  Bull. Chem. Soc. Jpn., 61, 2437—2442 (1988)

The Synthesis of *C*-Methyl Branched-Chain Deoxy Sugar Nucleosides by the Deoxygenative Methylation of *O*-Tosylated Adenosines with Grignard Reagents[1)]

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(Received January 7, 1988)

The reaction of appropriately protected 2′-*O*-tosyladenosines with methylmagnesium bromide (or iodide) gave 9-(2-deoxy-3-*C*-methyl-β-D-*threo*-pentofuranosyl)adenine after deprotection. The same reaction on 3′-*O*-tosyladenosine derivatives afforded an epimeric pair of 2′-*C*-methyl-3′-deoxy sugar nucleosides. The modified structures of the sugar moieties were determined unambiguously.

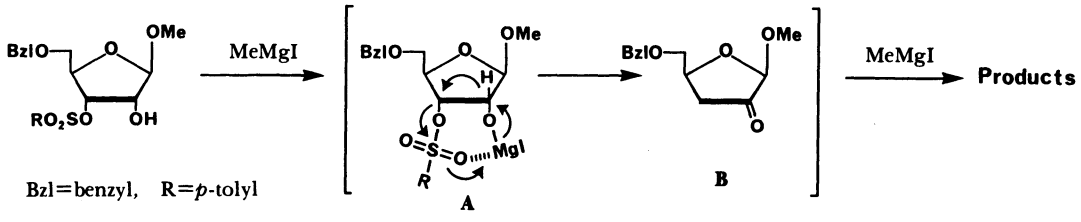
There has been considerable interest during the past decade in the synthesis and chemistry of branched-chain sugar nucleosides,[2)] because modification of the sugar moieties has produced compounds with biologically interesting properties. Walton et al.[3)] reported that 2′-*C*- and 3′-*C*-methyladenosines were resistant to adenosine deaminase (adenosine aminohydrolase; EC 3.5.4.4) and that they exhibited inhibitory activity against KB cells in a culture. These findings prompted us to develop a convenient method for synthesizing a new type of adenosine analogue, branched-chain deoxy sugar nucleosides.

Previously we have described that methyl 5-*O*-benzyl-2-*O*- or -3-*O*-tosyl-β-D-ribofuranosides reacted with methylmagnesium iodide (MeMgI) to produce the corresponding 2-deoxy-3-*C*- or 3-deoxy-2-*C*-methyl branched-chain sugar furanosides in an efficient one-pot procedure.[4)] These reactions involved a [1,2]-hydride shift and a concerted elimination of a sulfonyloxy group, as is depicted in **A** (Scheme 1).[5)] The resulting α-deoxygenated keto sugar **B** was converted into products in the presence of an excess of MeMgI.[6)] We have now extended the scope of this reaction to the preparation of adenosine analogues. (A preliminary report on this work has been published.)[7)] During the course of this work, a report on the preparation of 1-(2-deoxy-3-*C*-methyl-5-*O*-trityl-β-D-*erythro*-pentofuranosyl)uracil by using 2′-*O*-tosyl-5′-*O*-trityluridine and MeMgI appeared.[8)]

