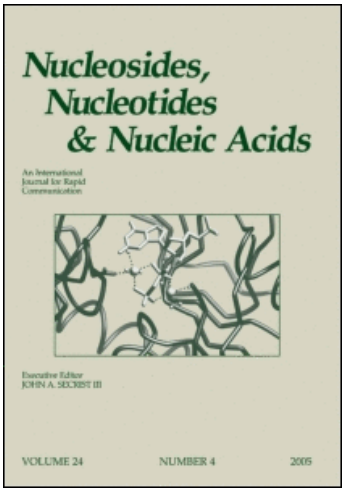

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7-Deaza-2'-deoxyguanosines Functionalized with 7-(ω-Aminoalk-1-YNYL) Residues

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7-DEAZA-2'-DEOXYGUANOSINES FUNCTIONALIZED WITH 7-(ω-AMINOALK-1-YNYL) RESIDUES

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ABSTRACT: The Pd(0)-catalyzed cross coupling reaction of 7-iodo-7-deaza-2'-deoxyguanosine (**1**, $I^7c^7G_d$) with the phthalimido-protected ω-aminoalkines **2a-c** gave the compounds **3a-c**. They were converted into the phosphoramidite building block **4a-c** as well as the phosphonates **5a-c**. Compounds **4a** and **4c** were incorporated into oligodeoxynucleotides of different sequence and their duplex stabilities were measured and compared with those of the unmodified counterparts.

The preparation of amino-functionalized oligonucleotides and their labeling with reporter groups has become an important tool of nucleic acid diagnostics. The incorporation of 7-substituents into 7-deaza-2'-deoxyguanosine is well accommodated in oligonucleotide duplexes [1]. Here, we report on the synthesis of the 7-(ω-aminoalk-1-ynyl)-7-deaza-2'-deoxyguanosines **4a-c** and their incorporation into oligonucleotides of different sequences.

The key reaction towards compounds **3a-c** and their building blocks for solid phase oligonucleotide synthesis is the Pd(0)-catalyzed cross coupling reaction of 7-iodo-7-deaza-2'-deoxyguanosine (**1**) [2] with the phthalimido-protected ω-aminoalkines **2a-c** under formation of **3a-c** [3]. They were converted into the phosphoramidites **5a-c** [3] and the phosphonates **6a-c** using isobutyryl as NH_2- and dimethoxytrityl as 5'-OH protecting groups.

The replacement of dG by **4a** in an alternating sequence causes a T_m increase of 12° while the incorporation of **4c** prevents duplex formation. Contrary, the replacement of four dG's in a random sequence by either **4a** or **4c** does not alter the duplex stability.

Compounds **5,6a-c** are useful for the preparation of NH_2-functionalized oligonucleotides with respect to the oligonucleotide stability and probably also to a subsequent

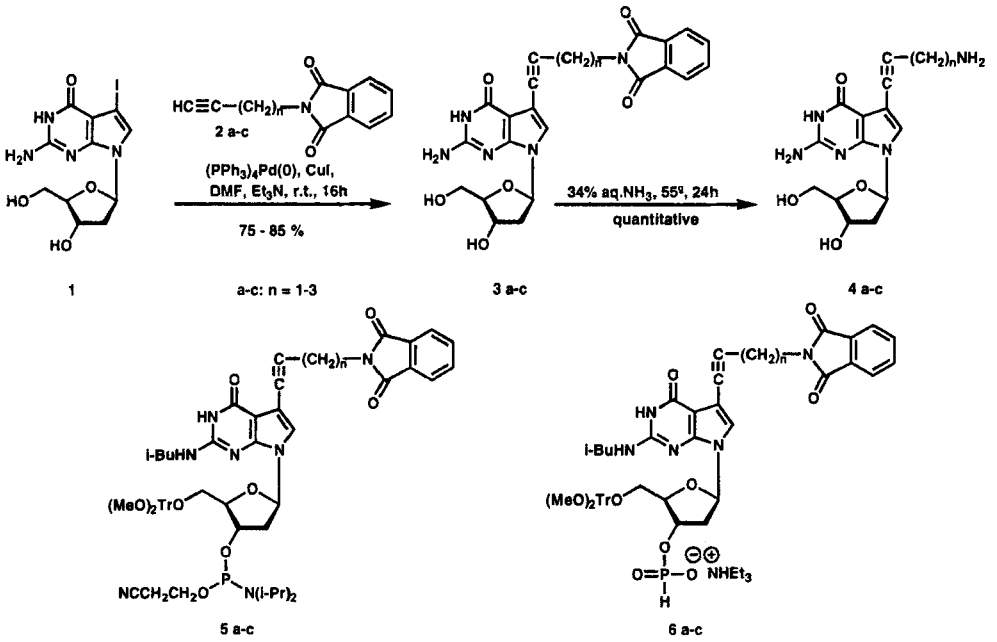

Table. T_m-Values of Oligomers in 10 mM Na-cacodylate, 0.1M NaCl, 10 mM $MgCl_2$.

Oligodeoxynucleotide	T_m [°C]	Oligodeoxynucleotide	T_m [°C]
5'-d(G-C)$_4$	60 [1]	5'-d((TAc^{7}Gc^{7}GTCAATACT)	
5'-d(c^{7}G-C)$_4$	53 [1]	d(ATCCAc^{7}GTTATc^{7}GA)-5'	44 [1]
5'-d(**4a**-C)$_4$	72	5'-d(TA**4a4a**TCAATACT)	
5'-d(**4c**-C)$_4$	-	d(ATCCA**4a**TTAT**4a**A)-5'	51
5'-d(TAGGTCAATACT)		5'-d(TA**4c4c**TCAATACT)	
d(ATCCAGTTATGA)-5'	47 [1]	d(ATCCA**4c**TTAT**4c**A)-5'	48

post-labeling [4] with an activated reporter group. However, depending on the sequence, already small variations of the spacer length are of critical importance.

REFERENCES AND NOTES

1 Ramzaeva, N, Mittelbach, C, Seela, F., *Helv. Chim. Acta* **1997**, *80*, 1809-1822.

2 Ramzaeva, N., Seela, F., *Helv. Chim. Acta* **1995**, *78*, 1083-1090.

3 **3a**: ^{1}H-NMR (D_6DMSO): δ, 2.07 (1H, m, $H_α$-2'), 2.29 (1H, m, $H_β$-2'), 3.49 (2H, m, H_2-5'), 3.75 (1H, m, H-4'), 4.27 (1H, m, H-3'), 4.59 (2H, s, CH_2), 4.87 (1H, t, 5'-OH), 5.18 (1H, d, 3'-OH), 6.26 (1H, "t", H-1'), 6.31 (2H, s, NH_2), 7.26 (1H, s, H-6), 7.87-7.94 (4H, m, Pht), 10.45 ppm (1H, s, NH).
5a: ^{31}P-NMR ($CDCl_3$): δ, 148.2, 148.6 ppm.

4 Cook, A. F., Vuocolo, E., Brakel, C. L., *Nucleic Acids Res.* **1988**, *16*, 4077-4095.