

mixture was filtered through a Teflon-wool plug and diluted to a suitable concentration for the UV measurement. A Beer's law calibration curve was made with the salt **15b**, and the UV absorption maximum (291 nm) plotted against concentration gave a straight line (correlation coefficient = 0.998). Unknown concentrations were determined by linear regression analysis using the derived equation (eq 1), where y is the UV absorbance and x is the concentration.

$$y = (2.844 \times 10^4)x + (1.808 \times 10^{-2})$$

Acknowledgment. This investigation was supported by Public Health Service Grants CA 22935 and CA 09166 awarded by the National Cancer Institute, DHHS. The authors thank Paul A. Corey for his initial work leading

to the preparation of **9** and Dr. Louis Malspeis, College of Pharmacy, The Ohio State University, for showing us his unpublished data concerning the hydrolysis of **1** and the details of his HPLC assay.

Registry No. 1, 74296-42-7; 2, 51-35-4; 3, 86421-96-7; 4, 86421-97-8; 5, 86421-98-9; 6, 86421-99-0; 7, 86422-00-6; 8, 86422-01-7; 9, 86422-02-8; 10, 86422-03-9; 11, 86422-04-0; 12, 86422-05-1; 13, 86422-06-2; 14, 86422-07-3; **15a**, 86422-09-5; **15b**, 86422-10-8; 3,4-dichlorobenzoyl chloride, 3024-72-4; dimethyl acetylenedicarboxylate, 762-42-5; (-)-*N*-(3,4-dichlorobenzoyl)-2-aza-5-oxabicyclo[2.2.1]heptan-6-one, 86422-11-9; *tert*-butyldimethylsilyl chloride, 18162-48-6; isopropyl isocyanate, 1795-48-8; chloroacetyl chloride, 79-04-9; dimethylamine, 124-40-3; succinic anhydride, 108-30-5.

Book Reviews

Drugs and the Pharmaceutical Sciences. Volume 14. Novel Drug Delivery Systems. Edited by Yie W. Chien. Marcel Dekker, New York. 1982. xii + 633 pp. 15.5 × 23.5 cm. \$65.00.

Fourteenth in the series of *Drugs and the Pharmaceutical Sciences*, this volume addresses the physicochemical principles, developmental concepts, and biomedical applications of controlled-release drug-delivery systems. One chapter is devoted to each of the following routes of drug administration: ocular, intravaginal, intrauterine, transdermal, parenteral, and subcutaneous implantation. The remaining four chapters discuss veterinary medicine applications, general pharmacokinetic principles, and the physical parameters governing drug release from capsule, matrix, and sandwich-type drug-delivery systems. The table of contents and author and subject indexes are very complete and thus allow the text to be easily utilized as a reference book.

Chapters dealing with a particular route of drug administration usually include historical development, a brief overview of anatomy and physiology, a comprehensive description of physical and pharmacokinetic principles of drug release, followed by examples of the clinical performance of several different drugs. The text is amply augmented by graphs and tables of research data from primary journal articles or directly from the investigator. A large majority of the primary reference citations are dated prior to 1979. As a result, the text discusses recent applications in this rapidly growing technology in a cursory fashion or not at all. For instance, transdermal nitroglycerin is only briefly discussed under governmental regulations. Routes of administration that are omitted are intranasal, sublingual, and bronchial aerosol. A reader might expect the latter topics to be included in a book about "novel" drug-delivery systems.

This book would serve the investigator in academia or industry who is contemplating research and development of controlled drug-delivery systems or the educator who wishes to include principles of rate-controlled drug dosage in a graduate pharmaceuticals course. Because of the pharmaceutical industry's recent intensive development in this field, the book should not be relied upon to provide a comprehensive description of all novel drug-delivery systems.

College of Pharmacy
Northeastern University
Boston, Massachusetts 02115

Barbara Ameer

Behavioral Models and the Analysis of Drug Action. Edited by M. V. Spiegelstern and Aharon Levy. Elsevier, Amsterdam and New York. 1982. xvii + 498 pp. 19 × 25 cm. ISBN 0-444-42125-4. \$139.50.

