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Synthetic Studies on Amino-sugars from Pyridines. I.* Synthesis of 1-O-Methyl-N-benzoyl-*dl*-nojirimycin[1]

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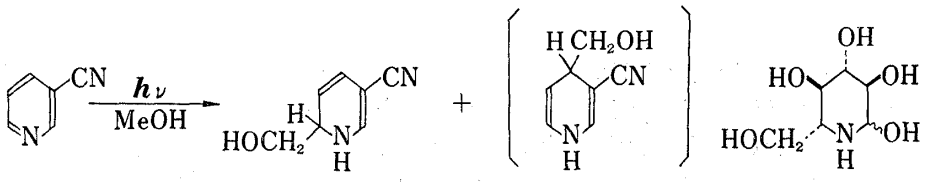
1-O-Methyl-N-benzoyl-*dl*-nojirimycin was synthesized from dihydropyridine derivative by stereoselective introduction of the hydroxyl function.

In the previous communication,[3] we reported a photochemical addition reaction of methanol into nicotinonitrile (**1**) to produce a mixture of dihydropyridines (**2** and **3**), and **2** was isolated as relatively stable crystals. Comparison of the structure of **2** and nojirimycin (**4**), a monosaccharide antibiotic,[4] suggested that the conjugate double bonds were suitably located in the structure of the 1,2-dihydropyridine (**2**) and the piperidinose form of the 5-aminohexose could be synthesized from **2** when the double bonds were hydroxylated in a stereoselective manner. The preliminary experiment, which we report elsewhere,[5] revealed that dihydropyridines such as **2** were stable in the form of an N-acyl derivative against various kinds of oxidations for introducing the polyhydroxyl function, and that oxidation could be carried out stepwise, due to the difference of reactivity between a simple double bond and the double bond involved in the vinylogous cyanamide. Thus, we synthesized a derivative (**15**) of nojirimycin, starting from nicotinonitrile (**1**).



1 **2** **3** **4**

Chart 1

The mixture of the photoproducts (**2** and **3**) was treated with sodium hydride in dimethylformamide in nitrogen atmosphere, followed by the addition of benzoyl chloride. Purification of the crude product by chromatography over silica gel afforded an O,N-dibenzoate (**5**) as a sole isolable compound. **5** was subjected to *cis*-dihydroxylation either with osmium tetroxide or with potassium permanganate. The reaction product was isolated as a diacetate (**6**)[6] in respective yields of 59.5% and 31%. The relation between the benzoyloxymethyl and acetoxyl groups could not be decided at this stage but was later deduced to be *trans* from the nuclear magnetic resonance (NMR) study of **11** and **14**. Oxidation of the second double bond was achieved by the treatment of **6** with N-bromosuccinimide (NBS) in anhydrous methanol to

* Dedicated to the memory of Prof. Eiji Ochiai.

1) Presented at the Symposium on the Progress of Syntheses and Reactions, Tokyo, Nov., 1974 (Abstr. Papers, p. 135).
2) Location: *Tamagawa 2-28-10, Setagaya-ku, Tokyo, 158, Japan.*
3) M. Natsume and M. Wada, *Tetrahedron Letters*, **1971**, 4503.
4) N. Ishida, K. Kumagai, T. Niida, T. Tsuruoka, and H. Yumoto, *J. Antibiotics* (Tokyo), Ser. A, **20**, 66 (1967).
5) M. Natsume and M. Wada, in Preparation.
6) All formulae hereafter depict only one enantiomer of the respective racemates.

produce **7** in 61% yield. Here again, there was no basis for the stereochemistry of the methoxyl group and at the final stage it was concluded to be axial, because of the small value of the spin-spin coupling constant between H_1 and H_2[7] in the NMR spectrum of **14**. Replacement of the bromine atom by the acetoxyl function in **7** was attempted initially with tetrabutylammonium acetate[8] but, actually, elimination of bromohydrin acetate took place in 91% yield and the formation of a new double bond was visible at 6.79 δ as a doublet in the NMR spectrum of **8**.

