Synthesis and Conformation of 9-(3′-*C*-Methyl-β-D-*xylo*-furanosyl)-adenine and 3′-*C*-Methyladenosine, Two Sugar-Methylated Nucleoside Analogues

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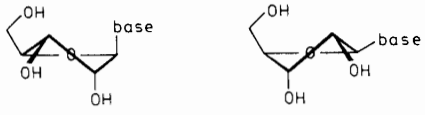
A novel synthetic route for the sugar-methylated nucleoside analogue 9-(3′-*C*-methyl-β-D-*xylo*-furanosyl)adenine (**1**) is reported. A Grignard reaction in THF with an appropriately protected keto nucleoside gave the *xylo* structure **4** in 60 % yield. Using diethyl ether as the solvent, the Grignard reaction furnished compound **4** in 35 % yield, along with the *ribo* epimer (ca. 1 %). The *ribo* epimer is the precursor of 3′-*C*-methyladenosine (**2**). Compounds **4** and **5** could be conveniently deprotected to obtain the title compounds in good yields. The conformational properties of **1** and **2** were analyzed using 500 MHz ^{1}H NMR spectroscopy. In line with earlier experiments, it is found that the methyl group on the sugar ring strongly prefers an equatorial location. For **1**, this results in the predominant population of the North ($^3T_2$) puckered form of the sugar ring, whereas compound **2** resides primarily in the South ($^2T_3$) conformation.

DNA or RNA nucleosides with a chemical modification frequently possess marked activity as antitumor or antiviral agents.[1–3] Initial studies in this field have been focussed mainly on base-modified nucleosides, such as 5-fluoro-2′-deoxyuridine, which is of current importance in cancer chemotherapy.[4] More recent investigations refer to nucleoside analogues in which the sugar moiety is modified. As examples, we mention 9-β-D-*arabino*-furanosyladenine and 1-β-D-*arabino*-furanosylcytidine,[5] which were found to be powerful cytostatic agents. Generally speaking, almost nothing is known about the detailed mechanism of action of modified nucleosides. It is fascinating that the activity seems to be correlated with the preferred conformation that is adopted in aqueous solution. It is known, for instance, that the naturally occurring cytostatic antibiotic cordycepin (3′-deoxyadenosine) is a functional analogue of adenosine, but not of the isomeric 2′-deoxyadenosine.[6] This may relate to the fact that cordycepin and adenosine both show a preference for a North ($^3T_2$) sugar conformation, whereas the sugar ring of 2′-deoxyadenosine resides primarily in the South ($^2T_3$) conformation.[7]



In this work we present a novel synthesis (via a Grignard reaction) and conformational analysis (via variable temperature 500 MHz ^{1}H NMR spectroscopy) of two analogues of adenosine. In compound **1** [9-(3′-*C*-methyl-β-D-*xylo*-furanosyl)adenine], a methyl group is introduced on the C(3′)-*exo* position; compound **2** (3′-*C*-methyladenosine) has a methyl group on C(3′)-*endo*.

A = adenine

Conformational analysis showed that **1** has a predominant preference for the North ($^3T_2$) sugar conformation, whereas inversion of the configuration at C(3′) (i.e., compound **2**) results in a pronounced population of the South ($^2T_3$) form. These findings reinforce our earlier conclusion that the sugar conformation in nucleosides can be finely tuned via the introduction of a methyl group on C(2′) or C(3′).[8,9]

Preparation of **1** *and* **2.** Syntheses of sugar-modified nucleosides have often been carried out by condensation of a suitably derivatized sugar with a nucleobase. In the case of compound **1**, this approach proved to be lengthy and difficult.[10–12] The modified sugar and the target nucleoside were

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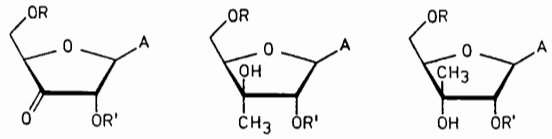
obtained in 6 and 2% overall yields in 8 and 10 steps, respectively; the precursor was 1,2,5,6-di-*O*-isopropylidene-3-methylenehexofuranose.

