from a highly successful career in industry after making major contributions in renal pharmacology and now is enjoying a new career in academia.

There are 37 review articles presented in this volume covering a wide range of pharmacological and toxicological subjects. Cardiovascular pharmacology is surveyed in four articles including the effects of calcium on myocardial and smooth muscle (A. Fleckenstein), cardiovascular drug interactions (D. Craig Brater and H. F. Morrelli), combination drug therapy of hypertension (C. T. Dollery), and the effect of hypolipidemic drugs on plasma lipoproteins. Renal pharmacology is discussed in two reviews including a discussion on the renal lithiasis (T. H. Steele) and a review on proximal tubular reabsorption (H. R. Jacobson and D. W. Seldin).

A number of articles deal with neuropharmacology, psychopharmacology, and drug–receptor interactions. J. W. Maas discusses the effects of various psychopharmacological agents on biogenic amine metabolism in the central nervous system, whereas J. L. Diaz discusses various aspects of the use of psychotropic plants by the Mexican Indians. Peptide neurotransmitters such as Substance P, proctolin, and enkephalin are discussed by M. Otsuka and T. Takahashi, whereas the effects of prostaglandins on autonomic transmission are discussed by P. Hedqvist. In addition, J. Schwartz reviews putative histaminergic mechanisms in the brain and O. Hornykiewicz examines dopamine and dopamine antagonists. The dynamic regulation of cholinergic function is discussed by D. L. Cheney and E. Costa in an article on acetylcholine turnover in rat brain. The interaction of catecholamine with its receptor and the activation of adenylyl cyclase are reviewed by B. B. Wolf, T. K. Harden, and P. B. Molinoff, whereas B. Weiss and W. N. Hait examine the role of cyclic nucleotides and the possible therapeutic use of inhibitors of cyclic nucleotide phosphodiesterases. In addition, receptor activation and the evolution of receptor proteins using aquatic invertebrates as model systems for study are summarized by H. M. Lenhoff and W. Heagy.

Review articles concerning the pharmacology of central homeostatic control mechanisms include the control of feeding (B. G. Hoebel) and the control of temperature and thermoregulation (B. Cox and P. Lomax). The pharmacology of local anesthetics and regional pain relief are discussed by J. Adriani and M. Naraghi. The pharmacology of experimental myopathies and its application to the development of models for progressive muscular dystrophies are reviewed by M. B. Laskowski and W. D. Dettbarn.

Cancer and cancer-related articles include a review on the chemistry of selected antineoplastic agents from plants (M. E. Wall and M. C. Wani), the application of cell kinetics to clinical cancer therapy (R. B. Livingston and J. S. Hart), and the immunological aspects on cancer chemotherapy (C. M. Haskell). In addition, the thymus and the role of thymic hormones in control of the immune system are reviewed by J. F. Bach.

Several articles concerning endocrine pharmacology include a discussion on the mechanisms of hormone secretion (J. M. Trifaro) and the clinical pharmacology of systemic corticosteroids (J. C. Melby).

Age and its effects on pharmacological agents is the subject of two reviews including pediatric clinical pharmacology (A. K. Done, S. N. Cohen, and L. Strebel) and the problems of aging on pharmacokinetics (D. P. Ritchey and A. D. Bender).

Miscellaneous, pharmacologically related articles include the pharmacology of laxatives (H. J. Binder), the pharmacology of magnesium (S. G. Massry), the therapeutic use of enzymes (J. S. Holcenberg and J. Roberts), and the pharmacological effects of hymenoptera venoms (R. I. Levy).

Although it is somewhat difficult to distinguish articles concerning pure pharmacology from those concerned only with

toxicology, a number of reviews do appear to be directly related to toxicological subjects. For example, A. R. Temple reviews the development of poison control centers and describes their general programs and capabilities. The toxicity of lead and exposure to lead are reviewed by P. B. Hammond, and the recent problem of vitamin toxicity due to the overconsumption of vitamins is discussed by J. R. DiPalma and D. M. Ritchie. In consideration of our environment, J. L. Hamelink and A. Spacie review the process of accumulation of chemicals by fish. The exposure of halogenated alkane propellants particularly certain fluoroalkanes is also of environmental interest and is aptly reviewed by K. C. Back and E. W. Van Stee.

The final review, in keeping with the tradition of this series, is the "Review of Reviews" by Chauncey D. Leake.

In considering the list of subjects presented in this volume, it is apparent that the scope of pharmacology has enlarged over the years. The addition of "Toxicology" to the "Annual Review of Pharmacology" in the previous volume, Volume 16, was necessary in keeping with the need for unity within the discipline. In view of the number of reviews and diversity of subject matter, there is quite a difference in the depth of coverage. Some of the articles are narrowly focused, whereas others are more broad in nature and might appeal to a wider audience.

