1, H_2 of Ar ring, $J_{2,3}$ = 7 Hz and $J_{2,4}$ = 3 Hz), 5.10 (q, 1, HCOH, J = 6 Hz), 4.37 (d, 2, OCH_2, J = 6 Hz), 4.03 [m (septet), 1, $NCH(CH_3)_2$, J = 7 Hz], 1.41 [d, 6, $(CH_3)_2$, J = 7 Hz]; CIMS (methane), m/z 274 (QM, 62), 256 (QM - H_2O, 91), 238 (QM - $2H_2O$, 45) 199 (36), 145 (naphthol QM, 100), 130 (67). Anal. ($C_{16}H_{19}NO_3$) C, H, N.

***N*-Nitroso-1-(isopropylamino)-3-(1-naphthoxy)-2-propanol (3, *N*-Nitrosopropanolol).** To a stirred solution of 4.00 g (14.0 mmol) of propranolol hydrochloride (Sigma Chemical Co.) in 150 mL of 10 M acetate buffer (pH 4.0) was added dropwise a solution of 18.7 g (0.270 mol) of $NaNO_2$ in H_2O over 1.5 h, while the temperature was maintained at 95 °C. After stirring for 3 h, the mixture was cooled and extracted with $CHCl_3$ (3 × 100 mL). The combined $CHCl_3$ extracts were washed with a saturated NaCl solution (2 × 100 mL) and aqueous 10% Na_2CO_3 (3 × 100 mL) and dried (Na_2SO_4), and the solvent was evaporated to yield an orange oil, which solidified on standing. Recrystallization from EtOAc–cyclohexane afforded 3.00 g (77%) of *N*-nitrosopropanolol (**3**) as a pale orange crystals: mp 83–89 °C; NMR (60 MHz) ($CDCl_3$) δ 8.25 (dd, 1, H_8 of Ar ring, $J_{8,7}$ = 8 Hz and $J_{8,6}$ = 2 Hz), 7.80–7.60 (m, 1, H_5 of Ar ring), 7.60–7.30 (m, 4, H_4, H_6, and H_7 of Ar ring), 6.75 (dd, 1, H_2 of Ar ring, $J_{2,3}$ = 8 Hz and $J_{2,4}$ = 2 Hz), 4.90–3.70 [m, 6, H_1, H_2, H_3, $NCH(CH_3)_2$], 3.60 (d, 1, OH, J = 4 Hz), 1.45 (d, 5.4, CH_3, J = 6 Hz), 1.15 (d, 0.6, CH_3, J = 6 Hz); IR (KBr) 3300, 3105, 3030, 2965, 1635, 1585, 1575, 1460, 1445, 1400, 1355, 1280, 1235, 1180, 1110, 1075, 1025, 1000, 965, 930, 795, 770, 740 cm^{-1}; CIMS (methane), m/z 289 (QM, 30), 288 (M, 18) 259 (QM - NO, 22), 215 (15), 145 (naphthol, 100), 72 (64). Anal. C, H, N.

Mutagenesis Testing. Male Sprague–Dawley rats (150–200 g) were obtained from the National Institutes of Health animal supply and maintained as previously described.[33] Animals were treated with Arochlor 1254 (500 mg/kg) dissolved in corn oil and sacrificed 48 h later. Preparation of liver fractions was performed as previously described.[34]

Mutagenesis assay was performed according to the method of Ames et al.[35] with minor modifications. To 2.2 mL of molten top agar containing 17 μmol of $MgCl_2$, 0.125 μmol of biotin, 0.215 μmol of histidine, 33 μmol of KCl, and 100 μmol of sodium phosphate buffer at 45 °C were added 0.1 mL of the bacterial tester strains (TA-98 or TA-100) grown in nutrient broth overnight (2–3 × 10^9 bacteria/mL), 0.1 mL of solution containing the compounds to be tested dissolved in Me_2SO, and 0.1 mL of the 9000*g* supernatant fraction containing 1.0 mg of protein. Prior to addition, liver fractions were diluted with phosphate-buffered saline to the desired protein concentrations and filtered through a 0.45-μm Swinnex filter unit (Millipore). The concentrations of protein in the filtrates were then determined after filtration to estimate losses during this process. NADPH (1 mg/plate) was added to 0.1 mL of phosphate-buffered saline. In all experiments, test compounds were added last. The colonies on each plate (histidine-independent revertants) were scored on a Count-all (Model 600) colony counter (Fisher Scientific Co., Pittsburgh, PA) after a 40-h incubation in the dark at 37 °C. The toxicity of the test compounds to the bacteria was tested by determining the number of colonies formed in histidine-enriched (4.5 mM) agar after the bacteria had been exposed to varying concentrations of the test compounds for 30 min at 37 °C and diluted to approximately 10^3 bacteria/mL before plating.

