of Dixon plots.[12] Data for these plots were obtained by measuring the reaction velocities of renin at three concentrations of porcine angiotensinogen (0.1, 0.2, and 0.3 μM) in the presence of varying concentrations of each inhibitor.

The enzymatic assay was carried out in a manner identical with that described previously.[1] Reaction velocities were expressed as the number of nanomoles of angiotensin I generated per milliliter per hour. Three determinations were made for each inhibitor concentration at each substrate level. A plot of $1/v$ vs. inhibitor concentration was made for each compound tested. All lines were calculated by linear regression analysis. The $-[I]$ value at the intersection of the three substrate line gave the K_i of the compound, while the competitive or noncompetitive nature of each inhibitor was determined by whether the point of intersection was above or on the x axis.

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Book Reviews

Progress in Macrocyclic Chemistry. Volume 2. Edited by Reed M. Izatt and James J. Christensen. Wiley, New York. 1981. xi + 347 pp. 15 × 23 cm. $50.00.

As the title denotes, this book contains information on synthetic multidentate macrocyclic compounds of which crown ethers were the first. The five chapters are (1) "Complexation of Arenediazonium Ions by Multidentate Ligands", (2) "Stability Constants of Cation–Macrocycle Complexes and Their Effect on Facilitated Membrane Transport Rates", (3) "Solute Binding to Polymers with Macroheterocyclic Ligands", (4) "Synthetic Chiral Receptor Molecules from Natural Products", and (5) "Cyclopeptide Macrocycles".

For the medicinal chemist interested in utilizing multidentate macromolecules, Chapters 1–3 will provide detailed information about the phenomena and help to explain the results of the experimental behavior. For example, Chapter 1 includes discussions of spectral studies of arenediazonium salt–crown ether complexes and crown ethers as phase-transfer catalysts in various arenediazonium salt reactions. Chapter 3 covers interaction of macrocycles with ions and ion pairs in media of low polarity and ion binding to poly(vinyl) crown ethers in nonaqueous media, while Chapter 2 deals with subjects like factors affecting complex stability and an electrostatic model for cation–macrocyclic binding. These latter two topics should interest people concerned with receptor-site binding and fit.

For the medicinal chemist with stereochemical interests, Chapter 4 will be a delight. The design and synthesis of various systems, utilizing chiral natural products, plus a discussion of complexation and catalysis of these multidentate macrocycles are covered. The fifth chapter on cyclopeptide macrocycles encompasses the total topic from conventions and nomenclature to design and synthesis to compounds with specific cation binding potential and compounds which mimic metal-binding sites of metalloproteins.

The book is good technically with very few typographical errors. The literature coverage is thorough through 1979 with selected references from 1980. This reviewer suggests that this book will be of value to medicinal chemists working in advanced aspects of multidentate macrocycles, to those involved in ion binding studies, and to those involved in stereochemical problems.

College of Pharmacy **C. F. Barfknecht**
University of Iowa
Iowa City, Iowa 52242

Advances in Cyclic Nucleotide Research. Volume 14. Edited by J. E. Dumont, P. Greengard, and G. A. Robinson. Raven Press, New York. 1981. 724 pp. 16 × 24 cm. $79.00.

This volume includes 55 of the invited lectures presented at the Fourth International Conference on Cyclic Nucleotides held in Brussels, July, 1980. Also included are 330 abstracts of poster presentations. Interestingly, many lectures cover areas not involving cyclic nucleotides but related through indirectly linked mechanisms. For example, questions are posed regarding the mechanisms of α- and β-adrenergic effects which are not mediated by adenylate cyclase. Consequently, the sections present several considerations of the role of calcium as a second messenger and of the significance of protein phosphorylation regulated by factors other than cyclic nucleotides or calcium. Many of the lectures are illustrated with helpful diagrams of models and hypotheses. Unfortunately, the sections and abstracts are not divided according to any scheme or field; this is a particular drawback in the abstracts part of the book. Several issues are addressed which clearly transcend the early phenomenological approach seen in the cyclic nucleotide field a decade ago. A functional and mechanistic approach is now being utilized to examine questions dealing with the role of GTP, calcium-binding proteins, "guanomodulin", and refractoriness in hormone–receptor activity. The mechanisms underlying the relationship between the phosphodiesterases and the regulation of cyclic nucleotide levels are also presented. Several investigations are now describing the architectural relationships among the various components of the cyclic AMP and cyclic GMP metabolizing systems in intact cells.

