

lyophilization of those comprising the single peak, detected by monitoring the absorbance of the eluate at 280 nm, yielded the ninhydrin-negative product (70 mg, 65% yield overall, 20%): R_f (A) 0.26, R_f (B) 0.37; $[\alpha]^{22}_D -12^\circ$ (c 0.5, 1 M acetic acid); homogeneous to electrophoresis in two pyridine acetate buffers (pH 3.5 and 6.5) and in aqueous acetic acid (30%). Amino acid analysis²¹ gave the following molar ratios: Gly, 1.00; Arg, 0.99; Pro, 1.08; Asp, 1.02; Val, 0.99; Phe, 1.02; Tyr, 0.99; Cys, 0.14; NH_3 , 2.0. A sample hydrolyzed identically after performic acid oxidation by the method of Moore²⁷ had a cysteic acid to Gly ratio of 1.02:1.00.

Acknowledgment. This work was supported in part by research grants from the National Institute of Child Health and Human Development (No. HD 06351), the National Institute of Arthritis, Metabolism and Diabetes (No. AM 01940), and the National Heart and Lung Institute (No. HL 12738). The authors wish to thank Ms. Jacqueline Moehring and Ms. Janny Seto for technical assistance and Ms. Cindy Licata for assistance in the preparation of the manuscript.

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Book Reviews

Receptors and Mechanism of Action of Steroid Hormones.

Part I. Edited by George R. Pasqualini. *Modern Pharmacology-Toxicology*. Volume 8. Marcel Dekker, New York, N.Y., and Basel, Switzerland. 1976. xi + 309 pp. 16 × 23.5 cm. \$29.75.

The discovery of proteins which can selectively bind the steroid hormones in target cells and that exhibit various properties likely attributable to the function of cellular receptors is a most significant development in this area. This monograph (part I of two parts) addresses this subject in detail describing recent (up to 1975) research on steroid hormones at the molecular level. Abridged chapter titles (authors) are 1, General Aspects of Receptor Interactions (Munck); 2, Autoradiographic Localization in Target and Nontarget Tissues (Stumpf, Sai); 3, Estrogen Receptor Purification by Affinity Chromatography (Sica, Cuatrecasas, Nola, Parikh, Puca); 4, Estrogen in Normal Human Endometrium (Gurpide, Tseng); 5, Androgen Receptors and Mechanism of Action (Liao); 6, Control of Tumor Growth (King, Cambray, Jagus-Smith, Robinson, Smith); 7, Progesterone Mechanism of Action (Spelsberg, Taft). Chapters 8-12 are found

in Part II and deal with Glucocorticoid Receptors (Munck, Leung); Mineralocorticoid Receptors (Pasqualini, Sumida); Aldosterone Mechanism of Action (Crabbé); Breast Cancer (Jensen, Desombre); Receptors in Brain, Hypothalamus and Hypophysis (Kato). It is unfortunate that all chapters are not found under one cover; the cumulative index is found in Part II. For Part I each chapter is individually referenced mainly through 1974 with some 1975 citations.

Chapter 1 sets the stage for this work by including discussions of historical aspects, terminology, definition of receptors, and an overview of theoretical considerations. This chapter is well written, informative, and very interesting to read. The remaining chapters found in Part I are also well done; in the remaining chapters the title subject is treated in considerably more detail. For example, chapter 2 contains discussions of autoradiographic methods used to search for and define steroid hormone target sites and the results of these experiments. In chapter 3, details of affinity chromatographic methods, estrogen and polymer properties, and assay methods for purified receptors and their characterization are considered. Chapter 4 contains a summary of the studies in

