Book Reviews

Cytokine Inhibitors. Edited by Gennaro Ciliberto and Rocco Savino. Marcel Dekker, New York. 2001. xiv + 372 pp. 15.5 × 23.5 cm. ISBN 0-0434-7. $165.00.

Reviewers usually complain about books in which each chapter has a different author—there is no continuity from one chapter to the next. But cytokines are a group of small signaling proteins which have numerous, sometimes opposing effects and complex interactions. They are so diverse that perhaps one should not expect continuity between chapters; cytokines may be a perfect justification for a multiauthored book.

This book covers a wide range of topics. Cytokines include the interleukins, tumor necrosis factors, a variety of growth factors, and colony-stimulating factors. They have been implicated in many disease states, including rheumatoid arthritis, graft vs host disease, Crohn's disease, allergy, asthma, cardiovascular disease, cancer/tumor angiogenesis, and HIV infection. While a few chapters focus mainly on the cytokines and their effects, most of the chapters take the next step, discussing drugs which may inhibit the cytokines. There is a fair amount of bioactivity and structure−activity information presented. Drug targets include the cytokines themselves, their receptors, and their converting enzymes.

Overall, the book is well-produced. There are few typographical or grammatical errors, the typesetting and layout are clear, and the illustrations are well-done. It appears that the editors were quite thorough in ensuring that the authors defined their jargon and acronyms on the first use in each chapter. Most chapters include literature references through 1998; a few include 1999 papers, and Chapter 11 includes a 2000 reference. At the other extreme, Chapter 5 covers literature as early as 1893. This book would be especially useful to medicinal chemists who are new to the field of cytokines or those who want to look at a broader range of cytokines.

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Solid Phase Synthesis.. Edited by Kevin Burgess. Wiley Interscience, New York. 2000. xiv + 277 pp. 15.5 × 23.5 cm. ISBN 0471318256. $69.95.

The explosion in the use of combinatorial chemistry in the pharmaceutical industry has necessitated the discovery of novel and reliable methods for conducting solid-phase transformations. This book is a compilation of reviews describing solid-phase techniques that have been developed for use in selected structural classes. As stated by the editor, this book does not cover all of the important aspects of solid-phase synthesis. However, in its eight chapters, it describes solid-phase approaches used to synthesize guanidines, benzofused heterocycles, phenylacetylene oligomers, and a number of natural products. Also included is a chapter outlining the use of solid-phase supports to conduct palladium-catalyzed C−C bond formation using the Heck, Stille, and Suzuki reactions. Chapter 5 is an excellent compilation of methods for using functionalized polymers to assist in solution-phase reactions (sequestering excess reagents and byproducts, use of polymer-supported quenching agents). Chapter 6 describes the application of radiation-grafted polymer surfaces to the synthesis of purines, guanidines, and polysaccharides, as well as generation of a number of functional groups. Perhaps the most generally useful is Chapter 7, which describes current methods for using vibrational spectroscopy (FT-IR) to monitor and optimize solid-phase synthetic transformations. Although this book will probably be of greater interest to industrial medicinal chemists, it does provide a valuable overview of the versatility and utility of solid-phase synthesis in any setting. In addition, the chapters are well-referenced, and for this reason, this book provides an excellent starting point for chemists interested in solid-phase organic synthesis. Certainly, this book should be considered as an addition to any medicinal chemistry library.

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Metal Ions in Biological Systems. Volume 38. Probing of Proteins by Metal Ions and Their Low Molecular Weight Complexes. Edited by Astrid Sigel and Helmut Sigel. Marcel Dekker, New York. 2001. xlvii + 690 pp. 16 × 23.5 cm. ISBN 0-8247-0289-1. $250.00.

