hypothesis of Belleau and Morgan.<sup>13</sup> The demonstration of the opioid activity of the quaternized compound 2, which presumably cannot penetrate the cell membrane, implies that the opiate receptors of guinea pig ileum myenteric plexus are located on the external surface of the neuronal membrane.

Acknowledgment. We thank Dr. Avram Goldstein for helpful discussion, Rekha Padhya and Asha Naidu for expert technical assistance, Hoffman-La Roche, Inc., for levorphanol and dextrorphan tartrates, and Endo Laboratories for naloxone. This work was supported by National Institute on Drug Abuse Grants DA-972 and DA-1199 and by the Drug Abuse Council.

## References and Notes

- A. H. Beckett and A. F. Casy, J. Pharm. Pharmacol., 6, 986 (1954).
- (2) P. S. Portoghese, J. Pharm. Sci., 55, 865 (1966).
- (3) H. W. Kosterlitz, J. A. H. Lord, and A. J. Watt in "Agonist and Antagonist Actions of Narcotic Drugs", H. W. Kosterlitz, H. O. J. Collier, and J. E. Villareal, Ed., Macmillan, London, 1972, p 45.
- (4) R. S. Foster, D. J. Jenden, and P. Lomax, J. Pharmacol. Exp. Ther., 157, 185 (1967).
- (5) A. Herz and H. Teschemacher, Adv. Drug Res., 6, 79 (1971).
- (6) Melting points were determined on a Kofler micro-heating

- stage and are uncorrected. Elemental analyses were performed by the Micro-analytical Laboratory, Department of Chemistry, Stanford University; results for elements indicated are within 0.4% of theoretical values.
- (7) The use of the guinea pig ileum preparation as a model for the in vivo analgesic action of opiates is well documented; see, for example, ref 3 and I. Creese and S. H. Snyder, J. Pharmacol. Exp. Ther., 194, 205 (1975).
- (8) W. D. M. Paton, Br. J. Pharmacol., 12, 119 (1957).
- (9) B. M. Cox and M. Weinstock, Br. J. Pharmacol., 27, 81 (1966).
- (10) R. Schulz and A. Goldstein, J. Pharmacol. Exp. Ther., 183, 404 (1972).
- (11) H. W. Kosterlitz and A. J. Watt, Br. J. Pharmacol., 33, 266 (1968).
- (12) E. J. Simon, J. M. Hiller, and I. Edelman, Proc. Natl. Acad. Sci. U.S.A., 70, 1947 (1973). Binding was measured in 0.1 M Tris-HCl buffer at pH 7.4 in the absence of added Na<sup>+</sup>. There is good agreement between relative inhibitory activity in this assay and relative analgesic potency for opiate drugs.
- (13) B. Belleau and P. Morgan, J. Med. Chem., 17, 908 (1974); see also B. Belleau, T. Conway, and A. D. Hardy, ibid., 17, 907 (1974).

Kent E. Opheim, Brian M. Cox\*
Addiction Research Foundation
Palo Alto, California 94304
Received November 5, 1975

## Book Reviews

Heterogeneity of Polypeptide Hormones. Edited by D. Rabinowitz and J. Roth. Academic Press, New York, N.Y. 1974. 181 pp. \$16.50.

This small volume is a special issue of the *Israel Journal of Medical Sciences*, dedicated to the memory of Soloman Berson. The papers incorporated here were received for publication between Sept 1972 and Oct 1973.

This compendium of papers is not a review of the subject of polypeptide hormone heterogeneity as is suggested by the title. Rather, it is a collection of research papers each of which has as its subject one or more of the polypeptide hormones. Several of the polypeptide hormones such as insulin, proinsulin, human growth hormone, glucagon, and luteinizing hormone are the subject of more than one paper, and several of the papers are more general in nature; however, since this volume is not a good general review of polypeptide hormone heterogeneity and since the information included here is readily available from the periodical literature, this book is recommended only for those who wish to own a copy in memory of Doctor Berson.

Lahey Clinic Foundation Boston, Massachusetts 02115 Ann Warner

Amino Acids, Peptides, and Proteins. Volume 6 (Specialist Periodical Reports). Edited by R. C. Sheppard with 18 contributors. The Chemical Society, London. xviii + 514 pp. 14 × 22 cm. £16.50.