In general, the reviews deal with subjects which are timely and, for the most part, well presented. However, it might be helpful if the reviews were presented in some logical sequence as opposed to an apparent randomized pattern. In all, this volume has continued to keep with the tradition and objectives of previous volumes and is a welcomed addition to this series.

*Northeastern University* **Leon Shargel**

**Progress in Drug Metabolism. Volume 2.** Edited by J. W. Bridges and L. F. Chasseaud. Wiley, New York, N.Y. 1977. xi + 348 pp. 15 × 22.5 cm. $29.50.

This is the second volume in a new and continuing series that is concerned with reviewing recent developments in drug metabolism, including techniques, metabolic pathways, and general subject areas.

This volume follows a format similar to that in Volume 1. The glucuronidation pathway is reviewed in "Newer Aspects of Glucuronidation" (G. J. Dutton and B. Burchell) and includes discussion on the mechanism of glucuronide formation, properties of UDP glucuronyltransferase(s), and factors affecting glucuronidation. There are three chapters that survey techniques that are applicable to metabolic studies. These include "Metabolism of Xenobiotics in Cell Suspensions and Cell Cultures" (J. R. Fry and J. W. Bridges), which is concerned with the metabolism of xenobiotics within isolated cells, a technique useful for detecting reactive metabolites which may not otherwise be detected in in vivo systems; "Role of Stable Isotopes in Drug Metabolism" (D. R. Hawkins) which deals with the application of stable isotopes to the solution of problems in drug metabolism, including the detection and structural elucidation of metabolites, as well as quantitation; and "Ion-Pair Extraction Methods" (G. Schill et al.), which offers a valuable method for the separation and extraction of ionic metabolites from biological fluids. Methods discussed include column chromatography, extraction selectivity, and use of ion pairs in quantitative determinations. The remaining two chapters review "Bioavailability of Drug Dissolution" (G. L. Mattok et al.) and "Transplacental Transfer of Foreign Compounds and Their Metabolism" (O. Pelkonen). This latter chapter reviews recent developments in the differences between fetal and neonatal metabolism and the ability of the fetus to metabolize xenobiotics.

The fine quality of the first volume of this series is followed in this volume—reviews are well written, illustrated, and referenced. An extensive author and subject index concludes this volume.

This book will be useful to those actively working in drug metabolism or who merely wish to stay abreast of this expanding field.

*Massachusetts College of Pharmacy* **David A. Williams**

**Recent Advances in the Chemistry of β-Lactam Antibiotics.** Edited by J. Elks. Special Publication No. 28. The Chemical Society, London. 1977. vi + 313 pp. 14.5 × 22 cm. $29.00.

In view of the fact that the β-lactam antibiotics have constituted an important field of chemical research for many years, it is surprising that the symposium organized by the Chemical Society at Cambridge in June 1976 should have been the first truly international meeting wholly devoted to their chemistry. The present, attractively produced book provides a permanent record of that highly successful meeting. It contains 32 papers, of which approximately two-thirds emanate from the pharmaceutical industry and the rest from academic laboratories, and nearly all of them contain substantial amounts of material not previously published elsewhere. The volume thus constitutes a representative picture of the state of β-lactam chemistry in the mid 1970's.

As might be expected, there is a heavy emphasis on synthetic organic chemistry, but structure–activity relationships are also discussed in considerable detail where appropriate. A nice balance is maintained between papers on side-chain modification of the familiar penam and cephem nuclei on the one hand and those on nuclear transformations and total synthesis on the other.

Among many excellent articles, two stand out for the elegance of their chemistry. One is by T. Tsuji and his colleagues of the Shionogi Research Laboratory describing a beautifully streamlined conversion of penicillins into 3-hydroxycephems. The other is R. B. Woodward's account of the total synthesis of the novel penem system, which combines structural features of both penicillins and cephalosporins.

Finally, the beginning of the current spate of novel types of β-lactam from natural sources is signaled by papers from T. Kamiya on the monocyclic β-lactam antibiotics, nocardicin A and B, and from A. G. Brown et al. on the β-lactamase inhibitor, clavulanic acid.

In summary, this is an essential book for chemists in the β-lactam field and is strongly recommended to anyone who enjoys synthetic organic chemistry.

*Beecham Pharmaceuticals* **John H. C. Nayler**

**Toxicology of Trace Elements.** Edited by Robert A. Goyer and Myron A. Mehlman. Halsted Press, New York, N.Y. 1977. xiv + 303 pp. 16 × 23.5 cm. $24.50.

