Synthesis of Some 3′,5′-Dideoxy-5′-*C*-Phosphonomethyl Nucleosides

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Ioannidis, P., Classon, B., Samuelsson, B. and Kvarnström, I., 1991. Synthesis of Some 3′,5′-Dideoxy-5′-*C*-Phosphonomethyl Nucleosides. – Acta Chem. Scand. 45: 746–750.

Ammonium [1-(3′,5′,6′-trideoxy-β-D-*erythro*-hexofuranosyl)thymine]-6′-phosphonate (**1**), ammonium 3′,5′-dideoxycytidine-5′-*C*-methylphosphonate (**2**) and 3′,5′-dideoxyadenosine-5′-*C*-methyl phosphonic acid (**3**) have been synthesized and tested for anti-HIV activity. The key steps involved an Arbuzov reaction between triethyl phosphite and 3,5,6-trideoxy-6-iodo-1,2-*O*-isopropylidene-α-D-*erythro*-hexofuranose (**7**), followed by condensation with the appropriate nucleoside bases. The substances **1**, **2** and **3** have been tested *in vitro* against HIV.

Inhibition of the replication cycle of the human immunodeficiency virus (HIV), the etiologic agent of AIDS, by inhibition of the virus-specific enzyme reverse transcriptase, using nucleoside or nucleotide analogues constitutes an attractive approach to anti-HIV therapy. 3′-Azido-3′-deoxythymidine[1] is the first and thus far the only drug approved for the treatment of AIDS. The mechanism of anti-HIV activity of 3′-azido-3′-deoxythymidine is believed to involve activation by cellular kinases to give the corresponding triphosphate which acts as a substrate/inhibitor for reverse transcriptase.[2,3] In attempts to circumvent the first phosphorylation step, which takes place *in vivo*, a number of 5′-*C*-phosphonomethyl derivatives of ribonucleosides,[4–6] such as 2′-deoxyribonucleosides,[6] 2′,3′-dideoxynucleosides,[7] 3′-azido-3′-deoxythymidine[8] and 3′-deoxy-3′-fluorothymidine[9] have been synthesized. None of these compounds have been reported to show anti-HIV activity.

Phosphonomethyl derivatives of nucleosides have previously been synthesized via an Arbuzov reaction of a trialkyl phosphite and a primary alkyl halide in the sugar moiety followed by condensation with a nucleoside base,[4–6,10,11] via a Wittig reaction between phosphoranylidene methylphosphonate and an 5′-aldehyde of the appropriate protected nucleodises,[5–7,12] or via photolysis of an *N*-hydroxy-2-thiopyridone ester of a carboxylic acid of a nucleoside in the presence of diethyl vinylphosphonate.[13]

Results and discussion

The synthesis (Scheme 1) of **1**, **2** and **3** was effected by means of an Arbuzov reaction between triethyl phosphite and 3,5,6-trideoxy-6-iodo-1,2-*O*-isopropylidene-α-D-*erythro*-hexofuranose (**7**) to give a sugar phosphonate which was condensed with silylated nucleoside bases. Commercially available 1,2-*O*-isopropylidene-α-D-glucofuranose **4** was reacted with *N*,*N*′-thiocarbonyldiimidazole in THF to yield the dithiocarbonate **5** in 92 % yield. The use of dichloroethane as the solvent, as suggested by Weigele *et al.*,[14] for making **5** failed in our hands probably due to low solubility of **4** in dichloroethane. Compound **5** was deoxygenated using tributyltin hydride with AIBN in refluxing toluene to yield 3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*erythro*-hexofuranose[14] (**6**) in 37 % yield. The primary hydroxy group of **6** was replaced with iodide to give **7** using triphenylphosphine, imidazole and iodine in refluxing toluene[15] in 78 % yield. An Arbuzov reaction[4,5,11] between the iodide **7** and triethyl phosphite gave the diethyl phosphonate **8** in 92 % yield. Hydrolysis of the isopropylidene group in **8** with 80 % acetic acid, followed by *O*-acetylation with acetic anhydride–pyridine (1:2),[11] afforded 1,2-di-*O*-acetyl-3,5,6-trideoxy-6-diethylphosphono-D-*erythro*-hexofuranose (**9**) in 93 % yield. Condensation of **9** with silylated thymine, cytosine and 6-chloropurine in acetonitrile promoted by *tert*-butyl dimethylsilyltriflate[4,16] afforded the β-anomeric nucleosides 1-[2′-*O*-acetyl-3′,5′,6-trideoxy-6′-(diethylphosphono)-β-D-*erythro*-hexofuranosyl]thymine (**10**), 2′-*O*-acetyl-3′,5′-dideoxy-5′-*C*-[(diethylphosphono)methyl]cytidine (**11**) and 9-[2′-*O*-acetyl-3′,5′,6′-trideoxy-6′-(diethylphosphono)-β-D-*erythro*-hexofuranosyl]-6-chloropurine (**12**) in 96, 87 and 97 % yield, respectively. Sequential deprotections[11] of **10**, **11** and **12** were performed by subsequent treatment with bromotrimethylsilane, water–pyridine and methanol saturated with ammonia. The thymidine and the cytidine analogues were isolated as ammonium salts. The 6-chloropurine analogue **12** was heated to 100 °C in 25 % ammonia[17] to give, after work-up, the phosphonic acid

