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Book Reviews

Biochemistry of Human Cancer. By Oscar Bodansky. Academic Press, New York, N.Y. 1975. xiv + 657 pp. 16 × 23 cm. $39.50.

From its earliest beginnings, biochemistry has had to deal with the cancer problem as a major issue. Almost a century ago the notion was put forward that there must be a fundamental metabolic difference between malignant and nonmalignant tissue, and the view persists even now that a cancer cure will be found by uncovering this difference and taking advantage of it to destroy tumor cells without harming "normal" ones. There are probably few medical chemists involved in the design and synthesis of antitumor agents today who do not accept this as a "central dogma" of their field. How fragile such an assumption may be is the theme of a scholarly and dispassionate new book by one of the world's authorities on human cancer biochemistry.

The first seven out of a total of 18 chapters in this excellent treatise are devoted to general aspects of the biochemistry of neoplastic disease. The rest focus on discrete tumor types and describe the many attempts that have been made over the years to relate tumors to specific metabolic or enzymic defects.

After a broad introductory chapter on the metabolism of proteins, lipids, and carbohydrates in cancerous vs. "normal" tissue, the reader is led through a meticulously arranged tour of the principal classes of enzymes—those concerned with glycolysis, those responsible for the cleavage of phosphate bonds, those involved in the breaking of amide and peptide bonds, and so on. This is followed by a chapter on immunoglobulins and the various immunoglobulinopathies associated with cancer (e.g., the existence of "Bence–Jones proteins" in the serum of patients with multiple myeloma). Two more chapters deal with the metabolism of tyrosine and tryptophan, a pair of amino acids for which cancer pathologists seem to have a special fascination. Tryptophan metabolites are implicated in the etiology of bladder cancer for example, whereas tyrosine and a plethora of catechols derived from tyrosine may be linked to neural crest tumors such as malignant melanoma and neuroblastoma.

The next 11 chapters, comprising approximately two-thirds of the total number of pages in the book, deal with specific tumor types and the biochemical correlates that pathologists sometimes rely upon in making a diagnosis.

In connection with tumors of the visceral organs, for example, may be cited the work of a number of investigators who believe that the serum of patients with colorectal carcinoma contains a unique glycoprotein, called carcinoembryonic antigen (CEA), which is absent in healthy subjects. Pancreatic tumors, also among the more common malignancies in the elderly, can be categorized with respect to their anatomical origin on the basis of certain biochemical criteria. Thus, one type of β-islet cell cancer, called insulinoma, appears to be correlated with hypoglycemia and elevated insulin production. Of course, hypoglycemia and a surplus of insulin do not in themselves signify that a tumor is present, and it is one of the virtues of this book that it stresses at every opportunity that such correlations mean very little in the absence of supporting histopathologic or clinical findings.

Leukemias and lymphomas, which are discussed together in a single chapter, occupy a special place among tumors because they often respond favorably to chemotherapy. Perhaps for this reason, more biochemical work seems to have been done with leukemic leukocytes than with other kinds of cancer cells. There is a detailed discussion of phosphatase and lysozyme levels in leukemic patients, but the most extensive coverage in this particular chapter is given to the labyrinthine complexities of purine and pyrimidine metabolism and nucleic acid biosynthesis in normal vs. leukemic cells. This discussion is particularly significant in relation to the widespread use of antimetabolites to arrest tumor growth.

Other chapters deal with bone tumors and associated disturbances in calcium and phosphorus metabolism, endocrine tumors and their hormonal correlates (e.g., the elevation of calcitonin in thryoid carcinoma), and tumors of the male and female reproductive organs. A very interesting chapter deals separately with a peculiar group of diseases called "ectopic syndromes". The word "ectopic" means "inappropriate" and refers to the fact that biochemical defects (especially those of a hormonal nature) are sometimes observed which are not those one would expect for a particular type of tumor. For instance, serum ACTH is sometimes elevated in patients whose pituitary gland shows no sign of malignancy but who turn out to have bronchial carcinoma. This would be referred to as an "ectopic

ACTH syndrome". Very little is known about the way ectopic tumors develop, and it has been suggested that these odd neoplasias may hold an important clue concerning the role of genetic control mechanisms in malignant disease.

Medicinal chemists will perhaps be a little disappointed by some of the implications of this thoughtful book. The point is forcefully made that, while biochemical "abnormalities" always signal an underlying state, it does not necessarily follow that malignancy is present or will ever appear. A case in point is serum alkaline phosphatase, which is said to be elevated in a large percentage of patients with hepatic metastases derived from primary tumors in other organs but may also be high in certain diseases totally unrelated to the liver, such as ulcerative colitis and congestive heart failure. Serum enzyme levels can be misleading because they are not necessarily a direct reflection of what is happening inside the tumor, and the problem is compounded by the fact that differences between normal and malignant tissue frequently involve isozyme patterns rather than total enzyme activity. Finally, of course, one cannot escape the vexing problem that even so-called "normal" tissues display widely divergent enzyme activities depending on the cytokinetic properties of the cells they contain. Thus, some compounds with no adverse effects on nonproliferative tissues may elicit catastrophic toxicity in rapidly dividing tissues such as the hematopietic system and intestinal epithelium.

While these reflections are obviously not meant to deter medicinal chemists from their efforts to cast "magic bullets", a careful reading of this book could turn out to be a beneficial, if sobering, experience.

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Peptide Synthesis. Second Edition. By Miklos Bodanszky, Yakir S. Klausner, and Miguel Ondetti. Wiley-Interscience, New York, N.Y. 1976. xiv + 208 pp. 15 × 23 cm. $19.50.

The first edition of *Peptide Synthesis* has been such an outstanding contribution that it would appear to be superfluous to review the second one. However, the completely rewritten text makes it, in my opinion, an even better book. The enormous expansion in the amount of information that has accumulated in the 10 years since the first edition was issued has been incorporated elegantly and seemingly effortlessly without space increase. (An apparent reduction in page numbers is mostly due to smaller type and omission of the author index.)

The disposition of chapters is conventional, i.e., Historical Aspects, Problems of Peptide Synthesis, Protecting Groups, Formation of the Peptide Bond, Racemization, Solid Phase Synthesis and other Facilitated Procedures, and Strategy and Tactics. The treatment is outstanding in its clarity, its exercise of authoritative evaluation and critique, and its concise and yet quite comprehensive format. The introduction includes a very useful listing of the proceedings of peptide symposia, of monographs, and of selected review articles. The chapter on protecting groups is excellent; that on coupling methods devotes, in my opinion, a bit too much space to outdated procedures somewhat at the expense of very recent ones. Both chapters contain several tables of protecting groups and reagents which provide information at a glance by being ingeniously simple and spacious. The literature references and the subject index are well proportioned.

All in all this is again an outstanding book, up to date, and an invaluable reference for anyone interested in peptide research.

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Synthetic Methods for Carbohydrates. Edited by Hassan S. El Khadem. American Chemical Society, Washington, D.C. 1976. ix + 285 pp. 14.5 × 22.7 cm. $19.50.

This text is part of the ACS Symposium Series, the result of a symposium on new synthetic methods in carbohydrate chemistry sponsored by the division of Carbohydrate Chemistry at the Centennial Meeting of the American Chemical Society, April 5–6, 1976. Fifteen papers cover several aspects of carbohydrate chemistry: applications of new blocking groups, the stereoselective synthesis of *O*-glycosides and *C*-nucleosides, the preparation and synthetic applications of unsaturated sugars, the synthesis of sugars containing atoms other than oxygen in the ring, and the synthesis of serologically active glycolipids, to mention a few. Most of the papers are reviews of the authors' work in the area, but a few are reports of research which include detailed experimental procedures. The contributors to this volume should be commended for providing coherent reviews of research in these important areas.

