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Synthesis of (+)- and (−)-nojirimycin and their 1-deoxy derivatives from *myo*-inositol

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ABSTRACT

The conversion of the naturally abundant cyclitol, *myo*-inositol (**4**), into (+)-nojirimycin (**1a**), its enantiomer (**1b**), and their 1-deoxy analogues (**2a** and **2b**) is described. Biological assay of **2a**, **2b**, and the bisulfite adducts of **1a** and **1b** (**3a** and **3b**) showed that the compounds having the unnatural L-*gluco* configuration (**2b** and **3b**) possess moderate-to-high inhibitory activity against almond β-D-glucosidase and bovine liver β-D-galactosidase.

INTRODUCTION

(+)-Nojirimycin[1] (**1a**) and (+)-1-deoxynojirimycin[2] (**2a**) are naturally occurring antibiotics that show potent inhibitory activity against glycosidases and glucoamylase[3]. The analogues of **1a** and **2a** having the D-*manno* configuration (mannojirimycin[4] and 1-deoxymannojirimycin[5]) and the analogue of **1a** possessing the D-*galacto* configuration (galactostatin[6]) are also found in Nature, and are reported to inhibit glycosidases. Recently, much attention has been focused on derivatives of **2a**, inhibitors of trimming glycosidases[7], which were shown to interfere with HIV-induced syncytium formation and viral infectivity[8]. Therefore, interest in the relationship between structure and enzyme-inhibitory activity, as shown by a study of chemically modified compounds, has increased[9].

A number of total syntheses of **1a** and **2a** have been achieved starting from carbohydrates[10], L-tartaric acid[11], and (*S*)-pyroglutamic acid[12], and by a combination of enzymic and chemical methods[13]. However, their enantiomers (**1b** and **2b**) have not been synthesized so far. In this article, we report a new synthesis of **1a**, **2a**, **1b**, and **2b** starting from naturally abundant *myo*-inositol (**4**), via bisulfite

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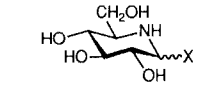
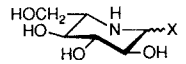


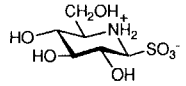
1a X = OH [(+)-nojirimycin]

2a X = H [(+)-1-deoxynojirimycin]

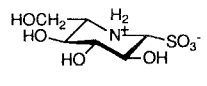


1b X = OH [(-)-nojirimycin]

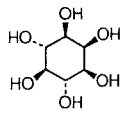
2b X = H [(-)-1-deoxynojirimycin]



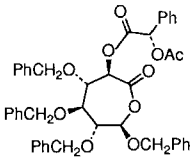
3a



3b



myo-Inositol (**4**)



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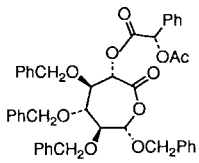

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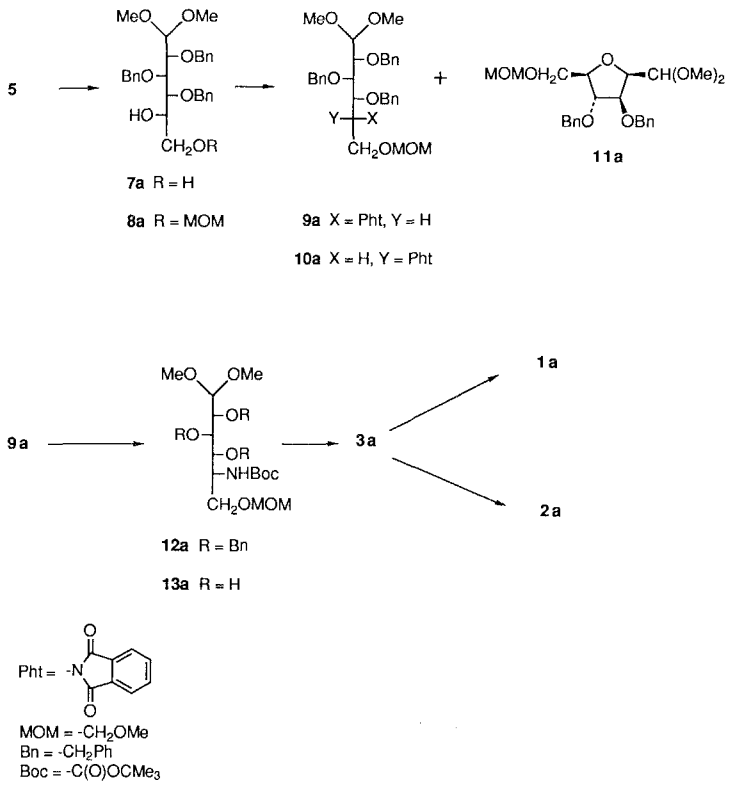
adducts (**3a** and **3b**), together with the inhibitory activities of **2a**, **2b**, **3a**, and **3b** against several enzymes[14].

