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# Nucleosides and Nucleotides

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Oligonucleotides Containing Consecutive 2'-Deoxy-Isoguanosine Residues: Synthesis, Parallel Duplex Formation and Identification of a  $d(T_4iG_4T_4)$  Tetraplex

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### OLIGONUCLEOTIDES CONTAINING CONSECUTIVE 2'-DEOXY-ISOGUANOSINE RESIDUES: SYNTHESIS, PARALLEL DUPLEX FORMATION AND IDENTIFICATION OF A $d(T_4iG_4T_4)$ TETRAPLEX

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ABSTRACT: Oligonucleotides containing consecutive 2'-deoxyisoguanosines were synthesized by using building blocks protected with a diphenylcarb-amoyl residue. Parallel duplexes were formed by  $iG_d$ -dC base pairs and a tetraplex of  $d(T_4iG_4T_4)$  was identified by ion exchange HPLC.

The 2-oxo group of 2'-deoxyisoguanosine ( $iG_d$ ) shows a higher reactivity than that of 2'-deoxyguanosine and the 6-amino group is difficult to acylate.<sup>1</sup> The nucleoside is very labile at the glycosylic bond. This encounters problems during oligonucleotide synthesis. The diphenylcarbamoyl (DPC) group which has been used for the protection of guanosine<sup>2</sup> is now applied for the protection of the 2oxo groups of 2'-deoxyisoguanosine<sup>3</sup> and 7-deaza-2'-deoxyisoguanosine ( $c^7iG_d$ ) (Scheme 1). Thus, the DPC-protected building blocks **1a**, **b** and **2a**, **b** were



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Scheme 2

synthesized as well as the 2-oxo unprotected compounds **3a**, **b** were prepared. It was found that oligonucleotides containing consecutive isoguanine residues requires oxo group protection.

Alternatively, the allyl group, which has been used for protection of the oxo group of isoguanine pyranosylnucleoside,<sup>4</sup> was investigated to block the 2-oxo group (compounds **4a**, **b** and Scheme 2).

It was reported that 2'-deoxyisoguanosine forms a base pair with 2'-deoxycytidine (dC).<sup>5</sup> In order to investigate this matter a series of oligonucleotides (Table) either containing iG<sub>d</sub> or c<sup>7</sup>iG<sub>d</sub>-residues were prepared. The self-complementary oligomers 5'-d(iG-C)<sub>3</sub> and 5'-d(C-iG)<sub>3</sub> show T<sub>m</sub>-values below 17°C. This points to incomplete hybridization of only 3 iG<sub>d</sub>-dC base pairs. When a hybrid was formed between 5'-d(iG-C)<sub>3</sub> and 5'-d(C-iG)<sub>3</sub> the T<sub>m</sub>-value was increased by 30°C (Table).

	<b>_</b>	
Duplexes	bp <sup>b</sup>	T <sub>m</sub> [°C]
[5' d(iGCiGCiGC)] <sub>2</sub>	5	31
[5' d(iGiGiGCCC)]₂	3	17
[5' d(CCCiGiGiG)]₂	3	16
5' d(CCCiGiGiG) 5' d(iGiGiGCCC)	6	47
[5' d(igCigCigC)]2 <sup>b</sup>	5	22

Table. T<sub>m</sub>-Values of Oligonucleotides<sup>a</sup>

<sup>a</sup> Measured in 1 M NaCl, 0.1M MgCl<sub>2</sub>, 60 mM Na-cacodylate buffer, pH 7.0. Oligonucleotide concentration was 10 μM.

<sup>b</sup> bp = the number of base pairs;  $ig = c^7 iG$ .



isoG<sub>d</sub>-dC

parallel strands

5'	т	т	т	т	т	3'
5'	Т	1	L	1	T	3'

Scheme 3



**Figure 1**. Ion exchange HPLC profiles of  $d(T_4iG_4T_4)$  (**a**) and  $d(T_4G_4T_4)$  (**b**) at 30°C. Tetrameric structure of  $d(T_4iG_4T_4)$  (**c**).

According to these observations the chain orientation is parallel. As the oligomer containing  $c^7iG_d$  and dC also formed a duplex Watson-Crick base pairing was established (Scheme 3).

Apart from the pairing with complementary bases an isoG-quartet structure has been proposed by Shugar<sup>6</sup> and others.<sup>7</sup> Nevertheless, a tetrameric species of  $iG_d$ -rich oligonucleotides has not been identified. Recently, the oligonucleotide  $d(T_4iG_4T_4)$  was synthesized and applied to ion-exchange HPLC. Two well separated peaks were observed (Figure 1a). The fast migrating peak belongs to the single-stranded oligomer while the slow migrating peak represents an aggregate. The same experiments were also performed on the oligomer  $d(T_4G_4T_4)$ . The chromatographic behavior of  $iG_d$ -aggregate is almost identical to that of  $d(T_4G_4T_4)$  (Figure 1b). As it is well established that ion-exchange HPLC discriminates molecules by the number of charges of the sugar-phosphate

backbone the aggregates of dG and  $iG_d$  have to show a similar structure. As  $d(T_4G_4T_4)$  forms a tetramer the  $d(T_4iG_4T_4)$  aggregate is also a tetramer. This experiment is the first example demonstrating the formation of a defined tetraplex species in the case of isoguanine-containing oligonucleotides. One possible tetraplex structure is shown in Figure 1c, which basses on measurements performed recently on monomeric isoguanosine.<sup>7</sup>

#### REFERENCES

- 1. Seela, F.; Wei, C.; Kazimierczuk, Z. Helv. Chim. Acta 1995, 78, 1843.
- Kamimura, T.; Tsuchiya, M.; Koura, K.; Sekine, M.; Hata, T. Tetrahedron Lett. 1983, 24, 2775.
- 3. Seela, F.; Chen, Y.; Melenewski, A.; Rosemeyer, H.; Wei, C. *Acta Biochim. Pol.* **1996**, *43*, 45.
- Pitsch, S.; Krishamurthy, R.; Bolli, M.; Wendeborn, S.; Holzner, A.; Mirton, M.; Lesueuer, C.; Schlönvogt, I.; Jaun, B.; Eschenmoser, A. *Helv. Chim. Acta* 1995, *78*, 1621 and private communication of Prof. Dr. A. Eschenmoser and Dr. J. Hunziker.
- 5. Seela, F.; Gabler, B.; Kazimierczuk, Z. Collect. Czech. Commun. 1993, 58, 170.
- Golas, T.; Fikus, M.; Kazimierczuk, Z.; Shugar, D. Eur. J. Biochem. 1976, 65, 183.
- Davis, J. T.; Tirumala, S.; Jenssen, J. R.; Radler, E.; Fabris, D. J. Org. Chem. 1995, 60, 4167.

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