210 mL of pyridine was stirred under 40 psi of H_2S for 7.5 h. The deep red reaction was poured into 960 mL of 2 N HCl, and the filtrate was washed with 700- and 500-mL portions of Et_2O. The combined organic phases were washed with four portions of 10% Na_2CO_3 and brine and dried over Na_2SO_4. The solvent was removed under reduced pressure to give a sticky yellow solid, smelling strongly of H_2S, which was taken up into boiling $CHCl_3$. The resulting granular yellow precipitate was discarded, the filtrate was concentrated, and the residue was treated again in a similar manner. After removal of the second crop of sulfur, the filtrate was concentrated and the residue was recrystallized from $CHCl_3$ or Et_2O to give combined 16.21 g of an off-white solid. Recrystallization from Et_2O gave 12.71 g (63.4%) of fluffy, off-white needles, mp 102.5–103.5 °C. Anal. ($C_{19}H_{20}ClNO_5$) C, H, N.

5-(4-Chlorobenzoyl)-4-(hydroxymethyl)-1-methyl-1*H*-pyrrole-2-acetic Acid (2). To a solution of 5.96 g (15.8 mmol) of **9** in 70 mL of absolute EtOH at 75 °C was added a solution of 34.7 mL of 1.0 N NaOH (34.7 mmol). After 20 min, the reaction was cooled to room temperature, filtered, and cooled in a crushed ice bath to afford three crops of yellow platelets. These crops were combined and recrystallized from EtOH–H_2O to afford 4.53 g (71.3%) of light yellow flakes, melting range dependent on rate of heating. Anal. ($C_{15}H_{13}ClHO_4{\cdot}Na{\cdot}4H_2O$) C, H, N, H_2O. With shaking, 402 mg (1 mmol) of that salt was partitioned between 75 mL of 2 N HCl and 175 mL of 1:1 EtOAc–Et_2O. The organic phase was washed with brine and dried over Na_2SO_4. Solvents were removed under reduced pressure to give an orange solid, which was recrystallized three times from EtOAc to yield 115 mg (37%) of a light yellow solid, mp 169–169.5 °C. This material was identical with the isolated metabolite by NMR, UV, TLC, high-performance LC, IR, and MS: ^1H NMR (Me_2SO-d_6) δ 7.62 (d, 2 H, J = 9 Hz), 7.50 (d, 2 H, J = 9 Hz), 6.17 (s, 1 H), 4.65 (br hump, 1 H, exchangeable with D_2O), 3.88 (s, 2 H, sharpened by the addition of D_2O), 3.73 (s, 2 H), 3.62 (s, 3 H); IR (KBr) ν_{max} 3411, 2952, 1737 (br), 1607 cm^{-1}; MS m/e 309, 307 (100%); UV (CH_3CN) λ_{max} 254 nm (ϵ 1.28 × 10^4), 315 (1.12 × 10^4). Anal. ($C_{15}H_{14}ClNO_4$) C, H, N.

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Book Reviews

Analytical Profiles of Drug Substances. Volume 7. Edited by K. Florey. Academic Press, New York. 1978. 15.5 × 22 cm. ix + 504 pp. $24.00.

The usefulness of this series to all pharmaceutical scientists and educators is well established. This seventh volume includes 18 detailed descriptions of drugs monographed in the official compendia: allopurinol, amoxicillin, chlorpheniramine maleate, dihydroergotoxine methanesulfonate, diphenoxylate hydrochloride, droperidol, epinephrine, ethambutol hydrochloride, fluoxymestrone, hexetidine, hydroflumethiazide, hydroxyzine dihydrochloride, 6-mercaptopurine, phenobarbital, sulfamethazine, thiostrepton, trimethoprim, and tubocurarine chloride.

More medicinally oriented chemists may be pleased to learn that a companion series covering the *Pharmacological and Biochemical Properties of Drug Substances*, the first volume of which is announced in the preface to this volume, will eventually create a truly encyclopedic work on our clinically useful drugs.

Staff

Mechanisms of Pain and Analgesic Compounds. Eleventh Miles International Symposium. Edited by F. Beers, Jr., and Edward G. Bassett. Raven Press, New York. 1979. xiii + 496 pp. 16 × 24 cm. $39.50.