Acknowledgment. The authors thank the U.S. Public Health Service (GM-25,373) for partial support of this work.

Registry No. 1, 84418-31-5; 1·0.5-oxalate, 84418-32-6; 1·HBr, 84418-33-7; **2**, 84418-34-8; **3**, 84418-35-9; *N*-hydroxyisopropylamine, 5080-22-8; 1-naphthoxy-3-bromo-2-propanol, 2007-16-1; propranolol hydrochloride, 318-98-9.

(33) Schut, H. A. J.; Thorgeirsson, S. S. *Cancer Res.* **1978**, *38*, 2501.
(34) Felton, J. S.; Nebert, D. W.; Thorgeirsson, S. S. *Mol Pharmacol.* **1976**, *12*, 225.
(35) Ames, B. N.; McCann, J.; Yamaski, E. *Mutat. Res.* **1975**, *31*, 347.

Book Reviews

Introductory Medicinal Chemistry. By John B. Taylor and Peter D. Kennewell. Halsted Press (A Division of Wiley), New York. 1981. 202 pp. 15.5 × 23.5 cm. ISBN 0-470-2752-X. $59.95.

The declared intention of the authors is to provide an introduction to medicinal chemistry research for scientists with an organic chemistry background but minimal knowledge of the biological and pharmaceutical sciences.

The book is divided into six chapters. Chapter 1 deals with definitions of subject areas, such as pharmacy, pharmacology, microbiology, etc. A historical drug development section is included, followed by a classification of pharmacological agents and a brief mention of the major processes involved in drug action. Chapter 2 deals with drug formulations, routes of administration, and dosage forms. The treatment is very concise and readable and is an adequate introduction to this branch of the pharmaceutical sciences.

Chapter 3 is entitled "The Pharmacokinetic Phase" and includes a section on cell biology (20 pages) and a useful section on QSAR. The pharmacokinetics of drug distribution are not discussed. Chapter 4 is concerned with the interaction of a drug with its site of action. The concept of receptors, receptor structures, agonists, and antagonists are discussed, and a section on radiolabeled ligands is included. The types of binding involved in drug–receptor interactions is also discussed, but the examples quoted deal mainly with enzyme models only. A section on receptor topography is given that is restricted to a summary of the structure–activity relationships of morphine and its synthetic derivatives. Finally, there is a topic on molecular design, which suffers from some rather poor illustrative examples chosen by the authors.

Chapter 5 is entitled "Neurotransmitters and Receptors". Half the chapter (16 pages) is concerned with the histology and anatomy off the nervous system and the rest is devoted to a rather classical pharmacological description of agonists and antagonists acting at peripheral receptors. A mention of receptors in the CNS is restricted to a list of central neurotransmitters. Surprisingly, there is no mention of the important role of enkephalins, endorphins, or γ-aminobutyric acid as neurotransmitters.

Chapter 6 deals with drug metabolism and is a concise, well-written, and useful introduction to this topic.

A useful reference section, a glossary of terms, and a subject index are provided. The book is adequately bound.

This book represents a rather basic introduction to medicinal chemistry, considering the intended readership suggested by the authors. Because of the broad, multidisciplinary approach chosen by the authors, the treatment is not comprehensive, some notable omissions being chemotherapeutic agents, prostaglandins, and antiinflammatory drugs. In addition, the authors have not emphasized the underlying chemical basis of drug action as forcefully as they might have done, and few examples of chemical mechanisms in drug action are given. Although this book may be of some interest to organic chemists wishing to persue a career in industrial medicinal chemistry, I doubt if it will become a useful text for undergraduate pharmacy or pharmacology students. At

$59.95, the book is expensive compared to similar size texts in this subject area.