This excellent volume will make medicinal chemists appreciate the sophistication that has been developed in behavioral pharmacology in the relatively short time the discipline has been

practiced. It comprises the proceedings of the 27th OHOLO conference, held in Israel in March 1982. There are manuscripts representing 22 invited papers grouped under the following subject headings: "Theoretical Issues in the Use of Animal Models"; "Memory, Learning, and Performance"; "Behavioral Toxicology and Addiction"; and "Behavioral Models Induced by Brain Manipulation". In addition, summaries of seven poster papers included at the conference are given.

The most significant theme appearing in the papers in the book appears to be the remarkable success achieved in developing specific animal models for various human behavioral anomalies. For example, the following techniques were reported to have been developed to represent the human condition shown in parentheses: an animal model of attention (schizophrenia), manipulation of brain cholinergic mechanisms by ethylcholine aziridinium (Alzheimer's disease), toxicity and self-administration (drug abuse liability), stress tolerance in rats (human behavioral depression), and threshold for brain reward stimulation (drug abuse potential). Also, techniques to measure hitherto unexplored behaviors such as attention, tardive dyskinesia, and aggression, are presented, as are references to social effects on behavioral experiments. Of particular interest to medicinal chemists are the several papers devoted to biochemical correlates of abnormal behavior. Examples include dopamine and rotational behavior, catecholamines and learning, and catecholamines and self-stimulation.

This book contains much information which should be highly useful to medicinal chemists engaged in design of drugs to alter CNS neurochemistry or behavior.

School of Pharmacy
University of Kansas
Lawrence, Kansas 66045

Robert A. Wiley

Solid-State Chemistry of Drugs. By Stephen R. Byrn. Academic Press, New York. 1982. xii + 346 pp. 16 × 23.5 cm. ISBN 0-12-148620-6. \$55.00.

Though it is common to consider solids as being inert, such is not always the case. There are instances where certain environmental conditions can initiate a reaction in or on a solid. In this monograph, S. R. Byrn has provided a fairly extensive overview of the types of reactions that take place in organic solids, especially drugs.

The subject is introduced by a brief description of the solid state (crystal forces, habits, crystalline and noncrystalline states) and the sequence of events that take place in a solid-state reaction. In the second chapter, the methods that are used to study solids and solid-state reactions are outlined: microscopy, X-ray diffraction, thermal methods, infrared, and analytical procedures for detecting chemical products. The various equations commonly used to treat solid-state kinetic data are presented in Chapter

3. The author points out that kinetic data alone is not sufficient to establish a mechanism for solid-state reactions.

The various types of solid-state reactions are discussed in the remaining chapters (4 to 11). The areas are polymorphism, loss of solvent of crystallization with emphasis on hydrates, oxidation, reaction of gases with solids, decomposition of solids with evolution of a gaseous product, photochemically initiated reactions (topochemically directed), and thermally induced rearrangements. Many examples of the reactions are presented and examined from a molecular viewpoint. Especially illuminating is the author's treatment of dehydration reactions, which drew heavily from investigations in his laboratory.

The concluding chapter summarizes the important molecular aspects of solid-state reactions and also provides a glossary of terms.

Pharmaceutical scientists involved in research with solid dosage forms will find it a worthwhile reference. It will provide an insight, which is not found in any other text, into the problems occasionally encountered due to the instability of a solid.

E. I. du Pont de Nemours & Co.
Glenolden, Pennsylvania 19036

Eli Shefter

Advances in Heterocyclic Chemistry. Volume 31. Edited by A. R. Katritzky. Academic Press, New York. 1982. ix + 350 pp. 16 × 23.5 cm. ISBN 0-12-020631-5. \$68.00.

This is a continuation volume in the well-established series *Advances in Heterocyclic Chemistry* and updates earlier reviews of the "Chemistry of Furans" and "Aromatic Quinolizines", as well as introduces topics new to the series covering the chemistry of 1,2-dithiol-3-ones and -3-thiones, azocines, Dewar heterocycles, and condensations under Vilsmeier conditions. This mix of material is excellent, and since the authors have all made contributions to their respective topics, the reviews are authoritative and reflect the present positions in these fields.

The chapter on "Aromatic Quinolizines" by Gurnos Jones is extremely thorough, well illustrated by numerous structural formulas, and presents a comprehensive picture of the interest in this group of compounds. "1,2-Dithiole-3-thiones and 1,2-Dithiol-3-ones" by Carl Th. Pedersen is a well-organized account of the chemistry of this interesting group of sulfur compounds covering their synthesis and reactions. Their photochemistry and electrochemistry, as well as spectral characteristics, are also described. "Azocines" by H. D. Perlmutter and R. B. Trattner covers in a thorough manner the chemistry of eight-membered rings containing one nitrogen atom and their benzo and dibenzo analogues. The vast amount of chemistry of these systems is presented in a readable and well-documented manner and will be of considerable interest to organic chemists in general.