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Progress in Bioorganic Chemistry. Edited by E. T. Kaiser and F. J. Kézdy. Wiley-Interscience, New York, N.Y. 1976. 15.8 × 23.4 cm. vii + 289 pp. $24.95.

This volume is No. 4 of a series which has in a way inaugurated the new bandwagon of "bioorganic chemistry". It is the aim of this new subdiscipline to fill the steadily widening gap between chemistry and biochemistry in plain terms of molecular structure. The progress of bioorganic chemistry is located on a razor's edge. On the one hand, it is very difficult to judge in many cases whether a given piece of organic chemistry deserves the prefix "bio". To give an example, riboflavin is a light-sensitive vitamin but its light sensitivity is efficiently quenched upon binding to an apoprotein which might devaluate flavin photolysis from a "bioorganic" down to a "nutritional" event. On the other hand, it is certainly extremely difficult, if not impossible, to describe the primary event of photosynthesis in terms of "Kékule structure". While this latter event is, of course, a main phenomenon of biochemistry, it seems very questionable whether it deserves the name "organic chemistry". With other words, it is, on the one hand, questionable whether a given chemical finding in a biologically relevant system has any biological meaning, and it is questionable, on the other hand, whether a given and maybe physically well-defined biological phenomenon can ever be expressed in terms of organic chemistry. This does not absolve us from making progress in this questionable context provided we would judge ourselves in terms of chemical as well as biological relevance.

A further handicap of the new bandwagon becomes obvious from the fact that there is no safe definition of organic chemistry apart from the idea that "organic" represents whatever is safe in chemistry. But since the human race is bound to make progress from the safe to the unsafe areas, the present volume penetrates from the "organic" into what must be addressed at least as "metalloorganic" if not inorganic areas. Hence it turns out that, since the most interesting ones among the centers of biological action are inorganic by chemical nature, the drivers of the new bandwagon should be honest enough to admit that, in view of the inherent difficulties, to distinguish life from dead matter one should at least drop the useless distinction of organic and inorganic matter in the area of "bio(in)organic" chemistry.

The present volume consists of four contributions, the second of which is touching inorganic domains: Models and Flavin Catalysis; Chemical Properties of the Phototrap in Bacterial Photosynthesis; A Basis for Biological Phosphate and Sulfate Transfers—Transition State Properties of Transfer Substrates; and Hydrolysis of Cyclic Esters.

The first contribution has been written by a notorious chemist and suffers from the first handicap mentioned above. Flavin is meant by nature to be an ambiguous catalyst, apt to deal with all kinds of redox equivalents, i.e., single electrons, hydride, and anionic group transfers with similar ease but with very different mechanisms. Hence, if one is happy enough to find a safe piece of flavin chemistry, one is easily tempted to take it for a model of any desired flavin-dependent biological event. Thorough cooperation of biochemists and chemists is required to ride on the edge of the bioorganic razor, while in the present flavin chapter the prefix "bio" remains questionable in large parts.

The second chapter suffers from the second handicap as mentioned above in spite of the obvious competence and excellence of the author which evokes the conviction that nothing better

could be done at all in the given context. This chapter remains the most exciting one in the present volume.

The two final chapters are minor ones as to the quantity of data reviewed. They cover well-defined and limited areas of transition-state chemistry and their clean and clear presentation might only suffer from the fact that no colored matter is involved in these acid–base catalyzed reactions in contrast to the full blossom of oxidoreductive centers encountered in the first two chapters.

This volume represents an excellent choice of interesting topics and claims for the continuation of this progress series, whose title could be improved by adding a hitherto hidden truth, yielding "Progress in Bio(in)organic Chemistry".

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Kinetics of Chemical and Enzyme-Catalyzed Reactions. By Dennis Piszkiewicz. Oxford University Press, London. 1977. 14.5 × 21.5 cm. ix + 235 pp. $12.50.

This unusual book joins several recent texts on the kinetics of enzymatic systems. What makes it somewhat out of the ordinary is the extensive, practically oriented use of graphical Lineweaver–Burk plots to distinguish between various possible enzymatic reaction mechanisms. Thus, the treatment of the various rate expressions expected for different mechanisms is built up from the simplest Michaelis–Menten mechanism to a useful range of different multisubstrate transformations. Dr. Piszkiewicz strikes a nice balance between rigorous mathematical derivation and the utility of kinetic relationships throughout the book, with well-chosen practice problems collected at the end of each chapter together with useful reading lists of original papers and the titles of other texts on the same topic. A careful solution of each text problem is given in an appendix.

Aside from the practical value of the author's approach, the book is clearly written in a style which should appeal to students. In fact, the author's sentence structure reminds this reviewer of that of Dr. Peter Sykes in his highly successful undergraduate book on organic reaction mechanisms. However, I do wish that the publisher had found a way of highlighting important relationships and terms in the text, rather than relying solely on the glossary at the end of the book. This reviewer found keywords hard to find on any given page and that obvious attention to keeping the book small has had the tendency of making it quite hard to read. If, as I suspect, this book is published in a second edition, careful attention to format would be appreciated. A second edition might also try to apply more of the thermodynamic concepts (developed in Chapter 3) in the later chapters of the book.

The text carries a good index and also includes a useful appendix of "Constants and Common Symbols". Among the very few errors noted are the use of the symbol K_a as an acid dissociation constant, e.g., on pp 6 and 54, and as an acid association constant on p 53. [In the glossary, K_a is defined as a dissociation constant (p 198)]. Also, confusion may arise between time and temperature in eq 21, 38, and 39 of Chapter 3, although this error is obviously typographical.

This is a good book. I enjoyed reading it and I think that students will find it both readable and useful.

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Inorganic Aspects of Biological and Organic Chemistry. By Robert P. Hanzlik. Academic Press, New York, N.Y. 1976. xvii + 402 pp. 15 × 22.5 cm. $37.00.

A number of books have appeared recently in the emerging discipline of bioinorganic chemistry, which comprises elements of inorganic chemistry and biochemistry, as well as medicinal chemistry. Dr. Hanzlik has modified this direction somewhat by including some of the aspects of organic chemistry which are affected by metal ions. This book is therefore an attempt to provide a common ground to all three areas, inorganic, organic, and biological chemistry. The result is a very useful text presenting a contemporary discussion of the interrelations of these areas of chemical knowledge.

Following an introductory chapter concerned with the role of metals in biological and organic chemistry, the next two chapters are devoted to a discussion of Group 1a and 2a metals and their complexes. The following section is concerned with brief but clear discussions of atomic structure and bonding in metal complexes. Ligand-exchange reactions and factors in complex stability, redox potentials and processes, and synthetic reactions involving metal ion chelation are taken up, and the conventional discussion of these topics is well supplied with examples from organic and biological chemistry.

A chapter of much interest to medicinal chemists is concerned with catalysis by metal ions, metal complexes, and metalloenzymes. Examples from enzyme chemistry include discussions of the mechanisms of aconitase, carboxypeptidase, and carbonic anhydrase action. Metal–oxygen and metal–nitrogen complexes are discussed; this of course includes treatment of hemoglobin and other porphyrin complexes. Both chemical and biological nitrogen fixation are also briefly described.

The final two chapters, comprising about one-fourth of the book, are devoted to organometallic complexes and their reaction mechanisms and the reaction of ligands in organometallic complexes. These chapters will probably be of greatest interest to organic chemists, involving such subjects as oxidative coupling–reductive decoupling, electrophilic and nucleophilic attack on coordinated ligands, carbon–carbon coupling reactions, and addition reactions of olefins and acetylenes. The discussion of these topics is thoroughly comparable with those of recent organic texts on these topics.

