

that, in the presence of an inhibitor of PNP, exogenously added 2'-deoxyguanosine is highly cytotoxic for T-lymphoblasts, presumably because it is phosphorylated to dGTP, a potent inhibitor of ribonucleotide reductase.^{16,17}

Human MOLT-4 T-lymphoblasts (H.E.M. Research, Inc.) and MGL-8 B lymphoblasts (a gift of Dr. B. S. Mitchell, University of Michigan) were maintained in RPMI 1640 containing 10% heat-inactivated fetal calf serum, 1% L-glutamine (2 mM/mL of medium), and 1% penicillin-streptomycin solution. For the cell line assay, RPMI 1640 plus 10% heat-inactivated horse serum was used. Lymphoblasts (100 μ L at 5×10^6 cells/mL) were added to the wells of 96-well U-bottom plates (Costar), and 100 μ L of

test compound or medium and 50 μ L 2'-deoxyguanosine (Sigma) or medium were then added. Cultures were incubated in a humidified atmosphere of 5% CO₂ in air at 37 °C for 48 h and labeled with 20 μ L of [³H]thymidine (New England Nuclear) for the final 16 h of culture. Incorporation of radioactivity was determined by liquid scintillography. Inhibitory activity of compounds was quantitated in counts/minute and expressed as a percent of the counts incorporated by control cultures. IC₅₀ values (the concentration of test compound required to inhibit by 50% the incorporation of [³H]thymidine by control cultures when assayed in the presence of 10 μ M 2'-deoxyguanosine) were calculated from log-transformed linear regression analysis.

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- (15) Carson, D. A.; Kaye, J.; Matsumoto, S.; Seegmiller, J. E.; Thompson, L. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 2430.
 (16) Moore, E. C.; Hurlbert, R. B. *J. Biol. Chem.* **1966**, *241*, 4802.
 (17) Thelander, L.; Reichard, P. *Ann. Rev. Biochem.* **1979**, *48*, 133.

Book Reviews

Nonsteroidal Antiinflammatory Drugs. Volume 5 of Chemistry and Pharmacology of Drugs. Edited by J. G. Lombardino. Wiley, New York, Chichester, Brisbane, Toronto, Singapore. 1985. xvii + 442 pp. 16 × 23.5 cm. \$99.50

This comprehensive work considers in four chapters (1) "Normal Articular Cartilage and the Alterations in Osteoarthritis" by H. J. Mankin of the Massachusetts General Hospital (Boston), (2) "Inflammation Mechanisms and Mediators" by W. Dawson of the Lilly Research Centre, Ltd. (Surrey), and D. A. Willoughby of St. Bartholomew's Hospital (London), (3) "Laboratory Models for Testing Nonsteroidal Antiinflammatory Drugs" by I. G. Oterness and M. L. Bliven of Pfizer Inc. (Groton), and (4) "Medicinal Chemistry of Acidic Nonsteroidal Antiinflammatory Drugs" by J. G. Lombardino of Pfizer Inc. (Groton). The volume is extensively referenced through 1983 and into 1984 and has a good index. All chapters are interesting, and the four adequately summarize the multidisciplinary aspects of acidic nonsteroidal antiinflammatory drugs and the inflammation process at the animal, organ, cellular, and molecular levels.

Volume 5 is recommended reading for medicinal chemists and others interested in the topic. Educators will find the book an excellent source of material for both graduate and undergraduate courses. In addition to biochemical mechanisms of inflammation and the modes of action and pharmacological properties of numerous clinically important drugs, synthetic schemes are presented for various prototypes. To limit the review size, only acidic antiinflammatory drugs having approved generic names and some clinical data are included. Generally, drugs withdrawn from clinical trials are excluded as are specialized salts, formulations, or obvious prodrugs. Also noteworthy reading for medicinal chemists are discussions on proteoglycans and metabolism of articular cartilage (Chapter 1), biochemical mechanisms and chemical mediators of inflammation (Chapter 2), and operant mechanisms of animal models and the importance of such mechanisms to human disease (Chapter 3).