This book is volume two of a continuing series in the "Advances of Modern Toxicology" edited by Myron A. Mehlman. This volume is composed of nine chapters which deal mainly with the environmental sources and toxicological properties of the various forms of trace metals, with particular emphasis given to potential adverse health effects to humans.

The first chapter by Suzuki deals with the absorption, transport, biotransformation, and excretion of various forms of mercurial compounds, along with the clinical and cellular consequences of exposure to mercurials. Goyer and Mushak in chapter two combine a review of the toxicology and metabolism of lead with the pathological effects (neural, hematopoietic, and renal) of lead poisoning. Also provided in the chapter is an excellent discussion of the various clinical tests used for the detection and quantitation of levels of lead in biological samples. In chapter three Fowler introduces the toxicology of arsenical compounds with a brief discussion of the sources of environmental arsenic and its accumulation in living organisms, including man. The pharmacokinetics, general toxicities of both inorganic and organoarsenicals in animals and humans, and proposed cellular mechanisms of arsenical poisoning conclude the chapter. Although copper does not pose a serious toxicological problem to the majority of the people, individuals with Wilson's disease and various domestic animals, especially livestock, are particularly sensitive to copper, and Hill in chapter four discusses these two circumstances. The metabolism and toxicology of nickel compounds are treated by Nielsen in chapter five. He points out that although the toxicological manifestations of nickel and its salts are relatively low, with the exception of contact dermitis, nickel inhalation, particularly of nickel carbonyl, presents a very serious industrial health problem.

Although vanadium is widely distributed in nature, it rarely occurs in high concentrations and up to now little attention has

been given to its toxicity. However, with man's increasing interest in oil and metallurgical refining, increased human exposure to vanadium-containing combustion products of residual oils and ores has stimulated interest in the study of its toxicity. After a brief review of the chemistry and environmental distribution of vanadium, Waters in chapter six presents a quite good discussion of the metabolism (including gastrointestinal, respiratory, and percutaneous absorption, transport, distribution, accumulation, and excretion) and potential toxicological effects of human exposure to vanadium salts. In chapter seven the carcinogenic, teratogenic, and mutagenic aspects of selenium and tellurium, along with their toxicities, are reviewed by Fishbein. The last two chapters of the book deal with nutrient interactions of toxic metals and metal carcinogenesis. Sandstead discusses various dietetic factors which can potentially increase the toxicities of three metals—lead, cadmium, and iron—while in the last chapter, Sunderman summarizes the current data regarding the carcinogenic properties of beryllium, cobalt, lead, nickel, zinc, and iron. For each metal epidemiological and experimental animal data are given, suggesting that these metals may also be carcinogenic in humans. Nickel carcinogenesis is treated in some detail, along with possible mechanisms for its carcinogenic potential.

In general the book is well organized and well written and free from typographical errors. It presents under one cover an excellent summary of what is currently known concerning the toxic effects of numerous widely distributed trace metals. Each chapter is well referenced and allows the reader easy access to additional information concerning each substance. This volume compliments the series quite well and would be of particular interest as a convenient reference source for toxicologists, as well as medicinal chemists and biochemists alike.

Note: The opinions expressed in this review are those of the reviewer only and do not necessarily represent those of either NIH or NCI.

*National Cancer Institute* **Peter J. Wirth**
*National Institutes of Health*

**The Specificity and Action of Animal, Bacterial and Plant Toxins.** Edited by P. Cuatrecasas. Halsted Press, New York, N.Y. 1977. ix + 345 pp. 16 × 24 cm. $35.00.

This book concerns a field of much significance to many medicinal chemists as well as to many pharmacologists and other researchers: the mechanisms of action of several of the most studied toxins of animal, bacterial, or plant origin. It is proposed that these studies may help shed light on various disease processes and that the toxins are excellent tools for probing and manipulating highly selective biological processes. All of this is true and the book does have such potential, but this only increases my unhappiness at the sloppy manner in which the book has been executed. In the first chapter alone, I noted well over a dozen typos, including such malapropisms as "the suspensions were then dilated..." and "the nonmenclature is that of Svennerholm...". The latter is not too far off the mark, since the nomenclature for this series of compounds is never defined.

Substantively, however, the first chapter (by Bennett and Cuatrecasas on cholera toxin) is quite thorough—through 1975. For my taste, it was (as also several other chapters) a bit too thorough; I feel that details on how many milliliters of what concentration reagent should be added is appropriate only in the original literature, not in a review—but this may be personal bias. Without much doubt, the reader will have a good concept of the thinking on the mechanism of action of choleragin (the cholera toxin, for the non-cognescenti) after completing the reading of this manuscript.

