residue obtained after removing the solvent was chromatographed on preparative TLC with use of methanol–chloroform (0.5:9.5). Elution of the fastest and major band gave a solid which recrystallized from ethanol to yield 0.92 g (48%) of **21**: mp 140–141 °C. Anal. ($C_{10}H_{15}N_3O_4$) C, H, N.

The slowest moving band afforded 20 mg (~1%) of **22**, which was identified by ^1H NMR spectroscopy.

1-[(2-Hydroxyethoxy)methyl]-2-methylimidazole-4-carboxamide (23). A solution of **21** (0.73 g, 3 mmol) in methanolic ammonia (45 mL) was allowed to stand at room temperature for 24 h. Evaporation of the solvent and coevaporation with ethanol gave a solid which was recrystallized from methanol to yield 0.59 g (98%) of **23**: mp 137–138 °C. Anal. ($C_8H_{13}N_3O_3$) C, H, N.

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Registry No. **8**, 51605-32-4; **9**, 77421-54-6; **10**, 77421-55-7; **11**, 77421-58-0; **12**, 85665-04-9; **13**, 77421-51-3; α-**14**, 95936-32-6; β-**14**, 95936-33-7; α-**15**, 95936-30-4; β-**15**, 95936-31-5; **17**, 95936-36-0; **18**, 95936-37-1; **19**, 95936-35-9; **20**, 95936-34-8; **21**, 95936-38-2; **22**, 95936-39-3; **23**, 95936-40-6; 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose, 13035-61-5; 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuranosyl chloride, 3601-89-6; (2-acetoxyethoxy)methyl bromide, 81777-40-4.

Book Reviews

Antimalarial Drugs I (Handbook of Experimental Pharmacology, Vol. 68/1). Biological Background, Experimental Methods, and Drug Resistance. Edited by W. Peters and W. H. G. Richards. Springer-Verlag, New York. 1984. xviii + 484 pp. 17 × 24.5 cm. ISBN 0-387-12616-3. $143.50.

This is the first of two monographs devoted to antimalarial drug development. The present one is concerned with the biological and clinical aspects of the subject, whereas the second is devoted primarily to a discussion of the various classes of compounds which have shown potential.

The 22 authors of Part I are specialists in their respective fields and, for the most part, have written their chapters in a lucid manner. The editors managed not only to bring cohesiveness to their contributions but also to minimize overlap of subject matter without incurring any obvious omissions. This is not a book for adherents to the off-the-shelf screening school of drug development. Rather, it is a guide for those who are interested in acquiring the biological background for intelligent antimalarial drug design.

In Chapter 1, P. C. C. Garnham describes the life cycles of various *Plasmodia* that infect humans, rodents, avia, and reptilia. The metabolic requirements of the malaria parasite and the characteristics of the host–parasite relationship are given by I. W. Sherman in Chapter 2. W. H. G. Richards, in Chapter 3, outlines the latest in vitro culture methods for malaria parasites and discusses their applicability in drug testing. In Chapter 4, G. H. Mitchell deals with the immune response to the malaria parasite at its various stages of development. A description of the clinical pathology of the disease is given in Chapter 5, written by V. Boonpucknavig, T. Srichaikul, and S. Punyagupta, and is accompanied by numerous black and white photographs showing the typical histological characteristics of the parasites. In Chapter 6, R. E. Desjardins describes recent in vitro culture technology, with emphasis on a semiautomated technique that is currently being used in antimalarial drug screening. Chapter 7, by W. H. G. Richards, is devoted to avian malaria and informs us that over 400 species of birds have been found to be afflicted with the disease. Details are given of how avian malaria models have been exploited for drug development. A. L. Ager, Jr., in Chapter 8, describes rodent malaria, first reported in 1948, and the manner in which the *Plasmodium berghei* model is used in primary and secondary screens. In Chapter 9, concerned with simian malaria, R. N. Rossan discusses the ability of the Colombian owl monkey to support *P. falciparum* infection and the application of this model to drug evaluation. S.-C. Chou and his collaborators in Chapter 10 describe alternative models for antimalarial testing, including isolated enzyme systems, use of protozoa other than *Plasmodia* for drug screens, and drug-induced clumping inhibition. In Chapter 11, G. A. T. Targett outlines the relationship between immune responses and antimalarial chemotherapy. Chapter 12, by M. H. Heiffer, D. F. Davidson, Jr., and D. W. Korte, Jr., details the organization of the Walter Reed antimalarial drug development program and considers the steps required to transform a promising lead into a drug for human therapy. Chapter 13, on phase I and II clinical trials by M. Fernex, lists the technical and ethical problems encountered in performing drug evaluations in human subjects. In the chapter which follows, the same author tells of the manner in which subjects are selected and in which field trials are conducted. H. M. Gilles in Chapter 15 details the pharmacogenetic factors which must be considered when testing antimalarial drugs. Chapter 16, by W. Peters, gives the history and present status of drug resistance and Chapter 17, by K. H. Rieckmann, tells how it is evaluated. The means of producing experimental drug resistance is reviewed by W. Peters in Chapter 18.

