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Original Scientific Paper

The Synthesis and Hybridization Studies of Oligodeoxyribonucleotides Containing the 2'-Deoxyguanosine Modification, 8-Aza-3-deaza-2'-deoxyguanosine

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Chemical and physical properties of the modified nucleoside 8-aza-3-deaza-2'-deoxyguanosine (**1**) are described. From the amino protected nucleoside **1a**, phosphoramidite **3** was prepared, and oligodeoxyribonucleotides were synthesized. Duplexes containing compound **1** are slightly less stable than the natural duplex.

Key words: synthesis, oligodeoxyribonucleotides, 8-aza-3-deaza-2'-deoxyguanosine, melting studies.

INTRODUCTION

Recognition points for the Watson-Crick base pairing within nucleic acids are provided by nucleobases or heterocycles. Any nucleotide modification must maintain the specific hydrogen-bonding interaction or the hydrogen-bonding pattern must be compensated by stronger stacking interactions.[1] However, these interactions, which determine nucleic acid structures, are not completely understood. Since the elucidation of the sequence dependence of such interactions is prohibited by the lack of variety among naturally occurring bases, use of unnatural bases while maintaining as much as possible the RNA or DNA structures, can circumvent this limitation.[2, 3] The

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examples include several pairs.[4] Among them, the nonpolar, non-hydrogen bonded base pair surrogates in DNA especially attracted our attention.

Kool[4] and others[5] have demonstrated that hydrogen bonds are apparently dispensable in maintaining the natural polymerase activity, proposing that the steric matching of bases within tightly confined active sites might be a substitute for the fidelity in DNA. In this way, the information content of DNA might be increased, since the pairing of natural bases is driven by the hydrophobic interaction instead.[5] The DNA polymerases are critical for a stable transmission of genetic information. Since the active site is apparently determined by a specific hydrogen bonding between the polymerase and O-2 and N-3 atoms in the minor groove region of the duplex DNA, the transposing of N-3 nitrogen from the pyrimidine moiety in guanosine at position C-8 → N-8 would represent an expanded genetic alphabet, provided a polymerase is capable of efficient and high fidelity synthesis of DNA containing 3-deaza-8-aza-2'-deoxyguanosine (**1**) in the unnatural pair.

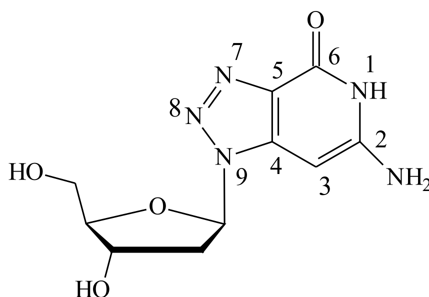


Figure 1. 8-Aza-3-deaza-2'-deoxyguanosine (purine numbering).

Very recently Kool *et al.*[4] extended the existing data on such contacts to the search for the significance of minor groove interactions at the extension step as well. While Spratt[6] finds the N-3 position in guanine crucial for the formation of the hydrogen bond between Arg and dG, proposing a general mechanism by which the polymerase checks the geometry of the newly forming base pair, Kool and coworkers[4] found that the polymerases for the majority of cases do not use hydrogen bonds between the bases during the insertion step when the correct geometry and specific minor groove interactions are obtained. Besides, the extension step reveals various abilities of sensing small changes in geometry in the absence of minor groove H-bond acceptors.[4] The efficient replication between non-hydrogen bonded shapes and recent structural data strongly supports the importance of non-polar isosteres of natural DNA bases.[7]

A practicable synthesis of **1** in our hands[8a,b] encouraged the idea of incorporating this isostere of guanosine into an oligonucleotide framework. The first successful attempt to incorporate 3-deaza-2'-deoxyguanosine was reported by Seela *et al*.[9] His work was continued[10] by a thorough investigation of 3-deaza and 7-deaza ODNs containing adequately modified guanine bases in alternating $d(CG)_n$. A strong destabilization effect was observed even when only one dG residue was replaced by c^3G_d, much more than with 7-deaza purine bases. On the other hand, an extra nitrogen at position 8 in ODNs possessing z^8G_d exhibits significantly higher T_m values than the parent purine oligomers, indicating a stabilization of 3–45 kcal mol^{-1} over the dG-dC base pair. This stabilizing effect is particularly evident within the 8-aza-7-deaza purine series, because of the missing steric constraints otherwise induced by the 8-substituents of purines.[11a,b] In our case, when the combination of both effects is present, we may expect a favourable issue and improved properties of the anticipated ODNs.