Dr. Collier gives a good rationale for the joining into one chapter of the exotoxins synthesized by the two disparate organisms, *Corynebacterium diphtheriae* and *Pseudomonas aeruginosa*: both catalyze covalent modification of elongation factor 2. Since this factor is essential in protein synthesis, such modification inhibits protein synthesis. After going through a review of relevant aspects from isolation, to inhibition kinetics, to structure–activity relationships, etc., the author concludes with hypotheses on how such similarly acting toxins arose in unrelated bacteria. I. B. Holland commits an unforgivable human sin in his chapter on bacteriocins: he neglects to define the abbreviations he uses. And since the book is void of a table of abbreviations and abbreviations are not included in the skimpy index, other readers and I are fated to go through life ignorant, unless we go back to the original literature and the authors have used the same abbreviations. Such a fault cannot be found with the next chapter—on abrin, ricin, and associated agglutinins—since the authors (Drs. Olsnes and Pihl) are almost compulsive not only in defining terms and abbreviations but even in tracing the historical origins of terms. (Did you know that a shekel represents $4^3$ seeds and an ounce $4^4$ seeds?)

Tetanus toxin chemistry is handled in almost classical fashion: from purification studies, to amino acid determination of sundry fractions, to attempts to determine antigenic sites, etc. Dr. Buzzini even points out the weaknesses in some areas of study and the putative value of increased knowledge of the nature of the toxin. In the chapter on the botulinum toxin, there is included an errata—14 errors which were introduced subsequent to the author's checking of the proofs. Unfortunately, there are errors in the errata! Some of the basic premises of the author are not self-evident to me; e.g., "In order to be poisonous, a substance must be active in miniscule quantities." Although the author's simplified description of nerve function may be of value to readers not familiar with such events, I wonder if those readers may not be unnecessarily confused when Dr. Simpson uses the same word (coupling) to refer to electrical coupling and to enzymatic coupling of acetate and choline. I also wonder why an acknowledged leader in the field uses the horrible (to me) abbreviation of "Ach" for acetylcholine, although he uses the more acceptable "ACh" in his figures; my guess is that the fault lies with the publisher.

Toxins from exotic sources are covered in the last chapter, authored by Drs. Albuquerque and Daly. Since Dr. Daly has recently returned from another Amazon expedition, other toxins of even greater specificity and utility may be on the way. In the meantime, researchers who are interested in studying receptors via reaction with toxins may profit from the contents of this book.

Note: This review was written by Dr. Usdin in his private capacity. No official support or endorsement by the NIMH is intended or should be inferred.

*National Institute of Mental Health* **Earl Usdin**

**Medical Botany. Plants Affecting Man's Health.** By Walter H. Lewis and Memory P. F. Elvin-Lewis. Wiley, New York, N.Y. 1977. xiii + 515 pp. 18 × 26 cm. $27.50.

Take a reasonable assortment of our well-known medicinal plants; arrange them according to the disease state or pharmacological effect for which they are used; add a dash of American Indian folklore, a few chemical formulas (some of which are incorrect), a bit of pharmacology (some of which will be quite beyond the layman to whom the book is, in part, directed), a liberal portion of untested folk remedies from around the world, the inevitable chapter on hallucinogens (which have no medical use), a representative collection of toxic plants, a glossary, and a selection of interesting old medical prints; wrap it up in a clear attractive type face (with too much white page space for the price); and the result is a light, palatable potpourri with a little bit for everybody but nothing very substantial for the health professional. However, the book may serve one of the authors' intentions: "...an interface between (a) more preprofessional course and that designed for a liberal educational experience."

*Northeastern University* **Robert F. Raffauf**

**Pesticide Chemistry in the Twentieth Century.** Edited by J. R. Plimmer. American Chemical Society, Washington, D.C. 1977. ix + 310 pp. 16 × 23.5 cm. $20.00.

This volume, No. 37 of the ACS Symposium Series, is collected from the Division of Pesticide Chemistry at the 171st National Meeting of the American Chemical Society, April 6–8, 1976.

The survey gives a historical approach to each class of pesticide, describing developmental problems and attempts to solve them. Chemical structure, as compared with biological activity, is outlined chronologically. Pharmacological action, as well as

resistance mechanisms, is described in conjunction with current usage. In most cases the fate of the chemical is followed both in the environment and metabolically in the pest. The effect on the environment is scientifically discussed. Usage figures are compared competitively in the market place, and the future of the pesticide is predicted. Pest control by a new generation of hormonal compounds or by generic resistance is discussed. Numerous references are given. The volume should be read by technical people in the field.