RESULTS AND DISCUSSION

The optically pure, diastereoisomeric, seven-membered lactones **5** and **6**, which were prepared from *myo*-inositol in 6 steps including optical resolution (using L-*O*-acetylmandelic acid) and a highly regioselective Baeyer-Villiger reaction[15], were chosen as the starting materials. Treatment of **5** with trimethyl orthoformate in methanol in the presence of *p*-toluenesulfonic acid, followed by reduction with lithium aluminum hydride, afforded 2,3,4-tri-*O*-benzyl-L-idose dimethyl acetal (**7a**) in 90% yield. Reaction of **7a** with chloromethyl methyl ether and *N*,*N*-diisopropylethylamine in dichloromethane gave **8a** (61%) with the recovery of some starting material (33%). To introduce the amino function into the 5-position of compound **8a** with inversion of configuration, the Mitsunobu reaction[16] using phthalimide as a nucleophile was carried out. Thus, treatment of **8a** with triphenylphosphine, diisopropyl azodicarboxylate, and phthalimide in dry benzene provided the desired compound **9a** in 46% yield. Two side products of this reaction could be isolated pure and their structures were tentatively assigned on the basis of elemental analysis as well as spectral data. One is the 5-phthalimido compound with the L-*ido* configuration (**10a**), and the other is the 2,5-anhydrohexose derivative **11a**. The ^{1}H NMR spectrum of **10a** was very similar to that of **9a**. Since compound **9a** could be converted into (+)-nojirimycin (**1a**), **10a** was assumed to be an epimeric phthalimide derivative. The ^{1}H NMR spectrum of compound **11a**

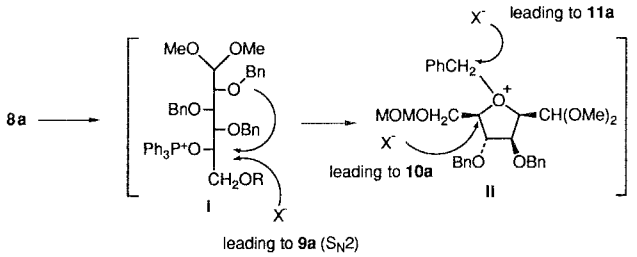


Scheme 1.

showed that there were only two benzyloxy groups, and there was no coupling between H-3 and H-4, indicating the cyclic structure **11a**. The observed strong NOE between H-2 and H-3 as well as H-4 and H-6 also supported the assigned structure.

The mechanism of this reaction involves the initial formation of an alkoxyphosphonium salt[16] (**i**). A direct nucleophilic attack of the phthalimide anion on **i** would provide the normal S_N2 product (**9a**), whereas intramolecular attack of the C-2 ether oxygen would afford the second intermediate (**ii**). The collapse of **ii** by attack of the nucleophile at C-5 would lead to the formation of compound **10a** and attack at the benzyl carbon would result in the formation of the 2,5-anhydro compound (**11a**). Similar formation of a 2,5-anhydro compound has been observed by Hashimoto et al.[17] in the reaction of 2,3,4,6-tetra-*O*-benzyl-D-glucose *S*-acetyl *O*-methyl monothioacetal with triphenylphosphine and triiodoimidazole.

