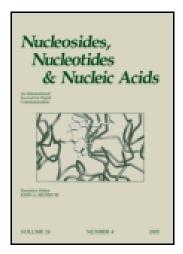
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Oligonucleotides Incorporating N⁷-(2'-Deoxy-β-d-erythro-pentofuranosyl)isoguanine

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Oligonucleotides Incorporating N^7 -(2'-Deoxy- β -Deoxy-pentofuranosyl)isoguanine

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ABSTRACT

The H-phosphonate and the phosphoramidite of N^7 -2'-deoxyisoguanosine (2) were prepared and incorporated into oligonucleotide duplexes. Their base pairing properties were investigated and compared with those of the parent purine nucleosides.

Oligonucleotides incorporating 2'-deoxyisoguanosine (1a) and its 7-deaza derivatives 1b,c as well as the N^7 -glycosylated adenine or guanine form stable duplex structures with parallel and antiparallel chain orientation. Now, the N^7 -(2'-deoxy- β -D-erythro-pento-furanosyl) isoguanine (2) was studied. The phosphoramidite 3 was prepared and employed in solid-phase oligonucleotide synthesis. Apart from this corresponding N^7 - nucleosides such as the methylthio derivative 4 were synthesized.

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Earlier, the synthesis of **2** was reported by our laboratory. [2] Its H-phosphonate was successfully employed in oligonucleotide synthesis. However, the application of phosphoramidite chemistry failed. Thus, the 2-oxo function of **2** was protected with the DPC-group ($\mathbf{5} \rightarrow \mathbf{6}$) and the dimethylaminomethylidene residue was used for aminogroup protection. Compound **6** was converted into the DMT-derivative **7** and subsequently into the phosphoramidite **3**.

Oligonucleotide duplexes containing **2** were prepared and hybridized with complemen-tary strands incorporating dA, dC and dT (data not shown) or $dG/^{5Me}iC_d$ opposite to 7iG_d .

From the T_m measurements it can be concluded, that only 2'-deoxyguanosine forms a strong base pair with **2**. Nevertheless, the stability of this base pair depends on the position of incorporation. It is not clear if this new base pair adopts a Watson-Crick or a Hoogsteen-motif. As it is weaker than a dG-dC pair only two hydrogen bonds are expected. As N^7G_d forms strong triplex structures^[3] similar results can be expected for compound **2**, also the formation of tetrameric structures has to be considered.

Table 1. T_m -values of oligonucleotide duplexes containing 7iG_d (2).

Duplex	$T_m [^{\circ}C]$	Duplex	$T_m \ [^{\circ}C]$
5'-d(TAGGTCAATACT) 3'-d(ATCCAGTTATGA)	51	5'-d(TAGGT G AATACT) 3'-d(ATCCA ⁷ iG TTATGA)	36
5'-d(TAG ⁷ iG ACAATACT) 3'-d(ATC G T GTTATGA)	44	5'-d(TAGGT i CAATACT) ^b 3'-d(ATCCA ⁷ iG TTATGA)	32

^aMeasured in 1 M NaCl, 0.1 M MgCl₂, 60 mM Na-cacodylate, pH 7.

 $^{^{}b}d(iC) = 5$ -methyl-2'-deoxyisocytidine.

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