Metal ions play a vital role in both organic and biological chemistry, and the principles underlying the processes in which they are involved have been well presented. The book is well organized and well written and is to be recommended to those who desire a better acquaintance with the role of metal ions in chemical and biological processes. The author is commended for a skillful blending of the disciplines.

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Textbook of Organic Medicinal and Pharmaceutical Chemistry. Edited by Charles O. Wilson, Ole Gisvold, and Robert F. Doerge. J. B. Lippincott, Philadelphia, Pa. 1977. xiv + 1085 pp. 18 × 26 cm. $33.00.

The appearance of a new edition of this standard textbook is always noteworthy. The new edition presents few surprises or innovations; the roster of authors of individual chapters is almost the same as in the previous edition, with a few added names. The somewhat encyclopedic, "monographic" format for discussions of the individual drugs is unchanged from previous editions. While some change from this traditional format seems desirable, this reviewer recognizes the difficulties attendant in devising alternatives. The book is based upon USP XIX and NF XIV and is stated to cover all products described in these two compendia.

Early chapters in the book are on general, theoretical aspects of medicinal chemistry: physicochemical properties, drug–receptor interactions, absorption phenomena, and metabolic reactions based on functional groups, inter alia. These discussions seem well-balanced, informative, and of an appropriate level of sophistication for an undergraduate text. It is a personal prejudice of this reviewer that editors/authors of some medicinal chemistry texts err in including far too much material on linear-free-energy techniques and molecular orbital theory of drug design, which tends to overwhelm the student and leads the reader to conclude that these techniques are widely and routinely employed in day-to-day medicinal chemical research.

The textual material on medicinal agents is categorized in general according to pharmacologic action, although one notes chapters titled "Phenols and Their Derivatives" and "Carbohydrates", which seem somewhat anachronistic.

One of the dilemmas facing authors of undergraduate medicinal chemistry texts is whether to produce a book of sufficient brevity

as to be readable from cover to cover by the student or whether to be comprehensive in scope and to attempt to present more facts, concepts, and theories than the student could reasonably be expected to grasp and master. In the view of this reviewer, a medicinal chemistry "textbook" serves the student best as a well-thumbed reference source-book, and adjunct to formal lecture material, rather than as a book of facts to be read, studied, and mastered in toto. This book fits the description of a "well-thumbed reference". Coverage of therapeutic agents seems quite complete and comprehensive and overall the narrative is maintained at a level that is useful and comprehensible to undergraduates. Narrative material in the preponderance of chapters utilizes modern organic chemical and pharmacologic concepts as the basis for discussion of drugs. Material on stereochemistry, structure–activity concepts, and drug–receptor interactions has been expanded, apparently at the expense of descriptions of synthetic organic aspects, although many synthetic procedures are still presented. This reflects current trends in teaching of medicinal chemistry to undergraduate pharmacy students.

Editing and printing of the book are good; few printing errors were noted. Overall, the book, like its predecessor editions, is a success and it is recommended for instructional use and as a first-level reference for the graduate student and the practicing medicinal chemist. The relatively high price of the book may be a deterrent to its extensive use in undergraduate courses.

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Encyclopaedia of Antibiotics. By John S. Glasby. Wiley, New York, N.Y. 1977. 372 pp. 18.5 × 26 cm. $42.50.

This handy volume is an alphabetical listing of some 1500 substances described as having antibiotic activity. By purposely choosing a broad definition of the term, the author has included many less-familiar compounds "derived from or produced by a living organism (which are) capable of inhibiting life processes of microorganisms in small concentration." Thus, many of the new mold metabolites with carcinostatic activity are described. For each substance source, chemical and physical properties, structure when known, methods of preparation, antibiotic spectrum, and key literature references are given. The book will serve as a convenient handbook not only for the research worker in the field but also for the teacher, the pharmacist, and allied health personnel to whom questions concerning the existence of some of the newer antibiotics currently in experimental use may be directed.

Staff Review

Birth Defects and Drugs in Pregnancy. By O. P. Heinonen, D. Slone, and S. Shapiro. Publishing Sciences Group, Littleton, Mass. 1977. 18 × 26 cm. 516 pp. $75.00.

The purpose of this book is to present data on drugs used by 50 282 pregnant women in relation to the birth defects identified in the children. The data are the analytical results of an 8-year study by a subgroup of the Collaborative Perinatal Project of the National Institute of Neurological and Communicative Disorders and Stroke. The book consists principally of 629 tables relating drug, malformation, distribution, relative risk factors, and other pertinent variables to each other. In an effort to avoid spurious positive associations, much of the work presented relies on multivariate statistical methods. The book adds substantially, albeit only in a quantitative fashion, to what is known about the general epidemiology of birth defects. The authors suggest that the most important conclusion to emerge with regard to the general epidemiology of malformations is that the etiology of birth defects appears to be multifactorial and that it is the exception, rather than the rule, for any birth defect to have a single cause. Material is presented that should be of interest to scientists concerned with all aspects of teratology, especially as a data base for hypothesis generation or testing. However, the cost of the book and its lack of any specific chemical perspectives will probably diminish the interest of medicinal chemists concerned about birth defects.

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Reagents for Organic Synthesis. Volume 5. By Mary Fieser and Louis F. Fieser. Wiley-Interscience, New York, N.Y. 1975. vii + 864 pp. 15.5 × 23.5 cm. $28.95.

This fifth volume in the series covers the synthetic organic literature from 1972 to August 1974. The format used previously is repeated with the reagents indexed not only as to subject but also as to reactions and compound type. Volume references are also provided for those reagents appearing in Volumes 1–4. About 400 new reagents are discussed, indicating the rapid rate at which new reagents are being introduced. The time period surveyed witnessed the design of new and interesting selenium and organotin reagents while phase-transfer catalysis and crown ethers continued to be extremely useful in organic synthesis. The series continues to be a most valuable reference source for synthetic organic chemists.

Staff Review

Drug Therapy Reviews. Volume I. Edited by Russell R. Miller and David J. Greenblatt. Masson Publishing, New York, N.Y. 1975. 260 pp. 16 × 23.5 cm. $26.00.

This is the first volume of what will presumably be an open-ended series of pharmacologic reviews on selected topics. Articles in this issue have previously appeared in the *Journal of the Maine Medical Association*. In fact, the New England origins of the editors and most contributors are frequently evidenced in the text.

Twenty-one topics are covered in this volume. They range from antacid therapy to the pharmacotherapy of cardiopulmonary arrest and tardive dyskinesia. The chapters were originally prepared to provide current reviews of drug therapy for hospital staff as guidelines for prescribing. There is, therefore, a tendency for the topics to be oriented toward medical practice in the hospital setting (e.g., Dosage and Choice of Parenteral Strong Analgesics; Guidelines for Total Parenteral Nutrition).

One weakness is that all topics are covered in approximately the same number of pages despite considerable differences in scope. This is presumably due to their having been tailored for use in a periodical.

Aside from the variability in depth, the reviews are uniformly concise and readable. Their strong suit is the attention paid to appropriate practicalities such as pharmacokinetic data, proprietary and generic names, and cost of therapy. In an attempt to provide prescribing guidance, a "drug of choice" approach is widely used.

The latter point raises the question: Who will find this series to be of unique value in the presence of other reviews of pharmacology? There are almost no drug structures to lure the chemist. The level of presentation in most cases is too superficial to be an important source for specialized physicians. It would seem most appropriate as a review for pharmacologists, staff physicians, and clinical pharmacists which was, after all, the original intention of the papers. Therefore, it could be a useful addition to a medical library, but individual ownership would probably not be worthwhile.

In summary, the series "Drug Therapy Reviews" should prove to be a concise collection of pharmacologic evaluations with an emphasis on practical prescribing rather than serving as a compendium.

