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Pion Advanced Biochemistry series  Editor J. R. Lagnado

Protein Phosphorylation
M. Weller

February 1979, 557pp., £29.00  0.85086.062.8

The literature on protein phosphorylation is large and increasing rapidly, thus it is a suitable time to present a book which summarizes, reviews, and critically discusses all the work which has been done on this subject, including studies of the properties and function of proteins containing covalently bound phosphorus. The early chapters describe and discuss the properties of the protein kinase and phosphatase enzymes. Other chapters deal with cyclic nucleotides, the action of hormones, and protein phosphorylation; nonenzymic proteins which contain covalently bound phosphorus—phosvitin, casein, ovalbumin, fibrinogen; phosphorylation in relation to enzymic function; the role of phosphorylation in the control of the movement of ions; and protein phosphorylation in the nucleus; ribosomes; the cell membrane; the nervous system; various tissues; and viruses. Appendices describe techniques useful in the investigation of protein phosphorylation and the properties of phosphoproteins.

The book will be of value to anyone carrying out research on protein phosphorylation, or on proteins which contain covalently bound phosphorus, and will provide instructive reading for advanced students, and workers in other fields who may not have appreciated the progress of research in protein phosphorylation.

A Pion publication distributed by Academic Press

Pesticide Microbiology
Microbiological Aspects of Pesticide Behaviour in the Environment

Edited by I. R. Hill and S. J. L. Wright

November 1978, xx + 844 pp., £38.00  0.12.348650.5

The growing world concern over the damage to the environment caused by man-made toxicants has recently confronted scientists with a new series of problems — how to comply with tightening legislation, how to monitor the fate of pesticides once discharged into the environment, how to safeguard food supplies and human and animal health while also recognizing the important role of microbial activities in the ecosystem. The harmful effects on birds, gardens and wild flowers caused when pesticides miss their specific target are easy to observe and control: equally serious and permanent is the possible wide-scale damage to microorganisms, which affect fertility and, consequently, productivity of environments. This book presents the subject of pesticide microbiology in a balanced and authoritative way, neither minimizing nor over-emphasizing the risks involved in our chemical interventions in the environment, and focusing attention on the diverse microbiological aspects of the fate and behaviour of pesticides. It describes how microbes can affect the activity and persistence of pesticides and how, in turn, pesticides can influence the activities of these members of the non-target biota. It recognizes, too, that interactions with microbes cannot be considered in isolation from other (physical, chemical and biological) factors concerned with pesticide behaviour in the environment.

Pesticide Microbiology will provide a timely appraisal of a rapidly expanding field for the wider scientific community in the areas of microbiology, soil science, ecology, biochemistry and crop protection. It is written with detailed attention to methodology, and will also serve as an ideal introduction to the subject for the post-graduate or advanced undergraduate, in including basic chapters on pesticides and microbial environments.

Mammalian Metabolism of Plant Xenobiotics

R. R. Scheline

November 1978, xii + 502pp., £28.00  0.12.623350.0

Plant xenobiotics, which can roughly be equated with those compounds termed 'secondary plant metabolites' are of considerable importance in many fields of research such as pharmacology, toxicology, medical and natural products chemistry, and food sciences. It is important therefore that information on their metabolites and the pathways leading to them, is readily available to those working in such active areas of research. A large quantity of literature on xenobiochemistry has been published in recent years, but references are scattered and location of an overall summary of the metabolism of a specific compound is often difficult and time consuming. Accordingly this volume has been compiled to provide a comprehensive survey of the current knowledge in a specific part of this large field, namely that of plant xenobiotics. The introductory chapter outlines the most common pathways of mammalian metabolism of plant xenobiotics. Subsequent chapters deal with the fate of individual plant compounds, which are grouped according to chemical class. The metabolic processes are extensively illustrated throughout with structural formulae.

