The Synthesis of Purine Nucleosides of L-Mycarose and L-Cladinose[1]

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Purine nucleosides of L-mycarose and L-cladinose, neutral branched-chain sugars of macrolide antibiotics, synthesized by a fusion method with the aid of dichloroacetic acid. The structure of these synthesized nucleosides was determined on the basis of the results of elemental analyses and the ultraviolet absorption and proton magnetic resonance spectra, as well as on the basis of the optical rotatory dispersion.

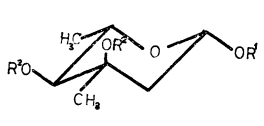
Since the first synthesis of cytotoxic nucleosides of branched-chain sugars by Walton *et al.*,[2] a number of synthetic studies of nucleosides of this class of sugars have been reported; some nucleosides exhibit considerable biological activity.[3] In the course of chemical studies of the macrolide antibiotics, the synthesis of purine nucleosides of the branched-chain sugar was carried out by the use of L-mycarose[4] and L-cladinose;[5] this was of chemical and biological interest. Recently, Howarth *et al.*[6] synthesized a purine nucleoside of arcanose.

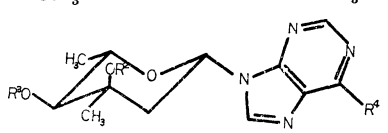
As the base components, purine[7] and 6-chloropurine were used. The condensation of the above-mentioned dideoxy branched-chain sugars with these bases was performed by a fusion method,[8] using dichloroacetic acid[9] as the catalyst.

4-*O*-Isovaleryl-L-mycarose, obtained by an acid hydrolysis of leucomycin A_3,[10] was converted into 1-*O*-acetyl, 1-*O*-isovaleryl, and 1-*O*-*p*-nitrobenzoyl derivatives (I, II and III). In the case of the preparation of II, 1-*O*-isovaleryl derivatives of 4-*O*-*n*-butyryl and 4-*O*-acetyl-L-mycarose (II′ and II″), arising from the minor components[11] of the leucomycin complex were also isolated from the reaction mixture.

The fusion procedure was carried out by quickly heating a mixture of the appropriate 1-*O*-acyl derivative of L-mycarose, the base, and dichloroacetic acid at a moderately elevated temperature (95±3°C). 1,4-Di-*O*-Acetyl-L-cladinose was coupled with these bases in an essentially similar fashion. The amount of dichloroacetic acid used was relatively high in comparison with that of the ordinary fusion method.[8] Excess dichloroacetic acid seems to act excellently as a solvent to form a homogeneous melt or to aiding in the smooth mixing of the reaction mixture, even if it is somewhat heterogeneous. In the course of the reaction, the mixture was fused after heating for 1—2 min. A thin-layer chromatogram showed essentially a single spot with the exception of the remaining base, which was detectable under ultraviolet light. The yields of nucleosides were not substantially affected by changing the leaving group. In the coupling of the 1-*O*-nitrobenzoyl derivative of L-mycarose (III) and purine, the yield was slightly improved. In this fusion, *p*-nitrobenzoic acid was quickly deposited from the reaction mixture, thus making evacuation unnecessary, and the duration of the reaction was so diminished that an undesirable decomposition of labile branched chain sugar could

Compds.	R^1	R^2	R^3	R^4
I	Ac	H	Iv	—
II	Iv	H	Iv	—
II′	Iv	H	Bu	—
II″	Iv	H	Ac	—
III	PNB	H	Iv	—
IV	—	H	Iv	H
V	—	H	H	H
VI	—	H	Iv	Cl
VII	—	H	Bu	Cl
VIII	—	H	H	OCH_3
IX	—	CH_3	Ac	H
X	—	CH_3	H	H
XI	—	CH_3	Ac	Cl
XII	—	CH_3	H	OCH_3





Ac= $-COCH_3$
Bu= $-COCH_2CH_2CH_3$
Iv= $-COCH_2CH(CH_3)_2$
PNB= $-COC_6H_4NO_2(p)$

Chart A

1) Presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971; Preprint, Vol. III (1971), p. 1838.

