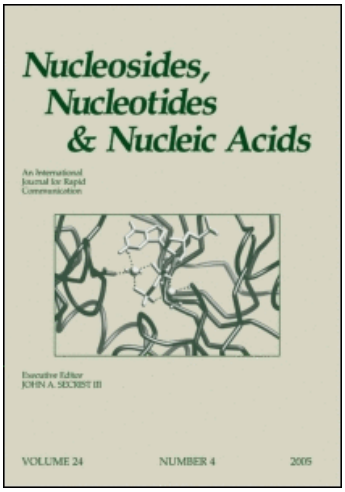

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Oligonucleotides Incorporating N^7-(2'-Deoxy-β-d-erythro-pentofuranosyl)isoguanine

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 N^7-(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 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.[1a–c] 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.

*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.

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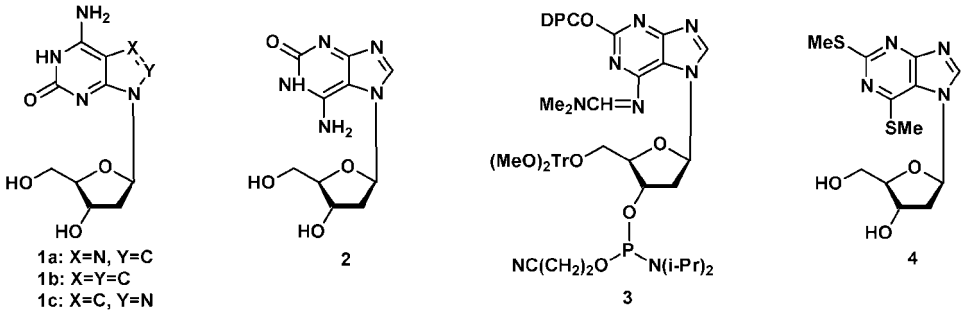
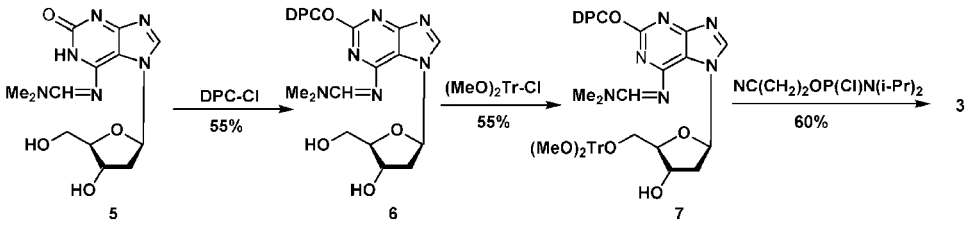


Earlier, the synthesis of **2** was reported by our laboratory.[2] Its H-phosphonate was successfully employed in oligonucleotide synthesis. However, the application of phosphoramidite chemistry failed. Thus, the 2-oxo function of **2** was protected with the DPC-group (**5** → **6**) and the dimethylaminomethylidene 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 complemen-tary strands incorporating dA, dC and dT (data not shown) or dG/^{5Me}iC$_d$ opposite to ^{7}iG$_d$.

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^{7}G$_d$ 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 ^{7}iG$_d$ (2).[a]

Duplex	T_m [°C]	Duplex	T_m [°C]
5′-d(TAGGTCAATACT) 3′-d(ATCCAGTTATGA)	51	5′-d(TAGGT**G**AATACT) 3′-d(ATCCA^{7}**i**GTTATGA)	36
5′-d(TAG^{7}**i**GACAATACT) 3′-d(ATC **G** T GTTATGA)	44	5′-d(TAGGT **i**CAATACT)[b] 3′-d(ATCCA^{7}**i**GTTATGA)	32

[a]Measured in 1 M NaCl, 0.1 M $MgCl_2$, 60 mM Na-cacodylate, pH 7.
[b]d(iC) = 5-methyl-2′-deoxyisocytidine.

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