g (27.8 mmol) of Na_2CO_3, and 1.5 g (9.7 mmol) of KI in 25 mL of dry DMF was heated at 150 °C for 2 h. Then the cooled reaction mixture was poured into 200 mL of H_2O and extracted with ether three times. The combined etheral extracts were dried, concentrated, and chromatographed on 150 g of silica gel using 1:1 benzene–ethyl acetate as eluent. Product-containing fractions were combined and evaporated, and the residues were dissolved in dry ether and treated with ethereal HCl to give 1.40 g (32%) of the desired product, mp 175–179 °C dec.

In a similar fashion, compound **2** was reacted with the appropriate ω-haloalkyl 4-fluorophenyl ketone to yield compounds **7** and **11** in the yields specified in Table I.

Preparation of Compound 10. A suspension of 700 mg (1.49 mmol) of compound **9** in 25 mL of THF and 5 mL of ethanol was treated with 282 mg (7.45 mmol) of $NaBH_4$ over a period of 30 min. After the solution was stirred an additional hour, the solvents were removed in vacuo, and the residues were taken up in water and repeatedly extracted with ether. The combined ether extracts were dried with $MgSO_4$ and then treated with a solution of dry HCl gas in ether to give 331 mg (47%) of compound **10**, mp 210.0–211.5 °C dec.

In a similar fashion, ketones **7** and **11** were reduced to give compounds **8** and **12** in the yields specified in Table I.

Biological Methods. Antagonism of (+)-Amphetamine-Induced Symptoms in Rats. Neuroleptic effects in vivo were estimated by the blockade of amphetamine stereotypy. Rats were placed individually in covered plastic compartments; after a brief period of acclimation in the cages, the rats in groups of five were treated intraperitoneally with compounds at doses separated by 0.5 log unit (i.e., ..., 1, 3.2, 10, 32, ... mg/kg). They were subsequently treated 1, 5, and 24 h later with *d*-amphetamine sulfate, 5 mg/kg ip. One hour after each amphetamine challenge each rat was assessed for its most characteristic behavior on a six-point scale.[10] These ratings represent increasing degrees of drug effect,[11] and the time of rating chosen coincides with the peak effect of amphetamine.[8] Scores were dichotomized (cf. ref 10), and approximate ED_{50} values were determined, based on the quantal data. Doses are expressed in terms of the respective salts.

Acknowledgment. The authors are grateful to Mrs. C. T. Lewis and to J. W. Homiski and R. L. Taylor for expert technical assistance.

(10) A. Weissman, B. K. Koe, and S. S. Tenen, *J. Pharmacol. Exp. Ther.*, **151**, 339 (1966).
(11) R. M. Quinton and G. Halliwell, *Nature (London)*, **200**, 178 (1963).

Book Reviews

The Chemistry of Heterocyclic Compounds. Volume 34. Thiazole and Its Derivatives. Part 2. Edited by Jacques V. Metzger. Wiley-Interscience, New York. 1979. xii + 590 pp. 16 × 23.5 cm. $80.00.

The thiazoles of greatest interest to the medicinal chemist are probably those based on the 2-amino derivative. The chemistry of these useful building blocks is discussed in a 361-page chapter in this second volume of a three-part set devoted to thiazoles edited by Professor Jacques V. Metzger. The authors contributing to this monograph hail from Metzger's institution, the University of Aix-Marseilles.

The first section, a nonchapter and running only 9 pages (by M. Chanon), gives a general introduction to protomeric thiazoles. Chapter 6 (by R. Barone, M. Chanon, and R. Gallo) discusses aminothiazoles and their derivatives from the synthetic, spectroscopic, and mechanistic viewpoints. In addition, at the end of the chapter there is a listing of mp/bp data and literature citations pertaining to some 6000 aminothiazoles. Chapter 7 (by C. Roussel, M. Chanon, and R. Barone) describes in a similar manner mercaptothiazoles, hydroxythiazoles and their derivatives. Both chapters have surveys of the medicinal applications of compounds possessing a thiazole ring.

As in Chapter 6, Chapter 7 has a large number (54) of tables listing mp/bp and literature references. The authors are to be complimented for undertaking such extensive compilations; however, locating specific compounds, other than the simplest, is not an easy task. An index to the tables (considering that Chapter 6 has 80 of them) would have been helpful. Furthermore, the tables in Chapter 6 also lack descriptive headings.