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5) P. F. Wiley, K. Gerzon, E. H. Flynn, M. V. Sigal, A. Weaver, V. C. Quark, R. R. Chautvett, and R. J. Monahan, *J. Amer. Chem. Soc.*, **79**, 6062 (1957).

6) G. B. Howarth, W. A. Szarek, and J. K. N. Jones, *J. Org. Chem.*, **34**, 476 (1969).

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8) W. Pigman, D. Horton, and A. Harp, "The Carbohydrates; Chemistry and Biochemistry," 2nd. ed., Academic Press, New York & London (1970), p. 9.

9) M. J. Robins and R. K. Robins, *J. Amer. Chem. Soc.*, **87**, 4934 (1965); F. Perini, F. A. Carey, and L. Long, Jr., *Carbohydrate Res.*, **11**, 159 (1969).

10) S. Omura, M. Katagiri, H. Ogura, and T. Hata, *Chem. Pharm. Bull.*, **16**, 1181 (1968).

11) S. Omura, M. Katagiri, and T. Hata, *J. Antibiotics*, **20**, 234 (1967); *ibid.*, **21**, 272 (1968).

be depressed.

In these fusion reactions, only the β-nucleosides were obtained as fine crystals and no significant formation of their α-anomer was observed. The anomeric configuration of synthetic nucleosides was confirmed by the measurements of their proton magnetic resonance spectra. All the synthesized nucleosides showed a quartet peak of the H-1′ proton, typical of axial anomeric the protons of 2-deoxy sugar, and a doublet of H-4′ with a large splitting constant, indicating the $\mathbf{C}_4^1$ conformation for the sugar moiety. It should be noted that 4′-*O*-isovaleryl derivatives of β-L-mycarosyl nucleoside (IV and VI) show a rather abnormal H-1′ quartet signal, indicating a slight deformation of their pyranosyl ring system. The removal of their isolvaleryl group made them again show the normal quartet pattern.

Table 1. PMR Spectral data (60 MHz)

Compds.	Solv.	(ppm) H-1 (H-1′)	(ppm) H-4 (H-4′)	*J* (Hz) $1,2_e$	*J* (Hz) $1,2_a$	*J* (Hz) 4,5
I	C^d	5.99	4.63	3.1	9.4	9.4
II	C^d	5.82	4.48	3.1	9.4	9.4
II′	C^d	5.83	4.48	2.9	9.1	9.4
II″	C^d	6.00	4.61	3.4	9.8	9.3
III	C^d	6.34	4.75	2.9	9.3	9.5
IV	C^d	6.36	4.88	5.7	8.1	9.8
V	W^d	6.17	3.27	2.7	11.2	9.4
VI	C^d	6.24	4.83	5.7	8.0	9.4
VII	C^d	6.26	4.83	6.9	8.2	9.3
VIII	W^d	6.13	3.33	3.2	10.8	9.6
IX	C^d	6.28	4.95	2.8	10.9	9.9
X	W^d	5.97	3.26	3.1	10.0	9.9
XI	C^d	6.24	4.92	3.1	11.0	10.0
XII	C^d	5.98	3.22	2.9	10.8	9.4

C^d=$CDCl_3$ (TMS, internal)
W^d=D_2O (TMS, external)

The assignment of the β-L-configuration described above was also supported by the optical rotatory dispersion data. All the dispersion patterns of synthetic nucleosides showed features opposite of those of a group of β-D-purine nucleosides.[12,13] In each case, a positive Cotton effect was observed.

The position of the *N*-glycosyl bond was assigned by measuring the ultraviolet absorption spectra.[13] The nucleosides of purine showed spectra similar to those of nebularine.[14] The spectra of the nucleosides of 6-chloropurine also indicated the *N*-9 substitution.[15]

The attempt to de-*O*-acylate the nucleosides of 6-chloropurine (VI and XI) without affecting the chloro group was unsuccessful. Treating them with dilute barium methoxide in methanol afforded corresponding 6-methoxyl derivatives (VIII and XII).