The following abridged chapter titles (authors) show the range of subjects included: Chlorinated Insecticides (Brooks), Insect Resistance Mechanisms (Brown), Herbicide Industry (Alder, Wright, and Klingman), Herbicide Action (Moreland), Triazine Herbicides (Knuesli), Environmental Herbicides (Crosby), Fungicides (Horsfall), Metallo-Organic Fungicides (van der Kerk), Sulfenimides (Kohn), Antibiotics (Misato), Hormonal Insecticides (Siddall), Pheromones (Blum), Chitin Description (Verloop and Ferrell), Future Insecticides (Bowers), and Plant Regulators (Lieberman, Luckwill).

*FMC Corporation* **W. G. Scharpf**

**Androgens and Antiandrogens.** Edited by Luciano Martini and Marcella Motta. Raven Press, New York, N.Y. 1977. xvi + 381 pp. 16 × 24 cm. $28.75.

This book is a collection of 30 papers covering research on androgens and antiandrogens in areas ranging from fundamental to clinical. The papers were originally presented at an International Symposium on Androgens and Antiandrogens, held in Milan in April 1976.

The book includes chapters dealing with androgen biosynthesis and its control, with the mode of action of androgens and antiandrogens, with androgen–antibody interaction, with androgen transport, and with numerous clinical applications of antiandrogens. The measurement of androgens in biological fluids is the subject of one excellent chapter and is an important theme in many of the other chapters.

The book is well indexed. Both the editors and the individual contributors are to be complemented for so rapidly producing a work which, given the number of authors, is unusual for its consistently high standards and readability. The wide scope of the material presented should prove stimulating to endocrinologists, to clinical practitioners, and to all medicinal chemists interested in current research on steroid hormones.

*State University of New York at Buffalo* **Alan J. Solo**

**The Alkaloids. Volume 7. Specialist Periodical Reports.** By M. F. Grundon, Senior Reporter. The Chemical Society, Burlington House, London. 1977. x + 332 pp. 14 × 22 cm. $50.00.

The seventh volume of *The Alkaloids* follows the policy and format adopted in previous volumes of this series. Thirteen chapters are concerned with literature published during July 1975–June 1976. Three chapters in Amaryllidaceae and Related Alkaloids, *Erythrina* and Related Alkaloids, and Miscellaneous Alkaloids cover a 2-year period up to June 1976. Chapters (authors) include Biosynthesis (R. B. Herbert); Pyrrolidine, Piperidine, and Pyridine Alkaloids (A. R. Pinder); Tropane Alkaloids (G. Fodor); The Pyrrolizidine Alkaloids (D. H. G. Crout); Indolizidine Alkaloids (J. A. Lamberton); The Quinolizidine Alkaloids (M. F. Grundon); Quinoline and Acridone Alkaloids (M. F. Grundon); β-Phenethylamines and the Isoquinoline Alkaloids (N. J. McCorkindale); The Aporphinoids (M. Shamma); Amaryllidaceae and Related Alkaloids (V. A. Snieckus); *Erythrina* and Related Alkaloids (V. A. Snieckus); Indole Alkaloids (J. E. Saxton); Diterpenoid Alkaloids (S. W. Pelletier and S. W. Page); Steroidal Alkaloids of the Apocynaceae Buxaceae and Related Compounds (F. Khuong-Huu and R. Goutarel); *Solanum* and *Veratrum* Steroidal Alkaloids (D. M. Harrison); and Miscellaneous Alkaloids (J. N. Reed and V. A. Snieckus) which include sections on muscarine, imidazole, purine, peptide, and a variety of unclassified alkaloids and alkaloid-containing plants.

As in the past this volume serves as an invaluable aid to the researcher interested in natural products as a source of potential medicinal agents and in keeping up with the ever-increasing literature in this field.

**Staff Review**

**Advances in Cyclic Nucleotide Research. Volume 8.** Edited by Paul Greengard and G. Alan Robison. Raven Press, New York, N.Y. 1977. x + 582 pp. 16 × 24 cm. $35.00.

Progress continues to be made toward a better understanding of the formation, metabolism, and biological function of the cyclic nucleotides. Several of the chapters in this volume review subjects previously covered in the series but with substantial amounts of new and informative material. The first chapter by M. E. Maguire, E. M. Ross, and A. G. Gilman presents a lucid discussion of the β-adrenergic receptor and ligand-binding interactions with adenylyl cyclase. The authors present a rigorous criteria for identification of the β receptor and, in this light, critically review current methodology, equilibrium and kinetic binding properties, and regulation of receptor number and sensitivity. The chapter concludes with a concise analysis of the relationship between the β-adrenergic receptor and adenylyl cyclase. D. M. Gill's chapter on the mechanism of action of cholera toxin details the events that lead to adenylyl cyclase activation in broken and intact cells and the altered properties of the enzyme.