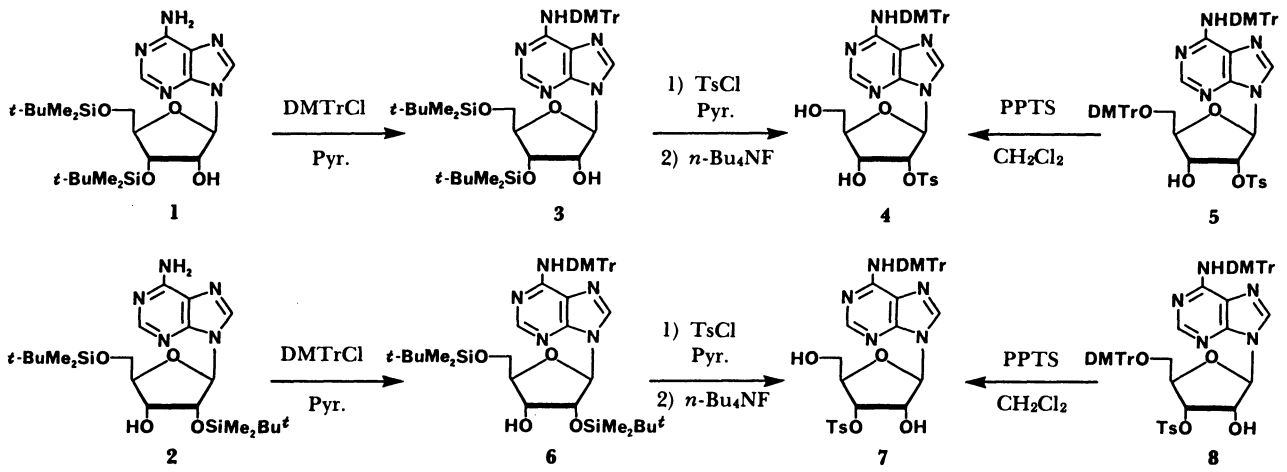
Results and Discussion

Appropriately protected 2′-*O*- and 3′-*O*-tosyladenosines were prepared from adenosine by the operations outlined in Scheme 2. Thus, the silylation of adenosine with *t*-butyldimethylsilyl chloride according to the method of Ogilvie et al.[9)] gave a mixture of 3′,5′-di-*O*- and 2′,5′-di-*O*-sililated adenosines (**1** and **2**), along with a 2′,3′,5′-tri-*O*-protected derivative; the compounds were isolated in a ratio of 51:41:8 by silica-gel column chromatography. The protection of an NH_2 group in **1** with 4,4′-dimethoxytrityl chloride (DMTrCl) afforded the corresponding N^6-(4,4′-dimethoxytrityl) derivative **3** in a good yield. A similar reaction conducted with **2** and DMTrCl gave the N^6-protected compound **6**. The conventional tosylation of **3**, followed by deprotection with tetrabutylammonium fluoride,[9b)] gave N^6-(4,4′-dimethoxytrityl)-2′-*O*-tosyladenosine (**4**). Alternatively, **4** was prepared from N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-2′-*O*-tosyladenosine[6i)] (**5**) by the selective detritylation of **5** with pyridinium *p*-toluenesulfonate (PPTS).[10)] Similarly, N^6-(4,4′-dimethoxytrityl)-3′-*O*-tosyladenosine (**7**) was obtained from **6** or N^6,$O^{5'}$-bis(4,4′-dimethoxytrityl)-3′-*O*-tosyladenosine (**8**).[6i)] The conventional tritylation of 2′-*O*-tosyladenosine provided the corresponding 5′-*O*-trityl derivative **9**.[6c,11)]

The deoxygenative methylations of **4**, **5**, and **7**—**9** were carried out in dry benzene with methylmagnesium bromide (MeMgBr; in tetrahydrofuran) or MeMgI (in diethyl ether) at room or an elevated temperature (Scheme 3). The products were not purified but were directly deblocked with 80% acetic acid or zinc bromide ($ZnBr_2$);[12)] in the former case, a depurination from 2′-deoxy nucleosides took place to some extent during the reaction and work-up. The

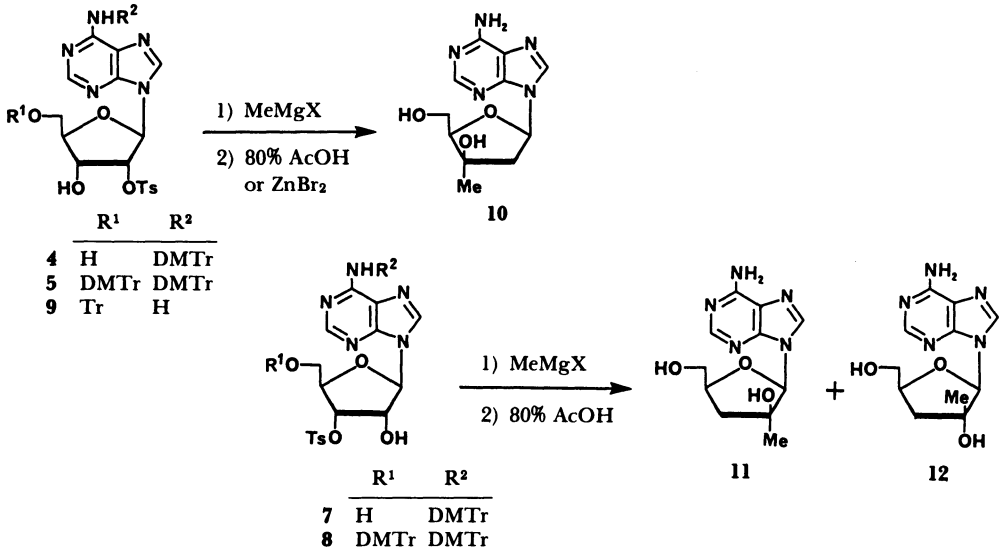


Scheme 1.



DMTr=4,4-dimethoxytrityl; PPTS=pyridinium *p*-toluenesulfonate; Ts=tosyl.

Scheme 2.



Tr=trityl; X=Br or I.

