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Synthesis and Antimicrobial Activity of 2′-Deoxypuromycin

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2′-Deoxypuromycin (2) was synthesized to learn the effect of the 2′-hydroxyl group on the biological activity. Acylated xylose 3 was condensed with silylated 6-chloropurine to give β-D-xylofuranosyl-6-chloropurine derivative 4, whose 6-dimethylamination, 2′-deoxygenation and deprotection afforded 2′-deoxy-β-D-xylofuranosyl purine analog 7. The latter was converted to 2′-deoxypuromycin (2) in 8 steps. 2′-Deoxy analog 2 showed only weak antimicrobial activity compared with that of puromycin (1).

An aminoacylnucleoside antibiotic puromycin (**1**), which was isolated from a culture broth of *Streptomyces alboniger* by Porter *et al.*,[1] has been found to inhibit protein biosynthesis as a 3′-end mimic of aminoacyl–t-RNA.[2] Many structural analogs of **1** have been synthesized in order to lower its toxicity and enhance its biological activities as an antimicrobial,[3–5] antitrypanosoma[3,6] and antitumor agent,[3,7,8] while puromycin has been used as a biological tool in an investigation of the mechanism for the peptide-elongation reaction.[2] Nathans *et al.* have also clarified that there are some structural requirements for the puromycin reaction.[9] The rigid configuration of aminonucleoside[10] and aromatic amino acid moieties[11] are required for biological activity. However, the methyl substituent on the dimethylamino group,[12] the hydroxymethyl group,[4] oxygen in the furanosyl ring,[13] the 5′-hydroxyl group[6] and the methoxyl group in the amino acid moiety[11] might be unnecessary for puromycin-like activity. The effect of the 2′-hydroxyl group of **1** on its biological activity is still obscure.[14] In this paper we describe the synthesis of

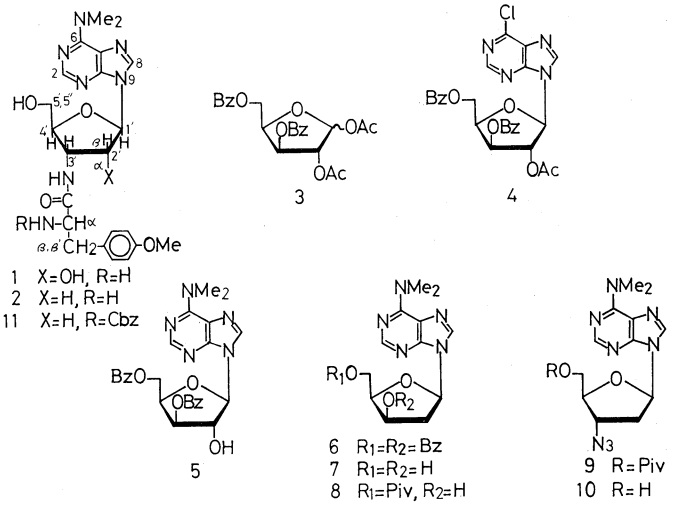

Fig. 1

2′-deoxypuromycin (**2**) to clarify its antimicrobial activity.

Generally for nucleoside synthesis, the lack of a 2-hydroxyl group has given an anomeric mixture of 2′-deoxynucleosides, except for a few examples.[15] From such a point of view, 2′-deoxypuromycin (**2**) was synthesized as outlined in Figure 1.

