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BOOK REVIEW/

MAKING PEPTIDES

By John Mark Carter

Synthetic Peptides: A User's Guide, edited by Gregory Grant, UWBC Biotechnical Resource Series, W. H. Freeman and Company, New York, 1992. $39.95.

The increasing need for high-quality peptides in biomedical research has been at least partly met through the development of improved technology for automated laboratory-scale peptide synthesis. This has led many non-peptide chemists to enter the field as part-time synthetic chemists. Such newcomers are the intended audience of this book. Indeed, the last chapter is a useful discussion of the set-up of a new peptide core facility. I recommend a close examination of this chapter by investigators interested in actually installing their own peptide core lab.

Throughout, the editor has encouraged incorporation of pertinent examples to illustrate the utility of synthetic peptides in the application of rational experimental design. The reader familiar with the peptide literature may find these anecdotes unnecessary or even a bit pedestrian. Nonetheless, they provide encouraging success stories, stimulate the reader's imagination, and otherwise enliven the topics.

An attractive feature is the inclusion of a summary at the end of each chapter. If you are trying to decide whether or not to buy the book, be sure to look at these chapter summaries. Another useful feature is a list of general rules for selecting sequences for antigenic peptide production, based on hydrophilicity and surface accessibility. These are extremely useful elementary guidelines: heed them. They summarize the paradigm, reflecting observations shared by numerous widely experienced peptide chemists.

The editor has also included an interesting and thorough discussion of antisense peptides, which are peptides synthesized according to the nucleotide sequence of the non-transcribed complementary strand of DNA. Some studies have shown that these complementary peptide molecules can bind to peptides synthesized according to the normally transcribed strand of a gene.

There is also an excellent discussion of "auxiliary" issues. The miscellaneous issues covered here are important for all stages of synthetic peptide experimentation: planning, synthesis, purification, and ultimate utilization. Although brief, it offers good advice that should be heeded. This information is has been gleaned from many years of experience in peptide synthesis and handling, but it rarely appears in the literature.

A related section contains a good (if not particularly comprehensive) discussion of common side reactions in peptide synthesis. This includes amino acid-dependent reactions, such as spontaneous cyclization of amino terminal glutamine to form pyroglutamic acid, as well as sequence-dependent problems, such as the hyperlability of the aspartylproline peptide bond to acid-catalyzed hydrolysis. Proper anticipation of these problems will prevent expensive resyntheses.

The book also presents some general information regarding the synthesis of amino acid derivatives for use as synthetic intermediates. However, most readers probably purchase all of their amino acids prederivitized, if not preweighed. Anyone interested in actually performing the synthesis of these other amino acid derivatives should consult the proven methods published in the literature. A rather comprehensive table of these amino acid derivatives, showing all the relevant chemical structures and indicating stability of the reagents, is provided; however, because of its encyclopedic scope, the list includes many (older) derivatives of arguable utility to a modern peptide chemist. Propitiously, the text points out which of the derivatives are currently most popular and why.

Unfortunately, other aspects of this book are less praiseworthy. For example, the author presents a general discussion of protection schemes without going through an example of their application to peptide synthesis. Because there are only two (or possibly three) commonly used protection schemes, this laudable attempt at generalization is probably unnecessary. Still worse, the terms "temporary" versus "permanent" are terribly awkward. If the reader doesn't already understand the difference between these concepts, reading this section would probably only confuse him/her. I don't understand why the authors avoided the use of the customary terms "protection" (indicating "temporary" encryption of the amino terminus of the nascent peptide) and "blocking" (indicating "permanent" derivitization of the amino acid side chains).

The treatment of immunology is the book's worst feature and in places is offensively inaccurate. For example, in this section the critical difference between linear and non-linear epitopes is thoroughly obfuscated. The importance of solubility and lack of homopolymerization of peptide antigen in generation of strong immune response is incorrectly asserted as fiat. And the structural requirements for antibody-epitope binding are so poorly written that I couldn't tell whether they were actually inaccurate, except for one part. In that passage the author miserably distorts the paradigm of epitope binding reactions. He concludes by describing the binding of a MAb to two separate epitopes on the lysozyme molecule. The landmark paper he refers to actually depicts the binding of this Mab to a single discontinuous epitope. The difference between two separate epitopes and a single discontinuous epitope may seem subtle, but their confusion constitutes a grave error, and it hints at a lack of understanding of this important application of synthetic peptide chemistry.

The use of synthetic peptides in biomedical research is currently enjoying tremendous popularity. Many investigators choose to obtain peptides from outside laboratories, including commercial suppliers. These scientists need a source of information about the practical problems of the use of peptides in their research. This "user's guide" attempts to be such a source. The material it presents on synthesis pitfalls and on the interpretation of quality control data is accurate and quite practically useful. The discussions of issues collateral to peptide chemistry, however, must be read with a modicum of salt.

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