# *Book Reviews*[*]

**Camptothecins: New Anticancer Agents**. Edited by Milan Potmesil (New York University School of Medicine) and Herbert Pinedo (Free University, Amsterdam). CRC Press, Boca Raton, FL. 1995. xxix + 935 pp. 15 × 22.5 cm. $129.95. ISBN 0-8493-4764-5.

The camptothecins represent a promising class of anticancer agents useful in the treatment of human diseases such as cancer. These agents display a unique mechanism of action, the inhibition of the DNA unwinding enzyme topoisomerase I. Topoisomerase I is an important nuclear enzyme for various DNA functions including transcription and replication. In the 1980's, topoisomerase I levels were found to be elevated in certain types of cancer cells, and this provided and important impetus to accelerate the development of these agents for the treatment of cancer. The current book by Potmesil and Pinedo provides an excellent summary of the basic science and clinical studies that eventually led to the clinical approval of two of the camptothecins (topotecan and CPT-11) by the Food and Drug Administration in 1996.

The book contains chapters from many of the international experts in the camptothecin area of research. Chapter 1, written by Leroy F. Liu, contains a concise summary of the biochemistry, biology, and genetics of DNA topoisomerase I. Also discussed in this chapter are some of the details known about the camptothecin−topoisomerase I interaction, mechanism of enzyme inhibition, drug-induced cell death, and drug resistance phenomena. Chapter 2, by natural products and medicinal chemistry experts Monroe E. Wall and Mansukh C. Wani, provides a complete and detailed historical background of the discovery of camptothecin. The chapter by Wall and Wani also covers the synthesis and testing of many of the water-soluble camptothecin analogs with ring A substituents. Chapter 4, by Milan Potmesil and Beppino C. Giovanella, provides an excellent summary of the testing of camptothecins in animals. Animal testing conducted in the laboratories of these two authors in the 1980's heightened the interest level of the cancer chemotherapy community in the potential therapeutic value of the camptothecins. Drs. Potmesil and Giovanella discuss how plasma levels of the lactone form of the drug are necessary for optimal therapeutic effects. Chapter 12, by Yves Pommier et al., expands on the discussion of resistance to the camptothecins that was initiated by Leroy Liu in Chapter 1. The chapter by Yves Pommier and coworkers contains a discussion of factors involved in cell sensitivity or resistance to these agents. Cell lines resistant to camptothecin developed in vitro are also covered, including two camptothecin-resistant cell lines, CPT-K5 and DC3F/C-10, with structural changes of the gene that encodes DNA topoisomerase I. This chapter includes comments on the possible implications of the findings for the molecular biology of the drugs.

Also covered in this book are chapters dealing with the clinical aspects of camptothecin therapy development. It seems most appropriate that the first chapter with a clinical theme was written by Franco Muggio, a physician and chemotherapy expert who was involved with the first clinical testing of camptothecin in the early 1970s. In the early studies camptothecin was administered in its less active sodium salt form, and Dr. Muggio analyzes this early clinical data in retrospect. Several considerations of camptothecin scheduling and pharmacology are presented by Dr. Muggia. Chapters 6, 7, and 8, by Drs. Taguchi, Rothenberg et al., and Chabot et al., respectively, summarize and discuss data from the clinical trials of CPT-11 conducted throughout the world. Chapters 9 and 10, by Howard Hochster and Jaap Verweij et al., summarize results concerning the clinical trials of topotecan. Chapter 5, by John Stehlin et al., concerns the oral administration of camptothecin lactone, while Chapter 11, by Howard Burris, III, et al., presents information of the dose-limiting toxicities of the camptothecins and their clinical management.

In summary, this well-written and appropriately referenced book is recommended for those individuals looking for a summary of the important basic science and clinical research developments that led to the clinical approval of the first camptothecin analogs for the treatment of cancer.

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**100 and More Basic NMR Experiments: A Practical Course**. By Siegmar Braum, Hans-Otto Kalinowski, and Stefan Berger. VCH Publishers, New York, NY. 1996. xii + 418 pp. 16.5 × 24 cm. $49.95. ISBN 3-527-29091-5.

The contents of this book are very accurately described by its title. The book consists of a detailed description of 115 experiments and variations of those experiments. A standard format is used to describe each experiment: purpose, literature, pulse scheme and phase cycle, acquisition, processing, result, comments, and space for recording the results obtained by the reader. Each experiment is written as a completely separate section with any necessary references to other experiments.

