showed it to be 9β,10β:7′,8′-diepoxyroridin H (H-10 at δ 3.18, $J_{10,11}$ = 4.1 Hz), mp 259–261 °C. NMR spectra of the minor components, 2 and 1.5 mg each, indicated that they were also diepoxides, with extra epoxidation apparently present at the 7′,8′ double bond, since the normal dienic splitting pattern downfield was not observed. Anal. Calcd for $C_{29}H_{36}O_9$: C, 65.84; H, 6.87. Found for 9α,10α-epoxyroridin H: C, 65.69; H, 6.89. Found for **15**: C, 65.75; H, 6.92. Anal. Calcd for $C_{29}H_{36}O_{10}$: C, 63.96; H, 6.66. Found for 9β,10β:7′,8′-diepoxyroridin H: C, 64.10; H, 6.51.

9β,10β-Epoxyroridin J (16). To a solution of 198 mg (0.37 mmol) of roridin J (**7**) in 20 mL of methylene chloride was added 94 mg (0.60 mmol) of MCPBA. This mixture was stirred overnight at room temperature, diluted to 25 mL with methylene chloride, and washed twice with 15 mL of saturated sodium bicarbonate solution. The organic portion was dried with $MgSO_4$, and the solvent was removed in vacuo to yield 200 mg of crude product; TLC analysis showed it to be composed of a single major product with two other minor products. Preparative TLC on 2-mm plates with 30% ethyl acetate in hexane, followed by crystallization from ether–hexane, gave 90 mg (43% yield) of 9β,10β-epoxyroridin J (**16**), mp 175–179 °C. Anal. Calcd for $C_{29}H_{36}O_{10}$: C, 63.96; H, 6.66. Found: C, 63.75; H, 6.79.

9β,10β-Epoxides of 8β-Hydroxy and 16-Hydroxy Derivatives of Verrucarin A and Roridin A. Synthesis of 21–24. Epoxidation of alcohols **10**, **11**, **18**, and **25** carried out in the usual fashion (MCPBA/CH_2Cl_2 overnight) gave the following epoxides (yield, melting point), isolated by PTLC (EtOAc/hexane): **21** (71%, 152–153 °C); **22** (59%, mp 149–152 °C); **23** (47%, 294–298 °C); **24** (35%, mp 138–142 °C). Anal. Calcd for $C_{27}H_{34}O_{11}$: C, 60.66; H, 6.41. Found for **21**: C, 60.88; H, 6.30. Found for **23**: C, 60.79; H, 6.27. Anal. Calcd for $C_{29}H_{40}O_{11}$: C, 61.69; H, 7.14. Found for **22**: C, 61.85; H, 7.00. Found for **24**: C, 61.50; H, 6.98.

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Registry No. **1**, 3148-09-2; **2**, 74560-38-6; **3**, 61251-97-6; **4**, 4643-58-7; **5**, 14729-29-4; **6**, 29953-50-2; **7**, 74072-83-6; **8**, 63783-94-8; **9**, 74516-67-9; **10**, 74608-63-2; **11**, 87583-91-3; **12**, 87532-25-0; **14**, 74516-66-8; **15**, 87532-26-1; **16**, 87532-27-2; **17**, 87583-92-4; **18**, 87532-28-3; **19**, 87532-29-4; **21**, 87532-30-7; **22**, 87532-31-8; **23**, 87532-32-9; **24**, 87532-33-0; **25**, 74516-64-6; 9β,10β:7′,8′-diepoxyroridin H, 87532-34-1.

Book Reviews

Alkaloids: Chemical and Biological Perspectives. Volume 1. Edited by S. William Pelletier. Wiley, New York. 1983. xi + 398 pp. 16.5 × 24 cm. 0-471-08811-0. $60.00.

Any new series of books on the alkaloids, such as this, must expect to be compared to the classic series, "The Alkaloids", edited by R. H. F. Manske until his untimely death in 1977. The first volume in that series appeared in 1950 and the 17th appeared in 1979. The present series indeed has a difficult act to follow. The editor of the present series himself contributed three chapters to the Manske series. It is stated on the fly jacket: "Here is the first volume in an outstanding new series that provides unprecedented interdisciplinary coverage of material relating to the chemical and biological properties of alkaloids... Because no other series provides this interdisciplinary approach to alkaloids...". One hopes that the high standards of the Manske series will be maintained regardless of the reasons or justifications presented for this new series.

This first volume is composed of five chapters, and each one is concerned with a different subject. We will briefly look at each chapter in turn.