The eleventh volume of the Miles International Symposium series is a collection of papers and the discussions which took place at the end of each of the sessions presented in Baltimore in June 1978. The symposium opened with a touching memorial tribute to the late Maurice Seevers presented by Dr. Walter Compton of Miles Laboratories.

The scientific part of the symposium is divided into six sections, the first of which deals mainly with current concepts of the nature of pain. The following section is comprised of a group of papers dealing with the neurophysiology of pain. Each of the contributions was written by an authority in this field, as is true for all of the other papers, but are primarily of interest to clinicians and neurophysiologists. The last four sections, which make up well over half the volume, are of greater interest to medicinal chemists.

The subject matter in the section entitled "Endogenous Substances Having Analgesic Action" is almost entirely limited to the enkephalins and endorphins—none of the newer opioid peptides, some of which were reported after this meeting was held, are discussed. The next section on peripheral mechanisms of pain and analgesics should be read by those engaged in research on nonopioid analgesics and antiinflammatory agents. The fifth section contains papers on the mode of action of opiates by such well-known investigators as Collier, Klee, North, and Herz.

The last section is entitled "New Leads for the Development of Analgesics". Even though the discussion leader, Julian Villareal, employed the term, "leads" in the sense that they are "presented as clues for action or objectives for focusing effort", this reviewer feels that the title of this section is misleading. Most if not all the material in this section is not new, and at least one reader does not feel that any new insights are presented to aid in designing new analgesics. Despite the misleading nature of the title, this section should prove to be quite useful to medicinal chemists in general and of particular interest to those engaged in analgesic research.

The organizers of the symposium and editors of the volume are to be congratulated for gathering a group of investigators whose papers were of uniformly high quality and for managing to publish them in a hard-cover book using conventional printing in so short a period of time.

Rensselaer Polytechnic Institute **Sydney Archer**

Progress in Drug Research. Volume 22. Edited by Ernst Jucker. Birkhäuser Verlag, Basel. 1978. 412 pp. 17 × 24.5 cm. $112.00.

Volume 22 contains eight contributions from various areas of drug research and therapy. Reviewed in this issue are "Aspects of Social Pharmacology" (by J. Venulet), "Fundamental Structure in Drug Research II" (by O. Schier and A. Marxer), "Antifungal Agents" (by P. F. D'Arcy and E. M. Scott), "Analgesics and their Antagonists: Recent Developments" (by A. F. Casy), "The Benzodiazepine Story" (by L. H. Sternbach), "Antiviral Agents" (by D. L. Swallow), "Clinical–Pharmacological Criteria in the Development of a New Antibiotic Basis and Methods" (in German) (by H. P. Kuemmerle), and "Drug Research and Human Sleep" (by I. Oswald). We call attention to the fact that this volume is the last which went into press during Dr. A. Birkhäuser's lifetime; he passed away on March 4, 1978. Dr. Birkhäuser founded this series of monographs and gave his strong support for the last 20 years. All in drug research are saddened by his passing and can think of no better memorial to him than the

continuation of these monographs in accordance with the excellent standards we have come to expect from Birkhäuser Verlag and the editor of this series, Dr. Ernst Jucker.

Staff

N-Nitrosamines. ACS Symposium Series. Number 101. Edited by Jean-Pierre Anselme. American Chemical Society, Washington, D.C. 1979. x + 204 pp. 15.8 × 23.5 cm. $22.50.

This work is a part of the "ACS Symposium Series" and it is based on presentations made at the Eighth Northeast Regional Meeting of the American Chemical Society in Boston, Mass., June 25–28, 1978. In addition to papers delivered at the symposium, several chapters have also been added or modified to give a more balanced presentation of the subject.

The major emphasis of the book is on the chemistry of nitrosamines rather than on the biological or environmental aspect of this important group of carcinogens. In addition to the introductory chapter on the basic chemistry of the compounds, chapters are presented on the photochemistry, stereochemistry, α substitution, and their oxidative (α and β) activation. The chapter by Lyle et al. on the role of stereochemistry in the carcinogenicity of the nitrosamines is rather speculative and ignores the report that 2,6-dimethylnitrosomorpholine is much more potent than nitrosomorpholine. The chapter by Keefer on the possible role of α-aminonitrite esters in the formation of nitrosamines is also rather speculative, but alternative explanations for their experimental observations are clearly presented. The chapter by Hecht et al. on the occurrence, carcinogenicity, and metabolism of tobacco-specific nitrosamines is excellent and it contains the type of information that would be of interest to the medicinal chemist. The volume also contains a subject index which increases the utility of the text, but it is poorly designed. Though nitrosation catalysts and nitrosamine metabolism are mentioned in many of the chapters, neither of these subjects is in the index.