"Dewar Heterocycles and Related Compounds" by Y. Kobayashi and I. Kumadaki discusses Dewar heterocycles containing oxygen, sulfur, and/or nitrogen atoms in five- or six-membered rings. The authors have presented a fascinating account of these relatively recent developments, and it will certainly stimulate applications of the ideas expressed to other systems.

"Cyclizations under Vilsmeier Conditions" by O. Meth-Cohn and B. Tarnowski further emphasizes the versatility of this reagent and its extreme usefulness in organic synthesis. The material has been organized in a way conducive to suggesting further applications of the reagent by the reader. "Recent Advances in Furan Chemistry", Part II, by F. M. Dean continues the updating of furan chemistry started earlier and emphasizes the versatility and usefulness of this heterocycle in organic synthesis. It presents a thorough, well-documented account of recent furan chemistry and will certainly suggest further applications to the reader.

This volume continues the high standards established by earlier volumes of this series. *Advances in Heterocyclic Chemistry* has become an indispensable part of any research library in organic chemistry, and this present volume shows that there are still interesting and exciting areas to be investigated.

Department of Chemistry
Rensselaer Polytechnic Institute
Troy, New York 12181

Kevin T. Potts

Studies in Organic Chemistry. 11. Flavonoids and Bioflavonoids. 1981. Edited by L. Farkas, M. Gabor, F. Kallay, and H. Wagner. Elsevier, Amsterdam, Chicago, and New York. 1982. xix + 534 pp. 17.5 × 25 cm. ISBN 0-444-99694-X. \$104.75.

The Flavonoids: Advances in Research. Edited by J. B. Harborne and T. J. Mabry. Chapman and Hall, New York. 1982. xii + 744 pp. 17 × 24 cm. ISBN 0-412-22480-1. \$114.00.

These two books approach the same topic from somewhat different points of view. The first represents a collection of 50 papers presented at the Proceedings of the International Bioflavonoid Symposium, effectively the Sixth Hungarian Bioflavonoid Symposium, held in Munich, FRG, in 1981. As such, it offers the more intimate glimpse into the current thinking and objectives of the scientists representing the flavonoid research of 15 nations. Without regard to organization into particular sections or chapters, the papers tend to emphasize synthetic methods and reactions (18) and the bioactivities of the compounds (16), with 12 devoted to isolation and characterization and 4 to physical-analytical methods. The book is produced by photo-offset from typed manuscript with the expected inconsistencies in type face, references, rendition of figures, etc. It is, nonetheless, quite readable.

The second is more properly a well-organized, typeset reference work covering additions to the literature, including those contributed by the Symposium authors, between the first such compilation (1975) and 1980. These are grouped into 12 chapters, largely on the basis of structural types, isolations, characterization, and analytical techniques. For the neophyte in flavonoid research, if not for the established worker in the field, it is difficult to underestimate the value of extensive check lists of the known flavonoid compounds which have been included in eight of the chapters. Perhaps even more welcome is the collection of 125 spectra which have been included in the chapter on ¹³C NMR as an aid in the solution of problems of structure elucidation in a group of closely related compounds.

However onerous the job of reviewing the ever-increasing literature, the contributors and editors are to be congratulated on the preparation of a definitive reference volume covering this fascinating group of natural compounds.

College of Pharmacy
Northeastern University
Boston, Massachusetts 02115

Robert F. Raffauf

Bioactive Carbohydrates. By J. F. Kennedy and C. A. White. Ellis Horwood, Chichester, England (outside England, distributed by Wiley, New York). 1983. 331 pp. 16 × 23.5 cm. \$79.95.

This small volume provided a broad coverage of the total field of carbohydrates, including the chemistry and biochemistry of monosaccharides, oligosaccharides, and polysaccharides. Similar information on carbohydrate-containing macromolecules (glycoproteins, glycolipids, nucleic acids, antibiotics, etc.) is presented, as is material on synthetically modified polysaccharides and on industrial applications of carbohydrates. The book can serve as a general reference for researchers who require general information about any of the above topics; it does not pretend to provide in-depth coverage but contains an adequate bibliography to which frequent references are made in the text.

