Page 1275. The last three entries in Table V should read as follows:

compd	K_i,[b] mM
5'-deoxy-5'-(methylthio)-adenosine	>5.4[c]
methionine	stimulates enzyme[c]
5'-deoxy-5'-(dimethylsulfonio)adenosine	6.0

Kuo-Chang Tang, Roy Mariuzza, and James K. Coward*: Synthesis and Evaluation of Some Stable Multisubstrate Adducts as Specific Inhibitors of Spermidine Synthase.

Page 1277. In the abstract, **2b** should read **2c**, and **3b** should read **3c** in all cases.

Page 1278. In line 28, left column, **2b** and **3b** should read **2c** and **3c**.

Page 1278. In line 1, right column, **2a** and **3a** should read **2b** and **3b**. Line 5, right column, should read "... from rat prostate reveal that **2c** and **3c** are potent and ...".

Page 1282. Analysis for **6g** should read $C_8H_{20}N_2O\cdot 2HCl$.

Page 1283. In line 3, right column, sentence should read as follows: "The iodide thus obtained was converted to the perchlorate salt by use of an AG-1X8 column ...".

1982, Volume 25

Yoko Yasuda,* Kunio Tochikubo, Yoetsu Hachisuka, Hisao Tomida, and Ken Ikeda: Quantitative Structure–Inhibitory Activity Relationships of Phenols and Fatty Acids for *Bacillus subtillis* Spore Germination.

Page 318. The phenol substituent for compound **27** should be 2,4-$(NO_2)_2$ instead of 2,5-$(NO_2)_2$.

Staff Review: Amino Acids, Peptides and Proteins. Volume 11. Specialist Periodical Reports.

Page 749. The correct price for Volume 11 is $104.00. Volume 10 is priced at $86.00, and Volume 6 is priced at $52.00.

Book Reviews

Steroids: Keys to Life. By Rupert F. Witzmann. Translated by Rosemarie Peter. Van Nostrand Reinhold, New York. 1981. xiii + 256 pp. 17 × 23 cm. $28.50.

Africa 1859. Livingston and his botanist John Kirk are in the bush collecting samples of arrow poisons. "Kirk was rather careless in (their) handling, carrying them in the same pocket into which he occasionally tucked his toothbrush. One morning, a little of the poison must have stuck to the bristles, and after brushing his teeth, Kirk suddenly noticed that his pulse was slowing down... Fortunately, nothing further happened. An intact mucous membrane save Kirk's life." The physiological effects of the steroid glycoside strophanthidin had been discovered.

The scene shifts to Mexico, 1941. "Marker found what he had been looking for: the (*Carbenza de negro*) root was full of steroids that could be converted into progesterone. This was the moment when Parke-Davis missed the boat. They declined to set up a small laboratory... Angrily, Marker moved to Mexico to start out on his own: a loner, a stubborn individualist, a genius who was going to take on the world's mightiest steroid producer all by himself. On top of everything, he did not have a penny to his name... One has to hand it to the two owners of the insignificant Laboratorios Hormona. When a nondescript man plunked $160,000 worth of progesterone down on the table and asked, 'Are you interested?' they gave the correct answer." Syntex was formed.

Rupert Witzman is a superb storyteller, a practicing physician and previous European Medical Director for two U.S. drug companies. His new book, *Steroids: Keys To Life*, is one of the very best books ever written for a mixed audience of drug scientists and for the lay public. Drawings of cardiac genins' A/B-cis ring junctures and 5α-androstane are as expertly drawn and described as EKG changes caused by digitoxin. The stories of Kirk, Livingston, and Russell Marker are blended with those of Butenandt, Windaus, Bloch, Huggins, and many other distinguished workers in the steroid field. They make for great reading.

The drama and politics of steroid product development are also well described. Although the world's first oral contraceptive product Enovid (with the steroid progestin norethynodrel) was marketed in 1956, it was not until 1959 that Searle actually dared to include contraception as one of the drug's indications for use. Witzman writes, "The opposition was armed and ready for such a product. There were even reports that the President of the United States had personally ruled out allocation of public funds for family planning... The FDA was furious, and refused to accept the claim. A three-hour, heated debate ensued, for which Searle had called in Professor (John) Rock, a Catholic (and co-developer of 'the pill')... Rock reportedly yelled at the FDA's departmental expert, 'what would *you* know about cancer? You talk about religion! What would you know about *my* religion?"

Illustrations in the book are well done. They include biochemical and physiological pathways (e.g., regulatory mechanisms for progestins including LH-RH, aldosterone and the sodium pump, estrone fitted into a hypothetical receptor, human chromosomes, and gene activation by steroids), as well as the structures of all major natural steroids. Photographs of the Nobel Laureates in steroid research are included, as well as drawings showing past contributors, such as Arnold Berthold (1803–1861). A collection of fine color photographs is included in the middle of the volume. Although a few have at best a distant connection to steroids, most do show the diversity of effects of steroids in nature—a deer (velvet on antlers from the effects of testosterone), a child with steroid excess (Cushing's syndrome), and catepillars (under the influence of steroids) being transformed into colorful moths.

Steroids: Keys to Life was written for the layman, but in the process, Witzman and his gifted translator Rosemarie Peter have also written a fine reference for drug experts—both chemists and nonchemists alike. Many of the historical narratives exist in no other place, assembled by good historical research and by interviews with mordern-day workers. Although the great accomplishments of some outstanding steroid chemists are omitted (e.g., Carl Djerassi, Josef Fried, and George Rosenkranz), this is generally a fine book which will be as enjoyable to the layman as to the medicinal chemist.

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Hormonal Proteins and Peptides. Volume 10. β-Endorphin. Edited by C. H. Li. Academic Press, New York. xvii + 359 pp. 16 × 23.5 cm. ISBN 0-12-447210-9. $44.50.

This book is the 10th in a series of volumes that are dedicated to the extensive review of a particular aspect of hormones and peptides. This volume deals with β-endorphin.