This extremely well-bound book contains yet another timely presentation of current essential metalloelement (primarily Ca, Cu, Fe, and Zn) research dealing with topics of special interest to medicinal chemists, biochemists, and others concerned with metalloelement physical and coordination chemistry in biological systems. At the onset it is pointed out that the remarkable stability of the amide bond and the phosphodiester bond gives rise to proteins and polynucleotides with half-lives estimated to be hundreds and one hundred million years, respectively, in physiological solution at neutral pH. Thus there are specific essential metalloelement-dependent enzymes required to catalyze specific protein bond and nucleotide bond hydrolysis as well as bond formation in enabling normal chemical protease and nuclease or synthetic transformations that are ongoing

in biochemical systems. The importance of metalloelement-dependent enzymes in the synthesis of peptides and polydesoxy and polyribonucleic acid syntheses and repair is also mentioned. It is remarkable that nature has fashioned ligands that increase the rate of essential metalloelement-dependent catalytic activity by many orders of magnitude and that these ligands protect biochemical systems from undesirable chemical consequences associated with the presence of free ionic bonded metalloelements. Small molecular mass essential metalloelement chelates are presented as active site enzyme mimetics in attempts to fashion chelates that might serve as useful agents capable of catalyzing reactions of interest in the development of new drugs and in gaining mechanistic understanding of essential metalloelement-dependent enzymes. As it turns out, the use of alkaline earth and transition essential metalloelements or nonessential metalloelements as ligands of interest is described in the synthesis of useful compounds that provide an understanding of known essential metalloelement-dependent enzyme catalases. There is also a substantial chapter dealing with electron transfer proteins and with what is described as "supramolecular" (involving rather large ligands) approach to modeling electron transfer and oxygen activation proteins.

In general, the preferred use of metalloelement oxidation state is employed by most of the authors; however, there is occasional use of plus charged species in the context of metalloelements bonded to ligands via coordinate covalent bonds. While most chemists will understand this, many biologists may have difficulty understanding that cationic species do not exist free of an anion. Another distraction is the use of the words "bind", "binding", "bound", and even "bounded" for some form of the word "bond", whether or not the exact character of electronic bonding interaction is known.

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Advances in Protein Chemistry. Volume 56. Drug Discovery and Design. Edited by Edward M. Scolnick. Academic Press, San Diego, CA. 2000. xi + 567 pp. 16 × 23.5 cm. ISBN 0-12-034256-1. $119.95.

This book consists of 11 chapters. An introductory chapter on the role of clinical trials in defining new chemical entities sets a context for the remaining 10 chapters. Each of the later chapters offers a current perspective on a case history in drug design and discovery. Collectively the chapter topics chosen represent clinically important drug discoveries. Some of the stories are classics, well-known to medicinal chemists. The topics covered include angiotensin-converting enzyme inhibitors, HMG-CoA- reductase inhibitors, cyclooxygenase-2 inhibitors, 5a-reductase inhibitors, peroxisome proliferator activated receptor agonists, HIV 1 protease inhibitors, calicurin inhibitors, selective estrogen modulators, monoclonal antibody therapy, and glucan synthase inhibitors. While the emphasis is decidedly not on telling the underlying chemical story of the design of such agents, most of the individual chapters nevertheless make interesting reading. The focus of most of the chapters is on the clinical evaluation of drugs or drug candidates that are providing increasing efficacy or selectivity of action. Nowhere are there extensive chemical discussions of SAR or of the underlying chemical approaches taken in drug design. Rather, the focus is on the drug targets and also on the value to the drug discovery process of an understanding of the biological regulation of the drug target. Structures of drugs or drug candidates are provided in some of the chapters, but details on the chemical design perspective are generally absent. That having been said, the reader should not take these comments as a serious criticism of the text, since the medicinal chemistry and drug design aspects of drug discovery have already been reviewed elsewhere and these references are cited in the early sections of some of the chapters. This volume will be of interest to medicinal chemists, particularly those involved in drug discovery programs. Most chapters make clear what kinds of ideal agents are desired and progress toward the goal of designing such agents. In general, the problems associated with less-specific earlier generation agents, from lack of receptor subtype selectivity to unexpected ease in the development of drug resistance as well as the absence of such difficulties in the newer agents, are discussed. Perhaps among the most interesting lessons to be learned from this text is that we are asking a lot from the drug design and discovery process, and that we are very often able to deliver.