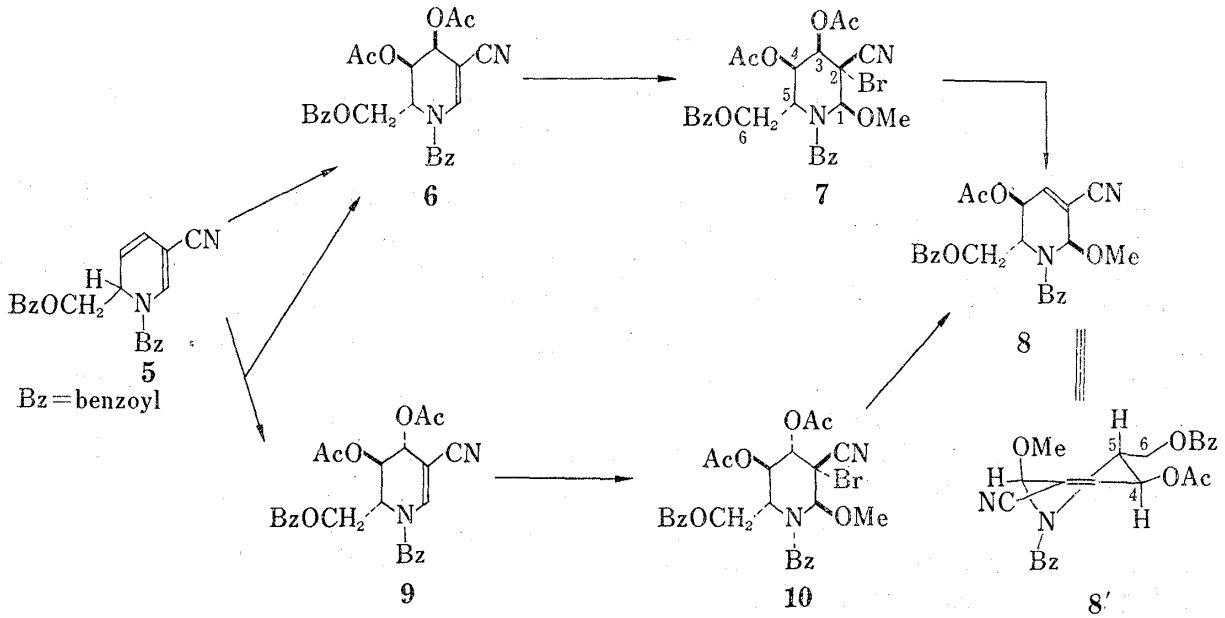


Chart 2

When **5** was warmed with 30% hydrogen peroxide in glacial acetic acid, a 5:1 mixture of **9** and **6** was obtained in 38.5% yield after acetylation. **9** was isolated and oxidized as above with NBS in methanol to **10** in 61% yield. As the treatment of **10** with tetrabutylammonium acetate afforded the same elimination product (**8**), **9** was different from **6** in the configuration of the 3-acetoxyl group. The proton signal at C-4 in **8** appeared as a double doublet with coupling constants of 8 and 3.5 Hz. The spatial structure (**8′**) was conceivable for **8** from this fact and oxidation of the double bond could be anticipated to occur from the less hindered side, that is, *trans* to the acetoxyl group. When **8** was hydroxylated with osmium tetroxide or potassium permanganate, followed by the work-up of the acetylation product, the expected compound (**11**) was obtained in 42% or 67.5% yield, respectively, and its structure was verified by the assignment of the NMR spectrum deduced from the spin-decoupling analysis as shown in Table I. A value of 10 Hz for the spin–spin coupling constant between H_3, H_4, and H_5 supported axial character for all these hydrogens, and stereoselective construction of substituents at C-3, C-4, and C-5 was achieved as desired.

In order to convert the cyanohydrin acetate grouping to the equatorial hydroxyl function, **11** was directly treated with sodium borohydride in methanol, the condition being effective in the case of the synthesis of a xylopiperidinose.[5] A major reaction which actually occurred was reduction of the cyano group to the primary amine and **13** was obtained in 59% yield after the acetylation reaction, accompanied with the formation of the expected product (**12**) in 31% yield. **13** possessed a formula of $C_{28}H_{32}O_{10}N_2$ and exhibited in its NMR spectrum a proton

7) Sugar numbering is used in this paper.
8) M. Fieser and L.F. Fieser, "Reagents for Organic Synthesis," Vol. 3, Wiley-Interscience, New York, 1972, p. 277; M. Sakai, *Tetrahedron Letters*, 1973, 347.