The experiments range from calibration and performance checks through all of the common 1- and 2-D experiments and one 3-D experiment. One section is devoted to pulsed-field gradient experiments. The book also includes very useful introductory sections with each

[*]Unsigned book reviews are by the Book Review Editor.

group of experiments. The first section, for example, discusses the NMR spectrometer and superconducting magnet and leads the reader through the "art" of shimming. Each experiment is clearly described and includes a description of the test solution needed and references to necessary calibration experiments. The experiments are described in terms of product operators, and the elementary product operator formalism rules are given in the appendix. In some cases, the authors gave their own evaluation of the value of the specific experiment.

The book is specifically written in Bruker terms and is, therefore, particularly useful for readers who operate Bruker instruments. To help the non-Bruker users, a very handy "dialect" table is given in the appendix, which gives the equivalent notation for each of the parameters used on three Bruker, two Varian, and two JEOL instruments. Bruker users would find it useful if the pulses sequences were identified in "Brukerease", the specific way that Bruker describes its sequences. The authors kindly offer to supply any pulse programs used in the experiments that are not in the readers' AM-, AC-, AMX-, or ARX-instrument library.

The space devoted in each experiment to "own observations" does not appear to be very useful, because spectra would have to be plotted to the proper size or reduced to fit in the spaces, and it seems unlikely that anyone would actually do this. The sections perhaps do help to fill out pages, and perhaps also encourage the reader to try it him/herself. The index should list "calibration" and cross reference it to "determination of". The INEPT sequence used for INAPT (Experiment 7.9) should have the hard carbon-13 pulses centered in the very long selective proton pulses. This removes the phasing problem seen in the spectra. It is more common to use the same spectral windows in both dimensions in the 2-D INADEQUATE experiment (Experiment 10.19) and accept the aliasing in the evolution dimension.

This is a very good book for anyone who operates an NMR spectrometer. It is clearly and honestly written, with inclusion of less than optimal results wherever they occurred (see the WATERGATE Experiment 11.13). It should be particularly useful as a laboratory text. It has much to offer both the beginner and the advanced NMR user.

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**Aspects of Organic Chemistry: Structure**. By Gerhard Quinkert, Ernst Egert, and Christian Griesinger (Johann-Wolfgang-Goethe University). VCH Publishers, Inc., New York, NY. 1996. xvii + 489 pp. 21 × 28 cm. $98.00. ISBN 3-906390-15-2.

This book provides a thorough if unorthodox treatment of the structure of organic molecules. The first seven chapters cover the structural model of classic organic chemistry, and the eighth chapter introduces quantum mechanical ideas. The next eight chapters cover specialized topics such as NMR, hydrogen bonding, and base pairing. Readers of this journal will be pleased with the frequent use of natural products as illustrative examples. For example, configurational analysis (Chapter five) is based on carbohydrate chemistry, and conformational analysis (Chapter six) is based on steroids. The main strengths of the book are its inclusiveness and logical rigor. The authors take a comprehensive view of organic chemistry, and Chapter seven, on macromolecular and supramolecular chemistry, contains a readily accessible but thorough introduction to the stereostructures of both biological and synthetic polymers. The authors use a consistent set of principles and nomenclature to illustrate how familiar conformational principles can be applied to polymeric systems. The book's logical rigor results in a thorough examination of the (often unstated) assumptions of organic chemistry. One particularly enlightening section is entitled "Is the entire set of causes of stereoisomerism known?" and argues that the answer is no. The book's unconventional charm is conspicuous in Chapter ten on the "description of molecules". This concise and complete discussion of the naming and drawing of organic molecules not only illustrates the strengths and weaknesses of our current system, it also serves as a subliminal introduction to semiotics complete with the famous Magritte painting *Ceci n'est pas une pipe* (*This is not a pipe*). Other highlights of the book are the clear black, white, and gray illustrations, the use of logical flow diagrams, the formal introduction of symmetry and group theory, and the vocabulary-enhancing language. The book contains no problems but does have an excellent selection of further readings. The authors' quest for rigor and completeness has a downside, and some material—space groups, irreducible representations, and some of the MO material—seems inappropriate. While the book will have a valued place in my library, it's intended to be an undergraduate text. Adopting this unconventional text would require a substantial revision of the typical curriculum, and given the sclerotic nature of most curricula, this doesn't seem likely. Too bad.