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Heterocyclic Chemistry. Volume 2. Specialist Periodical Reports. Edited by H. Suschitzky and O. Meth-Coh. The Royal Society of Chemistry, Burlington House, London. 1981. xx + 441 pp. 14.5 × 22 cm. ISBN 0-85186-813-4. $155.00.

The first volume of this series reviewed the heterocyclic literature from July 1978 to June 1979. Now, the second volume updates this review to June 1980. The organization and format of this issue are patterned after Volume 1 with one exception: a separate chapter on conformational analysis has been deleted. Again, the list of senior reporters is impressive, as are their reviews.

The coverage of oxirans and aziridines, e.g., their preparation, theoretical aspects, and reactivity, constitutes the major portion of Chapter 1 by T. J. Mason who surveys the literature on three-membered ring systems. In Chapter 2, R. C. Storr examines four-membered heterocycles and their analogues; a number of interesting papers on the preparation and transformations of β-lactams (azetidinones) are reviewed. Chapter 3, devoted to the literature of five-membered ring systems, is divided into three parts. In Part 1, S. Gronowitz reviews the extensive contributions to the thiophene area with mention of the synthesis of monocyclic and condensed selenophenes and NMR studies conducted on certain tellurophenes. Next (in Part 2), P. A. Lowe covers systems containing nitrogen and sulfur, selenium or tellurium. Isothiazoles, thiazoles, thiadiazoles, and their fused derivatives comprise the bulk of this material. Certain ring systems are categorized according to the Sprague–Land classification. G. V. Boyd reviews the literature on the remaining five-membered rings and their respective fused analogues in Part 3. The literature surveyed is broken down by the type of heteroatoms in the ring and by the ring size of the second ring in fused systems. Together, the topics reviewed in this chapter represent approximately 40% of this text.

S. O. Carter, G. W. H. Cheeseman, and G. P. Ellis review six-membered ring systems in Chapter 4, which like Chapter 3, is divided into two parts. In the first part, Carter and Cheeseman cover azines, oxazines, and thiazines. These reporters have used the same organization adopted by R. K. Smalley in Volume 1. Ellis follows in Part 2 with a review on the remaining six-membered ring systems and their fused counterparts. Both parts reference most of the notable research published on these systems. Literature on seven-membered ring systems is surveyed by J. T. Sharp in Chapter 5, a major portion of which is devoted to the chemistry of azepines and diazepines. In Chapter 6, G. M. Brooke covers eight-, nine-, and ten-membered rings and also includes an interesting section on macrocycles. In the last chapter (Chapter 7), J. M. Mellor reviews the literature on bridged systems. A section on physical methods assesses the conformational aspects of these systems.

Like Volume 1, this text contains a detailed table of contents that provides access to specific topics quickly and easily. Reviews on certain ring systems are cited at the beginning of each chapter or subtopic, and references to the material selected for review appear at the bottom of each page. An author index is provided at the end of the text. Although page constraints were applied to this volume, the individual reporters still provide comprehensive reviews on their topics and maintain the high quality established in Volume 1.

Chemists interested in all phases of heterocyclic chemistry will find this new series indispensable. Volume 2 has been reduced in price, but it is probably still to expensive for inclusion in personal collections. However, like its predecessor, it certainly belongs on the shelves of research libraries. This volume lives up to the promise of Volume 1 and it is hoped that The Royal Society of Chemistry continues to publish this series for years to come.

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The Chemistry of Heterocyclic Compounds. Volume 41. The Pyrazines. By G. B. Barlin. Edited by A. Weissberger and E. C. Taylor. Wiley-Interscience, New York. 1982. xxi + 687 pp. 16.5 × 24 cm. ISBN 0471-38119-5. $150.00.

Volume 41 of *The Chemistry of Heterocyclic Compounds* is a comprehensive review of synthetic methods in pyrazine chemistry. The work covers the literature cited in Beilstein (to 1929) and Chemical Abstracts (to 1978) and selected references (to 1980) including the patent literature. With few exceptions, the synthetic methodology is thoroughly cross-referenced between different but related sections of the text.

