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SYNTHESIS OF 2′- AND 3′-AZIDO-2′,3′-DIDEOXYADENOSINES. PREPARATIVE APPLICATIONS OF THE DEOXYGENATIVE [1,2]-HYDRIDE SHIFT AND β-ELIMINATION REACTIONS OF *O*-SULFONYLATED ADENOSINES*

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ABSTRACT

2′-Azido-2′,3′-dideoxyadenosine (**9**) has been synthesized from adenosine (**1**) in 6–8 steps. The key intermediate, N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-9-(3-deoxy-β-D-*threo*-pentofuranosyl)adenine (**6a**), was prepared in a one-flask manner by two methods, (a) in 95% yield by a deoxygenative [1,2]-hydride shift of a 3′-*O*-mesyladenosine derivative (**5e**) and subsequent reduction of an *in situ*-generated 2′-keto derivative (**10**) with mixed reagents, $Mg(OMe)_2$–$NaBH_4$; (b) by elimination of N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-3′-*O*-mesyl-2′-*O*-tosyl- and -2′,3′-di-*O*-tosyladenosines (**5b** and **5c**) to form an enol tosylate (**11**), which was converted into **6a** in good yield. In these reactions, KOH could be used in place of $Mg(OMe)_2$. 2′-Detosylation of **5b** occurred to some extent (~30%) prior to the β-elimination. The overall yields of **9** from **1** were 4 and 36% by the use of the first and second procedures, respectively. Similarly, 3′-azido-2′,3′-dideoxyadenosine (**17**) was synthesized from **1** in 17% overall yield *via* the known 9-(2-deoxy-5-*O*-trityl-β-D-*threo*-pentofuranosyl)adenine (**13**), which was prepared by the deoxygenative reduction of 2′-*O*-tosyl-5′-*O*-trityladenosine (**12**) with $LiEt_3BH$.

INTRODUCTION

Many azido-substituted sugar nucleosides show biologically interesting activities. 3′-Azido-3′-deoxythymidine (AZT) possesses significant inhibitory activity against human immunodeficiency virus (HIV)[1a]. The 5′-triphosphates of 2′-azido-2′-deoxyadenosine and 2′-azido-2′,3′-dideoxycytidine inhibited DNA and RNA polymerases from Ehrlich ascites tumor cells[1b] and cherry salmon testes[1c], respectively. We describe here new methods for synthesizing the unknown 2′-azido-2′,3′-dideoxyadenosine (**9**) and its 3′-azido analogue **17** (Schemes 1 and 3). The

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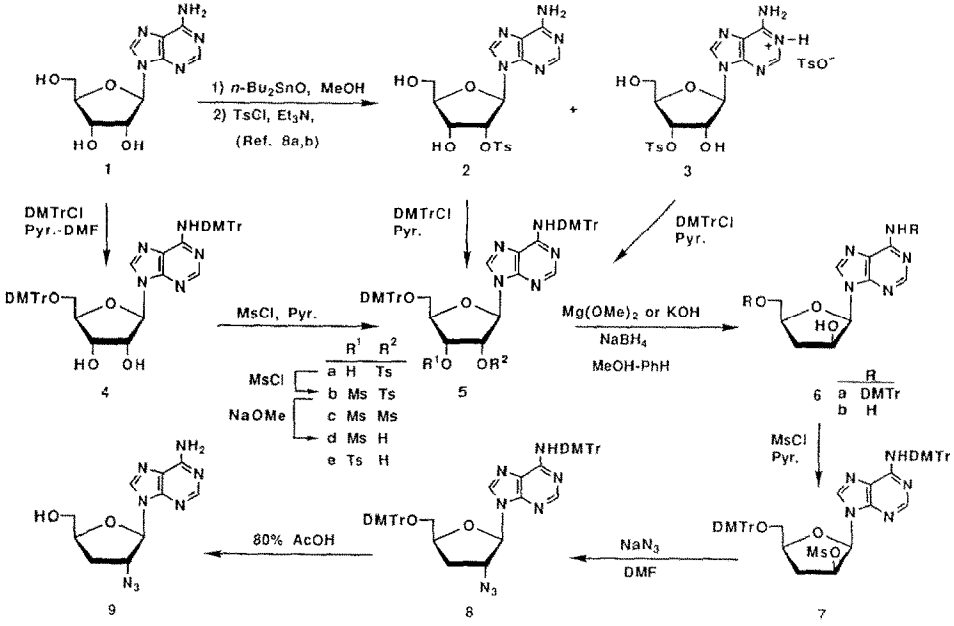
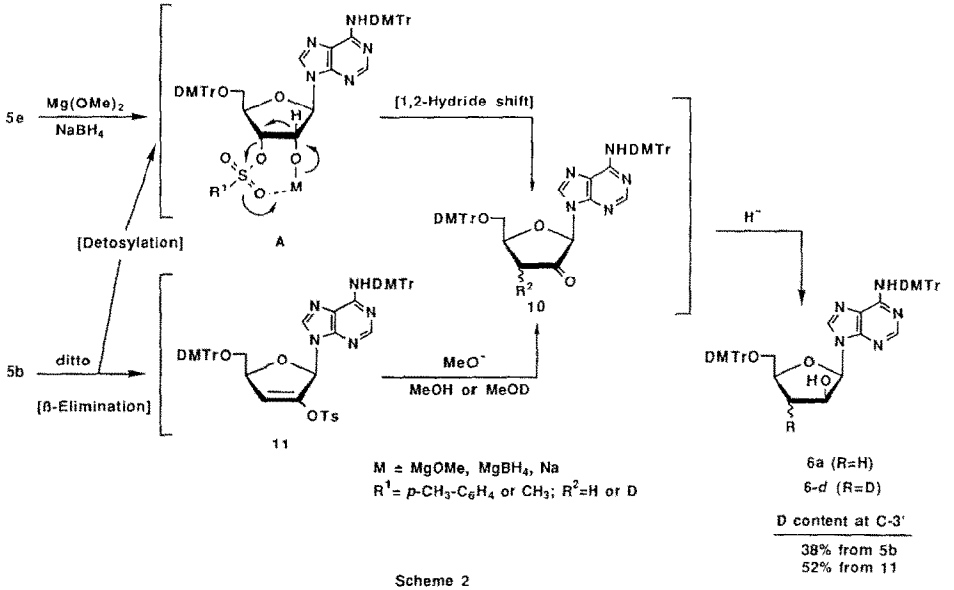
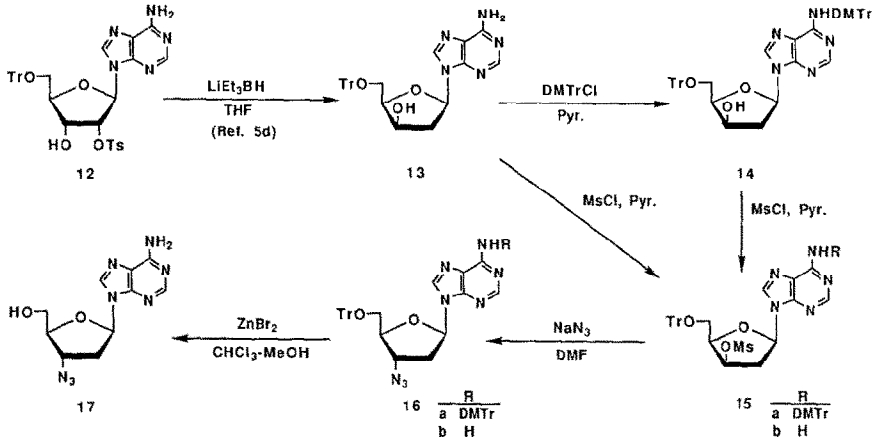
latter has been prepared by transglycosylation of an AZT derivative with a protected adenine base[2]. During the course of this work[3], similar syntheses of these compounds and their anti-HIV activity have been reported[4].