Removal of the phthaloyl group of **9a** was achieved by treatment with hydrazine in refluxing methanol and the resulting amine was successively converted into the *N-tert*-butoxycarbonyl derivative (**12a**) in 95% yield. Removal of the *O*-benzyl



Scheme 2.

groups by catalytic hydrogenation afforded the triol (**13a**), quantitatively. Treatment of an aqueous solution of **13a** with sulfur dioxide at 40°C for 2 days resulted in hydrolysis of the protecting groups and formation of the bisulfite adduct, to provide the known crystalline (+)-nojirimycin bisulfite adduct[10a,18] (**3a**) (58%), whose spectral properties (^{1}H, ^{13}C, and IR) were identical with those of an authentic sample[18] prepared from natural (+)-nojirimycin. The adduct **3a** was converted into (+)-nojirimycin (**1a**) by the known procedure[10a] [Dowex 1-X2 (HO^-) resin treatment]. On the other hand, hydrogenolysis of **3a** in the presence of Raney-Ni and $Ba(OH)_2$[10n] in water provided (+)-1-deoxynojirimycin (**2a**) in 53% yield, identical in all respects with the natural material.

Likewise, (−)-nojirimycin (**1b**) and (−)-1-deoxynojirimycin (**2b**) were prepared starting from the lactone **6** via the (−)-nojirimycin bisulfite adduct (**3b**).

The biological activities of **2a** and **2b** as well as those of the bisulfite adducts of synthetic **1a** and **1b** (**3a** and **3b**), natural **1a**, and mannojirimycin are shown in Table I. Although the bisulfite adducts show somewhat different inhibitory activity compared to their parent nojirimycins[18], their chemical stability allowed us to evaluate and compare the activity accurately. It is noteworthy that the synthetic (−)-nojirimycin bisulfite adduct (**3b**), which is the enantiomer of the natural form, possesses high inhibitory activity against both almond β-D-glucosidase and Jack bean α-D-mannosidase, almost comparable to that of mannojirimycin. It is also interesting that (−)-1-deoxynojirimycin (**2b**) showed moderate activity against β-D-glucosidase and β-D-galactosidase. The reasons why compounds having an enantiomeric relationship to the natural products **2b** and **3b** are moderate-to-strong inhibitors of β-D-glucosidase and β-D-galactosidase are not clear so far; this work provides a new approach to the study of the relationship between structure and enzyme-inhibitory activity of the compounds in this class.

EXPERIMENTAL

General methods.—Melting points were determined on a Mitamura Riken micro hot-stage and are uncorrected. Specific rotations were measured in a 0.1-dm tube with a Jasco DIP-370 Digital Polarimeter. ^{1}H NMR spectra were recorded on

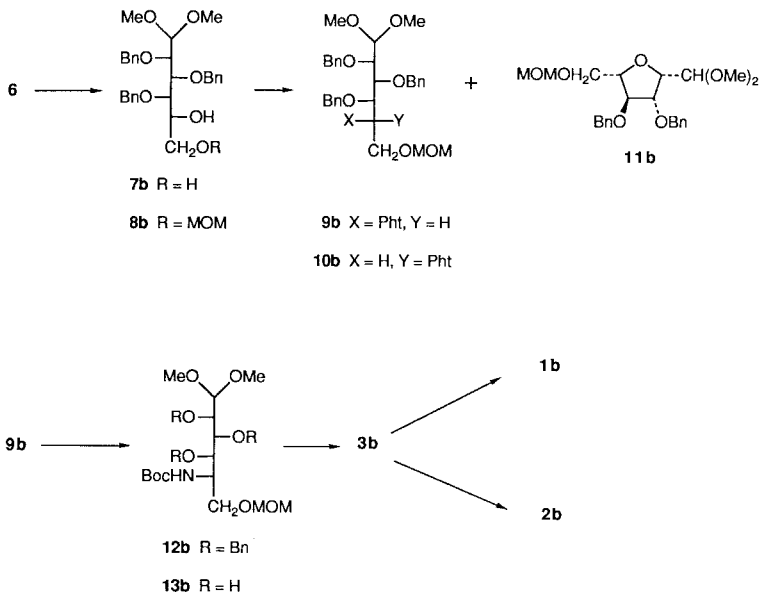
TABLE I

Inhibitory activity of compounds **2a**, **2b**, **3a**, **3b**, and the bisulfite adduct of mannojirimycin against several enzymes [a]