vitro carried out by Gurpide and Tseng relating to concentration, distribution, and disposition of estrone and estradiol in normal human endometrium. The apparatus used, methods, and results are discussed. Double-label experiments using [^{14}C]- and [^3H]-labeled estrogens allowing for the measurement of receptor levels and competition on nuclear binding by estradiol are presented. In chapter 5 Liao discusses experiments designed to assess uptake and retention of androgens by target cells and receptors in prostate. Discussions of α and β face binding of the steroid to the receptor, transformation and nuclear retention of cytoplasmic receptor, chromatin acceptor sites, and receptor binding of RNA and ribonucleoproteins are included. The chapter is concluded with an interesting discussion of the androgen receptor and gene expression. Cell culture experiments found in chapter 6 are considered in light of androgen influence on cell kinetics, the time course of the response, development of an androgen-responsive cell line, steroid specificity and metabolism, and receptor studies. The chapter includes a discussion of the biological significance of these studies. One conclusion reached is the "qualified yes" to the question "Is the interaction of steroid with a receptor an obligatory requirement for biologic activity?" The chapter is concluded with discussions of biochemical processes in relation to cell proliferation and a general discussion on the growth of responsive and unresponsive tumors. The final chapter in Part I considers experiments employed to identify progesterone receptors in chick oviduct and properties of the cytosol and nuclear receptors as well as progesterone receptors in mammalian uterus. Nuclear acceptor sites studies and progesterone-induced macromolecular synthesis are also reviewed. These studies showed that the action of progesterone closely resembles that of other steroid hormones in specific target cells.

This volume is certainly an excellent contribution and is recommended for reading by virtually all biomedical investigators. For individuals planning to enter this area of investigation this monograph serves to summarize in considerable detail much of the literature in this area into 1975. Various chapters should serve as an initial source of undergraduate and graduate lecture material in many fields including medicinal chemistry and pharmacology. This monograph is likely too expensive for individual ownership unless the individual is entering this field; nonetheless, the volume is a good one to have as part of virtually any biomedical investigator's private library.

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Hormone-Receptor Interaction: Molecular Aspects. Edited by Gerald S. Levey. Marcel Dekker, New York and Basel. 1976. xii + 474 pp. 15.5 \times 23 cm. \$45.75.

Not too many years have passed since receptors were compared by De Jongh to "beautiful but remote ladies". However, with the advent of improved methods for the purification of macromolecules and with the decline in standards before declaring a macromolecule to be "pure", there has been an explosion of papers dealing with the isolation of receptor molecules and with their interaction with pharmacologically interesting ligands. We have also learned that if receptors are to be compared with ladies, these have a tendency to be unstable.

The present volume deals with insulin receptors, cardiac and liver glucagon receptors, receptors for hypothalamic hormones, oxytocin, FSH, gonadotropin, growth hormones, glucocorticoids, and progesterone, the role of receptors in breast cancer, receptors for vitamin D₃, β -adrenergic receptors, receptors for thyroid hormones, prostaglandin, and with acetylcholine receptors.

Because of the very wide scope of this book, the space available for each topic is quite limited with the result that, in some cases, the coverage of the subject is quite incomplete. For example, it is unfortunate that the review on acetylcholine receptors has ignored the very important work with microsacs by Changeux and his co-workers, this being one of the few examples where attachment of ligands to membrane receptors induces a response which can be quantitated and related to the response in living cells or to binding data obtained with purified protein. However,

the reader of this book will be supplied with a great deal of useful information with some of the chapters, for instance, those by Jacobs and Cuatrecasas, Lefkowitz, and Kuehl doing an admirable job of condensation.

Numerous 1975 references are included in the bibliography making this book relatively timely. It is a pity that its price is so high.

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Methodicum Chemicum. Volume 11. Part 1. Nucleic Acids, Proteins and Carbohydrates. Edited by F. Korte and M. Goto. Academic Press, New York, N.Y., Georg Thieme Verlag, Stuttgart, and Maruzen Co., Tokyo. 1976. viii + 231 pp. 19 \times 26.5 cm. \$39.50.

The *Methodicum Chemicum* series aims to provide "a critical survey of proven methods and their application in chemistry, natural science and medicine". Although there is much of value in Volume II, part 1, it is unwieldy. The preface states, "Separation and determination of main classes of compounds were already discussed in Volumes 1A and 1B of this series, and, to avoid duplication, some important discussions on purification and isolation of classes of compounds are intentionally omitted from Volume II. Synthetic compounds with industrial importance or with physiological significance are to be discussed in Volumes 9 and 10". It is not clear how "compounds with physiological significance" were distinguished from the compounds included in the present volume which are of obvious physiological significance. There are 22 individual contributions including one on lipids which escaped mention in the title.

