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SYNTHESIS OF 3-*O*-ACETYL-2,6-DIAZIDO-4-*O*-BENZYL-2,6-DIDEOXY-L-IDOPYRANOSYL CHLORIDE, A GLYCOSYL HALIDE FOR THE SYNTHESIS OF NEOMYCIN B*

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ABSTRACT

3-*O*-Acetyl-2,6-diazido-4-*O*-benzyl-2,6-dideoxy-L-idopyranosyl chloride, a glycosyl halide useful for the synthesis of neomycin B, has been prepared from D-glucose. Key steps in this synthesis are the introduction of two azido groups at C-5 and -1 (after reduction) of the D-glucose structure, followed by oxidation at C-6 to give a head-to-tail inverted compound, 2,6-diazido-4-*O*-benzyl-2,6-dideoxy-L-idopyranose (**10**). The structure of **10** was confirmed by conversion into neosamine B, and its methyl α-L- (**16**) and β-L-glycosides (**17**). The anomeric configuration of **16** and **17** is discussed.

INTRODUCTION

Neomycin is a useful aminoglycoside antibiotic discovered independently by Umezawa *et al.*[1] and Waksman *et al.*[2]. Neomycin consists of three components, neomycin A, B, and C, and the absolute configuration was determined by Rinehart and assoc.[3,4]. Neomycin A (neamine) had first been synthesized from the components[5] or through paromamine by S. Umezawa *et al.*[6–9]. The total synthesis[10,11] of neomycin C was also achieved in this laboratory. In the case of neomycin B, the major component of neomycin complex, however, the synthesis of a protected 2,6-diamino-2,6-dideoxy-L-idosyl halide for β-L-glycosylation of the residual pseudotrisaccharide portion of neomycin B presents a major obstacle[12]. Although, the synthesis of several protected derivatives of neosamine B (2,6-diamino-2,6-dideoxy-L-idose, paromose) has been reported[13,14], none of the synthetic intermediates reported could be used for our present synthesis because of the presence of *N*-acyl protecting groups that will participate to form 1,2-*trans*-glycosides. This paper describes the synthesis of a protected 2,6-diazido-2,6-dideoxy-L-idopyranosyl chloride usable for the synthesis of neomycin B. The azido group

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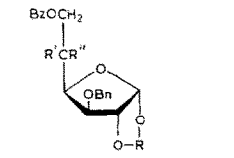
does not exhibit any neighboring group effect, is readily convertible into an amino group, and is stable in the glycosylation reaction.

The characteristic points of this synthesis are: (a) Introduction of the first azido group to C-5 (which corresponds to C-2 of the final product) of a D-glucofuranose derivative (**1**) with inversion of configuration; (b) reduction of the reducing group followed by introduction of the second azido group at that position (which corresponds to C-6 of the final product); and (c) oxidation at C-6 of the resulting L-iditol derivative (**9**) to obtain the head-to-tail inversion that gives the L-idose derivative (**10**) having two azido groups at C-2 and -6.

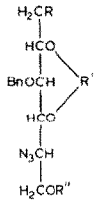
RESULTS AND DISCUSSION

The OH-5 group of 6-*O*-benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[15] (**1**) was treated with trifluoromethanesulfonic anhydride in pyridine–1,2-dichloroethane (1 h, 0°), and the resulting unstable triflate immediately treated with sodium azide in *N,N*-dimethylformamide (1 h, 70°) to give 5-azido-5-deoxy-L-idofuranose derivative (**2**) in high yield. When **1** was *p*-toluenesulfonylated, a higher temperature (60°) and a longer reaction period (20 h) were necessary to complete the reaction, and subsequent substitution by an azido group also required a higher temperature and longer reaction period (100°, 3 days). Acid-catalyzed deisopropylidenation of **2** gave crystalline, free sugar **3** as a mixture of anomers. The free sugar was carefully reduced with sodium borohydride, without reducing the azido group, to give the L-iditol derivative **4** in high yield. The primary hydroxyl group of **4** was then selectively protected. Among the procedures tested, silylation with *tert*-butylchlorodimethylsilane in pyridine–1,2-dichloroethane gave the best result, giving the 1-*O*-silyl ether **5** in 90% yield. Acid-catalyzed isopropylidenation of the 2,4-diol**5** with 2,2-dimethoxypropane in 1,2-dichloroethane gave the 2,4-*O*-isopropylidene derivative **6**. Desilylation with tetrabutylammonium fluoride in oxolane gave crystalline **7**. The free primary hydroxyl group of **7** was then triflated, and the unstable product was treated, without isolation, with azide ion to give the 1,5-diazido derivative **8** in high yield. When the 1-*O*-tosyl derivative prepared from **7** was treated in a manner similar to that just described, a higher temperature and a longer reaction period (120°, 10 h) than those used for the triflate derivative (room temp., 30 min) were required to complete the reaction. Debenzoylation of **8** with methanolic sodium methoxide gave **9**, and subsequent oxidation of the free hydroxyl group by the Pfitzner–Moffatt method[16] gave an aldehyde, that, without isolation, was deisopropylidenated under acidic conditions to give crystalline 2,6-diazido-4-*O*-benzyl-2,6-dideoxy-L-idopyranose (**10**) as a mixture of anomers (72%).