Acylated xylose **3**[16] was condensed with silylated 6-chloropurine and $SnCl_4$,[17] and then converted to β-D-xylofuranosylpurine derivative **4**. The glycosidation position of the purine base was assigned by ^{1}H-NMR.[18] **4** was heated in 50% aq. $HNMe_2$/THF to afford 6-dimethylamino purine derivative **5**. 2′-Deoxygenation of **5** was accomplished by phenoxythiocarbonylation[19] and successive reduction with n-Bu_3SnH and AIBN (α,α′-azobisisobutyronitrile) in toluene to yield 2′-deoxy-derivative **6**. Deprotection of **6** with methanolic ammonia gave 2′-deoxy-β-D-xylofuranosyl purine derivative **7**. The 5′-hydroxyl group of **7** was protected as pivalate **8**, whose 3′-hydroxyl group was mesylated and then converted to α-azide **9** in the S_N2 manner. When the 5′-hydroxyl group was protected as a trityl ether, by steric hindrance of the β-face, α-azide **9** was obtained in only a low yield (<40%; 2 steps). Saponification of **9** with sodium methoxide gave 6-dimethylamino-9-(3′-azido-2′,3′-dideoxyribofuranosyl)purine **10**. Firstly, the azide group was hydrogenated to an amino group and acylated by the conventional method for peptide synthesis (DCC–*N*-hydroxysuccinimide).[12] However, the reduction proceeded in a low yield, and acylation of the amino group proceeded slowly. Secondly, we applied the Staudinger reaction to form a peptide bond.[20] Treatment of **10** with triphenylphosphine in toluene resulted in the formation of an iminophosphorane, which was reacted with *N*-benzyloxycarbonyl-*p*-methoxy-L-phenylalanine[8] to give aminoacyl derivative **11**. This protocol has been reported by Zaloom and co-workers,[20] and from our studies, it was found to be useful for directly synthesizing an aminoacylnucleoside from an azide intermediate. Hydrogenolysis of **11** with 10% Pd on charcoal gave the desired 2′-deoxypuromycin (**2**).

Table I. COUPLING CONSTANTS FOR PROTON SIGNALS IN PUROMYCIN AND SOME 2′-DEOXYNUCLEOSIDES

	Puromycin	**2**	**10**	**11**
1′-2′β	2.7[a]	6.1[b]	5.4[c]	6.2[b]
1′-2′α	—	7.9	9.3	8.2
2′α-3′	—	7.6	6.1	7.8
2′β-3′	5.8	2.9	0[d]	2.3
2′α-2′β	—	13.4	13.7	13.9
3′-4′	8.0	2.9	6.8	6.2

[a] ^{1}H-NMR (360 MHz, D_2O); *cf.*, H. P. M. De Leeuw, J. R. De Jager, H. J. Koeners, J. H. V. Boom and C. Altona, *Eur. J. Biochem.*, **76**, 209 (1977).
[b] ^{1}H-NMR (270 MHz, $CDCl_3+D_2O$).
[c] ^{1}H-NMR (100 MHz, $CDCl_3$).
[d] The signal of H-2′ was observed as dd (J=5.4 and 13.7 Hz).

2′-Deoxypuromycin (**2**) and puromycin (**1**) were tested for antimicrobial activity. The minimum inhibitory concentration in a broth of **2** and **1** was as follows (μg/ml): *Staphylococcus aureus* 6243, >100 and 25; *Bacillus subtilis* var. *niger* IFO 3108, >100 and 50; *Escherichia coli* 6038, >100 and 25.

2′-Deoxypuromycin (**2**) lost its strong antimicrobial activity, this result being explainable by the fact that **1** is known to exist in an *N*-(3′-*endo*) conformation, whereas the 2′-deoxy nucleosides are more likely to exist in an *S*-(2′-*endo*) conformation.[2] This conformation was supported by ^{1}H-NMR measurements. The coupling constants of the proton signals of **1**, **2** and some intermediates are shown in Table I. Especially, the difference in $J_{2'\beta,3'}$ values of the proton signals of **1** and some 2′-deoxynucleosides could suggest the puckering of the ribose ring.[21] It could be supposed that such puckering of the ribose ring would cause a change in orientation of the aminoacyl moiety of puromycin (**1**) and influence the recognition by a peptidyl transferase and its biological activity.