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**The Alkaloids: Chemistry and Pharmacology, Vol. 46**. Edited by G. A. Cordell (University of Illinois at Chicago). Academic Press, Inc., San Diego, CA. 1996. ix + 364 pp. 15 × 22.5 cm. $110.00. ISBN 0-12-469546-9.

This book, the 46th volume in an important and prestigious series, offers two chapters on biosynthesis and three chapters on the occurrence, structures, and pharmacology of three unique classes of alkaloids.

Robins provides a thorough overview of the biosynthetic pathways in the pyrrolizidine and quinolizidine families. Significant advances in identifying and un-

derstanding the precursors, intermediates, and stereochemistry involved have been made in the past decade or so. The contributions from several groups are summarized.

Iwasa's chapter on the biotransformation of protoberberines in plant tissue culture reviews research on three pathways. It is somewhat difficult to follow. A great number of compounds and transformations are presented in tables and schemes, but numerous compound numbers (e.g., reticuline) and references are absent. Examples: The introduction should direct the reader to any reviews of the occurrence and identification of these alkaloids. The section (pp 314−6) on formation of benzophenanthridines from protoberberines in plant tissue cultures of three genera has no references to published or unpublished work. On p 320, the statement "These results differ from those utilizing the purified enzyme..." is not followed by citation of the work involved (O'Keefe, B. R.; Beecher, C. W. W. *Plant Physiol*. **1994**, *105*, 395−403).

Mueller, Roeloffs, and Jackson provide a concise, but richly detailed, review of the pharmacology of polyamine toxins from spiders and wasps. After a brief introduction to the ecology and chemistry of these organisms and their venoms, the authors offer a detailed summary of mechanism and site of action studies in both invertebrates and vertebrates and an overview of structure−activity studies.

Szántay, Kardos-Balogh, and Szántay have written a chapter focused on the various syntheses of epibatidine, a frog skin alkaloid with powerful and potentially important analgesic activity. The unique structure of epibatidine, its scarcity in nature, and its biological activity have prompted a good deal of synthetic work. This short chapter is nicely illustrated and brings together all work in this arena well into 1994.

Bringmann and Pokorny provide a richly detailed, thorough update of previous reviews (1977, 1986) on the naphthylisoquinoline alkaloids, thus far found only in two small, related plant families (Ancistrocladaceae and Dioncophyllaceae). In the past decade, over 40 new members of this class of alkaloid have been identified. This review not only summarizes the new structures and their sources, but also brings together work on their biological activity, stereochemistry, synthesis, biosynthesis, and ecology. This chapter suffers only from 18 citations of meeting abstracts and 33 citations of unpublished work among the 250 references. While the latter would seem to reflect the authors' desire to be as up to date as possible, the lack of access to experimental data in 20% of the chapter's references would be a hindrance to interested readers and scientists wishing to work in this area.

Like its predecessors in this venerable series, this book should be in library collections of the series. Those researchers with a direct involvement or interest in any of these five topic areas may want to obtain a personal copy.

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**Preservative-Free and Self-Preserving Cosmetics and Drugs: Principles and Practice**. Edited by J. J. Kabara (Technology Exchange, Inc., and Michigan State University) and D. S. Orth (Neutragena Corporation). Marcel Dekker, Inc., New York, NY. 1997. x + 274 pp. 15 × 22.5 cm. $150.00. ISBN 0-8247-9366-8.

This volume, which is volume 16 in the Cosmetic Science and Technology Series, is a multiauthor compilation with the following chapters and authors: Principles for Product Preservation (J. J. Kabara and D. S. Orth); The Effect of Acid pH on Microorganisms and Survival Strategies that Permit Growth in Products (D. S. Orth); Water Activity and Self-Preserving Formulas (D. C. Enigl and K. M. Sorrells); The Roles of Surfactants in Self-Preserving Cosmetic Formulas (O. Cozzoli); Fatty Acids and Esters as Multifunctional Components (J. J. Kabara); Biomimetic Phospholipids: Components for Self-Preservation (D. L. Fost and J. I. Yablonski); Use of Antioxidants in Self-Preserving Cosmetic and Drug Formulations (A. L. Branen and P. M. Davidson); Aroma Chemicals as Preservatives (J. J. Kabara); Chelating Agents as Preservative Potentiators (J. J. Kabara); The Role of Packaging in Product Preservation (D. K. Brannan); Preservative-Free and Self-Preserving Cosmetic and Drug Products: The Future (J. J. Kabara and D. S. Orth).

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