temperature, the reaction mixture was extracted with five 120-ml portions of diethyl ether. The combined extracts were dried (Na_2SO_4), and the residue (750 mg) obtained after removing the solvent was distilled [bp 118–119 °C (0.3 mm)]: NMR ($CDCl_3$)[8] δ 1.6–2.5 (m, 4 H, C-3′ and C-4′), 2.5–3.1 (m, 1 H, C-5′), 3.1–3.5 (m, 1 H, C-5′), 3.6 (t, 1 H, J = 7.5 Hz, C-2′), 3.48 (center of AB q, 2 H, J = 17 Hz, $\Delta\nu_{AB}$ = 17 Hz, CH_2CN),[9] 7.0–9.0 ppm (3 m, 4 H, typical splitting for aromatic H of 3-substituted pyridine); ir (neat) ν 2240 cm^{-1} (weak C≡N stretch); uv (EtOH) λ_{max} 260 nm (ϵ 1880).[10] Anal. ($C_{11}H_{13}N_3$) C, H, N. The dipicrate (from 2-propanol) melted at 149.5–151.5 °C. Anal. ($C_{23}H_{19}N_9O_{14}$) C, H, N. The GC and EI mass spectral characteristics of synthetic **10** were identical with those observed for the compound isolated from the nicotine incubation mixture.

It was not clear from these experiments if the cyanomethyl compound was formed indirectly by a Mannich base type condensation of cyanide ion with metabolically formed nornicotine and formaldehyde or by some process not involving initial cleavage of the C–N bond. This question was investigated by incubating nicotine-*N-methyl-d_3* (5×10^{-4} M) with the rabbit liver preparation in the presence of H_2CO (5×10^{-3} M). The H_2CO added would be expected to dilute any metabolically formed D_2CO at least 50-fold in which case **10**-*cyanomethyl-d_2* should be almost negligible compared to **10**-d_0. The GC–EI mass spectrum of the isolated cyanomethyl compound was found to be a 1 to 1 mixture of **10**-d_0 and **10**-*cyanomethyl-d_2* (*m/e* 109 vs. 111). Thus, to a significant extent, compound **10** appears to be formed without prior C–N bond cleavage suggesting that the reactive methyleniminium ion **9** is generated in the course of the in vitro metabolism of nicotine. The experimental details of these findings will be published separately.

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Trong-Lang Nguyen, Larry D. Gruenke
Neal Castagnoli, Jr.*
Department of Pharmaceutical Chemistry, School of Pharmacy, University of California
San Francisco, California 94143
Received April 22, 1976

Book Reviews

Atomic Absorption Spectroscopy. Second Edition (Revised and Expanded). By James W. Robinson. Marcel Dekker, New York, N.Y. 1975. ix + 183 pp. $14.95.

The second edition of this work has been expanded to include chapters on nonflame atomizers and on atomic fluorescence. The remainder of the text has been revised slightly. The work is a clear and concise statement of the basic theory and problems with which anyone wishing to use atomic absorption should be conversant. No prior knowledge of the technique is assumed. The fundamentals of AA are explained from a practical vantage point and should be particularly helpful for a novice wishing to use the technique. Discussions include fundamental theory, design and use of flame atomizers, spectral and chemical interferences, techniques for improving analyses, and statistical considerations. The fourth chapter is an element by element tabulation of operating conditions used for flame procedures.

Part of the expansion deals with nonflame atomizers (carbon rods, tubes, furnaces, etc.) which are currently being used to greatly enhance the sensitivity of the technique. This chapter provides an excellent introduction to these methods.

The other added chapter covers the fundamentals of atomic fluorescence spectroscopy. The coverage is an adequate introduction although no discussion of saturated atomic fluorescence using high-intensity sources (currently the most useful AF technique) is included.

In summary, the text affords an excellent introduction to the technique. It is not, nor does it purport to be, a definitive text covering state of the art research interests. It is highly readable and provides surprisingly thorough coverage of practical AA considering its brevity.

Chemistry Department
Northeastern University
Boston, Massachusetts 02115
T. R. Copeland

Structure–Activity Relationships for Some Conjugated Heteroenoid Compounds, Catechol Monoethers and Morphine Alkaloids. Volumes 1 and 2. By H. L. Holmes. Defence Research Establishment Suffield, Ralston, Alberta, Canada. 1975. 1498 pp. 21 × 28 cm. $30.00 (Canadian).

The two volumes achieve their principal objectives—to demonstrate whether the dominant factors, namely, the rate of

penetration of drugs, the rate of reaction between the drug and receptor site, the rate of loss of drug on its way to the locus of action, and, for certain structures, the fit factor between the drug and the receptor site, play a role in the degree of drug activity. The agents covered fall into the two major classes as the title implicates.