Experimental

Generally, the crude products obtained were purified by column chromatography on silica gel (20 weights of raw product), followed by the examination of each fraction by thin-layer chromatography. The organic layer was dried over sodium sulfate. After the removal of the salt, the solutions were concentrated below 40°C under reduced pressure, unless otherwise stated. Thin-layer chromatography was performed using Silica Gel G (Merck) as the adsorbent. The proton magnetic resonance spectra were measured with a Hitachi H-6013 and, in part, Varian, S-60A apparatuses. The optical rotatory dispersion was measured with a Nihon Bunko spectropolarimeter, Model ORD/UV-5, at 24—25°C.

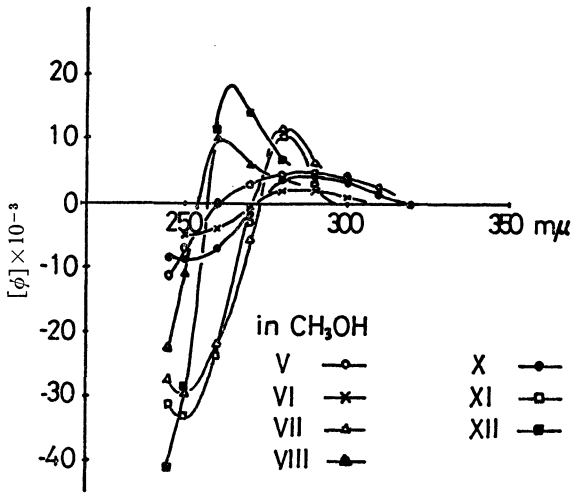

Chart B ORD Curves of Branched-chain Nucleosides

1-O-Acetyl-2,6-dideoxy-4-O-isovaleryl-3-C-methyl-β-L-ribo-hexopyranose (I). Acetic anhydride (3.0 m*l*) was added to a solution of crude 4-*O*-isovalery-L-mycarose[10] (carimbose) (0.32 g) in pyridine (1 m*l*). The solution was kept standing for 3 hr. Methanol (4 m*l*) was then added into the solution and the resulting mixture was kept standing at room temperature for 3 hr. It was concentrated below 55°C to afford a brown syrup (0.54 g), which was then subjected to column chromatography (benzene : 2-butanone=10 : 1). Five-gram fractions were collected. A combination of Fractions #4 and #5 afforded a syrup (0.27 g; 72%) which was then distilled to give an analytically pure acetate; mp 72—74°C, bp 133—135°C/0.01 mmHg, $[\alpha]_D^{25}$ −15° (*c* 1.1, chloroform). ν_{max}^{KBr} (cm^{-1}): 1761 (*O*-acetyl), 1738 (*O*-isovaleryl).

Found: C, 58.10; H, 8.56%. Calcd for $C_{14}H_{24}O_6$ (288.34): C, 58.32; H, 8.39%.

2,6-Dideoxy-1,4-di-O-isovaleryl-3-C-methyl-β-L-ribo-hexopyranose (II). Isovaleryl anhydride (3.3 m*l*) was added to a solution of crude 4-*O*-isovaleryl-L-mycarose[10] (4.0 g) in pyridine (40 m*l*), and the resulting mixture was left standing at room temperature for 18 hr. Additional anhydride (2 m*l*) was then added to the reaction mixture. After

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15) R. K. Robins, E. F. Godefroi, E. C. Taylor, L. R. Lewis, and A. Jackson, *J. Amer. Chem. Soc.*, **83**, 2574 (1961).

standing for a further 25 hr, methanol (20 ml) was stirred into the mixture under cooling. The solution was allowed to stand overnight and was then concentrated *in vacuo* at 65°C (oil pump), followed by repeated co-evaporation with toluene to give a brown residue with a disagreeable odor. This was fractionated on a silica-gel column (150 g; benzene : 2-butanone=20 : 1; 100 ml fractions). The third and fourth fractions afforded Compound II (2.8 g; 52%). A pure product was obtained by a high-vacuum distillation (79% recovery); bp 155—158°C/0.002 mmHg, n_D^{20} 1.4552, $[\alpha]_D^{23}$ −20° (*c* 4.1, chloroform). ν_{max}^{film} (cm^{-1}): 1735 (*O*-isovaleryl).