Nucleic acids are covered in 84 pages by Y. Iwanami (Nucleic Acid Components), E. Ohtsuka (Chemical Synthesis of Oligo and Polynucleotides), T. Uchida (Enzymic Degradation of Nucleic Acids), R. Flügel (Replication of DNA), T. Godefroy-Colburn (Synthesis of Nucleic Acids by Polynucleotide Phosphorylase), R. Flügel (mRNA Synthesis from DNA), R. Flügel (DNA Synthesis from RNA), S. Nishimura (Determination of Nucleotide Sequences of Nucleic Acids), M. Tsuboi (Physical Methods), Y. Inoue (Applications of Physical Methods), and K. Miura (Viruses—Chemistry of their Structural Unit). Although many of these articles are good, brief surveys of the literature, critical evaluation is not always provided as in the section by Y. Inoue which consists only of a bibliography of 146 references.

Proteins are covered in 48 pages by K. Narita (Primary Structure of Protein), K. Hotta (Glycoproteins), O. Minari (Lipoproteins), S. Iwanaga (Protein and Peptide Toxins), I. Kato (Microbial Toxins), and K. Onoue (Antibody, Antigen and Complement). Where would one find out about secondary and tertiary structure or about cross-linking reagents?

Carbohydrates are covered in 27 pages by K. Anno (Mono- and Oligosaccharides), A. Misaki (Polysaccharides), S. Suzuki (Mucopolysaccharides), and H. Nikaido (Cell Wall Substances).

Lipids are covered in 18 pages by K. Ohno and T. Shimojo. The subject index is inadequate. For example, the 50 modified bases discussed in Iwanami's chapter (thiouracil, pseudouracil, etc.) are not included. No author index is provided.

In summary, while many of the chapters are very good, the material is not covered evenly nor is information readily accessible.

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Synthetic Peptides. Volume 4. By George R. Pettit. Elsevier Scientific, Amsterdam-Oxford-New York. 1976. xvii + 477 pp. 15.5 \times 23 cm. \$59.95.

The explosive growth of literature necessitates—from time to time—major reviews in almost all areas of chemistry. The discovery of a multitude of biologically active peptides combined with recent improvements in the methodology of peptide synthesis led to a particularly productive period and the synthetic peptide

chemist is embarrassed by the intractable volume of published material. The complex nomenclature of synthetic products, and particularly of their protected intermediates, renders it quite difficult to locate them in key journals. Therefore a volume that contains a compilation of the physical constants of synthetic peptides together with references to original articles that describe the details of synthesis is of considerable assistance rendered to peptide chemists by G. R. Pettit for several years. The task becomes more and more arduous; volume 4 of his series is almost 500 pages long and must be the result of dedication and hard work.

The tables systematically deal with synthetic derivatives of amino acids, dipeptides, tripeptides, and so on to reach even hen-egg-white lysozyme with 129 residues. Not less valuable are the tables that summarize the results of syntheses leading to polypeptides, cyclopeptides, depsi-peptides, and steroidal, chromo-, and nucleopeptides. These tables are rich in information and, because of their practical organization, still can be scanned with reasonable speed for a particular material. They represent the more valuable part of the book.

Preceding the tables seven chapters were included with discussions of such topics as racemization, protecting groups, coupling methods, various strategies, and solid-phase peptide synthesis. Here the author introduced a very welcome new name for one of the strategies of peptide synthesis: "segment condensation" (rather than "fragment condensation"). These chapters, however, cannot compete in depth or precision with the yearly editions of the Specialist Periodical Report on Amino Acid Peptides and Proteins, published by the Chemical Society in Great Britain. There are some disturbing errors in the introductory chapters. E.g. (on page 1), fractional crystallization is mentioned as a method for the resolution of DL-amino acids. The original article, however, deals with preferential crystallization induced by heavy seeding of a mixture with the enantiomer that is present already in excess.

The examples of synthetic procedures, presented after the tabulation of synthetic peptides, are of limited value. They are reproduced from published material but without critical evaluation. E.g., the synthesis of Z-Gly-Phe-Gly-OEt from Z-Gly-Phe and Gly-OEt with ethoxyacetylene as condensing agent is described (on p 445) as an example for coupling with Ahrens' reagent. In the paper of Sheehan and Hlavka—who quite properly do not claim credit for this coupling method—the reporting of this tripeptide derivative (the Anderson model) was used for the demonstration of the absence of racemization and was certainly not meant to serve as a recommended example of synthesis. Also it is questionable whether or not the idea to reproduce some papers in their original language is justified. The German texts may create some difficulty for a few peptide chemists; the Italian versions will be valued only by a small group of them.

