EtOAc was removed under reduced pressure to yield an oil, which was purified by column chromatography (silica gel, 25% hexane–75% EtOAc) to yield **6** (410 mg, 30%): mp 160–165 °C. This compound was converted into its hydrochloride salt by stirring in a saturated solution of CH_3OH (HCl(g)) IR 3280–3120, 1430 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 4.55 (2 H, s), 6.81 (1 H, d, J = 7.5 Hz), 7.0 (1 H, t, J = 7.7 Hz), 7.11–7.64 (10 H, m), 8.05 (1 H, d, J = 7.8 Hz), 11.29 (1 H, s); MS (15 eV), m/e (relative intensity) 272 (100), 181 (59). Anal. ($C_{19}H_{17}N_2Cl \cdot 0.25H_2O$) C, H, N (high-resolution MS m/e 272.1316 ($C_{19}H_{16}N_2$ requires 272.1313)).

The potencies of **1a–c** as inhibitors of [^{3}H]diazepam binding to benzodiazepine receptors were determined as described[15] with minor modifications. In brief, cerebral cortex from adult, male Sprague–Dawley rats (Taconic Farms, Germantown, NY) was weighed and disrupted in 100 volumes of 50 mM Tris·HCl buffer (pH 7.4) with a Brinkmann Polytron (setting 6–7, 15 s). The tissue homogenization–centrifugation procedure was repeated two more times, and the final pellet resuspended in 50 volumes of Tris·HCl buffer. An aliquot (0.2 mL) of tissue suspension was added to 0.6 mL of assay buffer and 0.1 mL of varying concentrations of either **1a–c**, buffer, or flunitrazepam (final concentrations, 5 μM). Reactions were initiated by the addition of 0.1 mL of [^{3}H]diazepam (final concentration, 2 nM; sp act. 70 Ci/mmol) and terminated 90 min (4 °C) later by rapid filtration through Whatman GF/B filters and washing (two 5-mL aliquots of buffer) with a Brandel M-24R filtering manifold (Brandel Instruments, Gaithersburg, MD). Nonspecific binding, which was measured in the presence of 5 μM flunitrazepam, represented <5% of the total binding. Filters were air-dried and placed in scintillation vials containing 4 mL of Ready-Solv MP (Beckmann Instrument Co., Fullerton, CA), and radioactivity was measured with a Beckmann LS 5801 liquid scintillation spectrometer. The IC_{50} value (that concentration of compound inhibiting the specific binding of [^{3}H]diazepam by 50%) was estimated from a Hill plot[21] with six to eight concentrations of inhibitor. The IC_{50} values presented are $\bar{x}$ values obtained from three independent determinations with an SEM < 10%.

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(21) Bennett, J. P. In *Neurotransmitter Receptor Binding*; Yamamura, H., Enna, S., Kuhar, M., Eds.; Raven: New York, 1978; pp 57–90.

Book Reviews

Metal Ions in Biological Systems. Volume 20. Concepts on Metal Ion Toxicity. Edited by H. Sigel. Marcel Dekker, Inc., New York. 1986. xxiv + 386 pp. 16 × 24 cm. ISBN 0-8247-7540-6. $85.00.

Metal ion toxicity is a major focus of concern in environmental and health-related fields particularly in this technological age where the term pollution has become a household word. Thus this treatise on "Concepts on Metal Ion Toxicity" is a handy source of information that covers areas of interest to scientists ranging from geologists to biologists to chemists. The topics are divided into areas progressing from distribution descriptions to biological analytical methods.

Chapters 1 (G. Sposito) and 2 (R. B. Martin) provide an excellent background to metal ion distribution and transport on and over Earth in the former, and specific metal ion chemical and physical properties in the latter. These two chapters, while easy to read, provide fascinating tidbits of insight to metal ion occurrence and behavior.

Aquatic systems are discussed in Chapters 3 (E. Eichenberger) and 4 (G. K. Pagenkopf), respectively. These two chapters are nicely interlinked. Eichenberger provides background into the double role of the metals and the fine line between essentiality and toxicity as well as mechanisms that influence the response within the aquatic community. In Chapter 4 Pagenkopf develops a quantitative chemical model based on the results of toxicity studies on fish, whereby toxicity is related to a variety of chemical factors such as hardness and pH.