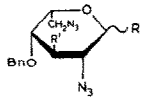
The structure of **10** was confirmed by conversion into 2,6-diamino-2,6-dideoxy-L-idose (neosamine B). Hydrogenation of **10** in the presence of palladium black, followed by purification by ion-exchange-resin chromatography to remove a slight L-iditol impurity gave neosamine B dihydrochloride. As this salt was



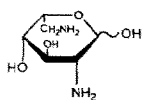
1 R = CMe_2, R′ = OH, R″ = H
2 R = CMe_2, R′ = H, R″ = N_3
3 R = H, H, R′ = H, R″ = N_3



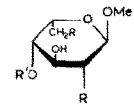
4 R = OH, R′ = H, H, R″ = Bz
5 R = $OSiMe_2(CMe_3)$, R′ = H, H, R″ = Bz
6 R = $OSiMe_2(CMe_3)$, R′ = CMe_2, R″ = Bz
7 R = OH, R′ = CMe_2, R″ = Bz
8 R = N_3, R′ = CMe_2, R″ = Bz
9 R = N_3, R′ = CMe_2, R″ = H



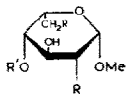
10 R = R′ = OH
11 R = R′ = OAc
12 R = Cl, R′ = OAc



13



14 R = N_3, R′ = Bn
16 R = NH_2, R′ = H



15 R = N_3, R′ = Bn
17 R = NH_2, R′ = H

Bz = PhCO
Bn = $PhCH_2$

strongly hygroscopic and inadequate for identification, it was converted into the crystalline dipicrate according to the procedure of Rinehart *et al.*[17]. An authentic sample of neosamine B dipicrate was also obtained from the hydrolyzate of lividomycin B according to the procedure of Oda *et al.*[18]. The two dipicrates gave identical m.p., specific rotation, and i.r. and ^{1}H-n.m.r. spectra. Further confirmation was obtained by converting **10** to methyl 2,6-diamino-2,6-dideoxy-α-L- (**16**) and -β-L-idopyranosides (**17**) by acid-catalyzed glycosylation of **10** in methanol, followed by hydrogenation. Authentic samples of **16** and **17** were obtained[19] from *N*-acetyllividomycin B by methanolysis in the presence of a strongly acidic resin. The specific rotations and the ^{1}H-n.m.r. spectra of synthetic **16** and **17** were identical with those of the authentic samples.

Since the idoside derivatives showed similar, small coupling-constants ($J_{1,2}$) of H-1 in the ^{1}H-n.m.r. spectra, their anomeric configurations could not be determined on the basis of the shift and J values as for α- and β-D-glucopyranosides. Therefore, they were determined on the basis of the specific rotations. Specific rotations of methyl α- and β-D-idopyranoside were reported as +101 and +103.3° (water)[20,21], and −49.2 and −40.8° (water)[20,22], respectively. The corresponding values observed for **16** and **17** were −89° (water) and +51° (water), respectively. It was assumed that the specific rotation is not much influenced by replacement of a hydroxyl with an amino group, and the α- and β-L configuration was assigned to **16** and **17**, respectively.

In the study of the conformation of **16** and **17**, it was observed that the latter compound (as the base) gave small J values ($J_{1,2}$, $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ 2–3.5 Hz) and a long-range coupling ($J_{2,4}$ ~1 Hz), indicating the favored conformation as $^1C_4$(L), a conformation having all axial substituents at C-2,3, and 4. The coupling constants of the α-L anomer **16** (as the base), on the other hand, showed 6–6.5 Hz with respect to $J_{2,3}$ and $J_{3,4}$, and $J_{2,4}$ was scarcely observed, indicating that **16** has a time-averaged conformation between the two chair forms, $^1C_4$(L) and $^4C_1$(L), with approximately equal contributions. These results correspond to those reported by Perlin *et al.*[20] for methyl α- and β-D-idopyranosiduronic acid. Incidentally, the ^{1}H-n.m.r. spectrum of neosamine B dipicrate in deuterium oxide solution showed the presence of three anomers [probably two pyranose (**13**) and one furanose] in the ratios of 8:1:1, the major anomer being suggested to have the β-L-pyranose form with an $^1C_4$(L) conformation (see Experimental section).