Anyone who has browsed through the Specialist Periodical Reports knows how valuable these little books are as a means of keeping pace with the latest advances in several important areas of chemistry that border on the life sciences. This sixth volume in the series on amino acids, peptides, and proteins is no exception.

With admirable terseness and modesty, the "reporters" have succeeded in condensing within the covers of this lightweight, hand-sized volume the information distilled from no fewer than 3000 journal articles, nearly all of which appeared during the year 1973 (only a few date back to 1971 and 1972). The number of papers abstracted in this book represents a 50% increase over the previous volume, which was reviewed here last year  $[J.\ Med.\ Chem.,\ 18,\ 444\ (1975)]$ .

The organization of the material follows very closely the outline of Volume 5. Chapter One deals with amino acids; Chapter Two with primary structure, chemical modification, x-ray studies, and conformation of peptides and proteins; Chapter Three with peptide synthesis; Chapter Four with special peptide types; and Chapter Five with structure—activity correlation. Major research efforts continue to focus on new coupling reagents and blocking groups, new sequencing techniques, the use of various physical methods to elucidate tertiary structure, and the design of biologically active synthetic peptides.

There is an author index and a very detailed table of contents, but in this Reviewer's opinion the usefulness of the book (and, in fact, of the entire SPR series) would be enhanced immeasurably by the addition of a subject index. Perhaps next year a cumulative subject index covering the first seven volumes would not be amiss.

Lastly, one notes with regret that the cost of Volume 6 is almost twice that of Volume 5 (for the same number of pages). No longer incredible bargains, these books—yet still very worthwhile, even at the current higher price.

Sidney Farber Cancer Center Boston, Massachusetts 02115 Andre Rosowsky

Synthetic Peptides. Volume 3. By George R. Pettit. Academic Press, New York, N.Y. 1975. vii + 438 pp. \$39.50.

This third volume of the series follows, in general, the format of its two predecessors. Thus, the bulk of the book comprises of a compilation of synthetic peptides arranged in 20 chapters of tables, each chapter having a brief introduction. The introductions to each group of tables contain selected examples from the literature in that particular area from Jan 1971 to July 1972 and complete coverage from then to Jan 1973. The tabular survey includes literature from Oct 1970 to July 1972.

Recent techniques for determining the extent of racemization produced by various coupling agents are discussed in Chapter 1 (2 pages) under the heading "racemization". Newer protecting groups and coupling agents are discussed in the introductions to Chapters 2 (amino acid derivatives) and 3 (dipeptides), respectively. Syntheses of tri- through polypeptides and cyclopeptides are grouped in Chapters 4-16 inclusive of a chapter on solid-phase synthesis. The remaining four chapters on depsipeptides, steroidal peptides, chromopeptides, and nucleopeptides are short ones (2-10 pages), demonstrating that these specialized areas indeed "still remain relatively neglected". It is the author's hope that the medicinal potential of compounds related to these latter areas will receive more attention in the future.

The book contains 734 references. The tabular surveys have been expanded to include, for each compound, data on chromatography, countercurrent distribution, electrophoresis, and spectral characterization methods. However, it is disappointing to note that for most of the compounds, these and/or other data columns of the tables are left blank due to the fact that no such data are available in the cited references. Compounds for which the only data available is the reference number are as good as unknown compounds and perhaps should not have merited an entry in the tables.

This series is of value to the peptide chemist because it is perhaps the only compilation available which can provide a convenient and continuing reference source on known peptides.

Schering Corporation Bloomfield, New Jersey 07003 A. Afonso

Solid-Phase Synthesis. Edited by E. C. Blossey and D. C. Neckers. Dowden, Hutchinson, and Ross, Stroudsburg, Pa. 1975. Distributed by Halsted Press, New York, N.Y. xxviii + 360 pp. \$27.00.

This is Volume 2 of the Benchmark Papers in Organic Chemistry series. The volume consists of reprints of 62 papers in which polymers are used as integral components of an organic synthetic technique. The technique has been widely applied to the synthesis of natural oligomers of peptides, nucleotides, and saccharides. This rapidly growing area of research finds its roots in the work of Merrifield and of Letsinger on polymer-supported polypeptide synthesis. Their ideas have been expanded in the 12 years following to include numerous substrates, reagents, catalysts, and sensitizers supported on or made an integral part of polymer backbones. There are several advantages to these procedures, of which ease of separation of products from excess or spent reagents and increased selectivity are the most obvious. However, there are also problems associated with these techniques and the editors have not neglected this in their selection of papers.