In the introduction to the tables of Chapter 7 one is referred to page 171 for "easier use of these tables". On page 171 one finds a few preliminary words regarding the tables of Chapter 6 and then one is referred to Part (Volume) 1, pages 2 and 3, for a guide to the abbreviations used. It is assumed that the reader has a copy available. Certainly, repetition of this list of 22 abbreviations in the second volume would have made life easier for the reader, especially one lacking a copy of Part 1. Furthermore, on page 171, the reader is warned to watch out for l's (ells) following reference numbers and not confuse them with 1's (ones). Indeed, an encounter with a reference number in the tables ending in an l or 1 does require the reader to take a particularly careful look.

The authors do not appear to have been overly concerned with the problem of nomenclature. Examples: one sees "1-morpholino" and "1-piperidino", wherein the 1's are superfluous; throughout Chapter 7 there is constant use of Δ's as in "Δ-4-thiazoline-2-thione". The deltas are also unnecessary and have not been used by Chemical Abstracts since the 1930's. Evidence of French authorship (e.g., ICH_3, pipéridine, NO_3H) is less apparent than in the preceding volume.

Yet, because of the extensive coverage of the subject matter, this volume can be recommended as an important new reference source for those involved in heterocyclic chemistry. The price of $80.00 will probably limit its sale to those individuals working with thiazoles, but scientific libraries will definitely want a copy.

Walter Reed Army Institute of Research **Daniel L. Klayman**

Immunochemistry in Clinical Laboratory Medicine. Edited by A. Milford Ward and J. T. Whicher. University Park Press, Baltimore, Md. 1979. 16.5 × 22.5 cm. x + 247 pp. $29.95.

This book contains the proceedings of a symposium held at the University of Lancaster, March, 1978, and is divided into three basic sections. The first deals with methods and problems in immunochemistry. The seven chapters in this section each give a general overview ranging from antisera production to their use for the quantitation of various body-fluid proteins. All chapters provide readers with a good introduction to both the potential and limitations of various methods utilized for clinical analysis. A major drawback is that the chapters lack sufficient detail to actually duplicate the procedures.

The second section includes chapters on specific proteins in laboratory diagnosis. Introductory chapters discuss the structure and function of the immunoglobulins. Other chapters review the role of albumin, the complement system, alphafetoprotein, α-antitrypsin, haptoglobin, and orosomuscoid in various benign and neoplastic diseases. The chapters are written for those that require a general review or introduction to these proteins as they relate to clinical medicine. As the authors clearly state, there is additional extensive detail published in other reference works.

The third section contains two chapters, one on urinary proteins and the other on the immunochemistry of CSF proteins. These

chapters, like the others in this book, provide readers with an introduction to these areas.

This book as written should be of value for those entering or working in a clinical chemistry laboratory. It is clearly written and provides an excellent introduction. This book is not recommended for those with a sufficient background in immunochemistry in clinical laboratory medicine.

Northeastern University **James Joseph Gozzo**

Terpenoids and Steroids. Volume 9. Edited by J. R. Hanson, Senior Reporter. The Chemical Society, Burlington House, London. 1978. xii + 352 pp. 14 × 22 cm. $72.00.

This Specialist Periodical Report is organized in the same fashion as its predecessors. It carries forward its unique and invaluable survey of these continually expanding areas of chemistry. The continuing isolation of natural products of fascinating structures is paced by the application of ingenious synthetic techniques. The inclusion of sections very briefly outlining outstanding advances in synthetic methodology is a welcome one, as it also serves the purpose of reviewing advances which will be of general interest to any chemist working in aliphatic and alicyclic chemistry. Similar sections on physical methods, particularly in the steroid section, are of analogous value. For chemists working in the area of natural products, this series continues to be one of the most valuable sets of books on the shelves.

Staff

Foundations of Molecular Pharmacology. Volume 1. Medicinal and Pharmaceutical Chemistry. Volume 2. The Chemical Basis of Drug Action. By J. B. Stenlake. The Athlone Press of the University of London, London. 1979. Volume 1: xi + 936 pp. 16 × 24 cm. $90.00. Volume 2: vii + 318 pp. 16 × 24 cm. $46.25.

The title of the two-volume series and for the first volume seem misleading. Volume 1 is intended as a foundation course in undergraduate organic chemistry for pharmacy and/or medicinal chemistry students. The book begins with an introductory chapter on atomic structure, bonds and bonding, and proceeds in a traditional fashion through chapters on alkanes, alkenes, benzenoid hydrocarbons, alkynes, alcohols, phenols, etc., through steroids, carbohydrates, and heterocyclic compounds. The narrative covers nomenclature, physical properties (extensive descriptive material), and reactions (not at all comprehensive). Wide use is made of the mechanistic approach to organic chemistry. Curved arrows are printed in red. References to the original literature are interspersed in the text, with a cumulative bibliography in the rear of the volume. Examples of chemical properties or reactions of functional groups are largely drawn from chemistry of drug molecules or from biochemical reactions. For example, when mixed anhydrides are discussed, the in vivo enzyme-mediated formation of acetyl phosphate is cited. A part of the exposition of the chemistry of urea is a reproduction of the ornithine cycle but without any discussion of it. This is soon followed by a brief, superficial discussion of barbiturates. No synthetic aspects are presented in the volume.