The ^{13}C-n.m.r. spectra of **16** and **17** for solutions in 20% ($^2H_3$)ammonia in deuterium oxide gave further information on the anomeric configurations. The signal of OCH_3 (δ 56.4) of the α-L anomer **16** appeared at a 0.9-p.p.m. higher field than that (δ 57.3) of the β-L anomer **17**. Since it was reported[23] that the signals for axially oriented OMe carbon atoms of methyl glycosides appear at a field higher by 1.5–2 p.p.m. than that of equatorially oriented carbon atoms, the aforementioned chemical-shift data indicate that the methoxyl group of **16** is more axially oriented than that of **17**, which is consistent with the results of the ^{1}H-n.m.r. spectra.

In order to obtain the protected 2,6-diazido-2,6-dideoxyidosyl chloride **12**, the free sugar **10** was acetylated, and the resulting 1,3-diacetate **11** was treated with hydrogen chloride in ether to give 3-*O*-acetyl-2,6-diazido-4-*O*-benzyl-2,6-dideoxy-L-idopyranosyl chloride (**12**), in 80% yield. When hydrogen bromide in ether was used instead of hydrogen chloride for the formation of the glycosyl halide, the azido group was displaced by a bromo group[11,24] to give a complex mixture. Treatment of **11** with titanium tetrabromide in 1,2-dichloroethane also gave a similar result.

EXPERIMENTAL

General methods. — Melting points were determined with a Kofler block and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 241 polarimeter. T.l.c was performed, unless stated otherwise, on Merck Kieselgel 60 plates, and spots were detected with a spray of 50% sulfuric acid, followed by heating. When t.l.c. was performed on Avicel SF (Funakoshi), components were detected by spraying the plates with 0.25% ninhydrin in pyridine and subsequent heating. For silica gel column chromatography, Wakogel C-200 was used. I.r. spectra were recorded with a JASCO A-202 grating spectrophotometer. ^{1}H-N.m.r. spectra were recorded, unless otherwise stated, at 250 MHz in the Fourier-transform mode with a Bruker WM-250 spectrometer. Spectra at 90 MHz were recorded with a Varian EM-390 spectrometer. The shift values were calculated from an in-

ternal reference (in both $CDCl_3$ and D_2O) of tetramethylsilane (Me_4Si) and determined by the decoupling method, except for easily assigned shifts. ^{13}C-N.m.r. spectra were recorded, in the Fourier-transform mode, with a Bruker WM-250 spectrometer operating at 62.9 MHz, and the shift values were calculated downfield from the signal of Me_4Si as $\delta(Me_4Si) = \delta(1,4\text{-dioxane}) + 67.4$.

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**2**). — To an ice-cold mixture of 6-*O*-benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[15] (**1**; 13.94 g) in dry pyridine (13 mL) and dry 1,2-dichloroethane (55 mL) was added trifluoromethanesulfonic anhydride (6.7 mL), and the solution was kept for 1 h at 0°. Methanol (0.2 mL) was added, followed by chloroform (150 mL) after 5 min, and the solution was successively washed with cold 10% aqueous potassium hydrogensulfate, saturated aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated to give an unstable 5-triflate as a syrup [18.74 g; t.l.c. (10:1 toluene–ethyl acetate) R_F 0.6; compound **1** R_F 0.2], which was dried for 30 min *in vacuo*. A mixture of the syrup and sodium azide (6.5 g) in *N,N*-dimethylformamide (110 mL) was stirred for 1 h at 70°. T.l.c. (in the same solvent system as just given) showed one major spot (R_F 0.5). After concentration, the mixture was extracted with toluene (300 mL), and the extracts were combined, washed with water, dried (sodium sulfate), and evaporated. The residue was chromatographed on a column of silica gel with 30:1 toluene–ethyl acetate to remove slight impurities, and the fractions containing the major product were collected and evaporated to give **2** as a syrup (yield 11.47 g; 78%, based on **1**). The syrup contained ~1% of impurity which had an R_F value close to that of **2** (R_F 0.53 in 10:1, v/v, toluene–ethyl acetate) and was detected on a t.l.c. plate by exposure to iodine vapor but not by spraying with 50% sulfuric acid. An analytical sample was obtained as a syrup from the latter part of the fractions; $[\alpha]_D^{24}$ −41° (*c* 1, chloroform); ν_{max}^{film} 2100 (N_3) and 1725 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.35 and 1.51 (each s, 3 H, CMe), 3.97 (d, 1 H, H-3), 4.14 (ddd, 1 H, H-5), 4.24 (dd, 1 H, H-6), 4.30 (dd, 1 H, H-4), 4.33 (dd, 1 H, H-6′), 4.60 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 4.68 (d, 1 H, H-2), 6.00 (d, 1 H, H-1), 7.34 (5 H, $CH_2C_6H_5$), and 7.47, 7.61, and 8.06 (2, 1, and 2 H, resp.; COC_6H_5); $J_{1,2}$ 4, $J_{2,3}$ 0, $J_{3,4}$ 3.5, $J_{4,5}$ 9, $J_{5,6}$ 6.5, $J_{5,6'}$ 3, and $J_{6,6'}$ 11 Hz.