Compound	Enzyme			
	α-D-Gluco-sidase [b]	β-D-Gluco-sidase [c]	α-D-Manno-sidase [d]	β-D-Galacto-sidase [e]
3a [f]	77.4 (14.5)	89.6 (8.0)	9.4	Not measured
Mannojirimycin bisulfite adduct [g]	1.3	98.0 (4.4)	55.5 (84.0)	Not measured
2a [h]	76.0 (15.0)	80.8 (24.0)	42.5	28.5
2b [h]	5.9	57.9 (74.0)	0	61.0 (43.0)
3a [h]	76.1 (17.0)	85.8 (9.4)	11.7	Not measured
3b [h]	2.1	91.7 (4.5)	31.2	Not measured

[a] Inhibition (*I*%) determined at the final concentration of 100 μg/mL; numbers in parentheses denote IC_{50} (concentrations required to cause 50% inhibition, μg/mL) values. [b] Yeast α-D-glucosidase, *p*-nitrophenyl α-D-glucopyranoside (0.66 mM), phosphate buffer (100 mM), pH 6.8. [c] Almond β-D-glucosidase, *p*-nitrophenyl β-D-glucopyranoside (0.33 mM), acetate buffer (100 mM), pH 5.0. [d] Jack bean α-D-mannosidase, *p*-nitrophenyl α-D-mannopyranoside (20 mM), acetate buffer (100 mM), pH 4.5. [e] Bovine liver β-D-galactosidase, *o*-nitrophenyl β-D-galactopyranoside (20 mM), phosphate buffer (50 mM), pH 7.3. [f] Obtained from natural (+)-nojirimycin. [g] Obtained from natural (+)-mannojirimycin. [h] Synthetic compound.

a Jeol JNM EX 90 (90 MHz), GSX 270 (270 MHz), or GSX 400 (400 MHz) spectrometer for solutions in chloroform-*d* with tetramethylsilane as internal standard, unless otherwise noted. ^{13}C NMR spectra were recorded with a Jeol



Scheme 3.

GSX 270 (67 MHz) or GSX 400 (100 MHz). IR spectra were recorded with a Jasco IR-810 spectrometer. Column chromatography was performed with Wakogel C-300 (Wako Pure Chemicals, Osaka, Japan). Organic solutions were dried over anhyd Na_2SO_4 and concentrated at $< 45°C$ under diminished pressure.

2,3,4-Tri-O-benzyl-L-idose dimethyl acetal (**7a**).—A solution of (2*R*,3*S*,4*S*,5*R*,6*R*)-2-(L-*O*-acetylmandeloyloxy)-3,4,5,6-tetrakis(benzyloxy)-7-hexanolide[15] (**5**; 3.05 g, 4.17 mmol), trimethyl orthoformate (15 mL), and *p*-toluenesulfonic acid monohydrate (0.24 g, 1.25 mmol) in MeOH (15 mL) was refluxed for 1 h, and then concentrated to dryness. To a stirred solution of the residue in tetrahydrofuran (20 mL) was added dropwise a solution of lithium aluminum hydride (0.63 g, 17 mmol) in tetrahydrofuran (20 mL) at 0°C under N_2. The mixture was stirred at ambient temperature for 2 h and then neutralized with M HCl. The mixture was filtered through a bed of Celite and washed with EtOAc. The filtrate and washings were combined, washed successively with M HCl, satd aq $NaHCO_3$, and brine, and dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (68 g) with 1:4 acetone–hexane to give **7a** (1.85 g, 90%) as a syrup; $[\alpha]_D^{27}$ +5° (*c* 3.4, $CHCl_3$), R_F 0.62 (1:5 EtOH–toluene). ^1H NMR data (90 MHz, $CDCl_3$) δ 7.5–7.1 (m, 15 H, 3 Ph), 5.0–4.4 (m, 7 H, 3 CH_2Ph and H-1), 3.98 (dd, 1 H, $J_{5,6}$ 2.4, $J_{6,6'}$ 8 Hz, H-6), 3.74–3.3 (m, 5 H, H-2,3,4,5,6′), 3.48 and 3.26 (2 s, each 3 H, 2 OMe), 2.8–1.9 (bs, 2 H, 2 OH). *Anal.* Calcd for $C_{29}H_{36}O_7$: C, 70.14; H, 7.31. Found: C, 69.75; H, 7.31.

