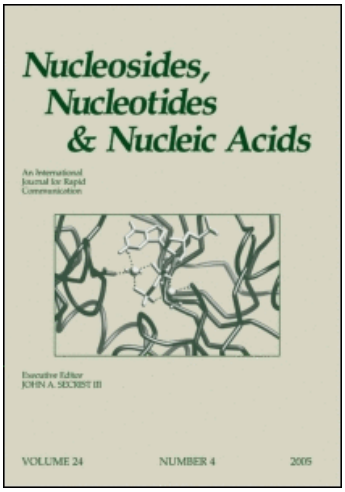

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The Incorporation of 2,6-Diaminopurine Into Oligodeoxyribonucleotides by the Phosphoramidite Method

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THE INCORPORATION OF 2,6-DIAMINOPURINE INTO OLIGODEOXYRIBONUCLEOTIDES BY THE PHOSPHORAMIDITE METHOD

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Abstract. A method has been developed to allow the synthesis of oligodeoxyribonucleotides containing 2,6-diaminopurine and avoiding depurination.

As part of a programme examining the factors affecting DNA duplex structure and stability we have recently synthesised a series of oligodeoxyribonucleotides containing the base analogue 2,6-diaminopurine A' (2-aminoadenine).

The incorporation of 2,6-diaminopurine into synthetic DNA is of interest due to the manner in which it forms base pairs with T. The replacement of A with A' increases base pair stability by virtue of an additional hydrogen bond between N2 of A' and O2 of T. This extra hydrogen bond gives A' containing sequences practical uses as sequence specific gene probes of high discrimination and stability.

Synthesis of such sequences by the phosphoramidite method is subject to a major side reaction,acid catalysed depurination of A' and subsequent chain scission during detritylation of the 5' hydroxyl terminus. The rate of depurination[1] is dependent on the choice of N6 protection as has been noted for A[1]. The process is accelerated by the use of electron withdrawing substituents to protect N6.

We investigated di-n-butylformamidine as possible N6 protection for A.

We have confirmed that the use of di-n-butylformamidine as N6 protection for cyanoethyl phosphoramidites allows the routine synthesis of A' containing oligodeoxyribonucleotides with high coupling efficiency and product quality.

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