Anal. Calc. for $C_{23}H_{25}N_3O_6$: C, 62.86; H, 5.73; N, 9.56. Found: C, 62.85; H, 5.78; N, 9.56.

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-5-deoxy-*L*-idofuranose* (**3**). — A solution of **2** (11.40 g) in 1,4-dioxane (250 mL)–M aqueous sulfuric acid (90 mL) was kept for 5 h at 80°. T.l.c. (2:1, v/v, toluene–ethyl acetate) showed one major product (R_F 0.25). Chloroform (300 mL) was added, and the lower layer successively washed with 10% aqueous sodium carbonate and 10% aqueous sodium chloride, dried (sodium sulfate), and evaporated. Purification of the syrupy residue by passing through a short column of silica gel with the aforementioned solvent system gave **3** as a syrup that crystallized spontaneously after 1 day, yield 9.67 g (93%). It was recrystallized from chloroform–hexane; m.p. 76–79°, $[\alpha]_D^{23}$ +34 (5 min)→ +31° (45

h) (*c* 0.8, chloroform); ν_{max}^{KBr} 2125, 2100 (shoulder), and 1720 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.80 (broad, 1 H, OH), 2.53 and 2.97 (each broad, 0.25 and 0.75 H, resp., OH), 4.67 and 4.69 (each AB q, 0.5 and 1.5 H, resp., *J* 11.5 Hz, $CH_2C_6H_5$), 5.20 (broad s, 0.25 H, H-1 of α-L anomer), 5.55 (d, 0.75 H, *J* 4 Hz, H-1 of β-L anomer), 7.35 (5 H, $CH_2C_6H_5$), and 7.47, 7.60, and 8.05 (2, 1, and 2 H, resp.; COC_6H_5).

Anal. Calc. for $C_{20}H_{21}N_3O_6$: C, 60.14; H, 5.30; N, 10.52. Found: C, 59.97; H, 5.38; N, 10.36

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-5-deoxy-*L*-iditol* (**4**). — A mixture of **3** (9.67 g) and sodium borohydride (1.87 g) in dry 1,2-dimethoxyethane (200 mL) was stirred for 1 h at 0°. After addition of 2M aqueous hydrochloric acid (25 mL), followed by sodium chloride (2 g), the mixture was extracted with chloroform (200 mL). The organic layer was washed with 10% aqeous sodium chloride, dried (sodium sulfate), and evaporated to a syrup, which showed a major spot (R_F 0.2) on t.l.c. in 1:1 toluene–ethyl acetate, and was purified by silica gel column-chromatography with the same solvent system to give **4** as a syrup, yield 7.86 g (81%); $[\alpha]_D^{23}$ −14° (*c* 0.6, chloroform); ν_{max}^{film} 2120 and 1720 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.64 (broad s, 1 H), 2.86 (broad d, 1 H, *J* ~6 Hz) and 3.04 (d, 1 H, *J* 6.5 Hz) (each disappeared on deuteration, OH), 3.66 (m, collapsed to dd on deuteration, 1 H, H-1), 3.69 (t, 1 H, H-3), 3.77 (m, collapsed to dd on deuteration, 1 H, H-1′), 3.87 (dt, 1 H, H-5), ~3.88 (m, 1 H, H-2), 3.97 (m, collapsed to t on deuteration, 1 H, H-4), 4.42 (dd, 1 H, H-6), 4.59 (dd, 1 H, H-6′), 4.62 (s, 2 H, $CH_2C_6H_5$), 7.36 (5 H, $CH_2C_6H_5$), and 7.46, 7.59, and 8.04 (2, 1, and 2 H, resp.; COC_6H_5), $J_{1,2}$ 4, $J_{1',2}$ 5, $J_{1,1'}$ 11.5, $J_{2,3} = J_{3,4}$ 4 or 4.5, and $J_{4,5}$ 4.5 or 4, $J_{5,6}$ 8, $J_{5,6'}$ 4, and $J_{6,6'}$ 11.5 Hz.