Chapter 1, entitled "The Nature and Definition of an Alkaloid", by S. William Pelletier is 31-pages long, containing 111 references and 10 sections. One of the author's colleagues is quoted in the beginning of the chapter as follows: "An alkaloid is like my wife. I can recognize her when I see her, but I can't define her." Finally, the author, after reviewing all of the types of compounds that apparently workers in the field agree are classified as alkaloids, suggests the following simple definitions: "An alkaloid is a cyclic organic compound containing nitrogen in a negative oxidation state which is of limited distribution among living organisms." While this chapter is interesting both from a historical perspective and as a brief summation of the field, it is unlikely that Pelletier's definition will affect the state of things.

Chapter 2, entitled "Arthropod Alkaloids: Distribution, Functions, and Chemistry", by Tappey H. Jones and Murray S. Blum contains 51 pages with 160 references, including several in 1982. There are 13 sections. Each of the heterocylic sections is divided into the three parts: "Distribution", "Function", and "Chemistry". These authors used a definition for alkaloids that was considered inappropriate in Chapter 1! The introduction contains some interesting and thought-provoking observations. Thus, arthropods have achieved an incredible degree of success in spite of great predatory pressure, and to a large measure this is due to the presence of potent defensive secretions, which are frequently alkaloids; since these animals, which account for 80% of all animal species, synthesize a wide variety of distinctive alkaloids, they will continue to be an outstanding source of nitrogenous compounds. The ability to utilize animal behavior in order to study the raison d'etre of these alkaloids presents zoologists with a luxury not generally available to those studying plant alkaloids. In the title at the top of each page, arthropod is misspelled.

Chapter 3, entitled "Biosynthesis and Metabolism of the Tobacco Alkaloids", by Edward Leete contains 67 pages and 388 references and is divided into 12 sections. Figure 1 shows the structures of 45 alkaloids of tobacco. Table 1 lists species other than Nicotiana in which nicotine and related alkaloids have been found and contains 85 entries. Table 2 lists 23 pages of tracer experiments relating to biosynthesis and metabolism of tobacco alkaloids. It is not difficult to believe the author's statement that tobacco has been more thoroughly examined than any other plant product. This chapter is clearly an exhaustive account for the expert but also provides much of interest to the nonspecialist.

Chapter 4, entitled "The Toxicology and Pharmacology of Diterpenoid Alkaloids", by M. H. Benn and John M. Jacyno contains 57 pages with 150 references and is divided into the three parts. Within Part 2, the properties of 64 alkaloids are discussed—this comprises the major part of the chapter. This treatment is uneven; sometimes detailed quantitative information is presented, whereas in other cases, perhaps by necessity, reference is made to a vague statement in the literature. Table 1 summarizes the acute toxicities of 42 diterpenoid alkaloids. Scrutiny of the pharmacological properties of the alkaloids is stated to reveal a broad range of symptoms, including impairment of the cardiovascular system (hypotension, cardiac arrhythmias), respiratory inhibition, muscular paralysis, and disturbances of the central nervous system. These effects appear to be due to the drugs acting as neurotoxins. Two main types can be characterized: those with aconitinelike (aconitiform) activity and those with curarelike (curariform) activity. This chapter is clearly of most interest to a relatively small group of specialists.

Chapter 5, entitled "A Chemotaxonomic Investigation of the Plant Families Apocynaceae, Loganiaceae, and Rubiaceae by Their Indole Alkaloid Content", by M. Volkan Kisakurek, Anthony J. M. Leeuwenberg, and Manfred Hesse comprises almost half the book with 166 pages. This chapter lists 754 references and was

part of the Ph.D. thesis of M. V. Kisakurek, Universitat Zurich, 1981. The chapter contains four sections. In addition, all of the indole alkaloids with a C9 or C10 monoterpene moiety isolated from the plant families Apocynaceae, Rubiaceae, and Loganiaceae are summarized in tables of nine Appendixes; these Appendixes occupy 76 pages, and an attempt was made to cite all references up to the end of 1978. It is stated that 3450 reports, which cover the isolation of 1200 different alkaloids, have been classified into eight different skeletal types. This chapter represents a monumental effort of great value to the specialist. The figures and chemical structures are beautifully done. Many pages of the Appendixes contain only three structures and very few words, and a number of the figures occupy an entire page and contain very few structures. It appears that these pages were taken directly from the above-mentioned thesis. While this is certainly restful to the eyes, one might question whether it is worth the increase in the cost of the book.

In conclusion, this reviewer enjoyed this first volume and recommends it to all interested in alkaloid chemistry. It indeed has an interdisciplinary character that would make it of interest to the nonspecialist as well as the specialist.

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Aging Series. Volume 23. Aging Brain & Ergot Alkaloids. Edited by Alessandro Agoli, Gaetan Crepaldi, Pier Franco Spano, and Marco Trabucchi. Raven Press, New York. 1983. xxii + 442 pp. 16.5 × 24.5 cm. ISBN 0-89004-853-3. $45.00.