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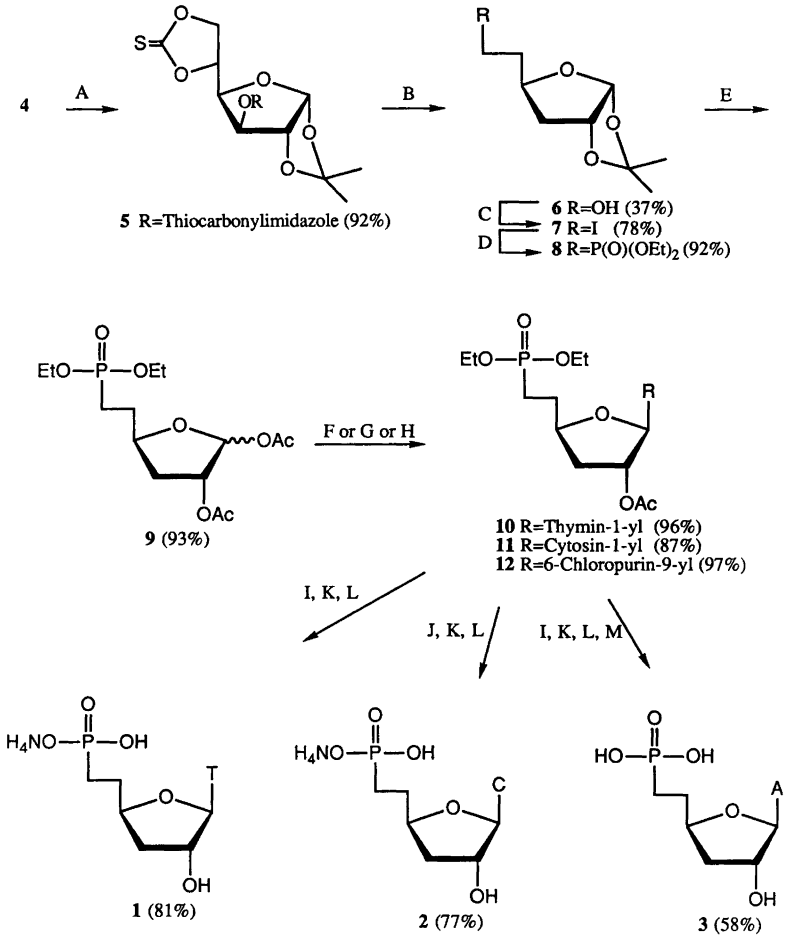

Scheme 1. Reagents: A, thiocarbonyldiimidazole, THF; B, tributyltin hydride, AIBN, toluene; C, Ph_3P, imidazole, I_2, toluene; D, $(EtO)_3P$; E, 80 % HOAc (aq.) then Ac_2O, pyridine; F, silylated thymine, TBDMSTf, CH_3CN; G, silylated cytosine, TBDMSTf, CH_3CN; H, silylated 6-chloropurine, TBDMSTf, CH_3CN; I, Me_3SiBr, $CHCl_3$; J, Me_3SiBr, DMF; K, pyridine, H_2O; L, NH_3, MeOH; M, 35 % NH_3(aq), precipitation, drying *in vacuo*.