We noticed that 3'-ketonucleosides had recently been made available in good yields starting from the appropriately protected β-D-*ribo* nucleotides.[13] Reduction of these compounds involved preferential attack of the nucleophile from the α-side of the system, i.e., the product mixture contains substantially more of the *xylo* compound than of the *ribo* compound. We reasoned that preferential attack from the α-side would also occur when a 3'-ketonucleoside is allowed to react with a Grignard reagent.[14] We have now studied the reaction of the ketonucleoside **3** with methylmagnesium iodide. As expected, this reaction afforded the partially protected 3'-methylated *xylo* nucleoside **4**; deprotection of **4** afforded compound **1**. It was found that the



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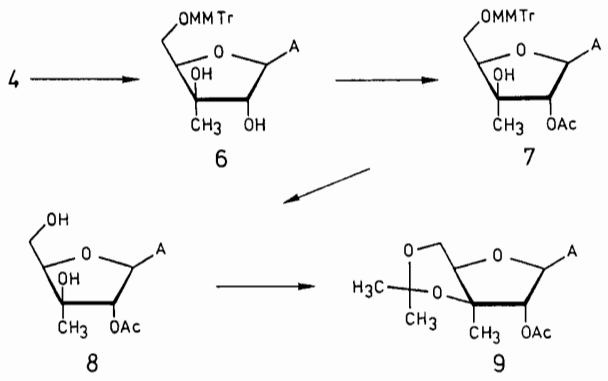
R = MMTr; R' = tBDMS

yield of **4** is highly sensitive to the order in which the reactants are added, the nature of the solvent, and the method of preparation of the Grignard reagent. Some important practical aspects are: (*i*), a large excess of iodomethane (2 equivalents with respect to Mg) is necessary to ensure complete conversion of Mg which otherwise causes reductive cleavage of the 5'-*O*-monomethoxytrityl group and/or reduction of compound **3** into *xylo*-adenosine, and (*ii*) the addition of compound **3** in THF or diethyl ether to a solution of the Grignard reagent leads to the best yield of **4**. The use of diethyl ether as the solvent results in partial cleavage of the 5'-*O*-monomethoxytrityl group, and also in formation of a trace of the *ribo* epimer **5** [ratio *xylo*-(**4**) / *ribo*-(**5**) approximately 50 : 1]. Compound **5** could be isolated, its deprotection finally affording the second title compound 3'-*C*-methyladenosine (**2**). Using THF as the solvent, we were able to suppress completely both the cleavage of 5'-*O*-monomethoxytrityl, and the formation of **5**. The absence of trityl cleavage in THF can be attributed to the fact that THF acts as a stronger Lewis base than does diethyl ether.[15]



Scheme 1.

The *xylo* configuration of compound **4** was assessed in a chemical fashion, i.e., by its conversion into the 3'-5'-*O*-isopropylidene derivative **9** (Scheme 1). Desilylation of **4** gave **6**; 2'-*O*-acetylation of **6** gave **7**; removal of the 5'-*O*-monomethoxytrityl group gave **8**; and reaction with 2,2-dimethoxypropane in the presence of a catalytic amount of 4-toluenesulfonic acid monohydrate furnished compound **9**. ^{1}H and ^{13}C NMR spectroscopy clearly showed resonances of the ketal fragment, which is feasible only for the *xylo* structure. Finally, compounds **4** and **5** were deprotected by reaction with tetrabutylammonium fluoride in THF for 30 min at 20 °C, and subsequent treatment with 80 % acetic acid.

Conformational analysis of **1** *and* **2**. As a consequence of the fact that compounds **1** and **2** carry two substituents on C(3') and one on C(2'), only one vicinal proton–proton coupling constant ($J_{1'2'}$) is available for conformational analysis. It must be stated, however, that in NMR studies of complicated RNA structures it is not uncommon for the conformational analysis of the sugar ring to rest exclusively on $J_{1'2'}$. In principle, two other vicinal coupling constants (i.e., $J_{2'3'}$, and $J_{3'4'}$) are available in RNA, but these couplings cannot usually be determined owing to extensive spectral overlap. We have monitored $J_{1'2'}$, of compound **1** as a function of the sample temperature in the range 4–92 °C (Table 1). As is well known, furanose rings are usually involved in a North ($^3T_2$) ⇌ South ($^2T_3$) equilibrium.[16] The North ($^3T_2$) form corresponds with a $J_{1'2'}$ value of 1.8 Hz, whereas the South conformation has $J_{1'2'}$ = 8.8 Hz. In this way, an estimation of the South ($^2T_3$) contribution to the North ($^3T_2$) ⇌ South ($^2T_3$) equilibrium can be made using the formula:

$$\% \text{ South} = \frac{J_{1'2'}(\text{exp}) - J_{1'2'}(\text{North})}{J_{1'2'}(\text{South}) - J_{1'2'}(\text{North})} = \frac{J_{1'2'}(\text{exp}) - 1.8}{7.0}$$

The results (Table 1) clearly show that the participation of the South ($^2T_3$) form in **1** is approximately 35 %, even at 92 °C. Alternatively stated; the furanose ring in compound **1** preferentially adopts the North ($^3T_2$) conformation.

For the *ribo* compound **2**, it also holds true that only $J_{1'2'}$, is available for conformational analysis. The results of the variable-temperature NMR analysis on **2** are also summarized in Table 1. In this case, is found that $J_{1'2'}$varies from 8.6 to 7.2 Hz, i.e., South ($^2T_3$) is the preferred sugar conformation.

It can be concluded that the orientation of the methyl group on C(3') actually dictates the conformation of the sugar ring in **1** and **2**. In line with our earlier work, it was found that a methyl substituent on the sugar ring strongly

Table 1. Variation of $J_{1'2'}$ with the sample temperature, measured for compounds **1** and **2**, along with the calculated percentage of the South conformer of the furanose ring (see the text).

Compound **1**			Compound **2**		
Temp./°C	$J_{1'2'}$/Hz	South/%	Temp./°C	$J_{1'2'}$/Hz	South/%
4	1.9	1	4	8.6	97
7	2.0	3	12	8.6	97
14	2.1	6	17	8.4	94
21	2.2	7	22	8.4	94
27	2.4	10	27	8.2	91
37	2.8	16	37	8.0	89
42	3.2	20	43	8.0	89
47	3.4	23	47	7.9	87
57	3.7	27	57	7.6	83
67	4.1	33	67	7.6	83
77	4.2	35	75	7.6	83
87	4.2	35	87	7.5	80
92	4.2	35	92	7.2	77

prefers an equatorial location. Hence, a methyl group on the C(3')-*exo* position gives North ($^3T_2$), and a methyl group on C(3')-*endo* gives South ($^2T_3$). This phenomenon may be of importance for the design of therapeutically useful nucleoside analogues, since the bioactivity seems to depend directly upon the intrinsic structural preference of the sugar ring.

Experimental

^{1}H NMR spectra were recorded at 500 MHz on a Bruker AM500 NMR spectrometer.[17] Tetramethylsilane was used as an internal chemical shift reference (δ 0) in the case of ^{1}H NMR in organic solvents. A trace of acetonitrile (δ 2.0) was used as an internal reference in the case of ^{1}H NMR in D_2O. ^{13}C NMR spectra were recorded on a Jeol FX 90Q NMR spectrometer at 22.9 MHz. Dioxane (δ 67.4) was used as an internal chemical-shift reference. UV absorption spectra were recorded with a Varian–Cary 2200 instrument; a Jeol DX 303 instrument was used for recording the mass spectra. Thin layer chromatography was performed with Merck precoated 60 F_{254} plates. Merck Kieselgel G was used for short-column chromatography. Solvent systems: A: ethyl acetate–hexane [5 : 1(v/v)]; B: ethanol–dichloromethane [2 : 8 (v/v)].

