Book Reviews

Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry. 8th Edition. Edited by Robert F. Doerge. J. B. Lippincott, Philadelphia. 1982. xiv + 876 pp. 22 × 28.5 cm. ISBN 0-397-52092-1. $47.50.

This revision replaces the 1977 edition of a textbook first published in 1949 under the title, *Organic Chemistry in Pharmacy*. The editor states that the book "...is written for the undergraduate pharmacy student...", but it is appropriate for anyone needing an introductory overview of the field.

The book is similar to previous ones on the subject in both size and content, while being written by multiple contributors. The advantage of multiple authors can be offset by some unevenness of topic presentation, but I found no "soft" chapter present. This 8th edition is reduced in the number of chapters from the previous edition by combining related topics (e.g., adrenergic agonists and antagonists in the same chapter). The metabolism chapter has been expanded and should provide a strong foundation for the nonspecialist in the area.

One expects a generally outstanding book without glaring errors of commission or omission in a standard textbook in its 8th edition, and this reviewer found it. Next, one can look to more subtle points whose significance varies with the individual. One can answer "yes" to each of the following questions: Are the chapters organized effectively? Are the drugs grouped into tables with a variety of important information and data? Are references to specific points appropriate and current? Are references to more thorough discussions of various aspects listed in the bibliography?

Each chapter provides a view of the broader therapeutic and pharmaceutical aspects of the topic, which aids in placing medicinal chemistry in proper perspective with other aspects of drug study. A useful feature of the index is the cross-listing of generic and tradenames. Consistent with most current undergraduate teaching in medicinal chemistry, synthesis of drug molecules is not emphasized, although selected syntheses are presented.

One aspect that I would like to see included in each chapter is a "drugs on the horizon" section. While it is difficult to predict which research areas under active investigation at the time of chapter writing will be promising new therapeutic categories when the book is read a year or more later, such a section can help. An example of a group of compounds that could have been included is the angiotensin II antagonist class in the cardiovascular chapter.

A good general medicinal chemistry textbook is a desirable part of the library of anyone working in the area. It provides background and breadth needed for understanding the specific area of current interest and its relationship to the whole field. It should compliment a general pharmacology textbook. From my brief examination and reading of this book, it appears this book meets the purposes for which it was written. However, after utilizing it in our medicinal chemistry survey course, I will feel more confident in giving it an unqualified recommendation.

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General and Synthetic Methods. Volume 5. Specialist Periodical Reports. G. Pattenden, Senior Reporter. The Royal Society of Chemistry, Burlington House, London. 1982. xiii + 439 pp. 14 × 22.5 cm. ISBN 0-85186-864-9. $122.00.

This report, similar in scope and format to the previous volumes in this series, covers the literature published during 1980. The subject matter is classified according to chapters entitled "Saturated and Unsaturated Hydrocarbons", "Aldehydes and Ketones", "Carboxylic Acids and Derivatives", "Alcohols, Halogeno-compounds, and Ethers", "Amines, Nitriles, and Other Nitrogen-Containing Functional Groups", "Organometallics in Synthesis", "Saturated Carbocyclic Ring Synthesis", "Saturated Heterocyclic Ring Synthesis", and "Strategy and Design in Synthesis". There is an additional section on "Reviews on General Synthetic Methods", which also includes a few entries from 1979.

The organization of the material in this volume is somewhat inconsistent. Chapter titles are misleading, since, for example, "Hydrocarbons" does not deal with hydrocarbons per se but rather with formations and transformations of the hydrocarbon components of functionalized compounds. Yet, Part I of "Organometallics in Synthesis", subtitled "The Transition Elements", is arranged by reaction type. Part II of the same chapter, entitled "Main Group Elements", is subdivided according to the periodic group of the specific element. In the absence of a subject index it is thus not possible to survey any particular functionality without a page-by-page perusal of the entire volume. There is an author index and a detailed table of contents.

The volume is an invaluable aid to synthetic chemists who are hard pressed to keep up with an ever expanding literature. This reviewer has previously commented on the prohibitive price of these otherwise desireable volumes, which has forced even libraries to become more selective in their acquisitions. (I have long since discounted the possibility of individual ownership.) Happily, the number of pages in this volume has increased by 16% over that of its predecessor, at a negligible increase in cost. While it is far too late to maintain continuity in library acquisitions, at least let us salute a small step in the right direction on part of the publisher.

