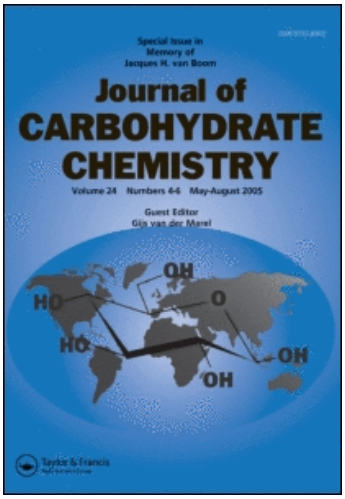

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BOOK REVIEW

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The concept of developing antisense therapeutic agents involves the inhibition of gene expression, at the message level, through the sequence specific binding of a synthetic drug analog to an RNA target. Seventeen years ago, the introduction of the antisense drug discovery approach was received with much interest and enthusiasm and has since generated a great deal of research activity principally in the area of modified oligonucleotides. The approach has been validated in a wide variety of experiments and is currently being used as an important tool in pharmacological and biochemical research. Furthermore, the value of antisense molecules as potential therapeutic agents is now well established and there are several drug molecules that have reached the level of human clinical trials. This book covers the most important current research efforts in carbohydrate chemistry required to develop new oligonucleotides from antisense applications. After a first overview chapter summarizing the synthetic methods and applications in antisense therapy the book includes three sections representing different structural modifications and a final three chapters covering miscellaneous subjects.

The first section covers nucleotides in which the phosphono linkages are replaced by other linkers such as amides, dialkylsiloxanes, sulfonic esters and amides as well as sulfides. The second section includes analogs in which the sugar component is modified while the third deals with modifications of the phosphodiester linkage. The last three chapters cover more diverse topics. One chapter discusses advances in the automated chemical synthesis of oligoribonucleotides while the second deals with the anti-HIV properties of some thiopurine-based oligonucleotides. The last chapter under the title "New Twists on Nucleic Acids" deals with the conformational properties of several oligonucleotides as determined from NMR and molecular mechanics data. An attempt is then made to correlate nucleotide conformations with the abilities of these molecules to form nucleotide duplexes. This approach is then used to identify the optimal features in the antisense oligomer required for interaction with a complimentary RNA target.

The book is generally well written and has a uniform and readable layout. It covers much of the relevant literature, but suffers from the usual shortcomings of multiauthored

publications being diffuse in content and somewhat disorganized. However, this should not detract from its value as a useful aid to all newcomers in the field and as a reference for chemists and biologists actively engaged in antisense research.

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