Found: C, 61.33; H, 9.02%. Calcd for $C_{17}H_{30}O_6$ (330.43): C, 61.80; H, 9.15%.

The fifth fraction gave crude 4-*O*-*n*-butyryl-2,6-dideoxy-1-*O*-isovaleryl-3-*C*-methyl-β-L-*ribo*-hexopyranose (II′) (1.0 g; 20%), which was purified by high-vacuum distillation; bp 140—145°C/0.06 mmHg, n_D^{20} 1.4543 $[\alpha]_D^{23}$ −29° (*c* 3.9, chloroform). ν_{max}^{film} (cm^{-1}): 1738 (ester).

Found: C, 60.49; H, 8.83%. Calcd for $C_{16}H_{28}O_6$ (316.40): C, 60.74; H, 8.92%.

The seventh fraction gave 0.20 g (4.3%) of 4-*O*-acetyl-2,6-dideoxy-1-*O*-isovaleryl-3-*C*-methyl-β-L-*ribo*-hexopyranose (II″); bp 125—130°C/0.002 mmHg. The proton magnetic resonance spectrum of this compound (in $CDCl_3$ with TMS) had a singlet peak at δ 2.05 attributable to acetoxymethyl.

2,6-Dideoxy-4-O-isovaleryl-C-methyl-4-O-p-nitrobenzoyl-β-L-ribo-hexopyranose (III). *p*-Nitrobenzoyl chloride (1.28 g) was added stirred into a solution of 4-*O*-isovaleryl-L-mycarose[10] (1.53 g) in pyridine (10 ml), and the resulting mixture was stirred at room temperature for 16 hr. The mixture was moistured with water (0.5 ml), agitated for a while, diluted with a mixture of dioxane (50 ml) and water (5 ml), and then concentrated at 45°C *in vacuo* to give a cake. This was dissolved in benzene (100 ml), and the solution was washed successively with aqueous sodium bicarbonate (1.3%) and water, dried, and evaporated to dryness to afford a syrup (2.42 g), which was then crystallized with isopropanol; yield, 0.58 g (24%); mp 110—112°C. The mother liquor gave a further crop. Recrystallization from isopropanol gave analytical sample. Mp 112.5—114.5°C, $[\alpha]_D^{25}$ −19° (*c* 0.64, chloroform). $\lambda_{max}^{methanol}$ 259 mμ (ε, 13.1×10^3). ν_{max}^{KBr} (cm^{-1}): 1737 (ester), 1607, 1526, 1350, 725 (*p*-nitrophenyl).

Found: C, 57.56; H, 6.38; N, 3.56%. Calcd for $C_{24}H_{25}NO_8$: (395.42); C, 57.71; H, 6.37; N, 3.54%.

9-(2,6-Dideoxy-3-C-methyl-β-L-ribo-hexopyranosyl)-purine (V). *A. From the 1-O-Acetyl Derivative*: A mixture of I (0.27 g), purine (0.11 g), and dichloroacetic acid (0.14 ml) were heated at 99°C for 3 min while being stirred well. A water aspirator vacuum (25 mmHg) was then applied, and the melt was stirred for more 10 min at the same temperature. The resulting greenish melt was quickly cooled with cold water and dissolved in ethyl acetate (20 ml). The solution was washed successively with aqueous sodium bicarbonate (1.3%) and water, dried, and evaporated to dryness to furnish a brown glass (0.27 g), which was then fractionated on a silica-gel column (benzene : acetone= 2 : 1; 5 g fractions). The product (0.14 g, 38%) obtained from Fractions #6 to #9 was dissolved in cold methanol (40 ml), and then chilled methanolic barium methoxide (1N; 5.3 ml) was showly added into the solution. After standing for 48 hr, the solution was carefully bubbled with carbon dioxide, quickly concentrated below 20°C, and purified by means of a silica-gel column (4 g, benzene : acetone= 1 : 1) to give homogeneous glass, 0.090 g (36% from I). Crystallization with diethyl ether (mp 197—199°C (colored)) and subsequent recrystallization from 2-butanone afforded colorless prisms; mp 215—216°C, $[\alpha]_D^{24}$ −25° (*c* 3.3, water). λ_{max}^{water} 265.5 mμ (ε, 6.9×10^3), $\lambda_{max}^{ethanol}$ 262.5 mμ (ε, 7.2×10^3). ν_{max}^{KBr} (cm^{-1}): 1595, 1584, 1497 (purinyl).

