Facile Transformation of β-D-Ribofuranosyl Purines and Pyrimidines into Their Respective 3′-Deoxy-*threo*-pentofuranosyl Nucleosides[1]

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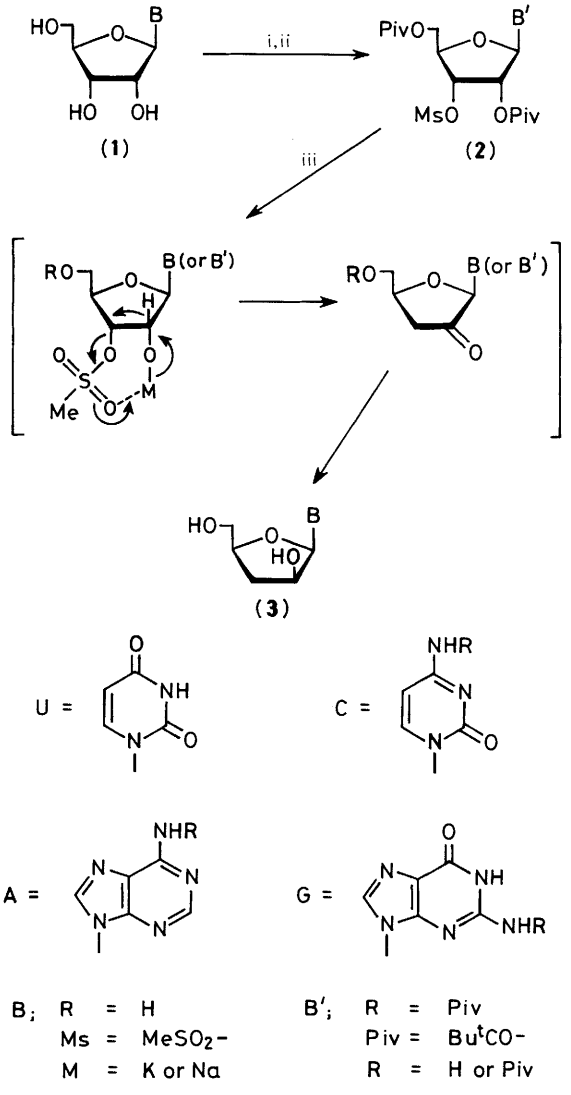
Practical syntheses of 3′-deoxy-β-D-*threo*-pentofuranosyl-uracil, -cytosine, -adenine, and -guanine (**3U**, **C**, **A**, **G**) from the corresponding ribonucleosides by two one-pot reactions with readily accessible reagents are described. The key reactions are the selective 3′-*O*-methanesulphonylations of the ribonucleosides, the deoxygenative [1,2]-hydride shift of the methanesulphonates, and the reduction of *in situ* generated 3′-deoxy-2′-keto nucleosides therefrom.

The deoxy analogues of arabinofuranosyl nucleosides, 9-(3-deoxy-β-D-*threo*-pentofuranosyl)adenine and 1-(3-deoxy-β-D-*threo*-pentofuranosyl)cytosine (**3A**) and (**3C**), are of biological interest because the parent nucleosides exhibit antitumor and antiviral activity.[2] Such 3′-deoxynucleosides also serve as useful synthetic intermediates [1b,3] for the preparation of 2′,3′-dideoxynucleosides and their analogues, which have recently received much attention as potential anti-HIV (human immunodeficiency virus) agents.[4] In this connection, we needed sufficient (**3A**) and (**3C**) as well as guanine and uracil derivatives (**3G**) and (**3U**) for biological evaluation and chemical modification of the sugar moiety. Until recently, no report on a general and useful method for synthesizing these nucleosides has appeared. Though the synthesis of (**3U**)[5] and (**3A**)[6] has been reported, the multi-step preparation *via* 2′,3′-epoxy-*lyxo*-nucleosides starting from the corresponding ribonucleosides was rather tedious. Some biological properties of (**3C**)[7] were investigated but neither synthetic procedures nor physicochemical data have been described. After this work had been completed,[1a] an efficient synthesis[8] of the 2′,3′-epoxyuracil nucleoside *via* a 2′,3′-di-*O*-methanesulphonated uridine and its conversion into (**3U**) and (**3C**) was reported, but the method seemed to be unsuitable for purine nucleosides.