Besides being suitable probes for PCR, short oligonucleotides may be also used to inhibit gene transcription *via* triple-helix formation on a double stranded gene[12, 13], while the contiguous dGs (> 3) prompt the formation of superstructures, like tetraplex (G – quadruplex) conformations.[14] Incorporation of the desired modification of the base presents a challenge with a hope of improving the hybridization properties and the influence on the structural stability of dG *vs.* dG* quartet in ODNs, which are critical determinants of HIV-1 replication in a cell culture.[15a–d,16]

In this study we wish to report the incorporation of **1** with the intention to collect the basic data, about the chemical and physical properties of the selected ODNs. The data describe the effect of the introduction of the assumed hydrophilic destabilization at position N-3 of guanosine replacing it with CH, and the effect of substituting C-8 by N-8.

RESULTS AND DISCUSSION

Monomers

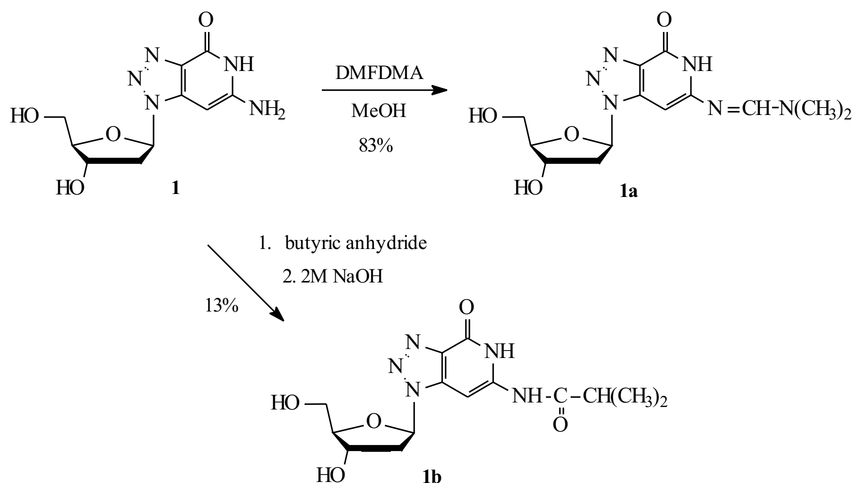
*Chemical and Physical Properties of Monomer **1***

A new, highly efficient procedure for 8-aza-3-deaza-2'-deoxyguanosine (**1**) was used for the preparation of the basic nucleosides.[8a,b] The Watson-Crick base pairing ability is expected to be the same for 2'-deoxyguanosine and the unnatural base **1**. Although the only difference is in the nitrogen content pattern, compound **1** shows a significantly different UV spectrum. The UV spectrum of **1** in water is bathochromically shifted and has a maximum at 286 nm. The pK_a value of deprotonation of **1** is between 10.4 and 10.5. At

pH = 1 and pH = 7 there was no difference in UV spectra of **1**, therefore we have concluded that **1** was protonated neither at N-7 nor at N-8 (2'-deoxyguanosine is protonated at N-7, p$K_{BH}{}^{+}$ = 3.5). Besides, compound **1** appeared to be more lipophilic than natural 2'-deoxyguanosine, due to its higher retention time on RP-18 HPLC.