Scheme 3

Our synthetic method utilizes two reactions developed for the deoxygenation of furanosyl moieties. One is the deoxygenative [1,2]-hydride shift of α-hydroxysulfonates with organometallic reagents[5], and the other is the β-elimination of 2′,3′-di-*O*-sulfonylated nucleosides with sodium methoxide[6].

We recently reported that N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-3′-*O*-tosyladenosine (**5e**) reacted with magnesium methoxide to give the corresponding 3′-deoxy-2′-keto derivative (**10**) *via* a [1,2]-hydride shift, as depicted in **A** (Scheme 2)[5k]. It has since been determined that when sodium borohydride was present in this medium, N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-9-(3-deoxy-β-D-*threo*-pentofuranosyl)-adenine (**6a**) was the main product. Furthermore, the mixed reagents [$Mg(OMe)_2$–$NaBH_4$] were found effective in the β-elimination of N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-3′-*O*-mesyl-2′-*O*-tosyladenosine (**5b**) to produce an enol tosylate[6] (**11**), which, under the reaction conditions, was converted into **6a** *via* **10** in a one-pot procedure. 2′-Detosylation of **5b** occurred to a substantial extent in this reaction. Compound **6a** thus obtained was a useful intermediate for synthesizing **9**.

The key intermediate for the synthesis of **17** was 9-(2-deoxy-5-*O*-trityl-β-D-*threo*-pentofuranosyl)adenine[7c] (**13**), obtained by the deoxygenative reduction of 2′-*O*-tosyl-5′-*O*-trityladenosine (**12**) with lithium triethylborohydride, this method being developed by Hansske and Robins[5d]. The reagent combination $Mg(OMe)_2$–$NaBH_4$ was unsuccessful in this case, presumably because of the instability[5d,k,7] of an *in situ*-generated 2′-deoxy-3′-keto nucleoside under the reaction conditions.

RESULTS AND DISCUSSION

The present work required various protected 2′- and/or 3′-*O*-sulfonylated

adenosines. Thus, 2′-*O*-tosyladenosine (**2**) and its 3′-isomer were prepared from adenosine (**1**) according to the modified method of Moffatt *et al.*[8a] and Uesugi *et al.*[8b]. The latter isomer was, for the first time, isolated as its *p*-toluenesulfonate salt (**3**), in 13% yield. Treatment of **2** and **3** with bis(4-methoxyphenyl)chlorophenylmethane ("4,4′-dimethoxytrityl chloride", DMTrCl) gave the corresponding N^6,$O^{5'}$-protected derivatives (**5a** and **5e**), respectively. The 5′-*O*-monotritylation of **2** was achieved with chlorotriphenylmethane (TrCl) to give 2′-*O*-tosyl-5′-*O*-trityladenosine[5d] (**12**). The 3′-*O*-mesyl-2′-*O*-tosyl derivative (**5b**) was obtained by mesylation of **5a**. Similarly the 2′,3′-dimesylate **5c** was prepared through N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)adenosine (**4**).

For the synthesis of **9**, **5e** was treated with $Mg(OMe)_2$ (10 mol. equiv.)–$NaBH_4$ (5 mol. equiv.) in C_6H_6–MeOH for 7 min at 65°. During the heating, hydrogen gas was liberated. The reaction proceeded well to give **6a** in 95% yield, but its overall yield from **1** was only 8%. No diastereomer was detected by t.l.c. or ^{1}H-n.m.r. spectroscopic analyses. In this reaction, $LiEt_3BH$[5d] could be used in place of $Mg(OMe)_2$–$NaBH_4$ to afford **6a** in 67% yield. The "up" configuration of the 2′-OH group in **6a** was ascertained by the conversion of **6a** into the known deblocked compound[9] (**6b**).

An alternative and superior preparation of **6a** has been accomplished by the use of the β-elimination of the 2′,3′-disulfonates[6]. Thus, when **5b** was treated with $Mg(OMe)_2$–$NaBH_4$ for 6 h under conditions similar to those described here, **6a** was formed in 86% yield (37% overall from **1**). As **5b** is readily synthesized from **2** (which in turn is the main product in the tosylation of the stannylated adenosine[8a]), this is the more preferred synthesis of **6a**.

It is considered that these mixed reagents produced NaOMe *in situ* according to the hard acid–soft base principle[10], and that this strong base played an important role in the β-elimination reaction[6]. In view of the fact that 2′-*O*-deacylation[11a], debenzylation[11b], and detosylation[11c] of ribonucleosides occurs under basic conditions, the 2′-*O*-tosyl group in **5b** might be partially cleaved prior to the β-elimination during the course of the reaction (from **5b** to **6a**). This cleavage would produce the intermediate (**A**; $R^1 = CH_3$, Scheme 2), which is potentially susceptible to a [1,2]-hydride shift. In order to clarify whether or not there is such a bypass, we performed experiments using a deuterium-labeled solvent (methanol-d_1) in the reaction of **5b**, and also treated the expected intermediate **11** with $Mg(OMe)_2$–$NaBH_4$*. The ^{1}H-n.m.r. spectroscopic analysis of partially deuterated products (**6**-*d*) thus obtained showed that the extents of deuteration at C-3′ were 38% (**5b**→**6**-*d*) and 52% (**11**→**6**-*d*). The large difference in deuterium content between these two compounds suggested that ~30% of the reaction for **5b** proceeded *via* **A** ($R = CH_3$). Additional evidence for the detosylation was obtained when **5b** was treated with NaOMe in C_6H_6–MeOH at room temperature. The reaction gave a complicated mixture of products, but the 2′-detosylated compound **5d** could be isolated in 21% yield. These findings prompted us to use the combined reagent KOH–$NaBH_4$

*We thank a referee for suggesing the use of **5c** and **11** in the reaction with $Mg(OMe)_2$–$NaBH_4$.

for the deoxygenative reduction. The reaction of **5b** and **5c** with these reagents smoothly proceeded at room temperature to provide **6a** in 87 and 96% yields, respectively. Consequently, the best synthetic route was **1→4→5c→6a**; the overall yield (3 steps) being 67%. The $N^6,O^{5'}$-bis(4-methoxytrityl) derivative of **6b** is known, but was prepared *via* an 8-step synthesis from **1** in 20% overall yield[9c].

Mesylation of **6a** gave $N^6,O^{5'}$-bis(4,4′-dimethoxytrityl)-9-(3-deoxy-2-*O*-mesyl-β-D-*erythro*-pentofuranosyl)adenine (**7**), which reacted with NaN_3 in *N,N*-dimethylformamide (DMF) at 110° to afford the (2′*R*)-2′-azido derivative **8** in good yield. The configuration of the azido group at C-2′ in **8** was assigned on the basis of the small value[12] of $J_{1',2'}$ (2.2 Hz) in the ^{1}H-n.m.r. spectrum and of the normal stereochemical course of an SN2 reaction[13]. Deprotection of **8** with 80% HOAc produced crystalline **9** in 75% yield. The overall yield of **9** from **1** *via* **2** or **4** was 20 or 36%, respectively, whereas *via* **3** it was 4%.

The 3′-tosylate (**5a**) was expected to be a good candidate as a reactant for the deoxygenative [1,2]-hydride shift rearrangement and subsequent reduction, which would provide an appropriate intermediate for the synthesis of **17**. Attempted [$Mg(OMe)_2$–$NaBH_4$]-mediated reaction of **5a**, however, gave complicated product-mixtures. Even when $LiEt_3BH$ (ref. 5d) was used instead of our mixed reagents, the yield of the desired product was extremely low. Therefore we utilized the known compound **13** as the key intermediate, prepared from **1** in 28% overall yield.