Previously, we reported a new deoxygenation at the C-3 position of 3-*O*-sulphonated D-allo- and ribo-furanoside derivatives with Grignard reagents.[9] In this deoxygenation, a [1,2]-hydride shift (from C-2 to C-3) and concerted elimination of the 3-sulphonyloxy group occurred to form a 3-deoxy-2-ketofuranoside, which in turn reacted with an excess of the Grignard reagent in a one-pot manner. Recently this reaction was extended to a field of nucleoside chemistry.[3,10] Hansske and Robins[10a] have succeeded in the synthesis of (**3A**) by the reaction of 3′-*O*-tosyladenosine with lithium triethylborohydride in a mixture of tetrahydrofuran (THF) and dimethyl sulphoxide (DMSO). In a large scale preparation of (**3A**), however, there are some disadvantages to the use of this method, *i.e.*, the multi-step synthesis of the starting 2′-unsubstituted 3′-sulphonate, strict anhydrous conditions, and removal of the nonvolatile solvent in a work-up step. We now report an improved, facile synthesis of (**3A**) as well as (**3U**, **C**, **G**) starting from the corresponding ribonucleosides by the use of the deoxygenative [1,2]-hydride shift as the key reaction (Scheme 1).

The preparation of our key intermediates, protected 3′-*O*-mesylribonucleosides was achieved by utilizing an efficient method for the regioselective acylation of the ribonucleosides developed by Ishido *et al.*[11] Thus uridine, cytidine, adenosine, and guanosine (**1U**, **C**, **A**, **G**) were partially acylated with pivaloyl chloride in pyridine,[11] followed by methanesulphonylation with methanesulphonyl chloride in a one-pot manner to give the corresponding *N*,*O*-pivaloyl protected 3′-*O*-mesylnucleosides (**2U**, **C**, **A**, **G**) as the major products. This process avoids the tedious stepwise synthesis of the 3′-sulphonylated nucleosides.[3c,10d] Among the methanesulphonylated nucleosides, (**2C**) and its deprotected counterpart could be easily purified and their structures were determined on the basis of



Scheme 1. *Reagents and conditions:* i, Bu^{t}COCl, pyridine; ii, $MeSO_2Cl$; iii, $NaBH_4$, MeOH, KOH (or NaOMe)

their elemental analyses, u.v., and ^{1}H n.m.r. spectral data (Tables 1 and 2). In the synthesis of (**3U**, **C**, **A**, **G**), these methanesulphonates were not purified, but directly subjected to the *next one-pot* reaction, which involved depivaloylation, the [1,2]-hydride shift, and reduction. We found that the use of reagent combinations, potassium hydroxide (or sodium methoxide)–sodium borohydride [KOH (or NaOMe)–$NaBH_4$] in methanol was extremely efficient for promoting further reactions. Under strong alkaline conditions the 2′-pivaloyl groups of (**2U**, **C**, **A**, **G**) were easily removed to generate molecules susceptible to the hydride-shift reaction. The *in situ* generated keto nucleosides from such molecules were reduced with sodium borohydride at room temperature in a one-pot manner to give the respective products (**3U**, **C**, **A**, **G**) in 40—60% overall yields from (**1**); the hygroscopic amorphous (**3C**) was characterized as its crystalline hydrochloride salt. The reduction of the keto nucleosides in the reactions proceeded with good stereoselectivity (>95:5, judging from the t.l.c. and ^{1}H n.m.r. spectroscopic analyses), presumably because of the steric hindrance due to the base moiety and of the mild reaction conditions. In practice, no isomers of (**3**) could be isolated by the present method for purification.