Anal. Calc. for $C_{20}H_{23}N_3O_6$: C, 59.84; H, 5.77; N, 10.47. Found: C, 59.66; H, 5.91; N, 10.39.

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-1-*O*-tert-butyldimethylsilyl-5-deoxy-*L*-iditol* (**5**). — To a solution of **4** (8.83 g) in 1,2-dichloroethane (40 mL)–pyridine (7.7 mL) was added a solution of *tert*-butylchlorodimethylsilane (3.65 g) in 1,2-dichloroethane (30 mL), and the mixture was kept for 17 h at 37°. T.l.c. (5:1 toluene–ethyl acetate) then showed one major product (R_f 0.3). Methanol (0.2 mL) was added, followed by chloroform (150 mL) after 1 h, and the solution was successively washed with 10% aqueous potassium hydrogensulfate, saturated aqueous sodium hydrogencarbonate, and 10% aqueous sodium chloride, dried (sodium sulfate), and evaporated. The resulting syrup was purified by passing through a short column of silica gel with the aforementioned solvent system to give **5** as a syrup that crystallized spontaneously after 2 days, yield 10.25 g (90%); m.p. 54.5–55.5° (hexane), $[\alpha]_D^{22}$ −19° (*c* 0.8, chloroform); ν_{max}^{KBr} 2130, 2100, and 1730 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 0.08 (s, 6 H, $SiMe_2$), 0.92 (s, 9 H, $SiCMe_3$), 2.47 (d, 1 H, *J* 5.5 Hz, OH-4; disappeared on deuteration), 2.77 (d, 1 H, *J* 5 Hz, OH-2; disappeared on deuteration), 3.66 (dd, 1 H, H-1), 3.73 (dd, 1 H, H-1′), 3.79 (dd, 1 H, H-3), 3.86 (m, collapsed to dt on deuteration, 1 H, H-2), 3.88 (dt, 1 H, H-5), 3.97 (dt, collapsed to dd on deuteration, 1 H, H-4), 4.48 (dd, 1 H, H-6), 4.61 (dd, 1 H,

H-6'), 4.75 (AB q, 2 H, *J* 11 Hz, $CH_2C_6H_5$), 7.36 (5 H, $CH_2C_6H_5$), and 7.45, 7.57, and 8.05 (2, 1, and 2 H resp.; COC_6H_5), $J_{1,2} = J_{1',2}$ 6, $J_{1,1'}$ 10, $J_{2,3}$ 3, $J_{3,4}$ 5.5, $J_{4,5} = J_{5,6'}$ 4, $J_{5,6}$ 8, and $J_{6,6'}$ 11.5 Hz.

Anal. Calc. for $C_{26}H_{37}N_3O_6Si$: C, 60.56; H, 7.23; N, 8.15. Found: C, 60.73; H, 7.22; N, 8.23.

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-1-*O*-tert-butyldimethylsilyl-5-deoxy-2,4-*O*-isopropylidene-*L*-iditol* (**6**). — A solution of **5** (10.11 g) in 1,2-dichloroethane (200 mL) containing pyridinium *p*-toluenesulfonate (520 mg) and 2,2-dimethoxypropane (9.6 mL) was kept for 2 h at 60°. T.l.c. (5:1 toluene–ethyl acetate) indicated conversion into a single product having R_F 0.8. The solution was washed with water, dried (sodium sulfate), and evaporated to give **6** as a syrup, yield 10.74 g (99%); $[\alpha]_D^{25}$ −13° (*c* 1.1, chloroform); ν_{max}^{film} 2110 and 1725 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 0.076 and 0.082 (each s, 3 H, SiMe), 0.91 (s, 9 H, $SiCMe_3$), 1.49 (s, 6 H, CMe_2), 3.53 (incomplete t, 1 H, H-3), 3.69 (dd, 1 H, H-1), 3.84 (t, 1 H, H-1'), 3.92 (ddd, 1 H, H-2), 3.92–3.97 (X part of ABX system, 1 H, H-5), 4.01 (dd, 1 H, H-4), 4.06–4.10 (AB part of ABX system, 2 H, H-6,6'), 4.80 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 7.20–7.44 (5 H, $CH_2C_6H_5$), and 7.48, 7.59, and 8.02 (2, 1, and 2 H, resp.; COC_6H_5), $J_{1,2}$ 4.5, $J_{1',2} = J_{1,1'}$ 9, $J_{2,3} = J_{3,4}$ 1.5, and $J_{4,5}$ 8.5 Hz.