monohydrate **3**. None of the nucleoside analogues **1**, **2** or **3** showed any anti-HIV activity when tested in an H9 cell system.[18]

Experimental

General methods. All solvents were distilled before use. Thin layer chromatography was performed using silica gel 60 F-254 (Merck) plates with detection by UV and/or by charring with 8 % sulfuric acid. Column chromatography was performed on silica gel (Matrix Silica Si 60A, 35–70 μ, Amicon). Organic phases were dried over anhydrous magnesium sulfate. Concentrations were performed under reduced pressure. Optical rotations were recorded using a Perkin–Elmer 241 polarimeter. NMR spectra were recorded on a JEOL GSX-270 instrument, shifts are given in ppm downfield from tetramethylsilane in $CDCl_3$ and CD_3OD, and acetone (δ 2.23) in D_2O.

3-O-Imidazolethiocarbonyl-1,2-O-isopropylidene-5,6-O-thiocarbonyl-α-D-glucofuranose (**5**). To a stirred solution of 1,2-*O*-isopropylidene-α-D-glucofuranose (**4**) (30.0 g, 0.163 mol) in THF (1.2 l) was added *N,N'*-thiocarbonyldiimidazole (60.7 g, 0.341 mol) at 50 °C. The mixture was refluxed for 3 h, cooled to room temperature, filtered and concentrated. Crystallization of the residue from ethyl acetate yielded the dithiocarbonate **5** (46.6 g, 92 %). Analytical data were in accordance with those published,[14]

3,5,6-Trideoxy-6-iodo-1,2-O-isopropylidene-β-D-erythro-hexofuranose (**7**). To a stirred mixture of 3,5-dideoxy-1,2-*O*-isopropylidene-α-D-*erythro*-hexofuranose[14] (**6**) (2.16 g, 11.48 mmol), triphenylphosphine, (6.02 g, 22.95 mmol) and imidazole (2.74 g, 40.25 mmol) in toluene (220 ml) was added iodine (5.82 g, 22.95 mmol) at 80 °C. The mixture was refluxed for 1.5 h and then cooled to room temperature. Aqueous $NaHCO_3$ (sat) (50 ml) was added with vigorous stirring. Aqueous $Na_2S_2O_3$ was added dropwise until the iodine colour in the organic phase disappeared.

The organic phase was washed with water, dried and concentrated. The residue was purified by column chromatography (toluene–ethyl acetate 20:1) to yield 2.67 g (78 %) of **7**: $[\alpha]_D$ +3.9° (*c* 1.46, $CHCl_3$): ^{13}C NMR ($CDCl_3$) δ 1.2 (C-6), 26.2 and 26.7 (2×CH_3, acetal), 38.4 (C-5), 38.6 (C-3), 77.7 (C-4), 80.4 (C-2), 105.3 (C-1), 111.1 (acetal); ^1H NMR ($CDCl_3$) δ 1.32 (s, 3 H, CH_3), 1.52 (s, m, 4 H, H-3′ and CH_3), 2.17–2.07 (3 H, H-5, H-5′ and H-3), 3.25 (m, 2 H, H-6 and H-6′), 4.25 (m, 1 H, H-4), 4.73 (m, 1 H, H-2), 5.79 (d, *J* 3.66, 1 H, H-1). Anal. $C_9H_{15}IO_3$: C, H.