This reviewer questions the philosophy of presentation of a special organic chemistry course to pharmacy or medicinal chemistry students, presumably based upon the premise that the organic chemistry needed by these students differs from that needed by an undergraduate chemistry major. The consistent use of drug molecules for examples of fundamental organic chemistry of functional groups is, in this reviewer's opinion, a detriment to learning and to teaching. The student, who may be overawed by beginning organic chemistry to begin with, may tend to be distracted further from learning basic chemical principles by the endless presentation of complicated drug molecules for the illustration of frequently simple chemistry. It seems undesirable to illustrate photolytic cleavage of ketones using androsterone as the sole example. The only chemistry described for the oxime moiety is the reaction of pralidoxime with a phosphorylated serine moiety of acetylcholinesterase.

Volume 1 is well written and well organized and seems to be free from errors. However, mastery of the material in the book will not, in this reviewer's opinion, provide any undergraduate student with adequate background in organic chemistry for pursuit of subsequent graduate study in medicinal or organic chemistry or even to cope with advanced undergraduate organic chemistry courses. Neither does this reviewer believe that the approach used in Volume 1 is adequate for the organic chemical education of undergraduate pharmacy students. Beginning graduate students might find the volume helpful as a reference work, for superimposition upon a prior basic course in organic chemistry.

Volume 2 (a much smaller volume) consists of chapters on "Drug–Receptor Interactions"; "Bonding and Biological Activity"; "Stereochemical Factors in Biological Action"; "Drug Ingestion, Transport, and Excretion"; and "Drug Metabolism". This volume may be of value as a reference work for undergraduate students in an "Organic Medicinals" course or for beginning medicinal chemistry graduate students. It can be read with profit by the organic chemist or the pharmacologist who wishes to gain a brief overview of certain aspects of medicinal chemistry. However, this volume seems too advanced and sophisticated for use as a text in a beginning course and too elementary and superficial for use in an intermediate or advanced level course in organic chemistry, medicinal chemistry, or pharmacology, either for health science practitioners or for research-oriented students.

An added deterrent to use of both volumes as texts is their cost. It is noted that printing of both volumes is excellent, but the binding is of poor quality: a leather texture cover which appears to be paper. Volume 1 reached this reviewer's hands with the inner paper binding already badly split and cracked, which presages poorly for the long-term survival of the integrity of the binding and the hard cover.

The two-volume set seems to be a useful addition to the library as a reference work, but it is not recommended as a text for any undergraduate or graduate chemistry or pharmacology course.

The University of Iowa **Joseph G. Cannon**

Mitomycin C. Current Status and New Developments. Edited by Stephen K. Carter and Stanley T. Crooke. Academic Press, New York. 1979. xiii + 254 pp. 15.5 × 23.5 cm. $20.00.

The purpose of this book as stated in the preface is "to provide a historical perspective on the development of mitomycin C, to summarize the recent developments, including studies on analogs, and perhaps to suggest new directions for future research". This theme is covered in 28 chapters, and data and personal viewpoints are presented on mechanism of action, analogue development, in vivo animal bioassay, morphological effects, toxicity, clinical pharmacology, suppressor cells/immune response, potentiation by lucanthone hydrochloride, and clinical studies (19 chapters).

The major thrust of the book is the chapters which describe clinical studies with mitomycin C, both as a single agent and in combination chemotherapy programs. In the final chapter, Stephen Carter gives a lucid summary of the book, in particular the chapters dealing with clinical studies. He reflects that it is often difficult to determine the value of a single agent or analogue when the clinician's urge is to go directly to a combination study. The need for a better understanding of the preclinical and clinical pharmacology of single agents is clearly suggested.

Useful references are omitted occasionally, i.e., "mass spectrometry has been tried to both detect and quantitate drug and metabolite", but no reference is given, even as unreported results. There are a number of typographical errors, which, although minor, should have been corrected easily by the editors. A point of personal and I would hope more general concern is the use of numerous names for mitomycin C, i.e., mytomycin, mito C, mito, MMC, MC, and M. The literature is confusing as is without resorting to nonconventional abbreviations for the title compound.

