Book Reviews

The Organic Chemistry of Biological Pathways. By John McMurry and Tadhg Begley (Cornell University). Roberts and Company Publishers. 2005. xxii + 490 pp. 24 × 19 cm. £35.00 (U.S.$66.00). ISBN 0-9747077-1-6.

This is a well-written book on the mechanistic aspects of the major biochemical pathways, and it is complementary to classical biochemistry textbooks, where the chemical reactions involved in the formation and degradation of primary metabolites are not discussed in detail.

The book is divided into eight chapters. The first chapter presents a good overview of the mechanisms of organic chemical reactions involved in biochemical transformations, including the reactivity of functional groups, acidity and basicity, and electrophiles and nucleophiles. Each mechanism is didactically presented, illustrated by colored atoms or groups that are directly involved in the chemical transformations. Such a presentation is consistently used throughout the book, in order to make clear every reaction within the biochemical pathways. The second chapter starts with a review on chirality and prochirality and its importance to biological compounds, followed by an introduction on primary metabolites, such as lipids, carbohydrates, amino acids, peptides, proteins, nucleic acids, enzymes, and coenzymes, including the principles of thermodynamics and kinetics of bioorganic reactions. Not only are the structures presented, but also the chemical properties of the main biological building blocks are discussed.

The next four chapters deal with the metabolism and catabolism of primary metabolites. In each chapter, every reaction sequence is first summarized, followed by a detailed discussion of the reaction steps involved in the functional group transformations and carbon−carbon bond formations or degradations in each of the biosynthetic pathways. The topics are presented very clearly; many recent references to the primary literature are provided at the end of each chapter, as well as a whole set of exercises of increasing difficulty from chapter to chapter. The selected topics are of prime importance to understanding biochemical reactions, and they are discussed in sufficient depth while avoiding overly lengthy explanations. The seventh chapter presents selected examples of the biosynthesis of secondary metabolites, including penicillins, cephalosporins, morphine, prostaglandins, erythromycin, coenzyme B_{12}, and other tetrapyrroles. Chapter eight summarizes all reaction mechanisms included in the book. Two appendices provide information on how to access protein structures from websites such as Protein Data Bank and to obtain further information of biosynthetic pathways from KEGG (Kyoto Encyclopedia of Genes and Genomes) and BRENDA websites. Finally, a third appendix gives answers for all exercises included in the book.

The book is beautifully illustrated and the structures have been drawn with great care in order to clearly present the mechanism of every single reaction discussed in the different chapters. The importance of the stereocontrol in different reactions is always considered. The text is easy to read, very enjoyable, in such a way that I consider it an ideal book for students interested in understanding the logic of organic reactions behind the main biochemical pathways such as triacylglycerol catabolism, fatty-acid and terpenoid biosynthesis, glycolysis, gluconeogenesis, the biosynthesis of every single amino acid, and both *de novo* and salvage nucleotide biosynthesis pathways, among others.

As a personal suggestion for a future edition, a few additional chapters could be included, covering topics such as the experimental tools used to establish biosynthetic pathways, the elaboration and proposal of biogenetic pathways, and additional examples of secondary metabolite biosynthesis, e.g., free radical coupling reactions involved in the formation of phenylpropanoid derivatives. However, the authors' choices are undoubtedly the most relevant today. It would be also very helpful if the authors could prepare a CD-ROM for teaching purposes. Since it is not an expensive book, I believe that this monograph deserves considerable attention as a serious first choice for those interested in detailed mechanistic explanations of biochemical pathways.

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***Anadenanthera*. Visionary Plant of Ancient South America**. By C. M. Torres and D. B. Repke (Florida International University). The Haworth Press, Binghamton. 2006. xvi + 256 pp. 6 × 8 in. $34.95 (paper). ISBN 0-7890-2642-2.