University of Mississippi **John K. Baker**

Conjugation Reactions in Drug Biotransformation. Edited by A. Aitio. Elsevier/North-Holland, Amsterdam. 1978. x + 529 pp. $69.75.

This book contains the proceedings of the symposium on conjugation reactions in drug biotransformation held in Turku, Finland, in July 1978, as a satellite symposium of the 7th IUPHAR Congress. It includes the invited lectures and abstracts of the poster presentations at the symposium, as well as summaries of the discussions which followed the presentation of papers. The book is a compilation of 43 papers, arranged in 8 sections, and 36 abstracts of the poster presentations. The list of authors include 159 names and many individuals contributed more than one article.

Four of the eight sections of the book deal with specific conjugation reactions. The first section discusses the metabolism of arene oxides and contains four papers dealing with the pharmacological and toxicological aspects of alkene and arene oxide metabolism, glucuronide formation in the metabolism of benzo[*a*]pyrene, and activation of benzo[*a*]pyrenephenols. The second section of the book deals with glycoside conjugation reactions and contains papers on the formation and metabolism of glycosides of phenolic steroids and bilirubin-1X. Conjugation reactions with amino acids and their derivatives are discussed in the third section of the book. Two papers in this section deal with glutathione conjugation reactions. The fourth section of the book is devoted to UDP glucuronyltransferases. This section contains nine papers which covered a wide range of topics, including the perinatal development of the enzyme, modulation of microsomal UDP glucuronyltransferase by membrane, and effectors of UDP glucuronyltransferases.

The remaining four sections of the book deal with general topics in conjugation reactions. One section is devoted to the presentation of papers on genetic variability in drug metabolism and another deals with conjugation reactions in isolated hepatocytes. The biochemical characterization of enzyme systems involved in drug biotransformations is the subject of a separate section that contains 11 papers which deal with a variety of topics, including the purification and characterization of UDP glucuronyltransferases from rat liver, properties of purified rat liver epoxide hydrase, and sulfation reactions. The final section of the book deals with the pharmacological and toxicological implications of conjugation reactions. It contains five papers, three of which deal with conjugates of *N*-hydroxyarylamines and -arylamides. One paper in this section discusses the pharmacokinetic and toxicologic implications of glucuronide and sulfate conjugation of salicylic acid and acetaminophen in man. The final paper in the book is a short review which attempts to underscore the importance of conjugation reactions in the action and fate of foreign compounds.

The poster abstracts cover a wide range of topics and, in general, are clear and informative. The inclusion of the summary of discussions which followed the presentation of papers is a useful feature of this book.

In the foreward to the book, the editor states "the main emphasis of the symposium was to elucidate the state of art of the conjugation reactions in toxication, detoxication and disposition of drugs". Reading the proceedings indicates that the symposium has achieved this goal. This book provides a convenient collection of timely papers and is recommended to the novice as well as to the serious worker in the field of drug metabolism.

The University of Minnesota **Mahmoud M. Abdel-Monem**

Analysis of Drugs and Metabolites by Gas Chromatography–Mass Spectrometry. Volume 6. Cardiovascular, Antihypertensive, Hypoglycemic, and Thyroid-Related Agents. By B. J. Gudzinowicz and M. J. Gudzinowicz. Marcel Dekker, New York. 1979. x + 446 pp. 15 × 22.5 cm. $47.50.

Volume 1 of this series was published in 1977, Volume 6 has recently appeared, and at least one more volume is in preparation. Together these represent a compendium of experimental data concerning GC and GC/MS analyses of important drugs. Volume 6 is divided into two chapters. Chapter 1 is a discussion of drugs used in treatment of cardiovascular abnormalities, including the glycosides, antiarrhythmic agents, coronary vasodilators, coumarin-type anticoagulants, diuretics, and antihyperlipidemics. Chapter 2 includes antihypertensives, hypoglycemic agents, thyroid hormones, and antithyroid drugs. These chapters are accompanied by a total of 478 references through 1977 and by both author and subject indicies.

