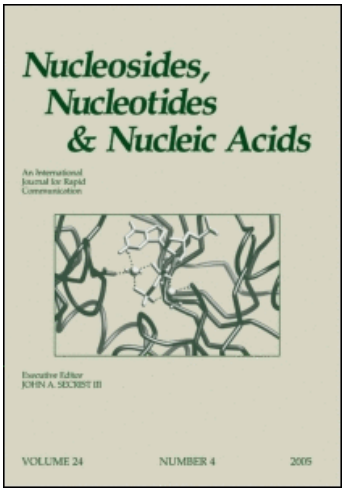


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# Oligomers Containing 2'-Deoxyinosine Isosteres as Ambiguous Nucleoside or 1,3-Propanediol as Nucleoside Substitute

Frank Seela[a]; Klaus Kaiser[a]
[a] Laboratorium für Organische und Bioorganische Chemie Fachbereich Biologie/Chemie, Universitat Osnabrvick, Osnabriick

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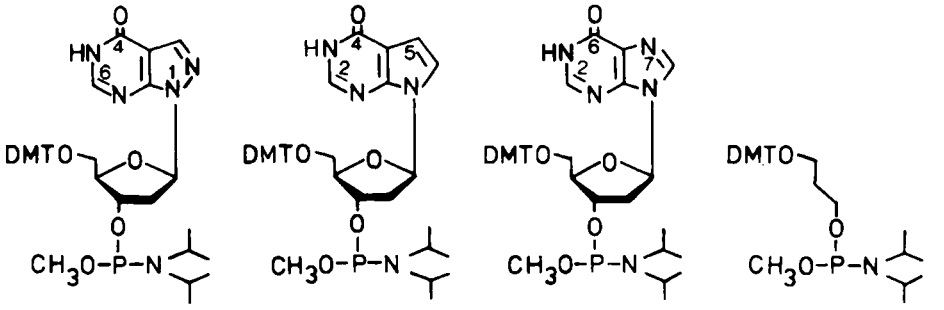
# OLIGOMERS CONTAINING 2'-DEOXYINOSINE ISOSTERES AS AMBIGUOUS NUCLEOSIDE OR 1,3-PROPANEDIOL AS NUCLEOSIDE SUBSTITUTE

Frank Seela* and Klaus Kaiser

Laboratorium für Organische und Bioorganische Chemie
Fachbereich Biologie/Chemie, Universität Osnabrück
D-4500 Osnabrück

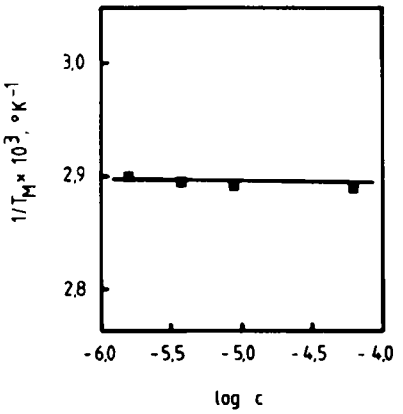


Three new appropriately protected phosphoramidites have been synthesized. Two of them (1 and 2) are isosteric to that of inosine (3) [1], one is a derivative of 1,3-propanediol (4). Whereas the inosine isosteres contain an ambiguous base recognizing adenine, guanine as well as cytosine residues in double stranded DNA-fragments the 1,3-propanediol unit can be seen as a simple nucleoside substitute in a DNA chain. It contains only those structural elements necessary to form the sugar/phosphate backbone, without supplying the DNA with either a base [2] or a 2'-deoxyribofuranosyl moiety.



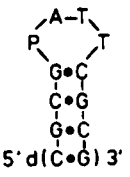

1 2 3 4

The phosphoramidites 1-4 have been employed in solid phase synthesis [3] of deoxyoligonucleotides. Self-complementary hexamers of the sequence d(GCI*CGC) (5-7) have been




d(CGCGPATTCGCG) d(CGCGAAPTCGCG)

9 10




IX

Figure 1. Plot of $1/T_m$ vs. log c for the oligomer 9



synthesized and were compared with the parent oligomer 8 with respect to duplex stability.

d(GCc$^7$z$^8$ICGC) d(GCc$^7$ICGC) d(GCICGC) d(GCGCGC)

5 6 7 8

Melting experiments show, that all three oligomers exhibited a lower $T_m$ than that of $[d(GpC)_3]_2$. From thermodynamic data of these alternating hexamers it was shown that allopurinol 2'-deoxyribofuranoside destabilizes such duplexes less strongly than 2'-deoxyinosine.

The 1,3-propanediol unit (P) was incorporated into different positions of the "Dickerson" dodecamer [4] by solid phase synthesis in an automatic DNA-synthesizer. Concentration dependend melting experiments of the modified dodecamer 9 show that these oligomers tend to form hairpin structures (IX) under appropriate salt conditions (see Figure 1).

Unexpected results were obtained from the cleavage pattern of the oligomers 9 and 10 by enzymatic hydrolysis with snake venom phosphodiesterase. This enzyme hydrolyzed all phosphodiesterbounds of the oligomers 9 and 10 except those between pGpP or pApP. As a result dimers such as ApP or GpP were detected (HPLC) after subsequent treatment with alkaline phosphatase.

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