The book appears to verify an unwritten law which states that the greater the number of contributors to a monograph, the further out-of-date it will be on publication. With few exceptions, the latest references are to papers which appeared in 1981; two chapters stop at 1980. The impression that one is left with is that, for whatever reason, the book is not quite as current as one would wish. Nevertheless, it is an excellent and highly recommended resource for malaria researchers and others interested in acquiring a good foundation in antimalarial chemotherapy.

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Comprehensive Heterocyclic Chemistry. Volumes 1–8. The Structure, Reactions, Synthesis, and Uses of Heterocyclic Compounds. Set Editors: Alan R. Katritzky and Charles W. Rees. Pergamon Press, Oxford, England, 1984. xvi + 1111 pp. 19.5 × 28 cm. ISBN 0-080-30708-6. $2200 for set, cannot be purchased individually.

The review, which consists of seven volumes devoted to the chemistry of heterocyclic compounds and one volume of indexes, is a masterful addition to the previous comprehensive reviews of inorganic (1973), organic (1979), and organometallic (1982) chemistry. One can appreciate the magnitude of the undertaking when one begins to consider all the permutations of heteroatoms, ring sizes, and sites of unsaturation possible. However, as the reader who examines this will attest, the editorial board has utilized well the choice of authors in achieving a truly comprehensive review of a field that is fascinating to chemists, particularly those involved with the design, synthesis, or evaluation of novel biologically active compounds.

Although comprised of eight volumes, the set is divided into six parts (including the indexes) in which ring size is the primary determinant and, in this way, it distinguishes itself from the more familiar pattern of heterocyclic reviews based on the identity of the heteroatom. Part 1 (Volume 1) provides an introduction to

the field of heterocyclic chemistry by giving an overview of the nomenclature involved, presenting some of the biological, pharmaceutical, and industrial uses of heterocyclic compounds, and reviewing heterocyclic compounds that contain the less common heteroatoms, e.g., transition metals and group 3 and group 4 elements. Part 2 (Volumes 2 and 3) describes the chemistry of the six-membered heterocycles and their benzo derivatives. Most of Volume 2 is devoted to aspects of the pyridine and benzopyridine ring systems as a significant quantity of information is given regarding the structure, reactivity of the ring atoms and substituents, reactivity of nonaromatic derivatives, synthesis, and applications. The remainder of Volume 2 and Volume 3 examines the six-membered rings and their annelated derivatives which contain multi heteroatom substitution. Because of the diversity of structures involved, e.g., diazines, triazines, pyrans, and thiopyrans, each chapter reviews the properties, reactivity, synthesis, and applications of the particular class of heterocycles. Five-membered rings having one heteroatom (O, S, or N) are reviewed in Part 3 (Volume 4) with several chapters given to the discussion of the general properties of the pyrroles, furans, and thiophenes, including the benzo derivatives of each, followed by series of chapters related to chemistry peculiar to each. Polyheteroatom-substituted five-membered heterocycles comprise Part 4 (Volumes 5 and 6). In the first of these two volumes the structure, reactivity, synthesis, and applications of the pyrazoles, imidazoles, triazoles, tetrazoles, pentazoles, and their benzo derivatives are examined. The second, Volume 6, covers all the remaining permutations of the five-membered ring heterocycles, including their fused derivatives, that contain two or more oxygen, sulfur, or nitrogen atoms. Part 5 (Volume 7) reviews other ring sizes with series of chapters that discuss the O-, S-, or N-containing three-, four-, and seven-membered rings, including individual chapters on penicillins and cephalosporins, and briefer synopses of the eight- and larger ringed heterocycles, crown ethers, and heterophanes. The indexes, which comprise Volume 8, very adequately compile the references and authors, as well as the systematic names and structures of the heterocyclic systems, cited in the set.