As in earlier volumes, data are presented in, for the most part, the same format as that used by the original authors. Adaptation of original data to a consistent format for presentation throughout these volumes would have substantially added to the value of the series. There is a definite improvement in organization and content with successive volumes. In Volume 6, the authors have made a genuine attempt to include information in each of the following categories for the drugs discussed: structures; methods of extraction from physiologic fluids; derivatization procedures; GC techniques and retention time data on various stationary phases; quantitation standards; mass spectra; quantitative GC/MS methods; and analytical data obtained in laboratory and clinical applications of these techniques. It should be emphasized, however, that this information is not complete in every case. Some irrelevant information is included and important data are often missing. For example, the authors have a particular fascination for reporting the manufacturers and models of equipment used (even when the equipment is obsolete) but often omit mass spectra of important compounds. Throughout the series, very little data are presented on analyses of major drug metabolites.

This volume and others in the series represent a substantial contribution to the field of drug analysis by providing an accessible source of information and references for sample preparation and gas chromatographic analyses of important drugs. Chemists with a knowledge of current analytical techniques and a file of appropriate reprints would probably not find the series useful. It is recommended, however, for libraries and large analytical laboratories.

University of Colorado **John A. Thompson**

Nutrition and the Brain. Volume 3. Edited by R. J. Wurtman and J. J. Wurtman. Raven Press, New York. 1979. ix + 309 pp. 16.5 × 24 cm. $29.50.

Volume 3 in this series is a collection of six chapters concerned with clinical and metabolic aspects of two disorders of nutrition—obesity and anorexia nervosa, with the use of dietary neurotransmitter precursors in the treatment of brain diseases, with the relationships of vitamins and megavitamin therapy to the nervous system, and with a general description of nutrients and cofactors that are required for monoamine synthesis in nerve tissue.

There is little direct application to medicinal chemistry in this volume, but those medicinal chemists interested either in obesity and other disorders related to nutrition or in the nervous system may find useful background material.

Cahill and his colleagues give a general picture of the overall metabolic economy of the body and list some pathologic changes associated with obesity and anorexia nervosa. Bruch has clinically oriented chapters on these two diseases. Growdon gives a detailed review of the still experimental use of neurotransmitter precursors such as tryptophan, tyrosine, and choline in the treatment of neurologic and psychiatric disorders. He emphasizes this as a "new" therapy based on recent findings, though tryptophan in the treatment of brain disorders has been tried for well over a decade. Lipton and others review megavitamin therapy, which they regard as identical with orthomolecular psychiatry, in the treatment of mental illnesses. They argue persuasively against the practices of many who advocate megavitamin therapy in treating psychosis. Sourkes discusses the substrates, cofactors, and metals required in the synthesis of monoamine neurotransmitters.

Overall the book is well done and furthers the objective of the series to appeal to scientists interested in nutrition as well as those interested in the brain.

Eli Lilly and Company **Ray W. Fuller**

Chemisty and Biology of Nucleosides and Nucleotides. Edited by Robert E. Harmon, Roland K. Robins, and Leroy B. Townsend. Academic Press, New York. 1978. xxi + 468 pp. 15.5 × 23.5 cm. $22.00.