Scheme 3.

deprotection of the 5′-trityl group in the product derived from **9** was achieved with $ZnBr_2$ at 65 °C without the depurination. The resulting free nucleosides were isolated by means of ion-exchange [Dowex-1 (OH^- form)] column chromatography. In these operations, **4**, **5**, and **9** were successfully converted into 9-(2-deoxy-3-*C*-methyl-β-D-*threo*-pentofuranosyl)adenine (**10**). The results are summarized in Table 1.

The structure of the modified sugar moiety in **10** was established on the basis of its elemental analyses, the UV and ^1H NMR spectral data, and the fact that the methanolysis of **10** gave isomeric mixtures of methyl pentosides, whose ^1H NMR spectrum was identical with those of specimens prepared from the known methyl 2-deoxy-3-*C*-methyl-β-D-*threo*-pentofuranoside[4] except for the intensity of the signals. No erythro isomer with the 3′-"up"-methyl group could be detected in the deoxygenative methylation of **4**, **5**, and **9**. In the case of the uridine derivative,[8] however, the erythro (3′-"up"-methyl group) derivative was the main product. The steric course of the methyl group in these reactions was strongly influenced by the nature of the base moiety attached to the anomeric position,[13] but the reason for this is not clear at this time. On the other hand, the reactions of **7** and **8** with MeMgBr or MeMgI proceeded at elevated temperatures to produce a pair of isomers, 9-(3-deoxy-2-*C*-methyl-β-D-*threo*- and -*erythro*-pentofuranosyl)adenine (**11** and **12**), after the deprotection (Table 1). Satisfactorily elemental analyses and spectral data were obtained for these products. The structure of the sugar moiety in **11** was correlated with that for the known methyl 3-deoxy-2-*C*-methyl-β-D-*threo*-pento-

Table 1. The Synthesis of Branched-Chain Deoxy Sugar Nucleosides with Grignard Reagents[a]

Starting material (mmol)	Grignard reaction			Deprotection			Product (Yield/%)
	Reagent (mmol)	Temp[b]	Time	Reagent	Temp[b]	Time	
4 (0.5)	MeMgBr (3)	rt	17 h	$ZnBr_2$	rt	2.5 h	**10** (17)
(0.5)	MeMgI (8)	1) rt	8 h	$ZnBr_2$	rt	2.5 h	**10** (53)
		2) 65 °C	50 min				
5 (2.0)	MeMgBr (12)	rt	5 h	AcOH	rt	0.5 h	**10** (55)
(0.5)	MeMgBr (11)	rt	5 h	$ZnBr_2$	rt	2.5 h	**10** (58)
(2.0)	MeMgI (12)	rt	8.5 h	$ZnBr_2$	rt	2.5 h	**10** (41)
9 (0.6)	MeMgBr (12)	80 °C	20 min	$ZnBr_2$	65 °C	1 h	**10** (51)
7 (0.7)	MeMgBr (4)	65 °C	30 min	AcOH	rt	2.5 h	**11** (40), **12** (19)
(0.8)	MeMgI (11)	rt	4 h	AcOH	rt	45 min	**11** (65), **12** (19)
8 (0.9)	MeMgBr (5)	65 °C	40 min	AcOH	rt	35 min	**11** (62), **12** (8)
(1.0)	MeMgI (17)	65 °C	15 min	AcOH	rt	60 min	**11** (67), **12** (15)

a) Some of the reaction conditions are described in the Experimental Section. b) rt=room temperature.

furanoside[4] by the methanolysis. In addition, the ^{1}H NMR spectrum (in DMSO-d_6) of **12** showed that the signal due to the methyl protons shifted upfield by 0.45 ppm relative to that for the corresponding protons in **11**, while the H-8 signal shifted downfield by 0.25 ppm. Similar shifts were observed in the ^{1}H NMR spectrum measured in MeOH-d_4. These facts indicated that, in **12**, the methyl group and the imidazole ring in a base moiety were located close to each other; the erythro structure of **12** was thus established.

Very recently Koole et al.[14] have reported the synthesis of **11** by the stereoselective addition of MeMgI to a protected 3′-deoxy-2′-keto nucleoside, followed by deprotection: the keto nucleoside was prepared from 5′-*O*-(4-methoxytrityl)-9-(3-deoxy-β-D-*erythro*-pentofuranosyl)adenine. The ^{1}H NMR (in MeOH-d_4) spectral data of **11** prepared by our method were almost identical with those previously reported.[14]

The reactions of 2′- or 3′-*O*-tosyladenosine derivatives with Grignard reagents other than MeMgI or MeMgBr gave various products, depending on the structure of the organic residues in the reagents; the preliminary results have been previously published.[7]