Found: C, 54.10; H, 6.12; N, 20.87%. Calcd for $C_{12}H_{16}N_4O_3$ (264.29): C, 54.53; H, 6.10; N, 21.20%.

B. From the 1-O-nitrobenzoyl Derivative: A mixture of III (0.20 g), purine (0.062 g), and dichloroacetic acid (0.07 ml) was heated in a test tube on a boiling-water bath for 3 min while being efficiently mixed by means of a glass rod. Then, the dark-colored mixture was quickly cooled by cold water and taken up with ethyl acetate (20 ml). The solution was treated as has been described above to give 0.17 g of a crude condensation mixture, which was then subjected to silica-gel column chromatography (5 g, benzene : acetone=2 : 1; 5 g each). The Fractions #3—#5 afforded a homogeneous syrup (0.07 g), which was then de-*O*-isovalerated with methanolic barium methoxide and subsequently treated in the above-described manner to give pure glass (0.049 g; 37% from III). Crystallization and recrystallization were carried out as above. The mixed melting point of this compound with the product from I was not depressed. The IR of the two were superimposable.

Found: C, 54.30; H, 6.16; N, 20.91% Calcd for $C_{12}H_{16}N_4O_3$ (264.29): C, 54.53; H, 6.10; N, 21.20%

6-Chloro-O-(4′-O-isovaleryl-2′,6′-dideoxy-3′-C-methyl-β-L-ribo-hexopyronosyl)-purine(VI). *A. From the 1-O-Acetyl Derivative*: A mixture of I (0.23 g), 6-chloropurine (0.20 g), and dichloroacetic acid (0.12 ml) was heated for 4 min at 95°C while being stirred well; the resulting melt was then stirred for a further 5 min under reduced pressure (25 mmHg, water aspirator) at the same temperature. The reaction was quenced by cooling, and the dark-colored mixture was diluted with 20 ml of ethyl acetate. After the recovery of the unreacted 6-chloro-purine (0.06 g) by filtration, the solution was treated as has been described above and then concentrated to furnish a heavy syrup (0.35 g), which was subsequently fractionated by means of a silica-gel column (benzene: 2-butanone=3 : 1; 5 g each). From Fractions #4 and #5, the product was obtained in a glassy state; yield, 0.11 g (36%). Crystallization and recrystallization were carried out with diisopropyl ether; colorless granular crystals; mp 130—131°C, $[\alpha]_D^{20}$ −28° (*c* 1.0, chloroform). $\lambda_{max}^{ethanol}$ 264 mμ (ε, 9.1×10^3). ν_{max}^{KBr} (cm^{-1}): 1737 (*O*-isovaleryl); 1599, 1567, 1499 (purinyl).

Found: C, 53.13; H, 5.89; N, 14.89%. Calcd for $C_{17}H_{23}O_4N_4Cl$ (382.85): C, 53.33; H, 6.05; N, 14.63%.

B. From the 1-O-Isovaleryl Derivative: 6-Chloropurine (0.15 g) and dichloroacetic acid (0.10 ml) were heated at 95°C for 2 min while being efficiently stirred, and then the reaction system was connected to a water aspirator while stirring and heating were continued for 2 min at the same temperature. From the resulting mixture, Compound VI was obtained after the above-mentioned treatment; yield, 0.10 g (27%). A mixed melting-point determination with the Compound VI obtained from I was not depressed. The IR of the two samples were superimposable.