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Fundamentals of Preparative Organic Chemistry. By R. Keese, R. K. Muller, and T. P. Toube. Wiley, New York. 1982. 149 pp. 15.5 × 23.5 cm. ISBN 0470-27522-7. $42.95.

This compendium, translated from the third German edition, gathers together valuable and practical information on the basic techniques needed by a laboratory worker for study, research, or advanced experimental work in organic chemistry. It lays emphasis on the role of practical hints, tips, and rules of thumb, accrued from everyday laboratory experimental work and the great experience of the authors and their colleagues and students over a number of years.

The authors provide just the sort of useful information that skilled and fully professional experimentalists would be likely to convey to those learning the subject: with an easy touch, ideal for instruction and from a practical angle, they cover all the main separatory techniques used in preparative organic chemistry, including crystallization and distillation.

Undergraduate and beginning graduate students in organic chemistry, organic chemistry researchers and workers, and those training in technical courses with an organic chemistry bias will find this little compendium quite helpful.

Staff

Advances in Pharmaceutical Sciences. Volume 5. Edited by H. S. Bean, A. H. Beckett, and J. E. Carless. Academic Press, London and New York. 1982. 230 pp. 15.5 × 23.5 cm. ISBN 012-032305-2. $19.80.

This volume contains contributions in three areas: "Germ Removal Filtration" by K. H. Wallhausser of Hoechst AG, Frankfurt; "Practical Pharmacodynamic Engineering in the Design, Development, and Evaluation of Optimal Drug Products" by V. F. Smolen of Pharmacontrol Corp., Englewood Cliffs, NJ; and "The Clinical Significance of Microbial Contamination in Pharmaceutical and Allied Products" by O. Ringertz and S. H.

Ringertz of the Karolinska Institute, Stockholm. The first section on germ removal filtration is extensive (116 pages). It gives a highly detailed and rather complete description of methods and evaluation of techniques used in germ removal from all types of delivery systems (parenteral solutions in ointment bases). There are many tables (29) and figures (31) describing methods and summarizing very pertinent information. The text is easy to follow and well documented. A close attention to detail is followed in each topic covered: the definition of terms (for example, flow efficiency), types of germs encountered, selection of apparatus, description of various filter types, controls needed before and after filter use, tests for sterility, air filtration, and others. The next section by V. F. Smolen (84 pages) is essentially a summary of the author's approaches to bioavailability studies that he has conducted over perhaps the last 7 to 10 years. The focus centers on pharmacodynamics and the quantitative relationship between drug bioavailability (inputs) and therapeutic and toxic effects (outputs). Terms used are probably foreign to the usual pharmaceutical reader, and reading therefore requires some concentration. The concepts are those of an engineer and, thus, general in their construction and evaluation of drug input–output relationships. The approach is mechanism independent involving "black box" analysis. Many examples make following the methodology easier, except that the legends in Figures 8–11 erroneously refer to Figures 3–5. It is demonstrated how in in vitro drug bioavailability testing it is unnecessary to compensate for actual mechanisms occurring in vivo, since it is only the predictive fidelity of the test that is important. This is where the "black box" systems analysis approach provides a simple (and general) means of developing optimal in vitro bioavailability requirements. A discussion of the selection of drug-response variables includes the resolution of pharmacokinetic data from biological signals utilizing biosignal changes in the time domain (plethysmographic changes with time for organic nitrates) or biosignal changes in the frequency domain (Fourier Transform of EEG for phenothiazines). In the last sections, examples are provided illustrating how optimizing drug input may be approached. The third major part of the book by the Ringertzs on microbial contamination in pharmaceutical and related products (26 pages) provides documentation of problems that have occurred with products that range from aqueous parenterals through thyroid tablets to eye mascara. The authors appear to be well acquainted with the problems that can occur. This section leaves the reader with a realization and a fear that many consequences of product contamination have not been reported, or even discovered, and makes the first section of this book on filtration even more significant.

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Antiepileptic Drugs. Second Edition. Edited by D. M. Woodbury, J. K. Penry, and C. E. Pippenger. Raven Press, New York. 1982. xvii + 879 pp. 18.5 × 26 cm. ISBN 0-89004-498-8. $65.00.