Experimental

All melting points (mp) are uncorrected. IR spectra were

recorded on a JASCO IR-810 infrared spectrometer. ^{1}H-NMR spectra were measured on a JEOL JNM FX-100 (100 MHz)/GSX-270 (270 MHz) spectrometer with TMS as an internal standard. High-resolution mass spectra were obtained with a JEOL JMX-HX110 mass spectrometer, while ultraviolet spectra were recorded on a Hitachi 124 spectrophotometer. Optical rotation values were measured with a JASCO DIP-4 digital polarimeter, and thin-layer chromatography was performed on silica gel (Merck 60 PF_{254}, 0.75 mm in thickness).

*6-Chloro-9-(2′-O-acetyl-3′,5′-di-O-benzoyl-β-*D*-xylofuranosyl)purine* (**4**). To a stirred suspension of 6-chloropurine (5.75 g, 37.2 mmol) in anhydrous acetonitrile (250 ml) were successively added hexamethyldisilazane (HMDS, 6.92 ml, 29.8 mmol), trimethylchlorosilane (TMS-Cl, 3.78 ml, 29.8 mmol) and $SnCl_4$ (a 4.96 M solution in CH_2Cl_2, 9 ml, 44.6 mmol). The mixture was stirred, and the temperature was raised to 60°C. To the stirred resulting clear solution was added acylated sugar **3** (16.46 g, 37.2 mmol) in anhydrous acetonitrile (100 ml) over a period of 15 min. The mixture was heated under reflux for 1 hr and cooled to room temperature. The reaction mixture was concentrated under reduced pressure, diluted with CH_2Cl_2 (400 ml), poured into a cold sat. $NaHCO_3$ soln. (400 ml) with vigorous stirring, and then neutralized. The emulsion was filtered through a Celite layer, the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine, and dried over $MgSO_4$. Evaporation of the solvent and subsequently silica gel chromatography (CH_2Cl_2–EtOAc = 7 : 1) of the residue afforded **4** (10.86 g, 54%) as a viscous syrup, $[\alpha]_D^{22}$ +65.1° (c = 0.67, $CHCl_3$). UV λ_{max} (EtOH) 265 nm ($\varepsilon = 1.31 \times 10^4$). IR ν_{max} cm^{-1}: 1750, 1730, 1590. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.22 (3H, s, acetyl), 4.76 (2H, m, H-5′,5″), 4.95 (1H, m, H-4′), 5.83 (1H, dd, $J_{2',3'}$ = 1.5 Hz, $J_{3',4'}$ = 4.0 Hz, H-3′), 5.97 (1H, dd, H-2′), 6.31 (1H, d, $J_{1',2'}$ = 2.0 Hz, H-1′), 7.41–8.00 (10H, m, Ph), 8.47 (1H, s, H-2), 8.63 (1H, s, H-8). *Anal.* Found: C, 58.00; H, 4.13; N, 10.21; Cl, 6.90. Calcd. for $C_{26}H_{21}ClN_4O_7$: C, 58.16; H, 3.94; N, 10.43; Cl, 6.60%.

In this reaction, a considerable amount of a polar by-product was produced (*ca.* 20%). This compound was assigned to be the N-7 isomer. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 6.71 (1H, d, $J_{1',2'}$ = 1.5 Hz, H-1′), 8.83 (1H, s, H-2), 8.91 (1H, s, H-8). However, no further investigation of this compound was made.