5'-O-(4-Monomethoxytrityl)adenosine. Adenosine (10.64 g, 40 mmol) was dissolved in 250 ml of dry pyridine, and 4-monomethoxytrityl chloride (6.2 g, 20 mmol) was added. The reaction was left overnight at room temperature with protection from light. A second portion of 4-monomethoxytrityl chloride (3.1 g, 10 mmol) was added, followed by a third portion (3.1 g, 10 mmol) after one day. A fourth portion was added (1.55 g, 5 mmol), and the mixture was stirred for one more day in order to drive the reaction to completion. Usual work-up furnished a brownish foam which was triturated with diethyl ether. This removed most of the 4-monomethoxytrityl alcohol. The yellow precipitate was redissolved in dichloromethane, from which the title compound crystallized out. Filtration followed by washing of the residue with dichloromethane gave pure 5'-*O*-(4-monomethoxytrityl)adenosine (9.3 g, 43 %). The mother liquors were pooled, concentrated, and the residue was applied to a short (10 cm) column of silica gel. Elution with dichloromethane and 2 % ethanol removed lyophilic by-products. Finally, 5'-*O*-(4-monomethoxytrityl)adenosine was eluted with 8 % ethanol in dichloromethane (2.6 g, 12 %). Total yield: 55 % (11.9 g).

^{1}H NMR ($CDCl_3$–CD_3OD 9:1): δ 8.25 [1 H,s,H(8)], 8.18 [1 H,s,H(2)], 6.02 [1 H,d,H(1'), $J_{1'2'}$ = 4.2 Hz], 4.56 [3 H,m,H(2')/H(3')/H(4')], 3.80 (3 H,s,OCH_3), 3.46 [2H,m,H(5')/H(5''), partially overlapped by CD_3OH].

5'-O-(4-Monomethoxytrityl)-2'-O-t-butyldimethylsilyladenosine. 5'-*O*-(4-Monomethoxytrityl)adenosine (5.4 g, 10 mmol) was dissolved in 100 ml of dry THF. Successively, dry pyridine (7 ml, 8.8 equiv.), and silver nitrate (2.04 g, 12 mmol) were added. After dissolution of the silver nitrate, t-butylchlorodimethylsilane (1.96 g, 13 mmol) was added and the reaction was allowed to proceed in darkness for 7–8 h. Silver chloride was formed during the reaction and removed by filtration through a Celite bed, which was subsequently washed with chloroform (100 ml). The filtrate was then diluted with chloroform (200 ml), and washed with saturated sodium hydrogencarbonate. All volatile matter was removed under vacuum, and the residue was purified by chromatography to give the desired product in 60 % yield (3.9 g) (R_f = 0.35 in solvent system A). In addition, the 3'-*O*-t-butyldimethylsilyl isomer was formed in 20 % yield (1.3 g, R_f = 0.25 in solvent system A). The latter compound could be partially isomerized into the desired product by treatment with triethylamine in methanol.

^{1}H NMR ($CDCl_3$): δ 8.26 [1 H,s,H(8)], 8.06 [1 H,s,H(2)], 6.03 (1 H,d,$J_{1'2'}$ = 5.4 Hz), 5.78 (2 H,s,NH_2), 5.01 [1 H,t,H(2'), $J_{3'4'}$ = 5.2 Hz], 4.31 [2 H,m,H(3')/H(4')], 3.79 (3 H,s,OCH_3), 3.47 [2 H,ddd,H(5')/H(5''), $J_{4'5'}$ = 3.0 Hz, $J_{4'5''}$ = 3.6 Hz], 2.77 (1 H,d,3'-OH), 0.84 (9 H,s,t-butyl of tBDMS), 0.00 and 0.12 (2 × 3 H, 2 × s, CH_3 of tBDMS).

9-[5'-O-(4-Monomethoxytrityl)-2'-O-t-butyldimethylsilyl-β-D-erythro-pentofuran-3'-ulosyl]adenine. Dry pyridine (2.5 ml, 30 mmol) was added dropwise to a vigorously stirred suspension of chromium trioxide (1.5 g, 15 mmol) in dry dichloromethane (30 ml), immediately followed by addition of acetic anhydride (1.5 ml, 15 mmol). Five minutes later, a solution of 5'-*O*-(4-monomethoxytrityl)-2'-t-butyldimethylsilyladenosine (3.27 g, 5 mmol) in dichloromethane (20 ml) was added. Oxidation was allowed to proceed for 45 min at 20 °C, after which the reaction mixture was applied to a short column of silica gel packed in ethyl acetate. The title compound was eluted with the same solvent. The eluate was collected in a 1 l Erlenmeyer flask

containing a solution of sodium hydrogencarbonate and EDTA. Extraction and evaporation of the organic phase gave a yellow foam which was further purified by column chromatography. The desired product was obtained in 55 °C yield (1.80 g) R_f = 0.48 in solvent system A.