Antiepileptic Drugs is an encyclopedic reference volume. The most useful drugs, such as phenytoin, carbamazepine, ethosuximide, and valproic acid, as well as the barbiturates, are covered in great detail. Less important drugs, however, are also fully covered, and information is provided on drugs that are rarely used, such as bromides, and some of the newer investigational compounds. The introductory chapters on pharmacokinetics are a useful outline of the subject but would probably be more important for physicians than pharmacologists. The chapters on testing antiepileptic drugs and controlled trials are of great general interest. It would have been useful for each of the individual chapter authors to have discussed how many of the claims of clinical efficacy for a particular drug are actually based on controlled data. There is relatively little information about mechanisms of actions in this volume, but it should be regarded as complimentary to the recent *Antiepileptic Drugs: Mechanisms of Action*, also published by Raven Press in the *Advances in Neurology* series. The references are variably up-to-date from chapter to chapter. Some chapters have references as recent as 1980, while others have none more recent than 1978. One disadvantage of the book is a poor index, making it very difficult to look up a subject involving several drugs. Some topics, such as the possible teratogenicity of antiepileptic compounds, are only superficially discussed. Nevertheless, this volume contains a very large amount of generally up-to-date pharmacologic information and is particularly strong in discussing the chemistry and assay methods for antiepileptic drugs, as well as their absorption, distribution, biotransformation, and excretion. Clinical topics, such as the relationship between plasma concentration, seizure control, and neurotoxicity, are also fully covered. This volume would be extremely useful for a laboratory actively involved in working in antiepileptic drugs or for a neurologist specializing in epilepsy. There are other volumes available that provide more succinct and well-organized discussions of anticonvulsant therapy, but none provides so much information about antiepileptic drugs themselves.

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Annals of the New York Academy of Sciences. Volume 389. C-Reactive Protein and the Plasma Protein Response to Tissue Injury. Edited by Irving Kushner, John E. Volkanis, and Henry Gerwurz. The New York Academy of Sciences, New York. 1982. xi + 482 pp. 15 × 23 cm. ISBN 0-89766-193-1 (ISBN 0-89766-194-x, paperback). $97.00.

This volume represents the proceedings of a New York Academy of Sciences conference held in September, 1981, dealing with aspects of the so-called acute phase response. This phenomenon is a response to inflammation or other tissue injury that is hallmarked by a dramatic increase in serum levels of certain proteins of hepatic origin.

The emphasis of this conference was on the biology and biochemistry of two acute phase proteins, C-reactive protein (CRP) and serum amyloid A, and of a molecule that is closely related to CRP and is an acute phase reactant in the mouse, serum amyloid P. The fascinating properties of these molecules are well reported by the presented papers. For example, CRP, in binding to certain ligands, notably pneumonococcal C-polysaccharide and phosphorylcholine, can activate the complement system. Because it can bind to damaged cell membranes in vivo, there is speculation that CRP promotes elimination of damaged cells. The molecule is remarkably conserved during evolution, and its ability to bind to certain types of lymphocytes hints at a role in immunoregulation.

Additionally, the mechanism of induction of the acute phase response is addressed, including the role of interleukin 1. Other aspects of the response receive considerably less attention, and relatively little new clinical data are presented.

This volume is considerably more cohesive and readable than most such published proceedings. Probably because this was, apparently, the first major meeting devoted to this subject, the presented papers contain a wealth of prior data in review. Although the book is enriched by the inclusion of transcripts of the discussion stimulated by the presented papers, the lack of a subject index severely restricts its usefulness as a reference. The price of this volume may generally preclude its worthy inclusion into personal libraries.

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Inflammatory Diseases and Copper. Edited by J. R. J. Sorenson. Humana Press, Clifton, NJ. 1982. xx + 622 pp. 15.5 × 23.5 cm. ISBN 0-89603-037-7. $69.50.

This collection of "camera-ready" manuscripts, poster sessions, and discussion transcripts records the scientific dynamics of an interdisciplinary meeting held in August 1981 at the University of Arkansas Medical Campus. The editor of this volume was not

only the chief convener but also a major contributor and living "guru" on the subject of copper and its relation to inflammation.