*6-Dimethylamino-9-(3′,5′-di-O-benzoyl-β-*D*-xylofuranosyl)purine* (**5**). To a stirred solution of **4** (28.03 g, 52.2 mmol) in THF (60 ml) was added dropwise 50% aq. $HNMe_2$ (100 ml) at 90°C (bath temp.) over 1.5 min. The mixture was heated under reflux for 1.5 min and then cooled to room temperature. After evaporating the solvent, the residue was treated with CH_2Cl_2 and water. The aqueous phase was reextracted. The organic layer was combined, and washed successively with dil. HCl, brine and a sat. $NaHCO_3$ solution, and dried over $MgSO_4$. After evaporating the solvent, the residue was chromatographed on silica gel (CH_2Cl_2–MeOH = 30 : 1) to give **5** (19.76 g, 75%) as a viscous syrup, $[\alpha]_D^{22}$ +47.1° (c = 0.52, $CHCl_3$). IR ν_{max} (film) cm^{-1}: 3300, 1720, 1595. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 3.50 (6H, s, 6-NMe_2), 4.70 (2H, m, H-5′, 5″), 4.9–5.2 (2H, m, H-3′, 4′), 5.74 (1H, m, H-2′), 6.05 (1H, d, $J_{1',2'}$ = 3.7 Hz, H-1′), 7.2–8.0 (10H, m, Ph), 8.04 (1H, s, H-2), 8.26 (1H, s, H-8). *Anal.* Found: C, 60.95; H, 4.90; N, 13.62. Calcd. for $C_{26}H_{25}N_5O_6 \cdot 0.5\,H_2O$: C, 60.93; H, 5.11; N, 13.67%.

*6-Dimethylamino-9-(2′-deoxy-3′,5′-di-O-benzoyl-β-*D*-xylofuranosyl)purine* (**6**). To a stirred solution of **5** (19.76 g, 39.2 mmol) and 4-dimethylaminopyridine (7.18 g, 58.8 mmol) in anhydrous acetonitrile (300 ml) was slowly added phenoxythiocarbonyl chloride[19] (8.13 ml, 58.8 mmol) with ice-cooling. The reaction mixture was stirred for 24 hr at room temperature, before the solvent was evaporated. The residue was then treated with CH_2Cl_2 (400 ml) and water (100 ml). The organic layer was washed with dil. HCl, sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. After evaporating the solvent, the residue was chromatographed on silica gel (CH_2Cl_2–MeOH = 60 : 1) to give 19.41 g (82%) of crude 6-dimethylamino-9-(3′,5′-di-*O*-benzoyl-2′-*O*-phenoxythiocarbonyl-β-D-xylofuranosyl)-purine. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 3.52 (6H, s, 6-NMe_2), 4.71–5.00 (3H, m, H-4′, H-5′ and H-5″), 6.05 (1H, dd, $J_{3',4'}$ = 4.0 Hz, $J_{2',3'}$ = 1.5 Hz, H-3′), 6.43–6.52 (2H, m, H-1′ and H-2′), 7.1–8.06 (15H, m, Ph), 8.06 (1H, s, H-2), 8.27 (1H, s, H-8).

The vacuum-dried crude product was dissolved in distilled toluene (400 ml), and AIBN (0.22 g, 1.34 mmol) and *n*-Bu_3SnH (12.9 ml, 47.9 mmol) were added. The solution was heated under reflux for 3 hr after passing through nitrogen gas. The mixture was then concentrated under reduced pressure, and the residue was chromatographed on silica gel. Initially, the column was eluted with CH_2Cl_2 to remove the non-polar alkyltin compounds, and then with CH_2Cl_2–MeOH (60 : 1) to give a crude product. Rechromatography of the crude product on silica gel with ethyl acetate afforded **5** (Rf = 0.42) at first, and then **6** (Rf = 0.33, 8.32 g, 53%) as a white solid, mp 126.5–127°C (from EtOH). $[\alpha]_D^{22}$ +33.5° (c = 0.49, $CHCl_3$). UV λ_{max} (EtOH) 275 nm ($\varepsilon = 2.70 \times 10^4$). IR ν_{max} (film) cm^{-1}: 1730, 1600. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 2.8–3.3 (2H, m, H-2′, 2″), 3.51 (6H, s, 6-NMe_2), 4.6–4.9 (3H, m, H-4′, H-5′ and H-5″), 5.90 (1H, m, H-3′), 6.53 (1H, dd, $J_{1',2'\alpha}$ = 5.0 Hz, $J_{1',2'\beta}$ = 6.4 Hz, H-1′), 7.3–8.1 (10H, m, Ph), 8.15 (1H, s, H-2), 8.28 (1H, s, H-8). *Anal.* Found: C, 63.94; H, 5.11; N, 14.32. Calcd. for $C_{26}H_{25}N_5O_5$: C, 64.05; H, 5.17; N, 14.37%.