*3,5,6-Trideoxy-6-diethylphosphono-1,2-*O*-isopropylidene-*α-D-erythro-*hexofuranose* (**8**). A solution of the iodide **7** (2.04 g, 6.84 mmol) in triethyl phosphite (10 ml) was refluxed for 24 h. Triethyl phosphite and diethoxyphosphinylethane were removed by distillation (46 °C/2 mmHg) and the residue was purified by column chromatography (toluene–acetone 1:1) to give **8**, 1.98 g (92 %): $[\alpha]_D$ −4.0° (*c* 1.02, $CHCl_3$): ^{13}C NMR ($CDCl_3$) δ 16.5 (d, *J* 5.5 Hz, 2×*C*$H_3$$CH_2$), 22.3 (d, *J* 143.0 Hz, C-6), 26.1 and 26.6 (2×CH_3, acetal), 27.1 (d, *J* 3.7 Hz, C-5), 38.6 (C-3), 61.5 (d, *J* 5.5 Hz, 2×CH_3*C*H_2,), 77.5 (d, *J* 8.3 Hz, C-4), 80.6 (C-2), 105.3 (C-1), 110.9 (acetal); ^1H NMR ($CDCl_3$) δ 1.28 (dt, s, 9 H, *J* 7.3, 3 Hz, 2×*CH*$_3$$CH_2$, CH_3, acetal), 1.45 (m and s, 4 H, H-3′ and CH_3, acetal), 1.72–2.12 (5 H, H-3, H-5, H-5′, H-6 and H-6′), 4.00–4.20 (dq and m, 5 H, *J* 7.33 Hz and 2.57 Hz, 2×CH_3*CH*$_2$, H-4), 4.70 (m, 1 H, H-2), 5.77 (d, *J* 3.66 Hz, 1 H, H-1). Anal. $C_{13}H_{25}O_6P$: C, H.

*1,2-Di-*O*-acetyl-3,5,6-trideoxy-6-diethylphosphono-*D-erythro-*hexofuranose* (**9**). A solution of **8** (1.74 g, 5.64 mmol) in 80 % acetic acid (100 ml) was stirred for 17 h at 80 °C. The mixture was concentrated and the residual acetic acid was co-evaporated three times with added toluene. The residue was dissolved in pyridine (12 ml) and acetic anhydride (6 ml) and stirred overnight at room temperature. The solution was concentrated and the residue was co-evaporated three times with added toluene. Purification by column chromatography (toluene–acetone 1:1) gave **9** as a 1:5 α/β-mixture, 1.84 g (93 %): ^{13}C NMR ($CDCl_3$) (selected signals) δ 16.4 (d, *J* 7.3 Hz, *C*$H_3$$CH_2$), 20.6, 20.9, 21.1, 21.2 (4×CH_3, acetates), 28.8 and 29.7 (2 d, *J* 3.6 Hz, C-5: α and C-5: β), 61.6 (d, *J* 7.4 Hz, *C*$H_2$$CH_3$), 94.7 (C-1: α), 99.3 (C-1: β), 169.4 and 170.0 (acetates); ^1H NMR ($CDCl_3$) (selected signals) δ 1.33 (t, *J* 6.96 Hz, 3 H, *CH*$_3$$CH_2$) 1.80–2.21 (s, s and m, 12 H, 2×CH_3, acetates, H-3, H-3′, H-5, H-5′, H-6, H-6′), 4.15 (dt, *J* 2.20, 2.57, 3.66, 6.96, 7.33 and 8.06 Hz, 4 H, 2×CH_3*CH*$_2$), 4.39 (m, 1 H, H-4), 5.18 (m, 1 H, H-2), 6.13 and 6.35 (2 d, 1 H, H-1β *J* < 1.5 Hz and H-1α *J* 4.40 Hz). Anal. $C_{14}H_{25}O_8P$: C, H, P.

