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

P. Leonard^a; R. Kröschel^a; F. Seela^{ab}

^a Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Osnabrück, Germany ^b Organische Chemie und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Osnabrück, Germany

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

P. Leonard, R. Kröschel, and F. Seela*

Laboratorium für Organische und Bioorganische Chemie
Institut für Chemie, Universität Osnabrück,
Osnabrück, Germany

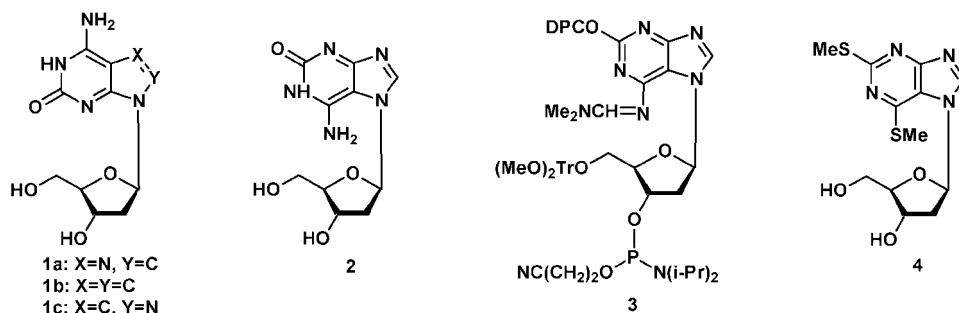
ABSTRACT

The H-phosphonate and the phosphoramidite of N⁷-2'-deoxyisoguanosine (**2**) were prepared and incorporated into oligonucleotide duplexes. Their base pairing properties were investigated and compared with those of the parent purine nucleosides.

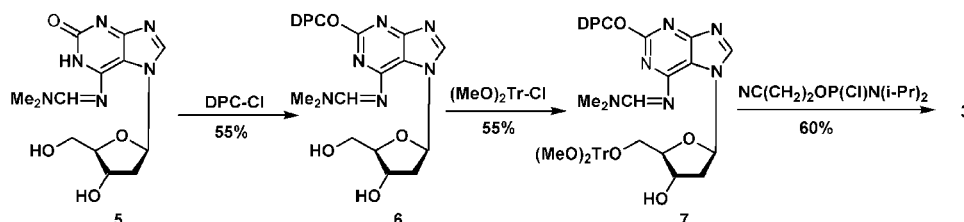
Oligonucleotides incorporating 2'-deoxyisoguanosine (**1a**) and its 7-deaza derivatives **1b,c** as well as the N⁷-glycosylated adenine or guanine form stable duplex structures with parallel and antiparallel chain orientation.^[1a–c] Now, the N⁷-(2'-deoxy-β-D-erythro-pento-furanosyl) isoguanine (**2**) was studied. The phosphoramidite **3** was prepared and employed in solid-phase oligonucleotide synthesis. Apart from this corresponding N⁷- nucleosides such as the methylthio derivative **4** were synthesized.

*Correspondence: F. Seela, Organische Chemie und Bioorganische Chemie, Institut für Chemie, Universität Osnabrück, Barbarastrasse 7, D-49069 Osnabrück, Germany; Fax: +49 541 969 2370; E-mail: frank.seela@uni-osnabrueck.de.





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 (**5** → **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 complementary strands incorporating dA, dC and dT (data not shown) or dG/⁵Me₂iC_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 N⁷G_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**).^a

Duplex	<i>T_m</i> [°C]	Duplex	<i>T_m</i> [°C]
5'-d(TAGGTCAATACT)	51	5'-d(TAGGTGAATACT)	36
3'-d(ATCCAGTTATGA)		3'-d(ATCCA ⁷ iGTTATGA)	
5'-d(TAG ⁷ iGACAATACT)	44	5'-d(TAGGT iCAATACT) ^b	32
3'-d(ATC G T GTTATGA)		3'-d(ATCCA ⁷ iGTTATGA)	

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

^bd(iC) = 5-methyl-2'-deoxyisocytidine.

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