Synthesis of Building Blocks for DNA Synthesis

Seela *et al.*[9, 10] reported that different nitrogen patterns in modified nucleosides can alter the reactivity of the 2-amino group. Following his experience, the use of two different protecting groups for exocyclic amino group was investigated. First, **1** was reacted with DMFDMA to furnish the (dimethylamino)methylidene derivative **1a**, while the synthesis of **1b** required two steps. Compound **1** was treated with isobutyric anhydride and the resulting *O,N*-tris-isobutyryl derivative was further selectively converted into the *N*-isobutyryl derivative using 2M NaOH. Reactions with overall yields are represented in Scheme 1.



Scheme 1.

Compounds **1a** and **1b** were hydrolyzed with saturated aqueous ammonia at 55 °C and the corresponding half-life values of the deprotection reaction of **1a** and **1b** were determined. The hydrolysis was followed UV-spectrophotometrically at the appropriate wavelength of the maximum absorbance difference between the adduct and the product. The half-life values were 12 min for **1a** and more than 3 days for **1b** (Table I). They are comparable with the results of Seela *et al.*,[9,10] who were the first to introduce DMFDMA for protection into 3-deaza-2'-deoxyguanosine and 3-deazaguanosine.

TABLE I

Half-life values ($t_{1/2}$) of two different amino protecting groups

Compd.	Wavelength λ / nm	Half-live value $t_{1/2}$ / min
1a	255	12
1b	260	> 3 days

It is obvious that only the (dimethylamino)methylidene intermediate **1a** could be cleaved off at a rate suitable for oligonucleotide synthesis. The deprotection profile for **1a** is shown in Figure 2 where the half-life value is represented by a circle.

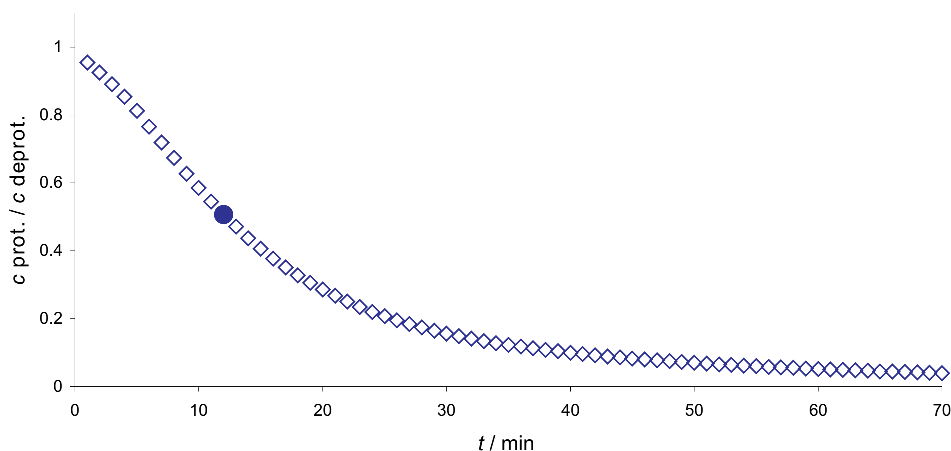
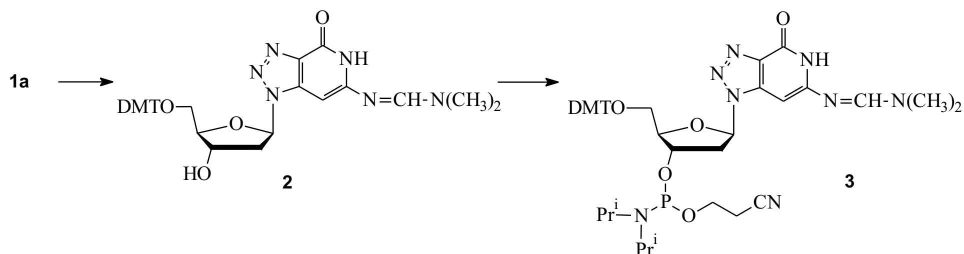


Figure 2. Deprotection profile of **1a**.

The synthesis of oligodeoxynucleotides containing **1** (Scheme 2) was carried out on a solid support applying the phosphoramidite approach.



Scheme 2.