This book is an exquisite labor of love, written by two experts who are well versed in the use of psychoactive plants as shamanic inebriants by indigenous cultures in the New World. Their information is presented from a multidisciplinary perspective and will appeal to those interested in phytochemistry, archeology, and the lure of forbidden fruit. The authors provide an exhaustive review of a tedious and obscure body of literature over the last 500 years, which is complicated by mistakes and misunderstandings that have been accepted without serious inquiry, with additional confusion from botanical reclassifications within the *Mimosa* genus during the 20th century. Moreover, the preparation and use of *Anandenathera* products varies widely over time and geography, while the reader is reminded that smoking, snuffing, and clysters were all unknown technologies in 15th century Spain, yet they were common features of indigenous life when Columbus and crew happened upon the Bahamas, most of the Greater Antilles, and the Virgin Islands in 1492. The mystery deepens as evidence of use appears throughout the Andes over millennia. The practice of insufflating powders derived from *Anandenathera* seeds still continues in some areas of South America, despite a sustained oppression. Apparently this ancient practice forms an important part of cultural values and is not just an interesting way to pass the time.

The gist of the text reveals the development of plant-based psychoactive inebriants, from simple smoking mixtures to snuffs, over the last 4000 years in Central and South America. The authors present solid evidence of a deliberate progression toward more efficacious products and delivery devices over time, in other words, more "bang for the buck", the hallmark of any advancing technology. Without much imagination, almost anything can be smoked in a jaguar bone pipe, while the science of preparing and delivering an effective dry powder, deep into the nasal cavity, is much like the difference between launching

a glider into the wind, down a slope, versus a brief rocket ride into the stratosphere. This gradual development demonstrates an empirical awareness of at least three important principles in the pharmaceutical sciences of today: (1) that a crude plant substance can be refined for higher potency, (2) that adding mineral lime, from burned seashells, can liberate alkaloids for more rapid and efficient absorption, and (3) that the human nasal cavity can absorb much more of this material than the lung. It is less clear at what point these innovative people developed the clyster as yet another way to appreciate these cherished alkaloids.

After a thorough introduction to the botany of *Anandenathera* species, subsequent chapters focus on the archeology and geographic distribution of this companion plant and the prehistoric cultures that used it. The known phytochemistry of *Anandenanthera* is completely described, along with an exposé on bufotenine and other methylated tryptamines. The book concludes with a summary, an extensive bibliography, and an index, in addition to 59 crisp, black and white photographs. One minor distraction is the poor resolution of molecular images in the first printing, which has been corrected for future printings of this magnificent work.

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Phage Display in Biotechnology and Drug Discovery. Edited by Sachdev S. Sidhu (Genentech, Inc.). CCR Press/Taylor & Francis Group, Boca Raton. 2005. xiii + 748 pp. 15 × 23 cm. $159.95. ISBN 0-532-42154-5.

This book is an important addition to the informative material on phage display technology. In contrast to the books previously published on the subject, which are mostly technical manuals, this text offers a comprehensive overview of the phage display technology and its applications in different areas in the study of proteins and is particularly relevant to the development of therapeutic proteins. Each chapter was individually prepared by a number of different authors from accredited institutions and biopharmaceutical companies to facilitate coverage on a wide range of topics. A detailed overview of filamentous phage biology and vectors is presented in Chapters 1 and 2. Methods for the construction of phage-displayed libraries and selection strategies are extensively covered in Chapters 3 and 4. The following chapters are dedicated to specific applications of phage display in different research areas, including vaccine and antibody development, protein characterization, and protein engineering. For each application, examples of development of therapeutic proteins are given. The last chapter, written by the editor, is a short but particularly elucidating review of the development of synthetic libraries and presents progress on this novel approach by different companies, with a look to the future of therapeutic antibody development. The material is presented in a logical and clear fashion, and each chapter has an extensive list of references. The text is supplemented with a good number of figures in most of the chapters, although some figures, especially those representing molecular structures, could be much more informative and easier to read with colors.