^{1}H NMR ($CDCl_3$): δ 8.25 [1 H,s,H(8)], 8.02 [1 H,s,H(2)], 6.07 [1 H,d,H(1'), $J_{1'2'}$ = 8.5 Hz], 5.77 (2 H,s,NH_2), 5.56 [1 H,dd,H(2'), $J_{2'4'}$ = 0.7 Hz], 4.33 [1 H,m,H(4')], 3.78 (3 H,s,OCH_3), 3,50 [2 H,d,H(5')/H(5''), $J_{4'5'}$ = 2.7 Hz], 0.75 (9 H,t-butyl of tBDMS), 0.06 and −0.13 (2 × 3 H, 2 × s, CH_3 of tBDMS).

^{13}C NMR ($CHCl_3$): δ 208.3 [s, C(3')], 159.6 (s, CH_3-bearing C of MMTr), 155.6 [s, C(6)], 153.2 [d, C(2), J_{CH} = 159.7 Hz], 150.3 [s, C(4)], 139.1 [d, C(8), J_{CH} = 205.2 Hz], 134.6 (s, C *para* to OCH_3 of MMTr), 143.8, 130.3, 128.3, 127.8, 127.0, aromatic C of MMTr, 119.9 [s, C(5)], 113.1 (s, C *ortho* to OCH_3 of MMTr). 87.0 (s, quaternary C of MMTr), 85.4 [d, C(1'), J_{CH} = 170 Hz], 80.9 [d, C(4'), J_{CH} = 150.9 Hz], 76.4 [d, C(2'), J_{CH} = 143.6 Hz], 67.8 [t, C(5'), J_{CH} = 145.0 Hz], 55.1 (q, OCH_3, J_{CH} = 143.6 Hz), 17.9 (s, quaternary C of tBDMS), 25.2 (t, t-butyl of tBDMS, J_{CH} = 124.6 Hz), −4.8 and −5.5 (q, CH_3 of tBDMS).

9-(2'-O-t-Butyldimethylsilyl-3'-C-methyl-5'-O-monomethoxytrityl-β-D-xylofuranosyl)adenine (**4**). The Grignard reagent was prepared by addition of iodomethane (2.5 ml, 40 mmol) to a suspension of magnesium turnings (486 mg, 20 mmol) in dry diethyl ether (10 ml). After the Grignard reagent had cooled to room temperature, 9-[5'-*O*-(4-monomethoxytrityl)-2'-*O*-t-butyldimethylsilyl-β-D-*erythro*-pentofuran-3'-ulosyl]adenine (652 mg, 1 mmol), dissolved in dry THF (20 ml) was added dropwise. After 1 h, the reaction mixture was carefully poured into water (100 ml), and extracted with chloroform (3 × 100 ml). The organic layers were pooled and concentrated to dryness. The crude material was dissolved in dichloromethane and loaded onto a column of silica gel. Elution with dichloromethane removed traces of the starting material, after which the product was eluted with 1 % ethanol in dichloromethane. Appropriate fractions were pooled and evaporation of the solvents furnished compound **4** as a colorless foam in 60 % yield. When diethyl ether was used as the solvent, the yield of **4** was reduced to 35 %, and formation of the *ribo* epimer **5** was also observed. Compound **5** was isolated after three purification runs by preparative TLC, using solvent system A as the eluent. Compound **4**: R_f 0.37 (solvent system A); compound **5**: R_f 0.39 (solvent system A).