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Testing and Screening for Drugs of Abuse. By G. G. DeAngelis. Marcel Dekker, New York, N.Y. 1976. 15.5 × 23 cm. viii + 140 pp. $17.50.

This book was written specifically for directors of drug maintenance programs. The author points out the many problems with urine analysis as an index of ilicit drug usage. The fact that two portions of a urine sample can be sent to two different analytical laboratories and the results be contradictory supports his doubts of the validity of these tests. It is pointed out in the book that in many cases the urine tests are correct only approximately 50% of the time. The author indicates that there are many schemes used by addicts to falsify their urine specimen. These are often hard to detect without careful supervision of the voiding process by technicians. He suggests that this scrutiny often is, or at least interpreted to be, an unwarranted violation of the dignity and personal rights of the individual. The concern of the author for the patients' rights is presented many times throughout the book.

There are a number of mistakes in this book, including misspellings and at least one misclassification of a drug. For instance, the author incorrectly classified propoxyphene as a tranquilizer rather than a moderate analgesic.

The techniques used to detect abused drugs in urine are presented in a clear and simplified manner so that those with limited experience in chemistry can obtain an appreciation for the procedures. References are given for those who would like more detail about these tests. This book is not intended to be a chemistry book and, therefore, is not appropriate as a text in a chemistry course. It also is not recommended for faculty, physicians, or graduate students in the medical sciences. The technical level of this book is such that it is most useful to nonprofessional workers in drug maintenance programs and the enlightened lay public.

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AMA Drug Evaluations. Third Edition. Edited by AMA Department of Drugs in Cooperation with the Society of Clinical Pharmacology and Therapeutics. Publishing Sciences Group, Littleton, Mass. 1977. lxi + 1326 pp. 19 × 26 cm. $29.50.

As with the previous editions of "AMA Drug Evaluations", this third edition has been organized into chapters and sections that are based, insofar as possible, on therapeutic classification. Each chapter discusses the therapeutic category, as well as evaluative monographs for individual drugs in this class. Drugs included for individual evaluations are all the therapeutic agents in the official compendia (U.S.P. and N.F.), the drugs most commonly prescribed in the United States and other drugs that are judged to be of particular importance to complete a discussion of a therapeutic category. Other nationally distributed preparations that are not individually evaluated are listed and indexed to give information about their therapeutic category and availability.

This book continues to provide the reader with evaluative or interpretive information, particularly on controversial matters. Statements are based on the convergent trend of information available from scientific literature, unpublished data, the advice of consultants, and the opinion of reviewers from the American Society for Clinical Pharmacology and Therapeutics.

This series continues to be a valuable source of current information on therapeutic agents available in the U.S.

Staff Review

The Fate of Drugs in the Organism. A Bibliographic Survey. Volume 4. By J. Hirtz. Marcel Dekker, New York, N.Y. 1977. 16 × 23.5 cm. xvii + 612 pp. $75.00.

This book is the fourth volume containing a survey of the recent literature in drug metabolism. This survey was compiled by the French Society for Pharmaceutical Science and Technology under the Chairmanship of J. Hirtz. The objective of this series of volumes is to provide a systemic compilation of references for rapid access to the literature.

The book is arranged into three sections. Part One contains 3000 references containing title, author(s), and journal references. These references are listed by number in no particular order. The second part contains a tabulation of drugs listed alphabetically by their common names (WHO) or by their chemical names according to the IUPAC regulations. For each drug there is a number for the reference(s) (Part One), the year of publication, and a series of 17 key words and an indication that the reference contains data corresponding to this particular key word. Part Three contains a tabulation of each drug by its empirical formula.

At present (1977) approximately 70 journals are surveyed for pertinent data relating to the metabolic fate of drugs. However, an exhaustive survey of the literature was not intended and, therefore, this volume may have omissions of some useful references. The most recent references in this volume are to 1974 which may be due to the difficulty in rapid publication of this book.

In summary, this series may be useful for a very rapid acquaintance with some of the more pertinent literature concerning the metabolic fate of many of the more commonly used drugs.

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First and Second Messengers—New Vistas. Advances in Biochemical Psychopharmacology. Volume 15. Edited by E. Costa, E. Giacobini, and R. Paoletti. Raven Press, New York, N.Y. 1976. 16 × 24 cm. xv + 498 pp. $30.00.

This volume is divided into two major sections, with the first indicating those "new" first messenger substances utilized for intercellular communication and the second detailing how such messages may be transduced into cellular events.

The new first messengers are grouped under biogenic amines (piperidine, tyramine, phenylethylamine, indoleamines, octopamine, histamine, 5-methoxytryptamine), amino acids (taurine, proline, glutamate, aspartate) and peptides, nucleotides, and proteins (substance P, purine nucleotides, and others). The inclusion in this section of nerve growth factor is suggested to be tentative and provisional and the addition of a "hormonal section" reporting the effect of a single hormone glucocorticoid on a single serotonergic system seems incongruous. With these exceptions, and a difference in coverage with the section on piperidine being as long as that covered by all the other biogenic amines, the accounts are competent and interesting.

In the second section the concept of second chemical messengers and the role of cyclic nucleotides is well defined. While studies relating to dopamine-sensitive cAMP are included and expected, considerable data relating drug action to cGMP are present. Finally, the last five chapters are pertinent to the effect of second messengers on the metabolic code.

The introductory chapter indicates that this is the first attempt to present a systematic body of evidence that supports a pluralistic system of neurotransmission. This has been achieved and the present volume is of importance to all researchers in the area and is a worthy addition to the series.

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Essays in Neurochemistry and Neuropharmacology. Volume 1. Edited by M. B. H. Youdim, D. F. Sharman, W. Lovenberg, and J. R. Lagnado. Wiley, London. 1977. 15.5 × 23.5 cm. xi + 195 pp. $21.50.

The goal of this important new series of "Essays in Neurochemistry and Neuropharmacology" is to provide readable, yet accurate, essays which are at the same time both critical and speculative.

The first volume does well in attaining these goals. Although the topics covered are rather diverse, all these contributions are primarily within the world of transmitter neurochemistry; less emphasis on neuropharmacology occurs in this first volume.

The first of the six topics is a masterful review by J. M. Saavedra on methylating enzymes in the brain. Considerably wide but succinct detail is provided on the localization, specificity, control, inhibition, and biological functions and purposes of these enzymes. A good critical review and analysis is given by G. G. S. Collins on the role of taurine in the brain. He rigorously applies the various criteria needed for establishing an amino acid as a neurotransmitter and then concludes that taurine has not yet quite achieved the status as a legitimate neurotransmitter.

The third contribution by H. Thoenen and U. Otten deals with nerve cell regulation and synthesis of neurotransmitter enzymes in a chapter entitled Molecular Events in Trans-synaptic Regulation of the Synthesis of Macromolecules. They have taken on a broad, challenging, and complex subject and helpfully supply the graduate student or other advanced reader a list of key references in the various subsections of enzyme induction, role of cAMP, hormonal modulation, and trans-synaptic events, as well as selective induction of specific enzymes such as tyrosine hydroxylase and DBH (dopamine β-hydroxylase). Because of the intricate nature of this subject, a diagram or two would have been helpful.

Brain aldehyde metabolism is covered by K. F. Tipton, M. D. Houslay, and A. J. Turner. This chapter is of interest to both neurochemists and neuropharmacologists, particularly those in the field of drug addiction, since a good summary is given of the alkaloid biosynthesis pathway from dopamine. Also reviewed here are the actions of ethanol, reserpine, and barbiturates on aldehyde metabolism.