J. N. Wells and J. G. Hardman review the current literature, with an emphasis on the last 2 years of publications, on cyclic nucleotide phosphodiesterases. They present a useful discussion of some potential problems with commonly employed assay techniques and then cover other topics such as multiple forms of the enzyme, the activator protein, and hormonal control of phosphodiesterase activity. H. G. Nimmo and P. Cohen review the hormonal control of protein phosphorylation first by characterizing the properties and in vivo regulation of the cyclic AMP-dependent protein kinases. The protein phosphorylation and hormonal control of glycogen metabolism are discussed in detail, while other systems, e.g., lipid metabolism and contractility and the cGMP-dependent protein kinase, are briefly discussed. E. M. Johnson also reviews cAMP-dependent protein kinase mechanisms but with a view to its nuclear substrate proteins (e.g., histone and protamine phosphorylation) and the role they may play in processes concerned with alterations in chromatin structure and with replication and expression of the genome. G. J. Strewler and J. Orloff review the role of the cyclic nucleotides in the transport of water and electrolytes, especially in the kidney and gastrointestinal epithelia. They summarize the evidence that regulation of the phosphorylation of pertinent proteins or lipid components of cell organelles and membranes by cAMP-dependent kinases may account for the alterations in solute and water flux. R. W. Tsien examines whether the elevation of cardiac cAMP is causally related to the subsequent increase in contractile force by looking at evidence supporting both "association" and "dissociation" experiments and providing some explanations for such conflicting data. Tsien suggests that some or perhaps all of the subcellular mechanisms of cAMP action in the inotropic response may be modified through the action of cAMP-dependent enzymes which phosphorylate or dephosphorylate functional proteins. The chapter by J. W. Kebabian covers the biochemical regulation and physiological significance of cyclic nucleotides in the nervous system. This review examines the recent work on the calcium-binding protein, the role of calcium ions in cAMP metabolism, and cyclic nucleotide interactions with neurotransmitters and protein kinase. A. E. Broadus' chapter reviews clinical cyclic nucleotide research with an emphasis on various disease states. In addition, Broadus also devotes considerable attention to the methodology of this area of clinical research by considering the kinetics, control conditions, expression of data, and pertinent pharmacologic and physiologic effects of hormones on extracellular cyclic nucleotides.

This latest of the "Advances..." series offers a useful method to researchers for keeping abreast of current information in the cyclic nucleotide field. It is interesting to note, while looking over this and preceding volumes, an increasing focus on the role of the protein kinases. There appears to be a growing acceptance that

cyclic nucleotide activation of protein kinases represents a nearly universal mechanism of action (a third messenger?) for hormone action.

*Northeastern University* **Jeffrey B. Blumberg**

**Organic Syntheses. Volume 56.** Edited by G. H. Büchi. Wiley, New York, N.Y. 1977. xviii + 144 + 13 pp. 16 × 23 cm. $12.50.

Editor George Büchi has included 27 checked and 21 unchecked procedures representing specific examples of important synthetic methods of general applicability and the preparation of a number of reagents and starting materials. The recently introduced technique of covalently binding reagents to a resin is represented by the preparation of polymeric carbodiimide and its use in Moffat oxidation. For the benefit of peptide chemists, there is a section on peptide syntheses utilizing *N*-ethyl-5-phenylisoxazolium 3′-sulfonate.

As in Volume 55, "common" names are used throughout this volume, accompanied by *Chemical Abstracts* indexing names. A future editor might consider adopting instead IUPAC nomenclature as it is designed for communication rather than for indexing.

The continuing diligence of the Editors in keeping chemists abreast of current developments and interests makes this volume a valuable addition to this important series. Many of the preparations are of more value as examples of techniques rather than for the specific products and should serve to attract students to the charms of skillfully planned and executed experimental work.

**Staff Review**

**Compendium of Organic Synthetic Methods. Volume 3.** Edited by Louis Hegedus and Leroy G. Wade, Jr. Wiley, New York, N.Y. 1977. xv + 495 pp. 16 × 23.5 cm. $17.00.