The first chapter by C. H. Li mentions briefly the synthesis of β-endorphin and describes extensively the synthesis of a large number of β-endorphin analogues. Biological activity of the analogues is also included.

The second chapter reviews the work reported on the trypsin-like proteinases that are involved in the generation of opioid peptides, while the third chapter discusses the biosynthesis of β-endorphin from proopiomelanocortin. Many timely references are given.

The fourth chapter is an extensive and scholarly review of many different aspects of the opiate receptor. Some of the topics covered are localization, molecular basis of binding, solubilization and purification of binding components, and biological roles of the opiate receptor.

Other chapters describe the anatomical location of β-endorphin structures in the brain, studies of β-endorphin in patients with mental illness (schizophrenia, unipolar and bipolar depression), and results of clinical studies of β-endorphin in patients with pain and drug addiction.

There also is a chapter on the neurobiology of β-endorphin and related peptides. Many different areas of pharmacology are reviewed, including EEG effects, neuroendocrine interactions, analgesia, thermoregulation, respiration, and cardiovascular function.

In general, the book is an excellent up-to-date review of what is known about β-endorphin. The book is well-organized and is recommended for anyone interested in opioid peptides.

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High-Density Lipoproteins. Edited by Charles E. Day. Marcel Dekker, New York. 1981. xii + 694 pp. 18.5 × 26 cm. ISBN 0-8247-1220-X. $65.00.

Serum lipoproteins are water-soluble combinations of lipid and protein that serve as fat transport vehicles in the bloodstream. They have been studied extensively over the last 30 years with particular emphasis on their role in coronary atherosclerosis, a major disease. Three broad classes were separated and designated as high-density (HDL), low-density (LDL), and very low-density lipoproteins (VLDL). High serum concentrations of LDL and VLDL were associated with an increased risk of developing atherosclerosis. Until 1975, therefore, most research efforts focussed on the study of these two classes. Also, the relatively more simple measurement of total serum cholesterol was judged equally reliable for assessing increased risk to atherosclerosis. It has now been suggested that high serum concentrations of HDL promote regression of atherosclerosis. In addition, since HDL also carries cholesterol, the value of total serum cholesterol determination to assess risk and the value of lowering serum cholesterol by diet or drugs for prevention of atherosclerosis were questioned. In order to obtain answers to these important questions, a tremendous amount of research activity has recently been dedicated to the study of HDL.

The editor of the present book on *High-Density Lipoproteins*, who earlier coedited a similar book on *Low-Density Lipoproteins* (1975), set himself the task to bring together into a single source most of what is known about HDL today. Written by experts from around the world, the book covers in 20 chapters various areas of research on HDL.

Four chapters deal with isolation, fractionation, chemical, and physicochemical characterization of HDL. HDL was shown to be heterogeneous and to be composed of a minimum of seven lipoprotein families. From physicochemical studies on HDL and reconstituted lipid–apolipoprotein fractions, much has been learned about lipid–protein interactions in general and the lipid-binding capacity of individual apoproteins in particular. The formulation of stimulating hypotheses, such as that of amphipathic α-helixes as a structural requirement for lipid binding, offers challenges for future experimentation. A chapter on assay methods for HDLs in clinical application reveals, not surprisingly, that there are considerable problems. Because of lack of standardization and lack of comparability between methods, it is difficult to compare serum HDL cholesterol determinations of one study with another. There is a need for improved accuracy and precision, on the one hand, and for simpler and cheaper methods, on the other.

Six chapters deal with biochemical studies on HDL. One chapter reviews studies of the biosynthesis of HDL; another reviews studies of its degradation. Studies on the effect of HDL on lipolylic enzymes and on lecithin:cholesterol acyltransferase (LCAT) are reviewed. A key chapter by P. J. Nestel and N. E. Miller deals with the effects of HDL on cholesterol metabolism. HDL is secreted by the liver in the form of bilaminar disks, composed predominantly of phospholipid and protein. Such nascent HDL particles have the capacity to take up cholesterol. Unesterified cholesterol within HDL is esterified by the action of plasma LCAT. Resultant cholesteryl esters enter the core of the HDL particle, which now assumes spherical shape, and are released in the liver for catabolism and excretion. These processes have been studied in vitro, mostly by use of cultured cells, and in vivo. A special chapter is devoted to mycoplasmas (a soft-skin microorganism) that provide a suitable model system for studying the transfer of cholesterol from serum lipoproteins to cell membranes.

The remaining nine chapters review physiological, clinical, and epidemiological studies of HDL. A general review of HDL in health and disease is followed by a chapter on Tangier disease, which is characterized by almost complete absence of HDL. Two chapters deal with the relationship of serum HDL to atherosclerosis. One of these is written by the Millers, whose 1975 publication is widely credited with having started the rush of HDL research. The evidence they review strongly supports the hypothesis that the plasma concentration and metabolism of HDL have an important influence on the rate of progression of atherosclerosis and that this is related, at least in part, to a role of HDL in the transport of cholesterol out of extrahepatic tissues. Probably only a fraction of HDL, the HDL_2 subclass, contributes to regression of atherosclerosis. Studies of HDL in nonmammalian vertebrates and in nonhuman primates are reviewed. Studies of lipoprotein patterns in animal models for hyperlipidemia and atherosclerosis are also reviewed and raise serious doubts regarding the relevance of these models for the human disease. The last three chapters review studies of environmental factors affecting HDL and epidemiological studies.

Overall, this book is excellent. The editor has been successful in coordinating the effects of many authors to arrive at a cohesive account with surprisingly little overlap. The material is discussed in depth with many references, yet an effort is made to arrive at coherent interpretations and to provide a perception of the many unresolved issues in HDL research. The material is easily accessible: each chapter has a table of contents and a summary; in addition, there is a brief subject index and an author index for the whole book. This book is of high interest to all those who continue to search for rational approaches to the treatment and prevention of atherosclerosis and other diseases of lipid metabolism.

