1 mL per kilogram of body weight. Three hours later, the ensuing edema was measured by electronic plethysmographic procedures. The amount of paw swelling (3 h minus 0 h value) was determined for each rat, and the mean value in the substance-treated animals was expressed as a percentage of the mean value obtained in the vehicle-treated controls. The method described above was utilized with the exception that the rats were bilaterally adrenalectomized under ether anesthesia and allowed to recuperate for 7 days prior to use. Adrenalectomized rats received 1.0% sodium chloride and 2.5% dextrose in their drinking water, together with the standard lab chow diet.

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Book Reviews

Concepts in Drug Metabolism. Parts A and B. Edited by Peter Jenner and Bernard Testa. Marcel Dekker, New York. Part A: 1980. xi + 409 pp. 16 × 24 cm. $49.50. Part B: 1981. x + 627 pp. 16 × 24 cm. $65.00.

Part A of this two-volume set contains a number of chapters that should be of particular interest to those medicinal chemists who include drug metabolism among their principal or ancillary activities. An extensive chapter (123 pages) by Testa and Jenner explores "A Structural Approach to Selectivity in Drug Metabolism and Disposition". Topics included in this presentation are substrate regioselectivity, substrate stereoselectivity, product regioselectivity, product stereoselectivity, and the application of quantitative structure–activity relationships in drug metabolism and disposition. Similarly, Trager's chapter entitled "Oxidative Functionalization Reactions" includes discussions of stereoselectivity and regioselectivity in monooxygenase-mediated reactions, as well as a rather detailed analysis of the concept of the oxenoid mechanism. An appreciation of the concepts presented in these two chapters, in conjunction with a knowledge of the potential toxicity of certain types of metabolites, should be of value to medicinal chemists who wish to incorporate metabolic principles into their approach to drug design.

Part A also contains a concise and useful review of the biochemistry and significance of conjugation reactions by Caldwell, as well as chapters on analytical techniques, extrahepatic drug metabolism, and developmental drug metabolism. The final chapter focuses upon the use of metabolite data in the evaluation of pharmacokinetics.

The first chapter of Part B is a review by Parke of the normal physiological functions of the endoplasmic reticulum (glycoprotein synthesis, lipid metabolism, cholesterol biosynthesis, etc.) and the pathological changes that occur when the endoplasmic reticulum is damaged as a result of aging or as a result of exposure to environmental chemicals. This chapter is followed by Mannering's comprehensive review (113 pages, 499 references) entitled "Hepatic Cytochrome P-450-Linked Drug-Metabolizing Systems". In this chapter the characteristics, functions, and interactions of the components of the monooxygenase system are considered with a particular emphasis being placed on cytochrome P-450 multiplicity.

The chapter titled "Toxification and Detoxification as a Result of Xenobiotic Metabolism" consists primarily of brief but lucid reviews of the metabolic activation and deactivation of paracetamol (acetaminophen), phenacetin, benzo[a]pyrene, 2-(acetylamino)fluorene and allyl alcohol. This presentation provides a useful introduction to the principles of metabolic toxification but it is not an in-depth treatment of the subject. Other chapters in Part B emphasize such topics as the relevance of enzyme induction and inhibition of drug action, the genetic aspects of drug metabolism, evolutionary consideration of drug metabolism and drug toxicity, the in vivo assessment of hepatic drug disposition, and altered drug disposition in disease states. The authors of the latter chapter conclude that the effects of disease states on protein binding, absorption, distribution, and elimination may be of greater relevance to alterations of drug actions than are the effects of disease states on drug metabolism. The final chapter, a philosophical discourse entitled "Xenobiotic Metabolism: Necessity, Chance, Mishap, or None of the Above?", raises some intriguing questions for which there may be no definitive answers.

There are certain topics that are covered in various degrees of depth in several chapters. Among the more prominent examples are induction and inhibition of cytochrome P-450, the multiplicity of cytochrome P-450, and metabolic activation as it relates to toxicity and carcinogenicity. As the editors point out in the preface, such overlap is unavoidable, and in some respects even desirable, if the goal of presenting a conceptual approach to major topics in drug metabolism and allied fields is to be achieved.

Both Parts A and B cover the literature through 1978 and a number of chapters cite papers that were published in 1979. These books constitute an important contribution to the literature of drug metabolism and they should serve as highly useful resources to anyone who is interested in the field. "Concepts in Drug Metabolism" is worthy of occupying space on the shelf next to the invaluable "Drug Metabolism: Chemical and Biochemical Aspects", which was published by Testa and Jenner in 1976.

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Annals of the New York Academy of Science. Volume 356. Calmodulin and Cell Functions. Edited by D. Martin Watterson and Frank F. Vincenzi. New York Academy of Science, New York. 1980. xii + 446 pp. 16 × 23.5 cm. $86.00.

Calmodulin is a ubiquitious intracellular protein which binds calcium ions and functions as one of several pathways for the expression of Ca^{2+}-mediated effects. Research interest in calmodulin is expanding at a rapid pace. This volume will certainly be the last to review the broad scope of calmodulin roles in under 500 pages at a price under $100. We will no doubt look forward to future volumes, each of which will deal with only one of the 30 or so major aspects outlined in this work.

This volume provides a summary of the 1980 New York Academy of Sciences conference of the same name. As is the custom for the annals from such conferences, there are about 30 papers of substantial size (average size = 12 pages) and abstracts of poster sessions (44 in number). Papers have been divided into six sections: (1) Biochemistry of Calmodulin; (2) Calmodulin and Supramolecular Structures; (3) Protein Phosphorylation and Calmodulin; (4) Cyclic Nucleotides and Calmodulin; (5) Membrane Transport and Calmodulin; (6) Cellular Receptors and Calmodulin. The contributors are an absolutely outstanding collection of investigators in each of these areas, including C. Y. Cheung, one of two individuals credited with the "definitive" recognition of calmodulin.

