yield after column chromatography. TLC (silica gel, chloroform) of this product showed only one component, and the R_f was identical with that of a sample of (−)-II prepared in 74% yield from (−)-I hydrochloride and diazomethane. The oily (±)-II was converted into a crystalline picrate, m.p. 187–189° dec., and a crystalline perchlorate, m.p. 263° dec.

The two preparations of apomorphine dimethyl ether [(−)-II and (±)-II] showed identical IR (film), UV, and NMR spectra; $\lambda_{max.}^{MeOH}$: 216 mμ (ε, 47,000), 269 (ε, 19,000), 306 s (ε, 2300); NMR ($CDCl_3$): 2.57 (3H, singlet), 2.66–3.37 (7H, multiplet), 3.73 (3H, singlet), 3.91 (3H, singlet), 6.91–7.18 (4H, multiplet), 8.28 (1H, doublet, J = 2 c.p.s.). (±)-Apomorphine dimethyl ether was converted to its hydroiodide salt with 57% hydriodic acid. Recrystallization from acetone–water yielded white needles, m.p. 279° dec.[1]

Anal.—Calcd. for $C_{19}H_{22}INO_2$: C, 53.91; H, 5.24; I, 29.98; N, 3.31. Found: C, 54.08; H, 5.40; I, 30.17; N, 3.13.

The demethylation of this hydroiodide proved an exceptionally facile reaction, considering the sensitivity of apomorphine to oxidizing agents as well as to acylating agents. The hydroiodide was heated with an equimolar mixture of 57% hydriodic acid and acetic anhydride at reflux for 1 hr. When the reaction mixture was diluted with ether, pure (±)-apomorphine hydroiodide was precipitated and isolated as a white crystalline powder, m.p. 282° dec.,[1] in 93% yield. This compound oxidized only slowly when stored in the cold under nitrogen. $\lambda_{max.}^{MeOH}$: 217 mμ (ε, 41,000), 273 (ε, 17,000), 309 (ε, 3300).

Anal.—Calcd. for $C_{17}H_{18}INO_2$: C, 51.66, H, 4.59, I, 32.11; N, 3.54. Found: C, 51.48; H, 4.69; I, 32.00; N, 3.40.

[1] Determined on a duPont differential thermal analyzer under nitrogen.

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JOHN L. NEUMEYER*
BERNARD R. NEUSTADT
KLAUS K. WEINHARDT
Arthur D. Little, Inc.
Acorn Park
Cambridge, MA 02140

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* To whom inquiries should be addressed. Present address: Department of Medicinal Chemistry, School of Pharmacy, Northeastern University, Boston, MA 02115

BOOKS

REVIEWS

International Encyclopedia of Pharmacology and Therapeutics. Section 13, Volume 1-Anticholinesterase Agents. Edited by C. RADOUCO-THOMAS, Pergamon Press Ltd., Oxford, England, 1970. ix + 508 pp. 15.5 × 23.5 cm. Price $24.00.

The number of compounds that inhibit the class of enzymes known as cholinesterases has increased markedly in recent years. These compounds, which have had only limited applications in medical therapy and have few equals as investigational tools in pharmacology, are now important industrially as insecticides and militarily as the highly toxic "nerve gases," *e.g.*, sarin, soman, and tabun. Concurrently, large numbers of papers have been published dealing with chemical and biological aspects of these inhibitors and of the enzymes with which they react. Many reviews have subsequently appeared, of which the one edited by Koelle in 1963, *Cholinesterases and Anticholinesterase Agents*, may be the most extensive and most widely used.

The present volume of anticholinesterase agents for the most part covers the same literature as that of the review of Koelle and attempts to include most papers published through late 1968. The material is presented in two major subsections, with an introduction, titled "History of the Research With Anticholinesterase Agents," by Professor A. G. Karczmar, the Section Editor. This part considers in brief, historic detail the pharmacology of physostigmine, the concept of neurohumoral transmission, some novel aspects of the cholinergic system, organophosphorous inhibitors, early work on cholinesterases, the therapeutic uses of inhibitors of these enzymes, and some interesting points of disagreement among investigators of these areas.

Subsection I, titled "Reactions of Cholinesterases With Substrates, Inhibitors and Reactivators," compiled by Dr. Earl Usdin, comprises the major portion of the volume. The author states that a somewhat different point of view has guided this review: an intention not only to describe the reactions of cholinesterases with substrates, inhibitors, and reactivators, but to make known the differences and similarities among the reactions of these three classes of compounds. In this effort, reference has been made to the active

sites of the enzymes, to the mechanisms and kinetics of the reactions, and to structure–activity relationships; stereoisomeric effects have been emphasized. Separate sections are included that are concerned with studies of the active sites of cholinesterases and on the "aging" of the organophosphate–enzyme product, since the latter phenomenon has particular significance in the therapy of poisoning by organophosphate inhibitors.

Subsection II, titled "Toxicity of Anticholinesterases and Treatment of Poisoning," by Dr. J. H. Wills, has two goals: (*a*) to complement and update reviews concerned with the pharmacology and toxicology of anti-ChE compounds, and (*b*) to describe and place on as firm a foundation as possible the treatment of poisoning by ChE inhibitors. Dr. Wills has assembled a large amount of basic data and information about the toxicology of a variety of inhibitors of ChE; and, more importantly, he has laid a foundation for therapy by a highly competent and thorough pharmacological analysis of the relevant material. The medical literature should still be consulted for clinical applications, to which the discussion of Dr. Wills is a prerequisite.