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Chemistry and Biochemistry of Amino Acids, Peptides and Proteins. Volume 6. Edited by Boris Weinstein. Marcel Dekker, New York. 1982. x + 327 pp. 15.9 × 23.5 cm. ISBN 0-8247-1363-X. $49.50.

This series continues to provide stimulating articles on advances in diverse areas related to amino acids and their derivatives. W. E. Hill in "Ribosomal Protein Synthesis and Structure" outlines the impressive progress made in this field, as well as our lack of understanding of the structure–function relationships of proteins and RNA in ribosomes. C. H. Stammer discusses the occurrence and synthesis of dehydro amino acids, as well as the effects of unsaturation of peptide conformation. Most of the naturally occurring dehydro amino acids so far discovered are products of microbial metabolism. Two examples are peptides formed by fungi that are pathogenic to plants. Alternariolide contains a dehydroalanine moiety and causes necrotic brown spots to form on apples. Tentoxin contains dehydrophenylalanine and induces chlorosis of germinating seedlings. E. Benedetti in his thoroughly documented chapter on "Structure and Conformation of Peptides as Determined by X-Ray Crystallography" also mentions tentoxin, which is a cyclic tetrapeptide (*N*-MeAla-Leu-dehydroPhe-Gly) because this substance has the same conformation in crystals as it does in solution (as determined by NMR spectroscopy). Benedetti's chapter emphasizes the factors responsible for the observed conformations, such as intramolecular hydrogen bonding, complexation, and solvation. The crystal structures of 20 naturally

occurring peptides are discussed. L. Pickert examines "Peptide and Protein Complexes of Transition Metals as Modulators of Cell Growth". Iron transferrin, a protein of molecular weight 76 000, delivers iron to cells after reacting with specific cell-surface receptors. The tripeptide Gly-His-Lys, a normal blood constituent, binds iron and copper and can stimulate or inhibit the growth of a wide variety of cell types. W. S. Chilton discusses "Secondary Amino Acids of Mushrooms". Derivatives of cysteine, proline, glutamic acid, leucine, tyrosine, and tryptophan are among the compounds reviewed. The function of these derivatives is not known, but their chemistry, odor, biosynthetic pathways, and toxic effects are intriguing. I. Ugi, D. Marquarding, and R. Urban describe the "Synthesis of Peptides by Four Component Condensation" as an alternative to conventional methods of peptide synthesis. The four-component method involves the combination of suitably protected peptide segments with an isocyanide and an aldehyde forming a cleavable condensation product. Many examples of stereoselective peptide syntheses are presented. The four-component method has also been used to synthesize derivatives of penicillin, furanomycine, and nocardicine, to attach peptides to solid supports for sequence analysis, and to immobilize enzymes.

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Metal Ions in Biological Systems. Volume 13. Copper Proteins. Edited by Helmut Sigel. Marcel Dekker, New York and Basel. 1981. xx + 394 pp. 16 × 23 cm. ISBN 0-8247-1504-7. $59.75.

Volume 12 of this series was concerned with general "Properties of Copper" and described mainly low-molecular-weight complexes of copper. Volume 13 takes up the copper-containing proteins. The expansion of our knowledge of the biological roles of copper in the animal is taking place at a rapid rate, and the nature and properties of the copper proteins are becoming better, although still not completely, understood. The attempt is made in the various chapters of this volume to describe the present knowledge of structural and physical properties, including information on the structure of the functional unit or the molecular environment of the copper ions, the nature of the electron transfer reactions involved, amino acid sequence, binding of ligands and substitution by other metals, other mechanistic studies, and biological significance of the copper proteins.

Although amino acid sequences are becoming known for a number of copper proteins, such as the copper "blue" proteins, the elucidation of the functional sites or mechanisms of action is still not complete in most cases. Such terms as "substantial approximation", "a difficult problem to treat", "interpretation remains difficult", "not yet clearly resolved", "other factors may be more important", "although there is some discrepancy", "recent evidence appears to favor", and "recent work has cast considerable doubt" appear all too often. The present picture of the copper monooxygenases, which include the tyrosinases and dopamine β-monooxygenase, is relatively well developed, however, and these enzymes may be of greater interest to most medicinal chemists than some of the other copper proteins.

There are individual chapters on the copper "blue" proteins, the properties of binuclear copper centers in model and natural compounds, ceruloplasmin: a multifunctional metalloprotein of vertebrate plasma, copper monooxygenases: tyrosinase and dopamine β-monooxygenase, cytochrome C oxidase, the active sites of molluscan and arthropodan hemocyanins, copper/zinc superoxide dismutase, and the chemistry and biology of copper metallothioneins. There is also an introductory chapter on the evolution of copper proteins, and a concluding one on metal replacement studies of blue copper proteins. All of the chapters are well written and well referenced with recent work.

In conformance with the rest of the series, there is both an author and subject index; these cover a total of 45 pages. The book should be of much value to biochemists, inorganic chemists interested in the structure of metalloproteins, and medicinal chemists who attempt to utilize protein structures in drug design. The editor and authors are to be commended for providing a volume that gives a useful if not wholly complete picture of the structural and chemical properties of the copper proteins, until recently rather poorly understood entities.

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Metal Ions in Biology. Volume 3. Copper Proteins. Edited by Thomas G. Spiro. Wiley, New York. 1981. ix + 363 pp. 15.5 × 23.5 cm. ISBN 0-471-04400-8. $54.50.

Each chapter of this excellent book is well written. Contributing authors present the current understanding concerning electronic structure, chemical reactivity, and bioinorganic chemistry of copper-dependent enzymes. References are current in all chapters and even include correspondence of unpublished data. Only two typographical errors were noted (arrow missing from the reaction $O_2 + 2H_2O \rightarrow 2H_2O + 2O$ on page 176 and laccose for laccase on page 177, second paragraph, last line).

H. B. Gray and E. I. Solomon begin with a nice abbreviated historical account of work done to establish the structure at active sites in blue copper centered enzymes. The chapter continues to develop the present understanding of the structural features of blue oxidases containing blue and other types of copper, which are represented by the laccasses, ceruloplasmin, and ascorbate oxidase, as well as blue oxidases, which contain only blue copper, the plastocynins, azurin, and stellacyanin. Of these, pure blue oxidases are presented as the best understood with regard to their electronic and quaternary structural features.

