Book Reviews

Drugs: Synonyms & Properties. Edited by G. W. A. Milne. Ashgate Publishing Co., Burlington, VT. 1999. xx + 1267 pp. 18 x 25.5 cm. ISBN 0-566-8228-4. $250.00.

The United States Pharmacopeia (USP) contains over 14 000 drugs, each of which is a specific chemical compound with a biological activity that is medically useful. Most of these drugs have been developed commercially by the international pharmaceutical industry and, as a consequence, are associated with one or more trade names. Several names are frequently assigned to drugs, mainly for marketing purposes. Drugs are often manufactured and sold under license agreements with the original developer and they acquire new names. In addition to these trivial names that may be associated with a drug, it may have several chemical names, developed according to various rules of nomenclature, which allow precise identification of the chemical entity involved. The consumer or researcher seeking information often has only one trivial name, one used (for example) in an advertisement, and this name contains no information on the composition or use of the drug. The chemical name is essential to the scientist, but this gives no hint as to the trade name(s) or general use of the drug.

Some 10 000 representative drugs in common use are described in Part I of this book. Every drug has been given an entry name, and within each drug category, entries are arranged alphabetically by that name. The entry name is the one most commonly used for the chemical entity and is usually the U.S. adopted name: the one under which the drug is listed in the USP. The book is organized into 201 therapeutic categories, with each category presented in alphabetical order. Drugs that have distinct activities, for example an antiarrhythmic agent with coronary vasodilator properties, are found in the appropriate sections. Thus, there is some duplication throughout Part I. However, this organization permits the reader to determine, at a glance, the number of drugs available, as well as the different chemical families which may be represented within a specific therapeutic category. For example, this database lists 483 penicillin-based antibiotics, 318 antihypertensives, 135 tranquilizers, and 68 drugs used to manage Parkinson's disease. The increasing sophistication of pharmaceutical research may also be discerned by noting the populations in such categories as ACE inhibitors (40 drugs) and histamine H2 receptor agonists (18 drugs).

Within each record the subject drug is associated with its Chemical Abstracts Service (CAS) registry number (also listed numerically in Part II, Index 1). Each record also provides, as available, two other numeric identifiers for the chemical: the monograph number from the 12th edition of *The Merck Index* and the European Inventory of Existing Commercial Chemical Substances (EINECS) number (also listed in Part II, Index 2). The chemical name, molecular formula (but not the chemical structure), and a list of trade names and synonyms are provided; the physical properties of each compound are described, and the known therapeutic utility and in some cases acute toxicity data are recorded in the main entries in Part I. Part III lists the manufacturers and suppliers of the drugs.

This comprehensive coverage of 10 000 drugs currently in use will be a valuable source of information to research chemists, pharmaceutical researchers, physicians and drug information centers, and others who have a need quickly to find basic information on a particular drug for which information sources are obscure. This volume, edited by a well-known and respected authority in the field of chemical information and computational chemistry, is highly recommended for all libraries involved with drugs. The price may preclude individual ownership.

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Biocatalysis. Edited by Ramesh N. Patel. Marcel Dekker, New York. 2000. xiii + 932 pp. 17.5 x 25.5 cm. ISBN 0-8247-8282-8. $250.00.

This book will be a welcome addition to the shelves of medicinal chemists, microbiologists, and biochemical engineers laboring in the pharmaceutical, agrochemical, and food industries to synthesize chiral products. The regulatory pressure for homochiral or diastereomerically pure drugs demands chiral synthetic approaches, of which biocatalysis has become a major player. Biocatalysis has evolved during the past 25 years to be an essential tool in drug discovery, total synthesis, and process chemistry. One may regard biocatalysts, usually enzymes or whole microbial cells, as chiral reagents that catalyze highly stereo- or regioselective transformations of organic compounds under extremely mild reaction conditions. Thus, reactions occur at ambient temperature and pressure, they need no blocking groups typical to synthetic chemical approaches, and the technique generally precludes problems of isomerization frequently encountered in chemical processes. This "green chemistry" approach can combine the best of chemical and enzymatic steps (chemo-enzymatic) for the synthesis of structurally complex, biologically active compounds. Biocatalytic processes today are done at the bench, at pilot scale, and they have been extended to thousands-of-tons scale reactions. The editor has gathered an impressive array of scientist authors who have contributed to the 30 chapters of the book.