^{1}H NMR ($CDCl_3$): δ 8.26 [1 H,s,H(8)], 7.96 [1 H,s,H(2)], 7.62–6.80 (14 H,m,MMTr), 5.79 (2 H,s,NH_2), 5,68 [1 H,d,H(1'), $J_{1'2'}$ = 1.7 Hz], 4.29 [1 H,d,H(2')], 3.95 [1 H,t,H(4'), $J_{4'5'}$ = 4.2 Hz], 3.77 (3 H,s,OCH_3), 3.56 [2 H,d,H(5')/H(5'')], 1.89 (1 H,s,3'-OH), 1.19 (3 H,s,3'-CH_3), 0.89 (9 H,s,t-butyl of tBDMS), 0.02 and −0.05 (2 × 3 H, 2 × s, CH_3 of tBDMS).

^{13}C NMR (CD_3COCD_3): δ 159.1 [d, C(2), J_{CH} = 189.2 Hz], 149.0 [s, C(4)], 138.6 [d, C(8), J_{CH} = 227.2 Hz], 145.0, 130.7, 128.7, 127.9, 127.0 (aromatic C of MMTr), 135.8 (s, C *para* to OCH_3), 120.2 [br s, C(5)], 113.2 (d, C *ortho* to OCH_3, J_{CH} = 159.9 Hz), 92.1 [d, C(2'), J_{CH} = 164.8 Hz], 86.9 (s, quaternary C of MMTr), 85.5 [d, C(4'), J_{CH} = 140.4 Hz], 84.9 [d, C(2'), J_{CH} = 156.2 Hz], 79.1 [s, C(3')], 63.1 [t, C(2'), J_{CH} = 140.0 Hz], 54.9 (q, OCH_3, J_{CH} = 144.1 Hz), 25.2 (t-butyl C of tBDMS), 19,2 (q, 3'-CH_3, J_{CH} = 127.0 Hz), 17.9 (s, quaternary C of tBDMS), −4.9 and −5.5 (2 × t, CH_3 of tBDMS,J_{CH} = 118.0 Hz).

UV (ethanol): λ_{max} = 259 (ε = 15800), 233 (17800); λ_{min} = 245 nm.

MS (FAB$^+$): $(M + H)^+$ Calc. 668.319; Found: 668.3308.

9-(2'-O-t-Butyldimethylsilyl-3'-C-methyl-5'-O-monomethoxytrityl-ribo-*furanosyl*)adenine (**5**). ^{1}H NMR ($CDCl_3$): δ 8.16 [1 H,s,H(8)], 7.92 [1 H,s,H(2)], 5.92 [1 H,d,H(1'), $J_{1'2'}$ = 7 Hz], 5.59 (2 H,s,NH_2), 4.83 [1 H,d,H(2')], 4.17 [1 H,dd,H(4'), $J_{4'5'}$ = 3.9 Hz, $J_{4'5''}$ = 6.6 Hz], 3.72 (3 H,s,OCH_3), 3.5 [1 H,d,H(5')], 3.44 [1 H,d,H(5'')], 1.18 (3 H,s,3'-CH_3), 0.73 (9 H,s,t-butyl of tBDMS), −0.06 (6 H,s,CH_3 of tBDMS).

MS (FAB)$^+$ Calc. 668.319; Found 668.3261.

9-(3'-C-Methyl-β-D-xylo-furanosyl)adenine (**1**). Compound **4** (242 mg, 0.36 mmol) was dissolved in dry THF (3 ml), and a 1 M solution of tetrabutylammonium fluoride (TBAF) in dry THF (0.4 ml, 0.4 mmol) was added. Complete removal of the 2'-*O*-tBDMS group took place within 30 min at 20 °C. The solution was then diluted with chloroform (30 ml), and washed with water (2 × 25 ml). Volatile components of the organic phase were evaporated off, the residue was redissolved in a minimum of dioxane, and 80 % aqueous acetic acid was added. Removal of the 5'-*O*-(4-monomethoxytrityl) group was complete within 2 h. Acetic acid was then evaporated and co-evaporated with dioxane. The residue was taken up in water and washed with chloroform and diethyl ether. Concentration of the aqueous phase under vacuum followed by lyophilization afforded the pure compound **1** in 84 % yield (85 mg) R_f = 0.41 (solvent system B).