signal due to the methylene group attached to the acetamino function as a doublet, which became a singlet by the addition of deuterium oxide. **11** was therefore hydrolyzed beforehand with diluted potassium hydroxide in methanol to ascertain the formation of a ketone derivative as an intermediate, and then reduced with sodium borohydride under ice-cooling. Acetylation of the reaction product afforded two compounds (**12** and **14**) in the respective yields of 17% and 67%, and for the purification, both were hydrolyzed to the same acetyl-free product (**15**), mp 73—75°. Examination of the NMR spectra of **12** and **14** suggested that a minor amount of the epimeric products having the opposite configuration at C-2 position were contaminated in each reduction product. **15** was converted back to **14**, which was obtained in a crystalline state this time, and the assignment of its NMR spectrum by the help of the spin-decoupling technique (Table I) fully satisfied the expected structure of **14**. The vicinal coupling constants

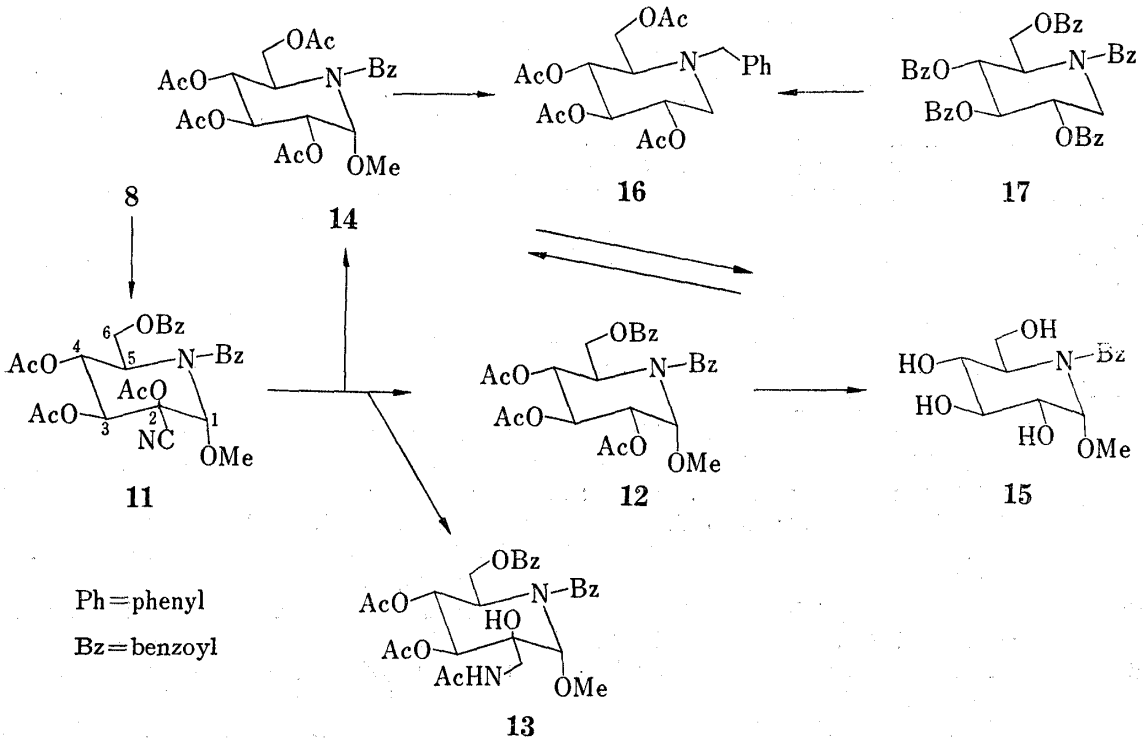


Chart 3

TABLE I. NMR Spectral Data[a] of 11 and 14

	11			14		
	δ		J (Hz)	δ		J (Hz)
H_1	5.70	s		5.25	d	3
H_2				5.13	dd	10, 3
H_3	6.23	d	10	5.92	dd	10, 8.5
H_4	6.10	dd	10, 10	5.75	dd	8.5, 8.5
H_5	4.14	ddd	10, 5, 5	4.03	ddd	8.5, 4.5, 3.5
H_6	4.98	dd	12, 5	4.74	dd	12, 3.5
H_6'	5.23	dd	12, 5	5.20	dd	12, 4.5
OMe	2.98	s		3.01	s	
OAc	1.47	s		1.52	s	
	1.70	s		1.66	s	
	1.80	s		1.76 (6H)	s	

a) obtained at 100 MHz in benzene-d_6

among H_2, H_3, H_4, and H_5 were 10, 8.5, and 8.5 Hz, respectively, suggesting that all substituents on the piperidine ring from C-2 to C-5 were oriented in an equatorial manner and $J_{1,2}$ value of 3 Hz clearly demonstrated that the methoxy group had been introduced axially in the NBS oxidation of **6** and **9**. **14** was reduced with lithium aluminum hydride and acetylated to form **16**, mp 80—82°, and the IR (in solution) and NMR spectra of **16** were completely identical with those of N-benzyl-tetraacetyl-D-deoxynojirimycin, mp 108—109°, derived from deoxy-nojirimycin perbenzoate (**17**) by the same reaction steps, and thus the synthetic material was correlated with nojirimycin. The deacetylated substance (**15**) mentioned above was therefore determined as 1-O-methyl-N-benzoyl-*dl*-nojirimycin.