Research on the ergot alkaloids has led to increased knowledge of the physiology and pathology of brain aging, more accurate methods for measuring impairment of brain function, and more effective drug therapies for many of the symptoms of brain aging.

This volume examines the contributions of ergot research to the study and treatment of brain aging. It highlights recent findings on altered neurotransmitter function in aging, particularly changes in dopaminergic activity. Chapters outline various clinical examination methods, such as psychometric assessment and quantitative EEG.

A substantial portion of the book examines the pharmacology of ergot alkaloids. Chapters define the actions of ergot compounds at various receptor sites, the effects of ergot derivatives on metabolic changes induced by hypoxia, and the behavioral pharmacology of ergot alkaloids.

This volume provides valuable directions for clinicians who manage elderly patients and for researchers investigating the pharmacology of dopamine agonists and the neurochemistry of brain aging.

Staff

Small Ring Heterocycles. Part 1. Aziridines, Azirines, Thiiranes, Thiirenes. Edited by Alfred Hassner. Wiley, New York. 1983. vii + 696 pp. 16.5 × 24 cm. $175.00.

This volume is a recent addition to the A. Weissburger–E. C. Taylor series of monographs on "The Chemistry of Heterocyclic Compounds". It represents a very successful effort at updating important developments since the last review of this area appeared in the series in 1964. As the editor points out, it was necessary to be selective rather than all-inclusive; nevertheless, with over 2000 references this work is a highly in-depth treatment of the title subjects. The volume is organized into three chapters written by James A. Deyrup ("Aziridines", literature to 1979), Vasu Nair ("Azirines", literature to 1981), and Uri Zoller ("Three Membered Rings Containing Sulfur", literature to 1979 with highlights of 1980). The majority of the last chapter is devoted to thiiranes, thiirenes, and derivatives but also contains a section on three-membered rings containing sulfur and other heteroatoms. Each chapter extensively covers physical properties (spectroscopy and theoretical calculations when applicable), synthesis, and reactions of the title compounds and derivatives, each chapter also has a detailed table of contents, which aids in quickly locating a particular topic of interest. The index is adequate, and, for the most part, equations are either numbered or grouped together in schemes, which, together with the well-done structures and production of this volume, enhance the overall readability of the detailed treatments of the title subjects. Specific examples of a given reaction are included in various tables that usually list yields, which assists one in forming a general impression of an unfamiliar reaction. Short sections on biologically active aziridines and uses of thiiranes are provided; however, an expanded treatment of relevant biological studies would have been welcomed by this reviewer, who would like to see a trend develop toward more emphasis on biological activity in forthcoming volumes of this series.

In general, this volume is a quality work, as are others in the series, and for many years it will be an essential reference for those with a serious interest in the topics reviewed.

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Controlled Release Delivery Systems. Edited by T. J. Roseman and S. Z. Mansdorf. Marcel Dekker, New York and Basel. 1983. xv + 402 pp. 16 × 23.5 cm. $57.50.

This volume includes selected manuscripts that were presented at the 8th International Symposium on Controlled Release of Bioactive Materials held July 26–29, 1981. The selected 25 papers are authored altogether by 77 people. The first 13 chapters deal with controlled delivery of drugs by means of liposomes, polymers, and complexes. The latter part of the work contains chapters on controlled release of various herbicides and other chemicals used in agriculture. As the editors note in their preface, there were at least eight books published in the last 7 years in this field. It seems that many of these contain some or most of the types of chapters and authors that are in the present book. Thus, we have certainly seen before contributions like Chapters 1–3 of the present volume. On the other hand, Chapter 4 discusses a potentially useful way to achieve zero-order release; however, so far there could not be one successful example given. The theoretical background for swelling zero-order release systems looks nice except there is no useful or successful formulation of this type known in the literature. What is truly disturbing in some cases, but which appears to be characteristic of a growing and potentially very rewarding field, is that in many of the papers presented the main objective is advertising performance, without disclosing the exact system and to discuss the basics for its advantages or disadvantages. A prime example of this is Chapter 10, which actually is discussing four different formulations of controlled release for quinidine, which are simply designated A–D. Comparison of these formulations to other known controlled release formulations concludes that one of them, formulation D, is the best in achieving the objective of controlled release. We do not learn, however, anything about what these formulations are, as the closest information given on these formulations is as follows: "The release characteristics of these products were controlled by the nature of the drug excipient mixture, the multiparticulate nature of the drug delivery system, and the properties of the rate-controlling membranes employed." This kind of work would certainly not be published in any journal that uses a reviewing system. The chapters on use of sustained release systems for herbicides and pesticides are interesting and informative. The controlled release of pheromones is a very attractive application, and several similar types of work were previously included in books on controlled release, such as the present Chapter 21. This one is, again, an advertisement of an industrial dispenser. The use of polymer–wood composites is discussed in Chapter 23. A porous polymer is finally advertised in the last chapter to be used for controlled release of volatile compounds. The system is presented using volatile model compounds.