2,3,4-Tri-O-benzyl-D-idose dimethyl acetal (**7b**).—(2*S*,3*R*,4*R*,5*S*,6*S*)-2-(L-*O*-acetylmandeloyloxy)-3,4,5,6-tetrakis(benzyloxy)-7-hexanolide[15] (**6**; 3.74 g, 5.12 mmol) was treated as described for the preparation of compound **7a**, to afford **7b** (1.89 g, 74%), which was identical with **7a** in all respects except for its optical rotation; $[\alpha]_D^{26}$ −7° (*c* 2.8, $CHCl_3$). *Anal.* Calcd for $C_{29}H_{36}O_7$: C, 70.14; H, 7.31. Found: C, 70.01; H, 7.22.

2,3,4-Tri-O-benzyl-6-O-methoxymethyl-L- (**8a**) *and -D-idose dimethyl acetal* (**8b**). —To a solution of **7a** (184 mg, 0.371 mmol) and *N*,*N*-diisopropylethylamine (0.16 mL, 0.93 mmol) in CH_2Cl_2 (2 mL) was added dropwise chloromethyl methyl ether (70 μL, 0.93 mmol) at 0°C, and the resulting mixture was stirred at 5°C for 4 h. The mixture was diluted with EtOAc, washed successively with M HCl, satd aq $NaHCO_3$, and brine, then dried. Removal of the solvent left a residue, which was chromatographed on a column of silica gel (10 g) with 1:10 EtOAc–toluene, to afford the starting material (**7a**; 61 mg, 33% recovery) and **8a** (123 mg, 61%) as a syrup; $[\alpha]_D^{24}$ ~0° (*c* 1.1, $CHCl_3$); R_F 0.24 (1:3 EtOAc–toluene). ^1H NMR data (90 MHz, $CDCl_3$) δ 7.5–7.2 (m, 15 H, 3 Ph), 5.1–4.4 (m, 9 H, 3 CH_2Ph, OCH_2, and H-1), 4.15–3.0 (m, 6 H, H-2,3,4,5,6,6′), 3.47, 3.29, and 3.24 (3 s, each 3 H, 3 OMe), 2.7–2.5 (bs, 1 H, OH).

Similarly, compound **7b** (919 mg, 1.87 mmol) was converted into the enantiomer **8b** (511 mg, 51%); $[\alpha]_D^{26}$ ~0° (*c* 2.7, $CHCl_3$); **7b** (311 mg, 34%) being recovered. *Anal.* Calcd for $C_{31}H_{40}O_8$: C, 68.87; H, 7.46. Found: **8a**, C, 68.71; H, 7.44. **8b**, C, 68.65; H, 7.32.

*2,3,4-Tri-*O*-benzyl-5-deoxy-6-*O*-methoxymethyl-5-phthalimido-*D- (**9a**) *and* -L-*glucose dimethyl acetal* (**9b**).—To a stirred solution of **8a** (332 mg, 0.614 mmol), phthalimide (271 mg, 1.84 mmol), and triphenylphosphine (322 mg, 1.23 mmol) in benzene (10 mL) was added dropwise diisopropyl azodicarboxylate (0.189 mL, 1.23 mmol) at ambient temperature under Ar. After 2 h, TLC [1:3 EtOAc–toluene] indicated the disappearance of **8a** and formation of one major (R_F 0.59) and two minor components (R_F 0.53 and 0.41). The mixture was concentrated and the residue was chromatographed on a column of silica gel (45 g) with 1:13 EtOAc–toluene to give **9a** (191 mg, 46%) as a syrup; $[\alpha]_D^{22}$ +31° (*c* 2.0, $CHCl_3$). ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.9–7.1 (m, 19 H, phenyl), 5.90–3.60 (m, 15 H, 3 CH_2Ph, OCH_2O, and H-1,2,3,4,5,6,6′), 3.31, 3.20, and 3.19 (3 s, each 3 H, 3 OMe).