Compound **13** was treated with DMTrCl to give the corresponding N^6-protected derivative (**14**), which, on mesylation, produced N^6-(4,4′-dimethoxytrityl)-9-(2-deoxy-3-*O*-mesyl-5-*O*-trityl-β-D-*threo*-pentofuranosyl)adenine (**15a**) in 79% yield from **13**. Careful mesylation of **13** also gave the corresponding 3′-mesylate (**15b**). Mesylates **15a** and **15b** were not purified, but were treated separately with NaN_3 in DMF at 110° to provide the corresponding 3′-azido derivatives (**16a** and **16b**) in 91 and 88% yields, respectively. Finally, deprotection of **16a** or **16b** was achieved with zinc bromide[14] in $CHCl_3$–MeOH for 3 h at 65°, giving **17** in 83 or 68% yield, respectively, without any depurination. The overall yields of **17** from **1** were 17% (*via* **15a**) and 14% (*via* **15b**). The physical properties of the product were in good agreement with those reported earlier[2].

Preliminary results for application of the deoxygenative [1,2]-hydride shift reaction with $Mg(OMe)_2$ (or KOH–$NaBH_4$) to other purine and pyrimidine nucleosides have been reported[5l,m]. Biological evaluation of **9** and **17** will be reported elsewhere.

EXPERIMENTAL

General methods. — Melting points were determined in capillary tubes with a Yamato micro melting-point apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 241MC polarimeter in a 1-dm cell for solutions in $CHCl_3$ unless otherwise stated. I.r. spectra were recorded with a Shimadzu IR-27 spectrophotometer, and u.v. spectra were measured with a Varian

Cary 2200 instrument using a 1-cm cell. ^{1}H-N.m.r. spectra were recorded with a JEOL JNM-GX 400 spectrometer, using Me_4Si as the internal standard, for solutions in $CDCl_3$ unless otherwise specified. Coupling constants were measured directly from the spectra, or calculated from the peak listings. T.l.c. was performed on precoated plates (0.25 mm) of Silica Gel 60 F_{254} (Merck). Detection was by u.v. (254 nm) or by spraying the plates with 16:3:1 (v/v) MeOH–H_2SO_4-*p*-anisaldehyde followed in the latter case by heating at >200°. Column chromatography was effected on Silica Gel 60 (Merck 70–230 mesh, ASTM). Elemental analyses were performed by the Microanalytical Laboratory of this Institute. Solvent extracts were dried with anhydrous $MgSO_4$, and solutions were evaporated under diminished pressure at 40–45°. Analytical samples were dried for 4 h *in vacuo* over P_2O_5 at 60°. The materials, $Mg(OMe)_2$, $LiEt_3BH$, and methanol-d_1 (min. content 99%) were purchased from Soekawa Chemicals (Tokyo, Japan), Aldrich Chemical Co. (U.S.A.), and E. Merck (W. Germany), respectively.

2′-O-Tosyladenosine (**2**) *and 3′-O-tosyladenosine tosylate salt* (**3**). — The method of Uesugi *et al.*[8b] was slightly modified. To a warm suspension of 2′,3′-*O*-(dibutylstannylene)adenosine [prepared from **1** (10.68 g, 40 mmol) and dibutyltin oxide (9.96 g, 40 mmol)][8a] in MeOH (20 mL) were successively added dry 1,4-dioxane (180 mL), Et_3N (18 mL), and TsCl (22.87 g, 120 mmol) with vigorous stirring. After the mixture had been stirred overnight at room temperature, crystalline salts were removed by filtration and washed with 1,4-dioxane. The combined filtrate and washings were evaporated, and the residue was dissolved in boiling MeOH (60 mL). After being kept overnight at room temperature, crude crystalline **2** was filtered from the mixture and washed with cold MeOH. The combined filtrate and washings were evaporated, and the residue was then triturated with boiling water (60 mL). After the mixture had been kept overnight at about 5°, undissolved materials were collected by filtration and washed successively with cold water (100 mL) and Et_2O (100 mL), and dried. Crystallization from MeOH gave **3** (3.12 g, 13%); m.p. 195–196° (dec.); $[\alpha]_D^{27}$ −23.0° (*c* 0.94, Me_2SO); λ_{max}^{MeOH} 259 nm (ε 16200); δ_H (Me_2SO-d_6) 2.29 (s, 3 H, Me), 2.43 (s, 3 H, Me), 3.42 (dd, 1 H, H-5′), 3.58 (dd, 1 H, H-5″), 4.12 (m, 1 H, H-4′), 4.83 (dd, 1 H, H-2′), 5.03 (dd, 1 H, H-3′), 5.95 (d, 1 H, H-1′), 7.12 (d, 2 H, arom.), 7.50 (m, 4 H, arom.), 7.88 (m, 2 H, arom.), 8.47 (s, 1 H, H-2), and 8.66 (s, 1 H, H-8).

Anal. Calc. for $C_{24}H_{27}N_5O_9S_2$: C, 48.56; H, 4.58; N, 11.80; S, 10.80. Found: C, 48.55; H, 4.57; N, 11.70; S, 10.71.

The crude **2** was placed in MeOH (80 mL), and the suspension was refluxed for 20 min. After being kept overnight at room temperature, the undissolved crystals were collected by filtration and washed successively with cold MeOH (80 mL) and CH_2Cl_2 (120 mL) to afford **2** (11.7 g, 70%), which was free from **3** and tin compounds, judging from the t.l.c. and ^{1}H-n.m.r. spectroscopic analyses: m.p. 221–222° (dec.) [lit.[8c] m.p. 222–223°].

N^6,$O^{5'}$-*Bis(4,4′-dimethoxytrityl)adenosine* (**4**). — Adenosine (**1**; 2.67 g, 10 mmol) was dissolved in dry C_5H_5N–DMF (2:3, 50 mL) at 100°. After cooling

(~25°), bis(4-methoxyphenyl)chlorophenylmethane (DMTrCl, 7.21 g, 21 mmol) was added, and the mixture was stirred for 7 h at room temperature. After cooling, 50% aq. C_5H_5N was added and the mixture was extracted with Et_2O containing a small amount of $CHCl_3$. The extract was washed successively with water, saturated aq. $NaHCO_3$, and water, dried, and evaporated. The C_5H_5N was removed by co-evaporation with PhMe. The residue was chromatographed on a column of silica gel with 7:3:0.1 C_6H_6–EtOAc–Et_3N as the eluant to give **4** (6.46 g, 74%) as a foam. A portion of the product was dissolved in a small amount of CH_2Cl_2 and precipitated by the addition of the CH_2Cl_2 solution to an excess of pentane under vigorous stirring. The resulting precipitate was collected and dried to afford an analytical sample: amorphous powder; $[\alpha]_D^{24}$ −4.5° (*c* 0.75); λ_{max}^{MeOH} 274 nm (ε 31000), 232 nm (shoulder, ε 42000); δ 3.13 (broad s, 1 H, OH), 3.20 (dd, 1 H, *J* 10.4 and 3.4 Hz, H-5′), 3.44 (dd, 1 H, *J* 10.4 and 3.7 Hz, H-5″), 3.767 and 3.773 (each s, 12 H, 4 OMe), 4.33 (broad d, 1 H, *J* 5 Hz, H-3′), 4.42 (m, 1 H, H-4′), 4.71 (t, 1 H, *J* 5.5 Hz, H-2′), 5.89 (d, 1 H, *J* 6.4 Hz, H-1′), 6.61 (broad s, 1 H, OH), 6.74–7.35 (m, 27 H, arom. and NH), 8.01 (s, 1 H, H-2), and 8.05 (s, 1 H, H-8).

Anal. Calc. for $C_{52}H_{49}N_5O_8$: C, 71.63; H, 5.66; N, 8.03. Found: C, 71.36; H, 5.77; N, 7.84.