Overall, the editors have done an excellent job of putting together a collection of timely and knowledgeable reviews on mitomycin C. The book should be of particular value to clinicians and, to a lesser extent, laboratory researchers, no matter which cancer chemotherapeutic drug is currently number one on their list.

Arthur D. Little, Inc. **Alan R. Branfman**

Physiological and Regulatory Functions of Adenosine and Adenine Nucleotides. Edited by H. P. Baer and G. I. Drummond. Raven Press, New York. 1979. xvii + 438 pp. 16 × 24 cm. $39.50.

Study of the regulatory role of adenosine and adenine nucleotides is in the midst of a period of rapid developments reminiscent of earlier cyclic-nucleotide studies. This volume contains the proceedings of a conference held in Banff, Alberta, Canada, in June of 1978 and is a broad-based collection of pharmacologic, biochemical, and physiologic studies. Major divisions include "Purinergic Nerves and Isolated Smooth Muscle Studies", "Cardiovascular Actions", "Cyclic AMP and Adenylate Cyclase Involvement (Structure Activity Studies)", "Transport and Metabolism of Adenosine", "Electrophysiological Studies", "Fat Cells", and "Immune System and Prostaglandin Involvement".

Typically, for conference proceedings there is a distinct lack of cohesion, while hypotheses abound. This is in part probably due to the rather limited level of current understanding of the precise mechanisms. On the other hand, the reader is likely to find a tissue (and a hypothesis) in harmony with his/her interests. One cannot overlook the similarity to the "Advances in Cyclic Nucleotide Research" series offered by the same publisher. However, this volume is more fully illustrated with less of a "review" format.

It is clear that adenosine and adenine nucleotides are involved with a series of interrelated processes, including adenylate cyclase, Ca^{2+} binding and transport, prostaglandins and catecholamine receptors. Much of the text provides testimony to these interactions. Structure–activity relationships among adenine derivatives are the basis for about six papers, and these provide the basis for receptor subclassification.

Overall, this book provides a well-presented gathering of basic research in an important, developing area of regulatory physiology. To the reviewer it seems that this volume could easily be the forerunner of a continuing series.

Northeastern University **Richard C. Deth**

The Porphyrins. Volume VII. Biochemistry. Part B. Edited by David Dolphin. Academic Press, New York. 1979. xxi + 550 pp. 16 × 23 cm. $55.00.

This constitutes the final volume of a series which must now take its place in every laboratory where porphyrins are seriously investigated. The major theme, the structure and function of hemoproteins, is well-defined by the following sentence: "The major role of the protein is to affect the properties of the heme so as to magnify one of them far out of proportion to the others and/or depress one or several of the other reactivities". It is occasionally necessary when using this book to recall that the heme group is the primary determinant of cytochrome function, although this may perhaps depend upon the reader's own interests.

Chapter 1 deals with cytochrome oxidases (including those of bacteria) and includes a brief historical introduction. A chapter on current (to 1978) information about cytochrome *b* in energy-transducing membranes is followed by one on the X-ray structure of cytochrome b_5 from calf liver. Structure/function relationships are discussed. Chapter 4 deals with the all-important electron-transfer function of cytochrome *c*. Stereoscopic diagrams are provided for those who possess the happy knack of viewing them. Chemical modification of the cytochrome, its nonphysiological redox behavior, and its reactions with enzymes receive detailed attention. The porphyrin nucleus comes to the fore in the description of cytochrome *c* structure given in Chapter 5, while Chapter 6 deals with the versatile peroxidase family and Chapter 7 with cytochrome P-450. In the last case, the value of using an array of spectroscopic techniques to probe the heme environment is well illustrated. The role of cytochrome P-450 in arene oxide formation and, possibly, chemical carcinogenesis is mentioned. Chapter 8 deals with the dissociation and reconstitution of hemoproteins and includes comment on the use of "unnatural hemes". Some experimental details are included. Chapter 9 describes the substitution of other metals (Co, Mn, Zn) for iron in hemo- and myoglobins as a probe of the influence of protein environment on the properties of the bound porphyrin. An essay on hemo- and myoglobin structure and function follows. This includes a discussion of the concerted vs. sequential controversy regarding the mechanism of cooperative binding of oxygen to hemoglobin. The final chapter is concerned with bacteriochlorophyll proteins from green photosynthetic bacteria. That obtained from a *Prosthecochloris aestuarii* strain has a trimeric structure, each subunit consisting of a hollow shell of protein with seven bacteriochlorophyll molecules in the core. Here, the spatial relationship between the porphine molecules is defined by binding to the protein, rather than by chl–chl interactions.

Typographical errors are rare in this book and footnotes to many of the chapters state clearly when literature coverage ends. There is a satisfactory subject index.