The utility of biocatalysis is demonstrated by chapters dealing with hydrolytic enzymes (hydantoinases and carbamoylases, aminoamidases, epoxide hydrolases, nitrilases, acylases), oxidations (hydroxylases, epoxidases, Baeyer−Villigerases), reductions, dehydrogenations, and decarboxylations. Chapters are devoted to chemo-enzymatic syntheses drawn from highly successful applications of the technology. Other chapters address biocatalyst selection and means for their use (immobilized and modified biocatalysts, biosensors, whole cell catalysis, reactions in supercritical carbon dioxide, enzyme transformations in organic solvents). Each chapter is well-referenced, and most chapters take the reader through fundamental principles, addressing how biocatalysts are identified for a given application and how they are used. The breadth of application to various drug classes is well-illustrated by the editor's own chapter on Stereoselective Biocatalysis for Synthesis of Some Chiral Drug Intermediates, where examples are given for ACE inhibitors, paclitaxel semisynthesis, a thromboxane A2 antagonist, anticholesterol drugs, calcium channel blockers, potassium channel openers, antiarrhythmics, antipsychotics, antiinfectives, antiinflammatories, antivirals, and prostaglandin syntheses. This is an excellent book for the shelf of anyone having an interest in expanding the repertoire of useful chiral reagents in organic synthesis to include enzymes or microbial catalysts. A minor criticism of the book is the lack of a "biocatalyst" index: one that links catalyst choice with specific applications. This detriment is offset by an excellent overall index in which relationships between biocatalysis and applications are extensively cited.

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Job$ in the Drug Industry. A Career Guide for Chemists. By Richard Friary. Academic Press, San Diego, CA. 2000. xxiii + 364 pp. 15 × 23 cm. ISBN 0-12-267645-9. $39.95.

The author, Richard Friary, is a very successful organic and medicinal chemist with more than 30 years experience; he is currently a senior principal scientist at the Schering-Plough Research Institute. In this book he describes the kind of work that is done by medicinal or process chemists in the pharmaceutical industry as well as the consequent satisfactions and rewards deriving from this work. The book gathers into a single volume all of the basics involved in getting a job as a medicinal or process chemist in the North American drug industry; it is intended to assist all levels of newly graduated chemists in finding suitable jobs in this field.

Job$ in the Drug Industry is divided into eight comprehensive chapters: (1) Enticements: Why Organic Chemists Work in the Pharmaceutical Industry, (2) Elements of Drug Discovery and Development, (3) Jobs in the Drug Industry, (4) Discovery and Developmental Chemical Research: Common Features, (5) Discovery Research: Medicinal Chemistry, (6) Chemical Development: Challenge in Organic Synthesis, (7) Qualifying and Searching for Jobs in the Drug Industry, and (8) Evaluating Companies and Job Offers. Each chapter treats its subject in comprehensive, frank, and realistic detail. For example, in Chapter 4 many different kinds of jobs and the various avenues of entry into these jobs are described. Discovery research jobs include those in medicinal chemistry, natural products, structural chemistry, drug metabolism, and radiochemistry. Jobs in service groups include ones in analytical chemistry, compound registration, cheminformatics (computer-related), patents (as coordinators, patent agents, and attorneys), chemical information, synthetic services, profiling and identification, chromatography and separations science, and regulatory affairs. Jobs in development research include those dealing with natural products, bioorganic catalysis, and safety, as well as temporary jobs. Jobs with satellite companies, government agencies, and nonprofit institutes include those with service firms, The Food and Drug Administration, The U.S. Patent and Trade Office, The Walter Reed Army Institute of Research, and The National Institutes of Health. Various miscellaneous entry-level jobs that do not involve laboratory work are also considered. Taken together, the eight chapters, all as clear, complete, and definitive as Chapter 4, definitively describe the activities (and their integration) that involve trained organic chemists in the pharmaceutical industry.

The book concludes with two appendices: (A) Prize-Winning Organic Chemists and (B) Indices of the North American Pharmaceutical Industry. The latter appendix is divided into two parts, namely a Geographical Index of the North American Pharmaceutical Industry and a Name Index of the North American Pharmaceutical Industry. These two parts of Appendix B provide the locations, names, and contact information for more than 500 companies and other organizations that comprise the major part of the pharmaceutical industry in the United States and Canada.

Job$ in the Drug Industry is an accurate presentation of opportunities and rewards for chemists in the pharmaceutical field. Primarily, it is intended as a guide for organic chemists, and special attention is not directed toward graduates with degrees in medicinal chemistry. Nonetheless, all chemists, as well as those trained in a variety of other scientific disciplines, will derive a great deal from this book. In my opinion, it will be of particular benefit to those who advise students, i.e., university professors, administrators, and faculty. It will enable these counselors to inform students early in their studies of the exciting variety of jobs available in the pharmaceutical industry and to plan a curriculum that

will facilitate the student's entry into a challenging and rewarding field.

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Metal Ions in Biological Systems. Volume 37. Manganese and Its Role in Biological Processes. Edited by Astrid Sigel and Helmut Sigel. Marcel Dekker, New York. 2000. xlvi + 761 pp. 16 × 23.5 cm. ISBN 0-8247-0288-3. $250.00.