N^6,O$^{5'}$-*Bis(4,4′-dimethoxytrityl)-2′-O-tosyladenosine* (**5a**). — To a suspension of **2** (4.21 g, 10 mmol) in dry C_5H_5N (50 mL) was added DMTrCl (7.45 g, 22 mmol), and the mixture was stirred for 20 h at room temperature. After cooling, 50% aq. C_5H_5N was added, and the mixture was extracted with $CHCl_3$. The extract was washed successively with water, saturated aq. $NaHCO_3$, and water, and dried. The $CHCl_3$ was evaporated, and the residual C_5H_5N was removed by repeated co-evaporation with PhMe. The residue was chromatographed on a column of silica gel with 9:1:0.2:0.1 PhMe–EtOAc–MeOH–Et_3N to give **5a** (7.74 g, 75%) as a foam. Precipitation from CH_2Cl_2–pentane gave an analytical sample: $[\alpha]_D^{24}$ −39.2° (*c* 0.5); λ_{max}^{MeOH} 274 nm (ε 26100); δ_H 2.29 (s, 3 H, Ts-Me), 3.31 (dd, 1 H, *J* 10.6 and 4.0 Hz, H-5′), 3.44 (dd, 1 H, *J* 10.6 and 3.5 Hz, H-5″), 3.77 (s, 12 H, 4 OMe), 4.19 (m, 1 H, H-4′), 4.65 (m, 1 H, H-3′), 5.73 (t, 1 H, *J* 5.6 Hz, H-2′), 6.07 (d, 1 H, *J* 6.1 Hz, H-1′), 6.78–7.55 (m, 31 H, arom. and NH), 7.73 (s, 1 H, H-2), and 7.81 (s, 1 H, H-8).

Anal. Calc. for $C_{59}H_{55}N_5O_{10}S \cdot 0.4\ H_2O$: C, 68.57; H, 5.44; N, 6.78; S, 3.10. Found: C, 68.60; H, 5.40; N, 6.75; S, 3.12.

N^6,O$^{5'}$-*Bis(4,4′-dimethoxytrityl)-3′-O-mesyl-2′-O-tosyladenosine* (**5b**). — Mesyl chloride (2.14 g, 18.6 mmol) was added to a solution of **5a** (9.50 g, 9.3 mmol) in dry C_5H_5N (40 mL), and the mixture was stirred for 1 h at room temperature. After cooling, 50% aq. C_5H_5N was added and the mixture was extracted with Et_2O. The extract was washed successively with water, saturated aq. $NaHCO_3$, and water, dried, and evaporated. The C_5H_5N was removed by coevaporation with PhMe. The residue was chromatographed on a column of silica gel with 95:5:1 C_6H_6–EtOAc–Et_3N, followed by 95:5:1:1 C_6H_6–EtOAc–MeOH–Et_3N, to give **5b** (8.35 g, 81%). Precipitation from CH_2Cl_2–pentane provided an analytical sample:

amorphous powder; $[\alpha]_D^{20}$ −34.1° (*c* 0.6); λ_{max}^{MeOH} 273 nm (ε 27900); δ_H 2.28 (s, 3 H, Ts-Me), 3.11 (s, 3 H, Ms-Me), 3.45 (dd, 1 H, *J* 11.0 and 3.4 Hz, H-5′), 3.54 (dd, 1 H, *J* 11.0 and 3.9 Hz, H-5″), 3.78 (s, 12 H, 4 OMe), 4.45 (q, 1 H, H-4′), 5.44 (dd, 1 H, *J* 5.4 and 2.5 Hz, H-3′), 5.89 (dd, 1 H, *J* 6.8 and 5.4 Hz, H-2′), 6.08 (d, 1 H, *J* 6.6 Hz, H-1′), 6.79–7.43 (m, 31 H, arom. and NH), 7.69 (s, 1 H, H-2), and 7.78 (s, 1 H, H-8).

Anal. Calc. for $C_{60}H_{57}N_5O_{12}\cdot C_5H_{12}$: C, 66.36; H, 5.91; N, 5.95; S, 5.45. Found: C, 66.26; H, 6.01; N, 5.80; S, 5.41.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-2′,3′-di-O-mesyladenosine* (**5c**). — To a solution of **4** (2.62 g, 3 mmol) in dry C_5H_5N (15 mL) was added mesyl chloride (0.7 mL, 9 mmol) at 0–5°. After being stirred for 2.5 h at room temperature, the mixture was processed in a manner similar to that described for the synthesis of **5b**. The crude products were chromatographed on a column of silica gel with 95:5:1 C_6H_6–EtOAc–Et_3N to give **5c** (2.89 g, 94%) as a foam. An analytical sample was obtained by precipitation from CH_2Cl_2–pentane: amorphous powder; $[\alpha]_D^{23}$ −14.6° (*c* 0.75); λ_{max}^{MeOH} 273 nm (ε 41000), 231 nm (shoulder, ε 44000); δ_H 3.05 and 3.06 (each s, 6 H, 2 SMe), 3.35 (dd, 1 H, *J* 11.0 and 3.3 Hz, H-5′), 3.59 (dd, 1 H, *J* 11.0 and 3.4 Hz, H-5″), 3.759 and 3.765 (each s, 12 H, 4 OMe), 4.43 (m, 1 H, H-4′), 5.72 (t, 1 H, *J* 5.0 Hz, H-3′), 6.11 (t, 1 H, *J* 5.0 Hz, H-2′), 6.20 (d, 1 H, *J* 5.2 Hz, H-1′), 6.76–7.35 (m, 27 H, arom. and NH), 7.88 (s, 1 H, H-2), and 7.94 (s, 1 H, H-8).

Anal. Calc. for $C_{54}H_{53}N_5O_{12}S_2\cdot 0.5\ C_5H_{12}$: C, 63.77; H, 5.59; N, 6.58; S, 6.02. Found: C, 63.70; H, 5.80; N, 6.36; S, 5.89.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-3′-O-mesyladenosine* (**5d**). — To a solution of **5b** (1.65 g, 1.5 mmol) in 1:1 C_6H_6–MeOH (18 mL) was added NaOMe (405 mg, 7.5 mmol), and the mixture was stirred for 2.2 h at room temperature. After cooling, the mixture was diluted with Et_2O, washed five times with water, dried, and evaporated. The residue was chromatographed on a column of silica gel with 90:10:1:1 C_6H_6–EtOAc–Et_3N–MeOH, followed by chromatography with the same solvent system (90:10:1:0.4), to afford **5d** (298 mg, 21%) as a foam. Precipitation from CH_2Cl_2–pentane gave an analytical sample: amorphous powder; $[\alpha]_D^{27}$ −12.3° (*c* 0.72); λ_{max}^{MeOH} 275 nm (ε 29300), 234 nm (shoulder, ε 42300); δ_H 3.17 (s, 3 H, SMe), 3.25 (dd, 1 H, *J* 11.0 and 3.1 Hz, H-5′), 3.47 (dd, 1 H, *J* 11.0 and 3.9 Hz, H-5″), 3.768 and 3.770 (each s, 12 H, 4 OMe), 4.56 (m, 1 H, H-4′), 5.00 (m, 1 H, H-2′), 5.18 (dd, 1 H, *J* 5.2 and 0.9 Hz, H-3′), 5.86 (d, 1 H, *J* 7.0 Hz, H-1′), 6.41 (d, 1 H, *J* 3.1 Hz, OH), 6.74–7.36 (m, 27 H, arom. and NH), 8.00 (s, 1 H, H-2), and 8.02 (s, 1 H, H-8).

