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## Nucleosides, Nucleotides and Nucleic Acids

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### 7-Deaza-2'-deoxyguanosines Functionalized with 7-( $\omega$ -Aminoalk-1-YNYL) Residues

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## 7-DEAZA-2'-DEOXYGUANOSINES FUNCTIONALIZED WITH 7-( $\omega$ -AMINOALK-1-YNYL) RESIDUES

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**ABSTRACT:** The Pd(0)-catalyzed cross coupling reaction of 7-iodo-7-deaza-2'-deoxyguanosine (**1**,  $I^{7c^{7}G_d}$ ) with the phthalimido-protected  $\omega$ -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 <sup>1</sup>. Here, we report on the synthesis of the 7-( $\omega$ -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**) <sup>2</sup> with the phthalimido-protected  $\omega$ -aminoalkines **2a-c** under formation of **3a-c** <sup>3</sup>. They were converted into the phosphoramidites **5a-c** <sup>3</sup> and the phosphonates **6a-c** using isobutyryl as NH<sub>2</sub>- and dimethoxytrityl as 5'-OH protecting groups.

The replacement of dG by **4a** in an alternating sequence causes a T<sub>m</sub> 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<sub>2</sub>-functionalized oligonucleotides with respect to the oligonucleotide stability and probably also to a subsequent

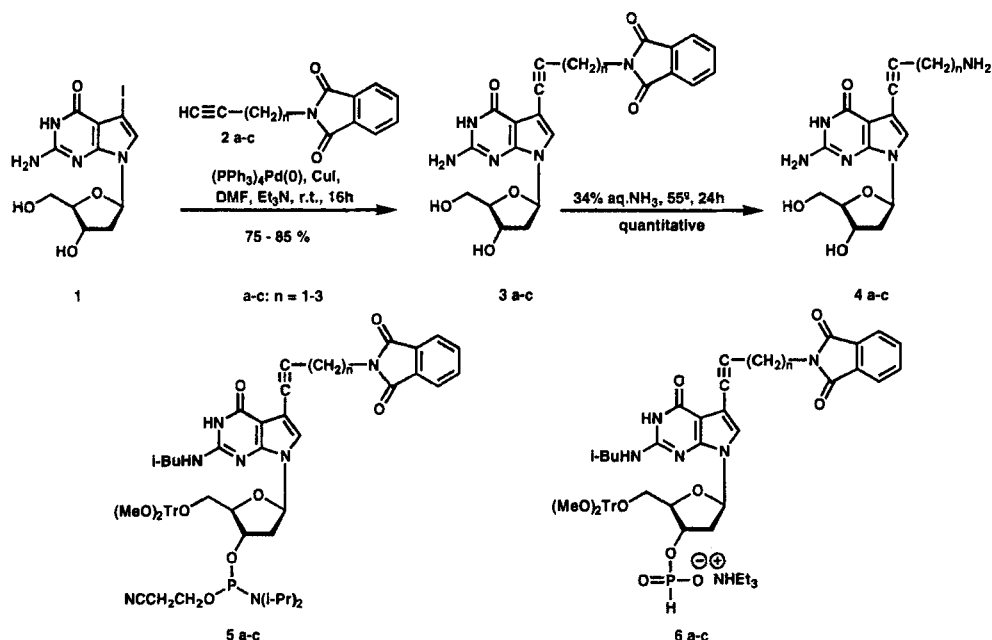


Table. T<sub>m</sub>-Values of Oligomers in 10 mM Na-cacodylate, 0.1M NaCl, 10 mM MgCl<sub>2</sub>.

Oligodeoxynucleotide	T <sub>m</sub> [°C]	Oligodeoxynucleotide	T <sub>m</sub> [°C]
5'-d(G-C) <sub>4</sub>	60 <sup>1</sup>	5'-d((TAc <sup>7</sup> Gc <sup>7</sup> GTCAATACT)	
5'-d(c <sup>7</sup> G-C) <sub>4</sub>	53 <sup>1</sup>	d(ATCCAc <sup>7</sup> GTTATc <sup>7</sup> GA)-5'	44 <sup>1</sup>
5'-d(4a-C) <sub>4</sub>	72	5'-d(TA4a4aTCAATACT)	
5'-d(4c-C) <sub>4</sub>	-	d(ATCCA4aTTAT4aA)-5'	51
5'-d(TAGGTCAATACT)		5'-d(TA4c4cTCAATACT)	
d(ATCCAGTTATGA)-5'	47 <sup>1</sup>	d(ATCCA4cTTAT4cA)-5'	48

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

## REFERENCES AND NOTES

- Ramzaeva, N, Mittelbach, C, Seela, F., *Helv. Chim. Acta* **1997**, *80*, 1809-1822.
- Ramzaeva, N., Seela, F., *Helv. Chim. Acta* **1995**, *78*, 1083-1090.
- 3a**: <sup>1</sup>H-NMR (D<sub>6</sub>DMSO): δ, 2.07 (1H, m, H<sub>α</sub>-2'), 2.29 (1H, m, H<sub>β</sub>-2'), 3.49 (2H, m, H<sub>2</sub>-5'), 3.75 (1H, m, H-4'), 4.27 (1H, m, H-3'), 4.59 (2H, s, CH<sub>2</sub>), 4.87 (1H, t, 5'-OH), 5.18 (1H, d, 3'-OH), 6.26 (1H, "t", H-1'), 6.31 (2H, s, NH<sub>2</sub>), 7.26 (1H, s, H-6), 7.87-7.94 (4H, m, Pht), 10.45 ppm (1H, s, NH).
- 5a**: <sup>31</sup>P-NMR (CDCl<sub>3</sub>): δ, 148.2, 148.6 ppm.
- Cook, A. F., Vuocolo, E., Brakel, C. L., *Nucleic Acids Res.* **1988**, *16*, 4077-4095.