The latest volume in this series presents new synthetic methods for preparation of monofunctional compounds reported from 1974 to 1976. As in previous volumes published in 1974 and 1971, sections appear corresponding to most of the possible interconversions between the major functional groups. This volume also contains examples of new methods of preparation of difunctional compounds formed from pairs of the major functional groups. Once the reader has familiarized herself/himself with the format, these volumes will faciliate the rapid location of methods for the interconversion of functional groups. This series will serve as an invaluable source of information at a very reasonable price for synthetic organic chemists, medicinal chemists, and biochemists.

**Staff Review**

**Aromatic and Heteroaromatic Chemistry. Volume 5.** Edited by C. W. Bird and G. W. H. Cheeseman, Senior Reporters. The Chemical Society, London. 1977. xv + 566 pp. 14 × 22 cm. $70.00.

The literature surveyed in this report is that abstracted by *Chemical Abstracts* in Volumes 83 and 84 (July 1975–June 1976). Medicinal chemists will be most interested in the final three chapters which discuss porphyrins, naturally occurring oxygen-ring compounds, and other naturally occurring compounds. This is the final volume to be compiled by the current senior reporters. Their efforts are very much appreciated and they are to be complemented for a thorough and comprehensive review.

**Staff Review**

**Survey of Organic Syntheses. Volume 2.** By Calvin A. Buehler and Donald E. Pearson. Wiley, New York, N.Y. 1977. x + 1105 pp. 16 × 23 cm. $25.00.

Volume 2 of this series covers the synthetic organic literature from 1969, where Volume 1 ends, to 1975. The organization of this volume parallels that of Volume 1 in that there are 20 chapters each dealing with a particular functional group. Chapter contents appear before each chapter and at the end of the book there is a Subject Index. Noteworthy, too, is the inclusion of a Reaction Index with useful synthons depicted by structural formulas. After each synthon, the reader is referred to Volume 1 or 2 for synthetic details.

Effort has been made not only to keep the reader abreast of newer synthetic methods but also to review these methods critically. The organization, literature references, and reasonable cost of Volume 2 will make it a useful addition to the library of many synthetic organic chemists.

**Staff Review**

**Aliphatic Chemistry. Volume 5. Specialist Periodical Reports.** By A. McKillop, Senior Reporter. The Chemical Society, Burlington House, London. 1977. xi + 337 pp. 13.5 × 21.5 cm. $47.00.

This volume reviews the literature published during 1975, except as noted below. After a 1-year lapse, there are again five chapters dealing with the following: Alkanes, Acetylenes, Allenes and Olefins; Functional Groups other than those above; Naturally Occurring Polyolefinic and Polyacetylenic Compounds; Chemistry of the Prostaglandins; and Fatty Acids and Related Compounds.

Of particular interest to medicinal chemists are the last three chapters listed above, and it should be noted that the chapter on fatty acids, a topic omitted in Volume 4 of this series, now covers the literature for 1974 and 1975.

There is a detailed table of contents and an author index. With the inclusion of the fatty acids, the number of references covered, 1750, is back to the level of 2 years ago. It should be noted that the Chemical Society has decided to discontinue this series after the present volume and that it will be replaced in the future, in part, by new titles, "General and Synthetic Methods" and "Aliphatic and Related Natural Product Chemistry". This volume constitutes a valuable aid to all researchers dealing with aliphatic chemistry who are hard pressed to keep up with the voluminous literature in their field.

*Northeastern University* **Alfred Viola**

**The Chemistry of Heterocyclic Compounds. Volume 30. Special Topics in Heterocyclic Chemistry.** Edited by A. Weissberger and E. C. Taylor. Wiley-Interscience, New York, N.Y. 1977. 601 pp. 16 × 23 cm. $57.50.

With this volume, a new type of review in the now standard series of Heterocyclic Chemistry has been presented in order to cover topics of more limited scope and not necessarily related to each other. In contrast to the former volumes of this series, which contained exhaustive discussions of syntheses, reactions, properties, structure, physical chemistry, etc., of compounds belonging to only one specific heterocyclic ring system, the present volume is mainly devoted to those disciplines of heterocyclic chemistry that are of general significance and application and of interest to all organic chemists. It is the main concern of this book that the special topic surveys the entire field of heterocyclic chemistry rather than a particular ring system and should therefore call attention more to the heterocyclic chemist in general than to the individual specialist in one field. Since there is a real need for additional discussions of various topics in heterocyclic chemistry as one of the most complex branches in organic chemistry, coverage of theoretical aspects, synthetic procedures, and physiological and industrial significances is especially appreciated.

