Book Reviews

Topics in Antibiotic Chemistry. Volume 4. The Chemistry and Antimicrobial Activity of New Synthetic β-Lactam Antibiotics. By Frederic A. Jung, William R. Pilgrim, J. Philip Poyser, and Patrice J. Siret. Ellis Horwood Limited, Chichester (Distributed by Wiley, New York). 1980. 278 pp. 15.5 × 24 cm. $75.00.

This volume is the fourth in the series edited by P. G. Sammes. It is devoted to a discussion of the chemistry and antibacterial activity of the β-lactam antibiotics synthesized in the 1974–1978 period. Earlier work, such as the original penicillin and cephalosporin syntheses, is included only as supporting material. Despite the small number of years covered in this review, the amount of interesting and valuable chemistry described is substantial. Of course, it is well known that large numbers of very talented chemists are engaged in the search for new clinically effective β-lactams. Thus, it is not surprising that the field is moving rapidly and producing numerous ingenious syntheses. The present volume presents a concise and authorative account of the results in this exciting field. It is well written by a team of investigators from I.C.I. Pharma S.A. in Rheims, France.

The volume is organized into a brief introduction and three major sections that are concerned with total synthesis, semisynthesis, and structural modification of the β-lactams. It is thorough and carefully planned. In the section on total synthesis, compounds of both natural and nonnatural skeletons are considered. The section on semisynthetic compounds gives an excellent account of recent application of the transformation of penicillin sulfoxides (Morin reaction) into cephalosporins and other β-lactams. It also emphasizes the preparation of C-3 exomethylene cephams. Chemical transformations of positions 2, 3, 6, and 7 in penicillins and the corresponding positions 3, 4, 7, and 8 in cephalosporins are the topic of the final section. There is a wealth of novel chemistry in this section, including that related to the cephamycins. Tables of antibacterial activity, generally expressed as minimum inhibitory concentrations against various organisms by the serial dilution technique in culture broths, are used effectively throughout the volume to establish structure–activity relationships for various types of β-lactams. Also very useful are the 575 pertinent literature references.

This volume is considered essential for anyone undertaking or contemplating research into β-lactam chemistry. It is recommended for libraries. Persons not involved with β-lactams might find it a valuable source of synthetic reactions and mechanisms, but the high price might be discouraging. Although the dust jacket of this volume indicates a readership of chemists, biochemists, pharmacologists, molecular biologists, and microbiologists, it can be recommended enthusiastically only to chemists. The treatment of the other fields is too cursory for specialists in them.

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Burger's Medicinal Chemistry. 4th Edition. Part I. The Basis of Medicinal Chemistry. Edited by Manfred E. Wolff. Wiley, New York. 1980. x + 497 pp. 17.5 × 25 cm. $29.50.

Part I of this well-known and valuable work in its fourth edition actually was published after Part II, presumably because all manuscripts for the former were not available. But the well-written introductory chapter by Alfred Burger himself, the originator of the work, was surely in the hands of Editor Wolff perhaps as early as 1977, the year of the last noted reference. Also, Burger's final entry in the table of important annual discoveries is dated 1975. More pertinent, Part I includes the perceptive preface by Manfred Wolff followed by the purpose of several competent researchers: contributions to the design of important new medicinal agents. Following the introduction there are 11 chapters concerning the following aspects of drugs: absorption, distribution, and elimination; biotransformations; receptor theories; design; quantitative analysis of structure–activity relationships; drug allergy; and chemical carcinogenesis. Obviously, the work constitutes a tremendous contribution through the time-saving device of making excerpts of the literature readily available and through inducing the reader to move toward finding new agents.

Trying to remember the well-documented facts of past researches cited by the various authors is mind boggling. Only such individuals as Thomas Macauley, the English writer, and Tomas Arias III, my former graduate student from Panama, are gifted with such computerized recall. Perhaps the computer is the answer. Beyond that, the human body is so seemingly arbitrary in its handling of drugs that integrating those established facts into meaningful conclusions and useful directions for research remains a most difficult but still challenging endeavor.

Considering the present state of biological knowledge and working as a traditional medicinal chemist who still dotes on hunch as well as Hansch, this reviewer is disturbed by the apparent paradox of devoting much space to awe-inspiring mathematical derivations with their implied exactitudes, while the present state of knowledge necessitates such discomforting statements as "Here we make two assumptions..." (line 8, page 354); "...water may exert a leveling effect..." (four lines up from the bottom of page 356); and "We realize the risk of generalizing in a most complicated area." (line 15, page 357).

Whether it is the intriguing nature of the subject or the skill of the writer or both, Kunz, in his chapter on "Drug-Receptor Geometry" creates excitement in his articulate and philosophic treatment of the subject. Also, his short summaries at intervals help the reader.