The fascinating and furiously growing subject of hypothalamic peptides is presented by A. J. Kastin, J. H. Miller, C. A. Sandman, A. V. Schally, and N. P. Plotnikoff. The approach and style of this chapter is commendable because of its consideration of both scientific problems and clinical applications; it also has refreshing paragraph headings which are in the form of simple questions. This is a very authoritative account of such alphabet-soup peptides as MSH, MSH/$ACTH_{4-10}$, MIF-I, FSH-RH, LH-RH, TRH, and GH-RH, including a review of both medical and memory-important aspects of some of these peptides.

Finally, E. D. Bird and L. L. Iversen describe the neurochemical findings in Huntingdon's chorea in a very up-to-date and crisp fashion. This neurochemical summary of Huntingdon's chorea is particularly timely for those ever-increasing number of neurochemists who are suddenly discovering that it is now possible to apply much "rat neurochemistry" toward analysis of human brain tissues.

Altogether this book provides an important addition to any neurochemistry laboratory. Future essays in this series might be advised to contain a few more diagrams which permit more clarity as well as more speculation. In these "xeroxable" days it might be advisable to insert the book's title, editors, and publishing details on the first page of each chapter, as is now becoming the custom in books emanating from symposia. While there are occasional amusing mistakes like in nitro (p 16), the book is to be applauded for its nonglare paper. The price is right at $21.50.

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Microbial Transformations of Non-Steroid Cyclic Compounds. By Klaus Kieslich. Wiley, New York, N.Y., and Georg Thieme Verlag, Stuttgart. 1976. xxii + 1262 pp. 18 × 26.5 cm. $90.00.

Dr. Kieslich's objective in preparing this volume is to summarize the information available on the use of microorganisms to carry out critical steps in the preparation of nonsteroid substances. The data on these reactions are widely dispersed and we are indebted to Dr. Kieslich for bringing together information on transformations of straight-chain and cyclic nonsteroid structures. In this sense this volume is a fitting companion to the "Microbial Transformations of Steroids" by Charney and Herzog (which appeared in 1967 and which will have a supplement published in 1978).

This volume is divided into six sections: (1) an introduction which includes information on methods used to study microbial transformations of the candidate compounds; (2) microbial transformations of individual substrate groups with special attention to Alicyclic Compounds, Terpenoids, Aromatic Compounds, O-Heterocyclic Compounds, N-Heterocyclic Compounds, Alkaloids, Di- and Triheterocyclics, S,O,S- and S,N-Heterocycles, and Carbohydrates; (3) Classification of the Transformations According to Reach Type with consideration of Oxidative Reactions, Reductive Reactions, Hydrolytic Reactions, Dehydration and Condensation Reactions, Degradation Reactions, Formation of Carbon–Carbon or Heteroatom Bonds, and Isomerization Reactions; (4) List of Microorganisms Used; (5) References; and (6) Subject Index. 800 pages are devoted to the Classification section with structures of the candidate compound, the microorganisms used, the products, the product yield, and the method of isolation all given in shortened but very useful form. Most of the 1932 references relate to this Classification section, and it and the Subject Index are among the best prepared the reviewer has had the opportunity to use. While the index of microorganisms is useful, taxonomy of microorganisms is a somewhat confused milieu for most chemists and the inevitable contradictions and duplications may be somewhat confusing. If the organism does the job we should not be too concerned about its taxonomy since (as the immortal bard is quoted to have written) "A rose by any other name smells just as sweet".

Dr. Kieslich has prepared this volume with the organic chemist in mind, and most of the arrangement of subject matter follows the groupings that discipline might favor. The text is remarkably free of errors, and the structural drawings are very well done, considering the space available. This is a reference work that will be useful for many years and this will justify the $90 cost for the volume. It should be a very useful volume by those organic chemists who after reading Jones et al., "Application of Biochemical Systems to Organic Chemistry", want quick reference to what may have been done and some advice on how to begin the experimental program. The volume should be included in all chemistry libraries as well as those of organic and biochemists who are trying to keep up to date for their particular projects.

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Handbook of Intermediary Metabolism of Aromatic Compounds. By B. L. Goodwin. Halsted Press, New York, N.Y. 1976. 19 × 25 cm. ix + 790 pp. $75.00.

This handbook represents a monumental task and as such is difficult to review in great detail. The author should be highly complimented for providing this encyclopedic treatise. Such an undertaking carries along the risk of potential omissions and errors. However, in reviewing this book, though by necessity, by "spot-checking", I did not detect errors of significance.

It is unfortunate that the information has been abstracted primarily from literature of up to 1971 and included only selected journals up to 1973. It is understandable, however, that a compilation of information of such dimensions necessitates deadlines beyond which further literature coverage cannot be conducted. The author states that: "It is *anticipated* that the material published will be included in supplements to this volume". It is hoped that these supplements materialize, since without these the value of the handbook will become limited within a brief period of time. In regard to supplements, it occurs to this reviewer that the handbook could have been presented in a loose-leaf format, so as to facilitate addition and deletion of material.

The treatise is presented in two parts. Part I (up to p 137), "Reactions and Enzymes", covers a variety of types of reactions and the enzymes catalyzing these reactions. Usually description of the enzymes involved in the various reactions is well documented and the coverage adequate. Occasionally, the description of a given enzyme is somewhat sketchy as exemplified by the

narrow coverage of microsomal hydroxylation of aromatic compounds (pp 26–29).

Part II, which covers reactions of individual compounds, represents the major portion of the book. The presentation in this section is clear, logical, and comprehensive. As a rule the description of reactions of a given compound involves (a) the *parent compound* from which the compound in question is derived, (b) the *transformation products* (metabolites), and (c) the *species* in which a given transformation product was demonstrated. For these reactions the references are documented so that the reader can judge for himself/herself whether the evidence for formation of a given product is satisfactory.

An index providing cross references of metabolites to their respective parent compounds would have been helpful to the potential users of this handbook. Similarly, cross referencing of American vs. British spelling of compounds (e.g., estradiol vs. oestradiol) would have facilitated the use of this book by American readers.

In its present form the handbook will probably be purchased primarily by scientific libraries and only to a limited extent for personal ownership. This conclusion is based on the relatively high cost of the book ($75.00) and on the fact that in the present age of specialization most scientists are interested only in limited areas and thus would not benefit significantly from information outside their narrow field of specialty.

In conclusion, the book is an important addition as a source for rapid information on a broad subject. Despite certain minor shortcomings, the book should receive frequent usage and library acquisitions should be welcomed.

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Methods in Receptor Research. Part II. Edited by M. Blecher. Marcel Dekker, New York, N.Y. 1976. xiv + 380 pp. 23.5 × 16 cm. $36.50.

"Methods in Receptor Research" (MRR) is a two-book series on the identification, isolation, and purification of cell membrane receptors. The material, which could easily have been included in a single volume, is divided equally and alphabetically between Parts I and II, Part I containing 11 chapters in 383 pages and covering the receptors for "acetylcholine through insulin" and Part II containing 11 chapters covering the receptors for "insulin through vasopressin". Part I was reviewed by this reviewer [*J. Med. Chem.*, **20**, 859 (1977)]; comments about the overall organization of MRR included in that review will not be repeated here.

Part II of MRR extends the list of receptors (and investigators who study them) to include insulin (Freychet; Hollenberg and Cuatrecasas), lectin (Jansons and Burger), opiate (Simon), oxytocin and vasopressin (Soloff; Jard, Bockaert, Roy, and Rajerison), parathyroid hormone (Zull and Malbon), prolactin (Shiu and Friesen), prostaglandin (Humes, Oien, and Kuehl; Rao), and thyrotropin (Lissitzky, Fayet, and Verrier).

As in Part I, the chapters of Part II are concerned with methods of identification (by means binding specificity) of receptors in cell-free preparations and with the isolation and purification of receptors. Thus there are sections of each chapter devoted to methods of preparing radioactively labeled ligands, cell membranes, measurement of the receptor specific binding of labeled ligands to cell membranes, and the solubilization of receptors from their membrane milieu and of the separation of receptor molecules from other cell membrane components by physical–biochemical techniques.