An occasional weakness of the work is its lack of mechanistic interpretation, which tends to make some of the facts presented less indelible. For example, oxidation of 2-chloropyrazines with normal peracids, such as peracetic acid, occurs with high regioselectivity at N-4 and with peroxysulfuric acid (Caro's acid) at N-1 (Mixan, C. E.; Pews, R. G. *J. Org. Chem.*, **1977**, *42*, 1869). The simple explanation of the regioselectivity at N-1 (protonation of N-4) is not mentioned. An exception to the lack of mechanistic detail is the adequate discussion of ANRORC rearrangements occurring during reactions of halopyrazines with hard nucleophiles, such as amide ion (Lont, P. J.; van der Plas, H. C. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 449).

A section on ionization and spectroscopic properties of pyrazines is very useful in understanding the regiochemistry of pyrazine substitution reactions. Reaction conditions are well described, but tables of compounds generally lack yield data. The utility of pyrazines as flavoring agents, chemotherapeutic agents, and ethical drugs and the occurrence of pyrazines as natural products are well described.

The subject index proved to be quite complete and very useful. Few typographical errors and no omissions of important chemistry were noted. The book is an indispensable reference work in the field of pyrazine chemistry.

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Reverse Phase-High Performance Liquid Chromatography: Theory, Practice, and Biomedical Applications. By A. M. Krstulovic and P. R. Brown. Wiley, New York. 1982. xi + 296 pp. 23.5 × 15.8 cm. ISBN 0471-05369-4. $35.00.

This book is an excellent compendium of knowledge in reverse-phase high-performance liquid chromatography (RP-HPLC). The authors estimate that 80% of HPLC chromatography being done is with RP methodology employing C_{18} columns of 5–10 μm sphere diameter. The aim of this book is primarily toward researchers with minimal experience in either RP-HPLC or HPLC, and this book provides that group with an excellent foundation with which to begin research. In addition, this book is an excellent review for researchers already using HPLC.

The book is presented in a logical and helpful manner and covers the following pertinent topics. Basic theory and terminology are given with definitions of solute–solvent interactions, peak broadening, column efficiency, resolution, etc. The chapter on instrumentation is a survey of all aspects of instrumentation presented in a briskly moving manner. The authors thoroughly discuss components in a HPLC system, including tubing, pumps, injectors, and detectors. The chapter on columns and column performance is a detailed collection of both basic chemistry underlining column supports and bonded phases, as well as assessment and characterization of individual columns. Another chapter is devoted to basic mechanisms involved in RP-HPLC wherein four mechanisms are proposed. No consensus is presented. Ion-pair techniques are treated briefly. For newcomers to the field of RP-HPLC, an excellent chapter is provided that is based on the authors' experience and philosophy for developing a strategy for HPLC analysis. General guidelines and specific chromatographic details are provided. A brief chapter outlines possibilities for spectroscopic and chemical characterization of fractions collected after RP-HPLC. Electrochemical detection, IR, NMR, and MS are discussed. Two brief chapters discuss chemical derivatization and quantitative analysis; the latter by

external standard, internal standard, and standard addition methods. The book concludes with a chapter that the authors hope will "whet the appetite" of researchers considering using RP-HPLC. Experimental details on analysis of nine different classes of compounds are discussed: amino acids, peptides, and proteins; biogenic amines; enzymes; lipids; nucleotides, nucleosides, and bases; steroids; vitamins; therapeutic drugs and drugs of abuse; and miscellaneous (uric acid and creatinine).

In summary, this book is highly recommended to both newcomers and practitioners of RP-HPLC. It is timely in its presentation—current literature (up to 1981) is extensively and intensively reviewed. The authors provide numerous diagrams, equations, and figures that are quite helpful to the reader.

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Modern Pharmacology-Toxicology. Volume 19. Hypertension Research: Methods and Models. Edited by Frederick M. Radzialowski. Marcel Dekker, New York. 1982. viii + 454 pp. 15.5 × 23.5 cm. ISBN 0-8247-1344-3. $67.50.

This volume was not meant to serve the medicinal chemist but rather as a sourcebook for experimental procedures and models in hypertension research. In this aspect it succeeds. The benefits and pitfalls of animal models and biochemical techniques are presented in a collection of well-referenced and generally thorough treatises.

