Book Reviews

Handbook of Drug Metabolism. Edited by Thomas L. Woolf. Marcel Dekker, New York. 1999. xi + 596 pp. 18 x 26 cm. ISBN 0-8247-0229-8. $225.00.

Woolf aims to provide a general and comprehensive text on drug metabolism, since the classic books in this field are now 20 or more years old. Part 1 (the first six chapters) provides excellent coverage of the fundamental topics. Chapter 2 (Mabic et al., Oxidative Metabolism of Xenobiotics) is an especially good "teaching" chapter. Chapter 5 (Non-P450 Oxidative Enzymes), by Rettie and Fisher, is also clearly written and nicely organized. Part 2 (Chapters 7−11) describes factors such as pharmacogenetics, enzyme inhibition, enzyme induction, and drug interactions. There is a strong practical orientation in the second half of the book, reflecting the fact that the editor and one-third of the book's authors are industrial scientists.

Part 3 consists of nine chapters on technologies for studying drug metabolism in vivo and in vitro. Methods involving whole organs, cells, subcellular fractions, and heterologously expressed enzymes are included. This part of the book is aimed squarely at those who are carrying out drug metabolism studies. Part 4 (Chapters 21 and 22) presents "the big picture", describing the roles of preclinical and clinical metabolism studies in drug development.

It is always difficult in a multiauthor book to coordinate the coverage of topics. In this volume, Chapters 12 and 13 both cover heterologous expression of human metabolic enzymes. The chapters are written quite differently, but there is much overlap of subject matter. Similarly, there is redundant coverage of the families of P450 enzymes in Chapters 2 and 4. Biochemists will be disappointed to see that Menten, of Michaelis−Menten fame, is misspelled on p 42.

The editor of this book envisions it as a textbook for a graduate course in drug metabolism and as a useful reference for industrial, academic, and government scientists. It could serve very well as a textbook, but it is not sufficiently comprehensive to be a reference source. For example, Chapter 14 contains some extensive tables of drug metabolism, but the drugs are not indexed. Still, the book strikes a very good balance between the didactic and the practical. It will be a most useful book for those interested in drug metabolism.

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JM0001323

10.1021/jm0001323

Handbook of Reagents for Organic Synthesis. Reagents, Auxiliaries, and Catalysts for C−C Bond Formation. Edited by Robert M. Coates and Scott E. Denmark. John Wiley & Sons, Inc., New York. 1999. xvi + 746 pp. 22 x 28.5 cm. ISBN 0-471-97924. $115.00. **Acidic and Basic Reagents.** Edited by Hans J. Reich and James H. Rigby. John Wiley & Sons, Inc., New York. 1999. xii + 494 pp. 22 x 28.5 cm. ISBN 0-471-97925. $115.00. **Oxidizing and Reducing Reagents.** Edited by Steven D. Burke and Rick L. Danheiser. John Wiley & Sons, Inc., New York. 1999. xviii + 550 pp. 22 x 28.5 cm. ISBN 0-471-97926-0. $115.00. **Activating Agents and Protecting Groups.** Edited by Anthony J. Pearson and William R. Roush. John Wiley & Sons, Inc., New York. 1999. xvii + 513 pp. 22 x 28.5 cm. ISBN 0-471-97927-9. $115.00.

A compilation of monographs on chemical reagents has tremendous value for anyone who is trying to decide which reagent is the most convenient for a given chemical transformation. The *Handbook of Reagents for Organic Synthesis* comprises four volumes, available for purchase on a single-unit basis, and includes selected monographs from the 3000 reagents that are contained in the eight-volume *Encyclopedia of Reagents for Organic Synthesis (EROS),* published 5 years ago. It was recognized that the large size and high cost of *EROS* might prevent research groups from having this valuable information in their laboratories. The editors of *EROS* selected 500 of the most important and useful reagents having the highest probability for repeated utilization and included these in this four-volume set.

More than a thousand practicing chemists around the world provided specific contributions in their area of expertise. Each of the monographs begins with some physical data on the reagent and other relevant information such as purification methods, handling/storing information, analysis of purity, and precautions. Some entries also begin with a useful general discussion. Although the monographs were copied directly from *EROS*, the *Handbooks* have included a "Related Reagents" section at the end of each monograph and have incorporated recent reviews (1992−98) and selected relevant new procedures from *Organic Syntheses* (Vol. 69−75) at the beginning of each volume. The *Handbooks* contain both a reagent formula and subject indices.

The volume entitled *Reagents, Auxiliaries, and Catalysts for C−C Bond Formation* contains 203 entries, which are organized into 22 classes based upon their chemical structure and function.

The volume entitled *Acidic and Basic Reagents* covers a fairly broad spectrum of reagents, from the usual acidic and basic reagents to ligands, complexing reagents, esterases, lipases, and other less commonly used reagents (e.g., phosphazene base), that are considered by the editors as being likely to become popular in the near future. Selected reactions from *Organic Syntheses* are grouped into four classes: Metalation; Acid Catalysts; Lewis Acids; and Hydrolyses−Enzymatic. Although these reagents are sometimes difficult to classify, a few examples may be misplaced in the classes. For

example, the enantioselective hydrolysis of 1,1′-bi-2-naphthol with pancreas acetone powder is found under "Metalation". Nevertheless, this does not detract significantly from an exceptionally useful volume.

The most important reagents to protect amine, alcohol, carbonyl, and other functional groups can be found in *Activating Agents and Protecting Groups*. Examples of reagents selected as "activating agents" include those capable of increasing the nucleophilicity of enolates, Lewis acids that increase the electrophilicity of some functional groups, and other more traditional reagents that convert alcohols into more reactive functionalities.