Although the chapters of Part II repeat, with minor variations, many methods which are already presented repetitiously in Part I, there are methods described in Part II which do not appear in Part I.

Among the methods introduced in Part II of MRR, several authors have successfully prepared suspensions of intact cells by treating whole tissues with enzymes, e.g., hyaluronidase, trypsin, and collagenase, which break intercellular bonds, the principal advantage being that suspensions of single cells, unlike homogenates, are still intact, physiologically, and they do not have the oxygen, metabolite, and drug diffusion problems that attend the use of organ preparations.

Part II offers some additional methods of preparing radioactively labeled ligands. Parathyroid hormone (PTH) is inactivated by conventional iodination methods (chloramine T, lactoperoxidase). As alternatives, Zull and Malbon were able to prepare [^{125}I]-PTH by the ^{125}I iodoelectrolytic technique and PTH acetimidate by reaction of [^{3}H]acetimidate with the amino terminal of PTH. Noting that ^{125}I iodination also reduced the biological activities of oxytocin and vasopressin, Jard et al. prepared tritiated isomers of these hormones having high specific activity (20–40 Ci/mmol) by first iodinating their tyrosine moieties and then displacing the iodines, in a substitution reaction, with tritium.

Receptors are identified in broken cell preparations on the basis of their unique and high affinity for receptor specific ligands, the subject specificity being partially demonstrated by the fact that pharmacological and binding studies yield identical ligand–receptor affinity constants. That such identification criteria appear to be met frequently is truly amazing in view of the fact that many receptor systems are not simple. For example, Freychet (Insulin) and Jard et al. (oxytocin and vasopressin) report finding two ligand specific binding sites and also that receptor mediated physiological events are fully activated when only one of these binding sites is occupied, results which make it impossible for these receptors to conform to accepted criteria for receptor identification.

Several authors report the use of catabolic enzymes, e.g., trypsin, RNase, galactosidase, neuraminadase, the phospholipases, etc., to modify the receptor in situ with the view of establishing the molecular character of the receptor. It would not seem wise to take the results of these studies seriously as is well known—partially as the result of evidence presented in other chapters of MRR—that alteration of the receptor's membrane milieu, e.g., by detergents, local anesthetics, etc., alters both the pharmacological activity and the binding specificity of the receptor. Thus, if phospholipase C abolishes a receptor mediated response, one cannot tell whether it did so because it altered the receptor or the membrane phospholipids which provide the matrix in which the receptor sits.

Finally, Part II of MRR extends the list of receptor molecules which have been isolated and partially purified. Among these are the insulin (Hollenberg and Cuactrecasas), lectin (Jansons and Burger), prolactin (Shiu and Friesen), and vasopressin (Jard et al.) receptors. Molecule isolation and purification is a difficult milestone to reach on the road to understanding the structure and function of a membrane receptor and those who get there are to be commended.

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Clinical Chemistry. Edited by D. T. Forman and R. W. Mattoon. ACS Symposium Series No. 35. American Chemical Society, Washington, D.C. 1976. ix + 293 pp. 14 × 22 cm. $19.75.

This volume consists of ten articles which were presented at the eighth annual series of lectures for continuing education sponsored by the Chicago sections of the American Chemical Society and the American Association for Clinical Chemistry. The editors indicate that two chapters of the book were not originally part of the lecture series but were added because of the current interest in the areas of protein binding assays and drug interference in clinical laboratory testing.

Chapter 1 provides a detailed discussion of the chemical structure, identification, and characterization of hemoglobin and its variants. The chapter is well referenced and contains a number of figures which illustrate the techniques employed in the analysis of hemoglobin variants.

In Chapter 2 the difficulties associated with the analyses for measuring serum levels of the calciotropic hormones, calcitonin, parathyroid hormone, vitamin D, and its metabolites are discussed.

In the brief space of 12 pages the fundamentals of competitive protein binding are presented in Chapter 3. The authors give the reader an overview of basic definitions, principles, separation techniques, data handling, equipment, assay set up, isotope safety, disposal of radioactive waste, and radioisotopic licensing.

Chapter 4, entitled "Prenatal Detection of Genetic Diseases", is divided into two parts. The first deals with the general background and theoretical introduction to the topic. In the second, the experiences of the author and other investigators with various diagnostic techniques are described. The frequency and types of genetic diseases are presented as well as approaches to prenatal diagnosis. The utilization and limitations of each technqiue are discussed in detail. Approaches to prenatal detection of genetic diseases are presented, such as direct and indirect fetal visualization, sampling of fetal blood and tissue, amniocentesis and examination of amniotic fluid cells, cytogenetic analysis and sex determination, biochemical analysis, and α-fetoprotein determinations.

The largest chapter in the book, Chapter 5 (58 pages), deals with the need for the establishment of laboratories dedicated to the performance of special techniques on specimens from the newborn. The neonate provides a special challenge to the clinical chemist in terms of adequate and proper sampling. The author discusses in detail the problems associated with specimen collection and handling. The necessity for microsampling and microtechniques is emphasized and specific examples are given of the equipment employed. Among the analyses discussed are those micro procedures for glucose, urea nitrogen, sodium, potassium, chloride, carbon dioxide, calcium, magnesium, bilirubin, protein, blood gases, blood pH, amino acids, and lipid screening.

In Chapter 6, a number of tables and nomographs are presented for the differential diagnosis between acid–base imbalance and types of hypoxia. Extensive tables provide the means for the classification of hypoxia and conditions associated with blood gas imbalance.

The determination of enzyme activity in the clinical laboratory is a well-established method for the detection of pathological conditions and for monitoring therapy. In Chapter 7, entitled "Analytical Aspects of Clinical Enzymology", a broad introduction to this topic is presented in the space of 50 pages. The authors discuss basic clinical enzymology including the nature of enzymes, instrumentation, proper specimen handling, and temperature control. The advantages of kinetic methods are considered as are the analytical criteria for enzyme procedures. Recommended methods for a number of clinically significant enzymes are presented in addition to a table of thermal stabilities of enzymes which should be of practical importance to the clinical chemist.

In Chapter 8, the theory and application of high-performance liquid chromatography to the clinical laboratory are presented. Included in the chapter are discussions of column selection and the function of various instrument components.

Increased interest in the analysis of trace metals in body fluids has led to the development of increased sensitivity, accuracy, and precision in atomic absorption spectrometry. The advantages and problems associated with electrothermal atomic absorption spectrometry are presented in Chapter 9. Each section of the chapter is well organized and documented. The influences on precision by electrothermal atomizers, inert atmospheres, graphite tubes, temperature calibration and regulation, sampling and contamination, standardization, and computation are discussed in detail. A table of trace metals complete with references to biological application is found in the chapter.

The fact that drugs interfere with clinical laboratory analyses has been well established. The authors of Chapter 10 provide references to publications containing extensive listings of these effects and discuss a computerized approach to assisting the physician in his interpretation of laboratory data where drug interference is possible. They also present tables of other specific agents and their influence on laboratory procedures. In addition, mechanisms of interferences are provided which include physical effects on spectrophotometric analyses, chemical effects which alter test results directly, or pharmacological effects which cause an indirect change in test results by altering normal biochemical pathways. Also included is a discussion of the potentiation or antagonistic action of one drug on another culminating in an anomalous test value.

The reviewer recommends the book for the libraries of both the clinical chemist and those chemists not directly involved in clinical analyses. The practicing clinical laboratorian will find some chapters too superficial; however, other chapters do provide valuable theoretical and practical information. To other chemists, the chapters of this collection offer an exposure to some of the types of procedures and problems associated with their use in the clinical laboratory. The book illustrates the growing sophistication of the clinical laboratory and the need for research to provide highly reliable instrumentation and testing procedures to meet the increasing demand of excellence in the clinical field.