Overall, this is a quite useful book to update this fast growing field.

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Advances in Enzymology. Volume 54. Edited by Alton Meister. Wiley-Interscience, New York. 1983. v + 512 pp. 16 × 23.5 cm. $50.00.

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. One article by J. E. Folk deals with the mechanism and basis for specificity of transglutaminase-catalyzed ϵ-(γ-glutamyl)lysine bond formation. Intermolecular ϵ-(γ-glutamyl)lysine cross-linking, which is catalyzed by the transglutaminases through the exchange of the ϵ-amino group of a lysine residue in one molecule of protein for ammonia at the carboxamide group of a glutamine residue in another protein molecule, is known to be the basic reaction underlying a number of physiological processes, including the covalent polymerization of fibrin during homostasis and the formation of the chemically resistant envelope of the stratum corneum during terminal differentiation of keratinocytes. Each of these biological events appears to be promoted by a different transglutaminase. This chapter focuses on these transglutaminases, their mechanism of catalysis, and their specificities.

Another article of obvious interest to medicinal chemists deals with fluorinated pyrimidines and their nucleosides. This chapter by Charles Heidelberger, Peter V. Danenberg, and Richard G. Moran concentrates on what is known about the biochemical mechanism of action of these fluorinated compounds and their complex metabolism. Of particular interest are the newer approaches to achieve improved chemotherapeutic results with fluoropyrimidines and their biochemical basis. The chapter does not deal with the pharmacological or clinical properties of these fluorinated pyrimidines.

In a very comprehensive and well-written chapter, Fritz Schlenk reviews the formation and metabolism of methylthioadenosine. Methylthioadenosine, which is formed from decarboxylated *S*-adenosylmethionine in enzymatic polyamine synthesis, has received increasing attention in recent years because of its highly diverse regulatory functions and because it appears to serve as a metabolic source of methionine. The other topics covered in this volume include the regulation of fructose bisphosphatase activity by Gopa A. Tejwani, cardiac cytochrome c_1 by Tsoo E. King, and the structure–activity relationships for creatinine kinase by George L. Kenyon and George H. Reed.

Some of the topics covered in this volume are of substantial current interest to medicinal chemists, making the volume worth the rather modest price tag.

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Electrophoresis '82. Advanced Methods. Biochemical and Clinical Applications. Edited by D. Stathakos. Walter de Gruyter, New York. 1983. xvi + 867 pp. 17 × 24 cm. ISBN 3-11-008791-X. $118.00.

The International Conference represented a broad spectrum of scientific disciplines and research fields and included most of the recognized leaders in the field. The aim was a maximal level of communication in theory and ideals, laboratory expertise, new results, layman's applications, as well as speculation in future trends.

This volume contains papers presented at "Electrophoresis '82". They are compiled in the following sections: "Plenary Lecture", "Theory and Methods", "Two-Dimensional Separations", "Biological and Biomedical Applications", "Round-Table Discussions", "Subject and Author Index".

Staff

Books of Interest

Methods in Enzymology. Volume 93. Immunochemical Techniques. Part I. Conventional Antibodies, Fc Receptors and Cytotoxicity. Edited by John L. Langone and Helen Van Vunakis. Academic Press, New York. 1983. xx + 448 pp. 16 × 23.5 cm. ISBN 0-120181993-0. $49.00.

New Drugs Annual: Cardiovascular Drugs. Volume 1. Edited by Alexander Scriabine. Raven Press, New York. 1983. 350 pp. 16 × 24 cm. ISBN 0-89004-730-8. $39.50.

Methods in Enzymology. Volume 94. Polyamines. Edited by Herbert Tabor and Celia White Table. Academic Press, New York. 1983. xxx + 497 pp. 16 × 23.5 cm. ISBN 0-12-181994-9. $55.00.

Liposomes. Edited by Marc J. Ostro. Marcel Dekker, New York. 1983. 416 pp. 16 × 23.5 cm. ISBN 0-8247-1717-1. $58.75.

Selected Topics in Clinical Enzymology, Proceedings (Selected) of the Third International Congress of Clinical Enzymology. Edited by D. M. Goldberg and M. Werner. Walter de Gruyter, New York. 1983. xviii + 363 pp. 17 × 24 cm. ISBN 3-11-009688-9. DM 160. $72.80.