Oxidizing and Reducing Reagents begins with oxidizing agents (24 classes) and reducing agents (35 classes), then lists reviews and selected *Organic Syntheses* procedures for oxidation and reduction. This volume contains 145 entries. The "Related Reagents" section of each entry refers to the corresponding oxidizing or reducing class, which makes the finding of possible alternate procedures very simple. This reviewer found the organization of the *Handbook* very useful, especially the graphical indexing of reactions *in Organic Syntheses*. All practicing chemists will definitely benefit by using any or all of the *Handbooks*.

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JM000115D

10.1021/jm000115d

Pharmaceutical Innovation. Revolutionizing Human Health. Edited by Ralph Landau, Basil Achilladelis, and Alexander Scriabine. Chemical Heritage Press, Philadelphia. 1999. xxiii + 408 pp. 16 × 24 cm. ISBN 0-941901-21-1. $44.95.

It seems almost inconceivable that the pharmaceutical industry that now plays such a major role in the world's economy had its origin less than 150 years ago with Henry Perkin's discovery of the first synthetic dyestuff in 1856. The industry's growth since then has been rapid and, in recent years, almost explosive. Further, this industry is unique because of its exceptional reliance on research and development, its close ties with the entire health care field, and its more recent entry into new areas of discovery, such as biotechnology and perhaps even gene manipulation. These considerations led to the preparation of this book with the objective of informing lay persons of the path of commercialization of science and technology that has resulted in the present state of the pharmaceutical industry.

A major part of the book is contained in the first two chapters which examine the historical evolution of the pharmaceutical industry from two different perspectives. In Chapter 1, Basil Achilladelis considers the development of the industry in five periods corresponding to five different generations of drugs. In the first period (1820−1880), drug therapy and research involved mainly natural plant products and their active principles and simple chemicals. The next phase of the industry's development (1880−1930) witnessed the establishment of research laboratories with scientists who devoted their research to the isolation, synthesis, and pharmacological testing of natural plant products. It was during this period that the first effective synthetic drugs and vaccines were marketed. In the third period (1930−1960), pharmaceutical companies began to evolve as we currently recognize them with a major focus on their own research to develop new therapeutic products. World War II stimulated Western governments to support the development of antibiotics, antimalarials, and other drugs needed because of the war. With this background, pharmaceutical companies prospered after the war and many new hormones, vitamins, antibiotics, and antiinflammatory drugs were developed. The fourth period (1960−1980), largely as a result of the thalidomide tragedy, was marked by stricter government regulations for drug approval with a consequent marked increase in the cost for developing new products. Nonetheless, many new drug products, ranging from antihypertensives to contraceptives to cancer chemotherapeutic agents, were introduced. The fifth period (1980 to the present) of the pharmaceutical industry has been marked by takeover threats, declining profitability, growth of biotechnology companies, competition from generic products, and pressure from HMOs and the government for lower prices. Nevertheless, a number of new products, e.g., for the treatment of osteoporesis, migraine headaches, benign prostatic hyperplasia, etc., have been developed. Also, biotechnology companies have begun to introduce new drugs and to produce novel avenues to the development of new therapeutic agents.

In Chapter 2, Alexander Scriabine reviews the major classes of therapeutic agents from the standpoint of their mechanism of action, effectiveness, and historical development. The first section deals with agents, such as vaccines and antibiotics, that block or attack infectious agents. This is followed by sections on cardiovascular agents, drugs affecting the central nervous system, drugs affecting the peripheral autonomic nervous system, hormones, nonsteroidal antiinflammatory agents, immunosuppressants, cancer chemotherapeutics, and the more recent "lifestyle" drugs, such as sildenafil (Viagra), minoxidil (Rogaine), finasteride (Propecia), tretinoin (Renova), etc. Recalling the historical development of many of these drugs is particularly enlightening and clearly illustrates the vital role of a variety of different scientific disciplines in the design, development, and recognition of a number of useful therapeutic agents in current use. The development of these agents, not unlike the development of the older therapeutic modalities, in many instances resulted from unexpected clinical observation.

Chapter 3 focuses on the history of eight companies to chronicle the development of the biotechnology industries since their origin in the 1970s. Chapter 4, *Pharmaceutical Taxonomy of Most Important Drugs*, is comprised mainly of tables in which new chemical entities (NCEs) judged to be most important are grouped by therapeutic area, chemical class, and time period of their introduction. In Chapter 5 the managerial and economic forces determining pharmaceutical firms' innovative performance and economic success are exam-

ined from historical perspective. In the final chapter, the torturous, multifaceted, interdisciplinary, risky, expensive, and sometimes serendipitous route of drug development is examined by focus on one case study, i.e., the basic science research on purines and pyrimidines by George Hitchings and Gertrude Elion at Burroughs Wellcome between 1942 and 1983 that culminated in a number of new and important drug products. This study also illustrates the importance of a champion, i.e., an individual with the knowledge, conviction, dedication, and perseverance, to lead and promote the progress of a drug through the often difficult path from conception to market. Clearly, many of the therapeutic agents in current use can be associated with such a champion.

This book is a comprehensive and realistic history of the pharmaceutical industry from the time of its inception to the present. It is more than just a compilation of company histories, but it treats all aspects of this vital industry from conception, through research and development, to the market, and to market acceptance. In the process, the importance of not only rational, well-planned research and development but also of observant chance discovery is given its due. Parts of *Pharmaceutical Innovation* will be important reading for all in the pharmaceutical industry; most will derive much from the entire book.

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JM000120H

10.1021/jm000120h