

## Book Reviews

**The Alkaloids. Volume 4.** J. E. Saxton, Senior Reporter. *Specialist Periodical Report of the Chemical Society*, London, 1974. xii + 443 pp. 13.5 × 21.5 cm. £14.00.

This fourth volume in the series of *Specialist Periodical Reports* on Alkaloids follows the pattern established by its predecessor and comprises summaries of progress in the whole field of alkaloid chemistry for the period July 1972–June 1973. A more extended review of the aporphine alkaloids by M. Shamma and S. S. Salgar deals with developments since 1967. The reporters describing the various classes of alkaloids are the same as in Volume 3 and the same high standard has been maintained. The reviews are often critical, questioning dubious structure assignments or interpretations of biosynthetic experiments. A large number of new alkaloids continue to be isolated, some with quite novel structures [nicotine blue (p 417), maytansine (p 423), zoanthoxanthine (p 424)]. Research activity in the area of alkaloid chemistry does not appear to be diminishing and many challenges remain for the organic chemist interested in natural product synthesis. However, seven total syntheses of camptothecin (three are described in the present volume) are probably excessive, especially when this alkaloid is of no medicinal value. The book is well illustrated with numerous structural formulas and reaction schemes, making it very readable and easily understood.

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**Advances in Enzymology. Volume 41.** Edited by Alton Meister. Wiley-Interscience, New York, N.Y. 1974. 364 pp. 16 × 24 cm. \$20.95.

The latest volume of this well-established series deals with six fairly unrelated areas in enzymology of which several would be of particular interest to chemists involved in drug design. These topics include an excellent article on the enzymology of gout by W. N. Kelley and J. B. Wyngaarden. Gout in the broadest definition of the term represents a heterogeneous group of diseases of diverse etiology usually characterized by hyperuricemia. This article concentrates on recent advances made toward elucidating the mechanisms responsible for the excessive production of uric acid; however, no attention is given to the area of defective uric acid excretion. The various proven and proposed enzyme abnormalities resulting in primary gout are extensively reviewed. A brief discussion is also provided about other enzyme abnormalities in purine metabolism in which the major clinical features are not related to uric acid precipitation (e.g., Lesch-Nyhan syndrome, xanthuria, etc.).

Another of the articles contained in this volume, which was written by I. Fridovich, a pioneer in the field, reviews the biochemistry of superoxide dismutases. The biochemical significance of superoxide radical ( $O_2^-$ ) has only recently been recognized. It has been proposed that superoxide radical may play an important role in oxygen toxicity and that superoxide dismutases constitute the primary defense against this radical. This article places particular emphasis on the current knowledge of the properties of these enzymes and of the substrate superoxide radical. Considering the potential biochemical importance of superoxide radical and the enzymes which catalyze its breakdown this article would serve as an excellent introduction to the literature in this rapidly expanding area.

Two of the chapters in this volume deal with the biochemistry of serum proteins. One of these chapters written by G. Ashwell and A. Morrell describes a new role for surface carbohydrates in regulating the serum survival time of plasma glycoproteins. The hypothesis was advanced and supporting data were presented to show that many, if not most, of the serum glycoproteins require surface carbohydrates such as sialic acid for continued viability in circulation. Another chapter dealing with serum proteins written by V. Najjar reviews in detail the physiological role of  $\gamma$ -globulin.

The comparative specificity of microbial proteinases is the subject of one of the review articles. In this chapter written by K. Morihara is described the classification of the microbial proteinases, their kinetics of hydrolysis of small substrates, and finally the effects of secondary interactions (the nature of the amino acids

surrounding the site of cleavage) on hydrolysis of large peptide or protein substrates. Some comparative data between microbial and animal proteinases are also described which might make the chapter appealing to those interested in antibiotics.

The final chapter written by G. J. Cardinale and S. Udenfriend deals with prolyl hydroxylase and its role in the biosynthesis of hydroxyproline. The abundance of hydroxyproline in fibrous proteins such as collagen has stimulated extensive studies of the enzyme responsible for its formation. Work in this area has been stimulated by the observation that the hydroxyproline residues in collagen play an important role in maintaining the structural integrity of this molecule. Also briefly discussed in this article is a related enzyme lysyl hydroxylase, which catalyzes the formation of hydroxylysine.

As is generally the case for the series "Methods in Enzymology", this latest volume very concisely, but yet extensively, reviews topics of current interest in enzymology and related areas of molecular biology. As is often the case with this series, this latest volume contains several articles which would be of particular interest to medicinal chemists.

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**Regulation in Metabolism.** By E. A. Newsholme and C. Start. Wiley, New York, N.Y. 1973. vii + 349 pp. \$17.50.

Some of this book could supplement a first course in biochemistry for senior undergraduates or first year graduates, but its various parts are quite uneven with respect to content and quality. The first chapter, Introduction to Regulation in Metabolic Pathways (33 pp), is weakest. As control of many biological processes amounts to control of a nonequilibrium process, much would have been gained by clearer definition of some of the concepts of nonequilibrium thermodynamics. The thermodynamic basis for why a nonequilibrium process must always be less efficient than an equilibrium process is easily understood in terms of entropy. Further, the relationships between flux, the thermodynamic idea of affinity, and kinetic coefficients never emerge clearly. Consequently, the puzzle of why "it must not be assumed that the rate of the pathway will be governed by the degree of displacement from equilibrium. The flux is usually governed by other factors that are quantitatively unrelated to displacement . . ." (p 9) is never really solved for the reader; yet, this is an important idea.

Chapter 2, Molecular Mechanisms in the Regulation of Enzyme Activity, gives a good treatment of the idea of allostery but the applicable kinetic models are short changed (5 pp) with respect to the treatment given the equilibrium binding models (27 pp). Those with a special interest in conformational responses of enzymes should study the superb treatment given the topic by Citri [*Adv. Enzymol.*, 37, 397–648 (1973)].

The heart of the book and its main merit lies in Chapters 3–7 where regulation of carbohydrate metabolism in muscle and regulation of glycogen metabolism, of fat metabolism, and of carbohydrate and fat metabolism in liver are given useful introductory treatment. There is no treatment of regulation of protein or glycoprotein metabolism and the publisher's claim that this book discusses "all the major energy producing and utilizing pathways in the cell" is not supportable.

Some metabolic effects of growth hormone, insulin, adrenaline, and glucagon are considered. There is, however, no discussion of thyroid hormones or estrogens, both of which have important regulatory effects. The index, printing, and layout of the book are good, but I would have preferred the various appendixes collected at the back. Dispersing them through the book interrupted its flow, at least for me.

I do not believe most medicinal chemists would choose to own this book. A few, perhaps those interested in drugs for control of diabetes and hyperlipidemias, might choose parts of it to review some of the underlying biochemistry.

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