Many are familiar with clinical folk tales concerning the wearing of copper bracelets to prevent the afflictions of arthritis and rheumatism. Most would dismiss, out of hand, any scientific rationale for such therapy. W. Ray Walker presents his results of a modest controlled study that seems to show some improvement of physical well-being. He also provides direct data for transdermal transport of various copper–amino acid complexes.

I enjoyed this "instant book". It represents the interesting interactions among chemists, biologists, biochemists, pharmacologists, and clinicians sharing a common interest in copper and how that trace element could be directly or indirectly involved in the causation or amelioration of inflammation. The major topics covered are physiological aspects of copper metabolism, biological aspects of copper metabolism in inflammation; antiinflammatory activities of copper complexes, antiulcer, antimicrobial, and anticancer activities of copper complexes, therapy of rheumatic diseases, and possible mechanisms of action.

The best feature of this volume is the assembling of diverse viewpoints and experimental approaches. Unfortunately, no integration or concensus was attempted or achieved. However, for those interested in trace-element metabolism, nutrition, and the complexities of inflammation and associated therapeutics, this collection provides a rich source of information. The papers on human copper nutrition, teratogenic effects, Menkes' disease, and Wilson's disease are of particularly high quality. The biochemistry of copper is uniformly well covered.

The situation becomes complicated as the roles of copper in inflammation are examined. The importance of superoxide as the generator or end product of pain and swelling in joints and the importance of ceruloplasmin as a scavenger for superoxide are examined. The thesis that copper complexes directly generate free radicals or are involved in the peroxidation of polyunsaturated fatty acids to prostaglandins and other pain of inflammation suppressants is discussed.

The discovery in 1976 by J. R. J. Sorenson that many antiinflammatory drugs used in treating arthritis were copper chelators stimulated researchers to explore animal models of hypersensitivity. Two of the most widely used therapeutic agents for arthritis, aspirin and D penicillamine, are strong copper complexing agents. Extensive data and discussion are presented on the use of these drugs.

Many therapeutic gold complexes are also directly or indirectly involved in copper and zinc homeostasis. Indeed, several papers describe the importance of copper–zinc interaction in trace-element nutrition and in the immune response systems. The modulation of lymphocyte response to copper and hepatocytes to a variety of trace elements represent new insights.

This book is timely; the references are up-to-date. The transcript of the discussion gives the reader a sense of doubts and validations. The errors of typing, spelling, grammar, etc., are trivial with respect to the multidisciplinary range the reader can experience in a single volume. There are some fascinating relationships emerging at the intersection of trace elements, chelation, and therapeutics presented here. If you were unable to attend the meeting, this volume is the next best thing.

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Human Cancer Markers. Edited by Stewart Sell and Britta Wahren. Humana Press, Inc., Clifton, NJ. 1982. xx + 428 pp. 15.5 × 23.5 cm. ISBN 0-89603-029-6. $59.50 in the U.S.A. ($69.50 elsewhere).

This book, *Human Cancer Markers*, contains an inclusive summary of many widely studied tumor markers and presents an objective view of their relevance to disease. While the identification of an unquestioned tumor-specific marker still eludes investigators, this book conveys optimism for the analysis of tumor-associated markers in the clinical management of disease. Since similar tumor-associated markers, such as carcinoembryonic antigen (CEA), alpha/fetoprotein (AFP), tissue polypeptide antigen, B_2-microglobulin, and other acute phase reactants and oncofetal antigens, are elevated in different cancers, the authors suggested that a detailed quantitative analysis of multiple markers may prove to be accurate indicators of disease. Future studies may show that the rise and fall of certain markers will accurately predict the disease course.

Each of the 16 chapters contains a well-organized and well-referenced update on separate organ site cancers and their respective associated markers. Lymphoid, skin, gastrointestinal, liver, pancreatic, prostratic, breast, endocrine, bladder, kidney, lung, and central nervous system associated markers are discussed. All chapters relate marker levels to both diagnosis and disease management. Each author appears to conclude that at present tumor markers are of most value in disease management rather than in diagnosis. There is, at present, no identifiable and generally acceptable tumor marker available for routine screening of individuals thought to be at high risk for cancer.

One chapter in the book presents an excellent review on hybridoma technology and specifically highlights the potential value of monoclonal antibodies in cancer diagnosis and therapy. With their exquisite specificity, it is conceivable that monoclonal antibodies will be able to deliver covalently bound toxic agents directly to the tumor cells.