University of Dublin, Trinity College **David Grayson**

Carcinogens and Related Substances. Analytical Chemistry for Toxicological Research. By Malcolm C. Bowman. Marcel Dekker, New York and Basel. 1979. x + 316 pp. 15 × 23 cm. $34.50.

Toxicological research, including routine in vivo and in vitro testing of chemicals for toxic properties, has traditionally been plagued by a lack of suitable and routinely instituted methods for the trace organic or inorganic analysis of these materials. If current and future testing of environmental or consumer product contaminants or constituents is to be more meaningful, it will be imperative for researchers to be more aware of the latest advances made in this area of analytical chemistry. Although the pertinent literature has been expanding rapidly in recent years, there has been an almost total lack of any comprehensive text which surveys and summarizes succinctly the latest results. Mr. Bowman's book attempts to accomplish this most worthwhile goal, and, in most aspects, it succeeds well. Having been directly responsible for the successful development of various trace methods of analysis for the National Center for Toxicological Research in Jefferson, Arkansas, Mr. Bowman is obviously well qualified and prepared to comprehensively discuss analytical chemistry for toxicological research.

This is not a general textbook of analytical chemistry, and it is not destined for popular consumption, but it is rather aimed directly at just those scientists directly involved in various areas of toxicological research and testing. In this regard, it is almost required reading for individuals responsible for the planning, performing, and interpretation of any biological testing for toxic properties of organic or inorganic chemicals. It obviously fills a long-standing need in the field and should be welcomed and well received by all interested parties. The book is divided into five chapters, with the third chapter making up almost 65% of the total material presented. This discusses the analysis of those substances being tested or already tested for toxicological properties and includes many of the more commonly studied materials, such as aromatic amines, estrogens, pesticides, and a small number of miscellaneous compounds. A variety of matrices are considered with regard to the extraction of these organics and sample preparation; these include animal chow, laboratory water, bedding, whole animals, urine, blood, etc.

The first chapter discusses the basic analytical requirements for undertaking research in toxicology, and this is excellent material for those now undertaking or about to undertake such work. An adequate discussion is provided of good laboratory practices, handling and storage of test substances, preparation of the final test items in food or water, safety practices, and the final disposal of all materials used. Chapter 2 presents a valuable discussion of the analysis of the basic animal diet for possible contaminants, such as aflatoxins, hormones, minerals and heavy metals, vitamins, proteins, fats, and pesticides and related chemicals. Finally, there is an excellent presentation of the analysis of animal bedding, feeder boxes, and water supplies for the animals. All of these subjects have been treated lightly in previous publications or texts; thus, their presentation here is extremely welcome and needed for future progress in animal testing. Too little attention has been given in the past to the presence of potentially carcinogenic and/or mutagenic materials present as contaminants in the laboratory environment. It should be obvious that all future work must include a complete analysis

of just these materials and for as large a number of possible contaminants as practical and feasible.

Chapter 4 deals with a comprehensive analytical procedure for a large number of carcinogens or mutagens that might be found together in human urine or waste water. The methods are valuable, sensitive, and somewhat specific for the compounds being studied. They allow for the rapid analysis of small samples in a reasonably short period of time, with some assurance that omissions will be few. Finally, the last chapter discusses the practical procedures for the almost total removal of trace levels of test substances from laboratory waste water. Again, this is an area that has been largely ignored in the past, just by those laboratories involved in toxicological research, but it is a subject that must be more rigorously dealt with in the future. Routine testing of such waste water, followed by any necessary treatment of such water for the removal of any substances found, must be more widely adopted.

In summary, Mr. Bowman's book provides all workers in toxicological research with an awareness and practical familiarity with the latest methods for trace organic and inorganic analysis of potentially toxic substances. It should find wide acceptance in the coming years by all researchers and administrators interested and/or involved in this field.

Northeastern University **Ira S. Krull**

Inorganic Biochemistry. Volume 1. Specialist Periodical Reports. Edited by H. A. O. Hill. The Chemical Society, Burlington House, London. 1979. xvi + 442 pp. 14 × 22 cm. $61.50.

The Chemical Society (London) Specialist Periodical Reports have long provided complete, concise, and, therefore, invaluable overviews of specific subdisciplines in chemistry. The addition of "Inorganic Biochemistry" to the list is indeed welcome. Allen Hill has assumed primary reportorial responsibility, and the reporters include a host of renowned workers in the field. The scope of coverage is quite broad, varying from purely inorganic "model systems" to trace element nutrition and clinical applications of metal-based drugs. Such "traditional" research topics as oxygen transport and electron transport are neatly summarized, noting much of the important detail of the references cited. In toto, the volume covers "current" literature through the end of 1977, incorporating some 2400 references in nine chapters. Further volumes should follow on an annual basis.