Anal. Calc. for $C_{53}H_{51}N_5O_{10}S\cdot 0.4\ C_5H_{12}$: C, 67.48; H, 5.75; N, 7.15; S, 3.27. Found: C, 67.48; H, 5.86; N, 7.24; S, 3.27.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-3′-O-tosyladenosine* (**5e**). — To a solution of the tosylate salt (**3**; 3.27 g, 5.5 mmol) in dry C_5H_5N (30 mL) was added DMTrCl (3.72 g, 11 mmol), after which the mixture was stirred for 3 h at room temperature. After cooling, 1:1 C_5H_5N–MeOH (3 mL) was added, and the mixture was extracted with $CHCl_3$. Processing similar to that described for the synthesis of **5a** and purifica-

tion by column chromatography on silica gel (9:1:0.1 PhMe–EtOAc–Et_3N → 9:1:0.1:0.1 PhMe–EtOAc–Et_3N–MeOH) gave **5e** (3.65 g, 65%) as crystals: m.p. 130 (sintered)–142° (from C_6H_6–Et_2O); $[\alpha]_D^{22}$ +4.8° (*c* 0.57); λ_{max}^{MeOH} 274 nm (ε 27200); δ_H 2.40 (s, 3 H, Ts-Me), 3.07 (dd, 1 H, H-5′), 3.39 (dd, 1 H, H-5″), 3.76 and 3.77 (2s, 12 H, 4 OMe), 4.42 (m, 1 H, H-4′), 5.02 (q, 1 H, H-2′), 5.08 (dd, 1 H, H-3′), 5.88 (d, 1 H, H-1′), and 7.97 (s, 2 H, H-2 and H-8).

Anal. Calc. for $C_{59}H_{55}N_5O_{10}S \cdot 0.2\ C_6H_6$: C, 69.41; H, 5.44; N, 6.72; S, 3.08. Found: C, 69.64; H, 5.50; N, 6.77; S, 2.95.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-9-(3-deoxy-β-*D-threo-*pentofuranosyl)adenine* (**6a**). — The purity of the products (**6a**) obtained according to methods A–F described below was more than 95% after chromatography, judging from the t.l.c. and ^{1}H-n.m.r. spectroscopic analyses.

(A) *From* **5b** *with* $Mg(OMe)_2$–$NaBH_4$. To a solution of **5b** (1.10 g, 1 mmol) in 1:1 C_6H_6–MeOH (20 mL) were added $Mg(OMe)_2$ (860 mg, 10 mmol) and $NaBH_4$ (190 mg, 5 mmol), whereupon the mixture was stirred for 5 h at 65° under an atmosphere of dry N_2. After cooling, the reaction was quenched with Me_2CO (5 mL). The mixture was diluted with Et_2O containing a small amount of $CHCl_3$, washed successively with aq. NH_4Cl and water, and dried. The organic solvents were evaporated, and the residue was chromatographed on a column of silica gel (9:1:0.1 C_6H_6–EtOAc–Et_3N → 9:1:0.1:0.1 C_6H_6–EtOAc–MeOH–Et_3N) to afford **6a** (740 mg, 86%) as a foam. Precipitation from CH_2Cl_2–pentane gave an analytical sample: amorphous powder; $[\alpha]_D^{22}$ +9.2° (*c* 0.9); λ_{max}^{MeOH} 274 nm (ε 30000); δ_H 2.15 (m, 1 H, H-3′), 2.47 (m, 1 H, H-3″), 3.19 (dd, 1 H, *J* 10.6 and 3.8 Hz, H-5′), 3.56 (dd, 1 H, *J* 10.6 and 2.6 Hz, H-5″), 3.78 (s, 12 H, 4 OMe), 4.34 (m, 1 H, H-4′), 4.53 (broad s, 2 H, H-2′ and OH), 6.06 (d, 1 H, *J* 2.9 Hz, H-1′), 6.78–7.42 (m, 27 H, arom. and NH), 8.02 (s, 1 H, H-2), and 8.24 (s, 1 H, H-8).

Anal. Calc. for $C_{52}H_{49}N_5O_7 \cdot 0.2\ H_2O$: C, 72.66; H, 5.79; N, 8.15. Found: C, 72.84; H, 6.08; N, 7.87.

(B) *From* **5b** *with KOH–*$NaBH_4$. To a stirred solution of **5b** (110 mg, 0.1 mmol) in 1:3 C_6H_6–MeOH (2 mL) was added a solution of KOH (56 mg, 1 mmol) in MeOH (1 mL) at room temperature, followed by addition of $NaBH_4$ (19 mg, 0.5 mmol). The mixture was stirred for 24 h at room temperature. After cooling, the reaction was quenched with Me_2CO (0.5 mL). The mixture was diluted with Et_2O, washed three times with water, dried, and evaporated. The residue was chromatographed on a column of silica gel with the same solvent systems as described in method A to give **6a** (75 mg, 87%).

(C) *From* **5c** *with* $Mg(OMe)_2$–$NaBH_4$. A stirred mixture of **5c** (103 mg, 0.1 mmol), $Mg(OMe)_2$ (86 mg, 1 mmol), and $NaBH_4$ (19 mg, 0.5 mmol) in 1:2 C_6H_6–MeOH (3 mL) was heated for 4.5 h at 65° under an atmosphere of dry N_2. Isolation and purification by chromatography as described in method A gave **6a** (66 mg, 77%).

(D) *From* **5c** *with KOH–*$NaBH_4$. To a solution of **5c** (1.03 g, 1 mmol) in 1:3 C_6H_6–MeOH (20 mL) was added a solution of KOH (560 mg, 10 mmol) in MeOH

(10 mL), followed by addition of $NaBH_4$ (190 mg, 5 mmol), whereupon the mixture was stirred for 24 h at room temperature. Isolation and purification by chromatography as described in method B afforded **6a** (822 mg, 96%).

(E) *From* **5e** *with* $Mg(OMe)_2$–$NaBH_4$. A mixture of **5e** (102 mg, 0.1 mmol), $Mg(OMe)_2$ (86 mg, 1 mmol), and $NaBH_4$ (19 mg, 0.5 mmol) in 1:1 C_6H_6–MeOH (2 mL) was treated for 7 min under conditions similar to those described in method A. Isolation and purification by chromatography gave **6a** (81 mg, 95%).

(F) *From* **5e** *with* $LiEt_3BH$. A solution of **5e** (3.08 g, 3 mmol) in dry C_6H_6 (16 mL) was added to a cooled M $LiEt_3BH$–THF solution (21 mL, 21 mmol) under an atmosphere of dry N_2, after which the mixture was stirred for 5 h at room temperature. After cooling, MeOH (2 mL) was dropwise added and the products were extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated. The residue was chromatographed on a column of silica gel with 99:1:0.1 $CHCl_3$–MeOH–Et_3N to give **6a** (1.71 g, 67%).

Preparation of partially deuterated compound (**6**-*d*). — *From* **5b**. A solution of **5b** (110 mg, 0.1 mmol) in dry 1:1 C_6H_6–MeOH-d_1 (2 mL) was boiled under reflux for 5 min, and the solvents were removed. This procedure was repeated once again. The residue was dissolved in dry C_6H_6 (1 mL), whereupon this solution was added to a stirred solution of $Mg(OMe)_2$ [prepared from Mg (turnings, 24 mg, 1 mmol) in MeOH-d_1] in dry 1:2 C_6H_6–MeOH-d_1 (3 mL). Sodium borohydride (19 mg, 0.5 mmol) was added, and the mixture was stirred for 6 h at 65° under an atmosphere of dry N_2. Isolation and purification by chromatography gave **6**-*d* (74 mg, 86%): δ_H 2.14 (m, 0.79 H, H-3′), 2.47 (m, 0.46 H, H-3″), 6.05 (m, 1 H, H-1′), 8.02 (s, 1 H, H-2), and 8.25 (s, 0.86 H, H-8).