The material in this series has been presented in a highly structured format. For chapters that cover an entire class of compounds, e.g., "Azetidines, Azirines, and Fused-ring Derivatives", the structure consists of an introductory section, followed by sections on structure, reactions or reactivity, synthesis, and biological properties of applications. Each of the sections contains more specific headings, which in turn may have subheadings. This has been codified with a numerical system in the following manner, e.g., 5 (part) .04 (chapter) .3 (main heading) .11 (subheadings), in order to assist the reader in both finding the desired information as well as providing a point of reference during a review of the material.

Another interesting feature in the comprehensive review is the manner in which the literature references are inserted into the text. This consists of a highly abbreviated form of the reference rather than a number which would require a reader refer elsewhere. This appears to be a very convenient feature for someone seeking information from a specific section. The complete references, of course, are compiled at the end of each volume as well as in the index volume.

The series "Comprehensive Heterocyclic Chemistry" provides an excellent comprehensive review of the field without being exhaustive. The highly structural format used by the editorial board has resulted in the individual chapters being quite uniform in style and depth of information. In general, the structural properties are well detailed and adequately referenced to provide a valuable resource and the examples used for reactions or syntheses are explicit enough to convey the intent of the author. In this area there was some variation in the means of portraying the reactions, but the effectiveness of the presentation is undiminished. The sections devoted to the applications are usually short, but it should be noted that the review is related principally to the chemistry and not the biology of the heterocyclic compounds.

As might be expected, the price for the entire eight-volume set is quite high; however, the information contained within it, as well as its accessibility, make it extremely worthwhile. Because of the high percentage of biologically active compounds that are heterocyclic or contain heterocyclic substituents, no library to which an organic or medicinal chemist needs access should be without it. It is a must.

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Heterocyclic Compounds. Volume 43. Parts 1 and 2. By B. Renfroe, C. Harrington, and G. R. Proctor (Part 1) and J. W. H. Watthey, J. Stanton, and N. P. Peet (Part 2); A. Rosowsky, Editor. Wiley, New York, 1984. xvi + 822 pp (Part 1), xix + 889 pp (Part 2). 16.5 × 24 cm. ISBN 0-471-01878-3 and 0-471-89592-x. $225.00 each Part.

This two-book volume is a comprehensive review of a large portion of azepine chemistry. Contrary to what might have been expected from the title, monocyclic azepines were not reviewed. Part 1 covers in an excellent manner bicyclic and tricyclic heterocyclics in which an azepine ring is fused to either another heterocyclic or a carbocyclic ring. Part 2 covers similar tricyclic diazepines and also monocyclic and condensed tri- and tetrazepines. Missing from Part 2 are the benzodiazepines, which are very important from a medicinal chemistry viewpoint.

The medicinal chemist is always very interested in any pharmacological activity of the compounds he may consider studying. Rosowsky, the editor of this volume, has contributed a fascinating, albeit brief, preface mentioning some of the varied biological properties of azepines, and some of the industrial authors reflect their interest in the utility of compounds and cite some of the reported biological activities in their chapters. However, the chapter on azepine ring systems containing two rings fails to address this aspect. Another serious shortcoming of this volume is a failure to cite relevant review articles which treat an area in much greater detail than is appropriate for discussion in this volume. For example two very excellent and lengthy review articles on benzazepines appeared in 1974 and 1975 which would be invaluable to further orient a newcomer contemplating work in this area, but they are not mentioned.

On the positive side all of the chapters are well written with adequate structures and flow charts to allow rapid comprehension of the text even by one unfamiliar with the nomenclature. The technical aspects of this two-book volume (author and subject indexes, table of contents, book quality) continue the traditional high standards of this invaluable series.

Although the two books comprising this volume are not primarily meant for browsing, and their cost will discourage individual ownership, the wealth of fascinating chemistry described and the biological importance of the types of compounds discussed makes this volume, like the others in this series, a must for any serious chemistry library.

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The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects. Edited by S. Agurell, W. L. Dewey, and R. E. Willette. Academic Press, Inc., Orlando, FL, 1984. xxii + 909 pp. 16 × 23.5 cm. ISBN 0-12-044620-0. $88.00.

The literature on *Cannabis* and its constituents is staggeringly extensive. Unfortunately, it is usually scattered. The mid-1970s saw the greatest activity in publication on the effects of cannabinoids, with a slackening following 1978; but there has since 1978 been a notable increase in interest in the potential therapeutic use of these compounds.

Here we are offered a comprehensive work by 148 internationally known authorities from 10 countries. Most contributions published in this book were written by scientists who participated in the very successful meeting held in Louisville, KY, in August 1982. All of the papers were reviewed by at least two specialists.

The general quality of the various contributions is high, though not consistently so. Most are timely, and each is provided with an up-to-date bibliography—often extensive. The easy-to-use