There remains a gap between the mathematic expressions derived in chapters such as that on "Drug Absorption, Distribution, and Elimination" and the actual design of novel or better drugs. Thus far, massive screening programs, molecular modification, keen observations of effects on animals and humans, the application of isosterism by Gertrude Elion and George Hitchings, and inhibition or protection of essential enzymes have produced the new drugs. Einstein was never able to derive a unifying theory of the universe. Nevertheless, compilations of new facts and theories such as those in Part I of Burger's Medicinal Chemistry are to be encouraged. Perhaps one day the 497 pages of Part I may be reducible to a single mathematical equation which will yield novel drugs with much less effort than is now being expended.

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Biochemical Applications of Mass Spectrometry. First Supplementary Volume. Edited by G. R. Waller and O. C. Dermer. Wiley-Interscience, New York. 1980. xvii + 1279 pp. $150.00.

"A good thing is improved by increasing it" (Irish proverb). This massive book, a supplement to the now-classic 1972 "Biochemical Applications of Mass Spectrometry", makes the case well. The new book is truly a supplement, not a revision, of the earlier work. Thirty-eight chapters build upon the well-laid foundation by presenting work done since 1971. Most of the original contributors, an international group all well-known in the areas they are discussing, have participated again. The high quality and broad scope are thus maintained and continuity provided. Introductory, historical, and theoretical material in each area is not repeated in the supplement. The reader is therefore at some disadvantage if the first book is not at hand

(but, by now, one assumes that any scientist doing biomedical mass spectrometry has access to that volume).

Reflecting areas of growing interest for mass spectrometrists, chapters have been added on clinical applications (the previous chapter under this title covered only respiratory MS), pollutants (two chapters: one on toxic residues, one on air pollutants), volatiles emitted by humans, flavanoids, and related plant phenolics, separation/identification systems for complex mixtures, quantitative MS and ^{252}Cf plasma desorption. The four appendixes offer practical guidelines, especially useful for workers in the U.S., on available computer program exchanges, biotechnology resources, short courses, and the development of criteria for good laboratory practices. A general glossary provides a ready reference to the most frequently used acronyms. A few chapters have not been updated. Some of these were more of an historical nature. It is unfortunate, however, that the chapters on chemical ionization and field ionization/desorption were not supplemented because both of these are areas in which there is a great deal of activity and for which many important advances have been made in the last few years.

Taken as a whole, the book represents an opportunity to place in context the developments of the last eight years in a discipline which is experiencing such a rapid growth that no one person can keep abreast of it all. The three major sections (Instrumentation, Interpretation of Mass Spectra, and Applications) constitute a broad-ranging dialogue written by the members of the mass spectrometry community for each other's use. The authors have, for the most part, seized the opportunity to review contributions in their fields in a manner which combines summary with constructive criticism.

The section on instrumentation underscores the fact that most of the innovation in both instrumentation and data systems continues to come from the users of mass spectrometers rather than the manufacturers. The parallel descriptions of hardware and software in a number of research laboratories allows the reader to make comparisons and to learn the reasoning behind the designs. Although most of the readers of the book will probably be purchasers/owners of commercial systems, the insight provided here can make them more discriminating customers/users. The chapters on interpretation focus on the attention now being directed to metastable analyses, particularly for complex mixtures (as does the chapter on "Mixture Analysis"), and on computer techniques for matching and interpretation of spectra.

The "Applications" chapters do have some overlap in their descriptions of instrumental approaches, but this is not a serious defect because these parts are generally short. Many chapters are of obvious interest to readers of this journal (e.g., "Steroids", "Hormones", "Nucleic Acids and Derivatives", "Antibiotics", "Stable Isotopes"), but a number of less likely chapters also include general discussions on topics such as separations and artifacts (in "Pheremones and Allelochemics") and sample preparation (in "Toxic Residues and Pollutants") which sould not be overlooked. The chapter on "Clinical Medicine" is particularly thorough (536 references). Although there is some repetition of topics covered elsewhere, different references are chosen for discussion, and the selection and presentation in this chapter is exceptionally good. The "Drug Metabolism" chapter is peculiarly short and lacks the insightfulness of the material under "Clinical Medicine", but for those interested in the subject the latter chapter and other related ones serve to compensate. Chapters on "Peptides", "Carbohydrates", and "Complex Lipids" continue the discussion of mass spectrometric approaches to the study of large molecules by providing critical reviews of the literature and thorough discussion of data. From the variety of experimental techniques being used, one can probably assume that all current procedures have limitations, but the level of activity in these areas reflects the optimism of the workers that solutions can be found. The chapter on "Quantitation" is particularly effective because the authors present an extensive table which not only lists references classified by analyte but includes information on the derivative and standard used and the levels measured.

This book is the state-of-the-art for biochemical mass spectrometry just as clearly as is the work described herein. For what it includes, its steep price is money well spent. It may be beyond the reach of most individuals, but it surely belongs in the collection of technical and university libraries and it is a prerequisite for any laboratory engaged in this type of research or dependent on its results.

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