Experimental

All melting points were taken on Yanagimoto micro-melting point apparatus and are not corrected. Infrared spectra were recorded on Hitachi 215 spectrophotometer and nuclear magnetic resonance spectra were determined on Varian A-60 A instrument, unless otherwise stated, using tetramethylsilane as an internal reference. Merck Silica gel PF_{254} was used for preparative thin-layer chromatography. Elemental analyses were performed by Mr. D. Ohata of this Laboratory.

5-Cyano-1,2-dihydro-2-picolyl Alcohol O,N-Dibenzoate (**5**)——A MeOH (100 ml) solution of nicotinonitrile (1.443 g) was irradiated by Hanovia 450 W high-pressure mercury arc lamp in N_2 atmosphere for 2 hr. The solvent was evaporated and the residue was purified by preparative thin-layer chromatography (prep-TLC) (5% MeOH–CH_2Cl_2) to afford a mixture of **2** and **3** (310 mg). A solution of this mixture (270 mg) in dry dimethylformamide (DMF) (3 ml) was added to a suspension of 50% NaH (400 mg, washed with dry benzene) in DMF (1 ml) under ice-cooling in N_2 atmosphere. After being stirred under cooling for 1 hr and at room temperature for 20 min, BzCl (1.2 g) in dry benzene (2 ml) was added to the mixture and the whole was kept to stand at room temperature for 25 min, diluted with H_2O, and extracted with benzene. The organic layer was washed with sat. $NaHCO_3$–H_2O, dried over Na_2SO_4, and evaporated *in vacuo* to give an oil, which was purified by chromatography over silica gel (15 g) with 50% benzene–CH_2Cl_2 and CH_2Cl_2 to afford 167 mg of crystals, which was recrystallized from ether. Colorless prisms, mp 127—128°. *Anal.* Calcd. for $C_{21}H_{16}O_3N_2$: C, 73.24; H, 4.68; N, 8.14. Found: C, 73.41; H, 4.89; N, 8.14. IR ν_{max}^{KBr} cm^{-1}: 2220, 1723, 1670, 1639, 1571. NMR δ ($CDCl_3$): 4.34 (dd, J=12, 5 Hz), 4.57 (dd, J=12, 4 Hz) (–CH_2–), 5.48—5.71 (1H, m, H_2[9]), 5.80 (1H, triple d, J=9, 5, 1 Hz, H_3), 6.16 (1H, dd, J=9, 1.5 Hz, H_4), 7.26 (1H, br s, H_6).

Osmium Tetroxide Oxidation of 5——A mixture of dibenzoate (**5**, 167 mg) and OsO_4 (115 mg) in benzene (7 ml) containing 5 drops of pyridine was stirred at room temperature for 2.5 hr, evaporated in reduced pressure, and diluted with CH_2Cl_2. H_2S gas was bubbled into the solution for 30 min and the solvent was evaporated *in vacuo*. The residue was acetylated with Ac_2O (1 ml) in pyridine (10 ml) under reflux for 1.5 hr. Treatment as above and purification by prep-TLC (CH_2Cl_2) afforded 132 mg (59.5%) of **6**. An analytical sample was obtained as a colorless glassy substance by repeated prep-TLC. *Anal.* Calcd. for $C_{25}H_{22}O_7N_2$: C, 64.93; H, 4.80; N, 6.06. Found: C, 64.59; H, 4.99; N, 5.89. IR ν_{max}^{KBr} cm^{-1}: 2222, 1754, 1727, 1686, 1627. NMR δ ($CDCl_3$): 2.08 (3H, s, OAc), 2.13 (3H, s, OAc), 4.42 (1H, dd, J=12, 4.5 Hz, H_6), 4.82 (1H, dd, J=12, 5.5 Hz, H_6'), 4.96—5.10 (1H, m, H_5), 5.75 (1H, dd, J=4.5, 3 Hz, H_4), 5.86 (1H, dd, J=4.5, 1.5 Hz, H_3).