The compounds (**3U**) and (**3A**) were identified with the corresponding known nucleosides by comparison of physical and spectroscopic data (m.p., $[\alpha]_D$, u.v., and ^{1}H n.m.r.). The structure of the modified sugar moiety in the compounds (**3C**) and (**3G**) was established on the basis of their ^{1}H n.m.r. spectral data and the following fact. The methanolysis of these compounds gave isomeric mixtures of methyl pentosides. The characteristic peaks of their ^{1}H n.m.r. spectra were identical with those for the methyl pentosides prepared from the known (**3A**).[3a]

The present method thus allows the synthesis of the 3′-deoxyarabino-nucleosides from the ribo counterparts by the two consecutive one-pot reactions, applicable to large scale preparations. The biological evaluation of the prepared 3′-deoxynucleosides is now in progress, and will be reported in due course.

Experimental

T.l.c. was performed on precoated plates (0.25 mm) of Silica Gel 60 F_{254} (Merck). Detection was done by u.v. (254 nm) or spraying the plates with a solution of methanol–sulphuric acid-*p*-anisaldehyde (85:15:5, v/v/v), followed in the latter case by heating on an electric plate. Column chromatography was effected on Silica Gel 60 (Merck 70—230 mesh, ASTM). Elemental analyses were performed by the Microanalytical Laboratory of this Institute. The solvent extracts were dried with anhydrous magnesium sulphate, 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 phosphorus pentaoxide. The physical and spectral data are summarized in Tables 1 and 2.

N^4,$O^{2'}$,$O^{5'}$-*Tripivaloyl*-3′-O-*mesylcytidine* (**2C**).—Pivaloyl chloride (4.84 g, 40 mmol) was added to a solution of (**1C**) (2.43 g, 10 mmol) in dry pyridine (40 ml) at 0—5 °C, after which the mixture was stirred at room temperature for 2 h. Methanesulphonyl chloride (6.9 g, 60 mmol) was added and the mixture was then stirred at room temperature for 2 h. After cooling, iced water was added, and the products were extracted with diethyl ether containing a small amount of chloroform. The extracts were washed once with aqueous sodium hydrogen carbonate and twice with water, 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 (8:2→6:4) as eluant to give (**2C**) (4.12 g, 72%) (Found: C, 51.9; H, 6.8; N, 7.2; S, 5.55. $C_{25}H_{39}N_3O_{10}S\cdot0.2H_2O$ requires C, 52.0; H, 6.9; N, 7.3; S, 5.55%); δ_H(400 MHz, $CDCl_3$) 1.26, 1.27, and 1.29 (9 H, each s, 3 × CMe_3), 3.07 (3 H, s, SMe), 4.44 (2 H, d, *J* 3.2 Hz, 5′,5″-H), 4.52 (1 H, m, 4′-H), 5.30 (1 H, t, *J* 5.9 Hz, 3′-H), 5.49 (1 H, dd, *J* 3.9 and 5.6 Hz, 2′-H), 6.01 (1 H, d, $J_{1',2'}$ 3.9 Hz, 1′-H), 7.47 (1 H, d, $J_{5,6}$ 7.3 Hz, 5-H), 7.82 (1 H, d, $J_{5,6}$ 7.6 Hz, 6-H), and 8.19 (1 H, br s, NH).

3′-O-*Mesylcytidine Hydrochloride*.—A solution of KOH (34 mg, 0.6 mmol) in MeOH (1 ml) was added to a stirred solution of (**2C**) (172 mg, 0.3 mmol) in MeOH (2 ml). After the mixture had been stirred at room temperature for 18 min, a solution of acetic acid (36 mg) in MeOH (0.2 ml) was added, and the mixture was concentrated at room temperature. The residue was chromatographed on a silica-gel column with $CHCl_3$–MeOH (9:1→85:15) to give 3′-*O*-mesylcytidine as a foam (68 mg, 71%), which was crystallized from a mixture of concentrated hydrochloric acid and ethanol to afford the hydrochloride salt (41 mg, 41%) (Found: C, 33.6; H, 4.5; N, 11.5; S, 8.65. $C_{10}H_{16}ClN_3O_7S\cdot0.1H_2O$ requires C, 33.4; H, 4.5; N, 11.7; S, 8.9%); δ_H[400 MHz, $(CD_3)_2$)SO] 3.26 (3 H, s, SMe), 3.64 (1 H, AB of ABX, *J* 2.7 and 12.2 Hz, 5′-H), 3.72 (1 H, AB of ABX, *J* 2.9 and 12.2 Hz, 5″-H), 4.23 (1 H, m, 4′), 4.38 (1 H, br t, *J* 5 Hz, 2′-H), 4.98 (1 H, t, *J* 4.4 Hz, 3′-H), 5.44 (1 H, br s, OH), 5.81 (1 H, d, $J_{1',2'}$ 5.8 Hz, 1′-H), 6.12 (1 H, d, $J_{5,6}$ 7.6 Hz, 5-H), 8.16 (1 H, d, $J_{5,6}$ 7.9 Hz, 6-H), and 8.40 and 9.34 (2 H, each br s, OH and NH).