The two volumes are divided into 14 chapters each. There are over 1000 compounds listed. The reviewer has limited his comments to Volume 1 since Volume 2 deals mainly with physical and biological data of the compounds which are well presented in the form of tables, graphs, diagrams, etc. The chapters in the latter volume parallel those in Volume 1 which make the reading and referencing more facile. In order to complete the spectrum of the compounds referenced, each chapter is richly supplemented with adequate data from the literature wherever available. Highlights of some of the chapters in Volume 1 are as follows. The author starts with an elaborate synthesis of selected classes of compounds, namely, styrenes, 1,4-naphthaquinones, catechol monomethyl ethers, and morphine alkaloids. Their reaction toward nucleophilic attack is discussed. The partition coefficient values of these compounds in different solvent systems are covered in Chapter 3. Frequently, dipole moment values of several compounds have been substituted into the equation to achieve a better fit in the evaluation of rate of penetration of the drug through the cell wall. The rationale for the anamolies in observed and calculated P values has been presented. The next three chapters (7–9) deal with NMR, ir, and uv absorption data of these systems. Specific parameters such as spatial arrangement of atoms, solvent effects, ring substituents, etc., have been taken into account. In Chapter 7, the different factors that govern the rate, equilibrium, and degree of biological activity have been elaborated. Chapter 8 deals with the polarographic half-wave potentials of those compounds used to evaluate the possible oxidation of the receptor (protein thiols) by these compounds. The chapter also entails a discussion of the existence of a certain degree of covariance between the log of the half-wave potentials and log of the in vitro rate constants and the dipole moments. Chapter 9 concerns mass spectral studies and an explanation for the fragmentation patterns is well covered.

Chapters 10 and 11 concentrate on the stimulatory activities determined by the sequential method on the frog reflex and also the growth inhibitory activities (nonspecific receptors) on more than one organism. Here the author has speculated on the cause of withdrawal symptoms on the observation that the bio-oxidant that converts morphine to pseudomorphine is a component of a cellular redox system and that this equilibrium is disturbed leaving a preponderance of the reduced form. The comparative study of the biological responses of one organism to another is given in Chapter 13 and in the final chapter, Dr. Holmes, the principal contributor, has made a commendable effort to explain all the concepts covered in Volume 1 in a summary form.

This is an exhaustive and monumental piece of work carried out at the Defence Research Board Laboratories, Alberta, Canada. These two volumes provide a good deal of information and will serve as a valuable reference addition to anyone interested in kinetic approach to structure–activity relationship of drugs. Finally, for those involved in the narcotic analgesic field Dr. Holmes' speculation on the cause of withdrawal system is indeed noteworthy.

Department of Biomedicinal Chemistry **Vasant G. Telang**
College of Pharmacy
Howard University
Washington, D.C. 20059

Sexual Behavior—Pharmacology and Biochemistry. Edited by Merton Sandler and G. L. Gessa. Raven Press, New York, N.Y. 1975. 354 pp. $22.50.

Recently, scientific interest in the pharmacology of sexual behavior has been given impetus by the discovery of drugs which can stimulate or inhibit it. These discoveries seemed particularly important because such compounds appeared to interact selectively with one or another brain neurotransmitter. It seems then that sexual behavior not only depends on classic hormonal influences but is under monoaminergic control as well. Several chapters of this book, in fact, deal with the functional interplay of hormones with the various CNS neurotransmitter systems in controlling sexual behavior. There is an emphasis in the book on the morphologic substrates that underlie copulatory behavior and the search for suitable methodologic approaches. The book is composed of 39 short chapters (average 9 pp) presented at an unnamed symposium in 1974.

Some of the major subject areas covered are neuroendocrinology and pharmacology of sexual behavior, drug abuse and sexual behavior, influence on sexual behavior of drugs acting on monoaminergic and cholinergic mechanisms, the pharmacological and psychosocial problems related to sex offenders, influence on sexual behavior of steroid and peptide hormones, drugs affecting human sexual behavior, and sexual behavior in psychiatric disorders. There is some problem with this last section of topics. The chapters on sexual arousal in females and homosexuals deal with a strict psychoanalytic approach to the subjects which seems rather inappropriate to the theme of the symposium. Similarly, a chapter on sexual behavior in schizophrenia completely ignores the advent and impact of drug therapy in mental patients.

An interesting question underlying several of the presentations is whether the developments in the neurochemistry of sexual behavior will allow a biochemical interpretation of sexual disorders at present considered to be of psychogenic origin. A related problem is the extent to which the data obtained in rats can be extrapolated to man. There are suggestions in the text that the sexual behavior in the rat and man is modulated by a not entirely different biochemical mechanism to judge from the aphrodisiac effect of *l*-Dopa and PCPA and the sexually inhibiting effects of the neuroleptics and MAO inhibitors in both species. These suggested answers, however, appear less precise when human drug–sex practices are reviewed. Various CNS stimulants and depressants, marihuana, and psychedelics have all been reported to increase libido, enhance enjoyment of sex, and lower inhibitions in man; on the other hand, these same drugs have been indicated as sexual depressants. Certainly, one important variable is a dose-related phenomenon. Other explanations for these reports, however, use personality-dependent factors for drug use in sexual behavior, e.g., drugs as anesthetics for sexual fears or even as substitutes for normal sexual desire. Such psychosocial factors again raise questions regarding the reliability of animal models. However, it should be noted that impotence and premature ejaculation are not exclusively human conditions but have also been noted in the laboratory rat.

This book offers an interesting introduction to the area of the pharmacological basis of sexual behavior. Unfortunately, most chapters are so brief that they often leave the reader with more questions than answers on the subject. This entire area of research is developing rapidly though and it seems likely that there will be further important developments in the near future.

College of Pharmacy **Jeffrey B. Blumberg**
Northeastern University
Boston, Massachusetts 02115