From **11**. The compound (**11**; 101 mg, 0.1 mmol) was treated under the same conditions as described for the preparation of **6**-*d* from **5b** except that the reaction time was 20 min, giving **6**-*d* (80 mg, 93%): δ_H 2.13 (m, 0.79 H, H-3′) and 2.45 (m, 0.17 H, H-3″).

*Preparation of 9-(3-deoxy-β-*D-threo-*pentofuranosyl)adenine*[9] (**6b**). — A mixture of **6a** (120 mg, 0.14 mmol) and 80% AcOH (6 mL) was stirred for 40 min at room temperature. The AcOH was removed by repeated coevaporation with EtOH–PhMe, and the residue was chromatographed on a column of silica gel with 99:1→8:2 $CHCl_3$–MeOH to give **6b** (30 mg, 86%): m.p. 193° (sintered), 207–208° (from EtOH); $[\alpha]_D^{25}$ −27.9° (*c* 0.2, DMF); $\lambda_{max}^{pH\,7}$ 259 nm (ε 13200) [lit.[9b] m.p. 192–193° (sintered), 203° (from EtOH); $[\alpha]_D^{23}$ −26.5° (*c* 0.50, DMF); $\lambda_{max}^{pH\,7}$ 258 nm (ε 14800)]; δ_H (Me_2SO-d_6) 2.02 (m, 1 H, H-3′), 2.28 (m, 1 H, H-3″), 3.55–3.68 (m, 2 H, H-5′ and H-5″), 4.09 (m, 1 H, H-4′), 4.50 (m, 1 H, H-2′), 5.16 (t, 1 H, *J* 5.4 Hz, 5′-OH), 5.40 (d, 1 H, *J* 5.6 Hz, 2′-OH), 6.14 (d, 1 H, *J* 5.6 Hz, H-1′), 7.21 (broad s, 2 H, NH_2), 8.12 (s, 1 H, H-2), and 8.28 (s, 1 H, H-8).

N^6,$O^{5'}$-*Bis(4,4′-dimethoxytrityl)-9-(3-deoxy-2-*O*-mesyl-β-*D-threo-*pentofuranosyl)adenine* (**7**). — To a cooled solution of **6a** (544 mg, 0.64 mmol) in dry C_5H_5N (4 mL) was added mesyl chloride (299 mg, 2.6 mmol), and then the mixture was stirred for 5 h at room temperature. Isolation as that described for the synthesis

of **5a** and purification by column chromatography on silica gel (99:1:1 $CHCl_3$–MeOH–Et_3N) gave **7** (556 mg, 93%) as a foam. Precipitation from CH_2Cl_2–pentane provided an analytical sample: amorphous powder; $[\alpha]_D^{22}$ +8.2° (*c* 0.9); λ_{max}^{MeOH} 274 nm (ε 29400); δ_H 2.47 (m, 1 H, H-3′), 2.52 (s, 3 H, Ms-Me), 2.62 (m, 1 H, H-3″), 3.38 (dd, 1 H, *J* 10.3 and 4.2 Hz, H-5′), 3.44 (dd, 1 H, *J* 10.3 and 5.6 Hz, H-5″), 3.78 and 3.79 (2s, each 6 H, 4 OMe), 4.34 (m, 1 H, H-4′), 5.32 (m, 1 H, H-2′), 6.34 (d, 1 H, *J* 4.6 Hz, H-1′), 6.77–7.48 (m, 27 H, arom. and NH), and 8.00 and 8.02 (2s, each 1 H, H-2 and H-8).

Anal. Calc. for $C_{53}H_{51}N_5O_9S \cdot 0.7\ C_5H_{12}$: C, 68.93; H, 6.08; N, 7.11; S, 3.26. Found: C, 68.89; H, 6.11; N, 6.94; S, 3.32.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-9-[(2R)-2-azido-2,3-dideoxy-β-*D-glycero-*pentofuranosyl]adenine* (**8**). — To a solution of **7** (523 mg, 0.56 mmol) in dry DMF (12 mL) was added NaN_3 (1.09 g, 16.8 mmol), and the mixture was stirred for 5 h at 105–110°. After cooling, the mixture was diluted with Et_2O containing a small amount of $CHCl_3$, washed three times with water, and dried. The organic solvents were evaporated and the residue was purified by column chromatography on silica gel with 97:3:1 $CHCl_3$–EtOAc–Et_3N to give **8** (382 mg, 78%) as a foam. Precipitation from CH_2Cl_2–pentane gave an analytical sample: amorphous powder; $[\alpha]_D^{20}$ −37.5° (*c* 0.4); ν_{max}^{KBr} 2110 cm^{-1} (N_3); λ_{max}^{MeOH} 274 nm (ε 28900); δ_H 2.13 (ddd, 1 H, *J* 13.4, 5.9, and 2.4 Hz, H-3′), 2.41 (m, 1 H, H-3″), 3.33 (dd, 1 H, *J* 10.5 and 4.9 Hz, H-5′), 3.41 (dd, 1 H, *J* 10.5 and 3.5 Hz, H-5″), 3.77 (s, 12 H, 4 *O*Me), 4.53 (m, 1 H, H-4′), 4.82 (m, 1 H, H-2′), 5.98 (d, 1 H, *J* 2.2 Hz, H-1′), 6.77–7.42 (m, 27 H, arom. and NH), and 7.94 and 8.03 (2s, each 1 H, H-2 and H-8).

Anal. Calc. for $C_{52}H_{48}N_8O_6 \cdot 0.5\ H_2O$ C, 70.18; H, 5.55; N, 12.59. Found: C, 70.26; H, 5.53; N, 12.45.

*9-[(2R)-2-Azido-2,3-dideoxy-β-*D-glycero-*pentofuranosyl]adenine* (**9**). — A mixture of **8** (182 mg, 0.21 mmol) and 80% AcOH (7 mL) was stirred for 4 h at room temperature. The AcOH was removed by repeated co-evaporation with EtOH–PhMe, and the residue was triturated with EtOH to provide crystalline **9**, which was separated by filtration (26 mg, 43%). The mother liquor was concentrated, and the residue was chromatographed on a column of silica gel with 19:1 $CHCl_3$–MeOH to give another crop of **9** (19 mg, 32%; total 75%): m.p. 203–204° (dec.) (from EtOH); $[\alpha]_D^{22}$ −66.0° (*c* 0.6, DMF); ν_{max}^{KBr} 2120 cm^{-1} (N_3); λ_{max}^{MeOH} 258 nm (ε 15000); δ_H (Me_2SO-d_6) 2.14 (ddd, 1 H, *J* 13.4, 6.4, and 3.9 Hz, H-3′), 2.46 (m, 1 H, H-3″), 3.54 (ddd, 1 H, *J* 12.0, 6.1, and 3.9 Hz, H-5′), 3.72 (ddd, 1 H, *J* 12.0, 5.2, and 3.3 Hz, H-5″), 4.32 (m, 1 H, H-4′), 4.85 (m, 1 H, H-2′), 5.25 (t, *J* 5.6 Hz, 1 H, OH), 6.01 (d, 1 H, *J* 3.2 Hz, H-1′), 7.36 (broad s, 2 H, NH_2), 8.16 (s, 1 H, H-2), and 8.40 (s, 1 H, H-8).

Anal. Calc. for $C_{10}H_{12}N_8O_2$: C, 43.47; H, 4.38; N, 40.56. Found: C, 43.47; H, 4.38; N, 40.60.