The papers are divided into topical areas introduced by brief editorial comments. The debt owed to Professor Merrifield is acknowledged by a biographical article as an introduction and by the inclusion of his and Professor Letsinger's first papers in this field in a Historical Perspectives section. Following this are 18 papers on polypeptide synthesis and four on problems of the solid-phase method. There are eight papers concerned with polynucleotide synthesis and six on polysaccaride synthesis. Most of these papers have been chosen to show the scope and strengths of the original concept.

The next section, entitled "Synthetic Applications of the Solid-State Method", consists of 14 papers and might be better titled, "Polymeric Reagents". The included works describe the use of polymers to support a wide variety of reagents from phosphoranes and carbodimides to transition metal complexes and aluminum chloride. The final section includes eight loosely connected papers which utilize polymer supports in reactions other than the synthesis of oligomeric materials. One paper does not deal with polymers at all. No reviews have been included but several are listed in the bibiliography. Author and subject indexes are also provided.

The editors' comments for each section may be best regarded as an introduction rather than as a critical evaluation of the papers or the techniques presented. This may be regarded as the weak point of the collection. The principal value of such a collection should be to put the field into perspective, point out mistakes as well as successes, and indicate directions for the future. This collection does offer historical significance and a limited amount of guidance. Its value to the medicinal chemist is limited to the historical presentation of a major breakthrough in polypeptide synthesis. There are other, more critical reviews which present an accurate view of the scope of the technique.

This volume may be a valuable addition to an institutional library. For personal purchase, however, one must consider that all of the articles were originally published in English and in readily available journals. Thus, its principal advantage may be that the cost of photocopying 330 journal pages is approximately that of this nicely bound volume.

Department of Chemistry Northeastern University Boston, Massachusetts 02115 James Quick

Advances in Heterocyclic Chemistry. Volume 18. Edited by A. R. Katritzky and A. J. Boulton. Academic Press, New York, N.Y. 1975. 468 pp (Index to Volumes 1–18).  $15.5 \times 23.5$ cm. \$48.50.

"Advances" represent the most difficult books to review. The wide scope covered by these books means that chances are slim indeed that the reviewer is equally expert in each of the topics covered. The same breadth of coverage makes it impossible to give an assessment of the volume as a whole. However, some comments can be made.

Volume 18 of this valuable series deals in depth with the chemistry of four heterocyclic systems. F. D. Popp has contributed an encyclopedic, albeit somewhat concise, review of progress in the chemistry of isatin and its derivatives over the past two decades. This treatise, which contains a high density of information (638 references for 58 pp), can interestingly serve as a primer to the chemistry of this interesting heterocycle. A fair amount of attention is devoted to the use of isatin as starting material for other heterocycles.

Thiochromanones have provided an extremely useful nucleus for medicinal agents (e.g., lucanthone, chlorprothixene) and have thus been the object of intensive work. The chemistry of this heterocycle system is reviewed in lucid fashion by S. W. Schneller. The reader unfamiliar with the area will find here not only the preparation of the parent hydrocarbons but their salient reactions as well. One notable feature of this chapter is a short paragraph detailing the uses of the compounds at the conclusion of each section, including the reported biological activities (references).

A clear and succinct account of the chemistry of chrom-3-enes is presented by L. Merlini. This chapter, too, presents the preparation and chemistry of the ring system which is to be found in a host of natural products. The author is to be particularly commended for including ranges of yields for the various synthetic schemes. The liberal use of mechanistic rationales makes the chemistry particularly easy to follow.

The first part of a review on the benzo[b] furans was written by P. Cagniant and D. Cagniant (Part 2 will presumably appear in a subsequent volume). This constitutes an extremely thorough, if occasionally repetitive, compendium of the many methods available for assembly of this ring system. Since many of the methods differ only in detail, one wishes the authors had taken a more critical approach to the chapter. How, for example, is a tyro to choose between two equally attractive syntheses without some idea of the yields characteristic of each?