The 4,4'-dimethoxytriphenylmethyl (DMT) residue was introduced into the 5'-OH position of compound **1a** under standard conditions, furnishing the DMT derivative **2**. Finally, **2** was reacted with (2-cyanoethoxy)-bis-*N,N*-diisopropylaminophosphine under anhydrous conditions, yielding phosphoramidite **3** as a diastereoisomeric mixture (observed by ^{31}P NMR). The overall yield is approximately 40%.

Oligonucleotides

ODNs were synthesized on an Expedite synthesizer (model 8909). Phosphoramidite **3** was dissolved in dry acetonitrile (0.1 M solution). The cycle for incorporation of **3** was modified by a longer coupling time. Compound **3** gave adequate coupling yields (>95%) during the solid phase synthesis (coupling efficiencies for **3**, based on the absorbance of the dimethoxytrityl cation released after each coupling, were consistent with those observed for DNA synthesis). After deprotection and purification, the ODNs were analyzed by RP-18 HPLC and characterized by ESI-MS.

The following 16 mers have been synthesized:

I GCC GAG GTC CAT GTC T$^{3'}$

II GCC GAG G*TC CAT GTC T$^{3'}$

III GCC G*AG G*TC CAT G*TC T$^{3'}$

IV G*CC G*AG* G*TC CAT G*TC T$^{3'}$

V AGA CAT GGA CCT CGG C$^{3'}$

G* = modified guanosine, 8-aza-3-deaza-2'-deoxyguanosine (**1**)

The sequence GCC GAG GTC CAT GTC T$^{3'}$ was found most convenient to study the influence of the incorporation of **1** on duplex stability. We have exchanged one, three and finally all of the 2'-deoxyguanosine residues by the more lipophilic 8-aza-3-deaza-2'-deoxyguanosine.

The ODNs structures were confirmed by mass spectroscopy. The results are represented in Table II.

TABLE II

Molecular weights of oligodeoxyribonucleotides determined by ESI-MS

ODN	MW / g mol^{-1}	
	calculated	measured
I	4871.3	4872.0
II	4871.3	4869.6
III	4871.3	nd
IV	4871.3	4872.0
V	4891.1	4890.0

nd = not detected.

The molecular weights of 8-aza-3-deaza-2'-deoxyguanosine **1** and 2'-deoxy-guanosine are identical. Therefore, we had to analyze the nucleoside composition. The incorporation of **1** into ODNs II, III, IV was proven by enzymatic hydrolysis using nuclease P_1 – penicillium citrinum and alkaline phosphatase – calf intestine. The mixture of nucleosides was analyzed by RP-18 HPLC. The separation of natural nucleosides and modified nucleoside **1** was efficient. When **1** was incorporated only once (ODN II), it was difficult to detect the corresponding peak due to a very low ε of **1** at 260 nm.

In all cases, integration of the peaks of HPLC analyses demonstrated the correct composition of ODNs.