Eight chapters, not closely related, are discussed by nine authors. J. P. Paolini wrote the first one, "5.5-Systems with a Bridgehead Nitrogen Atom", covering syntheses, reactions with electrophiles and nucleophiles, ring openings, and condensations as well as tautomerisms of various types. The contribution of H. L. Blewitt is concerned with "Indolizine and Aza Derivatives with Additional Nitrogens in the 5-Membered Ring". Physical properties, syntheses, general and specific reactions, and theoretical aspects are presented in a detailed manner. The following chapter, "Azaindolizine Systems having more than one Nitrogen Atom in the 6-Membered Ring", by G. Maury can be regarded as an extension of the former contribution, having concentrated

mainly on the changes in chemistry due to additional nitrogen atoms in the $\pi$-deficient part of the molecule. The chapter by A. Taurin on "The Chemistry of Cyclazines" collects all the information available about fused tricyclic conjugated ring systems held planar by the three covalent bonds to an internal nitrogen atom. R. D. Hamilton and E. Campaigne are responsible for the survey on "Dithiole and Dithiolium Systems" which have mainly been investigated in the last 15 years. Their interesting chemistry and properties are described and discussed in detail.

In chapter VI K. T. Potts offers a review of "Heteropentalenes", showing ylidic characteristics. This group of compounds is of special interest since their properties depend to a large extent not only on the nature of the heteroatoms but also on their orientation in the molecule. The next chapter by A. J. Fritsch is dealing with "Borazaromatic Compounds" which are derived from normal aromatic hydrocarbons by the replacement of adjacent carbon atoms by boron and nitrogen. These relatively new and interesting systems are discussed from a chemical and physical point of view leading to a better understanding of this field. The last chapter finally offers an excellent concentrate on "Syntheses and Properties of Cyanine and Related Dyes", written by D. M. Sturmer. All important information of this field has been covered and clearly presented, giving an overall picture of the development and the chemical and physical–chemical facts associated with this class of compounds.

The style of this book is consistent with the high standard of the conventional volumes of this series and the well-known high-quality production guarantees a long-lived use. The comprehensive collection of valuable information connected with extensive references and a detailed subject index will provide a wide distribution.

*Universität Konstanz* **Wolfgang Pfleiderer**

**Psychopharmacology.** By Lewis S. Seiden and Linda A. Dykstra. Van Nostrand-Reinhold, New York, N.Y. 1977. xi + 451 pp. 15 × 23 cm. $19.95.

This is a most competent introduction to the research literature in experimental psychopharmacology. The authors open with chapters describing the behavioral procedures for assessing drug action in animals, followed by the pharmacological and biochemical techniques most generally used in psychopharmacology. These two concise methodological chapters form a solid foundation on which the rest of the book is built. The autonomic nervous system is then presented as a model for the biochemical and physiological events that may occur in the brain, and the basics of neurotransmission, physiology, and pharmacology are succinctly tackled. Separate chapters discuss the biochemistry and pharmacology of serotonin, dopamine, norepinephrine, and acetylcholine, their roles in behavior, and their interactions with psychoactive drugs. This section covering the pharmacological and biochemical basis of psychopharmacology concludes with a chapter on the function of macromolecules in learning and memory. The final section deals with the behavioral analysis of drug action, with chapters covering drug effects on schedule-controlled behavior and on discrimination, as well as discussions of the role of drugs as reinforcers and discriminative stimuli.

In all chapters the authors have focused on salient data and methodological issues and have provided critical analyses. They are to be congratulated on the useful summary tables to the major literature sources for the particular phenomena under discussion. These are particularly valuable, as the text makes reference to over 1000 research papers. Psychopharmacology is a young and exciting science which draws on knowledge and techniques from several fields. The authors are careful to provide a basic description of fundamentals in each instance before moving to more critical discussions of complex areas. Numerous caveats are scattered throughout the text, pointing out the various pitfalls and misinterpretations of data that can and have been made in this interdisciplinary area.

It should be emphasized that the selection of behaviors and neurochemicals is not inclusive but is sufficiently broad to cover our present understanding of the mechanism of action of psychomotor stimulants, antidepressants, antianxiety agents, antipsychotics, analgesics, and hallucinogens. However, in this rapidly moving field one already notices the absence of chapters on peptides and behavior, and drug receptor binding studies. The subheading of this volume, "A Behavioral and Biochemical Approach", defines its scope and also its limitations. One wishes that the authors could have included discussion of recent electrophysiological studies of drug mechanisms, for example, the effects of hallucinogens on presynaptic serotonin receptors or neuroleptic-induced alterations in nigrostriatal activity. Nevertheless, this authoritative text provides an excellent sourcebook of current psychopharmacological research for pharmacologists, experimental psychologists, and psychiatrists, as well as for students in the neurosciences. It can be highly recommended.

*Johns Hopkins University School of Medicine* **Ian Creese**