rivative (II) with the proposed structure indicated. It seems appropriate to correct the record now since I was again proposed as the structure for silylated biotin in a recent review (3).

The possibility that the proposed structure for the silyl ester (I) might be incomplete appeared when we prepared the methyl ester of biotin using diazomethane. Although this methyl ester could be chromatographed, the compound had a much longer retention time compared with the silylated compound and produced a peak that tailed badly. This large difference in chromatographic behavior is not expected for two compounds that are supposed to be simple esters. It also was observed that when the silylating agent [bis(trimethylsilyl)trifluoroacetamide] (III) was added to the previously formed methyl ester, the late eluting broad peak disappeared and a sharp, early eluting peak was obtained. These observations led to a more definitive study of the derivatives formed.

The fully silylated derivatives can be formed by reacting 5 mg of biotin with 1 ml of a 1:1 (v/v) solution of III and pyridine. After heating at 60° for 15 min, the sample is ready for analysis. The partially silylated derivative can be formed by first reacting 5 mg of biotin in ether with excess diazomethane until the yellow color persists. After 10 min, the methyl ester solution is evaporated to dryness and then silylated as described.

These samples were then analyzed[1] on a gas chromatograph–mass spectrometer[2] using a 1.9-m 3% OV-17 on 100–120-mesh Gas Chrom Q[3] column. The mass spectrum of the fully silylated derivative produced molecular ion 460 together with a base peak at *m/e* 73, supporting Structure II. The mass spectrum of the methylated biotin trimethylsilyl derivative gave *m/e* 402, again with a base peak at *m/e* 73, supporting the biotin methyl ester *N,N*-trimethylsilyl structure.

(1) C. Plinton, F. P. Mahn, M. Hawrylyshyn, V. S. Venturella, and B. Z. Senkowski, *J. Pharm. Sci.*, **58**, 875 (1969).
(2) V. Viswanathan, F. P. Mahn, V. S. Venturella, and B. Z. Senkowski, *ibid.*, **59**, 400 (1970).
(3) S. Ahuja, *ibid.*, **65**, 163 (1976).

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BOOKS

REVIEWS

Annual Reports in Medicinal Chemistry. Vol. 11. Edited by FRANK H. CLARKE *et al.* Academic, 111 5th Ave., New York, NY 10003, 1976. 339 pp. 17 × 25.5 cm. Price $16.50.

The new editor-in-chief of this series, Dr. Frank Clarke, is to be congratulated on maintaining the quality of content, presentation, and timeliness found in earlier volumes. The 32 chapters of this volume are grouped into six principal sections. Six section editors (three of them new) have the responsibility for the contributions in their areas.

Most chapters survey the literature of 1975 on new compounds reported to have pharmacologic activity. A few chapters cover the years since a report last appeared in this series. Some of the most interesting chapters present a mini-review of some biological process or disease state and point the way to potential new approaches for drug therapy. A third type of chapter deals with general methods of possible utility in the synthesis, design, or testing of drugs.

The section on CNS Agents has three chapters that update previous coverage of antidepressants, antipsychotic agents, antianxiety agents, anticonvulsants, sedative–hypnotics, analgesics (including endogenous peptides), and narcotic antagonists. In addition, there are two excellent chapters on the currently "hot" areas of opiate receptors and biological factors in psychiatric disorders. The Pharmacodynamic Agents section covers pulmonary and antiallergy drugs, antihypertensives, diuretics, and the structure–activity relationships of prostaglandins. The Chemotherapeutic Agents section has chapters on antibiotics and antifungal, antiviral, antiparasitic, and antineoplastic agents.

The section on Metabolic Diseases and Endocrine Function has chapters devoted to immunosuppressive and immunostimulatory agents, steroids, peptide hormones, diabetes, disorders of lipid metabolism, drug metabolism, and antiobesity agents. The Topics in Biology section features particularly pertinent chapters on membrane regulators, active transport across membranes, the antimetabolite concept, comparative toxicology, and chronopharmacology. The last section on Topics in Chemistry has the usual chapter on synthetic reactions of interest plus chapters concerning the synthesis of β-lactam antibiotics, synthesis of cyclic adenosine monophosphate and cyclic guanidine monophosphate derivatives, syntheses employing polymeric reagents, quantitative drug design, and use of NMR for drug binding studies.

As expected with any work by 46 different authors, the writing style is far from uniform. However, the readability of this volume is generally quite good. Every medicinal chemist and most pharmacologists would surely find several chapters of interest.

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Chinese Herbs: Their Botany, Chemistry, and Pharmacodynamics. By JOHN D. KEYS. Tuttle, Rutland, VT 05701, 1976. 338 pp. 15 × 22 cm. Price $15.00.

This book is a compendium of monographs of Chinese medicinal plants arranged by botanical classification. Each monograph includes an illustration and Chinese characters as well as a botanical, chemical, and pharmacological description. There are also supplementary sections on mineral- and animal-derived drugs, a collection of Chinese prescriptions, and a table of toxic herbs.

This book is a good compilation of the medicinal plants of China, done mainly through translation of Chinese works, some as old as the 6th century. The botanical description seems quite complete, while the chemical and pharmacodynamic sections appear too outdated and su-

perficial for the pharmaceutical scientist. However, this book should be of interest to the lay reader or scientist specifically interested in Chinese herbs and herbal medicine.

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Advances in Modern Toxicology, Vol. 1, Part 1: New Concepts in Safety Evaluation. Edited by MYRON A. MEHLMAN, RAYMOND E. SHAPIRO, and HERBERT BLUMENTHAL. Halsted, 605 Third Ave., New York, NY 10016, 1976. 455 pp. 16 × 25 cm.