$KMnO_4$ Oxidation of 5——To an ice-cold solution of **5** (51 mg) in MeOH (3 ml), a solution of $KMnO_4$ (23 mg) in MeOH (1 ml) and H_2O (0.5 ml) was added dropwise with stirring. After 10 min, sat. $NaHSO_3$–H_2O solution was added, a solid was filtered off, and the solution was evaporated to dyness in reduced pressure. The residue was acetylated with Ac_2O (0.5 ml) in pyridine (1 ml) at room temperature for 19.5 hr, and usual work-up afforded 57 mg of syrup, which was purified by prep-TLC (1% MeOH–CH_2Cl_2) to obtain 20 mg (31%) of colorless glassy substance. This was identified as **6** from IR and NMR spectra.

NBS Oxidation of 6——A mixture of **6** (92 mg) and NBS (156 mg) in dry MeOH (5 ml) was kept to stand at room temperature for 5.5 hr and evaporated in reduced pressure. The residue was dissolved in CH_2Cl_2, washed with sat. $NaHCO_3$–H_2O, and dried over Na_2SO_4. Removal of the solvent afforded crystals, which were recrystallized from MeOH to give 57 mg of needles. Purification of mother liquor by prep-TLC (1% MeOH–CH_2Cl_2) followed by recrystallization gave 13 mg of **7**. Total yield was 70 mg, 61%. An analytical sample, mp 157—158°, was obtained by recrystallization from MeOH as colorless needles. *Anal.* Calcd. for $C_{26}H_{25}O_8N_2Br$: C, 54.46; H, 4.39; N, 4.89. Found: C, 54.73; H, 4.40; N, 5.10. IR ν_{max}^{KBr} cm^{-1}: 1766, 1750, 1720, 1676. NMR δ ($CDCl_3$): 2.02 (3H, s, OAc), 2.17 (3H, s, OAc), 3.58 (3H, s, OMe), 5.00 (2H, d, J=7 Hz, –CH_2–), 4.38—4.82 (1H, m, H_5), 5.22 (1H, s, H_1), 5.72—6.00 (2H, m, H_3 and H_4).

Treatment of 7 with Bu_4NOAc——A solution of **7** (70 mg) and Bu_4NOAc (166 mg) in acetone (3 ml) was allowed to stand at room temperature for 18.5 hr. The solvent was evaporated and the residue was dissolved

9) Numbering of pyridine was adopted only in this compound.

in CH_2Cl_2, washed with sat. $NaHCO_3$–H_2O and dried over Na_2SO_4. Removal of the solvent gave a pink oil, which was purified by prep-TLC (1% MeOH–CH_2Cl_2) to afford a colorless oil (**8**, 48 mg, 91%). *Anal.* Calcd. for $C_{24}H_{22}O_6N_2$: C, 66.35; H, 5.10; N, 6.45. Found: C, 65.99; H, 4.92; N, 6.42. IR ν_{max}^{KBr} cm^{-1}: 2236, 1747, 1725, 1668. NMR δ ($CDCl_3$): 2.10 (3H, s, OAc), 3.43 (3H, s, OMe), 4.44 (1H, triple d, J=8, 6.5, 5 Hz, H_5), 4.84 (2H, d, J=5.5 Hz, $-CH_2-$), 5.28 (1H, s, H_1), 5.87 (1H, dd, J=8, 3.5 Hz, H_4), 6.79 (1H, d, J=3.5 Hz, H_3).

Peracetic Acid Oxidation of 5——A mixture of **5** (440 mg), HOAc (10 ml), and 30% H_2O_2 (0.5 ml) was heated at *ca.* 45° for 8 hr. After cool, 10% Pd-C was added and the mixture was evaporated in reduced pressure. The residual oil was acetylated with Ac_2O (2 ml) in pyridine (2.5 ml) at room temperature for 15 hr and worked up in the usual manner. The oily product thus obtained was purified by prep-TLC (1% MeOH–CH_2Cl_2) to afford a mixture (1: 5.1) of **6** and **9** (255 mg, 38.5%). Separation of this mixture was performed by repeated prep-TLC and a fraction from the smaller *Rf* value was identified as **6**, which was prepared by using OsO_4. A fraction having a larger *Rf* afforded **9** as colorless amorphous material. *Anal.* Calcd. for $C_{25}H_{22}O_7N_2$: C, 64.93; H, 4.80; N, 6.06. Found: C, 64.65; H, 4.88; N, 6.26. IR ν_{max}^{KBr} cm^{-1}: 2224, 1755, 1723, 1691, 1622. NMR δ ($CDCl_3$): 1.82 (3H, s, OAc), 2.15 (3H, s, OAc), 4.45 (1H, dd, J=11, 8.5 Hz, H_6), 4.68 (1H, dd, J=11, 7 Hz, H_6'), 5.28 (1H, br t, J=*ca.* 8 Hz, H_5), 5.42 (1H, t, J=2 Hz, H_3), 5.56 (1H, t, J=2 Hz, H_4).

