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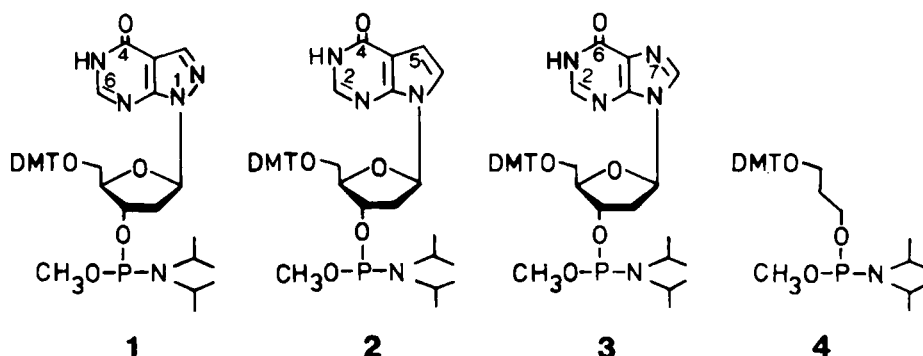
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OLIGOMERS CONTAINING 2'-DEOXYINOSINE ISOSTERES AS AMBIGUOUS
NUCLEOSIDE OR 1,3-PROPANEDIOL AS NUCLEOSIDE SUBSTITUTE

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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.



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

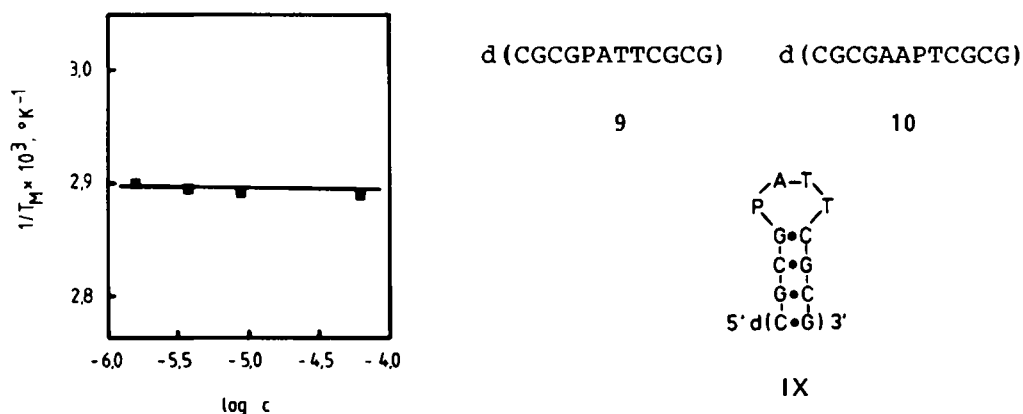
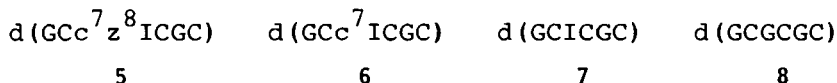


Figure 1. Plot of $1/T_m$ vs. $\log c$ for the oligomer 9

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



Melting experiments show, that all three oligomers exhibited a lower T_m than that of $[\text{d}(\text{GpC})_3]_2$. 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 dependent 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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