This book represents the continuation of an outstanding annual series dedicated to presenting research progress in essential metalloelement-dependent biological processes. All chapters are well-written, and they range from physical and coordination chemistry of prominent manganese oxidation states [Mn(II), Mn(III), and Mn(IV)] as well as Mn(V), found in manganese-dependent enzymes of microorganisms, plant cells, and extracellular spaces and in cells of humans, to fascinating presentations of X-ray crystal structures of many holoenzymes depicting covalent and coordinate-covalent bonding of manganese at the active site as supported with an array of X-ray, electron paramagnetic resonance, and ultraviolet−visible spectral measurements. Presentations of manganese metabolism and speciation of manganese in tissues provide a recognized understanding that the concentration of ionically bonded manganese in tissues (10^{-18} M) is too small to be measured with existing instrumentation, so that all measured manganese amounts in tissues represent small molecular mass chelates or large molecular mass manganese-dependent enzymes.

Medicinal chemists are likely to be interested in the more prominent manganese-dependent enzymes, including: ribozymes; heart 2-oxoglutarate dehydrogenase; many glycosyltransferases; sulfotransferases; kinases; phosphatases; integrins; cytidyl, adenyl, and guanyl cyclases; a superoxide dismutase; arginases; and catalases. Recognized participation of adenyl and guanyl cyclases in synthesis of second messengers involved in norepinephrine- and acetylcholine-mediated normal and disease-related responses (as well as nitric oxide-mediated responses and suggested roles for superoxide in causing tissue pathology in many disease states) should make the association of manganese-dependent enzymes with these processes of paramount interest. Many of the preceding enzymes as well as still other manganese-dependent enzymes identified as required for normal metabolism by fungi and bacteria (including restriction endonucleases) suggest approaches to design of new antibiotics and antimicrobial agents. Some of these enzymes have been modeled as biomimetic small molecular mass chelates.

This reviewer found the use of the designation Mn^{2+} versus Mn(II) or MnII to be distracting, since the former designation indicates ionically bonded forms of manganese. In addition, use of some form of the word "bond" to describe electronic interactions of this and other metalloelements with small molecular mass ligands or with proteins is less precise and accurate than is implied by use of the word "bond", whether the exact character of the interaction is known. All characterizations of specific oxidation states in electronic bonding interactions are most correct and less misleading state-of-the-science representations.

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The Alkaloids. Volume 52. Chemistry and Biology. Edited by Geoffrey A. Cordell. Academic Press, San Diego, CA. 1999. x + 391 pp. 15.5 × 23.5 cm. ISBN 0-12-469552-3. $135.00.

As users of this well-established series have come to expect, the latest volume of *The Alkaloids* is comprised of a limited number of chapters on disparate topics. Volume 51 contains one chapter on alkaloids from a geographic region, Sri Lanka, one on alkaloids from marine organisms, and three on chemical groupings of alkaloids. More than half of the book is occupied with tables, figures, and references, leaving only about 40% of the book for text.

The review of Sri Lankan alkaloids (by Gunatilaka) is justified by the high number of alkaloid-containing indigenous plants that have ethnomedicinal uses. About 260 endemic species of alkaloidal plants, in 21 families, are listed. This chapter will clearly serve as a standard resource and reference on Sri Lankan alkaloids.

The discussion of the sarpagine group of indole alkaloids (by Lounasmaa, Hanhinen, and Westersund) primarily emphasizes synthesis. The chapter contains a large table on NMR and MS data. As it is stated that few pharmacological effects have been found for this group, it is not surprising that only two short paragraphs are devoted to pharmacology. The ibogaine alkaloids, however, have a chapter (by Popik and Skolnik) devoted to their pharmacology. These alkaloids are derived from plants used in West Africa for tribal initiation rites. The interest in their pharmacology stems from anecdotal evidence that these alkaloids can be used to treat drug addictions without having abuse liability. The history of these claims might lead one to view such evidence with a degree of scepticism. That notwithstanding, this is a well-organized chapter on the history, chemistry, and pharmacology of ibogaine alkaloids.

Attar-U-Rahman and Choudhary discuss marine alkaloids unfamiliar to most investigators. Some of these complex compounds, such as the zoanthamine alkaloids, are derived from animals, stretching the traditional definition of an alkaloid. Such alkaloids tend

to be of structurally novel types. The cephalostatins, for example, are 13-ringed spiroketals found in marine worms. Many of these marine compounds are cell growth inhibitors and are thus of great interest to cancer researchers. The final chapter (by Cordell) brings the reader back to the familiar terpene alkaloids. Even here, however, some new notes can be sounded on the same old bells. Thus incarvillateine is a highly substituted 1,3-dicarboxycyclobutane terpenoid from a Chinese member of the Bignonia family.

The volume is a fit continuation of this magisterial series. As is the case with the earlier volumes, it will serve as a basic reference source for decades or more.

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