

mixture was then stirred 1 week at room temperature. The dark solution was poured in a thin stream on 2 kg of ice and treated with 2 l. of concentrated NH_4OH solution (28%). After filtration and washing with H_2O , the wet precipitate was dissolved in 2 l. of CHCl_3 . The CHCl_3 solution was dried (Na_2SO_4) and the volume was reduced to approximately 1 l. On cooling and subsequent filtration, 122 g of 4,5-bis(phthalimidomethyl)acridine was obtained as a whitish powder: mp 285–287°. From the filtrate a second crop of the same material was obtained after chromatography on silicic acid. Elution with benzene–ethyl acetate (95:5) afforded 14 g (total yield 136 g, 54%).

The 4,5-bis(phthalimidomethyl)acridine (136 g, 0.27 mol) was refluxed for 20 hr with 8 l. of 6 N HCl, then cooled to 0°, filtered, and washed with H_2O . The precipitate was suspended in 200 ml of MeOH, warmed to reflux, and then cooled to 10°. After filtration the yellow crystals were washed with MeOH to yield 49 g (58%) of crude material. An analytical sample was prepared by crystallization from water: mp >350°; pmr (DMF- d_7 - D_2O) δ 4.8 (s, 4, ArCH_2N), 7.8 (comp m, 6, H-1, H-2, H-3, H-6, H-7, H-8), 9.1 (s, 1, H-9). *Anal.* ($\text{C}_{15}\text{H}_{15}\text{N}_3 \cdot 2\text{HCl}$) C, H, N, Cl.

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Book Reviews†

The Treatment of Parkinsonism with L-Dopa. By John Marks. American Elsevier, New York, N.Y. 1974. vii + 165 pp. 16 × 24 cm. \$11.25.

The book is a compilation of reprints or translations of 12 "classical and original" papers, tracing the development of the use of levodopa in Parkinsonism, beginning with James Parkinson's 1817 essay on shaking palsy. The choice of the landmark contributions to the subject is defensible, although workers in the field might challenge the omission of other equally influential contributions. Some of the chapters are prefaced by an italicized brief historical outline or by a short interpretation of the findings described in the paper following. The book concludes with a terse italicized listing of "Further Problems" and a 3½ page appendix on current views on the clinical use of levodopa (unreferenced). While publication of the compilation of these 12 papers may be defended on the basis of historical value, all of them have appeared in print previously, and all are well known and are readily accessible in the original to the scientific community. The contribution of the author–editor–compiler (this reviewer is uncertain as to the proper designation) to the book seems minimal and, overall, the volume does not impress this reviewer as being useful or needed, either by active workers in the field or by those who might wish to gain knowledge of an insight into Parkinson's disease. Proofreading of the book has not been rigorous, as evidenced by misspelling of "vitamin" in the Index, p 165.

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Organic Reactions. Volume 21. William G. Dauben, Editor-in-Chief. Wiley, New York, N.Y. 1974. vii + 417 pp. 14.5 × 23 cm. \$22.50.

This volume follows the pattern previously established with each chapter containing a discussion of selected reactions and their mechanisms followed by tables listing reactants, conditions, products, and the references for specific reactions in each general category. Both chapters of volume 21 discuss methods for the synthesis of fluorine-containing compounds. The titles of these chapters are "Fluorination by Sulfur Tetrafluoride" and "Modern Methods to Prepare Monofluoroaliphatic Compounds."

How Modern Medicines are Discovered. Edited by Frank H. Clarke. Futura, Mount Kisco, N.Y. 1973. ix + 177 pp. 15.5 × 23 cm. \$10.00.

This is a book which is somewhat difficult to place in a category, either by content or by style. It does not fit the classification of a monograph or a journal, is not really a textbook, and yet its emphasis is more than historical. The editor and authors have attempted to tell the story of how new medicinal agents are developed, from the point of view of the medicinal researcher. They have chosen to go about this task by utilizing the rich historical framework from which the medicinal sciences have grown, by attempting to communicate the rewards and excitement as well as the disappointments which many have known during the progress of their work. They have also made every effort to highlight and put into perspective the considerable scientific insight and technological developments which have grown over the years. In my opinion, they have succeeded admirably.

The book begins with a chapter bearing the same title as the book, in which the editor eloquently describes the entire process involved in the creation of a new drug, from the initial concept to the final clinical trials. The interdisciplinary nature of the process is emphasized throughout. From this point, the story unfolds into chapters on the development of specific classes of medicinal agents, chosen mainly for their illustrative elegance. Chapter 2 relates the developments of the natural antibiotics, from the discovery of penicillin and chlortetracycline, through the testing methods to biosynthetic and chemical modifications. The third chapter is devoted to developments in the area of analgetics, again scanning the spectrum, this time from morphine to aspirin. Brief sections on narcotic antagonists and the development of the rational approach to analgetic drug design are also presented.

The fascinating story of the sulfa drugs is treated in chapter 4, from their origins in the dye industry to their use as antibacterials, diuretics, and antidiabetics. Chapter 5 deals with the progressive relationship in the early research in the areas of antimalarials and antihistamines which led to the discovery of the tranquilizers and antidepressants, represented best by the discovery of chlorpromazine. The chapter concludes with a short discussion of the function of the brain amines, particularly as related to mental illness and Parkinsonism. Chapter 6 contains a discussion of hormones and their analogs, touching on such topics as contraception and the sex hormones, steroidal antiinflammatory agents and other corticosteroids, and the polypeptide hormones insulin, ACTH, and oxytocin.