1-(3-*Deoxy*-β-D-threo-*pentofuranosyl*)*cytosine* (**3C**) *and its Hydrochloride*.—To a stirred suspension of (**1C**) (7.29 g, 30 mmol) in dry pyridine (100 ml) was added pivaloyl chloride (14.7 g, 121 mmol) at 0—5 °C. After the mixture had been stirred at room temperature for 40 min, methanesulphonyl chloride (20.6 g, 180 mmol) was added at 0—5 °C, and the mixture was then stirred at room temperature for 1.5 h. The work-up as described for the synthesis of (**2C**) afforded the crude methanesulphonylate (19.5 g) as a foam, one third (6.5 g) of which was taken up in MeOH (60 ml). To this solution was added a solution of KOH (3.36 g, 60 mmol) in MeOH (40 ml) at 0—5 °C, immediately after which $NaBH_4$ (1.13 g, 30 mmol) was added. The mixture was stirred at room temperature for 20 h. After the mixture had cooled, a mixture of concentrated hydrochloric acid (4.4 ml, 50 mmol) and MeOH (1.5 ml) was gradually added with vigorous stirring. The resulting precipitates were filtered off and washed with MeOH. The combined filtrate and washings were concentrated to *ca.* 20 ml, and the pH of the solution was adjusted to *ca.* 8 with concentrated hydrochloric acid–MeOH (3:1). To this mixture was added boiling Pr^iOH (60 ml) with vigorous stirring, and the stirring was continued for 30 min. After the mixture had cooled, the undissolved materials were filtered off and washed with Pr^iOH. The combined filtrate and washings were concentrated to dryness. The residue was triturated with Pr^iOH (50 ml), and the undissolved materials were filtered off and washed with Pr^iOH. The filtrate and washings were combined and concentrated to give a crude product (2.26 g). Chromatography on silica gel with $CHCl_3$–MeOH (95:5→8:2) as eluant gave (**3C**) (1.37 g, 60%) as a hygroscopic foam, which was crystallized by treating a solution of the foam in Pr^iOH with concentrated hydrochloric acid–Pr^iOH (1:4) to afford (**3C**)·hydrochloride salt (Found: C, 41.1; H, 5.4; Cl, 13.55; N, 15.9. $C_9H_{14}ClN_3O_4$ requires C, 41.0; H, 5.35; Cl, 13.45; N, 15.9%).

The Preparation of 1-(3-*Deoxy*-β-D-threo-*pentofuranosyl*)-*uracil* (**3U**).[5]—Pivaloyl chloride (9.08 g, 75 mmol) was added to a stirred solution of (**1U**) (7.32 g, 30 mmol) in dry pyridine (100 ml) at 0—5 °C, after which the mixture was stirred at room temperature for 30 min. Methanesulphonyl chloride (13.8 g, 120 mmol) was added at 0—5 °C and the mixture was then