NBS Oxidation of 9——A mixture of **9** (141 mg) and NBS (210 mg) in anhyd. MeOH (5 ml) was kept to stand at room temperature for 19 hr and evaporated in reduced pressure. The residue was dissolved in CH_2Cl_2, washed with sat. $NaHCO_3$–H_2O, and dried over Na_2SO_4. Removal of the solvent gave a crystalline solid, which was recrystallized from MeOH to afford **10** (99 mg). Purification of the mother liquor by prep-TLC, followed by recrystallization gave further 7 mg of crystals. Total yield of **10** was 106 mg, 61%. An analytical sample was obtained as colorless prisms, mp 187—188°, by further recrystallization from MeOH. *Anal.* Calcd. for $C_{26}H_{25}O_8N_2Br$: C, 54.46; H, 4.39; N, 4.89. Found: C, 54.52; H, 4.32; N, 5.00. IR ν_{max}^{KBr} cm^{-1}: 1756, 1711, 1681. NMR δ ($CDCl_3$): 2.06 (3H, s, OAc), 2.15 (3H, s, OAc), 3.64 (3H, s, OMe), 4.10 (1H, quintet, J=5 Hz, H_5), 4.85 (1H, dd, J=12, 5 Hz, H_6), 5.17 (1H, dd, J=12, 6 Hz, H_6'), 5.37 (1H, s, H_1), 5.47—5.88 (2H, m, H_3 and H_4).

Treatment of 10 with Bu_4NOAc——A mixture of **10** (33 mg) and Bu_4NOAc (58 mg) in acetone (3 ml) was allowed to stand at room temperature for 17 hr and then evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2, washed with sat. $NaHCO_3$–H_2O, and dried over Na_2SO_4. Removal of the solvent gave a brown oil, which was purified by prep-TLC (1% MeOH–CH_2Cl_2) to afford **8** (13 mg, 52%) as a colorless oil.

OsO_4 Oxidation of 8——A mixture of **8** (105 mg) and OsO_4 (107 mg) in pyridine (1.5 ml) was stirred at room temperature for 63 hr, evaporated *in vacuo*, and the residue was dissolved in MeOH and CH_2Cl_2. H_2S gas was introduced into the solution under ice-cooling for 45 min and the solution was evaporated in reduced pressure. The resulting crude diol was acetylated with Ac_2O (1.5 ml) in pyridine (2 ml) at room temperature for 17.5 hr, followed by treatment in the usual manner to give a brown syrup. Purification of the product by prep-TLC (1% MeOH–CH_2Cl_2) and recrystallization from MeOH afforded **11** (56 mg,-42%) as colorless prisms. An analytical sample, mp 188—189°, was obtained by recrystallization from MeOH. *Anal.* Calcd. for $C_{28}H_{28}O_{10}N_2$: C, 60.86; H, 5.11; N, 5.07. Found: C, 60.42; H, 4.96; N, 5.26. IR ν_{max}^{KBr} cm^{-1}: 1772, 1755, 1731, 1666.

$KMnO_4$ Oxidation of 8——To a solution of **8** (35 mg) in MeOH (2 ml), a solution of $KMnO_4$ (15 mg) in H_2O (1 ml) was added dropwise with stirring under ice-cooling. After 15 min, excess $KMnO_4$ was decomposed with a saturated solution of $NaHSO_3$ in 30% MeOH–H_2O. A solid was filtered off and the filtrate was evaporated to give crude diol, which was acetylated with Ac_2O (1 ml) in pyridine (1.5 ml). The product obtained by the usual work-up was purified by prep-TLC (1% MeOH-CH_2Cl_2) and recrystallized from MeOH to afford 30 mg (67.5%) of **11** as colorless prisms, mp 186°.