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Polyene Antibiotics, Present and Future. By Igor M. Tereshin. University of Tokyo Press, Tokyo. 1976. 15.5 × 23.2 cm. ix + 144 pp. $7.95.

This slim volume in the series marking the E. R. Squibb Lectures on The Chemistry of Microbial Products contains three chapters [Sources and Biosynthesis of Polyene Antibiotics; Physicochemical Properties and Separation of Polyene Antibiotics; and Application of Polyene Antibiotics in Medical Practice in the Soviet Union] which were originally presented at Rutgers on Jan 29–31, 1974. Unfortunately, the title implies a much broader coverage than the book succeeds in delivering. The introduction briefly recapitulates the long history of the institutions which ultimately became the Leningrad Research Institute of Antibiotics and its motivation in specializing in antifungal agents. A soil screening program led to the discovery of levorin and mycoheptin, polyene antifungal agents used clinically in Russia. Physicochemical investigations of the nature of the agents and their separation into a multitude of similar components differing in potency, etc., ensued, as well as studies of their pharmacokinetic characteristics.

The first chapter gives the morphology and growth characteristics of the levorin and mycoheptin producing organisms and the means of selecting and producing more potent mutant strains. Almost all of this work has been described in Russian journals, meeting abstracts, and patents so a resume of the data will be of interest to specialists. A brief and badly dated resume of the biosynthesis of antibacterial macrolides follows and this, in turn, by a discussion of polyene macrolide biosynthesis which is largely limited to media effects on potency and product distribution. This latter is highly important for production but, to the average medicinal chemist, "biosynthesis" promises to contain a different sort of subject matter. The second chapter deals with paper chromatographic and countercurrent distribution methods for separating polyene mixtures.

Unfortunately, the more recent spectacular power of HPLC to resolve such mixtures, even those believed based on PC and CCD to be homogeneous, is more recent than the literature coverage of this book. The subdivision of the polyenes into groups is done by the traditional UV methods as well as hydrogenation rates and ionic properties. By these methods, levorin is shown to be similar to candicidin. Experiments are briefly recorded in which solubilizing and stabilizing groups were sought, with some success. A section follows in which a structure is proposed for mycoheptin, in collaboration with Professor Borowski, based on degradative experiments, and a similar section deals with arenomycin B.

The last chapter is rather brief, describing the clinical place of nystatin, levorin, amphotericin B, and mycoheptin in Russia.

In sum, the specialist who does not read Russian will find a number of points of interest. The references are predominantly to the Russian literature and are up to date relative to the date of the Lectures (1974), whereas the coverage of non-Russian work is more limited and does not go beyond 1972. The nonspecialist seeking an up-to-date and general treatment of the polyene antifungal agents will not likely be pleased with this book because of its narrow scope and its slowness of publication despite its

attractive appearance, freedom from errors, and relative inexpensiveness.

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The Urea Cycle. Edited by S. Grisolia, R. Baguena, and F. Mayor. Wiley, New York, London, Sydney, and Toronto. 1976. xx + 579 pp. 16.5 × 23.5 cm. $31.00.

This book is a collection of studies on the urea cycle presented at a meeting at the University of Valencia in 1975 in honor of Sir Hans Krebs, father of the urea cycle (among others). In what appears to have been an unusually amicable meeting, students and students of students gathered to pay homage and discuss the past and present status of the urea cycle. This cycle, which prevents the buildup of toxic ammonia when nitrogen-containing amino acids derived from protein are broken down in the liver, is covered with great thoroughness. Its enzymology and regulation are discussed at length as are clinical enzyme assays. The role of the mitochondrial membrane in transport and control (the urea cycle has both cytoplasmic and mitochondrial components) is covered and a very interesting section is devoted to disorders of the urea cycle. Most of these disorders lead to the accumulation of ammonia in the blood and are accompanied by brain damage and mental retardation.

The progression from the discovery of the urea cycle by Krebs and Henseleit in 1932 to the identification of clinical signs of urea cycle disorders in the 1960's is well laid out and instructive to follow as an example of the shifting emphases in biochemistry.

This is a valuable and beautifully put together book which gives a comprehensive picture of past and present research on the urea cycle enzymes. It could be an excellent example to give a graduate student in biochemistry who needs to acquire a feel for his subject.

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An Introduction to the Chemistry of Heterocyclic Compounds. Third Edition. By R. M. Acheson. Wiley, New York, N.Y. 1976. xviii + 501 pp. 14.5 × 22.5 cm. $24.95.

This work, which has achieved three editions in 16 years, must be considered well established. The new edition has the following proportions. It opens with an 88-page account of the three- and four-membered ring systems. The next 260 pages deal with the five- and six-membered rings, first as single rings and then as fused structures such as indole and quinoline. The next 66 pages introduce compounds with two heteroatoms. However, only 22 pages are assigned to systems with more than two heteroatoms. Medicinal chemists, conscious of the unique function of ATP in energy storage, of purines in genetic coding, and of pteridines as coenzymes in the biosynthesis of DNA precursors, may find the treatment inadequate. Unusual as are the properties of rings where so much structural carbon has been replaced by nitrogen, almost a halfway house between organic and inorganic chemistry, these properties could helpfully have been shown to be the inevitable summation of trends already present in pyridine because of its π deficiency. The book concludes with a 20-page section on seven-membered and larger rings.

A more general defect is the treatment of heterocyclic compounds according to the size of the ring, rather than by separating aromatic, paraffinic, and ethylenic heterocycles to make three distinct but self-consistent divisions. A solution to this problem has been attempted by favoring the aromatic types and treating the other two as their minor derivatives. Thus, pyrrolidines and pyrrolines occupy 2 pages in the center of a 33-page treatment of the pyrroles.

Revision and expansion have introduced new historic allusions, physical data, electronic and mechanistic concepts (the latter only sparingly), and many references to biochemistry. Essentially the plan is that of a miniature encyclopedia without pretentions to teach heterocyclic chemistry through physical organic chemistry, a more favored contemporary approach. The style, bright and readable, should ensure pleasant browsing for the senior undergraduate. Errors are uncommon and a wealth of pleasantly reproduced chemical formulas illustrate the text.

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Porphyrins in Human Diseases. Edited by Manfred Doss. S. Karger, AG, Basel. 1976. 17.5 × 24.5 cm. xx + 512 pp. $77.75.

The purpose of this book is to present the papers given at the First International Porphyrin Meeting on Porphyrins in Human Diseases, held in Freiburg im Breisgau, May 1–4, 1975. The major goal of this meeting was to crystallize out the quintessence of the achievements of experimental and clinical scientists in understanding porphyrias through the presentation of papers by prominent scientists from each area of porphyria investigation. Over 170 participants and contributors from around the world participated in this First International Conference on Porphyrins.

The book consists of 76 papers presented at 11 sessions, a list of participants and contributors, and a short subject index. Session I included papers on porphyrin biosynthesis and the action of drugs on this process. The next two sessions were devoted to heme metabolism including the regulation of hepatic heme metabolism and enzymes of the heme pathway. Session IV included papers on the clinical biochemistry of proporphyria, and session V focused on the pharmacology and neurochemistry of porphyrin precursors. The next five sessions presented papers on various aspects of porphyrias including papers on the pathological biochemistry of hepatic porphyrias, the diagnosis and treatment of acute intermittent porphyria, the clinical biochemistry and therapy of chronic hepatic porphyrias, porphyrin metabolism in various experimental porphyrias, and experimental chronic hepatic porphyria. The last session presented a number of procedures under the title "Analytical Biochemistry of Porphyrins". The articles are well illustrated and include numerous references to previous work.

