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## Nucleosides, Nucleotides and Nucleic Acids

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## Synthesis of Spirannic Nucleosides and Their Incorporation into Oligonucleotides

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## SYNTHESIS OF SPIRANNIC NUCLEOSIDES AND THEIR INCORPORATION INTO OLIGONUCLEOTIDES

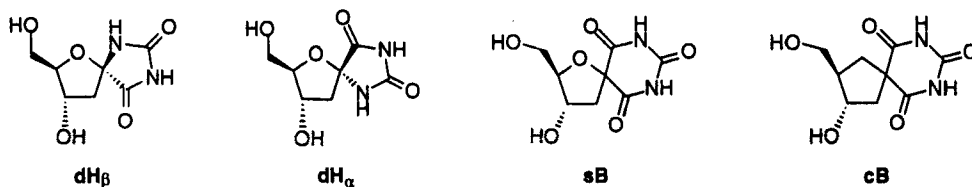
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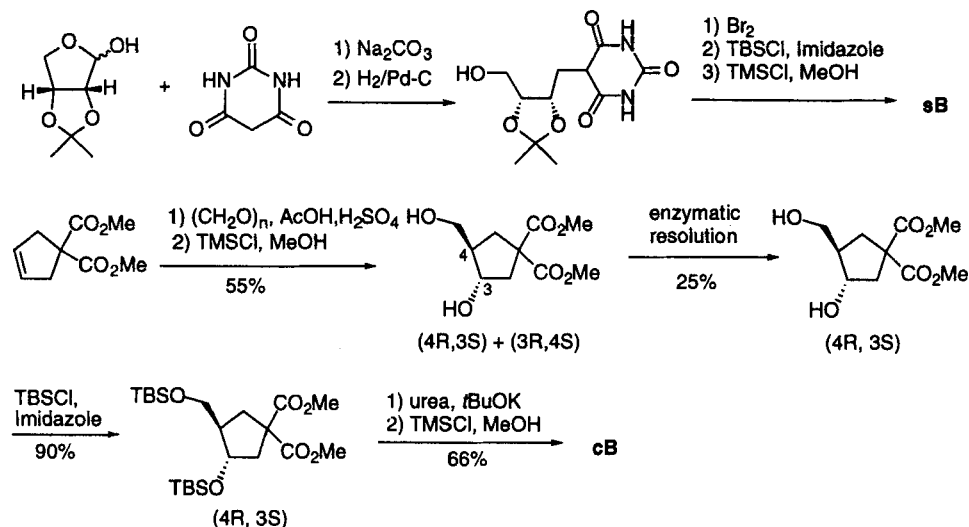
**ABSTRACT:** The spirannic nucleosides **dH<sub>α</sub>**, **dH<sub>β</sub>**, **sB** and **cB** were synthesized and incorporated into oligonucleotides using the cpg-oxalyl solid support strategy.

The ability of triplex forming oligonucleotides to recognize specific sequences of double stranded DNA can be used as a powerful means to control gene expression<sup>1</sup>. We designed a new type of chimeric oligonucleotides built from a track of spirannic nucleosides for the recognition of double stranded DNA sequences.

The hydantoin ring and the barbiturate ring are known to possess thymine-like hydrogen bonding capacity against adenine derivatives. These heterocycles were combined with the deoxyribose moiety or its carbocyclic analog to afford four spirannic nucleosides, 2'-deoxyhydantocidin (**dH<sub>β</sub>**), its C1'-epimer (**dH<sub>α</sub>**), 2'-deoxyribospiro barbiturate (**sB**) and carbaspispirobarbiturate (**cB**). These constrained units were chosen as target units to be incorporated into oligonucleotides. Indeed, according to preliminary molecular modeling study, a favorable preorganized geometry for triplex formation might be induced by incorporation of a continuous set of these spirannic units into oligonucleotides.



In a previous paper<sup>2</sup>, we described an efficient synthesis of 2'-deoxyhydantocidin (**dH<sub>β</sub>**) and its C1'-epimer (**dH<sub>α</sub>**). We newly developed stereocontrolled synthesis of the hitherto unknown spiro nucleosides **sB** and **cB** outlined in the following scheme.



#### Scheme Stereocontrolled Synthesis of **sB** and **cB**

We showed by  $^1\text{H}$  NMR spectroscopy that these spirannic nucleosides bind deoxyadenosine (diacetate) in organic solvent ( $\text{CDCl}_3$ ) with the spirobarbiturates showing the highest affinities. These spiro nucleosides turned out to be unstable in the alkaline conditions used for the final deprotection step in the conventional phosphoramidite approach. We circumvented this problem using a modified cpg-oxalyl solid support methodology<sup>3</sup>. We thus synthesized nine modified decamers  $\text{T}_4\text{YT}_5$ ,  $\text{T}_3\text{Y}_3\text{T}_4$  and  $\text{TY}_8\text{T}$  ( $\text{Y} = \text{dH}_\alpha$ , **dH<sub>β</sub>** or **cB**)<sup>4,5</sup>. The hybridization properties of these oligomers are currently under study.

#### REFERENCES

- (1) (a) Thuong, N. T.; Hélène, C. *Angew. Chem. Int. Ed. Engl.*, **1993**, 32, 666-690. (b) Soyfer, V. N.; Potaman, V. N. "Triple-Helical Nucleic Acids", Springer-Verlag New York, **1996**.
- (2) Renard, A.; Kotera, M.; Lhomme, J. *Tetrahedron Lett.*, **1998**, 39, 3129-3132.
- (3) Alul, H. R.; Cingman, C. N.; Zhang, G.; Letsinger, R. L. *Nucleic Acids Res.*, **1991**, 19, 1527-1532.
- (4) The deoxyribospiro barbiturate (**sB**) is too unstable to be incorporated into oligonucleotides.
- (5) The purity of oligomers was verified by HPLC and the successful incorporation in the case of three 8 units-incorporated decamers ( $\text{TY}_8\text{T}$ ) was confirmed by NMR analysis.