Formation of 13——To a solution of **11** (37 mg) in MeOH (3 ml), a solution of $NaBH_4$ (85 mg) in MeOH (3 ml) was added and the resulting mixture was kept to stand at −13° for 43 hr. The mixture was neutralized with AcOH and the solvent was evaporated *in vacuo*. The residue was acetylated with Ac_2O (0.7 ml) in pyridine (1 ml) at room temperature for 4.5 hr and treated in a usual way. The resulting mixture was separated by prep-TLC (3% MeOH–CH_2Cl_2) to afford crude **12** (11 mg, 31%) and **13** (22 mg, 59%), and the latter was purified by prep-TLC (5% MeOH–CH_2Cl_2), followed by recrystallization from MeOH–ether to afford an analytical sample as colorless needles, mp 185—186°. *Anal.* Calcd. for $C_{28}H_{32}O_{10}N_2$: C, 60.42; H, 5.80; N, 5.03. Found: C, 60.45; H, 5.72; N, 5.09. IR ν_{max}^{KBr} cm^{-1}: 1758, 1727, 1642. NMR δ ($CDCl_3$): 1.70 (3H, s, Ac), 1.98 (3H, s, Ac), 2.20 (3H, s, Ac), 3.27 (2H, d, J=5.5 Hz, $-C\underline{H}_2-NHAc$), 3.43 (3H, s, OMe), 3.86 (1H, triple d, J=10.5, 5, 5 Hz, H_5), 4.64 (1H, s, H_3), 5.76 (1H, dd, J=10.5, 9.5 Hz, H_4), 6.26—5.99 (1H, br m, $-N\underline{H}Ac$).

1-O-Methyl-N-benzoyl-*dl*-nojirimycin (15)——A mixture of **11** (139 mg) and 10% KOH–H_2O (0.1 ml) in MeOH (10 ml) was kept to stand at 3° for 3 hr 45 min, and a solution of $NaBH_4$ (155 mg) in MeOH (5 ml) was added. The resulting mixture was allowed to stand for 37 hr at −20—3°, neutralized with HOAc, and evaporated *in vacuo*. The residue was acetylated with Ac_2O (3 ml) in pyridine (3.5 ml) at room temperature for 4.5 hr. The acetylated mixture was separated by prep-TLC into two products and crude **12** (23 mg, 17%) obtained as a colorless oil from the larger *Rf* portion was probably contaminated with its C-2 epimer in the

ratio of 5.6: 1, which was estimated from the integrated value of MeO signals at 3.35 and 3.51 δ in its NMR spectrum. The smaller *Rf* fraction afforded crude **14** (77 mg, 67%) as a colorless oil and the ratio of **14** and its C-2 epimer was estimated to be 10: 1 from the NMR signals of MeO at 3.30 and 3.51 δ. Crude **14** was hydrolyzed by allowing a solution of 29 mg and 10% KOH–H_2O (0.03 ml) in MeOH (3 ml) to stand at 3° for 1 hr 15 min. The mixture was neutralized with ion-exchanger resin (Amberlite IR-120B H^+ form, 0.5 ml) and filtered. The filtrate was evaporated *in vacuo* to yield a crystalline solid (18 mg,) which showed two spots of TLC (10% MeOH–CH_2Cl_2). Recrystallization of the solid from CH_2Cl_2–ether afforded colorless prisms, mp 71—72.5°, (**15**, 4 mg), which was pure by TLC examination. An analytical sample, mp 73—75°, was obtained by further recrystallization from the same solvent. *Anal.* Calcd. for $C_{14}H_{19}O_6N \cdot H_2O$: C, 53.32; H, 6.71; N, 4.44. Found: C, 52.72; H, 6.41; N, 4.42. IR ν_{max}^{KBr} cm^{-1}: 1628. Crude **12** (23 mg) was hydrolyzed as above and the crystalline solid obtained was recrystallized from CH_2Cl_2–ether to yield 1 mg of **15** as colorless prisms, mp 74—77°.

1-O-Methyl-N-benzoyl-*dl*-nojirimycin Tetraacetate (14)——A solution of **15** (22 mg) and Ac_2O (1 ml) in pyridine (1.5 ml) was allowed to stand at room temperature for 1.5 hr and then warmed at 50—60° for 45 min. By treatment in the usual manner, a slightly yellow syrup (29 mg) was obtained, which was purified by prep-TLC (1% MeOH–CH_2Cl_2) twice to afford **14** (22 mg, 64%) as crystals. Colorless prisms, mp 111—112°, were obtained by two recrystallizations from MeOH. *Anal.* Calcd. for $C_{22}H_{27}O_{10}N$: C, 56.77; H, 5.85; N, 3.01. Found: C, 57.00; H, 5.89; N, 3.16. IR ν_{max}^{KBr} cm^{-1}: 1764, 1746, 1652.