The chapter (no. 2) concerning the classification of carbohydrates is particularly good in its discussion of the monosaccharides and oligosaccharides. It concisely and effectively correlates the various structural representations of these two classes, establishes the use of conformational structures in the book, and emphasizes the use of correct carbohydrate nomenclature. In my opinion, the three chapters on polysaccharides (no. 8), on glycoproteins and proteoglycans (no. 9), and on glycolipids (no. 10) are especially useful. They combine chemical, structural, and biological information in much more detail than is the case in most of the other sections.

The material on the organic chemistry of the carbohydrates that appear in Chapters 3 (on the general chemical reactions of carbohydrates), 4 (on chemical and biochemical syntheses), and 5 (on monosaccharides) is the least effective. Most of this material

is superficial and overgeneralized, which sometimes results in misleading statements (e.g., "Sulphonate groups can be removed by nucleophilic displacement with lithium aluminum hydride."). Such important topics as deoxy sugars and halogeno sugars are each covered in about one-half page of material that it is not further referenced to general texts on these subjects.

I was disappointed in the large number of errors that appeared in the text. Many structures are incorrect (e.g., a lactone on page 52 lacks the ring oxygen, the structures of L-ascorbic acid, its tautomer, and its oxidation product are all wrong on page 117, and numerous errors appear in the structures and the equations for the periodic acid oxidations on pages 70–72). Although the authors have carefully employed systematic carbohydrate nomenclature throughout the text, one finds carelessness in usage like D-ribitol, D-glycerol, 2-hydroxypropanaldehyde, and the use of the symbol Bz to designate *O*-benzoyl on one flow sheet and *O*-benzyl on another. Material in flow sheets is sometimes wrong (e.g., reference to NaBH₄ in the schemes on pages 122 and 123).

One aim of the authors has been to provide a coverage of carbohydrates suitable for undergraduate use. My own feeling is that the present volume does not succeed in this largely because too much material has been compressed in too small a space to make it useful as a textbook. Further, the price, as a textbook, is prohibitive. In spite of these negative statements the book contains a large amount of useful information and can be a convenient reference for workers requiring a broad general introduction to carbohydrate chemistry and biochemistry.

Department of Chemistry
University of Rhode Island
Kingston, Rhode Island 02881

Leon Goodman

Methods in Protein Sequence Analysis. Edited by Marshall Elzinga. Humana Press, Clifton, NJ. 1982. xxv + 589 pp. 15 × 22.5 cm. ISBN 0-89603-038-5. \$64.50 in the U.S.; \$75.40 elsewhere.

This book presents the Proceedings of the IVth International Conference on Methods in Protein Sequence Analysis, which was held at the Brookhaven National Laboratory, Upton, NY, September 21–25, 1981, and attended by approximately 200 participants. A wealth of new information about every aspect of the art of sequencing can be found in the 70 articles of this book. They are divided into two categories, i.e., papers dealing primarily with methods, which appear as full papers, and reports about new sequences, which are published as short communications.

The Conference lecture given by R. F. Doolittle, entitled "An Anecdotal Account of the History of Peptide Stepwise Degradation Procedures", is a fascinating story, which is enjoyable to read. The nuts and bolts of highly efficient sequencing operations, as well as strategic considerations, are comprehensively reviewed by Brigitte Wittman-Liebold.

These introductory chapters set the stage for a wide range of contributions, including instrumentation, microsequencing, solid-phase sequencing, manual procedures, sequencing by mass spectrometry, cleavage of proteins, coordination of protein and DNA sequencing, and HPLC purification of peptides and proteins. Each topic is introduced by an authoritative main chapter.

M. W. Hunkapiller et al. describe the principle and performance of the new gas-phase sequenator, followed by presentations on longer sequenator runs (G. Frank) and nonspecific peptide bond cleavage (W. F. Brandt et al.). Microsequencing techniques and applications are addressed by J. Y. Chang, A. S. Bhowan, K. Beyreuther, and L. Duffy and their collaborators. Precolumn labeling and radiolabel sequencing are recommended, and the elegant sequence analysis of corticotropin releasing factor served as an impressive example (J. Spiess et al.). Opportunities and constraints in solid-phase sequencing are addressed in six presentations, which also describe a variety of improvements. The use of DABITC [4-(dimethylamino)azobenzene 4'-isothiocyanate] in solid-phase sequencing provides good results at 1–20 nanomol of sample (Salnikow, Wittman-Liebold et al.). Although the majority of all sequencing work still seems to be carried out manually, only two contributions on manual methods are presented (G. E. Tarr, Clyde Zalut). When a partitioning method is used (G. E. Tarr), 10 samples are handled at a time in the 0.1–

10-nanomol range. With cycle times of under 1 h, 20–40 steps per day may be carried out!