*6-Dimethylamino-9-(2′-deoxy-β-*D*-xylofuranosyl)purine* (**7**). Through a stirred solution of **6** (2.63 g, 5.93 mmol) in methanol (30 ml) was passed ammonia gas to saturation at room temperature. The mixture was next stirred at room

temperature for 24 hr and warmed to *ca.* 50°C, before being evaporated to dryness. The residue was recrystallized from ethanol to give pure **7** (1.11 g, 73%) as a white needle, mp 210–211°C. $[\alpha]_D^{22}$ −22.7° (c=0.52, H_2O). UV λ_{max} (EtOH) 275 nm ($\varepsilon=2.17\times10^4$). IR ν_{max} (KBr) cm^{-1}: 3350, 3200, 1610. ^{1}H-NMR (DMSO-d_6, 100 MHz) δ: 2.25 (1H, dd, $J_{1',2'\beta}$=2.2 Hz, $J_{2'\beta,2'\alpha}$=13.2 Hz, H-2'β), 2.79 (1H, ddd, $J_{1',2'\alpha}$=8.5 Hz, $J_{2'\alpha,3'}$=5.2 Hz, H-2'α), 3.45 (6H, br.s, 6-NMe_2), 3.69 (2H, m, H-5', 5''), 3.86 (1H, m, H-4'), 4.33 (1H, m, H-3'), 4.70 (1H, t, $J_{5',OH}$=5.5 Hz, 5'-OH, disappeared by D_2O exchange), 5.91 (1H, d, $J_{3',OH}$=5.6 Hz, 3'-OH, disappeared by D_2O exchange), 6.29 (1H, dd, H-1'), 8.22 (1H, s, H-2), 8.36 (1H, s, H-8). *Anal.* Found: C, 51.39; H, 5.99; N, 25.08. Calcd. for $C_{12}H_{17}N_5O_3$: C, 51.60; H, 6.14; N, 25.08%.

6-Dimethylamino-9-(2'-deoxy-5'-O-pivaloyl-β-D-xylofuranosyl)purine (**8**). To a stirred solution of **7** (1.50 g, 5.37 mmol) in 1,4-dioxane–pyridine (1:1, 108 ml) was added dropwise a solution of pivaloyl chloride (0.73 ml, 5.91 mmol) in 1,4-dioxane (54 ml) at 0°C over a period of 45 min under an N_2 atmosphere. The mixture was then stirred at 5°C for 2 days. Ice chips were next added, before the mixture was stirred for 15 min and evaporated. The residue was diluted with $CHCl_3$ (50 ml), washed with a sat. $NaHCO_3$ soln., dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel (CH_2Cl_2–ethyl acetate=1:1) to give **8** (1.36 g, 69%) as white crystals, mp 140–141°C (from EtOAc-*n*-hexane). $[\alpha]_D^{22}$ −14.2° (c=0.48, $CHCl_3$). UV λ_{max} (EtOH) 275 nm ($\varepsilon=2.44\times10^4$). IR ν_{max} (film) cm^{-1}: 3200, 1730, 1600. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.20 (9H, s, pivalyl), 2.59 (1H, dd, $J_{1',2'\beta}$=3.4 Hz, $J_{2'\beta,2'\alpha}$=15.1 Hz, H-2'β), 2.90 (1H, ddd, $J_{2'\alpha,3'}$=6.1 Hz, $J_{1',2'\alpha}$=9.0 Hz, H-2'α), 3.53 (6H, br.s, 6-NMe_2), 4.07 (1H, m, H-4'), 4.22 (1H, dd, $J_{4',5'}$=4.9 Hz, $J_{5',5''}$=11.7 Hz, H-5'), 4.40 (1H, m, H-3'), 4.64 (1H, dd, $J_{4',5''}$=4.2 Hz, H-5''), 6.04 (1H, dd, H-1'), 7.80 (1H, s, H-2), 8.10 (1H, br.m, 3'-OH, disappeared by D_2O exchange), 8.28 (1H, s, H-8). *Anal.* Found: C, 56.17; H, 6.91; N, 19.23. Calcd. for $C_{17}H_{25}N_5O_4$: C, 56.18; H, 6.93; N, 19.27%.