A rather different approach is taken by T. S. Griffin, T. S. Woods, and D. L. Klayman in the chapter on thioureas in the synthesis of heterocycles. This section, organized on the basis of ring size of the product, undertakes the heroic task of examining the enormous utility of thioureas. Since very small variations in starting materials tend to change the nature of the product, the chapter is necessarily quite fragmented. This is, however, a quite thorough examination of the field.

An understanding of the fine structure of the purine and pyrimidine bases lies at the very heart of molecular biology. One need but recall Watson's account of the false spoor he followed when misled by a textbook which showed the wrong tautomers for those bases. The Pullmans discussed the structures of the purines in Volume 13 of this series. The present chapter constitutes an in-depth discussion of the pyrimidine bases: cytosine, uracil, and thymine as well as some of the rare bases. Thus, the tautomeric equilibria for each group, as determined by physical methods, are covered as are the same equilibria as calculated by the quantum mechanics. In addition, geometry, electronic structures, and MO energies for each group of bases are discussed in exhaustive detail. Some feel for the thoroughness of the chapter is indicated by the fact that it occupies better than one-fourth of the volume.

Though the Table of Contents at the head of each chapter provided by the author help guide one through the book, the omission of a traditional subject index is to be regretted. The price of this volume (\$48.50) seems to be an admission on the part of the publisher that this book is intended for library use.

Cardiovascular Diseases Research The Upjohn Company Kalamazoo, Michigan 49001 Daniel Lednicer

Adenine Arabinoside: An Antiviral Agent. Edited by Deborah Pavan-Langston, Robert A. Buchanan, and Charles A. Alford, Jr. Raven Press, New York, N.Y. 1975. xvii + 425 pp. 16 × 24 cm. \$21.50.

This book reports the proceedings of a symposium held in San Francisco in Sept 1974 on adenine arabinoside (ara-A) and brings together much of the data available on this nucleoside analogue, which is currently being investigated for its potential antiviral and anticancer activities. The book is a mixture of review articles and articles reporting original work. Some of the latter have apparently not been previously published but have been reviewed by a member of the editorial board prior to inclusion in the book. The major focus is on the antiviral activity of the drug. It is nicely divided into three sections: preclinical studies, parenteral studies, and ophthalmic studies.

The section on preclinical studies (196 pp) includes chapters on toxicology, effects on postnatal growth and development, and species differences in the metabolic disposition of the drug. The section on parenteral studies (96 pp) has chapters on human pharmacology, tolerance, and effects on the cellular immune response. This part of the book also contains the sole chapter on the use of the drug in cancer chemotherapy. The section ends with a good summary chapter by one of the editors. The section on ophthalmic studies (124 pp) seems disproportionately lengthy, considering the topics covered in each section. The chapters in this section seem to overlap more than in the other two sections but will probably be of particular interest to ophthalmologists.

Although a large amount of research on a potent drug such as ara-A tends to be done by the drug companies manufacturing the drug (12 of the 32 chapters in this book have at least one Parke-Davis by-line), the data seem to be presented in a relatively unbiased fashion. The book leaves one with the conclusion that there is still a long way to go to find the optimal antiviral drug but that ara-A does seem to have at least some definite advantages over other antiviral drugs.

The book has an adequate subject index, and the reference lists at the end of the chapters appear to be current; 1974 and even 1975 citations are given in most articles. The main shortcoming seems to be in the format of the tabulated data. Many of the figures and tables cannot be interpreted without consulting the text (legends are insufficient), and there are not infrequent duplications between tables and figures; some of the tabulated materials would be more appropriate as legends to other tables.

The prime advantage of the book is its bringing together a large body of data from both laboratory and clinical studies concerning ara-A. It provides a good review for those who are interested in this field and is a rapid way to get an introduction to the current problems, advances, and bibliography.

Department of Ophthalmology
Harvard Medical School and
Department of Connective Tissue
Research
Boston Biomedical Research Institute
Boston. Massachusetts 02114

Liane Reif-Lehrer

Advances in Carbohydrate Chemistry and Biochemistry. Volume 30. Edited by R. S. Tipson and D. Horton. Academic Press, New York, N.Y. 1974. \$37.50.

"Advances in Carbohydrate Chemistry and Biochemistry", Volume 30, like previous volumes in the series, is an asset to researchers in the area. It is also a useful reference book for any scientific library.