$N^6,O^{5'}$-*Bis(4,4′-dimethoxytrityl)-9-(2,3-dideoxy-β-*D-glycero-*pent-2-enofuranosyl)adenine* (**11**). — To a solution of 9-(2,3-dideoxy-β-D-*glycero*-pent-2-enofuranosyl)adenine[6] (140 mg, 0.33 mmol) in dry C_5H_5N (2 mL) was added DMTrCl

(268 mg, 0.79 mmol), after which the mixture was stirred for 12 h at room temperature. After cooling, the mixture was quenched with 50% aq. C_5H_5N, and extracted with Et_2O. The extract was washed successively with water, saturated aq. $NaHCO_3$, water, dried, and evaporated. The residue was chromatographed on a column of silica gel with 95:5:1 C_6H_6–EtOAc–Et_3N, followed by 95:5:1:1 C_6H_6–EtOAc–Et_3N–MeOH, to afford **11** (232 mg, 70%) as glasses. Precipitation from CH_2Cl_2–pentane gave an analytical sample: amorphous powder; $[\alpha]_D^{26}$ −21.6° (*c* 0.95); λ_{max}^{MeOH} 275 nm (ε 27500), 229 nm (shoulder, ε 51800); δ_H 2.40 (s, 3 H, Ts-Me), 3.22 (dd, 1 H, *J* 10.1 and 4.7 Hz, H-5′), 3.35 (dd, 1 H, *J* 10.1 and 5.5 Hz, H-5″), 3.762, 3.764, and 3.777 (each s, 12 H, 4 OMe), 5.00 (m, 1 H, H-4′), 6.13 (t, 1 H, *J* 1.5 Hz, H-1′), 6.65 (dd, 1 H, *J* 2.7 and 1.5 Hz, H-3′), 6.76–6.84 (m, 9 H, arom. and NH), 7.19–7.36 (m, 20 H, arom.), 7.66 (s, 2 H, arom.), 7.68 (s, 1 H, H-2), and 7.95 (s, 1 H, H-8).

Anal. Calc. for $C_{59}H_{53}N_5O_9S \cdot 1.4\ C_5H_{12}$: C, 71.47; H, 6.34; N, 6.31; S, 2.89. Found: C, 71.47; H, 6.46; N, 6.33; S, 2.83.

2′-O-Tosyl-5′-O-trityladenosine (**12**). — This compound was reported by Hansske and Robins[5d], but method of synthesis and physical properties have not been described.

To a stirred suspension of **2** (2.11 g, 5 mmol) in dry 5:1 C_5H_5N–DMF (12 mL) was added TrCl (2.09 g, 7.5 mmol). The mixture was first stirred overnight at room temperature and then for 4 h at 85°. Isolation similar to that described for the synthesis of **4** and purification by column chromatography on silica gel (4:1 $CHCl_3$–EtOAc→7:3:0.5 $CHCl_3$–EtOAc–MeOH) gave $N^6,O^{5'}$-ditrityl-2′-*O*-tosyladenosine (1.55 g, 31%) and **12** (1.84 g, 55%) as crystals: m.p. 195–196° (dec.) (from C_6H_6); $[\alpha]_D^{23}$ −52.6° (*c* 1.0); λ_{max}^{MeOH} 260 nm (ε 14300); δ_H 2.31 (s, 3 H, Me), 3.39 (dd, 1 H, *J* 4.0 and 10.7 Hz, H-5′), 3.51 (dd, 1 H, *J* 4.0 and 10.7 Hz, H-5″), 3.63 (m, 1 H, H-4′), 4.28 (m, 1 H, H-3′), 4.74 (broad s, 1 H, OH), 5.73 (broad s, 2 H, NH_2), 5.78 (dd, 1 H, *J* 5.0 and 6.7 Hz, H-2′), 6.08 (d, 1 H, *J* 6.7 Hz, H-1′), 6.96–7.48 (m, 19 H, arom.), 7.77 (s, 1 H, H-2), and 8.02 (s, 1 H, H-8).

Anal. Calc. for $C_{36}H_{33}N_5O_6S$: C, 65.14; H, 5.01; N, 10.55; S, 4.83. Found: C, 65.04; H, 4.99; N, 10.53; S, 4.78.

*Preparation of 9-(2-deoxy-5-O-trityl-β-*D-threo*-pentofuranosyl)adenine*[7c] (**13**). — This compound was synthesized according to the method of Hansske and Robins[5d].

To a stirred M $LiEt_3BH$–THF solution (100 mL, 100 mmol) was added a solution of **12** (9.30 g, 14 mmol) in dry THF (32 mL) at 5° under an atmosphere of dry nitrogen, after which the mixture was first stirred for 4 h at this temperature and then for 3.5 h at room temperature. After cooling, the reaction was quenched with MeOH, and the mixture was diluted with $CHCl_3$. The solution was washed three times with water, dried, and evaporated. The residue was chromatographed on a column of silica gel (99:1→9:1 $CHCl_3$—MeOH) to give **13** (5.03 g, 73%) as crystals: m.p. 175° (sintered), 215–216° (dec.) (from C_6H_6); $[\alpha]_D^{23}$ −13.7° (*c* 0.5); λ_{max}^{MeOH} 259 nm (ε 16600) [lit.[7c] m.p. 120–125° (melting and resolidification) and 216°;

λ_{max}^{MeOH} 259 nm (ε 15400)]; δ_H 2.50 (dd, 1 H, *J* 15.4 and 2.7 Hz, H-2′), 2.86 (m, 1 H, H-2″), 3.55 (dd, 1 H, *J* 10.5 and 4.5 Hz, H-5′), 3.60 (dd, 1 H, *J* 10.5 and 6.8 Hz, H-5″), 4.06 (m, 1 H, H-4′), 4.39 (m, 1 H, H-3′), 5.75 (broad s, 2 H, NH_2), 6.10 (dd, 1 H, *J* 9.3 and 2.7 Hz, H-1′), 7.00 (d, 1 H, *J* 10.0 Hz, OH), 7.16–7.45 (m, 15 H, arom.), 7.92 (s, 1 H, H-2), and 8.24 (s, 1 H, H-8).

Anal. Calc. for $C_{29}H_{27}N_5O_3 \cdot 0.2\ C_6H_6$: C, 71.24; H, 5.58; N, 13.75. Found: C, 71.25; H, 5.64; N, 13.46.

N^6-*(4,4′-Dimethoxytrityl)-9-(2-deoxy-5-*O*-trityl-β-*D-threo-*pentofuranosyl)-adenine* (**14**). — A mixture of **13** (490 mg, 0.99 mmol) and DMTrCl (0.41 g, 1.2 mmol) in dry C_5H_5N (7 mL) was stirred overnight at room temperature. Isolation as in the synthesis of **4** and purification by column chromatography on silica gel (9:1 C_6H_6–EtOAc) gave **14** (0.65 g, 82%) as a foam. Precipitation from CH_2Cl_2–pentane gave an analytical sample: amorphous powder; $[\alpha]_D^{23}$ −21.5° (*c* 0.4); λ_{max}^{MeOH} 275 nm (ε 24200); δ_H 2.47 (dd, 1 H, *J* 15.4 and 2.7 Hz, H-2′), 2.84 (m, 1 H, H-2″), 3.53 (dd, 1 H, *J* 10.4 and 4.5 Hz, H-5′), 3.59 (dd, 1 H, *J* 10.4 and 7.0 Hz, H-5″), 3.78 (s, 6 H, 2 OMe), 4.01 (m, 1 H, H-4′), 4.34 (m, 1 H, H-3′), 6.05 (dd, 1 H, *J* 9.3 and 2.6 Hz, H-1′), 6.78–7.43 (m, 30 H, arom., NH, and OH), 7.83 (s, 1 H, H-2), and 7.91 (s, 1 H, H-8).

Anal. Calc. for $C_{50}H_{45}N_5O_5 \cdot 0.2\ H_2O$: C, 75.11; H, 5.72; N, 8.76. Found: C, 75.09; H, 5.82; N, 8.67.