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Advances in Pharmacology and Chemotherapy. Volume 13.

Edited by S. Garattini, N. Goldin, F. Hawking, and I. J. Kopin.
Academic Press, New York, N.Y. 1975. 16 × 23 cm. ix + 415 pp. \$39.50.

As the title indicates, the book contains seven well-balanced chapters in pharmacology and chemotherapy. Brener reviewed the chemotherapy of *Trypanosoma cruzi* infections. He discusses the testing procedures and the drugs which are active against infections. Although the author did not include the side effects of these drugs, he emphasizes a need for a highly effective drug against the parasite infection. C. Hansch's formulations for quantitative structure-activity relationships are used by many investigators. In a 40-page chapter, the author describes enzyme study as a source of strategy in drug design. A multidisciplinary group of investigators wrote a relatively large chapter on the pharmacology, toxicology, and clinical aspects related to the cephalosporin group of antibiotics. Since the structure-activity relationship on the subject has been previously covered by others, only limited space is devoted to this aspect. Goble surveys the effects of CNS active myotrophics, hypoglycemics, anti-infectives, and antineoplastic drugs as influenced by sexual differences. Another timely topic on L-Dopa and extrapyramidal disease is

covered by Pelton and Chase. Authors not only discuss the pharmacology and therapeutics of Parkinson's disease, but the value of L-Dopa in other extrapyramidal disorders is also reviewed. In recent years many reviews and books have been written on the pharmacology of amphetamines. The effects of amphetamines on neurotransmitter and carbohydrate metabolism are reviewed by Estler. The latter aspect of the topic was not emphasized before. The last chapter is devoted to biological inhibitors of lymphoid cell division.

Since the book contains many unrelated topics, it may not be a wise investment for a scientist's personal library. The book could, however, serve as a general reference in the biological science library.

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Fundamentals of Integrated GC-MS. Part I. Gas Chromatography. By B. J. Gudzinowicz, M. J. Gudzinowicz, and H. F. Martin. Marcel Dekker, New York and Basel. 1976. 23.5 × 15.9 cm. vii + 382 pp. \$37.50.

Part I is the first of a three-book series comprising Volume 7 of Marcel Dekker's Chromatographic Science series. Parts I and II describe theory and principles of gas chromatography and mass spectrometry, respectively. Part III will describe the "integrated GC-MS analytical system" and is expected to be published in March 1977. The references cited cover material up to, and including, 1974.

The book is divided into four chapters: Fundamentals of Gas-Liquid Chromatography, Detectors—Operating Principles and Theory, Qualitative Methods for Molecular Structure Determination by Gas Chromatography, and Quantitative Methods of Analysis by Gas Chromatography. The chapters are well written and illustrated and would provide the basis for knowledgeable operation of most commercially available gas chromatographic systems.

The selection of topics is perplexing when considering the intent of Volume 7. As the authors note in the preface, understanding the components of an integrated system will result in achieving its maximum utility. But a preponderance of space is devoted to topics of little relevance to the GC-MS-computer system, i.e., a detailed discussion of detector types, functional group analysis, identification of compounds by degradation patterns, subtractive chromatographic techniques, and much of the last chapter on methods of peak area integration.

Contrary to the marked interest in glass capillary columns and the advantages of direct MS interfacing, the book is surprisingly devoid on topics of etching, coating, and related technology. The pages on derivative preparation (Chapter 3. VII. Formation of Derivatives by Chemical Means) do not discuss the importance these manipulations can have on structural interpretation.

It would appear the book was written to be a single basic text on gas chromatography for which it is most suited. However, it offers no better insight into the fundamentals of integrated GC-MS-computer instrumentation than any other gas chromatographic text.

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Fundamentals of Integrated GC-MS. Part II. Mass Spectrometry. By B. J. Gudzinowicz, M. J. Gudzinowicz, and H. F. Martin. Marcel Dekker, New York and Basel. 1976. 23.5 × 15.9 cm. vii + 326 pp. \$35.50.