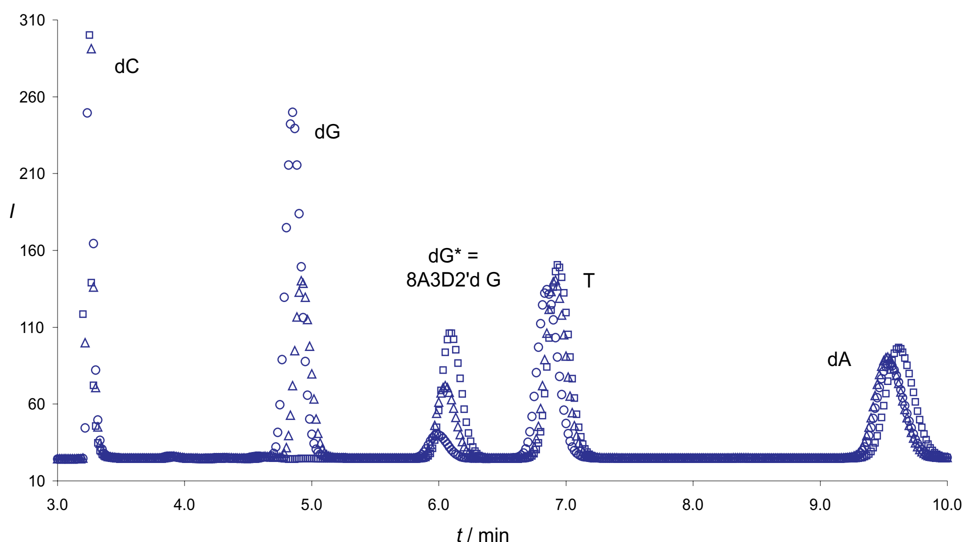


Figure 3. RP-18 HPLC profiles of oligodeoxyribonucleotides II (O), III (Δ) and IV (□) after enzymatic digestion.

Thermal Denaturation Studies

Compound **1** was incorporated into the 16 mers ODN I [d(GCC GAG GTC CAT GTC $T^{3'}$)], which forms a duplex with its complement V [d(AGA CAT GGA CCT CGG $C^{3'}$), T_m = 65.3 °C]. This structure is definitely devoid of higher ordered aggregates (triplexes, quadruplexes) and is consequently a useful model for studying either structural or thermodynamic properties of the anticipated duplexes.

Table III summarizes the T_m values (at 5.6 μmol dm^{-3} single strand concentration) as well as thermodynamic data of ODNs (I : V, control duplex

TABLE III

T_m values and thermodynamic data of 16 mer DNA duplexes

Duplex	$\frac{T_m}{°C}$	$\frac{\Delta T_m}{°C}$	$\frac{\Delta H°}{kJ\ mol^{-1}}$	$\frac{\Delta S°}{kJ\ mol^{-1}\ K^{-1}}$
Control duplex I : V	65.3	/	–577	–1.6
D1 = II : V 1 × G* in II	63.5	–1.8	–568	–1.58
D2 = III : V 3 × G* in III	59.8	–1.9	–538	–1.51
D3 = IV : V 5 × G* in IV	57.9	–1.5	–527	–1.49

and novel duplexes II : V, III : V, IV : V), where dG* indicates the position of the replacement of dG within a 16 mer sequence.

All duplexes were prepared in a 10 mmol dm^{-3} cacodylic acid buffer, 100 mmol dm^{-3} Na^+, pH = 7, by mixing equimolar concentrations of both strands. ODNs concentrations were determined from the absorbance at 260 nm with single strand extinction coefficients (Table IV in Experimental part) determined by phosphate analysis.[17] Cooperative melting profiles were observed in all cases. The T_m values were extracted from the first derivative. Transition enthalpies $\Delta H°$ and transition entropy $\Delta S°$ were determined from the dependance of T_m on the DNA concentration (ranging from 11.5 to 3.5 μmol dm^{-3} duplex concentration, 5–6 points).[18]

According to Table III, it is apparent that an increased number of 8-aza-3-deaza residues within the dG strand destabilizes the duplex structure, and that there is an almost linear dependence of the T_m values and the number of modified base residues. Namely, one replacement decreased the T_m by 2 °C (Table III), while the only example reporting comparable replacement with 3-deaza-2'-deoxyguanosine showed much stronger destabilization (9 or 11 °C) within a specific 12 mer.[10] When comparing the thermodynamic data of duplexes II : V, III : V, IV : V with the unmodified control duplex I : V, we may conclude that the less favourable enthalpy terms lead to a minor duplex destabilization and that entropy changes do not prevail. Now, we may conclude, that our findings (Table III) corroborate the earlier observations made on 8-aza-analogues that the introduction of N-8 might compensate for the lack of N-3 in our case.

Conclusions

The modified nucleoside **1**, 8-aza-3-deaza-2'-deoxyguanosine, can be easily prepared for oligodeoxynucleotide synthesis and incorporated into 16 mers.

It shows coupling yields of 95% or higher. It is apparent that the introduction of an extra nitrogen *vs.* CH at N-8 position leads to duplex stabilization when the changes caused by lipophilization at position N-3 are present. Elucidation of these changes on secondary and tertiary structures within these short DNAs is now in progress, including studies of the modified 8-aza-3-deazaguanine base with modifications in sugar moiety such as 2'-fluoro arabino and 2'-O-methoxy.