$LiAlH_4$ Reduction of 14——$LiAlH_4$ (48 mg) was added to a solution of **14** (52 mg) in dry tetrahydrofuran (THF) (6 ml) and the mixture was refluxed for 2 hr. Acetone was added to decompose excess of reagent, the whole was neutralized with HOAc, and inorganic material was filtered off. The solid which remained by filtration was extracted thoroughly with H_2O, the H_2O extracts were combined to the THF solution, and the whole was evaporated to dryness. The residue was acetylated and purified by prep-TLC (1.5% MeOH–CH_2Cl_2) to yield **16** (9 mg) as a crystalline solid. Recrystallization from ether–hexane afforded colorless prisms, mp 80—82°. *Anal.* Calcd. for $C_{21}H_{27}O_8N$: C, 59.85; H, 6.46; N, 3.32. Found: C, 60.07; H, 6.54; N, 3.21. Identity of this sample with **16** from natural origin was proved by mixed TLC (1% MeOH–CH_2Cl_2) and comparison of their IR (CS_2, $CHCl_3$) and NMR ($CDCl_3$) spectra.

16 from Nojirimycin-Bisulfite——Crude deoxynojirimycin[10] prepared from nojirimycin-bisulfite adduct (500 mg) was benzoylated with BzCl (5 ml) and Ac_2O (3 ml) in a mixture of pyridine (20 ml) and CH_2Cl_2 (10 ml) at room temperature for 18 hr. The mixture was evaporated to dryness *in vacuo* and work-up in the same manner as the acetylation process to obtain 5.498 g of brown syrup, which was chromatographed over 50 g of silica gel using CH_2Cl_2 as a solvent. Fraction showing two spots on TLC (1% MeOH–CH_2Cl_2) were combined and separated further by prep-TLC (1% MeOH–CH_2Cl_2). Crystals (333 mg) obtained from the larger *Rf* portion were recrystallized from ether to yield **17** (184 mg) as colorless prisms, mp 193—193.5°. *Anal.* Calcd. for $C_{41}H_{33}O_9N$: C, 72.02; H, 4.87; N, 2.05. Found: C, 72.22; H, 4.87; N, 2.13. IR ν_{max}^{KBr} cm^{-1}: 1730, 1646.

$LiAlH_4$ (48 mg) was added to a solution of **17** (71 mg) in dry THF (10 ml) and the mixture was refluxed for 1.25 hr. Treatment as above and acetylation with Ac_2O (1.5 ml) in pyridine (2 ml) at room temperature for 15.5 hr afforded a peracetate, which was purified by prep-TLC (1% MeOH–CH_2Cl_2), followed by recrystallization from ether–hexane to give N-benzyl-tetraacetyl-D-deoxynojirimycin (**16**) (11 mg) as colorless needles, mp 108—109°. *Anal.* Calcd. for $C_{21}H_{27}O_8N$: C, 59.85; H, 6.46; N, 3.32. Found: C, 59.77; H, 6.43; N, 3.27. IR ν_{max}^{KBr} cm^{-1}: 1743, IR $\nu_{max}^{CS_2}$ cm^{-1}: 1761. 1750 (sh). NMR δ ($CDCl_3$): 1.93, 2.00, 2.03, 2.08 (s, OAc), *ca.* 2.23 (m, H_1-axial), 2.62—2.90 (1H, m, H_5), 3.08 (1H, dif dd, J=12, 3.5 Hz, H_1-equatorial), 3.44 (1H, d, J=13.5 Hz, $C_6H_5C\underline{H_A}H_B$–), 4.12 (1H, d, J=13.5 Hz, $C_6H_5CH_A\underline{H_B}$–), 4.26 (1H, d, J=3.5 Hz, H_6), 4.48 (1H, d, J=3 Hz, H_6'), 4.85—5.32 (3H, m, H_2, H_3, H_4), 7.30 (5H, s, $C_6\underline{H_5}$).

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10) S. Inoue, T. Tsuruoka, T. Ito, and T. Niida, *Tetrahedron*, **24**, 2125 (1968).