N^6-*(4,4′-Dimethoxytrityl)-9-(2-deoxy-3-*O*-mesyl-5-*O*-trityl-β-*D-threo-*pentofuranosyl)adenine* (**15a**). — To a solution of **14** (0.54 g, 0.68 mmol) in dry C_5H_5N (5 mL) was added mesyl chloride (390 mg, 3.39 mmol), and the mixture was stirred for 4.5 h at room temperature. Isolation as described for the synthesis of **4** gave crude **15a** (0.57 g, 96%): amorphous powder; δ_H 2.69 (s, 3 H, SMe), 2.90 (m, 2 H, H-2′ and H-2″), 3.33 (dd, 1 H, *J* 9.7 and 6.9 Hz, H-5′), 3.67 (dd, 1 H, *J* 9.7 and 5.7 Hz, H-5″), 3.77 (s, 6 H, 2 OMe), 4.35 (m, 1 H, H-4′), 5.43 (m, 1 H, H-3′), 6.45 (dd, 1 H, *J* 6.3 and 4.2 Hz, H-1′), 6.76–7.43 (m, arom. and NH), and 7.95 and 8.05 (2s, each 1 H, H-2 and H-8). This product was used for next reaction without further purification.

*9-(2-Deoxy-3-*O*-mesyl-5-*O*-trityl-β-*D-threo-*pentofuranosyl)adenine* (**15b**). — Mesyl chloride (592 mg, 5.1 mmol) was added to a stirred solution of **13** (397 mg, 0.8 mmol) in dry C_5H_5N (5 mL) at 5°. After 5 min, the reaction was quenched with cold water. Isolation as described for the synthesis of **4** gave crude **15b** (393 mg, 86%): amorphous powder; δ_H 2.70 (s, 3 H, SMe), 2.92 (m, 2 H, H-2′ and H-2″), 3.35 (dd, 1 H, *J* 9.8 and 6.8 Hz, H-5′), 3.69 (dd, 1 H, *J* 9.8 and 5.9 Hz, H-5″), 4.37 (m, 1 H, H-4′), 5.44 (broad s, 1 H, H-3′), 5.72 (broad s, 2 H, NH_2), 6.50 (dd, 1 H, *J* 7.1 and 3.4 Hz, H-1′), 7.20–7.44 (m, arom.), 8.00 (s, 1 H, H-2), and 8.34 (s, 1 H, H-8). This product was used for next reaction without further purification.

N^6-*(4,4′-Dimethoxytrityl)-9-[(3S)-azido-2,3-dideoxy-5-*O*-trityl-β-*D*-glycero-pentofuranosyl]adenine* (**16a**). — A mixture of crude **15a** (0.57 g, 0.65 mmol) and NaN_3 (0.42 g, 6.5 mmol) in dry DMF (10 mL) was stirred for 2 h at 105–110°. After cooling, the mixture was diluted with Et_2O containing a small amount of $CHCl_3$, and the solution was washed three times with water, dried, and then evaporated.

The residue was chromatographed on a column of silica gel (19:1 C_6H_6–EtOAc) to afford **16a** (0.49 g, 91%) as a foam. Precipitation from CH_2Cl_2–pentane provided an analytical sample: amorphous powder; $[\alpha]_D^{23}$ −6.1° (*c* 0.4), ν_{max}^{KBr} 2100 cm^{-1} (N_3); λ_{max}^{MeOH} 275 nm (ε 25000); δ_H 2.49 (m, 1 H, H-2′), 3.02 (m, 1 H, H-2″), 3.37 (dd, 1 H, *J* 10.5 and 4.4 Hz, H-5′), 3.44 (dd, 1 H, *J* 10.5 and 4.9 Hz, H-5″), 3.77 (s, 6 H, 2 OMe), 4.09 (q, 1 H, H-4′), 4.50 (m, 1 H, H-3′), 6.26 (t, 1 H, *J* 6.2 Hz, H-1′), 6.39–7.40 (m, 29 H, arom. and NH), and 7.88 and 7.98 (2 s, each 1 H, H-2 and H-8).

Anal. Calc. for $C_{50}H_{44}N_8O_4 \cdot 0.2\ C_5H_{12}$: C, 73.33; H, 5.56; N, 13.41. Found: C, 73.23; H, 5.58; N, 13.30.

*9-[(3S)-3-Azido-2,3-dideoxy-5-O-trityl-β-*D*-glycero-pentofuranosyl]adenine* (**16b**). — A mixture of **15b** (286 mg, 0.5 mmol) and NaN_3 (325 mg, 5 mmol) in dry DMF (3 mL) was stirred for 50 min at 105–110°. Isolation similar to that described for the synthesis of **15b** and purification by chromatography on silica gel (99:1 $CHCl_3$–MeOH) gave **16b** (228 mg, 88%) as a foam. An analytical sample was obtained by precipitation from CH_2Cl_2–pentane: amorphous powder; $[\alpha]_D^{23}$ +4.0° (*c* 0.5); ν_{max}^{KBr} 2100 cm^{-1} (N_3); λ_{max}^{MeOH} 259 nm (ε 14600); δ_H 2.55 (m, 1 H, H-2′), 3.04 (m, 1 H, H-2″), 3.37 (dd, 1 H, *J* 10.5 and 4.4 Hz, H-5′), 3.46 (dd, 1 H, *J* 10.5 and 4.6 Hz, H-5″), 4.11 (q, 1 H, H-4′), 4.54 (m, 1 H, H-3′), 5.61 (broad s, 2 H, NH_2), 6.31 (t, 1 H, *J* 6.2 Hz, H-1′), 7.21–7.45 (m, 15 H, arom.), 7.96 (s, 1 H, H-2), and 8.28 (s, 1 H, H-8).

Anal. Calc. for $C_{29}H_{26}N_8O_2 \cdot 0.2\ H_2O$: C, 66.70; H, 5.10; N, 21.46. Found: C, 66.90; H, 5.10; N, 21.16.

*9-[(3S)-3-Azido-2,3-dideoxy-β-*D*-glycero-pentofuranosyl]adenine* (**17**). — *From* **16a**. To a stirred solution of **16a** (123 mg, 0.15 mmol) in $CHCl_3$ (0.75 mL) was added[14] a solution of $ZnBr_2$ (270 mg, 1.2 mmol) in 1:4 MeOH–$CHCl_3$ (1:4, 1.64 mL), whereupon the mixture was heated for 3 h at 65°. After cooling, MeOH (6 mL) was added, and the mixture was concentrated to a few mL, and then diluted with EtOAc (50 mL). The solution was washed with water (4 × 10 mL), and dried. The organic solution was concentrated to a few mL, and the residue was chromatographed on a column of silica gel (19:1 $CHCl_3$–MeOH) to give **17** (24 mg, 59%) as crystals.

The water extracts were passed through an column (1.8 cm × 10 cm) of activated carbon (70–300 mesh, Wako Pure Chemical Industries Ltd., Tokyo) packed in water, and the carbon was washed successively with water, 80% aq. MeOH, and MeOH. The product was eluted with 1:1 $CHCl_3$–MeOH, giving another crop of **17** (10 mg, 24%; total 83%): m.p. 186–187° (dec.) (from EtOH); $[\alpha]_D^{23}$ −8.4° (*c* 0.3, DMF); ν_{max}^{KBr} 2110 cm^{-1}; $\lambda_{max}^{H_2O}$ 259 nm (ε 16400) [lit.[2] m.p. 189–191°; ν_{max}^{KBr} 2120 cm^{-1}; $\lambda_{max}^{H_2O}$ 259.5 nm (ε 15300)]. The data for the ^{1}H-n.m.r. spectrum of **17** were identical with those reported earlier[2].

From **16b**. A solution of **16b** (78 mg, 0.15 mmol) in $CHCl_3$ (0.75 mL) was treated with $ZnBr_2$ (270 mg, 1.2 mmol) under conditions similar to those already described, giving **17** (28 mg, 68%). The i.r. and ^{1}H-n.m.r. spectra of the product were identical with those of the sample prepared from **16a**.

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