*1-[2′-O-Acetyl-3′,5′,6′-trideoxy-6′-(diethylphosphono)-*β-D-erythro-*hexofuranosyl]thymine* (**10**). A mixture of thymine (107 mg, 0.852 mmol), chlorotrimethylsilane (100 µl) and a catalytic amount of diammonium sulfate was refluxed in hexamethyldisilazane (2 ml) under nitrogen for 6 h. The solution was concentrated and then concentrated with added toluene (5 ml). The residue was dissolved in acetonitrile (5 ml) and to this was added a solution of diacetate **9** (200 mg, 0.568 mmol) in acetonitrile (5 ml). The mixture was cooled in an ice bath, flushed with nitrogen and *tert*-butyldimethylsilyl triflate (0.160 ml, 0.681 mmol) was added dropwise. The ice bath was removed after 15 min, and the reaction mixture was stirred for 18 h at room temperature. Pyridine (1 ml) was added and the solution was filtered through a pad of silica gel and concentrated. The product was purified by column chromatography (chloroform–methanol, 15:1) to yield **10**, 228 mg (96 %) as a syrup: $[\alpha]_D$ +11.60° (*c* 1.00, $CHCl_3$): ^{13}C NMR ($CDCl_3$) δ 12.6 (CH_3, thymine), 16.4 (d, *J* 5.5 Hz, 2×*C*$H_3$$CH_2$), 20.9 ($CH_3$, acetate), 22.7 (d, *J* 142.9 Hz, C-6′), 27.8 (d, *J* 5.5 Hz, C-5′), 36.9 (C-3′), 61.7 (d, *J* 5.5 Hz, 2×CH_3*C*H_2), 77.8 (C-2), 79.3 (d, *J* 6.5 Hz, C-4′), 91.6 (C-1′), 111.3 (C-5), 136.1 (C-6), 150.0 (C-4), 163.6 (C-2), 170.3 (acetate); ^1H NMR ($CDCl_3$) δ 1.33 (t, *J* 6.96 and 7.33 Hz, 6 H, 2×*CH*$_3$$CH_2$), 1.79–2.10 (s, s and m, 12 H, CH_3 thymine, CH_3 acetate, H-3′, H-3″, H-5′, H-5″, H-6′, H-6″), 4.11 (dt, *J* 6.96, 7.33 and 7.69 Hz, 4 H, 2×CH_3*CH*$_2$), 4.24 (m, 1 H, H-4), 5.29 (m, 1 H, H-2′), 5.71 (d, *J* 2.19 Hz, 1 H, H-1′), 7.01 (s, 1 H, H-6), 8.99 (s, 1 H, H-3). Anal. $C_{17}H_{27}N_2O_8P$: C, H, N.

2′-O-Acetyl-3′,5′-dideoxy-5′-C-[(diethylphosphono)methyl]-cytidine (**11**). A mixture of cytosine (95 mg, 0.852 mmol), chlorotrimethylsilane, (100 µl) and a catalytic amount of diammonium sulfate in hexamethyldisilazane (2 ml) was refluxed under nitrogen for 6 h. The solution was concentrated and then concentrated with added toluene (10 ml). The residue was dissolved in acetonitrile (5 ml) and to this was added a solution of diacetate **9** (200 mg, 0.568) in acetonitrile (5 ml). The mixture was cooled in an ice bath and *tert*-butyldimethylsilyl triflate (0.160 ml, 0.681 mmol) was added dropwise. The ice bath was removed after 30 min and the mixture was stirred at room temperature for 16 h. Pyridine (1 ml) was added and the solution was filtered through a pad of silica gel and concentrated. The residue was purified by column chromatography (chloroform–methanol 9:1) to yield **11**, 199 mg (87 %): $[\alpha]_D$ +36.56° (*c* 0.90, MeOH): ^{13}C NMR (CD_3OD) δ 16.7 (d, *J* 5.5 Hz, 2×*C*$H_3$$CH_2$), 20.8 ($CH_3$ acetate), 22.05 (d, *J* 141.1 Hz, C-6′), 28.5 (d, *J* 5.5 Hz, C-5′), 37.3 (C-3′), 63.3 (d, *J* 7.4 Hz, 2×*C*$H_3$$CH_2$), 79.7 (C-2′), 80.9 (d, *J* 6.5 Hz, C-4′), 94.1 (C-1′), 96.2 (C-5), 143.3 (C-6), 157.8 (C-4), 167.8 (C-2), 171.8 (acetate); ^1H NMR (CD_3OD) δ 1.30 (t, *J* 6.96 and 7.33 Hz, 6 H, 2×*CH*$_3$$CH_2$), 1.91–2.14 (s, m, 9 H, CH_3, acetate, H-3′, H-3″, H-5′, H-5″, H-6′, H-6″), 4.11 (m, *J* 1.83 and 6.59 Hz, 4 H, 2×CH_3*CH*$_2$), 4.26 (m, 1 H, H-4′), 5.28 (m, 1 H, H-2′), 5.72 (d, *J* 1.47 Hz, 1 H, H-1′), 5.88 (d, *J* 7.70 Hz, 1 H, H-5), 7.56 (d, *J* 7.70 Hz, 1 H, H-6). Anal. $C_{16}H_{26}N_3O_7P$: C, H, N.