E. I. Solomon presents electronic and quaternary structural features of binuclear copper centers in tyrosinase, hemocyanin, and other Type III EPR nondetectable copper oxidases. Current knowledge concerning chemical mechanisms for the biochemical transformation of phenols to *o*-hydroquinones and their conversion to *o*-quinones as catalyzed by tyrosinase is presented in detail.

D. Reinhammar and B. G. Malmstrom provide an overview of the current understanding of multicopper oxidases that contain four or more copper atoms in mononuclear and binuclear sites from the point of view of chemical composition and structure, as well as the catalytic reactivity of the Type I, II, and/or III sites in ceruloplasmin, ascorbate oxidase, laccases, cyanins, and azurin.

O. Farver and I. Pecht offer an alternative view of the electron-transfer pathway to blue copper sites using data obtained by pulse radiolysis in addition to spectrophotometric methods.

G. Hamilton presents oxidases with monocopper reactive sites: galactose oxidase and copper-containing amine oxidases. These oxidases have at their active sites only one atom of copper that is not close to any other metal atom. Mechanistic arguments for the involvement of the copper(III) oxidation state for galactose oxidase catalysis are well presented. Monoamine oxidases are suggested to possess a new modified-flavin cofactor for copper-dependent monoamine oxidation. Flavin containing and copper-requiring amine oxidases are also suggested to be closely related enzymes.

M. J. Ettinger and D. J. Kosman call into question the involvement of copper(III) as an oxidation state in the catalysis of galactose oxidation.

J. J. Villafranca suggests two models of copper binding in dopamine β-hydroxylase, which contains 2 to 10 atoms of copper in both the soluble and insoluble forms. Many mechanistic aspects are considered for conversion of the β-methylene group of dopamine to a secondary alcohol in norepinephrine with retention of configuration. Other substrates and inhibitors are also considered. It is pointed out that chelating agents which chelate copper in dopamine β-hydroxylase inhibit this enzyme.

J. S. Valentine and M. W. Pantolinao review quaternary structure, chemical reactivity, and metalloprotein interactions of superoxide dismutase, a cuprozinc protein. The section on physiological reactions of cuprozic proteins deals with copper and zinc metabolism and explores a very large body of much needed background information that might have been given more space in a first chapter to provide background information, justifying the need to know more about copper proteins. Unfortunately, this section contains a bit of misinformation. The notion,

presented in the 4th paragraph on page 343, that the normal daily diet contains more than required amounts of copper, 2 to 10 mg, can no longer be held in the light of 13 recent reports of low daily dietary intakes associated with the ingestion of three well-prepared meals per day. Many "well prepared and balanced" diets are now known to provide less than 2 mg/day (Klevay, In "Inflammatory Diseases and Copper". Sorenson, J. R. J., Ed.; Humana Press: Clifton, NJ; 1982; pp 123–136).

Copper Proteins is recommended for chemists who are involved with inorganic, bioinorganic, medicinal, or biochemical research pertaining to metalloelement-dependent enzymes, inflammation, or the adrenergic nervous system. Topics covered in this book should be appropriately presented in graduate and undergraduate course work in these areas.

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Understanding Enzymes. By Trevor Palmer. Ellis Horwood Ltd., England, and Wiley, New York. 1981. 405 pp. 15.5 × 23.5 cm. ISBN 0470-27186-8. $80.95.

This well-written introduction to enzymology should be very useful for undergraduate students in biochemistry, pharmacology, and other health sciences. It carefully develops the needed background in the nomenclature, organic chemistry, chemical reaction mechanisms, and biochemistry in concise chapters in the first section so that the student can understand the complex concepts of enzyme catalysis, enzyme inhibition, protein–protein interactions, and ligand–protein interactions in the second section. Most chapters conclude with summary paragraphs, several current references, and problems that illustrate the concepts (answers are provided at the back of the book). A third section, applications of enzymology, includes chapters on assay methods, localization of enzymes in cells, extraction and purification, and practical uses of enzymes.

There are many valuable discussions for the advanced student and researcher in the second and third sections. In particular, I enjoyed reading the mathematical equations and graphic presentations of the various types of enzyme inhibition, current approaches to dissect multisubstrate reactions, and the problems and assumptions associated with different assay methods. The weakest subsections concerned subcellular localization of enzymes and genetics of enzyme deficiency diseases, but they are adequate for introductory students. The price is high and may prevent its use as a text for undergraduate students.

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Carbohydrate Chemistry. Volume 12. Specialist Periodical Reports. J. F. Kennedy and N. R. Williams, Senior Reporters. The Royal Society of Chemistry, Burlington House, London. 1981. xv + 624 pp. 13.5 × 21.5 cm. $143.00.

The 12th volume in this series reviews the literature in carbohydrate chemistry published during 1978. The Report is now organized by two persons in order to facilitate production of the two parts of the volume concurrently. Dr. N. R. Williams is now the Senior Reporter for Part I (mono-, di-, and trisaccharides and their derivatives) and Dr. J. F. Kennedy is the Senior Reporter for Part II (macromolecules). The approximately 1000 references cited in Part I reflect particularly vigorous activity in the areas of antibiotic and nucleoside chemistry, whereas the >2000 references cited in Part II reflect research emphasis in the areas of glycoproteins, carbohydrate enzymology, and chemically modified carbohydrates. The two new Senior Reporters and the five other Reporters continue to maintain the standards of excellence set by their predecessors in this well-established series. The quality of the reporting and the extraordinary volume of literature abstracted continue to make this series an invaluable reference to all who work in the field.

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Neurotransmitters, Seizures, and Epilepsy. Edited by P. L. Morselli, K. G. Lloyd, W. Loscher, B. Meldrum, and E. H. Reynolds. Raven Press, New York. 1981. xvi + 361 pp. 18.5 × 26 cm. ISBN 0-89004-753-7. $42.00.