6-Dimethylamino-9-(2',3'-dideoxy-3'-azido-5'-O-pivaloyl-β-D-ribofuranosyl)purine (**9**). To a stirred solution of **8** (0.99 g, 2.72 mmol) and pyridine (2 ml, 24.48 mmol) in CH_2Cl_2 (30 ml) was slowly added mesyl chloride (0.63 ml, 8.16 mmol) with ice-cooling. The mixture was stirred at room temperature overnight. The reaction mixture was poured into a cold sat. $NaHCO_3$ soln., extracted with CH_2Cl_2 and dried over $MgSO_4$. The residue was passed through a short column of silica gel with CH_2Cl_2–MeOH (10:1) to give 1.21 g (quant.) of crude 6-dimethylamino-9-(2'-deoxy-3'-*O*-mesyl-5'-*O*-pivalyl-β-D-xylofuranosyl)-purine. IR ν_{max} (film) cm^{-1}: 1730, 1600, 1340, 1180. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.20 (9H, s, pivalyl), 2.95 (2H, m, H-2', 2''), 3.00 (3H, s, mesyl), 3.53 (6H, br.s, 6-NMe_2), 4.43 (3H, m, H-4', H-5' and H-5''), 5.44 (1H, m, H-3'), 6.51 (1H, dd, $J_{1',2'\alpha}$=5.4 Hz, $J_{1',2'\beta}$=5.4 Hz, H-1'), 8.06 (1H, s, H-2), 8.33 (1H, s, H-8).

To the vacuum-dried crude methanesulfonate were added DMF (25 ml) and NaN_3 (1.77 g, 27.2 mmol). The suspension was stirred for 5 hr at 120°C under an N_2 atmosphere. The mixture was filtered, and the residue washed with $CHCl_3$, and then the filtrate was evaporated to dryness. The residue was dissolved in $CHCl_3$, washed with sat. $NaHCO_3$, dried over $MgSO_4$, and evaporated. The residue was finally chromatographed on silica gel (CH_2Cl_2–MeOH=60:1) to give **9** (0.89 g, 84%) as a syrup, $[\alpha]_D^{22}$ −6.9° (c=0.51, $CHCl_3$). UV λ_{max} (EtOH) 273 nm ($\varepsilon=2.39\times10^4$). IR ν_{max} (film) cm^{-1}: 2100, 1730, 1600. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 1.21 (9H, s, pivalyl), 2.57 (1H, ddd, $J_{1',2'\beta}$=6.6 Hz, $J_{2'\beta,3'}$=6.1 Hz, $J_{2'\alpha,2'\beta}$=13.7 Hz, H-2'β), 2.9–3.1 (1H, m, H-2'α), 3.52 (6H, br.s, 6-NMe_2), 4.1–4.8 (4H, m, H-3', H-4' and H-5''), 6.28 (1H, dd, $J_{1',2'\beta}$=6.2 Hz, H-1'), 7.83 (1H, s, H-2), 8.32 (1H, s, H-8). *Anal.* Found: C, 51.96; H, 5.98; N, 28.44. Calcd. for $C_{17}H_{24}N_8O_3\cdot0.4H_2O$: C, 51.66; H, 6.22; N, 28.36%.