*9-(2′-O-Acetyl-3′,5′,6′-trideoxy-6′-diethylphosphono-*β-D-erythro-*hexofuranosyl)-6-chloropurine* (**12**). A stirred mixture of 6-chloropurine (263 mg, 1.70 mmol), chlorotrimethylsilane (200 µl) and a catalytic amount of diammo-

nium sulfate in hexamethyldisilazane (4 ml) was refluxed under nitrogen for 6 h. The solution was concentrated and then concentrated with added toluene (10 ml). The residue was dissolved in acetonitrile (10 ml) and to this a solution of diacetate **9** (400 mg, 1.135 mmol) in acetonitrile (10 ml) was added. The mixture was flushed with nitrogen, cooled in an ice bath and *tert*-butyldimethylsilyl triflate (0.320 ml, 1.362 mmol) was slowly added. The ice-bath was removed after 30 min and the reaction was stirred at room temperature for 16 h. Pyridine (2 ml) was added and the solution was filtered through a pad of silica gel and concentrated. Purification by column chromatography (chloroform–methanol 15:1) yielded **12**, 492 mg (97 %): $[\alpha]_D$ +6.09° (*c* 1.16, $CHCl_3$): ^{13}C NMR ($CDCl_3$) δ 16.5 (d, *J* 5.5 Hz, 2×CH_3CH_2), 20.9 (CH_3, acetate), 22.2 (d, *J* 132.9 Hz, C-6'), 27.8 (d, *J* 5.5 Hz, C-5'), 36.5 (C-3'), 61.7 (d, *J* 5.5 Hz, 2×CH_3CH_2), 78.4 (C-2'), 80.8 (d, *J* 6.5 Hz, C-4'), 90.4 (C-1'), 132.5 (C-5), 144.0 (C-8), 150.9 (C-6), 151.5 (C-4), 152.1 (C-2), 170.2 (acetate); ^1H NMR ($CDCl_3$) δ 1.22 (d, *J* 1.47, 6.96 and 7.33 Hz, 6 H, 2×CH_3CH_2), 1.70–2.49 (s, m, 9 H, CH_3, acetate, H-3', H-3", H-5', H-5", H-6', H-6"), 4.00 (dq, *J* 4.76, 6.96 and 7.33 Hz, 2×CH_3CH_2), 4.37 (m, 1 H, H-4'), 5.50 (m, 1 H, H-2'), 5.95 (d, *J* 1.47 Hz, 1 H, H-1'), 8.10 (s, 1 H, H-8), 8.66 (s, 1 H, H-2). Anal. $C_{17}H_{24}ClN_4O_6P$: C, H, N.

*Ammonium [1-(3',5',6'-trideoxy-β-*D*-*erythro*-hexofuranosyl)thymine]-6'-phosphonate* (**1**). To a solution of the protected thymidine analogue **10** (210 mg, 0.502 mmol) in chloroform (3 ml) was added bromotrimethylsilane (0.78 ml). The solution was stirred for 7 h at room temperature and then concentrated. The resulting disilyl ester was hydrolysed with a mixture of water–pyridine (5:2, 7 ml) for 1 h at room temperature. After concentration, the residue was dissolved in methanol saturated with ammonia (8 ml). The solution was allowed to stand overnight at room temperature and then concentrated. Precipitation from methanol yielded **1**, 137 mg (81 %) $[\alpha]_D$ +8.73° (*c* 1.02, water): ^{13}C NMR (D_2O, 25 °C) δ 12.3 (CH_3, thymine), 25.8 (d, *J* 133.8 Hz, C-6'), 29.9 (d, *J* 3.7 Hz, C-5'), 38.1 (C-3'), 76.2 (C-2'), 82.8 (d, *J* 18.3 Hz, C-4'), 93.0 (C-1'), 111.8 (C-5), 137.8 (C-6), 152.3 (C-4), 167.4 (C-2); ^1H NMR (D_2O, 25 °C): δ 1.56–2.2 (s, m, 9 H, CH_3, thymine, H-3', H-3", H-5', H-5", H-6', H-6"), 4.44 (m, 2 H, H-2' and H-4'), 5.8 (d, *J* 2.20 Hz, 1 H, H-1'), 7.4 (s, 1 H, H-6). Found: C 38.70; H 5.87; N 12.05. Calc. for $C_{11}H_{20}N_3O_7P$: C 39.17; H 5.98; N 12.46.