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Radiation-Protective Drugs and Their Reaction Mechanisms. By J. C. Livesey, D. J. Reed, and L. F. Adamson. Noyes Publications, Park Ridge, N.J. 1985. xii + 146 pp. 16 × 24 cm. ISBN 0-8155-1051-9. \$32.00

The concept that biological systems can be protected from lethal doses of ionizing radiation by chemicals first became established in 1948, from the work of Dale in England and Latarjet in France. In the nearly 40 years that have elapsed since, a variety of sub-

stances have shown some effect in preventing radiation damage to living cells, and a number of postulations have been put forth to explain their action. Considering the considerable amount of research on this subject, relatively few comprehensive treatments have been published, although reviews on various aspects of the subject have been adequate. The work by Livesey et al., which provides an up-to-date review of the radiation-protective mechanisms that have been postulated, is therefore most welcome. The coverage of chemical substances that provide protection is limited to a small selection of the more active agents, however.

The book begins with a concise account of the effects of radiation on biological systems. This considers the effects of ionizing radiation at the atomic and molecular levels as well as at the functional and systemic levels. Modes of energy transfer, critical radiation targets, and effects on cell survival are discussed briefly but adequately. Effects of nonionizing and ultraviolet radiation on biological systems are also included.

The second chapter is concerned with endogenous factors that influence radioresistance. A relatively extensive account of the oxygen effect on radiation damage is included, along with the mechanisms proposed. The endogenous radioprotective substances, including glutathione, other thiols, vitamins, and antioxidants, are treated in regard to the free-radical reactions involved. An explanation of the competition model for oxygen and glutathione is included.

Chemical radioprotection from exogenous substances is taken up in the third chapter and provides a thoroughly current treatment. The principal theories of radioprotection that are discussed were all elaborated more than 20 years ago, but much more information on the biochemical bases of these mechanisms is now available. Plausible explanations for the protective activity of specific types of agents can now be made, although no one mechanism has been generally accepted. Repair of radiation damage to macromolecules, including DNA, now a subject of much investigation, still requires further research to delineate the role of thiols and other protectors.

Therapeutic measures for treatment of radiation damage is taken up in the fourth chapter. This includes a discussion of the effects of interferon, tissue extracts, endotoxins, hormones, and exogenous thiols and enzymes. A very brief chapter five proposes recommendations by the authors for future research. There are two appendices: one is entitled "Chemical Radioprotection—Research in Progress" and lists a number of research projects supported by government agencies in the U.S. No dates for these projects are given. Appendix B includes "Some Compounds Showing Radio-Protective Activity" and includes a very brief discussion of structure-activity relationships and a list of protective compounds with relevant test data. The list is quite brief

but does cover the more important compounds used in mechanism studies.

The book should be of great interest to chemists and biologists concerned with radiation protection and the pros and cons of the various mechanisms proposed, particularly in view of the length of time since the last comprehensive review of this subject in English. The printing and illustrations, done by a photo-offset process, are clear and uniform. Close to 500 references are included, many of them to recent work. The authors are to be commended for a concise and critical treatment.

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Purines: Pharmacology and Physiological Roles. Edited by T. W. Stone. VCH Publishers, Deerfield Beach, FL. 1985. 284 + xix pp. 16 × 24 cm. ISBN 089573-444-3. \$47.50

The present volume originates from a satellite symposium of the 9th International Union Of Pharmacology (IUPHAR) Congress held in London in the summer of 1984. It contains 25 chapters on various aspects of purine, mainly adenosine, pharmacology together with 48 abstracts presented at the meeting. While the majority of articles are authoritative, much, if not all, of the information presented is available in other, more comprehensive and topical monographs: for instance, *Adenosine: Receptors And Modulation Of Cell Function*; edited by V. Stefanovich et al., IRL Press, Oxford, U.K., 1985. In addition, the present volume has poor production standards even allowing for the camera-ready nature of its presentation.