Table 1. Physical data for the nucleosides

Compound	M.p.[a] (°C)	Recryst. solvent	$[\alpha]_D$/°	(*c*, solvent)[b]	Temp. (°C)	$\lambda_{max.}$(MeOH)/nm[c] (ε/dm^3 mol^{-1} cm^{-1})
(**2C**)	Amorphous		+41.0	(0.3, $CHCl_3$)	23	250 (17 400) 298 (7 800)
3-*O*-Mesylcytidine·HCl	194—197 (decomp.)	EtOH	+38.3	(0.9, DMF)	23	280 (11 600)
(**3U**)	146—147	Pr^iOH	+97.7	(1.1, DMF)	20	263 (10 300)
	145—146	Acetone	+146	(0.8, H_2O)	27	
	[147—148][d]	Acetone	[+165	(0.77, H_2O)	26][d]	[262 (10 140)][d,e]
(**3C**)·HCl	183.5—184.5 (decomp.)	EtOH	+151	(0.5, H_2O)	26	283 (11 600)
(**3A**)	195—196	MeOH	−24.3	(1.1, DMF)	20	259 (14 200)
	[195—196][f]	MeOH	[−27	(1, DMF)	22][f]	[260 (15 800)][f,g]
(**3G**)	>235[h]	EtOH	+8.7	(1.1, DMF)	20	253 (14 800) 271sh (10 200)

[a] Uncorrected, measured on a Yamato micro melting-point apparatus. [b] Obtained with a Perkin-Elmer Model 241MC polarimeter. [c] Measured on a Varian Cary 2200 apparatus. [d] Ref. 5*a*. [e] $\lambda_{max.}$(EtOH). [f] Ref. 6*a*. [g] $\lambda_{max.}$(pH 7). [h] Sintering with gradual decomp.

Table 2. ^{1}H N.m.r.[a,b] spectral data (δ_H) for the 3′-deoxynucleosides

Compd.	1′-H ($J_{1',2'}$)	2′-H (m)	3′,3″-H (m)	(m)	4′-H (m)	5′,5″-H ($J_{A(B).X}$,$J_{A,B}$)		2 or 5-H ($J_{5,6}$)	6 or 8-H ($J_{5,6}$)	2′-OH (d)	5′-OH (t)	NH or NH_2 (s)
(**3U**)	5.87 (4.8)	4.33	1.75	2.24	4.00	3.55 (4.8, 11.7)	3.60 (3.7, 11.7)	5.55 (8.1)	7.74 (8.1)	5.35 (4)	5.05 (br)	11.18 (br)
(**3C**)	5.88 (4.3)	4.24	1.76 (ddd 4.0, 5.8, 13.4)	2.27	4.03	3.54 (4.9, 11.6)	3.59 (4.0, 11.6)	5.68 (7.3)	7.68 (7.3)	3.2—3.7 (2 H, br s)		
(**3C**)·HCl	5.90 (4.5)	4.39 (br q, 5)	1.76	2.26	4.11	3.58 (4.9, 12.0)	3.63 (3.8, 12.0)	6.17 (7.6)	8.15 (7.6)	8.76, 9.81 (1 H, each s, NH or OH)		
(**3A**)	6.15 (5.4)	4.51	2.02	2.29	4.09	3.58 (m)	3.66 (m)	8.14 (s)	8.30 (s)	5.42 (5.6)	5.17 (5.4)	7.24 (2 H, br)
(**3G**)	5.86 (5.1)	4.42	1.96	2.28	4.03	3.54 (m)	3.61 (m)		7.83 (s)	5.39 (br, 5.5)	5.06 (br)	6.64 (NH_2) 10.82 (NH, br)

[a] Obtained on a JEOL JNM-GX 400 spectrometer. [b] Determined in $(CD_3)_2SO$ with Me_4Si as an internal standard; coupling constants in Hz.

stirred at room temperature for 1 h. The work-up as described for the preparation of (**2C**) gave the crude methanesulphonate, which was dissolved in MeOH (100 ml). To this solution was added a solution of KOH (6.72 g, 120 mmol) in MeOH (80 ml) at 0—5 °C, immediately after which $NaBH_4$ (2.28 g, 60 mmol) was added. The mixture was stirred at room temperature for 24 h. The resulting undissolved crystals were filtered off and washed with MeOH. To the combined filtrate and washings was added a mixture of concentrated hydrochloric acid (9.8 ml, 118 mmol) and MeOH (37 ml) at 5 °C. The resulting precipitates were filtered off and washed with MeOH. The combined filtrate and washings were concentrated to *ca.* 40 ml. After the mixture had cooled a mixture of concentrated hydrochloric acid (2.1 ml, 25 mmol) and MeOH (10 ml) was added, and the undissolved materials were filtered off and washed with MeOH. The filtrate and washings were concentrated again, and the remaining water was removed by repeated co-evaporation with ethanol. The residue was chromatographed on a silica-gel column made in $CHCl_3$–MeOH (99:1). Elution with the same solvent system (97:3→9:1) provided (**3U**) (3.82 g, 56%) (Found: C, 47.4; H, 5.4; N, 12.0. Calc. for $C_9H_{12}N_2O_5$: C, 47.4; H, 5.3; N, 12.3%). The physical properties of the product were identical with those reported.[5]