In summary, this volume is an incredibly rich compilation of the current literature and research trends in the "metastatic" field of inorganic biochemistry. Anyone with even a tangential interest in the field would be well advised to peruse a library copy. Those directly involved in one or more areas of inorganic biochemistry, and possessed large unrestricted funds (the price of one is an incredible $61.50!), might seriously consider subscribing to the series.

University of Rochester **George McLendon**

Narcotic Plants of the Old World. By Hedwig Schleiffer. Lubrecht and Cramer, Monticello, N.Y. 1979. 193 pp. 15 × 23 cm. Paperback $7.95, Hard Cover $12.50.

The term "narcotic" is used here in the classical sense, to benumb or to induce a sense of stupor, rather than in the more usual medicinal chemical-pharmacological sense of "opioid". Hence, this attractive little volume includes reference to a large number of well-known plants, among them *Atropa*, *Cannabis*, *Datura*, and *Papaver*, whose constituents and biodynamic properties are well established. The author is to be congratulated, however, for presenting this material in the form of an anthology of texts or translations of original observations and writings spanning the centuries from Herodotus to modern authors. The result is a refreshing glimpse into the history of some of our most powerful medicinal and toxic plants. Perhaps more appealing to the interests of the modern medicinal chemist are the few lesser-known species whose constituents and pharmacological actions have not been as well defined. It is a companion volume to the author's earlier anthology dealing with the narcotic plants of the New World Indians.

Northeastern University **Robert F. Raffauf**

A History of the Life Sciences. By Lois N. Magner. Marcel Dekker, New York and Basel. 1979. xi + 489 pp. 16 × 23.5 cm. $23.50.

A true appreciation of the rapid advances in our understanding of disease and its treatment which have been made in this century lies in an awareness of the broad concepts in the life sciences which were developed in centuries past. These are presented in an attractive and readable fashion in this book.

The author points out in her preface (page ix) that "some problems"—and these include the modern contributions of what we know as medicinal chemistry—"may seem somewhat slighted" in this introduction to the history of the life sciences. Nonetheless, the roots of medicinal chemistry are apparent in chapters dealing with Arabic science and medicine, the scientific revolution, the development of microbiology, and the efforts of scientists through the centuries to define the physiological and pharmacological mechanisms to which our current efforts at therapy are directed. Concluding chapters deal with twentieth-century genetics and molecular biology and their portents for the future of the life sciences. While the book's major appeal will be to the allied health professions, I would not hesitate to recommend it to the medicinal chemist as recreational reading.

Northeastern University **Robert F. Raffauf**

Acupuncture Manual. A Western Approach. By Luke S. W. Chu, Samuel D. J. Yeh, and Denise D. Wood. Marcel Dekker, New York and Basel. 1979. xvi + 256 pp. 18 × 25.5 cm. $15.00.

This book is a serious attempt to present the history, philosophy, methods, and clinical applications of acupuncture to Western medicine. As a manual, much of the content is devoted to "how to"; as an introduction to the art, there is ample recognition of the need for research, controlled studies, clinical data, and the interpretation of results. Mindful of the controversial nature of the method, the approach, discussed in detail in the Preface, is cautious and reasoned enough to dispel any notions of charlatanism, although the mingling of the sophisticated vocabulary of anatomy with the patois of historical acupuncture may arouse suspicions in the minds of many.

The modern physiologist/pharmacologist will probably find much to argue about here. Since the method is not confined to the relief of pain but can be used, it is said, in the treatment of many disorders, the medicinal chemist, if he has any interest at all, will learn what the competition is up to.

It would be interesting to speculate on the response to be obtained in those "patients" who have their ears pierced for earrings—but that would spoil the plot!

Northeastern University **Robert F. Raffauf**

Chemical Stability of Pharmaceuticals: A Handbook for Pharmacists. By Kenneth A. Connors, Gordon L. Amidon, and Lloyd Kennon. Wiley-Interscience, New York. 1979. xi + 367 pp. 15.5 × 23.5 cm. $21.50.

This book approaches chemical kinetics, as it relates to drug stability, from the pragmatic viewpoint of the pharmacist (student or practitioner) who is primarily interested in being able to make a fast and reasonably reliable estimate of dosage form shelf life. Competence of this type requires an understanding of the basic theory underlying chemical kinetics, as well as a knowledge of typical values reported in the literature for various kinetic parameters. The authors have divided the book into two sections dealing with these aspects of kinetics on an individual basis.