W. E. Hageman and M. D. Brannan provide a comprehensive and very practical overview of the methods of arterial pressure measurement (Chapter 1). Telemetry is reviewed by T. B. Fryer and H. Sandler (Chapter 2). Techniques to demonstrate centrally acting drugs are described by J. P. Buckley and B. S. Jandhyala (Chapter 3). J. L. Perhach (Chapter 10) presents a meaningful discussion on the role of the CNS in the etiology of hypertention and the animal models relevant to research in this area.

An excellent review of the renin–angiotension system is provided by I. A. Reid (Chapter 4). The experimental utility and clinical relevance of models of renal hypertension are critically evaluated by J. Buggy and G. D. Fink (Chapter 11).

A thorough review of the background and biochemical techniques in the measurement of the prostaglandins and their metabolites in biological fluids is provided by L. M. Cagen and J. C. McGiff (Chapter 5). The excellent manner in which this topic is treated extends the benefits of this chapter beyond the scope of this book. A similar broad applicability is found in Chapter 9 wherein special emphasis is placed by M. M. Hall and J. H. Sanner on the utility of in vitro techniques in the evaluation of vasoactive agents.

The mechanism of action of β-adrenergic blocking agents and the techniques utilized in their experimental evaluation are effectively covered by C. S. Sweet (Chapter 8). In Chapter 12 a review of adrenal hypertensive models is provided (C. E. Hall and C. Gomez-Sanchez) and a monograph on the spontaneously hypertensive rat is presented in Chapter 13 (A. J. Tobia and G. M. Walsh).

This book is recommended as a practical reference for the pharmacologist in the initiation or development of a program in antihypertensive research.

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Chemical Derivatization in Analytical Chemistry. Volume 1. Chromatography. Edited by R. W. Frei and J. F. Lawrence. Plenum Press, New York and London. 1981. xi + 344 pp. 16 × 23.5 cm. ISBN 0-306-40608-X. $39.50.

Chemical derivatization is a very important technique in analytical chemistry and especially in chromatography. It is an established method of expanding the usefulness of both gas and liquid chromatography. This volume is the first in a series on derivatization and should prove valuable to chromatographers in all fields. Although the chapters are written by different authors, the book is uniformly well written. Each chapter has an extensive bibliography from early work in the 1960s through 1979, and because there are only four chapters, each author was able to present the material in-depth.

The first two chapters deal with gas chromatography. The first chapter is on chemical derivatization in pesticide analysis. While the topic that W. P. Cochrane covers is fairly specialized, some of the material can be generally applied to other GC analyses, especially clean-up techniques using chemical reactions.

The second chapter by W. C. Kossa explores the use of cyclic boronates as derivatization reagents for use in coupled GC—mass spectrometry analyses of functional organic compounds. When GC–MS is used, the derivatization techniques must be compatible not only with the GC but also with the mass spectrometry. This chapter includes a table of some cyclic boronates that have been used in GC–MS, the scope of applications, gas chromatographic and mass spectrometric properties of cyclic boronates, as well as preparation of these compounds. Also included is an excellent section on specific biochemical examples of the preparation and use of cyclic boronates.

The third and fourth chapters deal with high-performance liquid chromatography (HPLC). In the third chapter, L. A. Sternson discusses in-depth precolumn derivatization. Included in this chapter are sections on HPLC detectors and compatible derivatives, chemical reactions used in derivatization, and functional group analysis (amines, alcohols, carboxylic acids, aldehydes and ketones, nitrogen-containing compounds, and thiols). Also discussed are both theoretical discussions and practical applications of paired ion chromatography.

The final chapter, by one of the editors, R. W. Frei, is a comprehensive discussion of reaction detectors or postcolumn derivatization. Both the theoretical and technical aspects of tubular, bed, and segmented stream reactors are discussed. Also included are applications of these techniques, coupling of these techniques with other detection modes and techniques, and trends for the future.

This book is highly recommended for analytical chemists and for those in any discipline in which chromatography is used and who are interested in expanding the usefulness of their chromatographic systems.

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European Organization for Research on Treatment of Cancer, Monograph Series. Volume 9. Combination Antibiotic Therapy in the Compromised Host. Edited by Jean Klastersky and M. J. Staquet. Raven Press, New York. 1982. x + 250 pp. 16 × 24 cm. ISBN 0-89004-658-1. $28.50.