Found: C, 52.95; H, 6.01; N, 14.77%. Calcd for $C_{17}H_{23}N_4O_4Cl$ (382.85): C, 53.33; H, 6.05; N, 14.63%.

C. From the 1-O-p-nitrobenzoyl Derivative: A finely-divided IV (0.20 g) and 6-chloropurine (0.08 g) were mixed well with dichloroacetic acid (0.05 ml) in a test tube with the aid of a glass rod and then heated on a boiling-water bath for 2 min while being efficiently mixed. After the reaction had been quenched, the mixture was subjected to the same treatment as above. The titled compound, 0.06 g (31%), was thus obtained; its melting point was not depressed by ad-

mixture with that from I. The IR of the two were superimposable.

Found: C, 53.14; H, 6.08; N, 15.05%. Calcd for $C_{17}H_{23}N_4O_4Cl$ (382.85): C, 53.33; H, 6.05; N, 14.63%.

6-Chloro-O-(4'-O-n-butyryl-2',6'-dideoxy-3'-C-methyl-β-L-ribo-hexopyranosyl)-purine (VII). A mixture of III (0.295 g), pulverized 6-chloropurine (0.15 g), and dichloroacetic acid (0.10 ml) was heated at 95°C at atmospheric pressure for 3 min and then *in vacuo* (23 mmHg). The recovering of the unreacted 6-chloropurine and the extraction of the acidic substances were carried out as has been described in the case of VI. The crude product thus obtained was fractionated on a column of silica-gel (benzene : 2-butanone=10 : 1—3 : 1; gradient elution), having been cut into five-gram portions. The main oily product (0.094 g, 27%) thus obtained was crystallized by trituration with diisopropyl ether. Two recrystallizations from the same solvent gave a pure sample as colorless prisms; mp 144—145°C; $[\alpha]_D^{23}$ −10° (*c* 0.72, chloroform): $\lambda_{max}^{ethanol}$ 264 mμ (ε, 10.1×10^3). ν_{max}^{KBr} (cm^{-1}): 1740 (*O-n*-butyryl); 1598, 1561, 1497 (purynyl).

Found: C, 52.21; H, 5.91; N, 15.01%. Calcd for $C_{16}H_{21}N_4O_4Cl$ (368.83): C, 52.12; H, 5.74; N, 15.19%.

6-Methoxy-9-(2',6'-dideoxy-3'-C-methyl-β-L-ribo-hexopyranosyl)-purine (VIII). VI (84 mg) was dissolved in 0.1 N methanolic barium methoxide (10 ml), and the resulting mixture was kept standing at room temperature for 4 days. After the careful bubbling in of carbon dioxide, the reaction mixture was quickly concentrated below 20°C under reduced pressure to give a residue which was then passed through a silica-gel column (2 g). By elution with a mixture of benzene and acetone (1 : 1), a product was obtained as a homogeneous glass (42 mg, 65%); it was twice crystallized from a mixed solvent of benzene, acetone, and diisopropyl ether (2 : 1 : 2) to give colorless needles; mp 211—213°C, $[\alpha]_D^{23}$ −18° (*c* 1.0, methanol). $\lambda_{max}^{methanol}$ 249 mμ (ε, 11.5×10^3). ν_{max}^{KBr} (cm^{-1}): 1604, 1581 (purinyl).

Found: C, 53.05; H, 6.16; N, 19.04%. Calcd for $C_{13}H_{18}N_4O_4$ (294.31): C, 52.89; H, 6.22; N, 18.94%.