The one redeeming feature of the volume, and one that will no doubt result in its major claim to citation fame, is the contribution from the editor. Exercising what might be termed a literary droit de seigneur, Stone has written a forward and an "afterword", titled "Summary of a Discussion on Purine Receptor Nomenclature" and "Some Unresolved Problems", respectively, that while brief are thought provoking and lively. They do not, however, make the book worthwhile purchasing except for the most ardent adenophile.

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Chemotherapy in Psychiatry. Edited by Ross J. Baldessarini. Harvard Press, Cambridge, MA. 1985. 416 pp. 15.5 × 23 cm. ISBN 0-67411383-7. \$25.00

This is the second edition of Dr. Baldessarini's book that was originally published in 1977 numbering 201 pages, having now been expanded to 354 pages. Dr. Baldessarini stands in a unique position, as both a clinical psychiatrist and preclinical neuroscientist, to author a text on psychopharmacotherapeutics. His astute awareness of the complexities of psychiatric disorders coupled with his vast knowledge about the biological correlates of these illnesses has enabled him to compile a very even-handed text on the use of psychotropics. In addition to his intellectual grasp of psychopharmacology, he has been able to write a clear, concise, practical, yet not superficial book on the use of these agents.

His preface clearly states that the "aim in this book is to provide a brief but useful overview of principles and currently recommended practices for the clinical use of psychotropic agents in psychiatry and medicine". He goes on to say that "basic preclinical pharmacology is included since it contributes to well-informed and rational use of medications". In both these areas, the author succeeds well in covering adequately the information necessary to provide the practitioner and student with material that will aid with the actual use and prescribing of the drugs, as well as furnish relevant preclinical data that can aid the physician with a better understanding of the underlying mechanisms of drug

effect and toxicity. The balance achieved is excellent; if the preclinical and experimental material is understood, and the recommendations for prescribing are followed, the clinician will have learned well the rational basis for the use of these compounds and patients will have benefited from optimization of prescribing practice.

In the first chapter entitled "Modern Psychopharmacology and Psychiatric Treatment" Dr. Baldessarini demonstrates the breadth of his understanding of the illnesses treated by these agents as he recommends to professionals in this area that a balanced view that includes biologic, psychosocial, and environmental factors is best to optimally treat major psychiatric disorders. He also covers nicely the pitfalls evident in the development of psychotropic agents and describes the process of the clinical research that is used in the evaluation of drugs for psychiatric patients. Finally, he addresses the ticklish area of biological hypotheses in psychiatry, elucidating for the reader that although the success of medications for the treatment of psychiatric illnesses may generate interesting hypotheses about the etiology of these disorders, caution must be exercised in drawing premature conclusions as to pathophysiology of depression or schizophrenia, for example, based on drug effect. He supports the notion that psychiatry needs to continue using the scientific method to generate, test, and prove viable biologic models of psychiatric illnesses.

The chapter on antipsychotic agents is among the best of this book, evidencing the author's extensive preclinical research and clinical experience in the use of these drugs. He covers basic issues such as problems in drug development, structure-activity relationships, pharmacokinetics, clinical use, and the all-important area of drug toxicity. This chapter, as is true of all others, could be well understood by a nonclinical scientist involved with the preclinical aspects of drugs research and development. Individuals who have little or no experience in the clinical care of psychotic patients but who are familiar with basic concepts of pharmacology could follow very easily the material in this chapter.

The chapter on lithium demonstrates to the reader the scholarship and clarity of presentation also evident throughout the text; here we see tables concisely tabulating the literature on such areas as prevention of bipolar relapse, efficacy of lithium for rapid-cycling bipolar disorder, prevention of nonbipolar relapse, and the antidepressant efficacy of lithium for acute nonbipolar depression. In addition, there are very practical tables in this chapter for the practitioner such as one on conditions that have been proven to respond to lithium as opposed to those in which the evidence for efficacy is less secure, and recommended guidelines for the long-term use of lithium that offers the physician a ready access to those physiological parameters that need to be monitored in the prophylactic use of lithium.