6-Dimethylamino-9-(3'-azido-2',3'-dideoxy-β-D-ribofuranosyl)purine (**10**). A mixture of **9** (620.7 mg, 1.57 mmol) and NaOMe (Na, 361 mg, 15.7 mmol) in MeOH (40 ml) was stirred at room temperature for 20 hr. The solution was neutralized with CO_2 gas, and evaporated under reduced pressure. The residual solid was passed through a short silica gel column (CH_2Cl_2–MeOH=15:1) in order to remove the inorganic salt. The residue was puriffed by PTLC (CH_2Cl_2–MeOH=20:1) to give **10** (493.2 mg, 99%) as a white solid, mp 80.5–81°C (from $CHCl_3$-*n*-hexane). $[\alpha]_D^{22}$ +11.8° (c=0.39, $CHCl_3$). UV λ_{max} (EtOH) 274 nm ($\varepsilon=2.58\times10^4$). IR ν_{max} (film) cm^{-1}: 3200, 2100, 1600. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ: 2.33 (1H, dd, $J_{1',2'\beta}$= 5.4 Hz, $J_{2'\alpha,2'\beta}$=13.7 Hz, H-2'β), 3.21 (1H, ddd, $J_{2'\alpha,3'}$= 6.1 Hz, $J_{2'\alpha,1'}$=9.3 Hz, by D_2O exchange, H-2'α), 3.52 (6H, br.s, 6-NMe_2), 3.72 (1H, dd, $J_{4',5'}$=2.0 Hz, $J_{5',5''}$=13.9 Hz, H-5', by D_2O exchange), 4.01 (1H, dd, $J_{4',5''}$=1.5 Hz, H-5'', by D_2O exchange), 4.23 (1H, m, H-4'), 4.60 (1H, m, $J_{3',4'}$=6.8 Hz, H-3'), 6.18 (1H, dd, H-1'), 7.06 (1H, m, 5'-OH, disappeared by D_2O exchange), 7.74 (1H, s, H-2), 8.25 (1H, s, H-8). *Anal.* Found: C, 47.10; H, 5.37; N, 36.40. Calcd. for $C_{12}H_{16}N_8O_2$: C, 47.36; H, 5.30; N, 36.82%.

6-Dimethylamino-9-[3'-(benzyloxycarbonyl-p-methoxyphenyl-L-alanylamino)-2',3'-dideoxy-β-D-ribofuranosyl']-purine (**11**). To a stirred solution of **10** (51.5 mg, 166 mol) in toluene (4 ml) was added trihenylphosphine (47.1 mg, 180 μmol) at room temperature for 2 hr. After the N_2 gas evolution had ceased, to the reaction mixture was added *N*-benzyloxycarbonyl-*p*-methoxy-L-phenylalanine (68.8 mg, 209 mol), and then the mixture was stirred at reflux for 20 hr. The solvent was removed under reduced pressure, and the residue was purified with PTLC (CH_2Cl_2–MeOH =10:1) to afford **11** (19.7 mg, 31%), mp 197–201.5°C (from $CHCl_3$/*n*-hexane). $[\alpha]_D^{22}$ −16.4° (c=0.22, $CHCl_3$). UV λ_{max} (EtOH) 275 nm ($\varepsilon=2.87\times10^4$). IR ν_{max} (film)