Eluted second was the 5-epimer (**10a**; 79 mg, 19%) of **9a**, isolated as a syrup; $[\alpha[_D^{26}$ ~ 0° (*c* 0.5, $CHCl_3$). ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.9–7.1 (m, 19 H, phenyl), 5.00–4.40 (m, 9 H, 3 CH_2Ph, OCH_2O, and H-1), 4.40–3.60 (m, 6 H, H-2,3,4,5,6,6′), 3.40, 3.27, and 3.15 (3 s, each 3 H, 3 OMe).

Eluted third was 2,5-anhydro-3,4-di-*O*-benzyl-6-*O*-methoxymethyl-D-glucose dimethyl acetal (**11a**; 91 mg, 34%), isolated as a syrup; $[\alpha]_D^{27}$ +20° (*c* 2.7, $CHCl_3$). ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.40–7.20 (m, 10 H, phenyl), 4.67 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.65–4.45 (m, 6 H, 2 CH_2Ph and OCH_2O), 4.13 (ddd, 1 H, $J_{4,5}$ 1.9, $J_{5,6}$ 7.3, $J_{5,6'}$ 5.9 Hz, H-5), 4.09 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-2), 3.99 (d, 1 H, H-3), 3.94 (d, 1 H, H-4), 3.71 (dd, 1 H, $J_{6,6'}$ 10.3 Hz, H-6), 3.60 (dd, 1 H, H-6′), 3.43, 3.40, and 3.30 (3 s, each 3 H, 3 OMe). *Anal.* Calcd for $C_{39}H_{43}NO_9$: C, 69.94; H, 6.47; N, 2.09. Found: **9a**, C, 69.62; H, 6.51; N, 2.06; **10a**, C, 70.08; H, 6.48; N, 2.00. Calc. for $C_{24}H_{32}O_7$: C, 66.65; H, 7.46. Found: **11a**, C, 66.62; H, 7.34.

A similar Mitsunobu reaction of compound **8b** (68 mg, 0.13 mmol) afforded **9b** (41 mg, 49%); $[\alpha]_D^{20}$ −31° (*c* 1.0, $CHCl_3$); **10b** (17 mg, 20%); $[\alpha]_D^{20}$ −1° (*c* 1.9, $CHCl_3$); and **11b** (13 mg, 24%), $[\alpha]_D^{25}$ −18° (*c* 1.0, $CHCl_3$). *Anal.* Found: **9b**, C, 69.79; H, 6.44; N, 2.08; **10b**, C, 70.00; H, 6.59; N, 1.79; **11b**, C, 66.50; H, 7.23.

*2,3,4-Tri-*O*-benzyl-5-(*tert*-butoxycarbonylamino)-5-deoxy-6-*O*-methoxymethyl-*D- (**12a**) *and* -L-*glucose dimethyl acetal* (**12b**).—A mixture of **9a** (179 mg, 0.27 mmol), hydrazine monohydrate (132 μL, 2.67 mmol), and MeOH (2 mL) was heated at reflux overnight. The mixture was filtered and concentrated. The residue was dissolved in CH_2Cl_2 (3 mL), and the solution was treated with di-*tert*-butyl dicarbonate (116 mg, 0.54 mmol) and triethylamine (76 μL, 0.54 mmol) at ambient temperature for 3 h, then concentrated. The residue was chromatographed on a column of silica gel (10 g) with 1:10 EtOAc–toluene to give **12a** (162 mg, 95%) as a syrup; $[\alpha]_D^{18}$ +16° (*c* 1.0, $CHCl_3$); ν_{max} (neat) 1710 cm^{-1} (urethane). ^{1}H NMR data (270 MHz, $CDCl_3$): δ 7.4–7.2 (m, 15 H, 3 Ph), 5.20 (d, 1 H, $J_{5,NH}$ 5.1 Hz, NH), 4.85–4.56 (m, 8 H, 3 CH_2Ph and OCH_2O), 4.40 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1); 4.20–4.08 (m, 1 H, H-5), 3.98 (dd, 1 H, $J_{2,3} = J_{3,4} = 5.1$ Hz, H-3), 3.83 (dd, 1 H, $J_{4,5}$ 5.1 Hz, H-4), 3.77 (d, 1 H, H-2), 3.60 (d, 2 H, $J_{5,6}$ 5.5 Hz, H-6 and 6′), 3.38, 3.35, and 3.31 (3 s, each 3 H, 3 OMe), 1.39 (s, 9 H, *t*-Bu).