Chapter 5 (F. T. Bingham, F. J. Peryea, and W. M. Jarrell) bring the subject back to "solid ground" with an agriculturally related discussion of the factors affecting metal uptake by plants that includes diagnosis and corrective measures. This chapter complements the aquatic chapters quite well and provides a smooth link to the animal kingdom, the subject of the remaining chapters.

The next chapters deal with metal ion toxicity in humans. Chapter 6 (P. B. Hammond and E. C. Foulkes) is a well-written overview of eight specific metals, which includes historical background as well as absorption, distribution, excretion, and toxicity data. In Chapter 7 (M. R. S. Fox and R. M. Jacobs) a short background on general vitamin–mineral nutrients is provided, followed by an in-depth treatment of two essential nutrients, selenium and zinc. Chapter 8 (A. Leonard) leads the foray into chromosomal aberrations induced by heavy metals. After an introduction to chromosomal changes with helpful illustrative photos is provided, the results of cytogenetic monitoring for a variety of metals are outlined and discussed. Chapter 9 (M. Costa and J. D. Heck) continues on the cellular level, discussing metal ion carcinogenesis. Cellular uptake and distribution of metal ions and the effect of metal ions on cell growth, DNA, and the production of tumors are discussed.

Chapters 10 (J. D. Heck and M. Costa) and 11 (H. G. Seiler) provide the analytical finale: detection of metal ions and toxicity. Chapter 10 treats in vitro analysis, including biochemical, microbiological, and mammalian cell culture methods. In Chapter 11 the specifics and problems of analysis for toxic trace elements in biological materials are treated.

This volume is exceptionally well arranged with respect to presentation of the different aspects of metal ion toxicity in a logical fashion, starting with the overview of distribution, progressing through aquatic, agricultural, and animal studies, to closing with current analytical techniques. Each chapter provides sufficient background for a reader outside of the area as well as the current state of knowledge, with recent references, including a number of 1985 citations. This volume provides fascinating insight to the dual role of metal ions, essentiality and toxicity, and is clearly a welcome addition to the series.

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Modern Analysis of Antibiotics. Edited by Adorjan Aszalos. Marcel Dekker, New York. 1986. xvi + 535 pp. 18 × 26 cm. ISBN 0-8247-7358-6. $89.75.

This text describes a wide range of chemical and biological procedures for analyzing antibiotics. These procedures have many applications such as in the search for new antibiotics, determination of mechanism of biological activity, and quantitation for quality control of manufactured products. The book does not

include a number of special topics such as procedures for structure determination, methods of dereplication which are used to discover new antibiotics, and NMR analyses since each of these topics would require considerable space.

Three chapters cover the chromatographic techniques [gas chromatography (gc), thin layer chromatography (tlc), and high pressure liquid chromatography (hplc)]. Chapter 1 gives a rather comprehensive review of gc applications; however, this technique is limited to relatively few antibiotics since most are of too high molecular weight to be amenable to this approach. The chapter on tlc is very well written and gives a number of examples with references. It offers not only examples but also principles and guides for method development. Chapter 7 has an extensive collection of hplc procedures for a wide range of antibiotics and includes 493 references. As with several other chapters it reviews not only natural and semisynthetic antibiotics but also some synthetic antibacterial, antifungal, and antiviral agents.

Ultraviolet/visible, infrared, electron spin resonance, and mass spectrometry applications are reviewed in four separate chapters. The discussion of the UV/vis spectra describes spectral characteristics of the various antibiotic structure types, and includes spectrometric titration assays and quantitative methods of determining antibiotics by United States, European, and British Pharmacopoeia procedures. The chapter on mass spectrometry reviews the literature since 1977 and emphasizes newer ionization methods and applications of mass spectrometry to the various antibiotic structure classes. Extensive references are given for both the chapters on UV/vis spectra and mass spectrometry. The chapters on infrared and electron spin resonance spectroscopy (ESR) are focused primarily on special studies. The latter reviews applications of ESR spectroscopy to mechanism of action studies particularly those involving antibiotic–metal binding and antibiotic–DNA interactions. A final chapter on physical methods describes applications of thermal analyses to study antibiotic stability, purity, and compatibility of formulations.

Biological methods are covered in separate chapters describing antimicrobial, mammalian cell culture, immunological, and antiviral assays, and the use of sea urchin eggs for detecting cell division inhibitors. The chapters on antimicrobial and antiviral assays are comprehensive with extensive references. The other chapters are well written and provide details on experimental procedures.