This volume contains the proceedings of the first Workshop on Neurotransmitters in Epilepsy under the patronage of Epilepsy International held in May, 1981. A great deal of information on the neurochemistry of epilepsy has been published in recent years in widely scattered journals and books. A symposium pulling together this widely scattered information is thus a valuable contribution.

This volume contains papers dealing with most aspects of the neurochemistry of epilepsy that are under active investigation, although the neurochemistry of absence seizures is not dealt with. The authors are eminently qualified to write in their areas. The articles are uniformly scholarly and up-to-date. The chapters contain original data, references, and formal discussion, making them of particular value to researchers in the area. There is an excellent subject index.

The chapters in this volume consist chiefly of research data from the laboratory of the chapter's author(s). The book thus represents a collection of reports from many of the leading latoratories in neurochemistry on many of the areas currently under investigation. The book does not contain comprehensive reviews of various areas of the neurochemistry of epilepsy. Many, but not all, chapters have summaries.

Overall, this volume contains reports from many leading laboratories on recent work in the neurochemistry of epilepsy. The book is highly recommended for researchers in the field and persons wishing to read accounts of recent original work in the field.

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Receptors and Recognition. Series B. Volume 13. Receptor Regulation. Edited by R. J. Lefkowitz. Chapman and Hall, London and New York. 1981. viii + 253 pp. 16 × 24 cm. ISBN 0-412-15930-9. $40.00.

This volume is a collection of reviews that are intended to describe the regulation of exemplary receptor systems. Because the literature on this topic is vast, the editor has opted for a representative rather than encyclopedic approach in order to highlight organizing principles. A number of principles and useful approaches to problems do emerge, and the reader gets a sense of the particulars of some systems that have made them fruitful study. Yet it seems that research findings are not very substantial for review in many cases, the result being either a short review or one full of interesting information not pertinent to receptor regulation. So, as illustrative as these examples are—and they have been judiciously chosen—this volume might have said less about more systems.

The volume is organized into eight chapters. The first five involve regulation as a physiological phenomenon. Particularly interesting among these is the one on adrenergic receptors for Lefkowitz's conception of β-receptor regulation and the one on cholinergic receptors of skeletal muscle as a chronicle of Fambrough's elegant work. Discussion of the insulin receptor is interesting for its global insights into receptor function and for consideration of technique. A chapter on EGF is illuminating but has little to say about regulation. The chapter on prolactin, which like angiotensin II apparently induces its receptor, is a little pedestrian in its tissue by tissue discussion, though it does stick to the topic of regulation. The last three chapters discuss medical conditions in which receptor regulation and autoimmune disorders play a role. This second chapter on insulin primarily summarizes

a number of conditions due to different disorders. Chapters on myasthenia gravis, in particular, and thyroid disorders explain more of the mechanism of these dysfunctions. These chapters were especially interesting as illustrations of how many different molecular mechanisms can cause similar dysfunctions, and they probably give the best sense of what a complicated phenomenon receptor regulation is.

These reviews highlight the literature through early to mid-1980. In general, they are well organized and easy to read for someone not working in the particular area. In fact, the great value of this book resides in the opportunity to spend an afternoon shopping for ideas in other systems. It is less useful as a comprehensive treatment of receptor regulation. With this in mind, it probably makes a wiser purchase for a department or university rather than individual library.

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The Future of Antibiotherapy and Antibiotic Research. Edited by L. Ninet, P. E. Bost, D. H. Bouanchaud, and J. Florent. Academic Press, New York. 1981. xx + 508 pp. 16 × 23.5 cm $60.00.

This volume contains 30 chapters, together with discussion and summary chapters, which represent the presentations made at the Second Rhône-Poulenc Round Table that was held in Paris in February, 1980. The book is divided into three main sections: one detailing the needs of current antibacterial therapy, a middle section dealing with several miscellaneous subjects but primarily with criteria of evaluating antibiotics or improving their efficacy, and, finally, one suggesting methods of identifying and isolating new antibiotics. The last section contains a summary and the general discussion of the three main parts. As might be expected, there is a considerable variation in quality and interest of the individual contributions. Also, it should be pointed out at the outset that despite the breadth suggested by the title, this text is only concerned with antibacterial therapy; there is no attempt to deal with the important areas of antiviral, antifungal, or antiparasitic chemotherapy.

Part 1, "Analysis of the Present Situation: Needs, Constraints and Objectives for the Antibiotics of the Future", comprises about 40% of the book's total and deals almost exclusively with the clinician's view of the current status of antibiotherapy. The analyses of the major problems of current antibiotherapy are augmented by an excellent discussion of the ecology of transferable antibiotic resistance by M. H. Richmond and the evolution of resistance patterns by J. Duval. Further chapters discuss clinical needs and ways to prevent the overuse of antibiotics. Finally, three chapters discuss the use of antibiotics in animal health and the potential for resistance in the use of antibiotic food additives. This reviewer felt that this section of the book was much too long—certainly not the fault of the individual authors, most of whom covered their subjects with admirable clarity, but rather of the conference organizers. Certainly the deficiencies of current antibacterial therapy are well known, and a much more concise presentation would have allowed for a more useful presentation, not of current status, but of the future of antibiotic research as the title implies.

Part 2, "Suggestions on Methods for Selection and Assessment of New Antimicrobial Agents", is concerned primarily with the in vitro and in vivo evaluation of new agents and the means by which drug efficacy can be improved. The chapter on in vitro evaluation presents a realistic overview of the problems involved when one evaluates a product in vitro and attempts to position the drug in the clinical scene. M. A. Sande's chapter on animal models discusses only two specialized models, rabbit endocarditis and rabbit meningitis, and thus the nonspecialist is left knowing very little about in vivo evaluation of antibiotics or the problems of the future other than those two. T. Bergan does an excellent job of not only providing an introduction to pharmacokinetics but of presenting some of the problems of current antibiotic usage. Clearly, alteration of the pharmacokinetic properties of new antimicrobial agents will be an essential adjunct to this development in the future. Finally, the perceptive chapter by A. Tomasz points the way to more selective antibacterial agents by developing a mode of action structure–activity relationship of cell-wall biosynthetic inhibitors. This chapter and D. Vazquez' chapter on screening of inhibitors of protein biosynthesis should more logically be part of the succeeding section. Chapters on the adhesion properties of *E. coli* strains, immunomodulating activities of antibiotics, chemotherapy of intracellular infections, and drug combination present some specialized problems in antibacterial chemotherapy, and a chapter by C. Gilvarg suggests a means of transporting antibacterial agents into cells by peptide conjugation. The development of alaphosphin is given as a successful example of this "Trojan horse" strategy.