Similarly, **9b** (583 mg, 0.87 mmol) was converted into **12b** (497 mg, 89%); $[\alpha]_D^{25}$

−13° (*c* 1.9, $CHCl_3$). *Anal.* Calcd for $C_{36}H_{49}NO_9$: C, 67.58; H, 7.72; N, 2.19. Found: **12a**, C, 67.47; H, 7.69; N, 2.29; **12b**, C, 67.32; H, 7.62; N, 2.28.

*5-(*tert*-Butoxycarbonylamino)-5-deoxy-6-O-methoxymethyl-*D- (**13a**) *and* -L-*glucose dimethyl acetal* (**13b**).—A solution of **12a** (454 mg, 0.71 mmol) in EtOH (5 mL) was hydrogenolyzed in the presence of $Pd(OH)_2$ on carbon (50 mg) at ambient temperature under an atmospheric pressure of H_2 for 4 h. The catalyst was removed by filtration and the filtrate was concentrated to afford **13a** (294 mg, 100%) as a white powder, mp 75–77°C; $[\alpha]_D^{28}$ +5° (*c* 0.9, $CHCl_3$); ν_{max} (neat) 1710 cm^{-1} (urethane). ^1H NMR data (270 MHz, $CDCl_3$): δ 5.30 (bs, 1 H, NH), 4.65 (s, 2 H, OCH_2O), 4.52 (d, 1 H, $J_{1,2}$ 6.8 Hz, H-1), 4.09 (bs, 1 H, OH), 4.05–3.62 (m, 7 H, H-2,3,4,5,6,6′ and OH), 3.48, 3.47, and 3.39 (3 s, each 3 H, 3 OMe), 2.96 (bs, 1 H, OH), 1.47 (s, 9 H, *t*-Bu).

Similarly, **12b** (196 mg, 0.31 mmol) was converted into **13b** (113 mg, 100%), isolated as a white powder; mp 71–72°C; $[\alpha]_D^{20}$ −8° (*c* 1.0, $CHCl_3$). *Anal.* Calcd for $C_{15}H_{31}NO_9$: C, 48.77; H, 8.46; N, 3.79. Found: **13a**, C, 48.79; H, 8.07; N, 3.79; **13b**, C, 48.89; H, 8.02; N, 3.98.

(+)-1-Deoxy- (**3a**) *and (−)-1-deoxy-nojirimycin-1-sulfonic acid* (**3b**).—A suspension of **13a** (162 mg, 0.44 mmol) in water (2.3 mL) was saturated with sulfur dioxide at ambient temperature, and stirred at 40°C for 2 days. White precipitates were collected by filtration and washed with MeOH. The mother liquor was treated with sulfur dioxide again to afford **3a** (62 mg, 58%); mp 133–140°C (dec); $[\alpha]_D^{20}$ 0° (*c* 1.0, H_2O). ^1H NMR data (270 MHz, D_2O; acetone as internal standard at 2.05 ppm): δ 4.08 (d, 1 H, $J_{1,2}$ 10.6 Hz, H-1), 3.89 (dd, 1 H, $J_{5,6}$ 3.1, J_{gem} 12.0 Hz, H-6), 3.82 (dd, 1 H, $J_{5,6'}$ 4.4 Hz, H-6′), 3.81 (dd, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 3.60 (dd, 1 H, $J_{3,4}$ 9.2, $J_{4,5}$ 10.6 Hz, H-4), 3.47 (dd, 1 H, H-3), 3.17 (ddd, 1 H, H-5). ^{13}C NMR data (100 MHz, D_2O; acetone as internal standard at 30.5 ppm): δ 76.14, 70.62, 69.58, 67.36, 60.36, 57.62.