Experimental

General. The melting points were determined in capillary tubes with a Yamato micro melting-point apparatus and are uncorrected. The optical rotations were measured with a Perkin-Elmer Model 241MC polarimeter in a 1-dm cell. The UV spectra were measured with a Varian Cary 2200 apparatus using a 1-cm cell. The ^{1}H NMR spectra were recorded with a JEOL JNM-GX 400 spectrometer, using tetramethylsilane as the internal standard. The coupling constants were measured directly from the spectra or were calculated from the peak listing. The TLC was performed on precoated plates (0.25 mm) of Silica Gel 60 F_{254} (Merck). Detection was done by means of UV (254 nm) or by spraying the plates with a solution of methanol–sulfuric acid–*p*-anisaldehyde (85:15:5, v/v), followed in the latter case by heating at above 200 °C. The column chromatography was effected on Silica Gel 60 (Merck 70—230 mesh, ASTM). The elemental analyses were performed by the Microanalytical Laboratory of this Institute. The solvent extracts were dried with anhydrous magnesium sulfate, and the solutions were evaporated under diminished pressure at 40—45 °C. The analytical samples were dried at 60 °C for 4 h in vacuo over diphosphorus pentaoxide. The Grignard reagents were purchased from the Tokyo Chemical Industry Co., Ltd.

3′,5′-Bis-*O*-(*t*-butyldimethylsilyl)adenosine (1) and Its 2′,5′-Isomer (2). The method of Ogilvie et al.[9] was slightly modified.

To a stirred solution of adenosine (2.67 g, 10 mmol) in a mixture of dry pyridine (4 ml) and DMF (10 ml), we added silver nitrate (3.40 g, 20 mmol), after which the mixture was stirred at room temperature for 2 h. After cooling with iced water, THF (20 ml), and *t*-butyldimethylsilyl chloride (3.02 g, 20 mmol) were added and the mixture was stirred at room temperature for 1 h. The undissolved materials were removed by filtration through a Celite pad and washed with THF. The combined filtrate and washings were diluted with ether containing a small amount of chloroform. The mixture was then washed successively with aq. sodium hydrogencarbonate and water (three times), dried, and concentrated. The pyridine was removed by repeated co-evaporation with toluene. The residue was chromatographed on a silica-gel column with benzene–ethyl acetate (7:3). The compound emerging first was 2′,3′,5′-tris-*O*-(*t*-butyldimethylsilyl)adenosine (427 mg, 7%). The second product eluted with the same solvent system (1:1) was **2** (1.74 g, 35%). The elution of **1** (2.18 g, 44%) was effected with benzene–ethyl acetate–methanol (25:25:1).

1: ^{1}H NMR ($CDCl_3$) δ=0.07 and 0.09 (3H, each s, 3′-SiMe), 0.17 (6H, s, 2×5′-SiMe), 0.90 (9H, s, 3′-SiBu^t), and 0.95 (9H, s, 5′-SiBu^t), 3.43 (1H, br d, OH), 3.77 (1H, dd,

J=2.9 and 11.4 Hz, H-5'), 3.93 (1H, dd, J=3.5 and 11.4 Hz, H-5''), 4.13 (2H, br s, H-2' and H-3'), 5.94 (2H, br s, NH_2), 6.04 (1H, d, J=4.3 Hz, H-1'), 8.10 (1H, s, H-2), and 8.34 (1H, s, H-8).

2: ^{1}H NMR ($CDCl_3$) δ=−0.12 and −0.05 (3H, each s, 2'-SiMe), 0.14 and 0.15 (3H, each s, 5'-SiMe), 0.84 (9H, s, 2'-*t*-Bu), 0.96 (9H, s, 5'-SiBu^t), 2.85 (1H, d, J=4.3 Hz, OH), 3.86 (1H, dd, J=2.4 and 11.5 Hz, H-5'), 4.02 (1H, dd, J=2.4 and 11.5 Hz, H-5''), 4.22 (1H, m, H-4'), 4.29 (1H, m, H-3'), 4.64 (1H, t, J=5.0 Hz, H-2'), 5.92 (2H, br s, NH_2), 6.12 (1H, d, J=5.2 Hz, H-1'), 8.23 (1H, s, H-2), and 8.35 (1H, s, H-8).