The book, Volume 9 in the monograph series of the *European Organization for Research on Treatment of Cancer*, consists of 14 chapters written by a total of 23 authors. It is directed primarily to the clinician concerned with antibiotic therapy in compromised hosts. Infection poses a serious complication in cancer patients, and while some progress has been made in treating some infections, other new types of organisms, not previously regarded as pathogenic, are causing serious problems. Mixed infections and the development of resistant organisms offer further complications. The book, as stated in its preface, "will contribute to a still more rational use of combinations of antibiotics and will suggest new areas for microbiological and clinical investigation".

The first three chapters cover the "Significance of In Vitro Tests", "Evaluation of Combination Antibiotic Therapy in Experimental Animal Models of Infection", and "Serum Bactericidal Test: A review with Emphasis on Its Role in the Evaluation of Antibiotic Combinations". The first chapter details and critiques the various in vitro techniques for evaluation of combination effects and discusses correlations with human infections. The second chapter covers some discriminative models of infection that simulate the characteristics of the infection in man. This chapter gives the features of the models discussed and describes the effects of antibiotic combination in infections such as endocarditis, meningitis, and osteomyelitis. The third chapter details the application of serum bactericidal tests as clinical guides for the course of therapy of serious infections.

The next four chapters deal with the "Theoretical Basis of Antibiotic Synergy and Antagonism", "Pharmaceutical Interactions Involving Parenteral Antibiotics", "Toxicity of Combined Antibiotic Regimens", and "Clinically Useful Combinations of Antibiotics". The first of these chapters briefly categorizes the types of synergies and antagonisms but does not discuss them from a biochemical perspective. The chapter on pharmaceutical interactions first discusses the stability of single antibiotics (penicillins, cephalosporins, aminoglycosides, and "other" antibiotics) in solution at room temperature and in deep frozen solution. The second part of the chapter deals with chemical interactions between antibiotics in solution (in vitro) and in vivo interactions, and the discussion focuses upon the β-lactam–aminoglycoside interaction. Other antibiotics are only briefly discussed.

The chapter on toxicity of combined antibiotic regimens emphasizes results from clinical trials. Topics that are discussed include the cephalosporin-induced increase in aminoglycoside nephrotoxicity, the toxicity of carbenicillin-aminoglycoside regimens, the toxicity of isoniazide–rifampicine, and the toxicity of "other" combinations.

The chapter on clinically useful combinations argues against the philosophy "if one is good, two must be better". Data, both in vitro and clinical, are given to support the use of specific antibiotic combinations.

The remaining half of the book contains seven chapters. These are, "Antibiotic Therapy for Febrile Granulocytopenic Patients", "Clinical Evaluation of Antibiotic Combinations", "Combination Antibiotics for Mixed Infections", "Antibiotic Combinations and Bacterial Endocarditis", "Combination of Antifungal Agents for Systemic Mycotic Diseases", "Clinical Use of Antiviral Chemotherapy", and "Adjuvant Therapy for Severe Infections".

These latter chapters examine clinical situations that commonly require combination antibiotic therapy. The chapters provide data concerning clinical experiences with one agent, two agents, and multiple agent therapy, and the authors have made suggestions for the use of combination therapy in the management of these conditions.

The book has a short but useful index, and each chapter has an extensive list of references (about 1125 references in all) that appear to give coverage through 1979 with only a few (less than 1%) later citations. The format of the individual chapters is quite consistent, and each chapter gives useful summary conclusions. The book will be of value to onocologists, students of clinical oncology, and clinical pharmacologists interested in antibiotic management of infections.

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Typical and Atypical Antidepressants. Volume 31. Molecular Mechanisms. Volume 32. Clinical Practice. Edited by Erminio Costa and Georgio Bacagni. Raven Press, New York. 1981. Volume 31: xviii + 391 pp. 16.5 × 24 cm. ISBN 0-89004-686-7. $45.00. Volume 32: xxii + 400 pp. 16.5 × 24 cm. ISBN 0-8900-830-4. $39.50.

The introduction into medicine, during the 1950's, of the first two antidepressant drugs, imipramine and iproniazid, made available for the first time therapeutic intervention for endogenous depression. Pharmacological evidence suggested that the two drugs had different mechanisms of action: the former inhibited the neuronal receptor uptake of norepinephrine and serotonin, while the latter blocked the normal brain function of the monoamine oxidases. The extensive use of iproniazid in man ended with the recognition that the drug was capable of inducing intolerable toxicity. The major defects of imipramine were (1) a slow onset of action and (2) a limited therapeutic effectiveness.