Similarly, the enantiomer **3b** was obtained from **13b** (247 mg, 0.67 mmol); yield, 110 mg (72%); mp 133–140°C; $[\alpha]_D^{20}$ ~0° (*c* 1.0, H_2O).

The IR and the ^1H and ^{13}C NMR spectra of compounds **3a** and **3b** were superimposable on those of an authentic sample. *Anal.* Calcd for $C_6H_{13}NO_7S \cdot 0.5H_2O$: C, 28.61; H, 5.59; N, 5.56. Found: **3a**, C, 28.01; H, 5.81; N, 5.12; **3b**, C, 28.78; H, 5.39; N, 5.63.

(+)-(**1a**) *and (−)-Nojirimycin* (**1b**).—A solution of **3a** (21 mg, 0.081 mmol) in water (0.7 mL) was charged on a short column of Dowex 1-X2 (HO^-) resin (7 mL) and the column was eluted with water (200 mL). The eluent was lyophilized to give **1a** (5.8 mg, 40%) as a white powder; $[\alpha]_D^{23}$ +74° (*c* 0.3, H_2O; after 30 h).

Similarly, the enantiomer **1b** was obtained from **3b** (28 mg, 0.12 mmol); yield, 7.8 mg (38%); $[\alpha]_D^{20}$ −74° (*c* 0.4, H_2O; after 24 h).

(+)-(**2a**) *and (−)-1-Deoxynojirimycin* (**2b**).—A mixture of **3a** (30 mg, 0.17 mmol) and barium hydroxide octahydrate (52 mg, 0.17 mmol) in water (1 mL) was hydrogenolyzed in the presence of Raney-Ni (W-4, ~30 mg) under an atmospheric pressure of H_2 at room temperature for 8 h. The insoluble materials were

removed by filtration and the filtrate was concentrated. The residue was purified by a column of Amberlite IR-120B (H^+) resin (3 mL) with water and M aq NH_4OH as eluent, to give **2a** (15 mg, 53%) as plates; mp 196–198.5°C (lit.[10a] 196°C); $[\alpha]_D^{22}$ +53° (*c* 0.19, H_2O) {lit.[10a] $[\alpha]_D^{21}$ +47° (H_2O)}. ^1H NMR data (270 MHz, D_2O; acetone as internal standard at 2.05 ppm): δ 3.63 (dd, 1 H, $J_{5,6}$ 2.9, $J_{6,6'}$ 11.7 Hz, H-6), 3.42 (dd, 1 H, $J_{5,6'}$ 6.2, H-6′), 3.29 (ddd, 1 H, $J_{1e,2}$ 5.1, $J_{1a,2}$ 10.6, $J_{2,3}$ 9.2 Hz, H-2), 3.12 (dd, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 3.03 (dd, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 2.91 (dd, 1 H, $J_{1a,1e}$ 12.5 Hz, H-1e), 2.34 (ddd, 1 H, H-5), 2.26 (dd, 1 H, H-1a). ^{13}C-NMR data (100 MHz), D_2O; dioxane as internal standard at 67.4 ppm) δ 79.18, 72.30, 71.66, 62.16, 61.27, 49.46.

Similarly, the enantiomer **2b** was obtained from **3b** (110 mg, 0.48 mmol); yield 54 mg (69%); mp 199.5–201.5°C; $[\alpha]_D^{22}$ −47° (*c* 0.27, H_2O).

The IR and the ^1H and ^{13}C NMR spectra of compounds **2a** and **2b** were superimposable on those of an authentic sample.

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