3',5'-Bis-*O*-(*t*-butyldimethylsilyl)-N^6-(4,4'-dimethoxytrityl)adenosine (3). Compound **1** (3.14 g, 6.33 mmol) was dried by co-evaporation with dry pyridine-toluene. This product was then dissolved in dry pyridine (30 ml), and 4,4'-dimethoxytrityl chloride (2.79 g, 8.2 mmol) was added. The mixture was then stirred at room temperature for 17 h. After cooling, 50% aq. pyridine was added; the products were extracted with ether. The extracts were washed with water, dried, and concentrated. The residual pyridine was removed by co-evaporation with chloroform–toluene, and the residue was chromatographed on a silica-gel column with toluene–ethyl acetate–triethylamine (9:1:0.1) to give **3** (4.34 g, 86%) as a foam. A portion of the product was dissolved in a small amount of dichloromethane and precipitated by the addition of the dichloromethane solution to an excess of pentane under vigorous stirring. The resulting precipitates were collected and dried to afford an analytical sample: amorphous powders: $[\alpha]_D^{22}$ −23.1° (*c* 0.49, $CHCl_3$); UV λ_{max}^{MeOH} 275 nm (ε 20200); ^{1}H NMR ($CDCl_3$) δ=0.03 and 0.07 (3H, each s, 3'-SiMe), 0.16 (6H, s, 2×5'-SiMe), 0.88 (9H, s, 3'-SiBu^t), 0.94 (9H, s, 5'-SiBu^t), 3.29 (1H, d, J=6.4 Hz, OH), 3.78 (6H, s, 2×OMe), 3.75 (1H, dd, J=2.9 and 11.2 Hz, H-5'), 3.89 (1H, dd, J=3.8 and 11.2 Hz, H-5''), 4.10 (1H, m, H-4'), 4.58 (2H, m, H-2' and H-3'), 5.97 (1H, d, J=4.6 Hz, H-1'), 6.76—7.43 (14H, m, Arom. and NH), and 8.00 and 8.05 (1H, each s, H-2 and H-8). Found: C, 64.77; H, 7.43; N, 8.70; Si, 7.04%. Calcd for $C_{43}H_{59}N_5O_6Si_2$: C, 64.71, H, 7.45; N, 8.77; Si, 7.04%.

N^6-(4,4'-Dimethoxytrityl)-2'-*O*-tosyladenosine (4). From **3.** Compound **3** (2.85 g, 3.6 mmol) was dried by co-evaporation with dry pyridine–toluene. This was then dissolved in dry pyridine (32 ml), and tosyl chloride (2.75 g, 14.3 mmol) was added. The mixture was stirred at room temperature for 5 d and then quenched with 50% aq. pyridine. The products were extracted with diethyl ether containing a small amount of chloroform. The extracts were washed successively with water, aq. sodium hydrogencarbonate, and water, and then dried. The solvents were evaporated, and the residual pyridine was removed by repeated co-evaporation with toluene. The residue was dissolved in THF (30 ml), and tetrabutylammonium fluoride (1 mol dm^{-3} solution in THF; 7.2 ml) was added. The mixture was then stirred at room temperature for 30 min. After cooling, it was diluted with diethyl ether and a small amount of chloroform. The solution was washed three times with water, dried, and concentrated. The residue was chromatographed on a silica-gel column with chloroform–ethyl acetate (9:1), followed with chloroform–ethyl acetate–methanol (9:1:0.1), to give amorphous **4** (2.12 g, 82%). Precipitation from dichloromethane–pentane gave an analytical sample: amorphous powders: $[\alpha]_D^{23}$ −13.9° (*c* 0.49, $CHCl_3$); UV λ_{max}^{MeOH} 275 nm (ε 22700); ^{1}H NMR ($CDCl_3$) δ=2.24 (3H, s, CMe), 3.28—3.37 (1H, br s, 5'-OH), 3.78 (6H, s, OMe), 3.63 (1H, br t, J=12 Hz, H-5'), 3.81 (1H, br d, J=11 Hz, H-5''), 4.21 (1H, br s, H-4'), 4.63 (1H, dd, J=1.7 and 4.4 Hz, H-3'), 5.47 (1H, dd, J=4.4 and 7.8 Hz, H-2'), 5.93 (1H, d, J=7.8 Hz, H-1'), 6.37 (1H, dd, J=2.0 and 12.0 Hz, 3'-OH), 6.78—7.44 (18H, Arom. and NH), 7.68 (1H, s, H-2), and 7.84 (1H, s, H-8). Found: C, 63.06; H, 5.25; N, 9.40; S, 4.38%. Calcd for $C_{38}H_{37}N_5O_8S$: C, 63.06; H, 5.15; N, 9.68; S, 4.43%.

From **5.** A solution of PPTS (450 mg, 1.8 mmol) in dichloromethane (8 ml) was added to a solution of **5** (4.56 g, 4.4 mmol) in dichloromethane (40 ml). The mixture was stirred at room temperature for 3 h and then diluted with dichloromethane. The solution was washed successively with aq. sodium carbonate and water, dried, and concentrated. The residue was chromatographed on a silica-gel column with chloroform–ethyl acetate (9:1), followed with chloroform–ethyl acetate–methanol (9:1:0.1), to give **4** (2.56 g, 80%).