This book is highly recommended to those desiring an exclusive update on the status of various tumor markers.

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Modern Methods of Pharmaceutical Analysis. Volumes I–III. CRC Press, Boca Raton, FL. 1982. Volume I: Edited by Roger E. Schirmer. xii + 274 pp. 18 × 26 cm. ISBN 0-8493-5244-4. $79.95 ($89.95 outside U.S.A.). Volume II: Edited by Roger E. Schirmer. x + 252 pp. 18 × 26 cm. ISBN 0-8493-5245-2. $81.00 ($91.00 outside U.S.A.). Volume III: Edited by Roger E. Schirmer. viii + 243 pp. 18 × 26 cm. ISBN 0-8493-5246-0. $72.00 ($83.00 outside U.S.A.).

The purpose of these volumes is to review methods used in drug analysis with emphasis on practical aspects, such as factors that influence proper application and tabulations of useful data. This purpose is, for the most part, accomplished in a comprehensive manner, and extensive references are provided. The advanced technical level of many of the chapters makes it most meaningful to the experienced pharmaceutical analyst, for whom it should prove an invaluable reference.

Volume I, Chapter I, "Separation of Drugs from Excipients", discusses liquid–solid and liquid–liquid extractions, ion pair extraction, and column chromatography. Chapter 2, "UV and Visible Absorption Techniques", includes theory, principles, extensive tables of spectral data, spectrophotometer design, and selection of instrumental parameters. There is a large section on applications, containing a thorough treatment of indirect methods such as diazotization and the Bratton–Marshall reaction. Chapter 3, "IR Methods of Analysis", covers theory, comprehensive lists and descriptions of characteristic bands arising from various functional groups, principles and features of IR spectrophotometers (including a short but lucid explanation of Fourier transform), selection of analytical parameters and quantitation. Applications to qualitative and quantitative analysis are discussed. Chapter 4, "Fluorometric Analysis", contains excellent treatments of phenomena on the molecular and atomic levels, quantum efficiency, experimental factors affecting fluorescence intensity, fluorometer design, and relation of fluorescence to molecular structure. Applications are given for more than 100 compounds of pharmaceutical interest. Chapter 5 is a short treatment of optical rotation measurement and calculation, much less detailed than the previous four chapters.

Volume II, Chapter 1, "NMR", deals with theory, including an extensive discussion and tabulation of chemical shifts and splitting, design of instrumentation, instrumental parameters for quantitative analysis, and shift reagents. Applications are included for

about 65 drugs, as well as excipients, impurities, and isomers. Chapter 2, "Polarography", contains qualitative and quantitative theoretical and practical treatments of the reversible, diffusion-limited situation and deviations therefrom; related techniques, such as differential pulse polarography, cyclic voltametry, and stripping analysis; method development; validation; and instrumentation. The short application section consists of a general discussion and a list of review articles. Chapter 3, "Coulometry", discusses controlled potential coulometry and coulometric titrations. For each subject, principles, calculations, mechanisms, instrumental design and parameter selection are reviewed. Applications are given: 32 for controlled potential coulometry and about 80 for coulometric titrations.

Volume III, Chapter 1, covers gas–liquid chromatography. After a rather superficial discussion of theory, instrumental considerations are dealt with in detail, with emphasis, on, and tabulation of, the nature of column packings. Method development considerations and derivatization are also covered. The applications section lists GLC methods in USP XIX and NF XIV and refers to 22 methodological papers and a review. A useful trouble-shooting table is presented. Chapter 2, "High-Performance Liquid Chromatography", includes basic theory and nomenclature, instrumentation, columns (with extensive tabulations and comparisons), separation mechanism, solvent selection, data handling, derivatization, preparative techniques, method development, trace analysis, purity analysis, troubleshooting, and maintainance, all covered in a fairly comprehensive manner, with emphasis on practical aspects. A listing of 102 methods for 93 compounds, with column (including brand name), mobile phase, and references, makes up the application section. Chapter 3, "Thermal Analysis", covers principles, procedures, and applications of thermogravimetric analysis, differential thermal analysis, and differential scanning calorimetry. References for the application of differential scanning calorimetry to 152 drugs are listed. Chapter 4 discusses phase solubility analysis. Theory and experimental procedure are presented, and applications to about 85 pharmaceuticals are listed. Chapter 5, "The Determination of Isomeric Purity", differs from the preceding material in that it is organized by type of isomer rather than analytical method. For positional isomers, GC, TLC, HPLC, NMR, IR, UV, and mass spectrometry are discussed. For stereoisomers, the methods considered include optical rotation, GC, HPLC, NMR, mass spectrometry, and IR. Four applications are reviewed in more detail.