EXPERIMENTAL

General

NMR spectra were obtained on a Varian (299.97 MHz). ^{1}H and ^{13}C were referenced to TMS and 85% phosphoric acid was used as an external standard for ^{31}P. MS spectra were recorded on a Pneumatic Assistant ESI-MS (AutoSpecE).

The UV spectra were recorded on a BioLambda 40 Perkin Elmer spectrophotometer. Melting points were determined with a Buchi and are uncorrected. Precoated merck Silica gel $60F_{254}$ plates were used for TLC.

Anhydrous solvents were freshly distilled from appropriate drying agents.

All other chemicals were of reagent grade or better quality and were used as received.

Alkaline Hydrolysis of Nucleosides

The half-lives of nucleosides were measured in concentrated aqueous ammonia at 55 °C. The reaction was followed UV-spectrophotometrically at a wavelength as indicated.

Synthesis, Purification and Characterization of Oligodeoxyribonucleotides

The solid-phase synthesis of ODNs was carried out on an automated DNA synthesizer (Expedite 8909, PerSeptive Biosystem) by standard phosphoramidite chemistry. A longer coupling time was used for incorporation of modified guanosine **1**.

Cleavage from solid support and deprotection were accomplished by treatment with concentrated aqueous ammonia at 55 °C for 8 hours. ODNs were synthesized as 5'-O-DMT derivatives and purified on C-18 RP column (pump A: 50 mmol dm^{-3} triethylammonium acetate + 5% acetonitrile; pump B: acetonitrile + 5% 50 mmol dm^{-3} triethylammonium acetate; gradient: 95–45% A in 37 min; flow rate 2.5 ml/min at preparative scale, flow rate 1 ml/min at analytical scale), then detritylated and further purified by size exclusion chromatography.

ODNs were extra desalted for MS on Dowex. ODNs were characterized by ESI-MS spectrometry and/or by the HPLC analysis of the constituent nucleosides obtained by digestition with nuclease P_1 – penicillium citrinum and alkaline phosphatase – calf intestine.

ODNs purity were verified by analytical C-18 RP column.

Melting curves were measured with a LambdaBio 40 Perkin Elmer UV/Vis spectrophotometer equipped with the Peltier system. The temperature was increased by 1 °C/min. The duplex was heated and cooled for 5 cycles at 1 °C/min. The first cycle was discarded and the T_m was calculated as the maximum of dA_{260}/dT *vs.* T for the remaining heating and cooling cycles.

Determination of ODN Extinction Coefficients

Molar extinction coefficients (ε) for the single strand ODNs were determined by phosphate analysis as described.[17] The extinction coefficients at 260 nm and 25 °C for ODN I, II, III, IV and V are represented in Table IV.

TABLE IV

Molar extinction coefficients of oligodeoxyribonucleotides at 260 nm and 25 °C

ODN	ε / mol^{-1} dm^3 cm^{-1}	λ_{max} / nm
I	132000	259.1
II	130000	260.3
III	113000	267.8
IV	104000	270.1
V	138000	

Enzymatic Hydrolysis of the ODNs II, III, IV

ODNs II, III, IV (0.4–0.5 A_{260} units) were dissolved in 10 mmol dm^{-3} cacodylic acid buffer (pH = 7) and treated with nuclease P_1 – penicillium citrinum and alkaline phosphatase – calf intestine at room temperature at least overnight. The mixture was analyzed on RP-18 HPLC (solvent system pump A: 50 mmol dm^{-3} triethylammonium acetate + 5% acetonitrile, pump B: acetonitrile + 5% 50 mmol dm^{-3} triethylammonium acetate, gradient 100% A, 5 min, 100–94% A in 18.5 min, flow 1 ml/min). Quantification was made on the basis of the peak areas, which were divided by the extinction coefficients of the nucleoside constituents (ε_{260}: dA 15400; dC 7300; dG 11700; 8-aza-3-deaza-dG **1** 3350; T 8800).