One of the few omissions in the book is that phage display with lytic phage is not even marginally considered. This is not a serious omission, considering that phage display is mainly based on the use of filamentous bacteriophages, which is also the editor's and the authors' area of expertise. However, display of peptides on T7 and other lytic phage has been shown to overcome some of the limitations of display on filamentous phages, and the utility of this system for some applications is well documented by a number of publications. Therefore, the presence of a brief section that deals with T7 peptide display and its applications in the development of therapeutic proteins would probably be appreciated by a number of readers and make this textbook more complete. In particular, the section concerning phage library diversity (VI, Chapter 1), after discussing the peptide censorship by the M13 host system, may point out the possibility of using the T7 lytic phage display as an alternative system to display peptide libraries. It has been previously proposed that T7-displayed peptide libraries could achieve maximum peptide sequence diversity (Rodi et al., 2002, *J. Mol. Biol.*); however, only recently have Krumpe and colleagues (2006, *Proteomics*) demonstrated that the use of T7 enhances the functional diversity of a peptide library compared to M13 due to the differing processes of phage morphogenesis.

In my opinion, this book is specifically directed and of great interest to experts in filamentous phage display who want to broaden their knowledge on different aspects of this technology or to well-informed molecular biologists interested in specific applications.

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Flavor Chemistry and Technology. By Gary Reineccius (University of Minnesota). CRC Press/Taylor & Francis, Boca Raton. 2006. xxiv + 489 pp. 16 × 24 cm. $149.95. ISBN 1-56676-933-7.

The world of flavor is complex and fascinating; any attempt to explain it is an ambitious task that is welcome. This book, combining comprehensive, accurate, and profuse data concerning the chemistry of flavor and its technology, deserves much more than regular support.

As anticipated from its title, this book is comprised of two almost equal parts: flavor chemistry and flavor technology. In the first chapter, the author succeeds in summarizing the anatomical aspects of taste and odor perception in an easy to read manner. The second chapter is probably the weakest (fortunately, it is only 9 pages long); it covers the different sources of information concerning flavor. Section 2.5.10 (how to use the Internet effectively) can hardly be considered essential. Methods to analyze volatile (aroma) and nonvolatile (taste) compounds are depicted in Chapter 3. Limits and concerns of these methods are clearly indicated, making this chapter much more than a catalog of techniques. Chapters 4−6 explain the biogenesis of aroma compounds, their possible transformation during food processing, and their interaction with the other food components. The origin of the bad smell sometimes encountered in food is explained in Chapter 7.

The flavor technology part of the book comprehensively describes the naturally occurring flavoring materials (Chapter 8), those obtained during food processing (roasting, fermentation, smoking, etc., Chapter 9), and the synthetic flavoring materials

(Chapter 10). Flavor enhancers are the specific topic of Chapter 11. Chapters 12−15 are more devoted to the industrial aspects of flavor (i.e., flavor creation, production, application, legislation). The last chapter deals with quality control, an essential field of food analysis that is predicted to grow dramatically in the near future.

Students eager to embrace a career in the flavor field will perhaps regret that the economic aspects of flavor chemistry and technology are the subject of only three lines in the preface. It should be noted that, despite the author's recommendation in section 10.6 to use IUPAC nomenclature rules, he sometimes still uses *cis*/*trans* instead of *Z*/*E* nomenclature. Nevertheless, this book is strongly recommended for anyone interested in one of the various flavor chemistry/technology domains.

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Combinatorial Synthesis of Natural Product-Based Libraries. Edited by A. M. Boldi (Codexis, Inc.). CRC Press/Taylor & Francis, Boca Raton. 2006. x + 347 pp. 7 × 10 in. $199.95. ISBN 0-8493-4000-4.

This book covers a range of topics related to high-throughput synthesis of natural product-based compounds. A highlight of this book is the first two chapters. These chapters discuss the importance of natural products to past, present, and future drug discovery and discuss in a fairly impartial and nonpartisan manner where the combination (marriage) of combinatorial chemistry and natural products is now and may have the most impact in the future. The remaining chapters each address an area of high-throughput, putative high-throughput, or envisioned approaches for future high-throughput design and synthesis of natural product derivatives or libraries based on natural product scaffolds. The various chapters in this book can be summarized into one or more of the following categories: (A) computational approaches to the design of natural product-based libraries; (B) engineering biosynthetic pathways; (C) scaffold modification and pendent groups; and (D) approaches to synthesize natural product scaffolds.