Tufts University **Jeffrey B. Blumberg**
Boston, Massachusetts 02111

Alkaloid Chemistry. By Manfred Hesse. Translated by I. Ralph C. Bick. Wiley, New York. 1981. xii + 231 pp. $28.50.

This volume is a translation of *Alkaloidchemie*, which was published in 1978. It was written for the scientist who is just beginning the study of alkaloidal natural products. Thus, it is not encyclopedic in its coverage of the field nor exhaustive in its discussion of individual topics. Leading references are given for each chapter or major section. Structural examples are used liberally throughout the text.

The brief initial chapters include the "Concept and Definition of an Alkaloid", "Nomenclature", and "Artifacts". "Classification of Alkaloids" is the longest chapter, covering all of the major classes and subclasses with examples and species of origin. The examples are well chosen to illustrate the structural variations within each class. The "Dimeric Alkaloids and Bisalkaloids" are covered in a separate chapter. The concepts of alkaloid biogenesis are illustrated with the benzylisoquinoline alkaloids. A discussion of the techniques used to study the biosynthesis of the *Papaver* alkaloids serves to demonstrate the methodology of such studies. Plumerane alkaloids are used to illustrate "Aspects of Chemotaxonomy".

The structural elucidation of villastonine in an excellent example with which to demonstrate the use of modern methods of structural investigation. From these mostly spectral techniques the author moves into a detailed description of the use of degradation reactions (Hofmann, Emde, and von Braun). The final chapter contains "Examples of Alkaloid Synthesis". A synthesis of mesembrine, the biomimetic synthesis of porantherine, the synthesis of oncinotine (from Hesse's own work), and a stereoselective synthesis of vincamine are discussed in detail. These

examples provide an excellent cross-section of the approaches and chemical reactions used in this broad field.

This volume is well suited for its stated purpose. It could serve as a text (albeit an expensive one) for part of a course on natural products. A better use, however, is as an introduction, and a standard, for those students embarking on a research career in the isolation and structure determination of, the study of the biogenisis of, or the synthesis of alkaloids.

Lexington, Massachusetts 02173 **James Quick**

Enantiomers, Racemates and Resolutions. By Jean Jacques, André Collet, and Samuel H. Wilen. Wiley, New York. 1981. xv + 447 pp. 16 × 24 cm. $52.50.

The monograph is the result of an international collaboration among Jacques and Collet at the Collège de France (where Biot first described optical activity in organic compounds in 1815) and Wilen at City College, CUNY. Its practical importance is well known to readers of this review, who are aware that the predicted demise of classical optical resolutions has not occurred. Asymmetric syntheses giving the preparatively useful 3:1 ratio of enantiomeric products are encountered rarely. The book appears to be the best single volume on the subject. All topics are referenced fully, some references being to articles published in 1980. Graphic formulas, tables, and phase diagrams are used extensively.

The first half of the work, "Racemates and Their Enantiomer Constituents", contains chapters on types of crystalline racemates, binary mixtures of enantiomers, and the solution properties of enantiomers and their mixtures. This material is not only needed to guide one in carrying out resolutions but also constitutes an encyclopedic survey of the physical chemistry of this area. To comprehend it fully, the reader must reacquaint himself with phase rule diagrams and the experimental technics involved in their construction. An unsuspected use to which the material might be put is its use as a teaching tool in physical chemistry; at least it's a good source of exam questions: The authors reiterate their assertion that the material is indispensable for a description of the properties of enantiomers and their mixtures and that such a description is a prerequisite for the proper attack of a resolution problem. The choice of resolution methods and the probability of their success depend to a large extent on the type to which racemates belong in the solid state. Additionally, failure to recognize the importance of solubility properties of enantiomers and their mixtures can lead to gross errors in resolutions and confusion between optical integrity and racemization. After 45 years of involvement with small- and large-scale resolutions, your reviewer now suspects that he has been living in a fool's paradise; at no time was he in a position to devote the time needed to acquire the comprehension recommended by the authors, but such was never needed. About 40 years ago, Chicago's James K. Senior wrote an amusing article about a mythical chemist named Zilch who discovered a new class of isomers (later named optical isomers) by use of melting points alone, without access to a polarimeter. Part I of the book describes the technics used.

