ACE using uncoated capillaries.[13]

Affinity capillary electrophoresis has six advantages as a method of determining binding constants. First, it requires only small quantities of protein and ligand: the complete series of experiments in Figure 1 (with five replicates of each experiment) consumed ~22 ng of carbonic anhydrases (CAB + CAA), and 1.3 mg of 1. Second, it does not require high purity for the protein or an accurate value of its concentration, since values of K_b are based on migration times, not peak areas. Measurement of K_b can, as a result of the high resolving power of capillary electrophoresis, be carried out on mixtures of proteins. Third, it is applicable simultaneously to several proteins in the same solution (for example, CAA and CAB in Figure 1). Fourth, it does not require the synthesis of radioactive or chromophoric ligands, although (as with 1 and 2) it will require the synthesis of a charged analog of a ligand if the ligand is itself electrically neutral. Fifth, it is capable of distinguishing forms of a protein that bind ligand from forms of the same protein that are denatured and do not bind ligand. Sixth, the commercial availability of automated instrumentation, and the high reproducibility of data, make it experimentally convenient.

Acknowledgment. We thank several members of the group for their contributions to this work: A. Jain, E. C. Blossey, J. Mathias, C. Seto, V. Narayan, and J. Kingery-Wood.

Supplementary Material Available: Experimental details for the preparation of 1–3 (5 pages). Ordering information is given on any current masthead page.

(13) Rapid equilibration of protein between the buffer and the wall of the capillary does not influence the value of K_b obtained by this method, unless the equilibration is influenced by the concentration of L or K_b is substantially different for adsorbed and soluble protein.

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Book Reviews

Compendium of Organic Synthetic Methods. By Michael B. Smith. John Wiley & Sons, Inc., New York. 1992. xix + 547 pp. 16 × 23.5 cm. ISBN 0-471-60713-4. $59.95.

This volume presents in abstract form the key functional group transformations, as well as many carbon bond forming reactions, described in the chemical literature from 1987 to 1989. New sections have been added to include the oxides of sulfur, nitrogen, and phosphorus, all of which are integral to the preparation of difunctional compounds. As with previous volumes, chemical transformations are classified first by the reacting functional group of the starting material and then by the functional group formed. The chemical reaction, reagents, yield, and stereochemistry are clearly shown. Indexes for monofunctional and difunctional compounds conveniently guide the user to specific tranformations as well as to specific reviews. Volume 7 also includes alphabetized headings and other minor format changes which add to its overall utility and ease of use. The book contains a complete author index.

This volume contains about 1250 examples of published methods for the preparation of monofunctional compounds, updating the 8100 in the first six volumes. In addition, 850 examples of the preparation of difunctional compounds and almost 100 reviews are included. All organic chemists will find this book a useful and convenient access to references to recently described synthetic methods.

Staff

Chemical Immunology. Volume 50. Integrins and ICAM-1 in Immune Responses. Edited by Nancy Hogg. S. Karger AG, Basel. 1991. viii + 168 pp. 17.5 × 24.5 cm. ISBN 3-8055-5429-X. $134.50.

The regulation of cell adhesion is a prerequisite for establishing and maintaining a normal host defense system. A broadly distributed family of transmembrane receptors, the integrins, are one of the main classes of molecules mediating cellular adhesion. This book provides a comprehensive overview of the structure and function of a number of integrins and also of intercellular adhesion molecule-1 (ICAM-1). Topics covered in the 10 chapters comprising this volume include the regulation of leukocyte integrin function, the role of VLA integrins in lymphocyte migration and recognition, common and ligand-specific integrin recognition mechanisms, and the role of $\alpha 4\beta 1$ in lymphocyte–endothelial cell interactions. The second part of the book details the importance of ICAM-1, an immunoglobulin and ligand for the leukocyte integrin LFA-1. Its role in inflammation and tumor development and its relevance as a receptor for rhinovirus and *Plasmodium falciparum*-infected erythrocytes are comprehensively reviewed.

The roles of integrins and ICAM-1 in the intricate network of the immune response have only recently been recognized. Thus, this volume will be vitally important to those concerned with modern immunology. Medicinal chemists researching in the areas of inflammation, tumor development, and rhinovirus infections will likewise find this book a valuable source of information.

Staff

Annual Reports in Medicinal Chemistry. Volume 26. Editor-in-Chief, James A. Bristol. Academic Press, Inc., San Diego, CA. 1991. xii + 369 pp. 17 × 25 cm. ISBN 0-12-040526-1 (alk. paper). $65.00.

Volume 26 continues in the format which is familiar to medicinal chemists. It is divided into seven sections which incorporate a total of 32 chapters. The major sections are as follows: (1) CNS Agents, (2) Cardiovascular and Pulmonary Agents, (3) Chemotherapeutic Agents, (4) Immunology, Endocrinology and Metabolic Diseases, (5) Topics in Biology, (6) Topics in Drug Design and Discovery, and (7) Trends and Perspectives. Each chapter updates, in 10 pages or less, including an exhaustive list of references, a significant area of research in medicinal chemistry of an emerging area of biological science anticipated to impact the future discovery and development of new therapeutic agents. In general, the chapters cover all aspects of the topic being addressed for 1990 or since the subject was last reviewed in *Annual Reports in Medicinal Chemistry*.