The chapter on antidepressants very thoroughly presents what is known about the action of antidepressant drugs via well-chosen figures that illustrate the major sites of action of these compounds, tables that give the in vitro data on the effects of these drugs on various biogenic amine systems, and clearly written text that guides the reader through all the material. Again, there are excellent tables on practical clinical use, literature reviews of efficacy of these agents in various types of depressive illnesses, and an excellent drug interaction table that will be of particular interest to clinicians. For the preclinical scientist, this chapter will offer concisely what is understood about the neurochemical mechanism of action of these drugs and realistically talks about those areas that are well understood, those areas that are more speculative, and those areas that lack coherence.

In conclusion, this book is a very detailed, expanded version of the first edition, which can be useful for a very broad range of individuals of varying backgrounds. For clinicians, it may be most helpful for those who are beyond the medical school years, and preferable for those who are familiar with psychiatric diagnosis. For the preclinical scientist, this is an ideal book to learn about the state of the art in psychiatric biological treatments. From a scientist who is fully versed in clinical psychiatry, it offers to his bench colleagues without a background in clinical phenomenology a rich compendium of well-presented and excellently researched material that will enable an understanding of what is known in psychopharmacology. Given that the area is fraught with mythology and misconceptions, this will allow preclinical

investigators a realistic view of psychiatry and the treatment of its major illnesses in a language that is free of jargon and very readable. Compliments to the author for integrating matters of clinical care of psychiatric patients with the science that serves as the foundation for these treatments in both a scholarly and practical manner.

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Amino Acids and Peptides. Edited by J. S. Davies. Chapman and Hall, London. 1985. ix + 430 pp. 21 × 27 cm. ISBN 0 412 26950 3. \$69.95

The publishers of this volume have responded to a perceived need for a "sourcebook" on amino acids and peptides by issuing a compendium of data drawn from the latest edition (1982) of the *Dictionary of Organic Compounds*. Entries are listed alphabetically, numbered for cross-reference, and indexed separately at the end of the book by name, empirical formula, and *Chemical Abstracts* registry number. Included are not only the common amino acids found in proteins but also the more exotic types present in peptide antibiotics and in peptide alkaloids. A large number of naturally occurring as well as synthetic dipeptides are also given. A typical entry includes the common and systematic name, chemical structure, empirical formula, molecular weight, melting point, specific rotation, solubility properties, and names and physical constants of a selected number of known derivatives (e.g., salts, esters, amides, and carbamates). Data are given for the (*R*), (*S*), and (*R,S*) forms when these are available, and appropriate journal and patent citations are provided. Biological activities and toxicities are also given for many of the entries.

The intent behind this sourcebook is certainly commendable, and the publishers have sensibly chosen to use soft covers to make the book affordable to as many individual buyers as possible. While the book is a handy desktop reference and will save many a trip to the library, the reader should be prepared for some disappointments. For example, Boc, Cbz, and Fmoc derivatives of the amino acids are extensively covered in the survey, but (nitrophenyl)sulfonyl, phthaloyl, and (trichloroethoxy)carbonyl and many other N-protected derivatives are not. Moreover, the statement in the Preface that "virtually every known rare amino acid has been included..." is quite unrealistic. For example, the reviewer looked in vain for 2-aminopimelic acid, though oddly enough 3-aminopimelic acid is described. α -Amino- α,ω -alkanedioic acids beyond 2-aminoadipic could not, in fact, be found at all. There are also some peculiar inconsistencies in nomenclature. Thus, 3,4-dihydroxyphenylalanine is listed as 2-amino-3-(3,4-dihydroxyphenyl)propanoic acid, and the corresponding 2,3- and 2,4-dihydroxy isomers are similarly named as propanoic acids, whereas the 2,5-dihydroxy compound is listed as 2,5-dihydroxyphenylalanine rather than as 2-amino-3-(2,5-dihydroxyphenyl)propanoic acid. As a result of this lack of consistency, the 2,5-dihydroxy compound could not be found without first looking for it in the name index and seeing that it is not named in the same way as the other isomers. The reviewer also happened at random to look for the well-known and commercially available *N*- α -glutamyltyrosine but was frustrated to find only the isomeric compound *N*- γ -glutamyl tyrosine. How many more such omissions could be found is anyone's guess.