2',5'-Bis-*O*-(*t*-butyldimethylsilyl)-N^6-(4,4'-dimethoxytrityl)-adenosine (6). Compound **2** (2.94 g, 5.9 mmol) was treated under conditions similar to those used in the preparation of **3.** The usual work-up and purification by silica-gel column chromatography [toluene–ethyl acetate–triethylamine (9:1:0.1)] gave **6** as crystals: mp 186 °C (sintered), 193.5—194.5 °C (benzene–hexane); $[\alpha]_D^{22}$ −29.7° (*c* 0.52, $CHCl_3$); UV λ_{max}^{MeOH} 275 nm (ε 24700); ^{1}H NMR ($CHCl_3$) δ=−0.17 and −0.07 (3H, each s, 2'-SiMe), 0.12 and 0.14 (3H, each s, 5'-SiMe), 0.80 (9H, s, 2'-SiBu^t), 0.95 (9H, s, 5'-SiBu^t), 2.71 (1H, d, J=3.9 Hz, OH), 3.78 (6H, s, 2×OMe), 3.84 (1H, dd, J=2.5 and 11.3 Hz, H-5'), 4.00 (1H, dd, J=2.8 and 11.3 Hz, H-5''), 4.19 (1H, m, H-4'), 4.26 (1H, m, H-3'), 4.65 (1H, t, J=5.1 Hz, H-2'), 6.05 (1H, J=5.1 Hz, H-1'), 6.76—7.34 (14H, m, Arom. and NH), 8.04 (1H, s, H-2), and 8.11 (1H, s, H-8). Found: C, 64.62; H, 7.41; N, 8.66; Si, 6.84%. Calcd for $C_{43}H_{59}N_5O_6Si_2$: C, 64.71; H, 7.45; N, 8.77; Si, 7.04%.

N^6-(4,4'-Dimethoxytrityl)-3'-*O*-tosyladenosine (7). From **6.** Compound **6** (1.78 g, 2.2 mmol) was treated under condition similar to those described for the synthesis of **4** from **3,** giving **7** (1.37 g, 85%): amorphous powders; $[\alpha]_D^{21}$ −29.6° (*c* 0.64, $CHCl_3$); UV λ_{max}^{MeOH} 275 nm (ε 21100); ^{1}H NMR ($CDCl_3$) δ=2.46 (3H, s, CMe), 3.05—3.2 (1H, br s, OH), 3.76 and 3.77 (6H, s, 2×OMe), 3.55 (1H, br t, J=13 Hz, H-5'), 3.82 (1H, d, J=13.7 Hz, H-5''), 4.37 (1H, m, H-4'), 5.11 (2H, m, H-2' and H-3'), 5.76 (1H, d, J=7.1 Hz, H-1'), 6.72—7.34 (15H, m, Arom., NH, and OH), 7.39 (2H, d, J=8.6 Hz, Arom.), 7.85 (2H, d, J=8.5 Hz, Arom.), 7.76 (1H, s, H-2), 7.95 (1H, s, H-8). Found: C, 62.92; H, 5.14; N, 9.57; S, 4.33%. Calcd for $C_{38}H_{37}N_5O_8S$: C, 63.06; H, 5.15; N, 9.68; S, 4.43%.

From **8.** A solution of PPTS (270 mg, 1.08 mmol) in dichloromethane (5 ml) was added to a solution of **8** (2.77 g, 2.7 mmol), and the mixture was stirred at room temperature for 8 h. The resulting fine crystals of 3'-*O*-tosyladenosine tosylate salt[6i] were filtered off, and the filtrate was diluted with dichloromethane. The solution was washed successively with aq. sodium carbonate and water, dried, and concentrated. The residue was chromatographed on a silica-gel column with chloroform–ethyl acetate (9:1), followed by chromatography with chloroform–ethyl acetate–methanol (9:1:0.4), to afford **7** (1.33 g, 68%).

9-(2-Deoxy-3-*C*-methyl-β-D-*threo*-pentofuranosyl)adenine

(10). Some of the reaction conditions and the results are summarized in Table 1.