The second half of the book deals with resolutions of enantiomer mixtures. It includes chapters on resolution by direct crystallization, on the formation and separation of diastereomers (both dissociable compounds and covalent compounds), on crystallization-induced asymmetric transformations, and on the experimental aspects and art of resolutions. The last-named chapter has as its purpose the demystification of the unit process so that there need be few, if any, failures in intelligently and systematically executed resolutions based on the information and concepts set forth in the earlier chapters.

The authors believe that crystallization technics are still the best for resolutions involving 100-g lots or tons. They reject the claim that liquid chromatography will soon be the only technic to use. Where the use of diastereomers is needed, a systematic procedure for choosing the correct resolving agent is described, as is a method for choosing the correct recrystallizing solvent. A statistical summary of 819 resolutions is given. The analytical scale technics for monitoring enantiomeric purity during the resolution process are discussed in detail. They include nuclear magnetic resonance, lanthanide shift reagents, chromatography, etc. The chapter concludes with a description of the technics needed to effect the final purification of an enantiomer; these are of course useful in the isolation of pure enantiomers from mixtures formed in most asymmetric syntheses.

The authors make no claim to have written a textbook on the subject of optical isomerism. While some lead references are provided, there is no discussion of meso compounds, asymmetric synthesis, enzymatic resolutions, absolute configuration, the relation between structure and optical rotatory power, the physical basis for optical activity, and polarimetry itself. Perhaps polarimeters aren't important. After all, old Zilch didn't need one. He didn't have to worry about misinterpreting resolutions because he used an impure solvent or an incorrect wavelength when measuring α.

Years ago I had a friend who succeeded in introducing President James B. Conant to a group of chemists without once using the word "Harvard". By the same token, your reviewer hereby lays claim to the distinction of having written the above review without having used "chiral", a word coined in my lifetime by one who couldn't believe that chemists who wrote and spoke all the languages of the civilized world were happy with their vocabulary of terms used to describe optical isomers during the past 150 years.

Amherst, Massachusetts **Edward R. Atkinson**

Amino Acid Analysis. Edited by J. M. Rattenbury. Ellis Horwood Ltd., Chichester, England (outside England, distributed by Wiley, New York). 1981. 380 pp. 15 × 23 cm. $89.95.

The techniques and applications of amino acid analysis have become increasingly sophisticated in recent times. This is reflected in the contributions to the symposium "Amino Acid Analysis in Clinical Chemistry and Medical Research", held in June, 1979, in Edinburgh, which are presented in this book along with subsequently added material.

The historical survey of methods for amino acid determination with which the book opens demonstrates the crucial role which chromatographic techniques play in this field. Subsequently, developments in fluorometric detection with particular emphasis on *o*-phthalaldehyde, gas chromatographic methods and the derivitizations required, high-performance liquid chromatographic analysis of phenylthiohydantoin amino acids, applications of mass spectrometry to peptide sequencing, and derivative spectroscopy of aromatic amino acids are discussed. The coverage of the last topic is substantially more detailed than that of the preceding ones. The presentation of chromatography, particular HPLC, suffers from the very rapid developments in this field in the last 3 or 4 years, so that it is unfortunately rather obsolete. A thought-provoking review of the factors affecting amino acid analysis in studies of protein structure, physiological fluids, and food hydrolysates, an analysis of the results of 11 collaborative studies on amino acid analysis, and a short report on the use of chemiluminescent nitrogen analysis for determination on urine, food stool, serum, and plasma conclude the first part of the book.

The remainder of the volume is devoted to applications. Part 2 discusses amino acid analysis in the study of physiological processes, including protein digestion and absorption, amino acid levels in the plasma of human newborns, and nitrogen metabolism in fetal lambs. Additional chapters in Part 2 cover the use of 3-methylhistidine and hydroxyproline levels in muscle and urine to monitor catabolic processes and the role of amino acids in neural funcion. Part 3 covers applications of amino acid analysis to investigations of systemic disease, including chronic renal failure, acute liver failure, alcoholism, and infant prematurity. In Part 4 the use of amino acid analysis in the study of congenital disorders is reviewed, including a general treatment of the methodology used in inherited disorders of amino acid metabolism, a discussion of the use of fluorometric detection in the investigation of these disorders, and a more detailed review of work done on homocystinuria, Wilson's disease, spina bifida, and anencephaly.