*1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-{[(dimethylamino)methylidene]-amino}-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on (**1a**)*

N,N-dimethylformamide dimethylacetal (1.2 ml, 9.2 mmol) was added to a solution of **1** (0.61 g, 2.3 mmol) in dried methanol (10 ml) and the solution was stirred at room temperature overnight. The precipitate was filtered, washed with cold methanol and dried, yielding **1a** (0.73 g, 83%, m.p. > 250 °C).

UV (H_2O) λ_{max} / nm: 238.9 (peak), 262.8 (base), 308. 5 (peak); log ε / dm^3 mol^{-1} cm^{-1} : 4.14, 3.58, 4.34; IR (KBr) ν_{max} / cm^{-1} : 3528, 3394, 3354, 3092, 2920, 1697, 1668, 1628, 1585 (C=N), 1485, 1428, 1378, 1322, 1255, 1221, 1120, 1089, 1055, 1034,

1000, 958, 940; ^{1}H NMR (DMSO-d_6) δ/ppm: 10.99 (1H, br. s, NH), 8.07 (1H, s, N=CH), 6.38 (1H, t, H-1'), 6.14 (1H, s, CH), 5.37 (1H, d, 3'-OH), 4.82 (1H, t, 5'-OH), 4.46 (1H, m, H-3'), 3.87 (1H, dt, H-4'), 3.50 (1H, m, H-5'b), 3.39 (1H, m, H-5'a), 3.09 (3H, s, NCH_3), 2.97 (3H, s, NCH_3), 2.89 (1H, m, H-2'b), 2.35 (1H, m, H-2'a); ^{13}C NMR (DMSO-d_6) δ/ppm: 156.0, 155.9, 154.5, 141.5, 132.9, 88.1 (C-1'), 85.7 (C-4'), 74.0, 70.6, 61.8 (C-5'), 34.2 (C-2');.

MS (EI) *m/z*: 322 (M^+, 5%), 206 (M^+ – 166, 100%); (FAB) *m/z*: 323 (MH^+, 40%), 207 (MH^+ – 166, 100%).

*1-[2-Deoxy-5-*O*-(4,4'-dimethoxytriphenylmethyl)-β-D-*erythro*-pentofuranosyl]-6-{[(dimethylamino)methylidene]-amino}-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on (**2**)*

4,4'-Dimethoxytriphenylmethyl chloride (1.53 g, 4.6 mmol) was added to a solution of **1a** in dry pyridine (20 ml) and triethylamine (0.63 ml, 4.6 mmol). After stirring at room temperature for 1.5 h, the mixture was poured into ice-cold water (150 ml) and extracted with dichloromethane (4 x 50 ml). The organic layers were dried (Na_2SO_4), filtered and evaporated. FC (60 x 140 mm; CH_2Cl_2 : MeOH + 1% Net_3, 100 : 1 to 20 : 1) afforded compound **2** (1.28 g, 90%) as foam.

^{1}H NMR (DMSO-d_6) δ/ppm: 11.05 (1H, br. s, NH), 8.09 (1H, s, N=CH), 7.26–7.09, 6.77–6.71 (13H, m, Ar-H) 6.41 (1H, q, H-1'), 6.17 (1H, s, CH), 5.44 (1H, d, 3'-OH), 4.53 (1H, m, H-3'), 3.99 (1H, m, H-4'), 3.71, 3.70 (6H, 2 x s, 2 x OCH_3), H-5'a, b, 3.05, 2.96 (6H, 2 x s, 2 x NCH_3), 2.91 (1H, m, H-2'b), 2.42 (1H, m, H-2'a).