Today there is increased governmental and industrial concern regarding the toxicity of chemicals, with emphasis on development of test procedures designed to reveal adverse effects before a particular substance becomes available for direct or indirect human ingestion. A text such as this one can assist scientists in fulfilling this objective.

Three of the 13 chapters focus on teratogenicity. Chapter 6, Current Methodology in Teratology Research, provides useful information regarding selection of the animal model and time of administration. Chapter 12, Distribution, Metabolism and Perinatal Toxicity of Pesticides with References to Food Safety Evaluation: A Review of Selected Literature, is a compilation of previously reported data on various pesticides, *e.g.*, DDT, aldrin, and dieldrin. Chapter 13, Transplacental Toxicity of Diethylstilbestrol: A Special Problem in Safety Evaluation, includes detailed descriptions of the pharmacology and toxicology of diethylstilbestrol in both animals and humans.

Two interesting sections devoted to methodology are Chapter 3, Potential Contribution of Inbred Syrian Hamsters to Future Toxicology, and Chapter 9, Radioautographic Methods for Physiologic Disposition and Toxicology Studies.

Chapter 8 is especially timely since it describes fundamental pharmacokinetic principles and their application to toxicological investigations.

Nonlethal Parameters as Indices of Acute Toxicity: Inadequacy of the Acute LD50 is the title of Chapter 7, which stresses the need to look beyond the LD50 value itself, *e.g.*, careful observation of all animals in the postadministration period, and pathological examination of survivors to detect latent toxicity.

Portions of the book suffer from inadequate editorial supervision. Numerous tables (*e.g.*, Chapter 4, Table 13, and associated Appendix; and Chapter 11, Tables 1 and 20) contain facts that are not organized on any basis. Individual chemicals could have been listed alphabetically within each table but instead appear in semirandom fashion. It is unfortunate that these defects, which could have easily been corrected, were overlooked.

On the positive side, background data are accompanied by extensive reference sections, and potential sources of error in development and interpretation of toxicity studies are emphasized. This text is a good comprehensive source of information for those conducting toxicological research.

Reviewed by Frederick J. Goldstein
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International Nonproprietary Names (INN) for Pharmaceutical Substances. Cumulative List No. 4. World Health Organization, Health and Biomedical Information Programme, 1211 Geneva 27, Switzerland, 1976. 314 pp. 17.5 × 24 cm. Price $19.20.

This book is a computer printout of international nonproprietary names (INN) of pharmaceutical substances in alphabetical order of the Latin names. Each entry includes the INN in English, French, Russian, and Spanish; indicates the national compendia in which the names appear; and lists national compendial names that differ from the INN. The Chemical Abstracts Service (CAS) registry number and molecular formula are also given. The book includes all INN published in the *WHO Chronicle* through March 1976. In addition, there is an appendix of national names that differ from INN, a molecular formula index, and a CAS registry number index. All of the text appears in both English and French.

Staff review

Molecular Connectivity in Chemistry and Drug Research. By LEMONT B. KIER and LOWELL H. HALL. Academic, 111 Fifth Ave., New York, NY 10003, 1976. 257 pp. 15 × 24 cm. Price $27.00.

This book represents the results of recent research into the utility of the connectivity index as a parameter for correlating physical, chemical, and biological properties. The 10 chapters in the book may be divided into roughly three sections.

The first section contains Chapters 1–3 on Structure and Properties, Elements of Graph Theory and Topological Indices, and Molecular Connectivity, respectively. These provide a general introduction to their topics. Both Chapters 2 and 3 may appear to be more abstract and formal than necessary on first reading. However, the equations and algorithms provided for the calculation of the various connectivity indices are very general. Computational facility may be gained through working the many examples provided in the numerous tables and in Appendix A.

The second part of the book, Chapter 4 on Molecular Properties and Chapter 5 on Molar (Bulk) Properties and Molecular Connectivity, provide examples of the correlation between the various connectivity indices and such properties as heat of formation and atomization, molar polarizibility, diamagnetic susceptibility, heat of vaporization, boiling point, aqueous solubility, and partition coefficient. In general, for each physical property the discussion is organized and correlations are presented by functional group.

The third part of the book focuses on biological activity correlations. Chapter 6 considers nonspecific biological activity (anesthetic and narcotic activity), while Chapter 7 considers more specific responses such as enzyme inhibition and microbial inhibition. Chapter 8 considers the use of multiple chi (connectivity) and chi-squared terms in correlating biological activities, while Chapter 9 considers the use of chi terms plus other physical property terms, primarily the Hammett sigma values, in correlation analyses. Finally, Chapter 10 concludes the book with reflections on the nature and future of connectivity. In this chapter, the authors ask such questions as: "Is the particular choice of chi important?" and "How is one to interpret the chi terms?", note problem areas such as *cis–trans*-isomerism, conformation, and high structural complexity, and suggest some possible future uses of chi.

While much of the content is available in the literature, the book pulls everything together, plus offers more of an introduction to graph theory and the development of the various connectivity indices. As the authors clearly state, much remains to be investigated. In the reviewer's opinion, it is too early to assess the value of molecular connectivity relative to other parameters. However, the index is no more difficult to compute than other commonly employed parameters, and the technique is easily generalized to the computation of number of indices. The method certainly merits the attention of researchers in structure–activity work as another (more fundamental?) parameter to aid in drug design. Although the book is more introductory and preliminary than one might like (it represents, for the most part, the results of investigations by one research group over the past 2–3 years), it can be recommended, particularly to investigators interested in structure–activity methodology, as a new and potentially useful technique.

Finally, some simple calculations reveal a cost of over 10 cents per page. This seems particularly steep since approximately one-third of the text is occupied by tables.

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