*Ammonium 3',5'-dideoxycytidine-5'-*C*-methylphosphonate* (**2**). A mixture of the protected cytidine analogue **11** (175 mg, 0.434 mmol) and bromotrimethylsilane (1.00 ml) in DMF (2 ml) was stirred for 4 h at room temperature, the mixture was concentrated and a mixture of water–pyridine (5:2, 7 ml) was added. After 1 h, the mixture was concentrated and then concentrated with added ethanol. The residue was dissolved in methanol saturated with ammonia (6 ml), stirred overnight at room temperature and concentrated. Precipitation from water–acetone yielded **2**, 108 mg (77 %): $[\alpha]_D$ +59.47° (*c* 0.95, water): ^{13}C NMR (D_2O, 80 °C) δ 25.3 (d, *J* 133.8 Hz, C-6'), 29.7 (d, *J* 3.7 Hz, C-5'), 32.8 (C-3'), 76.7 (C-2'), 82.7 (d, *J* 18.3 Hz, C-4'), 94.1 (C-1'), 96.4 (C-5), 142.3 (C-6), 157.6 (C-4), 166.8 (C-2); ^1H NMR (D_2O, 80 °C) δ 1.68–2.16 (m, 6 H, H-3', H-3", H-5', H-5", H-6', H-6"), 4.43 (m, 2 H, H-2', H-4'), 5.77 (d, *J* 1.83 Hz, 1 H, H-1'), 6.04 (d, *J* 7.69 Hz, 1 H, H-5), 7.69 (d, *J* 7.69 Hz, 1 H, H-6). Found: C 37.56; H 5.90; N 16.80. Calc. for $C_{10}H_{19}N_4O_6P$: C 37.27; H 5.94; N 17.39.

*3',5'-Dideoxyadenosine-5'-*C*-methylphosphonic acid* (**3**). A solution of the protected 6-chloropurine derivative **12** (389 mg, 0.871 mmol) and bromotrimethylsilane (1.56 ml) in chloroform (6 ml) was stirred at room temperature for 7 h. The solution was concentrated and a mixture of water–pyridine (5:2, 14 ml) was added. The solution was stirred for 1 h and then concentrated. The residue was dissolved in methanol saturated with ammonia (12 ml) and the solution was stirred at room temperature overnight. The mixture was concentrated, dissolved in 25 % aqueous ammonium hydroxide (10 ml) and heated to 100 °C for 20 h in a sealed steel vessel. After being cooled the mixture was concentrated and precipitated from water–acetone to yield **3**, 175 mg (58 %): $[\alpha]_D$ −11.51° (*c* 1.06, H_2O): ^{13}C NMR (D_2O, 80 °C) δ 25.1 (d, *J* 135.7 Hz, C-6'), 29.9 (d, *J* 3.6 Hz, C-5'), 38.1 (C-3'), 76.2 (C-2'), 82.4 (d, *J* 18.3 Hz, C-4'), 91.6 (C-1'), 119.8 (C-5), 140.5 (C-8), 149.4 (C-4), 153.6 (C-2), 156.3 (C-6); ^1H NMR (D_2O, 80 °C) δ 1.40–2.29 (m, 6 H, H-3', H-3", H-5', H-5", H-6', H-6"), 4.54 (m, 1 H, H-4'), 4.77 (m, 1 H, H-2'), 6.00 (d, *J* 1.83 Hz, H-1'), 8.18 (s, 1 H, H-8), 8.21 (s, 1 H, H-2). Anal. $C_{11}H_{18}N_5O_6P$ *x* H_2O: C, H, N.

Acknowledgements. We thank the Swedish National Board for Technical Development for financial support, Medivir AB for the biological testing and Dr. N. G. Johansson, Medivir AB for useful discussions.

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Received December 21, 1990.