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# Book Reviews

**Control of Renin Secretion.** Edited by Tatiana A. Assaykeen. Plenum Press, New York, N. Y. 1972. 290 pg. 17 cm × 26 cm. $17.50.

The subjects covered in this book are the proceedings of a workshop held in 1971 at the Kroc Foundation in Santa Ynez, California. Consideration is given to most, if not all, factors known to influence renin release and is up-to-date with respect to the knowledge in this field. Emphasis is on the physiology of the sympathetic regulation of renin release. Although the conclusions drawn from some of the investigations are not in complete agreement, in general it can be said that sympathetic stimulation and administration of epinephrine and isoproterenol activate β-receptors, possibly located in the juxtaglomerular apparatus, which mediate the process of renin release. There are suggestions that renal cyclic AMP might also be brought into play to evoke renin release, but this is by no means a certainty. Other mechanisms of renin release, beside nervous regulation, rely on alteration of sodium load delivered to the distal tubule and arterial pressure change detected at some site in the kidney. In one investigation the nonfiltering kidney preparation was used as a means of determining the participation of the three factors cited above. Related topics concerning release of prostaglandin $E_2$ from renal medullary interstitial cells and influences on aldosterone secretion from the adrenal cortex are also touched upon. In regard to aldosterone there is evidence that another humoral substance exists in addition to angiotensin II which may regulate its secretion. Human studies are presented in which relationships between renin and aldosterone plasma levels and various disease states were sought. It was apparent from the results of these studies that in certain clinical conditions a simple inverse relationship between sodium concentration in plasma and renin and aldosterone does not exist. An interesting result of one of these studies was that angiotensin II generated intrarenally may produce deleterious effects in acute renal failure. All in all, these presentations make worthwhile reading for both experts in the field and for those who seek to bring themselves up-to-date in the renin-angiotensin field, particularly in relation to renin release.

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**Chemical Modification of Proteins.** By G. E. Means and R. E. Feeney. Holden-Day, Inc., New York, N. Y. 1971. 254 pp. 17.5 × 23.5 cm. $12.50.

Despite the increasing dependence of the protein chemist upon the X-ray crystallographer for definitive, detailed answers to questions of protein shape and binding site topography as well as presumptive evidence for functional residues in enzymes, the literature on the chemical modification of proteins, most often with the same goals in mind, has not abated, but rather continues to grow at an impressive rate.

This observation attests to the tremendous utility of modification methodology which still characterizes many areas of contemporary protein research. Very often chemical probes of active sites and functional residues may be the only feasible approach in characterizing enzymes unsuitable for X-ray diffraction studies by virtue of insufficient quantities; instability; lack of success in obtaining *any* crystals, suitable crystals, or isomorphous derivatives; or which are simply too complex for the present state of the art.

Even when crystallographic data on an enzyme are available, chemical modification studies, buttressed by kinetics measurements, are required to confirm catalytic activity in residues implicated by X-ray. A particularly instructive example of such corroboration work is found in the recent chymotrypsin study of Robinson and Belleau (*J. Amer. Chem. Soc.*, 94, 4376 (1972)). Furthermore, chemical approaches—often a probe of "buried" *vs.* "exposed" residues—may be the method of choice to grapple with the vexing problem of whether a protein's structure under physiological conditions is the same as that in the crystal.

The study of modified enzymes, *per se*, has provided new insights into the relationship between structure and function and the mechanism by which enzymes act. Several have shown *enhanced* activities toward synthetic substrates, increased stabilities, or effective pH ranges. In the case of ribonuclease, an active "dimer" can even be put together from inactive monomer components. Superfluous residues or sequences have been ascertained by modification or cleavage reactions, respectively.

Chemical modifications leading directly to cleavage or combined with proteolytic enzymes in which new sites for attack are created are playing an ever growing role in the sequencing of proteins.

These are only a few of the reasons that a comprehensive yet digestible survey of modification techniques and applications is welcome and timely.

This book, intended as a graduate school text, is thorough and critical enough for experienced workers to profit from. They will find particularly useful the thoroughly cross-referenced, tabular presentation of much of the material. Tables on side-chain reactivities, reversible modifications, and bifunctional reagents are representative.

The book is organized in three main parts. The first section treats briefly the history of early work ("preautoanalyzer"), the development of methodology, current applications such as affinity labeling, the redirection of proteolysis for sequencing, and the introduction of "reporter" groups. A survey of general aspects of protein reactivity and a particularly important, critical section on monitoring changes in the structure and activity of enzymes to ascertain that changes in these properties are due solely to the reaction being studied complete this section.

The second and by far longest section covers the great bulk of the modifying reagents which have been used, organized by reaction type. This scheme echoes the approach used by Cohen in his excellent treatment of this subject in *Annu. Rev. Biochem.* (1968). A general discussion of the scope and mechanism of each reaction type, *e.g.*, acylation, is followed by details on the dozen or so particular acylating reagents, *e.g.*, *N*-acetylimidazole, presently in use. In this manner, alkylations; esterification; amide formation, reduction, and oxidation, electrophilic substitution; and a miscellaneous class are covered. One might quibble with the pigeonholing of a few reactions (cyanogen bromide, sulfenyl halides, and *N*-bromosuccinimide all behave as electrophilic reagents yet appear in other sections), still the organization should serve the biochemist well. Each section is adequately illustrated with reaction schemes as well as data and a number of well-chosen applications from the recent literature. In this regard, particularly, the authors have done an excellent job. The searching of the biochemical literature for modification work can be a frustrating and time-consuming job since very often a particular modification will not be abstracted or appear in the title but will lie buried in the text of the paper.