This review will be helpful to the student, investigator, and teacher interested in the various phases of ChE enzymes and their inhibitors, especially those for whom the historiographic approach is important. The subsection by Dr. Usdin, in addition to almost 300 pages of data and discussion, includes over 50 pages of references, a testimony to literature searches aided by computers. The computer, however, cannot be faulted for the fact that in an important table listing inhibitor constants the references are identified by number, whereas they are listed alphabetically. More rigorous editing here and throughout the text would have added to the readability and importance of this very useful review.

Reviewed by A. A. Kondritzer
Medical Research Laboratory
Edgewood Arsenal, MD 21010 ■

The Chemistry and Biochemistry of Steroids. Edited by N. KHARASCH, Intra-Science Research Foundation, Santa Monica, Calif., 1969. iv + 166 pp. 21.5 × 28.5 cm. Price $12.00.

This book represents a compilation of a series of lectures presented by Drs. Leland J. Chinn, John S. Baran, Paul D. Klimstra, and Raphael Pappo at the University of Southern California during the fall of 1968. The authors are all research chemists with G. D. Searle and Company and considerable discussion is given to research conducted in the Searle laboratories over the past two decades. Taken in this light, the book represents informative reading for students in medicinal chemistry interested in an industrial career.

The book is not, however, a complete text describing "The Chemistry and Biochemistry of Steroids" as represented by the publishers. Only selected areas of steroid chemistry are emphasized, and often times repeated (*e.g.*, synthesis of 19-norsteroids), and the biochemical aspects are even more limited in scope. For example, the initial chapter by Dr. Chinn represents an excellent discussion of mineralocorticoids, but little mention is made of the equally important glucocorticoids. Moreover, the chapter on conformational analysis is lucidly presented, but the section on structure–receptor interaction fails to evaluate critically the various hypotheses associated with this nebulous subject.

The chapters on biosyntheses of cholesterol and hypocholesterolemic agents by Dr. Baran are an up-to-date summary of the research in these fields. To confuse the matter, however, these chapters are followed by another given the same title as the text itself, but which deals largely with the metabolism of cholesterol. Similarly, a chapter entitled "Biological and Clinical Aspects of Estrogenic Hormones" is four pages in length and describes mainly Dr. Baran's own research with 11β-methyl-19-norsteroids.

The chapters by Dr. Klimstra on oral contraceptives and androgenic and anabolic steroids are well-documented reviews. As pointed out by the author, however, similar reviews recently have been published in other texts.

The final two chapters are written by Dr. Raphael Pappo and pertain to a discussion of the chemistry and biology of 2-oxasteroids and total and partial synthesis of steroids. The author has contributed significantly to the former and describes in detail the chemical development of the 2-oxa isostere of methyltestosterone which is marketed as an anabolic agent under the name of Anavar. A considerable portion of the chemistry presented in this chapter describes the author's own work and has not been published elsewhere.

Thus, this book represents an interesting and easy-to-read series of lectures representing selected areas of steroid chemistry and biology. It is not, however, a text on "The Chemistry and Biochemistry of Steroids" as the title implies.

Reviewed by Raymond E. Counsell
Laboratory of Medicinal Chemistry
College of Pharmacy
University of Michigan
Ann Arbor, MI 48104 ■

International Encyclopedia of Pharmacology and Therapeutics. Pharmacology of the Endocrine System and Related Drugs: The Neurohypophysis. Executive Editor, G. PETERS; Section Editors, H. HELLER and B. T. PICKERING. Pergamon Press Ltd., Oxford, England, 1970. x + 486 pp. 15 × 23.5 cm. Price $16.00.

This volume I of section 41 of the *International Encyclopedia of Pharmacology and Therapeutics* is composed of 12 chapters by 19 distinguished contributors. The subject matter includes the history of neurohypophysial research, the chemistry of the natural and synthetic neurohypophysial hormones, their distribution and evolution in vertebrates, structural–activity relationships of the natural and synthetic hormones, and the latest theories on their storage, release, biosynthesis, and analysis in body fluids. There is also an expanded chapter on the physiological and pharmacological effects of posterior pituitary peptides and their derivatives on the kidney, uterus, and mammary gland. In addition, there are chapters on the effects of posterior pituitary hormones and their derivatives in lower vertebrates, their cellular mode of action and fate, as well as a concluding discourse on the clinical pharmacology of oxytocin and vasopressin.

Through this text which deservedly carries the term encyclopedia are extensive references to books, reviews, monographs, and original papers which easily bring the researcher up to date on the most recent data available concerning every conceivable aspect of the neurohypophysis. Appended is a complete author and subject index.

The reader is urged to spend some time studying a series of electron-micrographs which very clearly demonstrate the ultrastructural changes and the effects on hormone release of ether anesthesia, and ether-and-hemorrhage on rat and rabbit neural lobes.

One major and obvious oversight is the unintentional absence of pages 264–265, 268–269, 272–273, 276, and 277. It is hoped that the publisher can, at this time, still rectify this before the book begins to circulate widely. It is too fine a reference source to be known for its missing pages and accompanying facts. This work should be included in all medical research libraries and is recommended to all investigators interested in the most up-to-date information concerning the pharmacology and endocrinology of the posterior pituitary.

Reviewed by Ronald F. Gautieri
Department of Pharmacology
School of Pharmacy
Temple University
Philadelphia, PA 19140 ■