The editor has prepared an excellent presentation of the papers. For technical reasons (unstated), discussions held after the session are not included in this book but are available in a separate volume. This book will be of primary interest to those actively working in the area of porphyrin-related human diseases.

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Chemical Mutagens. Principles and Methods for Their Detection. Volume 4. Edited by A. Hollaender. Plenum Press, New York and London. 1976. 16 × 23 cm. xviii + 364 pp. $29.95.

This volume is fourth in a series and consists of a direct continuation of the material presented in the first three volumes. The fourth book discusses in detail methods of determining different chemical mutagens in different systems, including cell cultures and various human cells. The best systems for certain purposes are described and the relative strengths and weaknesses of the different test systems are developed. It mentions the difficulties of interpretation one is likely to incur, especially in human test systems. The book covers the available methods in detail and presents with care those recently developed. The bibliography for most chapters is fairly extensive and covers the recent literature. For example, in the chapter on Atmospheric Mutagens over 600 references are given.

Chapter headings include such topics as Cytological Methods; The Micronucleus Test for Cytogenetic Analysis; The Function of Drosophila in Genetic Toxicology Testing; Plant Test Systems; Indirect Indicator Systems; and Carcinogenic and Mutagenic *N*-Nitroso Compounds.

Many problems of the day are addressed. Included under Atmospheric Mutagens are such topics as sulfur and nitrogen oxides; halogenated hydrocarbons; fluorine; pesticides; poly-

chlorinated biphenyls; lead; and mercury. The last chapter of the book discusses a most timely topic, The Cytogenetic Surveillance of Industrial Populations.

Overall the book is highly informative, practical, and sufficiently detailed with adequate attribution to be of general use as a reference. For those working in the field or otherwise interested, this is an excellent book and is highly recommended.

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The Enzyme Molecule. By W. Ferdinand. Wiley, London and New York. 1976. 15 × 22.5 cm. 289 pp. $22.00.

The title of this book is somewhat misleading. A more descriptive one would be "An Introduction to Enzyme Kinetics". The majority of the book is devoted to the development of the usual equations of enzyme kinetics. In general, a careful step-by-step derivation of the various equations is given. The necessary assumptions and their implications are pointed out. The author's stated purpose has been to produce a "single source which is up-to-date and reasonably brief to which one can direct students and in which they can find all they need to know about the biological, structural, and kinetic facets of the study of enzymes". He has succeeded well with the kinetic part. The discussion of enzyme structure and mechanisms is too brief to be of any real value. On p 138 the question is raised, "Why study kinetics?", but is never really answered. One is left with the feeling that the answer is largely that enzyme kinetics is an end in itself.

The following chapter headings and number of pages give one a rough idea of structure and content of the book: 1. The Enzyme in the Cell (12 pp); 2. Bioenergetics and Kinetics (22 pp); 3. The Structure and Properties of Proteins (35 pp); 4. The Enzyme Structure and Function (30 pp); 5. Enzyme Kinetics I: The Kinetics of Independent Active Sites (23 pp); 6. Enzyme Kinetics II: The Kinetics of Interacting Sites (28 pp); 7. Enzymes and the Control of Metabolism I: Fine Control of Enzymic Activity (20 pp); 8. Enzymes and the Control of Metabolism II: Coarse Control of Enzyme Activity (7 pp); Appendix 1: Nomenclature and Classification of Enzymes (10 pp); Appendix 2: The Purification of Proteins (14 pp).

For the medicinal chemist who needs a good introduction to enzyme kinetics, "The Enzyme Molecule" can be recommended. However, to someone who is interested in the relevance of theoretical studies of enzymes to the development of new or better drugs, "The Enzyme Molecule" has little to offer.

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International Review of Neurobiology. Volume 19. Edited by C. C. Pfeiffer and J. R. Smythies. Academic Press, New York, N.Y. 1976. 15.5 × 23.5 cm. vii + 323 pp. $33.50.

Nowadays the word neurobiology covers a multitude of sins. The recent explosion in research in the neurosciences includes an area ranging from biochemistry and genetics to psychology and sociology. Obviously it is quite impossible for anybody to have a great depth of knowledge in so many different areas. With this in mind "review" publications are particularly useful either for those who need detailed articles directly related to their own area of research or for others who require some introductory information in another area of neurobiology in order for them to assess the overall impact and potential of their work in this area.

The "International Review of Neurobiology" is certainly one of the oldest review publications in this rapidly expanding field. Previous volumes have contained articles of extremely high calibre by experts in several areas of neurobiology. In addition, the publication can be commended for the fact that it has often included papers by authors in this area who hold unconventional views.

Volume 19 (1976) contains an interesting potpourri of articles. These are (titles abbreviated) (1) Hippocampal lesions and memory, S. D. Iversen; (2) Synaptosomal transport, G. Levi and M. Raiteri; (3) Glutathione and the nervous system, M. Orlowski and A. Karkowsky; (4) Ethanol and the nervious system, A. K. Rawat; (5) Octopamine and related amines, H. A. Robertson and A. V. Juorio; (6) Apomorphine, F. C. Colpaert et al.; (7) Plasma levels of thymoleptics and neuroleptics, T. B. Cooper et al.

Although all the chapters are well written and interesting, some are of immediate interest to medicinal chemists. The chapter on apomorphine is an example of this. Apomorphine and related drugs cannot be said to have suffered from a lack of interest in recent years owing to their use as tools to probe the neurological and neurochemical basis of Parkinson's disease and schizophrenia and other behavioral syndromes related to central dopaminergic systems. The review here treats the chemistry of these compounds briefly but then forms an excellent introduction to all the behavioral and neuroendocrine sequelae resulting from administration of these compounds (certainly essential reading for all medicinal chemists in this area).

Chapters on ethanol and the nervous system and on plasma levels of neuroleptic and thymoleptic drugs will certainly be of interest to medicinal chemists associated with the clinical aspects of pharmacology. The chapter on octopamine will also interest those who may be looking for "newer" biogenic amines to serve as templates for drug development.

On the whole, therefore, this volume, as previous volumes in the series, can be highly recommended. It may not be an essential purchase for the individual scientist but is a must for any library which expresses even a meager interest in the neurosciences.

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Advances in Mass Spectrometry in Biochemistry and Medicine. Volume II. Edited by Alberto Frigerio. Halsted Press, New York, N.Y. 1977. 15.5 × 23 cm. 609 pp. $47.50.

This volume is the compilation of the Proceedings of the Third International Symposium of Mass Spectrometry in Biochemistry and Medicine held at the Mario Negri Institute for Pharmacological Research, Milan, Italy, in June 1975.

While the topics in this symposium covered many different areas of biochemical and medicinal research, they generally fall into three major mass spectral topics—metabolic studies, quantitation, and structure elucidation. The format of the chapters should be very useful to the researcher since considerable experimental detail is included in each presentation as well as references and a discussion of the results. The metabolic studies (13 chapters) contain descriptions of techniques as varied as structure elucidation of metabolites isolated by TLC, HPLC, extraction, and GC and monitoring of compounds in biological matrices by mass fragmentography. The chapters on quantitation (15) also describe extensive use of mass fragmentography. Of particular interest is the emphasis on monitoring specific compounds in complex biological matrices. The powerful analytical utility of GC–MS as well as the limitations is well documented. The third topic, structure elucidation, is represented by several examples which describe the use and utility of chemical ionization, field ionization, and field desorption as alternatives or as complements to electron-impact ionization in structure identification.

This volume will be of interest to all investigators in the fields of biochemistry and medicine who wish to keep abreast of the latest mass spectral techniques for studying the metabolic fate of molecules, for quantitating biological samples, and for those who are interested in excellent examples of the use of gas chromatography–mass spectrometry for the analysis of complex biological molecules.

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