The chapter on the application of gas-liquid chromatography to carbohydrates (Part II) by Dutton is well written. It summarizes the use of various methods of methylation available in the literature and points out the merits and difficulties encountered in them. Purification of the methyl ethers using liquid chromatography, Sephadex, and gas-liquid chromatography has been described. For mass spectral studies the preparation of trimethylsilyl ethers has been recommended because of their increased volatility and recognizable modes of fragmentation. The tables at the end of the chapter will be very helpful because they provide the references for the method of preparation of many useful carbohydrate derivatives and the type of column and the temperature used for their gas-liquid chromatographic studies.

Sumio Umezawa's chapter entitled "Structure and Synthesis of Aminoglycoside Antibiotics" is informative and covers key literature since 1963 with emphasis on recent advances. The elucidation of the structures of the streptomycins, the neomycins, the paromomycins, the hybrimycins, the lividomycins, the kanamycins, tobramycin, the gentamicins, sisomicin, ribostamycin, the butirosins, hygromycin B, destomycin A, and apramycin is delineated. Also covered are other less important amino sugar antibiotics. It should be noted that the elucidation of the structures of the kanamycins was undertaken in two laboratories, in Japan and in the United States, and the first publications on the subject appeared simultaneously in these two countries. Documentation of proper references would have been more appropriate on p 121. It should be noted that kanamycin A was first synthesized by M. Nakajima (1968) and subsequently by S. Umezawa (1969). Hence, Nakajima's synthesis is hardly an alternative route as claimed by the author in the last sentence of p 157. The article also describes syntheses of many of the antibiotics mentioned above and related substances. There are some errors, however; e.g., the word racemic is used when it is meant epimeric.

The chapter on the biochemical mechanism of resistance to aminoglycoside antibiotics by H. Umezawa is excellent. The author describes the biochemical mechanism of resistance of the strain isolated from patients. Many of the currently known active enzyme systems, e.g., kanamycin-neomycin phosphate transferases I and II, kanamycin-neomycin phosphate transferase in *Pseudomonas aeruginosa*, in staphylococci, gentamicin-kanamycin nucleotidyl transferase, kanamycin-neomycin acetyltransferase, gentamicin acetyltransferase, streptomycin adenylyltransferase, and streptomycin phosphate transferase, are described and the methods of isolation of these active enzymes are described. Also discussed by the author are the methods of elucidation of the structures of the inactivated antibiotics.

The chapter on the metabolism of  $\alpha,\alpha$ -trehalose by Elbein is difficult to read but contains many useful references. It summarizes the occurrence of  $\alpha,\alpha$ -trehalose and its isomers in nature. It also discusses the mechanism of biosynthesis and catabolism of  $\alpha,\alpha$ -trehalose. The role of  $\alpha,\alpha$ -trehalose in metabolism as a structural compound, supply of energy, and as an intermediate in D-glucose resorption has been outlined.

J. J. Marshall's article on the application of enzymic method to the structural analysis of polysaccharides, Part I, is timely, well written, and extremely useful to all chemists and biochemists involved in polysaccharide analysis. The reviewers look forward to Part II of the article.

R. L. Sidebottom covers, in his review on dextran, methods of elucidation of structures of dextran, the biosynthetic aspects of dextran, and the importance of dextran in dental carries and in the sugar industry. The article is well written.

The last chapter is a bibliography of crystal structure of carbohydrates, nucleosides, and nucleotides compiled by Jeffrey and Sundaralingam. As they have clearly defined the various symbols they use in the bibliography, it is easy for an organic chemist to use the data. A brief comment has been included in

the bibliography on the conformation of the molecule, terminal angles of the linkage bonds in di- and trisaccharides, and glycosyl torsional angles in nucleosides and nucleotides.

Research Division Schering Corporation Bloomfield, New Jersey 07003

A. K. Ganguly T. L. Nagabhushan

Advances in Radiation Research. Volume 3. Biology and Medicine. Edited by J. F. Duplan and A. Chapiro. Gordon and Breach, New York, N.Y. 1973. 522 pp. \$42.00.