Part 3, "Suggestion of Methods for Obtention of New Antibiotics", is understandably the section of most interest to the antibiotics researcher. H. A. Lechevalier proposes the isolation of rare forms of microorganisms as the most likely source of novel antibiotics. In the following chapter, S. Ōmura proposes screening for inhibition of cell-wall peptidoglycan synthesis as nontoxic antibiotics and gives the details of the screen used at the Kitasato Institute for this purpose. Perhaps the most provocative chapter in this text is the one by D. A. Hopwood on the possible applications of genetic recombination in antibiotic discovery. Two methodologies are suggested. The first involves mutation of regulatory genes so that normally repressed biosynthetic pathways are expressed, leading to the appearance of new antibiotics. The second recombinational strategy involves transferring genes coding for antibiotic biosynthetic enzymes from one organism to another, thus producing a hybrid capable of producing a new antibiotic. Undoubtedly, both procedures will find application in the future. A. L. Demain discusses the biosynthetic production of new antibiotics by directed and mutational biosynthesis. Finally, after a chapter on structure elucidation, the theory of antagonist design is briefly discussed.

The book concludes with Part 4, "General Discussion", with summations of the preceding sections. In general, these authors do a commendable job in summarizing the relevant points of the previous sections and putting the diverse presentations into perspective. The reader gets an excellent survey of current clinical practice—its needs and its accomplishments. However, for the researcher interested in discovering the antibiotics of the future, there are too few suggestions. For the readers of this journal, in particular, there is no mention of medicinal chemistry (other than the brief chapter on antagonist design) as a means of drug discovery. Surprisingly, there was not a single speaker from industry at this symposium even though it was sponsored by Rhône-Poulenc. This oversight understandably contributed to the imbalance in these presentations, for members of the pharmaceutical industry will undoubtedly continue to be major contributors to the future of antibiotic research.

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Nonisotopic Alternatives to Radioimmunoassay. Principles and Applications. Edited by Lawrence A. Kaplan and Amadeo J. Pesce. Marcel Dekker, New York and Basel. 1981. xi + 342 pp. 16 × 23.5 cm. ISBN 0-8247-1581-0. $45.00.

This book serves as Volume 10 of the series "Clinical and Biochemical Analysis". The volume was motivated, as the authors state in its preface, by a potential need for alternatives that supplant the use of radioisotopes in the clinical laboratory, a particularly timely consideration in view of the recent lack of suitable disposal sites for radioactive waste materials. The editors have drawn contributions both from university-based medical centers and from commercial organizations that have been instrumental in the development of high-performance liquid chromatographic and immunological technologies. The first three chapters consider applications of high performance liquid chromatography (HPLC; including a chapter on electrochemical detection) in clinical analysis. These chapters thoroughly cover methodology developed or used in the respective author's laboratories for a limited selection of drugs and endogenous chemicals. Chapter 1 contains the misstatement that refractive index de-

tectors are one of the most widely used detectors in HPLC. In Chapter 3, all electrochemical detectors are erroneously referred to as polarographic detectors. Otherwise, Chapters 1 and 3 are satisfactory. This is not the case with Chapter 2. Here, one finds numerous errors, including the omission of one or more sentences between pages 21 and 22. The second complete sentence on page 22 reads, "In reality, reagent stability, specificity, and the possibility of monitoring several compounds simultaneously." Figure 2 on page 26 contains incorrect formulas for sodium carbonate and hydrochloric acid. The concepts of accuracy and precision are presented confusingly on page 29. Finally, the description of an HPLC assay for gentamicin (page 40) suggests direct fluorometric detection, which is not possible.

Chapter 4 gives both background material and methodological information on the exploding field of hybridoma-generated monoclonal antibodies, which will undoubtedly replace less specifically produced antibodies as immunological reagents in the future. There follows five chapters dealing with fluorescence-related methodologies: fluorescence protection immunoassays (including assays that use antibody-coated particles), high-sensitivity photon counting techniques, homogenous substrate-labeled fluoroescent immunoassays, the fluoroimmunometric system known as FIAX, and fluorescence polarization techniques. All of these interim chapters are contributed by individuals associated with companies that market specific products. This might explain the apparent imbalance in coverage in each chapter. Remaining chapters cover comparisons of immunoassay techniques in therapeutic drug monitoring, diagnostic enzyme-labeled immunoassays (ELISA), immunological methods of measuring carcinoembryonic antigen (CEA), problems associated with enzyme immunoassays, immunodiagnostic assay systems for clinical use, principles and clinical applications of nephelometry, and measurement of plasma lipoproteins by automated immunoprecipitation–nephelometry. These last sections are satisfactorily written, though are somewhat limited in scope.

Practically all chapters contain references through 1980 and, overall, the book has few typographical errors. The book should be of interest to clinical chemists and other investigators concerned with the analysis of drugs and endogenous components in biological fluids. It therefore merits purchase through reference libraries. The cost/benefit ratio for purchase by individuals may be poor due to the book's limited coverage of applications.

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Radiopharmaceuticals: Structure–Activity Relationships. Edited by Richard P. Spencer. Grune & Stratton, New York. 1981. viii + 843 pp. 18 × 26 cm. $45.00.