^{1}H NMR (D_2O): δ 8.21 [1 H,s,H(8)], 8.07 [1 H,s,H(2)], 5.87 (1 H,d, $J_{1'2'}$ = 2.4 Hz), 4.33 [1 H,s,H(2')], 1.32 (3 H,s,3'-CH_3). Other sugar protons could not be assigned owing to severe overlap of the resonances.

^{13}C NMR (D_2O): δ 155.4 (d, J_{CH} = 11 Hz), 152.6 [d, C(2), J_{CH} = 202.6 Hz'], 148.3 [s, C(4)], 141.5 [d, C(8), J_{CH} = 217.3 Hz], 128.9 [d, C(5), J_{CH} = 161 Hz], 90.6 [d, C(1'), J_{CH} = 166 Hz], 87.0 [d, C(4'), J_{CH} = 145.3 Hz], 82.9 [d, C(2'), J_{CH} = 152.6 Hz], 79.4 [s, C(3')], 60.9 [t, C(5'), J_{CH} = 144.0 Hz], 18.8 (q, 3'-CH_3, J_{CH} = 127.0 Hz).

UV (H_2O): λ_{max} 259 (ε 13300; pH = 7), 257 [ε 13700; pH = 1), 259 nm (ε = 13385; pH = 11). $[\alpha]_D^{20}$ −13.2 (*c* = 1, H_2O).

3'-C-Methyladenosine (**2**). Deprotection of 5'-*O*-(4-monomethoxytrityl)-3'-*C*-methyl-2'-*O*-t-butyldimethylsilyl-adenosine (**5**) (8 mg, 10 μmol) to 3'-*C*-methyladenosine (**2**)

was carried out using the procedure described for the *xylo* epimer **4**. Yield: 36% (1 mg).

^{1}H NMR (D_2O): δ 8.26 [1 H,s,H(2)], 8.13 [1 H,s,H(8)], 5.95 [1 H,d,H(1′), $J_{1'2'}$ = 8.1 Hz], 4.58 [1 H,d,H(2′)], 4.15 [1 H,t,H(4′), $J_{4'5'} = J_{4'5''}$ = 3.1 Hz], 3.79 [2 H,dd,H(5′)/H(5′′)], 1.40 (3 H,s,3′-CH_3).

9-(2′-O-Acetyl-3′-C-methyl-β-D-furanosyl)adenine (**8**). ^{1}H NMR ($CDCl_3$–CD_3OD): δ 8.24 [1 H,s,H(8)], 8.04 [1 H,s,H(2)], 5.81 [1 H,d,H(1′), $J_{1'2'}$ = 3 Hz], 5.38 [1 H,d,H(2′)], 3.99 [4 H,br s,H(3′)/H(4′)/H(5′)/H(5′′)], 2.16 (3 H,s,2′-acetate), 1.41 (3 H,s,3′-*C*-methyl).

9-(2′-O-Acetyl-3′-C-methyl-3′,5′-O-isopropylidene-β-D-xylo-furanosyl)adenine (**9**). ^{1}H NMR ($CDCl_3$): δ 8.42 [1 H,s,H(8)], 8.35 [1 H,s,H(2)], 6.16 [1 H,d,H(1′), $J_{1'2'}$ = 1.7 Hz], 5.85 (2 H,s,NH_2), 5.51 [1 H,d,H(2′)], 4.13 [2 H,d,H(5′)/H(5′′), $J_{4'5'} = J_{4'5''}$ = 2.2 Hz], 3.93 [1 H,t,H(4′)], 2.19 (3 H,s,3′-acetate), 1.52 and 1.38 (2 × s, 2 × 3H, isopropylidene), 1.40 (3 H,s,3′-CH_3).

^{13}C NMR ($CDCl_3$): δ 155.2 [C(6)], 153.1 [C(2)], 139.4 [C(8)], 99.0 [C(5)], 87.8 [C(1′)], 82.9 [C(4′)], 79.0 [C(3′)], 77.8 [C(2′)], 58.6 [C(5′)], 29.4 and 24.7 (CH_3 groups of isopropylidene), 20.7 (CH_3 group of 2′-acetate), 18.6 (3′-CH_3), −0.08 (quaternary C of isopropylidene).

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