Not to be confused with the well-known older review series entitled "Current Topics in Radiation Research", this book is part of a five-volume series intended to cover the various fields of radiation research from the fundamental physical aspects such as the deposition of energy into matter to the theoretical approaches to radiobiology in vitro and its application to radiation therapy in vivo. This is the third of the three volumes devoted to Biology and Medicine, the other two volumes being related to Physics and Chemistry. This volume is a collection of 49 essays covering radiobiology, radiotherapy, and radiation biochemistry in their broadest sense. The primary emphasis is on immunology, immune mechanisms, and the relationship between radiation and the immune response. Almost without exception, the articles are well written and superbly illustrated with tables, line drawings, and graphic material. Photographs are used sparingly but are most effective when employed. Two articles in particular, The Growth of Chinese Hamster Cells as a Tumor Model for Studying Radiation Effects by Sutherland, Inch, and McCredie and Ultrastructure of Lung Parenchyma and Permeability Changes of the Blood Air Barrier after Local Exposure to 2000 R of X-rays by Maisin, Oledzka-Slotwinska, and Lambiet-Collier, are noteworthy for both the verbal and pictoral content.

A significant number of papers deal with the topic of the microanatomy of supporting tissue and the acute and long-term effects of high- and low-level irradiation on these tissues. It is of interest to see that modern day radiobiological studies are not confined solely to the effects of radiation on tumors but also includes normal tissue.

This volume is not appropriate for students nor as an introduction to the field of radiation research. It is a rather broad overview of current research and knowledge and future trends. None of the papers can be considered extensive or exhaustive in content or literature citations. By itself, the usefulness of this volume is somewhat limited to serve as a general reference for advanced workers in the field. The complete five-volume set, however, gives one a much larger perspective of the overall area as well as a greater in depth feel for each specific scientific discipline covered by the term Radiation Research and is a most valuable addition to the radiation scientists' library.

Radiology Department Harvard Medical School Boston, Massachusetts 02115 Michael A. Davis

Antiinflammatory Agents. Chemistry and Pharmacology. Edited by Robert A. Scherrer and Michael W. Whitehouse. Academic Press, New York, N.Y. 1974. Volume I, xxii + 417 pp.  $16 \times 23.5$  cm, \$32.50. Volume II, xvi + 382 pp.  $16 \times 23.5$ cm, \$28.50.

This is a two-volume set in the Academic Press "Medicinal Chemistry" series of monographs, with chapters by a number of workers active in the field. The editors intended that authors assess and interpret the literature and present their opinions, and this seems to have been attempted by most authors. Volume I is chemically oriented. The book is divided into chapters according to chemical types of antiinflammatory drugs, and the chapters contain discussions of synthetic aspects, SAR, and some pharmacology. Especially intriguing is the survey chapter on gold compounds, perhaps due to the exotic nature of the subject matter. One chapter contains an exposition of the Scherrer definition and diagram of the antiinflammatory receptor, which this reviewer found to be enjoyable reading. The chapter on antiinflammatory

steroids covers the literature from 1962 to early 1972 and, due to the monumental scope of the topic, is perhaps one of the less satisfying sections of the volume, through no fault of the authors or editors. It seems impossible to do justice to steroids in 50 pages.

Volume II is biologically oriented. Especially useful are the chapters, "Evaluation for Antiinflammatory Activity" and "Evaluation for Immunosuppresive and Antiallergic Activity". These seem to be intended for the enlightenment of the chemist who desires a speaking knowledge of bioassay techniques. Only a brief discussion of clinical testing is included, as a part of the introductory chapter to the volume. The volume ends with a discussion of drug effects on connective tissue metabolism and a survey of metabolism of antiinflammatory compounds.

In the two volumes, literature through 1972 is cited, and there are a selected references from 1973 and early 1974. The set is well written and comprehensive in its coverage of topics, although some topics are not covered in the depth that might be desired. Overall, the effort is a success, and the two-volume set provides an excellent beginning for the chemist and the pharmacologist who wish to enter into some area of antiinflammatory research. The set is highly recommended.

College of Pharmacy The University of Iowa Iowa City, Iowa 52242

Joseph G. Cannon

Immunological Tolerance. Mechanisms and Potential Therapeutic Applications. Edited by D. H. Katz and B. Benacerraf. Academic Press, New York, N.Y. 1974. 645 pp. Cloth, \$21.00.

The title of the book suggests that both basic mechanisms of immunological tolerance and clinical applications are discussed. Of the 645 pp, 608 are devoted to a discussion of mechanisms and only 34 pp concern potential therapeutic application. Herein lies a problem for a person who is not working in this important but confusing area of investigation. For the expert immunologist, however, the book succeeds in presenting the results of many current studies.