This should have been a "state of the art" book, for it is the permanent record of the symposium on the Chemistry and Biology of Nucleosides and Nucleotides, held in San Francisco in 1976. The meeting was held in conjunction with the celebrations of the 100th anniversary of the founding of the American Chemical Society, and the editor of the book draws attention to the fact that it was also about 100 years ago when Miescher published the first paper on "nuclein", thus launching chemical research on nucleic acids. This must have lent a real sense of fitness to the occasion. It was also particularly appropriate that the symposium should begin with two papers of such import as those which were presented by Khorana and his co-workers. These two papers, which take up the first 36 pages of the book, describe the total syntheses of an *E. coli* tyrosine suppressor tRNA gene, in which the entire duplex has an overall length of 207 nucleotide base pairs. The synthetic gene was also shown to be fully functional in vivo. This was, of course, a monumental achievement. As Khorana himself points out, however, it must not be allowed to overshadow completely the solid basis on which its success depends, namely, the specialized chemical synthetic methods which have been developed over the years, and the remainder of the book reflects an ever increasing activity in this area. Indeed, the emphasis in the symposium seems to have been more on chemistry than on biology, and there are many papers describing methods for the synthesis of new nucleosides, nucleotides, and their analogues. This area of chemistry is technically a very difficult one, and it is obvious that newer laboratory techniques are being exploited to advantage. In particular, reversed-phase high-pressure liquid chromatography has proved to be an extremely powerful tool for carrying out separations both on the analytical and preparative levels, and it was a key technique in the gene synthesis which has already been mentioned.

In this preface, the editor expresses the hope that this volume will serve as reference and source material for many workers in biomedical research and also as teaching material for instructors of advanced science courses. It is fair to say that his hopes have probably been realized. Any chemist, and to a lesser extent biologist, who intends to introduce himself to modern aspects of this highly specialized field could not do better than to buy a copy. It is well written, nicely produced, is full of information, and carries a subject index as well as a list of those who contributed to the symposium. It should earn a place on the bookshelves of those interested in nucleosides and nucleotides. For many workers active in the field, however, the book has to some extent been overtaken by events; its late appearance, 2 years after the symposium, somewhat belies any claim that it represents a "state of the art" account of research in its area. This is a pity, because the volume otherwise constitutes a very valuable addition to the literature of this important and highly interesting field of research.

Trinity College, Dublin **Peter H. Boyle**

Schistosomiasis. III. Abstracts of the Complete Literature, 1963–1974. Volumes I and II. By K. S. Warren and D. B. Hoffman, Jr. Hemisphere Publishing Corp., Washington, D.C. (distributed solely by The Halsted Press, a division of Wiley, New York, N.Y.). 1976. 730 pp. 22 × 28.5 cm. $90.00.

Schistosomiasis. IV. Condensations of the Selected Literature, 1963–1975. Volumes I and II. Edited by D. B. Hoffman, Jr., and K. S. Warren. Hemisphere Publishing Corp., Washington, D.C. 1978. 537 pp. 22 × 28.5 cm. $90.00.

The volumes "Schisto III" and "Schisto IV" came for review simultaneously despite several years between their publication dates. This does admit of intercomparison of the two individual units in the series of definitive reference volumes on schistosomiasis which Warren, his associates, and computer back-up have developed.

"Schisto III" provides abstracts of the literature on schistosomiasis which was published between 1963 and 1974 as a continuation of the bibliographic *tour de force* which was begun with Warren's 1973 work "Schistosomiasis. The Evolution of a Medical Literature". This set represents the integrated blending of citations and abstracts numbering 8148, as stated in the preface. No single source was adequate to provide such coverage, developed from "Tropical Diseases Bulletin", "Helminthological Abstracts", and "Index Medicus". The material was arranged in alphabetic sequence based on the first author; however, the complete author index and the keyword index make truly accessible the superb quality of material compiled.

In "Schisto IV", the editors enlisted 17 deep specialists in the area to provide definitive condensations of literature in schistosomiasis embodying parasitology and studies done on experimental animals and in the clinic. The depth of the selections is further enhanced by inclusion of selected monographs and review articles. It has been developed as a vademecum, not as a cookbook for methods and procedures. When indicated, illustrative material has been supplied, and discussions, observations, and interpretations are all combined to make these well-indexed volumes fitting for the total compendium.

The compilation of volumes by Warren and his team was prompted by diverse considerations on the dispersed diffuse literature of schistosomiasis. One certainly has been the fact that clinicians and others in endemic areas have relatively little access to pertinent source material to aid in their work. These beautifully handled, highly successful efforts have been assembled in very attractively bound, well printed, highly expensive books. There is no doubt that they constitute a very substantial investment, from start to ownership. Their true worth may be established through their resistance to fungi, bugs, humidity, and other associates of tropical regions where they do especially deserve to find great use. The series certainly must be included in the budget of facilities involved in work on schistosomiasis.

Walter Reed Army Institute of Research **Edgar A. Steck**