Part II of the Fundamentals of Integrated GC-MS is entitled "Mass Spectrometry" and contains chapter 5 (Mass Spectrometry: General Theory, Principles and Instrumentation) and chapter

6 (Qualitative and Quantitative Methods of Analysis by Mass Spectrometry).

The vast majority of the material covered in both chapters is related to papers that appeared in the 1950's and 1960's with very few references from the early 70's, the most recent one being 1973. This demonstrates one of the deficiencies of this book, namely, that it is not up to date with respect to the field which the title of Volume 7 indicates, namely, integrated GC-MS. In fact, very little of Chapter 5 has any relationship to this subject, except that it happens to describe also the principle of those mass spectrometers that are presently used in GC-MS systems. While it is of general educational interest to see a diagram of Dempster's double-focusing mass spectrograph of 1935 or a block diagram of the batch inlet systems used in the 1940's for the quantitative analysis of light hydrocarbons, it has no bearing on integrated GC-MS. These subjects have been described well and in considerable detail during the past two decades in a number of expertly written books on the instrumental aspects of mass spectrometry and the authors of the present volume merely selected the material from these sources.

How unrelated the text is to the subject of the book is best illustrated by the fact that in the subject index there is only a single entry to be found under "GC-MS" and it refers to an obscure statement on page 5. Slightly more useful may be chapter 6 which makes an attempt to outline the use of mass spectra for qualitative and quantitative analysis. Since the authors appear not to have much practical experience in this field, they have relied heavily on a somewhat uncritical assemblage of published material mainly from textbooks or *Analytical Chemistry* and even *Chemical and Engineering News*. Under qualitative analysis approaches to the interpretation of mass spectra are discussed and much of this chapter (pp 189-223) consists of a list of masses either lost as neutral fragments (Table 6.20) or of common fragment ions (Table 6.21) and their possible structure and origin, i.e., structural indication. While it is debatable whether or not this is a useful approach to the interpretation of mass spectra, there is no need to repeat these tables which already have appeared in other textbooks. This is then succeeded by sections on computer-aided identification of mass spectra which is again done in a rather uncritical way, summarizing each one of the published approaches but neither in chronological nor logical order. It even begins by quoting verbatim a lengthy section of a paper by Groch covering a full page in the book.

The ultimate example of outdatedness is Section 6 in Chapter 5 (p 105) on magnetic tape recording of mass spectral data which follows a detailed description of mass spectral digitizers, an approach that uses electromechanical devices and was briefly used 15 years ago for quantitative analyses unrelated to GC-MS. After discussing at some length the relative merits of analogue vs. digital tape recording for mass spectral data, neither of which is used any longer except in very exceptional circumstances, it very briefly spends two paragraphs on computer-based data acquisition systems. If one considers the fact that these are now an indispensable part of any GC-MS system that is efficiently used, one cannot avoid the conclusion that the present work is of little relevance to the present or future users of integrated GC-MS systems and does not add anything new to the existing array of text and reference books in this field.

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Introduction to Mass Spectrometry, Biomedical, Environmental and Forensic Applications. By J. Throck Watson. Raven Press, New York, N.Y. 1976. 15.5 × 24 cm. ix + 239 pp. \$20.00.

The past decade has seen the establishment of mass spectrometry as an essential tool in the organic analytical laboratory. The number and diversity of scientists depending on mass spectrometry for their research have increased significantly and

so have their need for a concise and comprehensive summary of the field to educate them on its basic principles and familiarize them with both the breadth and limitations of the technique. This book represents not only a fine survey of the general utility of mass spectrometry in organic analysis but can also provide a text or supplemental reference book in the teaching of a basic course in the area.

The author has wisely avoided any elaborate discussion of the interpretation of mass spectra, fragmentation mechanisms, etc., which are well covered in other texts. The brief discussion in Chapter 6, in conjunction with the presentation of the different ionization techniques, provides sufficient information for the novice to acquaint him with the principal features of a mass spectrum and some of the factors governing the fragmentation of organic molecules. Instead, the principal focus is on instrumentation and analytical techniques, most notable among them topics such as inlet systems, sample handling, and selected ion monitoring. The last chapter contains a valuable summary of the publicly accessible reference libraries of mass spectral data based on information made available by the American Society for Mass Spectrometry. While the coverage of these topics is by no means complete—the field is obviously too extensive to be thoroughly covered in a book of this length—the author has provided an excellent list of references and bibliography, which makes indeed for a very thorough piece of work.