cm^{-1}: 1710, 1660, 1600. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.10 (1H, symmetrical m, H-2′β), 2.92 (1H, dd, $J_{\alpha,\beta}=8.4$ Hz, $J_{\beta,\beta'}=13.6$ Hz, H-β), 3.05 (1H, ddd, $J_{1',2'\alpha}=8.2$ Hz, $J_{2'\alpha,3'}=7.8$ Hz, H-2′α), 3.15 (1H, dd, $J_{\alpha,\beta'}=6.2$ Hz, H-β'), 3.53 (6H, br.s, 6-NMe_2), 3.70 (1H, m, $J_{4',5'}=1.9$ Hz, $J_{5',5''}=13.3$ Hz, H-5′), 3.78 (3H, s, OMe), 3.91 (2H, m, H-4′ and H-5″), 4.33 (1H, dd, H-α), 4.54 (1H, ddd, $J_{2'\beta,3'}=2.3$ Hz, $J_{2'\alpha,3'}=7.8$ Hz, $J_{3',4'}=6.2$ Hz, H-3′), 5.10 (2H, s, $PhCH_2$), 5.45 (1H, m, α-NH), 5.94 (1H, dd, $J_{1',2'\beta}=6.2$ Hz, H-1′, by D_2O exchange), 6.15 (1H, m, 3′-NH, by D_2O exchange), 6.87 (2H, d, $J=8.6$ Hz, anisyl), 7.14 (2H, d, $J=8.6$ Hz, anisyl), 7.33 (5H, s, Ph), 7.33 (1H, m, 5′-OH, by D_2O exchange), 7.74 (1H, s, H-2), 8.24 (1H, s, H-8). HR-FAB-MS *m/z*: 590.2763 (MH^+, 590.2725 calcd. for $C_{30}H_{36}N_7O_6$).

*6-Dimethylamino-9-[3′-(p-methoxyphenyl-*L*-alanyl-amino)-2′,3′-dideoxy-β-*D*-ribofuranosyl]purine* (*2′-deoxypuromycin*) (**2**). A suspension of **11** (50.3 mg, 85 μmol) and 10% Pd on charcoal in 1,4-dioxane–ethanol (1 : 1, 5 ml) was stirred under hydrogen at ordinary pressure and room temperature for 18 hr. After filtration through Celite, the filtrate was evaporated. The residue was purified with PTLC (CH_2Cl_2–MeOH = 8 : 1) to give **2** (24.7 mg, 63%) as a solid, mp 153.5–155°C (from 99% EtOH). $[\alpha]_D^{22}$ −25.5 ($c=0.20$, 1,4-dioxane). UV λ_{max} (EtOH) 275 nm ($\varepsilon=3.28\times10^4$). IR ν_{max} (film) cm^{-1}: 3300, 1670, 1600. ^{1}H-NMR ($CDCl_3$, 270 Hz) δ: 2.05 (2H, br.s, α-NH_2), 2.29 (1H, ddd, $J_{1',2'\beta}=6.1$ Hz, $J_{2'\beta,3'}=2.9$ Hz, $J_{2'\alpha,2'\beta}=13.4$ Hz, H-2′β), 2.81 (1H, dd, $J_{\alpha,\beta}=8.1$ Hz, $J_{\beta,\beta'}=13.9$ Hz, H-β), 3.01–3.14 (2H, m, H-2′α and H-β'), 3.53 (6H, br.s, 6-NMe_2), 3.61 (1H, dd, $J_{\alpha,\beta}=4.4$ Hz, $J_{\alpha,\beta'}=8.1$ Hz, H-α), 3.78 (1H, dd, $J_{4',5'}=2.2$ Hz, H-5′, hidden under the signal of OMe), 3.79 (3H, s, OMe), 3.96 (1H, dd, $J_{4',5'}=1.7$ Hz, $J_{5',5''}=12.7$ Hz, H-5″), 4.11 (1H, m, H-4′), 4.65 (1H, ddd, $J_{2'\alpha,3'}=7.6$ Hz, $J_{3',4'}=2.9$ Hz, H-3′), 6.17 (1H, dd, $J_{1',2'\alpha}=7.9$ Hz, H-1′), 6.85 (2H, d, $J=8.6$ Hz, anisyl), 7.13 (2H, d, $J=8.6$ Hz, anisyl), 7.69 (1H, m, 3′-NH), 7.85 (1H, s, H-2), 8.27 (1H, s, H-8), 8.27 (1H, m, 5′-OH, disappeared by D_2O exchange). HR-FAB-MS *m/z*: 456.2358 (MH^+, 456.2357 calcd. for $C_{22}H_{30}N_7O_4$).

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