Annual updates are provided in many traditional areas. For the first time, in 1990, the chapter on antihypertensives has been replaced with three more mechanistically-related chapters: renin–angiotensin system, potassium channel activators, and vasoactive peptides. Several chapters address topics of great current interest, e.g. neuronal calcium channels, neurokinin antagonists,

thrombosis, CCK, osteoporosis, and mechanism-based immunosuppressants. Today's increased focus on viral disease therapy is reflected by three chapters on this topic, with appropriate emphasis on AIDS. The importance of molecular biology as an enabling technology in medicinal chemical research is apparent in all chapters in these sections.

The Topics in Biology sections includes chapters that review cytokine receptors, amyloidogenesis, bacterial adhesions, and the ras GTPase cycle. Topics in Drug Design and Discovery include chapters on molecular diversity, receptor modeling by distance geometry, and sequence-defined oligonucleotides as potential therapeutics. Trends and Perspectives contains the traditional chapter on NCE introductions and concludes with a chapter on perspectives in human gene therapy.

This volume of *Annual Reports in Medicinal Chemistry* continues the fine tradition of its predecessors. All medicinal chemists require a desk copy of this important compilation. Researchers in all other disciplines involved in pharmaceutical research and development will also find this Division of Medicinal Chemistry of the American Chemical Society-sponsored volume a most valuable resource.

Staff

Pharmacokinetics and Pharmacodynamics. Volume 3. Peptides, Peptoids and Proteins. Edited by Pamela D. Garzone, Wayne A. Colburn, and Michael Mokotoff. Harvey Whitney Books, Cincinnati, OH. 1991. viii + 200 pp. 15.5 × 23 cm. ISBN 0-929375-04-01. $35.00.

This book is a product of the Fifth Annual Pharmacodynamic Conference held at the University of Pittsburgh on May 23 and 24, 1989. Researchers from a number of pharmaceutical organizations constitute the majority of the contributing authors. The book is organized into three main sections: (1) Design, Synthesis, Activity of Peptides, Peptoids, and Proteins (four chapters); (2) Assay, Delivery, Pharmacokinetics of Peptides, Peptoids, and Proteins (eight chapters); (3) Safety and Regulatory Aspects of Peptides, Peptoids, and Proteins (three chapters). The organizers of the conference intended to provide the attendees with discussion on the problems and potential solutions to the development of peptide-, peptoid, and protein-containing pharmaceuticals. By way of concise summaries of background information and presentations of specific examples, the compilation of material in this book offers a valuable resource to researchers who are active or have interest in the field of synthetic or genetically-engineered peptidic compounds as potential pharmaceuticals, and issues associated with safety and delivery.

In the first section, a very brief discussion on peptide syntheses with emphasis on solid-phase method is provided in chapter 2. The advantages of the Fmoc method and newer resins are highlighted. Chapters 1, 3, and 4 provide detailed discussion on structure–activity studies of a number of selected peptide analogues relating to melanotropin, somatostatin, cyclosporine, and luteinizing hormone-releasing hormone. Issues of receptor selectivity, evaluation of conformational constraints, and potential clinical uses provide the sense of a trend of current basic-research methodology.

In the main section of the book, chapters 5, 6, and 7 on assay, delivery, and pharmacokinetics, offer highly valuable discussions on issues concerning analytical methods of peptides in biological fluids (bioassay, immunoassay, HPLC-method development, pit-falls, validation, and implementation), and issues of nonoral routes of peptide delivery such as nasal and pulmonary routes. Chapter 8 provides an excellent short-course on pharmacokinetics and pharmacodynamics of peptides (models and mathematical calculations) with consideration of ADME and emphasis on delivery and routes of administration. Chapters 9, 10, and 11 follow with specific illustrations with evaluation of data in animals and in man of the pharmacokinetics and pharmacodynamics of a number of examples which include interferon-α-2a, growth hormone-releasing factor, human insulin, growth hormone, and relaxin. Chapter 12 provides a brief and informative discussion on the regulation of the passage of peptides across the blood–brain barrier.

In the last section of the book, chapter 13 addresses the issue of immunogenicity induced by recombinant proteins with a brief survey of some preclinical and clinical studies. Chapter 14 offers a very comprehensive case study of recombinant human tissue-plasminogen activator (tPA) with emphasis on a number of pioneering issues (source, purity, safety) which were required for process development and FDA approval for human use. Chapter 15 by an FDA supervisory pharmacologist provides a highly useful and concise comment on a number of preclinical issues with emphasis on purity and safety assessment of human peptide drugs that meet the evolving FDA requirements for clinical trials.

The subject matter of this book is certainly of contemporary interest. The content spans the many issues of concern, from the basic molecular study to the consideration of human clinical trials. The references cited are generally up to the time of the conference. The organization of the book makes for a nice flow of reading and for quick reference. This book is definitely informative and very educational.

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