All those actively involved in the fields of biochemical pharmacology, toxicology, natural products chemistry and biochemistry, phytochemistry and related fields will find this book a most useful reference source for years to come.
Biochemical Mechanisms of Liver Injury

Edited by T. F. Slater

November 1978, xii + 824pp., £40.00 0.12.649150.X

The book is primarily concerned with describing the variety of biochemical disturbances underlying a number of important liver injuries and diseases. Certain aspects in particular are emphasized, such as the role of metabolic activation of many hepatotoxins and hepatocarcinogens in the development of liver injury; the transient nature of such activated intermediates which makes rapid reaction studies necessary for their investigation; the importance of free radicals in the biochemical disturbances produced by these transient intermediates; and the multiplicity of protective mechanisms that may be applied. The book also includes some chapters dealing with the application of relatively new techniques to problems of liver injury, such as electron spin resonance, nuclear magnetic resonance microdensitometry and hepatocyte culture. The contributions are all by acknowledged experts in the field, and include substantial amounts of previously unpublished material together with several novel concepts introduced for the first time. The book is an important contribution to research on the biochemical aspects of liver injury, providing a detailed and up-to-date survey of the subject as well as a good source of reference. It will be invaluable for all involved in research in the area, such as clinical researchers, biochemists, toxicologists, pharmacologists and virologists.

FEMS Symposium No. 5
Antibiotics and other Secondary Metabolites

Biosynthesis and Production

Edited by R. Hütter, T. Leisinger, J. Nüesch and W. Wehrli

November 1978, xii + 256pp., £14.40 0.12.363250.1

This volume presents the main lectures given at the 5th FEMS Symposium, held in Basel, Switzerland, from September 14-16, 1977.

The book begins by considering some general aspects of secondary metabolism including its importance for the producing organisms themselves. When considering secondary metabolism as a 'play-ground of evolution' it was proposed that 'secondary metabolites' should be regarded as 'specific metabolites of restricted distribution'. Following this are full discussions on both the contributions of deregulation or changed regulation of metabolism and the role played by biotechnology in increasing the production of secondary metabolites. Microbial transformations are discussed as type reactions as well as with respect to their application in natural product chemistry.

Photosynthetic Oxygen Evolution

Edited by H. Metzner

October 1978, xvi + 532pp., £18.00 0.12.491750.X

The book is a collection of the papers presented during the Symposium "Photosynthetic Oxygen Evolution" held at Tübingen in September, 1977. Photosynthesis specialists, photochemists and electrochemists have contributed towards this multidisciplinary discussion of the problems of light-induced oxygen evolution. Dealing mainly with the energetics and mechanisms of light-induced charge transfer reactions in green plant cells, the papers include discussions on how plant cells can create a strongly oxidizing power; how the oxidized donor regains its missing electrons; and the role of organically bound manganese in the charge transfer. There are also sections on the structure and ontogenetic development of the oxygen producing system of the chloroplasts. Throughout, emphasis is placed on the need to integrate the experimental results and current hypotheses, both to gain a better understanding of the problem and also to look for practicable new techniques to perform crucial experiments.

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Uptake of citrate by synaptosomes and synaptosomal mitochondria from rat brain. Urzula Rafalowska and Hanna Ksiezak.
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Diphenylphosphoryl azide (DPPA) is a stable, non-explosive liquid with unique applications in organic synthesis, some of which are described below.

**Synthesis of Carbamates**

DPPA effects the conversion of carboxylic acids to carbamates under mild conditions without isolation of a potentially explosive carbonyl azide, thus providing a one-pot equivalent of the Curtius reaction:

\[
\text{RCO}_2\text{H} + (\text{PhO})_2\text{P(=O)}\text{N} = \text{O} \xrightarrow{\text{ROP}} \text{RNH-C=O}^\circ
\]