All in all, however, users of this compendium are more likely than not to find it a helpful laboratory companion and will enjoy browsing through its many pages of intriguing chemical structures.

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Carbohydrate Chemistry, Volume 17, Part I. Mono-, Di-, and Trisaccharides and Their Derivatives. Specialist Periodical Reports. N. R. Williams, Senior Reporter. The Royal Society of Chemistry, Burlington House, London. 1985. x + 275 pp. 14 × 22 cm. ISBN 0-85186-182-2. \$87.00

Volume 17, Part I, of this series reviews the literature in carbohydrate chemistry for 1983 and includes abstracts of over 1400 references. This extraordinary volume of literature has been abstracted and organized in a concise and well-written manner. The 24 chapters include coverage of the well-established fields of glycoside and antibiotic chemistry as well as separate chapters on various types of sugar derivatives, including ethers, acetals, esters, halo-, amino-, thio-, and deoxysugars, and inorganic and unsaturated derivatives. Chapters on synthesis of chiral natural products from carbohydrate precursors and oligosaccharides reflect the increasing interest in these areas over recent years. Also included are chapters on spectroscopic, separatory, and analytical methods. This volume maintains the high standards of excellence that have been set for this well-established series. However, the Senior Reporter of this volume notes that there is a disturbing trend of declining sales and profitability for the general series of *Specialist Periodical Reports* and indicates the dependence on readers, and especially purchasers, to keep the particular volumes of the series viable. It is hoped that those workers in the field of carbohydrate chemistry will continue to recognize the invaluable nature of this reference source and support its continued publication.

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Modern Methods in Protein Chemistry. Review Articles. Vol. 2. Edited by H. Tschesche. deGruyter, Berlin, New York. 1985. 434 pp. 17 × 24 cm. ISBN 0-89925-079-3. \$94.00

This is the second volume in a series begun in 1983 to publish reviews surveying the status of analytical methods available to protein chemists for characterizing and analyzing proteins. This volume contains 21 chapters, presented at a conference entitled *Modern Methods in Protein Chemistry* held in Bielefeld, FRG, June 1984, that review the following topics: modern micro-methods; chromogenic peptide substrates for serine proteases; immobilized metal ion affinity chromatography; use of synthetic dyes for affinity chromatography of proteins; advantages and disadvantages of immunoassays; the chemical modification of proteins and the use of cross-linking reagents for labeling proteins; microanalysis of peptides using color reagents; fluorescence-activated cell sorting; FPLC system for fast and high resolution of proteins; amino acid analysis by HPLC using precolumn derivatization; use of cation-exchange HPLC for separation of protein fragments; purification and detection of cysteine peptides by HPLC; on-line detection of Edman degradation products by HPLC; improved separation of Pth-amino acids by HPLC; use of microcomputers to control peptide sequencers; use of computer programs for analysis of sequence alignment and secondary structure in proteins; DNA and RNA sequence analysis; use of Raman spectroscopy for secondary structure determination; standard methods for synthesizing peptides.

In the Preface to this book, the editor states his hope "that the book will satisfy the current need to all those involved in the aims of protein chemistry to keep up with the rapid development and perfection of all analytical and preparative methods". The book succeeds in addressing a wide variety of topics of current interest to protein chemists, but the limited space allocated to each topic precludes an adequate in-depth treatment of most subjects.

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