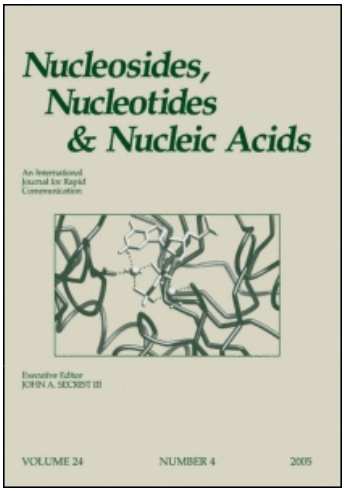

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8-Aza-7-deazapurine DNA: Synthesis and Duplex Stability of Oligonucleotides Containing 7-Substituted Bases

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8-AZA-7-DEAZAPURINE DNA: SYNTHESIS AND DUPLEX STABILITY OF OLIGONUCLEOTIDES CONTAINING 7-SUBSTITUTED BASES

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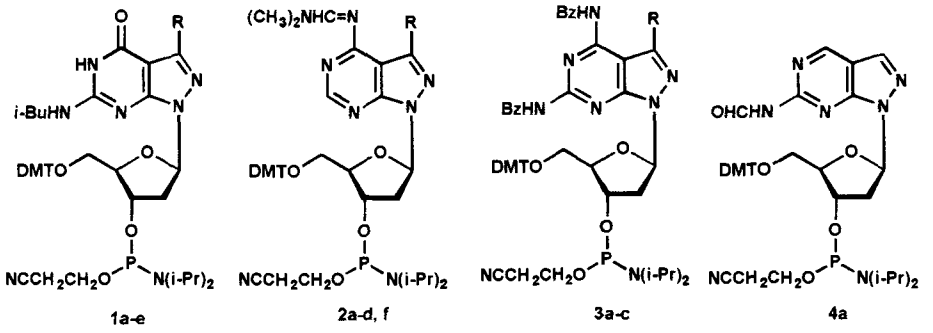
ABSTRACT: The 7-substituted 8-aza-7-deazapurine phosphoramidites **1a - 3c** as well as the phosphoramidite **4a** were synthesized. In comparison to the parent purine oligonucleotide duplexes, the 7-substituted 8-aza-7-deazapurine residues lead to a significant duplex stabilization.



For the synthesis of the corresponding 8-aza-7-deazapurine nucleosides related to **1a - c, 1e** and **2a - c** see [1-3]. The nucleosides related to **1d ,2d** and **2f** were obtained by the cross-coupling reaction on the 7-iodo precursor compounds with either hex-1-yne or phenylacetylene. According to the Table 8-aza-7-deazaguanine (→**1a**) already stabilizes the duplex compared to the parent guanine, whereas 8-aza-7-deazaadenine (→**2a**) does

Table. T_m-Values of Oligonucleotides [a,b])

Oligodeoxynucleotide	T_m [°C]	Oligodeoxynucleotid	T_m [°C]
5'-d(TAGGTCAATACT) d(ATCCAGTTATGA)- 5'	46	5'-d(T**2a**GGTC**2a2a**T**2a**CT) d(ATCC**2a**GTT**2a**TGA)- 5'	47
5'-d(TA**1a1a**TCAATACT) d(ATCCA**1a**TTAT**1a**A)- 5'	51	5'-d(T**2b**GGTC**2b2b**T**2b**CT) d(ATCC**2b**GTT**2b**TGA)- 5'	57
5'-d(TA**1b1b**TCAATACT) d(ATCCA**1b**TTAT**1b**A)- 5'	55	5'-d(T**2c**GGTC**2c2c**T**2c**CT) d(ATCC**2c**GTT**2c**TGA)- 5'	58
5'-d(TA**1c1c**TCAATACT) d(ATCCA**1c**TTAT**1c**A)- 5'	55	5'-d(T**2d**GGTC**2d2d**T**2d**CT) d(ATCC**2d**GTT**2d**TGA)- 5'	58
5'-d(TA**1d1d**TCAATACT) d(ATCCA**1d**TTAT**1d**A)- 5'	53	5'-d(T**3a**GGTC**3a3a**T**3a**CT) d(ATCC**3a**GTT**3a**TGA)- 5'	57
5'-d(TA**1e1e**TCAATACT) d(ATCCA**1e**TTAT**1e**A)- 5'	60	5'-d(T**4a**GGTC**4a4a**T**4a**CT) d(ATCC**4a**GTT**4a**TGA)- 5'	41

[a]) 10 mM Na-cacodylate, 10 mM $MgCl_2$, 0.1 M NaCl, pH 7. [b]) The numbers refer to the phosphoramidites used in the oligonucleotide synthesis.

not show this stabilization. Halogeno-, alkynyl-, and alkyl- [4-6] substituents in position 7 increase the T_m-value of oligonucleotides significantly. Incorporation of **1b - e** and **2b -d, f** enhance the T_m by about 2°C per residue [5,6]. The strongest increase was found for the derivative **1e** (4°C per residue). When **3a-c** were employed the T_m-value was raised by 2 - 4°C per residue. The phosphoramidite **4a** leads to duplexes which are destabilized. The B-DNA structure is retained in the case of the duplexes, which is shown by CD-spectroscopy. The nucleosides of **2f** and **4a** show strong fluorescence, while those of **1a - e**,**2a - d**, and **3a -c** are only minimal fluorescent. Treatment of the parent nucleosides of **3a - c** with adenosine deaminase converted only **3a** into the guanine derivative, while the halogeno-substituted compounds are resitent.

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