*1-[2-Deoxy-5-*O*-(4,4'-dimethoxytriphenylmethyl)-β-D-*erythro*-pentofuranosyl]-6-{[(dimethylamino)methylidene]-amino}-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on 3-*O*-(2-Cyanoethyl-*N,N*-diisopropylphosphoramidite) (**3**)*

(2-cyanoethoxy)-bis-*N,N*-diisopropylaminophosphine (0.7 ml, 2.2 mmol) was added to a stirred solution of **2** (0.98 g, 1.6 mmol) and anhydrous *N,N*-diisopropylamine tetrazolide (80 mg, 0.5 mmol) in dry dichloromethane (20 ml) under an Ar atmosphere at room temperature *via* a syringe in one portion. The reaction mixture was stirred overnight. After completion, the reaction mixture was filtered and the filtrate was extracted with saturated sodium bicarbonate and water. The organic phases were dried (Na_2SO_4) and evaporated to dryness. The solid material was purified by FC (45 x 115 mm, EtOAc : CH_2Cl_2 + 1% NEt_3 = 100 : 0 to 50 : 50), yielding a colourless foam (0.64 g, 48%).

^{31}P NMR ($CDCl_3$) δ/ppm: 147.45, 146.97; MS (FAB) *m/z*: 825 (MH^+, 5%), 303 (MH^+ – 522, 100%).

*1-[2-Deoxy-3,5-bis-*O*-(2-methylpropionyl)-β-D-*erythro*-pentofuranosyl]-6-[(2-methylpropionyl)amino]-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on*

Compound **1** (50 mg, 0.2 mmol) was dissolved in dry pyridine (2 ml). After addition of pyridine/isobutyric anhydride (1 : 1, 4 ml), the mixture was refluxed for 4 h and then evaporated. The oil residue was purified by TLC (20 x 20 cm, 2 mm, MF = CH_2Cl_2 : MeOH = 30 : 1, 3x). A white solid was obtained (42 mg), which was used in the next step.

MS (FAB) *m/z*: 338 (MH^+, 15%), 154 (MH^+ – 184, 100%).

*1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-[(2-methylpropionyl)amino]-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on* (***1b***)

To a suspension of 1-(2-deoxy-3,5-bis-*O*-(2-methylpropionyl)-β-D-*erythro*-pentofuranosyl)-6-[(2-methylpropionyl)amino]-1,2,3-triazolo[4,5-*c*]pyridine-4(5*H*)-on in MeOH (3 ml), 2M NaOH was added until pH=13 was reached (yellow solution). After 0.5 h, ion-exchange resin (Dowex WX-8 pyridinium form) was added until neutral pH. The solution was filtered, and the resin was washed with MeOH. The filtrate was evaporated, yielding 9 mg **1b** (13% from **1**) as a white solid (m.p. = 218–222 °C).

UV (H_2O) λ_{max}/nm: 205.0 (peak), 244.9 (base), 292.9 (peak); log ε / dm^3 mol^{-1} cm^{-1} : 4.39, 3.29, 4.26; ^{1}H NMR (DMSO-d_6) δ/ppm: 11.45 (1H, br.s, NH), 10.48 (1H, br.s, NH), 6.67 (1H, s, H-3), 6.45 (1H, t, J = ≈ 6 Hz, H-1'), 5.41 (1H, d, J = 4.4 Hz, 3'-OH), 4.75 (1H, 't', 5'-OH), 4.44 (1H, m, H-3'), 3.88 (1H, m, H-4'), 3.49–3.40 (2H, m, H-5',5''), 2.99–2.90, 2.65–2.56 (2H, m, H-2',2''), 1.15, 1.13 (6H, 2 x s, 2 x CH_3).

MS (FAB) m/z: 338 (MH^+, 15%), 154 (MH^+ – 184, 100%).

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SAŽETAK

Sinteza i studij hibridizacije oligodeoksiribonukleotida koji sadrže 2'-deoksiguanozinsku modifikaciju, 8-aza-3-deaza-2'-deoksiguanozin

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Opisana su kemijska i fizikalna svojstva nukleozida 8-aza-3-deaza-2'-deoksiguanozina (**1**). Iz amino-zaštićenog nukleozida **1a** pripravljen je fosforamidat **3** i niz oligodeoksiribonukleotida. Spoj **1**, koji sadržava dupleks, nešto manje je stabilan od prirodnog dupleksa.