Hypotheses for the involvement of calmodulin in cellular regulation abound. However, true to the inquisitive basis of science, more new questions are raised than are answered. For instance, the activation of phosphodiesterase activity and inhibition (or activation) of adenylate cyclase by calmodulin has fueled further interest in the complex manner in which these two

second messenger substances are interrelated. The excitement engendered by the recognition of calmodulin's widespread occurrence must be tempered by the difficulties encountered in determining the appropriate perspective for its roles. Despite the fact that this volume will eventually be superceded by more extensive treatises, it does provide a high quality overview of this important area of biomedical research.

The price of the hard-bound volume seems a bit expensive at first, but the quality of materials is first rate, and the text is replete with tables and figures as well as micrographs which have certainly contributed to its price. Overall, it is a recommendable resource for graduate students or other investigators who would like to get a feel for the way in which nature has employed this remarkable transducer—calmodulin.

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Reviews in Biochemical Toxicology. Volume 3. Edited by Ernest Hodgson, John R. Bend, and Richard M. Philpot. Elsevier/North Holland, New York. 1981. ix + 368 pp. 17 × 25 cm. $49.50.

This is the third volume in a continuing series devoted to reviews of the biochemical mechanisms of toxicity elicited by xenobiotic substances. As in the previous volumes, high standards of scholarship have been maintained, the only drawback being that a typewriter format is still being used. In this age of high-speed composition and printing by computer technology, the compromised readability due to the light type is unfortunate. However, structural formulas—where they occur—are faithfully reproduced. For example, the interesting chapter by D. H. Swenson on the metabolic activation and detoxication of aflatoxins, the highly carcinogenic fungal metabolites, abound with structures without which the chapter would be incomprehensible. Similarly, the review by C. E. Carniglia on the metabolism of aromatic hydrocarbons by bacteria, fungi, and algae gives metabolic pathways with complete structures showing the stereoselectivity of the enzymatic reactions. By contrast, what is otherwise an excellent review by L. L. Paulson on the oxidation of foreign sulfur compounds by the microsomal flavin-containing monooxygenases suffers from the absence of structural formulas depicting thioamide sulfoxides, formamidine sulfenic acids, or carbodithioic acids. This could confuse those who are unfamiliar with organic sulfur chemistry and its specialized nomenclature.

Two other reviews deserve special mention. "Mechanisms of Fibrosis" by G. C. Fuller gives an accurate overview of the present state of knowledge of collagen biosynthesis and focuses on fibrotic lesions of the liver and lungs, the two organs most frequently affected. The other is the review by D. Mansuy on the use of heme complexes as models for cytochrome P-450 reactions. Both oxidations (hydroxylation) and reductions (of polyhalogenated compounds, aromatic nitro compounds) are discussed, and a proposed interpretation of the molecular mechanism for CCl_4 biotransformation catalyzed by the heme vis-a-vis cytochrome P-450 system is presented.

The volume is divided into discrete subject categories entitled Xenobiotic Metabolizing Enzymes (UDP-glucuronyl transferase; flavin containing monooxygenase), Biochemical Toxicology of Organs and Organ Systems (lungs), Toxic Compounds (benzene; aflatoxins), Modes of Toxic Action (mechanisms of fibrosis; tumor promotion), Methodology of Biochemical Toxicology (heme models), and Comparative Toxicology (H.C. metabolism by bacteria, etc.). This makes for diversity and balance, thereby serving the needs of and attracting a wider readership.

This third volume complements the first two and should be part of any toxicology collection.

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Books of Interest

Basic and Clinical Endocrinology. Volume 1. Radioassay Systems in Clinical Endocrinology. Edited by Guy E. Abraham. Marcel Dekker, New York. 1981. xiv + 669 pp. 18 × 26 cm. $67.50.

Textbook of Clinical Neuropharmacology. By Harold L. Klawans and William J. Weiner. Raven Press, New York. 1981. x + 371 pp. 16 × 24 cm. $32.50.

Advances in Epileptology. XIIth Epilepsy International Symposium. Edited by Mogens Dam, Lennart Gram, and J. Kiffin Penry. Raven Press, New York. 1981. xvii + 699 pp. 16.5 × 24 cm. $75.00.

Lange's Handbook of Chemistry. 12th Edition. Edited by J. A. Dean. McGraw-Hill, New York. 1979. xv + 1464 pp. 16 × 23.5 cm. $38.50.

Organ-Directed Toxicity: Chemical Indices and Mechanisms. IUPAC Proceedings of the Symposium on Chemical Indices and Mechanisms of Organ-Directed Toxicity, March, 1981, Barcelona, Spain. Edited by S. S. Brown and D. S. Davies. Pergamon Press, Elmsford, NY. 1981. xii + 341 pp. 19 × 27.5 cm. $90.00.

Chemiosmotic Proton Circuits in Biological Membranes. Edited by V. P. Skulachev and P. C. Hinkle. Addison-Wesley Advanced Book Program, Reading, MA. 1981. xviii + 633 pp. 16.5 × 24 cm. $29.50.

Techniques of Chemistry. Volume 16. Separations by Centrifugal Phenomena. By Hsien-Wen Hsu. Wiley, New York. 1981. xvi + 466 pp. 15.5 × 23.5 cm. $54.50.

CIBA Foundation Symposium. Number 78. Metabolic Activities of the Lung. Excerpta Medica, Amsterdam. 1981. ix + 401 pp. 17 × 24.5 cm. $66.25.