The overriding theme of most chapters relates to combinatorial chemistry or high-throughput synthesis strategies for identifying new natural product-based therapeutics. Some chapters cover specific examples of the authors' efforts in preparing natural product-based compounds/libraries for a specific purpose. Alone or as a component of this book, these chapters are interesting. A number of chapters essentially review a range of examples of natural product-based libraries from the authors' perspective or in the context of the authors' approach to natural product-based library synthesis. To this end, the compilation of these reviews into one book affords a number of topics that get a bit redundant and can be found in primary review journals. These reviews will be of interest to an audience with an interest in gaining a broader perspective of approaches for preparing natural product-based libraries. Most examples of natural product-based library synthesis discussed in these chapters are timely. However, it is noteworthy that some examples provided in detail in a few chapters have been covered in multiple prior review articles since their original report a decade or more ago.

The subject index of this book is thin, but adequate. Some of the chapters suffer from a very limited number of references. However, an extensive number of references are effectively provided with other chapters and readily direct readers to both primary literature and additional topical reviews. In general, this book will be of primary interest to individuals with an interest in the synthesis of natural product-based libraries, as appropriately advertised by the title. In addition, the first two chapters, as well as components of some additional chapters, will be of interest to an audience looking to gain some insight into the past, the present, and the possible future role of high-throughput synthesis in facilitating drug discovery based on natural products and natural product structural templates.

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Industrialization of Drug Discovery. From Target Selection through Lead Optimization. Edited by J. S. Handen (Merck Research Laboratories). Drug Discovery Series, Vol. 2. CRC Press/Taylor & Francis, Boca Raton. 2005. xviii + 305 pp. 16 × 24 cm. $139.95. ISBN 0-8247-2391-0.

This multiauthored volume attempts to cover a wide variety of topics in drug discovery, "from barcodes to bioethics", and thus may have a chapter to suit the needs of many different readers. The editor leads off with an overview of current trends in drug discovery, with the often-mentioned observation that small molecule drugs are getting harder and more expensive to find, despite massive investments in research and development within pharmaceutical companies. Of note, he states that currently industry averages 5 new lead molecules per year per 1000 discovery employees and that management would like to improve that ratio to 14 leads per 1000. Without a doubt, automation can and will assist in this process, if applied appropriately.

In a later chapter, Peakman exhorts the reader that industrialization, not automation, is the proper focus. He makes a good point that process analysis can be a useful way to identify bottlenecks and redirect resources; however, I think that the industrialization analogy is, by and large, false. Henry Ford (who makes an appearance in the chapter) successfully industrialized automobile manufacturing, not the development of new models of cars. The track record of the automobile industry in introducing new, successful models is probably not so much better than that of pharma with new drugs. No one disputes that pharmaceutical *manufacturing* benefits by industrialization, but pharmaceutical *discovery*, to my mind, is very much a craft dependent on careful examination of data for competing leads, and one which cannot be truly industrialized.

The fourth chapter, by Perakslis and Iorns, is a very good overview of most issues in compound management, although the authors make no mention of the important problem of compound precipitation from DMSO solution, which has been widely discussed elsewhere. A fifth chapter, on high-throughput screening, makes the point that major improvements can be made in coordination within the lead identification process without the introduction of new technology.

A chapter on ADME/PK and toxicology makes a good case that parallel development of multiple lead series can avoid starting over

when one series fails. This, of course, requires higher throughput methods, which are now becoming available. However, the diversity of reasons that compounds fail at this stage makes it hard to develop an integrated approach.

Further chapters discuss the economic valuation of research, electronic collaborative workspaces, and bioethics of genomic medicine.

It is unlikely that a single reader will be interested in all of these topics, but most scientists will profit from some of them. The book is well-edited in general and very readable.

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