**Peptide Synthesis**

As an azide transfer reagent, DPPA effects the coupling of N-acetylcarboxylic acids or peptides with amino acid or peptide esters without racemization:

\[
\text{R} - \text{NCOHCH}_2\text{CO}_2\text{H} + \text{H}_2\text{NCHCO}_2\text{Me} \xrightarrow{1 \text{ DPPA/DMF}} \text{R} - \text{C=O}\text{Me} + \text{H}_2\text{O}
\]

**Synthesis of Thiol Esters**

Treatment of a carboxylic acid and a thiol with DPPA and triethylamine affords the thiol ester:

\[
\text{RCO}_2\text{H} + \text{R''SH} \xrightarrow{1 \text{ DPPA/DMF}} \text{R''C-SR'}
\]

Again, the reaction proceeds with little or no racemization; even a highly functionalized cephalosporin derivative afforded the corresponding thiol ester.

**Stereo-specific Synthesis of Azides from Alcohols**

The reaction of alcohols with DPPA, triphenylphosphine and diethyl azodicarboxylate gives azides in 60 to 90% yield without racemization.

\[
\text{ROH} \xrightarrow{\text{EtOCON=NOCOEt/Ph,P}} \xrightarrow{\text{DPPA/THF}} \text{RN}_3
\]

**References**

4. 17,875-6 Diphenylphosphoryl azide (DPPA) 25g $24.45
100g $65.15

**2-Chloro-1-methylpyridinium Iodide**

Recent reports in the chemical literature have established 1-alkyl-2-haloazepyrindinium salts as effective reagents for the synthesis of carboxylic esters, carboxamides, 2-pyridyl sulfides, lactones, alkyl halides, and carbodiimides.

Reactions of carboxylic acids and alcohols with 2-chloro-1-methylpyridinium iodide (1) in the presence of two molar equivalents of tri-n-butylamine afforded the corresponding carboxylate esters.  

\[
\text{RCO}_2\text{H} + \text{RNCOH} \xrightarrow{\text{1 DPPA/DMF}} \text{R'C-O = O}^\circ + \text{Me}_2\text{N}
\]

Carboxamides are formed rapidly in high yields by the reactions of free carboxylic acids and amines with 2-chloro-1-methylpyridinium iodide. This reaction is applicable to both secondary and tertiary alkyl-substituted acids and amines.

\[
\text{RCO}_2\text{H} + \text{R'NH-R''} \xrightarrow{\text{1 DPPA/DMF}} \text{R'C-O = O}^\circ + \text{Me}_2\text{N}
\]

Direct lactonization of \(\omega\)-hydroxy acids has been successfully carried out under mild conditions by treatment with 2-chloro-1-methylpyridinium iodide in the presence of triethylamine.

\[
\text{HO(CH}_2\text{)}_n\text{COOH} + \text{1 Et,N} \xrightarrow{n = 5,7,10,11,14} \text{O(CH}_2\text{)}_n
\]

Aromatic and aliphatic carbodiimides, which are useful coupling reagents for the synthesis of peptides and nucleotides, have been prepared in high yields by treating N,N'-disubstituted thiourea with 2-chloro-1-methylpyridinium iodide in the presence of triethylamine.

\[
\text{S} \xrightarrow{\text{Et,N}} \text{R'NH-C=NHR''} + \text{Me}_2\text{N} \xrightarrow{n = 5,7,10,11,14} \text{R'N=C=N-R''} + \text{Me}_2\text{N}
\]

All of the above synthetic transformations using 2-chloro-1-methylpyridinium iodide proceed in 60-90% overall yield. Reactions of 2-chloro-1-methylpyridinium iodide can be carried out in a variety of solvents such as toluene, dichloromethane, dimethoxyethane, and pyridine at temperatures ranging from ambient to the boiling point of the solvent.

**References**

9. 19,800-5 2-Chloro-1-methylpyridinium iodide
25g $19.95; 100g $57.00
10. 13,206-3 Triethylamine
500g $7.70; 2kg $19.80
11. 74,935-2 Tri-n-butylamine
500g $6.20; 1kg $8.85