The third and briefest section—a series of "recipes" comprising a short "cook book" for protein chemists—may be handy for students but will be of dubious benefit to anyone with access to a good library or even to such bibles as Volume 11 of "Advances in Enzymology." Still, hardly a reason not to add this book to one's own library.

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**L-Dopa and Behavior.** Edited by Sidney Malitz, with 19 contributors. Raven Press, New York, N. Y. 1972. 144 pp. 23 × 16 cm.

As a sequel to the therapeutic use of L-dopa in parkinsonism, the pharmacology and the role of dopamine in mental function have been studied extensively. Since dopamine, like other catecholamines, 5-HT, etc., does not cross the blood–brain barrier, many of the clinical observations are based on the precursor amino acid, L-dopa. This compound increases alertness and causes a little euphoria bordering on hypomania, but has no striking effect on depression. Dopa does not restore the dopamine-depleted nigrastriatal neurons but may restore, at least in part, the functions of the motor system controlled by these neurons. Since dopa is administered clinically in the range of a food rather than at therapeutic doses, a relatively large amount of hydroxylated and methylated metabolites of both dopa and dopamine appears, with consequent "side effects" including a depletion of biochemical methyl donors and of the level of

multifunctional enzymes involved in amine metabolism. These complex and interwoven processes can be traced to dopaminergic and related mechanisms, and have already stimulated much thought about the biochemical causation of mental illnesses.

A stereochemical comparison by Snyder, *et al.*, of the activities of the stereoisomers of norepinephrine, amphetamine, and tranylcypromine lists interesting experimental findings but in their explanation overlooks the absolute configurations of these amines. The book should be of great interest to biochemists, psychopharmacologists, experimental behaviorists, and modern experimental psychiatrists.

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**Antiepileptic Drugs.** Edited by D. M. Woodbury, J. K. Penry, and R. P. Schmidt, with 52 contributors. Raven Press, New York, N. Y. 1972. xxiii + 536 pp. 19.4 × 26 cm. $19.75.

This may well be the definitive book on anticonvulsants for the neurologist, neuropharmacologist, and general physician. It gives the history and development of anticonvulsant drugs, describes laboratory tests in animals and in man, and for the experimenter spells out the procedures prescribed for clinical trials. Each known clinically useful antiepileptic agent is described in detail. Dosage forms, mode of action, drug metabolism, side effects (useful and untoward), toxic manifestations, indications, and contraindications are discussed. Even drugs still in an experimental clinical stage are included. Format and print are unusually good, chemical formulas are correct, and the air of authoritative compilation pervades each chapter.

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**Mass Spectrometry: Techniques and Applications.** Edited by George W. A. Milne. Wiley-Interscience, New York, N. Y. 1971. x + 521 pp. 15 × 22.6 cm. $24.95.

The editor has attempted to critically review recent developments which have had, and will continue to have, a great impact on mass spectrometry. Since the chapters were all completed during the first part of 1970, the presentations are well documented up to that time. Each of the 19 contributors to the 12 chapters is an expert in an area of application or in a technique associated with the broad field of mass spectrometry, and each writes about his area of experience. Thus the book consists of a series of reviews of the state of the art and is not intended to be an introduction to mass spectrometry or a reference book.

Approximately a third of the book will be especially useful for medicinal chemists and biochemists who use mass spectrometry and are not concerned with the operation of the instrument. A chapter describes the areas of medicine and biochemistry to which mass spectrometry has been applied. Since this is a rapidly expanding area of research, the reader must remember that the 232 references cover the chemical literature through the first of 1970. More specialized chapters treat the employment of stable isotopes, emphasizing biosynthesis and metabolism, and the determination of the sequence of amino acid units in peptides. A chapter on recent developments in ionization techniques contains a section on ion–molecule reactions in which the mass spectra of natural products obtained by chemical ionization can be compared with the mass spectra obtained by electron impact. Since peaks in the molecular ion regions are much more intense in the chemical-ionization mass spectra, the two ionization techniques complement one another.

The other chapters discuss the applications of data acquisition and analysis systems to mass spectrometry, use of computers for storing and searching complex files of mass spectra and for interpretation of mass spectra, types of interfaces used in gas chromatography–mass spectrometry combinations, methods by which mechanisms of reactions in the mass spectrometer can be studied, and various aspects of metastable transitions. Mass spectrometrists would find these chapters more useful than would the medicinal chemist who uses mass spectrometry as an analytical technique. A considerable background in mass spectrometry is helpful when one reads these chapters. For example, photographic recording and electrical recording of data from high-resolution mass spectrometers are covered in separate chapters, but there is no impartial comparison of these two techniques. Also, a long and detailed chapter on an application of artificial intelligence to the interpretation of mass spectra is included. It is difficult to sort out the actual application from the considerations of creativity, human *vs.* artificial intelligence, and other philosophical problems.

In general, the chapters are written by relatively young mass spectrometrists, active in research, and are easy to read. One finds a few problems in the editing, such as structures being left off some chemical-ionization mass spectra, the use of the symbols $A$ and $\nu$ for frequency factors in separate chapters with no cross-reference, etc. It is unlikely that every subject will be interesting to a reader. Since the chapters are not closely related and there is little cross-referencing, one can choose chapters and feel free to read them in a different order than the one in which they are presented.

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