The last chapter of the book reviews animal models for evaluating antibiotic toxicity. It provides a very good coverage of this topic, but the general subject seems to fall outside the scope of analytical methods for antibiotics.

The text is unique in that it is the only up-to-date compilation of both chemical and biological analytical techniques for antibiotics. In general, it brings together some very good reviews of these analytical methods and provides a good source of references for investigators wanting to gain familiarity with these procedures.

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Neuropsychopharmacology of the Trace Amines. Edited by A. A. Boulton, L. Maitre, P. R. Bieck, and P. Riederer. Humana Press, Clifton, NJ. 1985. 510 pp. 16 × 25 cm. ISBN 0-89603-099-7. $69.50.

This volume contains the proceedings of the 2nd Trace Amines Symposium held at Weitenburg Castle, West Germany, in May 1985. That this meeting occurred so soon after the 1st Trace Amines Symposium in Edmonton, Canada, in 1983, indicates how fast this field is moving due, for the most part, to the introduction of increasingly sophisticated physicochemical techniques for the detection and identification of trace amines. The book comprises 47 short papers divided approximately equally between a Neuropsychopharmacology section, covering studies of the effects of several trace amines on a variety of neurochemical and behavioral parameters, and a Clinical Pharmacology section, which contains details of trace amine measurements in certain neuropsychological states and also in healthy volunteers.

In the Neuropsychopharmacology section, there are interesting papers on the effects of 2-phenylethylamine (PEA), *p*-tyramine, octopamine, and tryptamine on brain chemistry and behavior, with particular emphasis being placed on their interactions with brain serotonin (5-HT) and dopamine systems. Data are also presented on the localization of possible pathways for trace amine-containing neurons in the central nervous system. Presented in the Clinical Pharmacology section are papers describing the association of trace amines with personality, stress, and depression, in addition to neurochemical analyses involving the measurement of trace indoleamines and [^{3}H]tryptamine binding sites in post-mortem human brain tissue.

Unfortunately, the book is sadly lacking in review chapters and as such will not appeal to researchers working outside this highly specialized area. However, for these scientists currently investigating the neuropsychopharmacology of the trace amines, this book will represent a valuable addition to their shelves.

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CRC Handbook of Autonomic Drugs and Autacoids. Edited by Matthew Verderame. CRC Press, Boca Raton, FL. 1986. 250 pp. 18 × 26 cm. ISBN 0-8493-3289-3. $105.00.

This handbook is one of a series of six medicinal chemical compendia written to present a systematic collection of selective chemical and pharmacological reference data on drugs from the major categories of therapeutically important agents. This volume is divided into six sections, namely "Adrenergics, Antiasthmatics, and Anorexigenics", "α- and β-Adrenoceptor Blocking Agents", "Direct and Indirect Cholinergics", "Cholinergic Antagonists", "Histamine H_1 and H_2 Histamine Receptor Antagonists, and Disodium Cromoglycate", and "Prostanoids and Leukotrienes". In addition to a brief introduction that generally describes the historical development and general mechanism of action, e.g., receptor modulation, of the various pharmacological classes of drugs, mechanism of action, structure–activity relationships, pharmacokinetics, uses and dosage, toxicity (including drug interactions), physical–chemical and other data are presented for the most significant drugs within those classes. In some instances the introductory parts of the various sections are clearly written and informative, but they are generally poorly referenced, often outdated, and contain little that is not presented in standard medicinal chemistry and pharmacology texts. A notable exception is the final section dealing with prostanoids and leukotrienes. In this section that deals with a complex recent topic, general principles as well as realized and anticipated therapeutic applications are treated in a well-written, informative fashion. Many typographical errors were noted in many parts of the handbook. Also, as such a broad range of topics is covered for each class of drugs, apparently with the objective of appealing to students and practitioners of pharmacy, pharmacology, medicinal chemistry, and medicine, as well as to researchers in the pharmaceutical industry and other allied health professions, none of the topics with the exception of prostanoids and leukotrienes, is treated in sufficient depth to make this handbook particularly useful to any of the cited disciplines. In my opinion, this volume is overpriced and will have only limited value to most medicinal chemists, although it may be useful to those who want a quick overview of the various topics of the book.

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