The field of radiopharmaceutical sciences has greatly expanded from its early beginnings employing radiolabeled iodine-131 in the 1940's to its current state of sophistication. Many of those scientists involved in this development participated in a symposium held on March 21–23, 1980, in Hartford, CT, culminating in this book on radiopharmaceuticals. The 38 papers were divided into five major sections. The first five chapters focus on basic aspects of structure–activity relationships. Included in this section are presentations on general quantitative structure–activity relationships, receptor binding, and enzyme inhibitors and suicide substrates as rationales for drug and radiopharmaceutical design. The final two chapters of this first section deal with the chemistry, biochemistry, and pharmacology of radiopharmaceutical design and distribution. Each chapter provides a thorough overview and several relevant examples from current research. The second section (consisting of 11 chapters) deals with metallic radionuclides, such as iron, gallium, platinum, ruthenium, and mercury, and various organometallic derivatives. The successes, limitations, and the future potentials of these radionuclides bound to biologically active molecules as radiopharmaceuticals are addressed in each chapter. The final three major sections of the book demonstrate the application of biochemical and pharmacological principles to the development of effective radiopharmaceuticals. In addition, these final 22 chapters emphasize the utility and, consequently, the potential for employing small organic molecules (substrate, hormone, biochemical, drug) with a covalently bound radionuclide as an imaging agent. Chapters 17 through 23 concern lipid-soluble materials, such as cholesterol, androgens, estrogens, glucocorticoids, and liposomes, for diagnostic imaging. In the fourth section consisting of Chapters 24 to 33, the structure–activity relationships of radiopharmaceuticals are arranged according th the major organ systems. The final six chapters examine the development of cyclotron-produced radionuclides, their incorporation in biochemicals and drugs, and their resulting biological activities.

Each chapter in this book relates the structures of the radiopharmaceuticals—biochemical, drug, macromolecule—to their biological activities. The papers reflect the individual style of the authors and most consist of a brief introduction, the presentation of results, and discussion sections. However, the book does not contain any question–answer discussions that might have occurred following the presentations. Such discussions can add pertinent information to the work presented or shed light on unsolved problems. Every paper does contain an extensive list of references, and the book has an adequate subject index. Thus, this book is a fine collection of both overviews and the present research efforts of the leading investigators in the radiopharmaceutical sciences. It is an excellent example of the rapid development of this field and the application of chemistry and biochemistry to nuclear medicine. This book is highly recommended for medicinal chemists, radiochemists, pharmacologists, nuclear pharmacists, and radiologists involved in radiopharmaceutical development.

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pK_a Prediction for Organic Acids and Bases. By D. D. Perrin, Boyd Dempsey, and E. P. Serjeant. Chapman and Hall: London. 1981. x + 146 pp. 14 × 22 cm. ISBN 0-412-22190-X. $22.95.

pK_a values, measures of acid–base strength in dilute aqueous solution, are used in all fields of solution chemistry and related areas. They are important quantitites in analytical chemistry (titrimetric equilibria, metal ion–ligand equilibria, solvent extraction, spectroscopy, chromatography), physical organic chemistry (pH–rate profiles, general acid–base catalysis, nucleophilic reactivity, substituent effects), medicinal chemistry and pharmaceutics (drug stability and solubility, bioavailability, pharmacokinetics), and other areas. Although thousands of pK_a values have been measured, it frequently happens that the pK_a for a compound of interest is not available. Of course it can usually be determined experimentally, but often an approximate value would serve the experimentalist's needs adequately, and then the capability of making a (nonexperimental) pK_a estimate is highly desirable. This little book describes methods for making such estimates.

The approach is pragmatic. pK_a prediction in the sense of the title merely means estimation of a reasonable number by any available means. Theoretical predictions from first principles are not of practical value from this point of view. Rather, effective estimates are made by analogy, correlation, and the assumption of additivity of substituent effects. Linear free energy relationships (LFER), primarily Hammett and Taft correlations, are described for many systems. The goal is a pK_a estimate that is within several tenths of a unit of the actual value.

LFER are expressed in the form $pK_a = pK_a^\circ - \rho\sum\sigma$, where pK_a° and ρ are given. A few correlations of the type pK_a (substituted phenol) = 6.46 ± 0.72pK_a (substituted aniline) are described. Rough guides are suggested for estimating unknown substituent constants and ρ values. The tables include extensive listings of Hammett and Taft substituent constants. A very helpful feature of the book is the inclusion of many worked examples, which is essential for the reader because the procedure for a complex structure may involve several steps.

Although LFER are central to the calculational methods used in this book, the explanation of σ values (pp 44–46) would surely

confuse anyone not already familiar with the concepts and the various model processes. Nevertheless, the very practical aim of this book has been largely achieved, and it conveniently furnishes the experimentalist with methods that will usually generate a reasonable pK_a estimate.

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Pharmaceutical Analysis. Modern Methods. Part A. Edited by J. W. Munson. Marcel Dekker, New York. 1981. xi + 485 pp. 15.5 × 23.5 cm. ISBN 0-8247-1502-0. $55.00.

This book is half of Vol. 11 of a series on "Drugs and the Pharmaceutical Sciences". It comprises six chapters. The first, by B. J. Kline and W. H. Soine, is a review of the theory, instrumentation, and pharmaceutical applications of gas chromatography (GLC), including 74 pages of text, a 17-page table of applications of GLC to pharmaceuticals, and 338 references. The second, by T. A. Roy and S. G. Schulman, devotes 36 pages to pyrolysis–gas chromatography, including 96 references. The third is a chapter by E. J. Cone on analysis of drugs in biological samples by GLC–mass spectrometry. This has 84 pages, of which 56 are didactic, 17 are an appendix containing tables of applications, and the remainder present 241 references. The fourth chapter is by S. C. Schulman and R. J. Sturgeon on "Fluorescence and Phosphorescense Spectroscopy". This has 65 pages of text, 18 pages of appendixes containing tables on fluorometric and phosphorimetric methods for drugs, 249 references, and a bibliography of 10 texts. The fifth chapter is by J. W. Munson on principles of liquid scintillation counting, consisting of 54 pages, including 94 references. Finally, there is a chapter on radioimmunoassay and other immunoassay techniques by W. A. Colburn. This is a 52-page review, including a glossary and 262 references. Indexes are provided by drug name, author, and subject. So much for a quantitative analysis of this book.