Part I, entitled "Principles", is comprised of six chapters, the first three of which present elementary theory relating to the

development of rate equations, the order of reactions, temperature effects, preliminary shelf-life estimations, transition-state theory, and medium effects, including homogeneous catalysis and pH effects. Chapters 4 and 5 consider various mechanisms of degradation, such as hydrolysis and other acyl transfers, and free radical mediated processes. Chapter 6 discusses GMP regulations, as related to drug stability, together with a presentation of methods for shelf-life estimation based on accelerated stability studies. An introduction to the experimental design of stability tests and the fundamentals of protocol design is also included. Throughout this section, theory is presented in terms of specific, pharmaceutically relevant examples which have been well chosen for both scope and content.

Part II, entitled "Stability Monographs", makes up approximately two-thirds of the book and consists of 30 such monographs. These are written by various contributors and have been edited to a uniform style and format for easy reading and reference. They focus sharply on the major routes of chemical degradation contributing to instabilities of pharmaceutical significance. The drugs treated in this section have been well selected both in terms of therapeutic class and for the variety of catalysis and degradation mechanism they comprise. A very selective use is made of published data, and sufficient key references are provided to allow the reader an easy entreē to the literature.

The book represents an excellent balance between its presentations of fundamental theory and of kinetic data. Its style is crisp and lucid, and it makes good use of many examples, figures, and tables. This text should be of value in graduate and advanced undergraduate courses in drug stability.

University of Minnesota **Edward G. Rippie**

Immunotherapy of Human Cancer. Published for the University of Texas System Cancer Center, M.D. Anderson Hospital and Tumor Institute, Houston, Texas, by Raven Press, New York. 1978. xix + 417 pp. 16 × 24 cm. $35.00.

This book contains 25 separate papers stemming from the 22nd Annual Clinical Conference on Cancer. Foremost among these is the Health Memorial Award Lecture by Dr. Georges Mathē entitled "Active Immunotherapy: Experimental and Rational Basis". Other discrete sections of this book include (1) "Immunologic and Clinical Basis of Immunotherapy"; (2) "Approaches to Immunotherapy"; (3) "Clinical Immunotherapy"; and (4) "Principles and Prospects for Immunotherapy".

As with books of this type with multiple authors and involving specific research programs and projects, there is a lack of continuity. However, the quality of the scientists and their obvious involvement at the cutting-edge of new research developments in immunotherapy makes it very relevant to immunologists and clinicians concerned with this mode of cancer therapy. This book is not totally concerned with immunotherapy in man, but the earlier sections present the studies in animals that have provided the basis for current clinical applications. Though immunotherapy of cancer yet remains in the early developmental stages, frequently with crude and poorly defined substances, as shown from this text, nevertheless, there is promise that there will be future clinical successes as judged by the studies presented in patients with acute myelocytic and acute lymphocytic leukemias, melanomas, genitourinary and gynecologic malignancies, sarcomas, and breast, lung and colorectal cancers. Evidence is shown that this relatively new therapeutic modality increases the rate of remission and its duration.

The last three chapters of this book present the limitations as well as the future approaches and opportunities of cancer immunotherapy in man. For example, there is a discussion on the removal of blocking factors, both circulating and membrane-bound, that may adversely effect the immunocompetence of patients. Use of plasmapheresis is presented as well as the potential and present use of immunorestorative agents. Discussion on the use of interferon, however, is outlined in only a very cursory manner. The variability of immunotherapy in cancer patients indicates the ultimate need for identifying individual immunological mechanisms that are operative and appropriately correcting them. The present status of knowledge, however, precludes such an approach at this time. However, the future of cancer immunotherapy as a fourth major modality for treatment in conjunction with surgery, radiation and chemotherapy is promising.

Ohio State University **Albert H. Soloway**

The Peptides. Analysis, Synthesis, Biology. Volume 1. Major Methods of Peptide Bond Formation. Edited by E. Gross and J. Meienhofer. Academic Press, New York. 1979. xvii + 435 pp. 15 × 23 cm. $39.50.

This is the first volume of an open-ended series whose aim is to provide comprehensive and critical reviews of major topics in the field of "peptidology". The inaugural volume deals mainly with methods of peptide synthesis and consists of seven chapters.

Chapter 1 (by E. Gross and J. Meienhofer) sets the stage by delineating in broad strokes the contemporary issues in peptide chemistry. Among the topics addressed here are the fundamental nature of the peptide bond (for instance, is it as rigidly planar as was once thought?), the specificity of proteolytic enzymes both in a physiological context and in relation to sequencing methodology, the need for novel new reagents for functional-group protection during polypeptide synthesis, and the importance of searching for improved racemization-free coupling reagents.