Those circumstances led to extensive searches for more effective and less toxic drugs for the treatment of endogenous depression. Significantly, the pharmacological evaluation of several of those newer drug candidates has revealed that the mechanism by which they, and imipramine, exert their antidepressant effects are so varied that at the present time there exists no single unifying understanding of their mode of activity but rather a kaleidoscopic array of speculations.

This conclusion becomes inescapable from an examination of the 34 articles included in the first of the volumes. From a review of the 41 contributions in the second volume it is evident that none of the candidate drugs has shown significant clinical superiority over imipramine.

The two volumes are to be highly recommended as a means of developing a comprehensive overview of the current (1980) and older literature, as well as the points of view of the foremost investigators in this area of drug development. The typescript of the contributors are replicated throughout, and this has led to an almost errorless text.

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Advances in Biochemical Psychopharmacology. Volume 30. GABA and the Basal Ganglia. Edited by Gaetano Di Chiara and Gian L. Gessa. Raven Press, New York. 1981. x + 241 pp. 16 × 24 cm. ISBN 0-89004-752-9. $28.00.

The book is subdivided into three main sections: "Anatomy and Electrophysiology of GABA Neurons in the Basal Ganglia", "Interactions of GABA with Other Transmitters in the Basal Ganglia", and "Role of GABA in Motor and Behavioral Functions of the Basal Ganglia". In the first section, the mapping of GABA neurons using lesioning and immunocytochemical techniques and electrophysiological methods is described. Based on these studies, reviewed in five chapters which summarize recent relevant literature, models for the neuronal interactions in the basal ganglia are outlined. These schematic models, which emphasize the central role of the inhibitory neurotransmitter GABA, demonstrate the complexity of the anatomy of this part of the brain. The four chapters in Section 2 describe the use of electrophysiological and pharmacological methods supported by techniques for in vivo studies of neurotransmitter release in studies of neuronal interactions. Such studies have recently provided new information about the structure and function of the basal ganglia. In this section some authors demonstrate combined use of electrophysiological and neurochemical methods. The first two chapters of Section 3 are also dealing with neuronal interactions in the brain areas concerned, and these chapters represent quite comprehensive reviews. The authors describe the application of lesioning and microinjection techniques supported by behavioral studies. In this section, the circling behavior of rats, induced by unilateral administration of different drugs into various areas of the basal ganglia, is extensively described. The relevance of this animal model in elucidating the functional role of different neuronal pathways is discussed. In the last chapter of Section 3 the possible involvement of GABA in various movement disorders is reviewed. Although neurochemical and anatomical studies strongly suggest that GABA has a major complicity in such diseases, the authors demonstrate that attempts to affect the symptoms and the progress of the diseases concerned via pharmacological manipulation of GABA-ergic mechanisms have, so far, not been very successful. The authors emphasize the urgent need for GABA-ergic agents capable of stimulating selectively GABA neurotransmission in the basal ganglia or in other restricted brain areas—indeed, a challenge to medicinal chemists!

The various chapters, which are written by scientists with high degrees of expertise, represent updated reviews, making the book useful to virtually all groups of neuroscientists. Unfortunately, a few chapters have been written not only by experts but also primarily for experts in the fields concerned. Since progress in neuroscience depends on communication and collaboration between scientists with expertises ranging from neuroanatomy and physiology to chemistry and biophysics, neuroscientists must learn to write reviews readable by other groups of colleagues. In any case, the book summarizes our present knowledge of the role of GABA in the basal ganglia, and it is a valuable resource for scientists currently active in neurotransmitter research. Unfortunately, a major part of the reference list of Chapter 4 is missing,

making reading of this interesting and valuable chapter somewhat difficult.

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Brain Neurotransmitters and Hormones. Edited by Robert Collu, Jacques R. Ducharme, Andre Barbeau, and George Tolis. Raven Press, New York. 1982. xviii + 409 pp. 18.5 × 26 cm. ISBN 0-89004-763-4. $46.00.