Of particular value in this book are the examples of "case studies" given in chapters 2 and 3. These sections provide an immediate impression upon the reader of the types of problems that mass spectrometry can be used for. The examples have been selected very well and in some respects form the backbone of the book. The early presentation of this material may not be proper for the novice to mass spectrometry, as the detailed discussion of the data in these examples may be hardly meaningful at first glance. For the novice it is advisable, after a cursory look at chapters 2 and 3, to begin an earnest study of this book with chapter 4. This is also recognized by the author in the preface.

The book is well written and easy to read. Its readability is further enhanced by the clarity and excellent reproduction of the spectra, chemical structures, and other diagrams. The author has used a lot of cross-referencing by referring to examples in various parts of the book. This has prevented too much repetition and has been generally successful. Some editorial omissions have been noted (e.g., p 146). In conclusion, this book will be a useful addition to the library of the mass spectrometry teacher, student, and user.

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Topics in Carbon-13 NMR Spectroscopy. Volume 2. Edited by George C. Levy. Wiley, New York, N.Y. 1976. 15.5 × 23.5 cm. xi + 485 pp. \$18.50.

One of the characteristics of modern science has been the regularity with which new and important spectroscopic methods have been developed. Every decade since 1930 has seen the addition of a new spectroscopic analytical tool to the armament of the organic chemist. In the 1930's, ultraviolet spectroscopy first started being used by organic chemists. This was followed in the 1940's by infrared spectroscopy. The 1950's witnessed the flowering of proton nuclear magnetic resonance. While mass spectrometry had its inception much earlier, it is in the 1960's that it started being used extensively for characterization purposes.

As if these developments were not enough, our present decade has seen still one new and important spectrometric development, namely that of ¹³C NMR. The present volume, edited by Professor George C. Levy, includes eight chapters dealing with such varied topics as conformation of peptides, structural characterization of natural products, the use of ¹³C NMR in biosynthetic studies, biopolymers, organometallic and transition metal complexes, structural assignments using ¹³C spin relaxation data, computers and Fourier transform NMR, and the theory of indirect nuclear spin-spin coupling constants with application to ¹³C NMR. The variety in these topics is sufficient to indicate the wide scope in the uses of ¹³C NMR spectroscopy.

^{13}C NMR is well on its way to revolutionizing biosynthetic studies in the realm of natural products chemistry. The low natural abundance of ^{13}C , a disadvantage from the viewpoint of sensitivity, affords simpler spectra since signals due to ^{13}C spin-spin coupling are not usually observed. Again, one can state that ^1H NMR has been exceedingly important in the structural elucidation of natural products, and ^{13}C NMR promises to be at least as powerful a tool.

The book is generally well written, the discussions are lucid, and the explanations and rationalizations can be easily followed. The printing job is of exceptionally high quality even though the price of the book is not excessive.

The editor, authors, and publisher should be congratulated for an especially fine addition to the literature on NMR spectroscopy.

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Molecular Connectivity in Chemistry and Drug Research.

By Lemont B. Kier and Lowell H. Hall. Academic Press, New York, N.Y. 1976. xiii + 257 pp. 15.5 × 23.5 cm. \$27.00.

Since its inception over 100 years ago by Sylvester, the subject of molecular connectivity has attracted inordinately little concern among chemists. The past 5 years, however, have seen the awakening of a germ of interest in the application of topological graph theory to elucidation of molecular properties. These advances are largely the issue of chemists and applied mathematicians from the Zagreb circle and their adherents in England, Germany, and the United States. Almost invariably, the work has involved predictions of thermochemical and other basic physical properties of hydrocarbons. These workers have been wary of dealing with any compounds containing heteroatoms since the topological approach in its present state has not been considered amenable to species more complex than the binary hydrides. The topological treatment of boranes by Lipscomb, for example, has consistently held to this limit.