Almost all the analyses in Parts 2 through 4 were conducted by automated ion-exchange chromatography. Unfortunately, the method is not given in a few cases, which seems inappropriate in a book devoted to analysis.

The wide range of applications covered by this book makes it of value for those analytical, clinical, and medicinal chemists,

pathologists, and perhaps pharmacologists and toxicologists interested in which types of questions modern amino acid analysis is trying to answer, best techniques for sample treatment, and special problems associated with biological samples. Those interested in the most up-to-date discussion of the determinative step will need to consult the recent literature.

Department of Medicinal Chemistry **Loren Gelber**
Graduate School of Pharmacy and Allied Health Professions
Northeastern University
Boston, Massachusetts 02115

Enzymes as Drugs. Edited by John S. Holcenberg and Joseph Roberts. Wiley, New York. 1981. x + 455 pp. 17 × 24.5 cm. $59.50.

When medicinal chemists connect enzymes with drugs their first intuitive thoughts will be of enzyme inhibition. It is timely to broaden this attitude and point to the roles enzymes may play in reversing manifestations of disease, not just by exerting increased concentration effects but by acting as therapeutic agents. The enzymes best known for such activities are proteases, which hydrolyze and thereby decrease the size of certain tissue, especially tumors and blood clots. In favor of enzyme-induced therapy is the specificity of many enzymes which permits targeting their action on the cells and tissues to be treated. The major problems in the development of enzymes as drugs are their antigenicity and, since they are hydrolyzable proteins, their short biological half-life. Both the therapeutic applications and the modification of antigenicity and stability are treated in several chapters of the present book for an astonishingly large number of enzymes.

A few specific neoplasias, such as acute lymphoblastic leukemia, can be treated with asparagninase from selected microbial sources, as well as with other nonessential amino acid degrading enzymes. Another biochemical approach is to deprive the tumor of essential amino acids, based on the poorly developed blood supply of many tumors and their sensitivity to loss of essential nutrients. Enzyme therapy is by no means the only way to achieve this, but administration of amino acid antagonists can be tried, to be sure with less specificity for the tumor tissue. Similar conditions prevail for fibrinolytic and defibrinating enzymes (streptokinase, urokinase, and plasmin) and those that replace clotting factors. Membrane permeability of the necessarily high-molecular-weight enzymes counterweigh these advantages. For digestive disorders, the age-old "pepsin" treatment is still in force, and superoxide dismutase, especially from phagocytizing polymorphonuclear leukocytes, can scavenge and thus interfere with a number of pathologies, especially inflammation.

The stability of enzymes intended for therapy can be enhanced by entrapment, immobilization, or formation of polymer–enzyme adducts. Several comprehensive chapters are devoted to these processes. The most imaginative use of enzymes lies perhaps in enzyme replacement in genetic diseases; the successes and failures of this possibility are described vividly and accurately.

The book is illustrated with many tables, referenced thoroughly, and balances enzyme utilization all the way from structural and biochemical to complex medical–therapeutic aspects.

Department of Chemistry **Alfred Burger**
University of Virginia
Charlottesville, Virginia 22901

Brain Neurotransmitters and Receptors in Aging and Age-Related Disorders. Volume 17. Edited by S. J. Enna, T. Samorajski, and Bernard Beer. Raven Press, New York. 1981. xiii + 277 pp. 16 × 24 cm. ISBN 0-89004-643-3. $32.00.

This volume was prepared in conjunction with a symposium held in Houston, TX, in October 1980. The topics covered range from discussions of the effects of aging on brain structure, chemistry, and electrophysiology to the latest advances made in the clinical management of age-related disorders. The relationships between aging, brain neurotransmitters, and their receptors are emphasized, because an understanding of these interactions is necessary for the design and development of more specific and effective pharmacological agents.

This volume will be of interest to neuroscientists in general and neuropharmacologists, neurologists, and psychiatrists in particular. In addition to providing an up-to-date review of this area, the text should also be useful as a reference guide to current laboratory and clinical procedures being used in this field.

Staff