To a stirred mixture of MeMgI (2 mol dm^{-3} solution in diethyl ether) or MeMgBr (1 mol dm^{-3} solution in THF) and dry benzene (3 ml), we added a solution of **4**, **5**, or **9** (ca.0.5 mmol) in dry benzene (3 ml) at room temperature, after which the mixture was stirred at the given temperature for the given reaction time. After cooling, aq. ammonium chloride was added, and the products were extracted with diethyl ether containing a small amount of chloroform. The extracts were then washed with water, dried, and concentrated. The residue was dissolved in chloroform (2.5 ml), and the solution was added to a solution of $ZnBr_2$ (450 mg, 2 mmol) in a mixture of methanol (0.54 ml) and chloroform (2.2 ml).[12] After the mixture had been stirred at the given temperature for the given reaction time, it was diluted with methanol and then concentrated to a few ml at room temperature in vacuo. The residue was chromatographed on a silica-gel column with chloroform–methanol (9:1 → 8:2). The combined eluates containing the product were concentrated to about 10 ml, and then the concentrate was diluted with methanol. This solution was then concentrated to a few ml and placed in an ion-exchange column (Dowex 1X-2, OH^-, 100—200 mesh) made up with water. Elution with the same solvent gave **10**: mp 166—167 °C (from MeOH–diisopropyl ether); $[\alpha]_D^{25}$ +4.7° (*c* 0.44, H_2O); UV λ_{max}^{MeOH} 259 nm (ε 15100); ^1H NMR (DMSO-d_6) δ=1.34 (3H, s, Me), 2.36 (1H, dd, *J*=2.7 and 14.4 Hz, H-2′), 2.65 (1H, dd, *J*=8.8 and 14.4 Hz, H-2″), 3.55—3.73 (3H, m, H-4′ and H-5′, 5″), 4.67 (1H, t, *J*=5.5 Hz, 5′-OH), 6.06 (1H, s, 3′-OH), 6.20 (1H, dd, *J*=2.8 and 8.7 Hz, H-1′), 7.36 (2H, br s, NH_2), 8.14 (1H, s, H-2), and 8.35 (1H, s, H-8). Found: C, 49.00; H, 5.70; N, 26.32%. Calcd for $C_{11}H_{15}N_5O_3 \cdot 0.2H_2O$: C, 49.14; H, 5.77; N, 26.05%.

9-(3-Deoxy-2-*C*-methyl-β-D-*threo*-pentofuranosyl)adenine (11) and Its Erythro Isomer (12). Some of the reaction conditions and the results are listed in Table 1.

Compound **7** or **8** (ca. 0.5 mmol), was subjected to a Grignard reaction under conditions similar to those used in the synthesis of **10**. After the reaction mixture had been worked up, the residue was dissolved in 80% acetic acid (10 ml) and the solution was stirred at room temperature for the given reaction time. The acetic acid was removed by repeated co-evaporation with ethanol–toluene, the residue was partitioned between chloroform and water. The water solution was washed with chloroform and then concentrated. The residue was chromatographed on a column of ion-exchange resin (Dowex 1X-2, OH^- form, 100—200 mesh) packed with water. Elution with the same solvent gave **12**, and then **11**.

11: Mp 218—219 °C (from MeOH–diisopropyl ether); $[\alpha]_D^{27}$ +34.9° (*c* 0.45, H_2O); UV λ_{max}^{MeOH} 259 nm (ε 16200); ^1H NMR (DMSO-d_6) δ=1.30 (3H, s, Me), 2.17 (2H, m, H-3′,3″), 3.55—3.70 (2H, m, H-5′,5″), 4.16 (1H, m, H-4′), 5.34 (1H,s, 2′-OH), 5.36 (1H, t, *J*=4.9 Hz, 5′-OH), 5.88 (1H, s, H-1′), 7.24 (2H, br s, NH_2), 8.13 (1H, s, H-2), and 8.28 (1H, s, H-8); (MeOH-d_4) δ=1.38 (3H, s, Me), 2.26 (1H, dd, *J*=5.5 and 13.4 Hz, H-3′), 2.37 (1H, dd, *J*=8.5 and 13.4 Hz, H-3″), 3.72 (1H, dd, *J*=3.7 and 11.9 Hz, H-5′), 3.87 (1H, dd, *J*=2.8 and 11.9 Hz, H-5″), 4.33 (1H, m, H-4′), 6.01 (1H, s, H-1′), 8.19 (1H, s, H-2), and 8.43 (1H, s, H-8). Found: C, 48.72; H, 5.65; N, 26.12%. Calcd for $C_{11}H_{15}N_5O_3 \cdot 0.3H_2O$: C, 48.81; H, 5.81; N, 26.12%.

12: Mp 233—234 °C (from EtOH); $[\alpha]_D^{22}$ −32.3° (*c* 0.54, H_2O); UV λ_{max}^{MeOH} 259 nm (ε 14900); ^1H NMR (DMSO-d_6) δ=0.85 (3H, s, Me), 1.84 (1H, dd, *J*=4.9 and 13 Hz, H-3′), 1.87 (1H, br t, *J*=12 Hz, H-3″), 3.63 (1H, m, H-5′), 3.84 (1H, m, H-5″), 4.40 (1H, m, H-4′), 5.22 (1H, t, *J*=5.1 Hz, 5′-OH), 5.55 (1H, s, 2′-OH), 5.92 (1H, s, H-1′), 7.29 (2H, br s, NH_2), 8.14 (1H, s, H-2), and 8.53 (1H, s, H-8); (MeOH-d_4) δ=0.97 (3H, s, Me), 1.95 (1H, dd, *J*=5.0 and 13.3 Hz, H-3′), 2.32 (1H, dd, *J*=11.3 and 13.1 Hz, H-3″), 3.77 (1H, dd, *J*=2.9 and 12.4 Hz, H-5′), 4.04 (1H, dd, *J*=2.6 and 12.4 Hz, H-5″), 4.55 (1H, m, H-4′), 6.06 (1H, s, H-1′), 8.20 (1H, s, H-2), and 8.64 (1H, s, H-8). Found: C, 49.19; H, 5.70; N, 26.51%. Calcd for $C_{11}H_{15}N_5O_3 \cdot 0.1H_2O$: C, 49.47; H, 5.74; N, 26.22%.