Mass spectrometry is well presented, starting with a review (Morris et al.). K. Biemann presents an exciting approach using "The Complementarity of Mass Spectrometry to Edman Degradation or DNA Based Protein Sequencing". The use of fast atom bombardment has clearly revolutionized this area. Small peptides may also be sequenced by using direct chemical ionization (S. A. Carr and V. N. Reinhold), and Y. Shimonishi computerized his operation.

Coordination of protein and DNA sequencing is an important new strategy. In four excellent contributions to this approach, the sequencing of the ATP-synthase complex (J. E. Walker et al.) of *E. coli* RNA polymerase (V. M. Lipkin, Yu. A. Ovchinnikov et al.), of *E. coli* β-galactosidase (A. V. Fowler and I. Zabin), and of mutants of the alcohol dehydrogenase gene (A. R. Place et al.) are described.

Purification of peptides and proteins and preparation of suitable fragments for sequencing are of critical importance. Thus, nearly one-half of the book is devoted to purification by high-performance liquid chromatography and to cleavage of proteins. B. Keil surveys recent advances in enzymatic cleavage of proteins. Trypsin remains as the most used proteinase in sequence studies. Unusual cleavages in the sequencing of tubulin are presented by Ponstingl et al. M. A. Hermodson and A. Fontana et al. discuss chemical cleavage procedures.

Altogether, 15 full papers are devoted to the application of HPLC for the preparation of purified material for sequencing. Although sequencing of mixtures may be carried out efficiently in favorable cases, careful preparation of highly purified starting materials has certainly been widely recognized as producing good sequencing results most consistently. Reverse-phase systems in their various modifications have been used in all of these studies for both purification and peptide mapping.

Sequences reported under "Communications" range from collagen to frog-skin peptides.

This book provides an outstanding account of very useful up-to-date information not only to the practitioners of peptide and protein sequencing but also to chemists, molecular biologists, and those concerned with recombinant DNA synthesis. It should also be on the shelves of all scientific libraries, since it will be useful for a long time due to the several excellent review articles.

Research Division
Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Johannes Meienhofer

Books of Interest

Molecular Biology of the Cell. By B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts, and J. D. Watson. Garland Publishing Co., New York and London. 1983. xxxvii + 1179 pp. 22 × 28.5 cm. ISBN 0-8240-7282-0. \$33.95.

Mycology Series. Volume 3. Fungi Pathogenic for Humans and Animals. Part A. Biology. Edited by Dexter H. Howard. Marcel Dekker, New York. 1983. xiii + 652 pp. 18.5 × 26 cm. ISBN 0-8247-1875-5. \$79.50.

Methods in Enzymology. Volume 90. Carbohydrate Metabolism. Part E. Edited by Willi A. Wood. Academic Press, New York. 1982. xxix + 602 pp. 16 × 23.5 cm. ISBN 0-12-181990-6. \$58.00.

Methods in Enzymology. Volume 75. Cumulative Subject Index. Volumes 31, 32, 34–60. Edited by M. G. Dennis and E. A. Dennis. Academic Press, New York. 1982. xxix + 824 pp. 16.5 × 23.5 cm. ISBN 0-12-161975-2. \$85.00.

Advances in Cardiology. Volume 31. Comprehensive Cardiac Rehabilitation. (2nd World Congress on Cardiac Rehabilitation, Jerusalem, Nov. 1981.) Edited by J. J. Kellermann. S. Karger AG, Basel. 1982. vii + 245 pp. 17.5 × 24.5 cm. ISBN 3-8055-3539-2. \$72.00.

Introduction to Semimicro Qualitative Analysis. 6th Edition. By C. H. Sorum and J. J. Lagowski. Prentice-Hall, Englewood Cliffs, NJ. 1983. xi + 340 pp. 15 × 22.5 cm. ISBN 0-13-496067-X. \$15.95 (paperback).