In its initial three chapters, the present work does adhere to the traditional development, although coverage is sparse and omits more significant work than it includes. Here, the authors rely principally upon calculations of the Yugoslavian theoretician, Milan Randich (now at Iowa), which are contrasted with several less successful treatments. The remainder of their exposition, however, stands aloof from the main bulk of the literature.

Beyond chapter three, the authors depart severely from convention and begin to deal with heteroatom-containing species. In order to do so, they have found it necessary to eschew the rigors of graph theory and to incorporate in its place a very loosely derived conception of Randich's topological branching index. This descriptor, which in some cases is derived empirically, is correlated to various fundamental properties of an almost unlimited array of heteroatomic substances by multiple regression. Having unveiled this Medusa, the prodigal authors unhesitatingly venture into the perilous arena of biological activity prediction. Boldly they disclaim the previous work in QSAR analysis which is based upon partitioning and linear free-energy relationships, maintaining that these are nothing more than property-activity correlations, in contrast to their more direct approach. Here they have missed several important connections which were drawn by Hansch in his review of "The Structure of Medicinal Chemistry" [*J. Med. Chem.*, 19, 1 (1975)].

Despite such peccadillos, and a litany of others which are raised whenever Kier and Hall have chosen to engage the rancor of their critics, this book is strongly recommended to all who admire radical departure, courageous innovation, and unbridled controversy. Examination of the graphs and data tables, taken from the authors' own publications, clearly reveals that these methods are capable of achieving correlations of structure with physical properties and biological activity which rival the best predictions

of established QSAR studies. If the development appears to be nonrigorous and defiant of logical, mathematical derivation, it must be borne in mind that this approach is new and radical. Indeed, it challenges the reader to become involved in its further development and criticism. This book does not provide an adequate background in graph theory sufficient to establish a basic understanding of molecular connectivity. Such a review is still sorely needed to bring together a scattered and obscure literature. Rather, this book is recommended as a very exciting and exotic approach to theoretical chemistry and drug design.

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Quantitative Analytic Studies in Epilepsy. Edited by Peter Kellaway and Ingemar Petersén. Raven Press, New York, N.Y. 1976. 16 × 24 cm. xiv + 588 pp. \$35.00.

This book could have been published as two volumes. The first 12 chapters (182 pages) are concerned with procedures for the determination of antiepileptic drugs and their metabolites in body fluids and tissues, and with the significance of such measurements. The remaining 23 chapters (381 pages) describe quantitative methods of analyzing EEG signals. The potential overlap of these two topics—i.e., changes in the EEG induced by known plasma or brain concentrations of antiepileptic drugs—is hardly explored. Two chapters describe analysis of EEG frequency changes in man following drug administration (but the drugs were not antiepileptics and plasma levels were not determined). One chapter (on experimental epilepsy in monkeys) does report correlations between plasma anticonvulsant drug levels and an (manual) analysis of EEG changes. It is to be presumed that the editors intend this book to bring chemical techniques to the attention of EEG analysts and EEG techniques to the attention of chemical analysts and thereby initiate collaborative research.

The development of techniques for assaying drugs and their metabolites in plasma and saliva has led to greater understanding of individual variability in response to antiepileptic therapy. Such measurement now plays a key role in the management of patients. The first 12 chapters review some methodological topics (including radioimmunoassay and enzyme immunoassay) and present some selected studies derived from chemical data (e.g., pharmacokinetics of phenytoin in man). It provides stimulating reading for anyone involved in this area of clinical chemistry. A moderate amount of technical detail is included but this is in no sense a laboratory manual, nor does it provide a comprehensive review of methodologies and results. The presentation is compressed, informative, and accurate (on p 175 there is a discrepancy between the text and figure plasma phenobarbital levels).

The latter part of the book very adequately documents recent dramatic improvements in the range of computer techniques for EEG analysis. Emphasis is now moving away from procedures adopted because the technology was available and toward procedures that select and process data of biological and clinical significance. In epilepsy this includes using the computer to detect and analyze transient and "paroxysmal" signals. Petersén and his colleagues report substantial progress in the use of digital signal processing to automate EEG diagnosis, yielding computer reports closely comparable to those written by trained electroencephalographers.

Many scientists will benefit from consulting this volume; very few will read it from cover to cover. Its insistence on placing together two disparate subjects may yield practical benefits but means that a substantial part of the book will be irrelevant for the majority of readers.

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