The Preparation of 9-(3-*Deoxy*-β-D-threo-*pentofuranosyl*)-*adenine* (**3A**).[3a,6]—Pivaloyl chloride (6.87 g, 56.8 mmol) was added to a stirred suspension of (**1A**) (5.0 g, 18.7 mmol) in dry pyridine (50 ml) at −15 °C. The mixture was stirred first at this temperature for 1.5 h and then at 0 °C for 2 h. Methanesulphonyl chloride (6.39 g, 55.6 mmol) was added and the mixture was stirred at room temperature for 3 h. After the work-up as described for the synthesis of (**2C**), the crude methanesulphonate was dissolved in MeOH (150 ml). To this solution was added NaOMe (8.10 g, 150 mmol) and $NaBH_4$ (2.51 g, 66.1 mmol) at −15 °C. The mixture was stirred first at room temperature for 14 h and then at 50 °C for 5 h. The reaction mixture was cooled and acetone was added. On cooling, the mixture was neutralized with concentrated hydrochloric acid and evaporated under reduced pressure. The remaining water was removed by repeated co-evaporation with ethanol. The residue was suspended in a mixture of $CHCl_3$ and MeOH, and placed on a silica-gel column made up in $CHCl_3$–MeOH (8:1). Elution with the same solvent system (8:1→5:1) gave (**3A**) (2.7 g, 57%) (Found: C, 47.75; H, 5.25; N, 28.1. Calc. for $C_{10}H_{13}N_5O_3$: C, 47.8; H, 5.2; N, 27.9%). The physical properties of this product were identical with those reported.[6]

9-(3-*Deoxy*-β-D-threo-*pentofuranosyl*)*guanine* (**3G**).—To a stirred suspension of (**1G**) (5.0 g, 17.7 mmol) in dry pyridine (50 ml) was added pivaloyl chloride (9.63 g, 79.6 mmol) at 0—5 °C, and the mixture was stirred at room temperature for 45 min. Methanesulphonyl chloride (6.10 g, 53 mmol) was added at 0—5 °C, afrter which the mixture was stirred first at this temperature and then at room temperature for 3 h. The work-up as described for the synthesis of (**2C**) gave the crude methanesulphonylate, which was dissolved in MeOH (120 ml). To this solution was added NaOMe (7.61 g, 141 mmol) and $NaBH_4$ (2.71 g, 71.4 mmol) at 0—5 °C. The mixture was stirred first at room temperature for 1 h and then at 50 °C for 5 h. After the mixture had cooled, acetone was added. In order to remove boric acid derivatives, MeOH (100 ml) was added and the mixture was then concentrated to a half volume. After this procedure had been repeated once again, the mixture was carefully made neutral with concentrated hydrochloric acid. The

methanol was removed by repeated co-evaporation with water. The residue was suspended in water (*ca.* 150 ml) and placed in a column of Diaion HP 20 (600 ml, highly porous resin, Mitsubishi Chemical Co., Tokyo) made in water. After inorganic materials had been eluted with water (*ca.* 1.5 l), the adsorbed organic compounds were eluted with 5% aqueous MeOH, followed with 5% aqueous MeOH–0.1M aqueous ammonia to give a crude product, which was crystallized from refluxing ethanol to afford (**3G**) (1.31 g, 28%). The mother liquor was concentrated to dryness, and the residue was treated with HP 20 as described above to give an additional amount of the product (0.55 g, 12%).