The major defect that must be noted for these volumes is that the material covered dates only to 1977, except for the chapter on HPLC, which has many references through 1980. While this is only a minor problem for most of the work, it is a serious flaw in the GC chapter, especially in the discussion of capillary columns. Nevertheless, a great deal of very useful information has been collected here. This set is recommended to any chemist who desires an in-depth understanding of pharmaceutical analysis.

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Introduction to High Performance Liquid Chromatography. Second Edition. By R. J. Hamilton and P. A. Sewall. Chapman and Hall, London. 1982. viii + 248 pp. 16 × 24 cm. ISBN 0-412-23430-0. $29.95.

This is a good book for the beginner in high-performance liquid chromatography. It is well organized and clearly written.

There are eight chapters in the book: (1) "Introduction to HPLC", (2) "Chromatography Theory", (3) "Equipment", (4) "Stationary Phases", (5) "Mobile Phases", (6) "Developing a Chromatogram", (7) "Preparative HPLC & Trace Analysis", and (8) "Applications". Although there is a compound index as well as a subject index, there is no author index.

The figures are well drawn, and the tables that are used present the material clearly. Most of the material was in the first edition of this book, which was published in 1977. The new material includes a table of bonded phase packings and sections on electrochemical detectors, microprocessor-controlled HPLC, bonded stationary phases, and the ion-pairing technique. The chapter on applications leaves something to be desired. First, the information could have been presented in a table or tabular form, which would have saved space and/or more applications could have been presented. Second, without chromatograms it is difficult to tell how good the separation and/or resolution was. For example, in 8.2.1 d, how many of the sugars were actually resolved with retention times of 3.4, 3.6, 4.0, 4.3, 4.4 min, etc. One picture sometimes is worth a thousand words. Since tremendous progress has been made in HPLC separations in the last few years, especially with the development of bonded phase packings, it was disappointing to see so many chromatograms used from the middle 1970s instead of current ones. In this book there is minimal use of the current literature. The list of references cited at the end of each chapter is very short and, for the most part, is comprised of early books or articles.

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Books of Interest

Mutagenicity: New Horizons in Genetic Toxicology. Edited by John A. Heddle. Academic Press, New York. 1982. xvi + 471 pp. 16 × 23.5 cm. ISBN 0-12-336180-X. $55.00.

Handbook of Enzyme Inhibitors (1965–1977). By Mahendra K. Jain. Wiley, New York. 1982. ix + 447 pp. 22 × 28.5 cm. ISBN 0471-86727-6. $100.00.

Adolescent Marijuana Abusers and Their Families. NIDA Research Monograph. Number 40. By H. Hendin, A. Pollinger, R. Ulman, A. C. Carr. U.S. Department of Health and Human Services, Rockville, MD. 1981. 114 pp. 14.5 × 23 cm. GPO stock, $4.50. NTIS PB, $12.00.

Benzodiazepines: A Review of Research Results, 1980. NIDA Research Monograph. Number 33. Edited by Stephen I. Szara and Jacqueline P. Ludford. U.S. Department of Health and Human Services, Rockville, MD. 1981. vii + 101 pp. 15 × 23 cm. GPO Stock, $4.75. NTIS PB, $12.00.

Behavioral Pharmacology of Human Drug Dependence. NIDA Research Monograph. Number 37. Edited by Travis Thompson and Chris E. Johanson. U.S. Department of Health and Human Services, Rockville, MD. 1981. xii + 294 pp. 15 × 23 cm. GPO Stock, $6.50. NTIS PB, $24.00.

Virus Infections: Modern Concepts and Status. Microbiology Series. Volume 6. Edited by Lloyd C. Olson Marcel Dekker, New York. 1982. x + 289 pp. 16 × 23.5 cm. ISBN 0-8247-1859-3. $39.75.