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Solid Phase Synthesis: A Practical Guide. Edited by Steven A. Kates and Fernando Albericio. Marcel Dekker, Inc., New York. 2000. xx + 826 pp. 15.5 × 24 cm. ISBN 0-8247-0359-6. $250.00.

It was a pleasant surprise to see two such capable chemists take on the monumental task of offering a practical guide to the solid-phase synthesis of peptides, oligonucleotides, oligosaccharides, glycopeptides, oligonucleotide−peptide conjugates, and their derivatives. Included in this ambitious venture are chapters on resin chemistry, convergent (segment condensation) methods for the preparation of large proteins, combinatorial chemistry using peptides and amino acids, a review on instrumentation for automated synthesis, peptide purification and analysis, and the chromatographic analysis of combinatorial arrays (HPLC-MS). In general, Kates and Albericio do an excellent job of selecting hot topics and reputable authors for the (14 out of 20) chapters

covering aspects of solid-phase peptide synthesis which is, after all, the primary field whence other topics have blossomed.

As a researcher who trained both with R. B. Merrifield (the pioneering peptide chemist at Rockefeller University, who wrote an excellent Forward to the volume) and Robert L. Letsinger (the pioneering oligonucleotide chemist at Northwestern University), I feel compelled to mention that oligonucleotide chemistry was not covered in equivalent depth to peptide chemistry in this volume. In all fairness, I suspect that if the authors had tried for equal depth of coverage in all subjects, this excellent volume would have of necessity become a series of volumes. Despite this small limitation, the book provides the most comprehensive, authoritative, and up-to-date coverage of solid-phase synthesis that I have yet seen. One of the book's great strengths is the attention to detail and the practical orientation of the articles. This ensures that practitioners of the art will want to keep it close at hand for constant reference.

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Combinatorial Chemistry. Edited by Hicham Fenniri. Oxford University Press, Inc., New York. 2000. xxxii + 476 pp. 19 × 24.5 cm. ISBN 0-19-963754-7. $70.00 (paperback).

This book's stated objective is to provide students with a text that will serve as an introductory reference to key methods of combinatorial library generation and procedures for library screening. In addition, the editor hoped to provide a review of the application of these technologies to drug, catalyst, and materials discovery and development. The approximately 500-page volume more than meets its goals, and it will serve as a useful reference to both student and researcher, its main value to the latter being to provide insight into the application of familiar technologies in fields other than those of one's primary interest. The book consists of 16 chapters, each written by recognized leaders in the field and each covering a key aspect of combinatorial technology. All common methods of solid- and solution-phase library generation are reviewed, including directed sorted techniques and positionally addressable library synthesis on continuous membranes. A condensed but extensive review of organic reactions performed on solid phase is also provided, with additional chapters covering multicomponent reactions used for library generation, and a timely review of multistep solution-phase combinatorial synthesis. Combinatorial methods for the discovery and optimization of electrocatalysts and combinatorial approaches to the identification of chiral catalysts significantly extend the scope of the text. Rounding out this extensive review is a discussion of the application of automation methods to combinatorial synthesis. All chapters provide well-referenced bibliographies covering the literature up to 1999, and an extensive general index provides ready access to all of the salient aspects of each of the topics reviewed in the general text. Overall, this book is very well balanced, providing sufficient coverage of each of the topics discussed to introduce all of the key aspects of the concept. In addition, an extremely useful feature is the inclusion throughout most chapters of a series of experimental protocols, which provide a practical framework onto which the newly introduced concepts can be hung. Importantly, the experiments described can for the most part be conducted in an academic laboratory without the need for specialized equipment typically found only in industrial locales. In conclusion, I found this book to be one of the most useful texts recently produced in this field, and I would strongly recommend it to both student and practitioner alike.

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