Methanolysis of (**3C**, **A**, **G**).—A mixture of (**3C**, **A**, or **G**) (20—50 mg) and Dowex 50W-X8 (80—150 mg, H^+ form, 100—200 mesh) ion exchange resin in MeOH (3—10 ml) was refluxed until the starting material disappeared. After the mixture had cooled, the resin was filtered off and washed with MeOH. The combined filtrate and washings were concentrated to give the crude methyl pentosides. The characteristic peaks of the ^1H n.m.r. spectra of the pentosides obtained were identical with those of the sample prepared from the known (**3A**); [3a] δ_H[400 MHz; $(CD_3)_2SO$] 1.77 (dd, *J* 2.9 and 13.8 Hz, 3-H), 2.27 (sextet, 3-H), 2.44 (octet, 3-H), and 3.34 (s, OMe), 3.54 (AB of ABX, *J* 2.1 and 11.8 Hz, 5-H), 3.90 (AB of ABX, *J* 2.1 and 11.9 Hz, 5-H), 4.08 (d, *J* 5.5 Hz, 4-H), 4.32 (dd, *J* 2.1 and 4.9 Hz, 2-H), and 4.84 (s, 1-H).

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References

1 (*a*) Presented at the 11th Japanese Carbohydrate Symposium, Gifu, July 1988, Abstr., p. 31; (*b*) Preliminary communication of a part of this work, M. Kawana, N. Yamasaki, M. Nishikawa, and H. Kuzuhara, *Chem. Lett.*, 1987, 2419.
2 R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley-Interscience, New York, 1970, p. 123.
3 (*a*) M. Kawana and H. Kuzuhara, *Tetrahedron Lett.*, 1987, **28**, 4075; *Carbohydr. Res.*, in the press; (*b*) P. Herdewijin, J. Balzarini, E. De Clercq, R. Pauwels, M. Baba, S. Broder, and H. Vanderhaeghe, *J. Med. Chem.*, 1987, **30**, 1270; (*c*) P. Herdewijn, R. Pauwels, M. Baba, J. Balzarini, and E. De Clercq, *ibid.*, p. 2131.
4 H. Mitsuya and S. Broder, *Nature*, 1987, **325**, 773 and the references cited therein.
5 (*a*) J. P. Horwitz, J. Chua, M. A. Da Rooge, M. Noel, and I. L. Klundt, *J. Org. Chem.*, 1966, **31**, 205; (*b*) T. Naito, M. Hirata, and Y. Nakai, Jap. P. 6 811 457—8/1968 (*Chem. Abstr.*, 1968, **69**, 107013h—j).
6 (*a*) A. P. Martinez, W. W. Lee, and L. Goodman, *J. Org. Chem.*, 1966, **31**, 3263; (*b*) R. Mengel and H. Wiedner, *Chem. Ber.*, 1976, **109**, 1395; (*c*) A. Nyilas and J. Chattopadhyaya, *Synthesis*, 1986, 196.
7 G. W. Kreis, K. A. Watanabe, and J. J. Fox, *Helv. Chim. Acta*, 1978, **61**, 1011; B. M. Mehta and D. J. Hutchison, *Ann. N.Y. Acad. Sci.*, 1975, **255**, 559.
8 T. R. Webb, H. Mitsuya, and S. Broder, *J. Med. Chem.*, 1988, **31**, 1475.
9 M. Kawana and S. Emoto, *Tetrahedron Lett.*, 1975, 3395; *Chem. Lett.*, 1977, 597; *Bull. Chem. Soc. Jpn.*, 1980, **53**, 222; M. Kawana, T. Koresawa, and H. Kuzuhara, *ibid.*, 1983, **56**, 1095.
10 (*a*) F. Hansske and M. J. Robins, *J. Am. Chem. Soc.*, 1983, **105**, 6736; (*b*) A. Grouiller, H. Essadig, H. Pacheco, S. Juntunene, and J. Chattopadhyaya, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 52; (*c*) M. Kawana, K. Takeuchi, T. Ohba, and H. Kuzuhara, *Nucleic Acid Res. Symp. Ser.*, 1986, No. 17, p. 37; (*d*) M. Kawana, K. Takeuchi, T. Ohba, and H. Kuzuhara, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 2437.
11 K. Kamaike, F. Uemura, S. Yamakage, S. Nishino, and Y. Ishido, *Nucleosides, Nucleotides*, 1987, **6**, 699.

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