The book contains the precedings of a conference held in May 1974. B and T cell tolerance and mechanisms for achieving tolerance are discussed. Another major theme is the activity of suppressor cells as a mechanism of tolerance. The importance of suppressor cells in a variety of diseases in human beings is now emerging and thus it is important that we understand mechanisms of suppression of the immune response. The potential role of blocking factors in tumor immunity and allograft tolerance was presented by the Hellstroms.

Several features beyond the subject matter make this book difficult to read. Virtually no introductory remarks are made to provide orientations for what follows in a long series of articles. No cross-index is present. The book has been designed for the convenience of the publisher and not the reader. For instance, the figures are all grouped at the end of the articles and thus one is forced to flip pages back and forth between the figures and narrative. Also, the references lack titles of the articles. Long discussions follow the articles and may confuse rather than clarify. The space may have been better used for summarizing or interpretating the data presented in the articles. But we should remember that brilliant flashes of insight, such as Thomas experienced, have been recorded in discussions. In 1957 he first articulated the immunological surveillance theory in a discussion.

Most disappointing to me was the failure of most participants to apply their ideas and expertise to pressing clinical problems that are vitally linked to immunological tolerance: pregnancy, autoimmune disorders, malignancy, transplantation, slow viral infections, and persistent infectious diseases. Surely, these clinical problems are being studied and our understanding will grow as a result of the studies presented in this book.

The book is a valuable summary of recent (1974) experiments on immunological tolerance. Immunologists and persons using immunological techniques for understanding mechanisms of immune function would benefit by reading it.

University of Massachusetts Medical Center Worcester, Massachusetts 01605 David T. Purtilo

Pro-drugs as Novel Drug Delivery Systems. ACS Symposium Series 14. Edited by T. Higuchi and V. Stella. American Chemical Society, Washington, D.C. 1975. ix + 245 pp. 15 × 22.5 cm. \$13.50.

As stated, the intent of this series is "to provide a medium for publishing symposia quickly in book form" and to this end "papers are not edited or reviewed except by the symposium chairman" and "are reproduced as they are submitted by the authors". Bearing these comments in mind, the variety of letter-type and the fact that certain chapters have several typing errors should, perhaps, be overlooked as shortcomings of this volume.

On the more important side of the coin is the subject material of the six chapters in this volume and, for these, the book merits praise. Chapter 5 (A. Repta) is exceptionally well written. It begins with a clear description of the steps taken in the general design and development of pro-drugs followed by specific examples of "pro-drugs for use in the formulation of cytotoxic agents in parenteral solutions". Because of the clarity and completeness of the opening dialogue, I would recommend that this chapter be read first. These same thought processes involved with pro-drug design will then protrude more clearly in the chapters by the other contributing authors. These chapters include the design of pro-drugs for antibiotics (Chapter 2, A. Sinkula), of dephenylhydantoin (Chapter 3, V. Stella, T. Higuchi, A. Hussain, and J. Truelove; Chapter 4, A. Glazko, W. Dill, R. Wheelock, R. Young, A. Nemanich, L. Croskey, V. Stella, and T. Higuchi), and of epinephrine (Chapter 6, D. McClure). The first chapter, "Pro-drugs: An Overview and Definition" (V. Stella), is also noteworthy for its completeness in terms of a survey of existing pro-drugs. The rather large number of examples and references cited in this chapter almost causes one to scratch the word "novel" from the title of this volume.

The book is a remarkable collection of data and references and the inclusion of a subject index is an asset. Because of "the importance of the use of an interdisciplinary approach in the synthesis and testing of" pro-drug derivatives, I feel that the book is of potential interest to individuals from a variety of disciplines and of an invaluable nature to scientists specifically interested in the design of pro-drugs.

Department of Medicinal Chemistry and Pharmacology
College of Pharmacy and Allied
Health Professions
Northeastern University
Boston, Massachusetts 02115

USAN and the USP Dictionary of Drug Names. 1975 Edition. Published by the United States Pharmacopeial Convention, Inc., and printed by Mack Printing Company, Easton, Pa. 1975. 352 pp. \$18.50.