9-(2',6'-Dideoxy-3'-C-methyl-3'-O-methyl-β-L-ribo-hexopyranosyl)-purine (X). 1,4-Di-*O*-acetyl-β-L-cladinose[16] (0.26 g) was fused and, after quick cooling to room temperature, was well mixed with purine (0.12 g) with the aid of dichloroacetic acid (0.18 ml). The mixture was heated with stirring at 98°C for 5 min under atmospheric pressure and then for a further 5 min under reduced pressure (water aspirator). After the quenching of the reaction by cooling with cold water, the greenish-colored mixture was diluted with 30 ml of ethyl acetate. The solution was washed and concentrated as in the case of the preparation of VI to afford an oily product (0.297 g), which was fractionated by a silica-gel column (5 g). The column was eluted with a mixed solvent of benzene and acetone (2 : 1). Five-gram fractions were collected. Fractions #3—#6 gave a main product (0.17 g) whose proton magnetic resonance spectrum did not show the presence of the α-anomer. This product was dissolved in methanol (30 ml) and treated with 4 ml of methanolic 1 N barium methoxide, as has been described in the preparation of V, followed by a similar working-up; it was then passed through a silica-gel column (4 g; benzene : acetone=3 : 2) to afford a glass (0.099 g, 35%). Two crystallizations and recrystallization from diisopropyl ether afforded colorless prisms; mp 155—156°C, $[\alpha]_D^{27}$ −10° (*c* 2.5, water). λ_{max}^{water} 262.5 mμ (ε, 7.2×10^3), $\lambda_{max}^{ethanol}$ 262.5 mμ (ε, 7.1×10^3). ν_{max}^{KBr} (cm^{-1}): 1596, 1581, 1499 (purinyl).

Found: C, 55.90; H, 6.48; N, 19.89%. Calcd for $C_{13}H_{18}N_4O_3$ (278.31): C, 56.10; H, 6.52; N, 20.13%.

6-Chloro-9-(2',6'-dideoxy-3'-C-methyl-3'-O-methyl-4'-O-acetyl-β-L-ribo-hexopyranosyl)-purine (XI). A mixture of 1,4-di-*O*-acetyl-β-L-cladinose[16] (0.26 g), pulverized 6-chloropurine (0.20 g), and dichloroacetic acid (0.13 ml) was heated for 4 min at 92—95°C with stirring in an open system and then *in vacuo* (25 mmHg) for 5 min to give a colored mixture; this mixture gave 0.36 g of an oily product after cooling, extraction, and concentration. This was subjected to silica-gel column chromatography (10 g, benzene : 2-butanone=5 : 1; 5 g each). Fraction #3 and #4 gave 0.10 g (28%) of a glass; this glass was subsequently crystallized with diisopropyl ether; mp 126—127°C. Two recrystallizations from the same solvent gave colorless prisms; mp 133—134°C, $[\alpha]_D^{25}$ −26° (*c* 2.5, chloroform). $\lambda_{max}^{ethanol}$ 264 mμ (ε, 9.5×10^3). ν_{max}^{KBr} (cm^{-1}): 1731 (*O*-acetyl); 1590, 1564, 1487 (purinyl).

Found: 50.73; H, 5.57; N, 15.63%. Calcd for $C_{15}H_{19}N_4O_4Cl$ (354.80): C, 54.53; H, 6.54; N, 15.79%.

6-Methoxy-9-(2',6'-dideoxy-3'-C-methyl-3'-O-methyl-β-L-ribo-hexopyranosyl)-purine (XII). XI (61 mg) was treated with 0.1 N methanolic barium methoxide (9 ml) for 3 hr, followed by neutralization with carbon dioxide and purification by means of a silica-gel column (5 g; benzene : acetone=2 : 1), to afford a colorless glass (53 mg, quant.). Three crystallizations from diisopropyl ether gave long, colorless needles; mp 179—180°C, $[\alpha]_D^{23}$ −15° (*c* 1.9, methanol), $\lambda_{max}^{methanol}$ 249 mμ (ε, 11.6×10^3), ν_{max}^{KBr} (cm^{-1}): 1608, 1582 (purinyl).

Found: C, 54.54; H, 6.63; N, 18.32%. Calcd for $C_{14}H_{20}N_4O_4$ (308.34): C, 54.53; H, 6.54; N, 18.17%.

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