The Editor's preface states that the book is intended to bridge the gap between basic texts and highly specific journal articles, is "... designed for the graduate student studying pharmaceutical analysis" and for "the researcher in another field ... who wants to increase his knowledge ... of the modern techniques of pharmaceutical analysis." This Reviewer would be afraid to walk that bridge, not having seen a good basic text on pharmaceutical analysis in more than a decade and having many reservations on the solidity of the span. "Pharmaceutical Analysis" encompasses obtaining information useful in solving problems on the characterization of drug substances, the nature and amounts of synthetic precursors and process contaminants in them, their incorporation in forms for administration to animals in preclinical pharmacology and toxicology studies, preformulation studies of their physicochemical properties, and development of specifications and tests for dosage forms, their bioavailability and metabolism in animals and man, etc. This reviewer is unsympathetic to a picture of pharmaceutical analysis as a collection of methods using drugs as the analytes. One could just as well depend on monographs, reviews, or manufacturers' literature for details of the instrumental methods used. The general chapter on GLC provides a heading on "purpose" in the applications tables, which are reminiscent of those that appeared in the biennial *Analytical Chemistry* reviews on "Pharmaceuticals and Other Drugs", which were generated by computer, presumably *for* computer.

References in most of the chapters are as recent as 1979. The chapter on pyrolysis–GC has a couple of late references; however, most of the papers cited are of historical interest, if that. Typographical errors that pepper the text are annoying but harmless. Discussions of methodology are well presented, but discussions of applications are scarce; hence, few structures of drugs are shown in the text. This Reviewer found reading the text unstimulating, but he has been known to chide his colleagues as "mechanics, not chemists". *De gustibus non disputandem est!*

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Optical Resolution Procedures for Chemical Compounds. Volume 2. Acids. Parts I and II. By Paul Newman. Optical Resolution Information Center, Manhattan College, Riverdale, NY. 1981. Part I, x + 566 pp. Part II, 580 pp. 22 × 28.5 cm. ISBN Set 0-9601918-3-6. $79.00 (set).

This volume continues Dr. Newman's project, the aim of which is to collect all existing information about optical resolutions. Volume 1 covered amines and related compounds, while Volume 3 will cover alcohols, aldehydes, and ketones, and Volume 4 will cover organometallic compounds, inorganic compounds, compounds containing heteroatoms, and hydrocarbons. More than 50 journals, Chemical Abstracts, Chemical Titles, and Dissertation Abstracts International are being scanned page by page, from the first issue to the time of writing, in order to accomplish this amazing feat.

Section 1 of this volume lists 120 resolving agents for acids and amino acids, with structures, melting or boiling points, specific rotations, and references to their preparation and/or resolution. Section 2 contains resolution procedures for 1424 compounds, including carboxylic acids, amino acids, sulfonic acids, phosphonic acids, hydantoins, lactones, and barbiturates. An additional 90 methods are included in an addendum. These procedures involve fractional crystallization of diastereomeric derivatives, are usually offset copies of the experimental section of the primary source, and are arranged by molecular formula. The methods are mainly in English, French, or German, with a few in Italian or Spanish. Literature was reviewed through 1980, with some citations from 1981.

Section 3 contains 32 gas chromatographic and 72 liquid chromatographic methods for resolution of enantiomers and diastereomers, complete with experimental sections and chromatograms. The accomplishments in this field from 1972 through the beginning of 1981 are well represented. The methods are categorized by type and arranged chronologically within each type. Section 4 contains a summary of, and 33 references to, methods for α-amino acid resolution by preferential crystallization and enzymatic synthesis or hydrolysis. Section 5 lists 52 references to methods for determining optical purity. Section 6, by Spiro Alexandratos, discusses asymmetric synthetic methods for carboxylic acids, including asymmetric hydrogenation and the use of chiral reagents, gives 43 references, and compiles data for 58 specific reactions.

The usefulness of this compendium to the chemist cannot be overestimated. Large amounts of valuable time that would otherwise be spent searching the literature can be saved by referring to it. Indeed, several of the methods were personal communications to the author or were buried in papers dealing with other topics and can thus be easily obtained in no other way. One wishes only for indexes: a compound-type index for Section 2 and comprehensive indexes for Sections 3–6. Perhaps someone should consider writing a "Guide to Newman". In any event, all chemists with interest in chiral compounds will want to have easy access to this work.

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Annals of the New York Academy of Science. Volume 367. Quantum Chemistry in Biomedical Sciences. Edited by H. Weinstein and J. P. Green. New York Academy of Sciences, New York. 1981. ix + 552 pp. 15 × 23 cm. ISBN 0-89766-122-2. $106.00.

This book is a collection of 32 articles from a conference held in June 1980. The prompt publication is commendable, making the articles timely to investigators in this area. The book is divided into five sections: "Quantum Chemical Methods for Large Molecules", "Calculation of Solvent Structure and Effects on Biological Mechanisms", "Molecular Conformation and Structure–Activity Relationships", "Theoretical Treatment of Drug–Receptor and Enzyme–Substrate Interactions", and "Quantum Chemistry and Drug Design".

Most chapters are well written and usually long enough for some background development. In a few cases, the discussions at the end of the chapters make contributions. The level at which most chapters are written puts the book beyond the understanding of

the beginner. It is, however, a useful review of current work in biological applications of quantum chemistry for the practicing scientist.

The tabular material and the illustrations are of great value for someone seeking this particular information. It is regrettable that their presence and location could not be documented in an appendix.

The medicinal chemist, pursuing a course of research in a particular biological system, may find some information of value in the book. Those interested in solution effects will find that section particularly valuable. The drug design section consists of six articles of quite specific nature. The book is of value to theoretical scientists and should be accessible to them, although the high cost may make personal copies less attractive than a library holding.

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