The next chapter is nominally concerned with the chemical transmitters in both the sympathetic and parasympathetic nervous system. The authors have approached the topic from a very current viewpoint, that of antihypertensive therapy. The balance in the autonomic nervous system is clearly, if somewhat simply,

† Unsigned book reviews are by the editorial staff.

described, followed by a discussion of several antihypertensive mechanisms of specific medicinal agents. The final chapter is entitled "Biochemical Approaches to Medicinal Research and Development" and is probably the chapter which most has an eye toward the future. It makes a case for the need for a solid biochemical rationale in future medicinal research. The author points out the desirability of a greater understanding of molecular biology, pharmacodynamic behavior, and drug interactions in the next generation of progress and gently nudges us in that direction.

If one would ever sit around a campfire telling stories about drug discovery, this book would be a transcript of those stories. The material flows freely and easily and offers not only a unique perspective to the medicinal researcher but also an easily understandable overview of the drug discovery process to anyone with minimal training in organic chemistry and biology. Ideally, it would be directed to the undergraduate contemplating further study in the areas of the health sciences. Two other particularly useful features of the book are (1) an index and (2) listings of suggested reading at the end of each chapter, for those who wish to pursue a topic to greater length. Summing up, this book is easily worth having in one's personal library.

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Chemical Carcinogenesis (Volume 4 of the *Biochemistry of Disease Series of Monographs*). Edited by Paul O. P. Ts'o and J. A. Di Paolo. Marcel Dekker, New York, N.Y., 1974. 16 × 24 cm. Part A: xx + 440 pp. \$29.75. Part B: xviii + 351 pp. \$26.50.

A symposium on Model Studies in Chemical Carcinogenesis, sponsored jointly by the National Cancer Institute and the Atomic Energy Commission, was held Oct 31 to Nov 3, 1972, at the Johns Hopkins Medical Institutions, Baltimore, Md. This monograph is a collection of the 42 papers presented. The intent of the symposium was to facilitate interaction between those individuals engaged in chemical carcinogenesis so as to identify promising areas that might be exploited in future research. The program was addressed to five major areas of carcinogenesis: mechanisms of action of chemical carcinogens, particularly the polycyclic aromatic hydrocarbons; interrelationships of chemical, physical, and viral carcinogenesis; cell transformation and mutagenesis; interruption of the carcinogenic process by metabolic modification of the carcinogen or repair of altered cellular molecules; and recent advances in cancer biology, particularly in the area of immunology. The monograph begins with a review of French research on chemical carcinogenesis with special reference to the careers and contributions of the late Professors A. Lacassagne and N. P. Buu-Hoi. The emphasis on hydrocarbons is most evident in the section on the physicochemical, organic, and biochemical studies of the carcinogenic process, in which 13 of 15 papers deal with these compounds. Although the emphasis on this class of carcinogens limits the scope of these books, it does permit the juxtaposition of several alternative approaches to this important and unsettled area of research. Additionally, those sections dealing with the biochemical and biological response of the cell or host draw, often by necessity, on a wider area of chemical carcinogenesis studies.

The presentations vary in format from concise reviews of published material to extensive descriptions of experimental work not

previously reported. Discussion and comments that these presentations most probably evoked are not included. A subject and author index for both Parts A and B is in Part B. The books are printed by use of a photo offset process.

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Conformation of Biological Molecules and Polymers. Volume V. Proceedings of International Symposium on Quantum Chemistry and Biochemistry. Edited by E. D. Bergmann and B. Pullman. Academic Press, New York and London, and Jerusalem University Press, 1973.

This book contains the talks presented at the fifth Jerusalem Symposium held in April of 1972. The editors state in their preface that the symposium set two goals for itself: "to collect the experimental facts and theoretical points on which there is agreement and to formulate precisely those questions that remain open to further theoretical treatment and new experimental approaches." Not surprisingly, the symposium was more successful in achieving its goals in some areas than others.

The talks presented at the symposium included a number of theoretical papers on quantum mechanical and classical approaches to conformational energies, as well as nmr, ORD-CD, X-ray, and dipole moment studies to determine structure and conformation.

The general areas covered were (1) theoretical and experimental studies of small peptide conformations (this area was one in which the reviewer feels the goals of the symposium were successfully reached), (2) protein tertiary structure, (3) small nucleoside and nucleotide conformation, (4) conformational analysis of neurotransmitters, hallucinogens, and histaminic compounds, and (5) conformational changes accompanying intermolecular interactions. As one can see, the subjects cover an extremely wide area. This is the main weakness of this volume; it tries to cover too much and thus the depth of coverage in specific areas often leaves something to be desired. This weakness is somewhat remedied by including the discussions which followed the papers; the reviewer found these discussions often interesting and illuminating.

Some of the results presented that this reviewer found most interesting were the utility of the PCIO quantum mechanical method in studying conformational effects, most clearly documented by the studies of B. Pullman and coworkers; the small molecule *ab initio* internal rotation studies of Radom and Pople; the studies of small ring conformations in dipeptides; the studies of nucleoside and nucleotide conformation by Sundaralingam; P. Pauling's discussion of the conformations of neurotransmitters; and the contributions on semiempirical potential functions by Scheraga and Lifson.

This book should be in every library where there is interest in relations between physical properties of molecules and their biological activity. Most scientists who have an interest in these relations will find some of the articles in this volume of interest.

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