Chapter 2 (by J. H. Jones) is a useful summary of the principal methods of peptide bond formation currently in use. The purpose here, apparently, is to point out to the general reader with little or no prior knowledge the various roads that are open to him as he attempts to synthesize a peptide for the first time. Techniques discussed in this chapter range from the classical ones (mixed anhydride synthesis and carbodiimide reagents) to some of the more modern options such as the use of isoxazolium reagents. Each topic is covered in a concise manner, and specific examples from the literature are provided in order to acquaint the novice with the scope and limitations of the method.

Chapter 3 (by M. Bodanszky) is devoted to a comprehensive review of active esters in peptide synthesis. The various classes of active esters (alkyl, aryl, enol, hydroxylamine, and so on) are introduced, along with an explanation of the importance of solvent catalysis, metal catalysis, and acid–base catalysis in the formation of peptide bonds via this route. Also considered in meticulous detail are various side reactions that can be encountered when certain functional groups (e.g., the guanidino group in arginine or the hydroxy group in serine) are not appropriately blocked during an active ester synthesis. Strategic factors that have to be evaluated when choosing between stepwise elongation and fragment condensation in the synthesis of a peptide of moderate chain length are also discussed.

Chapter 4 (by J. Meienhofer) deals with the azide method of peptide bond formation, which has gained much in popularity during recent years because of the low degree of racemization associated with it. Methods of preparation of azide intermediates, either by oxidation of the corresponding hydrazides or by use of special reagents such as diphenyl phosphorazidate, are critically reviewed, with particular attention to side reactions and overall synthetic strategy.

Chapter 5 (by D. H. Rich and J. Singh) concerns itself with the venerable carbodiimide technique, which is still a mainstay in peptide synthesis. Many interesting improvements in this method have been devised in recent years, especially in respect to trapping agents such as *p*-nitrophenol, *N*-hydroxysuccinimide, and 1-hydroxybenzotriazole, which are intended to prevent racemization and also decrease the likelihood of side reactions via the *O*-acylurea pathway. Once again, the relative merits and disadvantages of these "second generation" diimide-based techniques are reviewed in a careful, critical style.

Chapter 6 (by J. Meienhofer) presents the same kind of well-balanced assessment of the mixed anhydride technique, another cornerstone of this field. Despite the very widespread use of this procedure, less experienced peptide chemists sometimes fail to appreciate the importance of rigorously standardizing the experimental conditions under which the reaction is carried out. This chapter goes a long way toward rectifying this problem by offering useful laboratory tips that may actually interest not only hardcore "peptidologists" but also synthetic organic chemists at large (this Reviewer was not previously aware, for example, that

one can remove the 0.1% dimethylamine impurity in commercial dimethylformamide by distillation from ninhydrin). As in other chapters, considerable space is devoted to side reactions and the question of racemization at the α carbon. Also considered are certain reagents, such as EEDQ, whose ability to bring about coupling is assumed to involve the formation of a mixed anhydride intermediate.

Chapter 7 (by D. S. Kemp) addresses itself, finally, to the thorny issue of racemization during peptide synthesis, which can occur at any of several stages, including blocking, coupling, and deblocking. The problem becomes acute during the synthesis of large peptides, as one can readily appreciate by considering that if there is even a 0.2% contamination by the D enantiomer in each of 100 residues, 82% of the resultant peptide will consist of a single stereochemically pure product, but 16% will be made of a mixture of 100 diastereomeric peptides. If one is endeavoring to synthesize a biologically active peptide, this is obviously of more than passing theoretical interest, since one or more of the diastereomers might turn out to be an antagonist of the desired product or else might have potent agonist activity of its own. This chapter presents an extremely thorough analysis of the entire problem from a mechanistic point of view, identifies specific amino acids that are especially vulnerable to racemization, discusses the experimental techniques employed to detect and quantitate small amounts of racemized products, and points out possible ways to reduce the likelihood of racemization during a peptide synthesis.

All in all this is an impressive and authoritative book, obviously written by individuals who are highly expert in their field. The editorial work is superb, the text is remarkably error free, and there is ample use of structural formulas, diagrams, and tables. There is a comprehensive subject index, as well as an author index, and each chapter is introduced with an outline of the topics to be covered. In addition, there is an explanation of peptide nomenclature and a most welcome list of abbreviations at the beginning of the book. Although there is a certain amount of repetition stemming from the fact that some topics are discussed again and again in different chapters, the Reviewer did not find this objectionable and, in fact, found it helpful to have key points stressed several times. If subsequent volumes maintain the excellent standards established by this one, the series will surely become a classic.

Sidney Farber Cancer Center **Andre Rosowsky**