Since 1961, an annual, cumulative compilation of United States Adopted Names (usually abbreviated USAN) and other names for drugs has been published under the auspices of the United States Pharmacopeial Convention which is one of the three organizations which sponsor the USAN program and form the USAN Council. The other two sponsors are the American Medical Association and the American Pharmaceutical Association and, since 1967, a liason representative from the Food and Drug Administration also sits on the USAN Council.

The USAN program attempts to meet "the need for order in assigning nonproprietary names to new drugs as they are developed", and is currently the only organized effort in the United States for doing so. In meeting this need the USAN Council "is committed to following established principles for coining nonproprietary names and to enlisting the cooperation of the pharmaceutical industry in this country and of nomenclature groups abroad with a view to selecting a single, good nonproprietary name for each promising new drug". It should be noted that the USAN designation usually is selected by the FDA as the "established" or "official" name which federal law empowers the Secretary of Health, Education and Welfare to select in the interest of simplicity and usefulness whenever considered desirable or necessary.

This current volume is the 13th compilation of United States

Adopted Names being cumulative for such names from June 15, 1961, through June 15, 1975. The format and the outlook of the publication are a continuation of the style adopted with the 10th edition in 1971. This book contains more than 10 000 entries of which 1403 are U.S. Adopted Names, the balance being brand names, foreign nonproprietary names, and various code designations and registry numbers. These entries are arranged in a single, consolidated list in alphabetical order.

The amount of information provided with each entry varies in scope with USAN entries the most complete. For USAN entries the following are included: U.S. Adopted Name; year of publication as a USAN; pronunciation guide; molecular and graphic formula; systematic chemical name; Chemical Abstracts Service registry number; pharmacologic activity claim; brand name(s) currently or formerly in use; name(s) of manufacturer(s) or distributor(s); code designation(s).

In addition to the largest section devoted to alphabetic listing of drug names, other sections or appendixes give a listing of CAS registry numbers of drugs included in the volume; a categorization by pharmacologic activity of all USAN, USP XVII and XIX, and NF XIII and XIV drugs; guiding principles for coining U.S. Adopted Names for drugs; molecular formulas and corresponding USAN; names and addresses of domestic firms associated with compounds for which USAN have been chosen.

This book probably should be part of any library servicing persons interested in drugs, whether such persons are actual professional practitioners in the various health sciences or researchers in the basic sciences associated with drugs. It would be a useful reference volume in the various "drug information centers" found in many places associated with hospitals. It is not likely that individuals would find it so frequently useful to warrant acquisition of personal copies particularly since annual, cumulative volumes apparently will continue to appear.

College of Pharmacy University of Minnesota Minneapolis, Minnesota 55455 John D. McRae

Affinity Techniques. Methods in Enzymology. Volume 34, Part B. Edited by W. B. Jakoby and M. Wilchek. Academic Press, New York, N.Y. 1974. xxix + 810 pp. 15 × 22 cm. \$39.00.

Perhaps no technique has advanced from a state of novelty to a condition of routine use in so short a time as affinity chromatography. However, routine use does not guarantee maturity for a methodology, and affinity chromatography is anything but mature at the present time. The procedures are not fully standardized; the mechanisms are not fully elucidated, and the potential is not fully achieved. It is, however, a most appropriate time for a "progress report" type of book on the subject, and this book admirably provides this service. Section I (10 pages, mostly references and a table listing proteins purified by affinity chromatography) references methodology not covered in detail in this particular book. Section II covers coupling reactions and general methodology including more novel techniques such as 'affinity density perturbation" and "affinity electrophoresis". Section III shifts the attention to specific ligands, each of which is given a chapter. This section is organized into "Coenzymes and Cofactors", "Sugars and Derivatives", "Amino Acids and Peptides", "Nucleic Acids, Nucleotides, and Derivatives", and "Other Systems". Thiol-disulfide interchange is an example of "Other Systems". The last three sections, which are much smaller than Section III, cover, respectively, the purification of synthetic macromolecules like synthetic oligonucleotides, the purification of receptors (for example, insulin receptors, adrenergic receptors), and immunological approaches (immunoadsorbents). The book certainly represents the best overall treatment currently available on the topic of affinity techniques.

Department of Medicinal Chemistry and Pharmacology College of Pharmacy and Allied Health Professions Northeastern University Boston, Massachusetts 02115 R. W. Giese