This book represents the proceedings of the XII Congress of the International Society of Psychoneuroendocrinology held in Montreal in May, 1981. The articles form an eclectic mix of topics ranging over nonstriatal dopaminergic systems, γ-aminobutyric acid and benzodiazepam actions, brain peptides, clinical psychoneuroendocrinology, the chronobiology of affective disorders, stress, and ethanol tolerance. Many of the articles are written by leaders in these fields and provide up-to-date reviews or current research reports on selected topics. Although the 33 articles in this book cover too much territory for detailed review here, a few of the main topics are pituitary dopamine receptors, comparisons between γ-aminobutyric acid receptors and benzodiazepine recognition sites, physiological effects of opiate peptides, neutrotensin, bombesin and ACTH, current clinical views on schizophrenia, tardive dyskinesia and affective disorders, and the endocrine effects of stress and ethanol.

The quality of the figures and drawings is generally very good, and the subject index is surprisingly detailed considering the rapid publication format used in this book. Although this collection of articles lacks the cohesiveness that can occur at more tightly focussed meetings, the individual articles are often excellent and will be of certain interest to clinicians and researchers in these rapidly moving research areas.

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PCP (Phencyclidine): Historical and Current Perspectives. Edited by Edward F. Domino. NPP Books, Ann Arbor, MI. 1981. xx + 537 pp. 15.5 × 23.5 cm. ISBN 0-196182-03-7. $40.00.

This monograph is the outgrowth of a workshop held December 13, 1979, in San Juan, Puerto Rico, by the American College of Neuropsychopharmacology. It outlines the development, pharmacology, clinical use, and abuse of PCP. Fifty-eight primary investigators of PCP from the U.S., France, and Israel have authored 25 chapters. This volume is essentially a collection of individual papers, some of which are reprinted from research journals; others are synopses of previously published research or minireviews. Accordingly, there is no uniform organizational style to the chapters and little, if any, cross-referencing from chapter to chapter. Nevertheless, this volume provides a timely comprehensive reference source on current knowledge on PCP. The mixture of disciplinary perspectives presented should make this volume interesting reading for both researchers in medicinal chemistry and pharmacology, as well as clinicians in the drug abuse and mental health fields.

Professor Domino has contributed significantly to both the basic scientific understanding of PCP and to the emergency room management of PCP overdose. He shares his wisdom most eloquently in the final chapter, which speculates on the future of PCP. He proposes three specific therapeutic goals to guide future research and outlines some major scientific questions that need to be answered. Professor Domino's analysis significantly enhances the value of this volume, especially to new investigators in this field.

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Advances in Fertility Research. Volume 1. Edited by D. R. Mishell, Jr. Raven Press, New York. 1982. x + 192 pp. 16 × 24 cm. ISBN 0-89004-577-1. $24.50.

Followers of research trends in the pharmaceutical industry are well aware of the fact that fertility research is not attracting appreciable attention in most companies. One of the recurring themes in this volume is that the opportunities for progress in this field are numerous, but the difficulties are substantial. Unlike most other areas of research that the pharmaceutical industry is engaged in, contraceptive research is frequently beset with social, cultural, and moral overtones, thus placing additional burdens on progress.

In this first volume of what will be a series, Dr. Mishell has invited leaders in the field of contraceptive research to provide chapters on natural family planning, vaginal contraception, oral contraceptives, intrauterine contraception, long-acting injectable steroids, subdermal implants, contraceptive vaginal rings, prostaglandins, male contraception, and contraceptive vaccines. A chapter discussing LRF analogues in female contraception is noticeable by its absence. In the majority of chapters, the reader is brought up to 1979–1980 in terms of timely references. Thus, while providing an excellent reference volume and an introduction to these areas of contraceptive research, the reader may have the feeling that *Time Magazine*, the *Wall Street Journal*, and the *New York Times* are providing more current information.

In general, this volume is well written with few errors. Among those detected are incorrectly designating norgestimate as the oxime of norgestrel rather than the oxime acetate and referring to malonaldehyde as propanediol rather than propanedial. Systematic names for a variety of long-acting steroids are incorrect in Table I, and the structural formula for 17α-hydroxyprogesterone caproate does not show the caproate as an ester group.

This relatively expensive volume will no doubt be well accepted by both established investigators and those entering the field. Future volumes are awaited with enthusiasm.

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