Methanolysis of Methyl 2-Deoxy-3-*C*-methyl-β-D-*threo*-pentofuranoside and 10. A mixture of methyl 2-deoxy-3-*C*-methyl-β-D-*threo*-pentofuranoside[4] (15 mg, 0.09 mmol) and Dowex 50W-X8 (125 mg, H^+ form, 100—200 mesh) in methanol (1.5 ml) was stirred at room temperature for 6 h. The resin was then removed by filtration through a Celite pad and washed with methanol. The combined filtrate and washings were concentrated to give methyl 2-deoxy-3-*C*-methyl-α- and -β-D-*threo*-pentosides (14 mg, 93%): ^1H NMR ($CDCl_3$) δ=1.23 (0.6H, s, CMe), 1.36 (1.1H, s, CMe), 1.39 (0.3H, s, CMe), 1.43 (1.0H, s, CMe), 3.39, 3.40, 3.446, and 3.448 (each s, OMe), 4.62 (0.4H, dd, *J*=3.4 and 6.6 Hz, H-1), 4.81 (0.2H, br d, *J*=3.2 Hz, H-1), 5.02 (0.1H, dd, *J*=2.1 and 3.5 Hz, H-1), and 5.16 (0.3H, dd, *J*=3.2 and 5.9 Hz, H-1).

The methanolysis of **10** (32 mg, 0.012 mmol) with Dowex 50W-X8 (127 mg, H^+ form, 100—200 mesh) in methanol (1.5 ml) was carried out at room temperature for 2.3 h. A work-up similar to that described above gave methyl pentosides (17 mg, 89%), whose thin-layer chromatographic behavior and ^1H NMR spectrum were identical with those for the pentosides prepared by the methanolysis of methyl 2-deoxy-3-*C*-methyl-β-D-*threo*-pentofuranoside.

Methanolysis of Methyl 3-Deoxy-2-*C*-methyl-β-D-*threo*-pentofuranoside and 11. A mixture of methyl 3-deoxy-2-*C*-methyl-β-D-*threo*-pentofuranoside[4] (15 mg, 0.09 mmol) and Dowex 50W-X8 (126 mg, H^+ form, 100—200 mesh) in methanol (1 ml) was stirred first at room temperature for 1.5 h and then at 50 °C for 5.5 h. The resin was removed by filtration and washed with methanol. The combined filtrate and washings were concentrated to give methyl 3-deoxy-2-*C*-methyl-α- and -β-D-*threo*-pentosides (13 mg, 89%): ^1H NMR ($CDCl_3$) δ=1.34 (s, CMe), 1.35 (s, CMe), 1.86 (0.74H, dd, *J*=2.7 and 13.4 Hz, H-3a,b), 1.94 (0.52H, d, *J*=7.6 Hz, H-3a,b), 2.25 (0.74H, dd, *J*=10.0 and 13.4 Hz, H-3a,b), 3.36 (s, OMe), 3.50 (s, OMe), 3.57 (0.74H, dd, *J*=1.7 and 11.7 Hz, H-5a,b), 3.71 (0.26H, dd, *J*=2.7 and 11.7 Hz, H-5a,b), 3.91 (0.74H, dd, *J*=2.1 and 11.6 Hz), 4.40 (0.25H, s, H-1), and 4.59 (0.75H, s, H-1).

A similar methanolysis of **11** (41 mg, 0.15 mmol) with Dowex 50W-X8 (H^+ form, 130 mg) in methanol (2 ml) afforded the pentosides (22 mg, 92%), whose thin-layer chromatographic behavior and ^1H NMR spectrum were identical with those for the pentosides prepared from methyl 3-deoxy-2-*C*-methyl-β-D-*threo*-pentofuranoside.

We wish to thank Dr. Jun Uzawa and Mrs. Tamiko Chijimatsu for the measurement of the ^1H NMR spectra, and Dr. Hiroshi Yamazaki and his staff for the

elemental analyses. This work was supported, in part, by a Research Grant for Life Science granted by this Institute.

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