Anal. Calc. for $C_{29}H_{41}N_3O_6Si$: C, 62.67; H, 7.44; N, 7.56. Found: C, 62.50; H, 7.49; N, 7.85.

*5-Azido-6-*O*-benzoyl-3-*O*-benzyl-5-deoxy-2,4-*O*-isopropylidene-*L*-iditol* (**7**). — To an ice-cold solution of **6** (10.40 g) in oxolane (100 mL) was added a M solution of tetrabutylammonium fluoride in oxolane (21 mL), and the solution kept for 1 h at 0°. T.l.c. (2:1 toluene–ethyl acetate) showed one major product (R_F 0.3). The solution was concentrated to ~20 mL, chloroform (200 mL) added, and the solution washed with water, dried (sodium sulfate), and evaporated. The residue was purified by silica gel column-chromatography with the aforementioned solvent system to give **7** as a syrup that crystallized on being kept at room temperature, yield 7.16 g (87%); m.p. 93–94° (ether–hexane), $[\alpha]_D^{24}$ −14° (*c* 1, chloroform); ν_{max}^{KBr} 2100 and 1720 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.50 and 1.52 (each s, 3 H, CMe), 1.85 (dd, 1 H, OH), 3.48 (t, 1 H, H-3), 3.72 (ddd, 1 H, H-1), 3.84 (ddd, 1 H, H-1'), 3.96 (ddd, 1 H, H-5), 4.00 (ddd, 1 H, H-2), 4.06 (dd, 1 H, H-4), 4.16 (dd, 1 H, H-6), 4.25 (dd, 1 H, H-6'), 4.73 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 7.24–7.44 (5 H, $CH_2C_6H_5$), and 7.47, 7.60, and 8.03 (2, 1, and 2 H, resp.; COC_6H_5), $J_{1,2}$ 5.5, $J_{1',2}$ 7, $J_{1,OH}$ 8, $J_{1',OH}$ 3.5, $J_{1,1'}$ 11, $J_{2,3} = J_{3,4}$ 1.5, $J_{4,5}$ 8.5, $J_{5,6}$ 5.5, $J_{5,6'}$ 3, and $J_{6,6'}$ 12 Hz.

Anal. Calc. for $C_{23}H_{27}N_3O_6$: C, 62.57; H, 6.17; N, 9.52. Found: C, 62.44; H, 6.15; N, 9.42.

*1,5-Diazido-6-*O*-benzoyl-3-*O*-benzyl-1,5-dideoxy-2,4-*O*-isopropylidene-*L*-iditol* (**8**). — To an ice-cold mixture of **7** (7.16 g) in dry 1,2-dichloroethane (70 mL) and dry pyridine (6.3 mL) was added trifluoromethanesulfonic anhydride (3.3 mL), and the solution was kept for 15 min at 0°. Methanol (0.2 mL) was added, followed by chloroform (150 mL), and the solution was successively washed with cold 10%

aqueous potassium hydrogensulfate, saturated aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated to give an unstable 1-triflate as a syrup (t.l.c. in 5:1 toluene–ethyl acetate: R_F 0.7). A mixture of the syrup, dried for 20 min *in vacuo*, and sodium azide (3.1 g) in *N,N*-dimethylformamide (70 ml) was stirred for 30 min at room temperature. After concentration, toluene (200 mL) was added, and the mixture was washed with water, dried (sodium sulfate), and evaporated to give a brown syrup which was chromatographed on a column of silica gel with 30:1 toluene–ethyl acetate. The fractions containing the main product (**8**; t.l.c. in the aforementioned solvent system: R_F 0.3) were collected and evaporated to give **8** as a syrup (yield 6.91, 91%) which contained ~2% of an impurity having R_F 0.4 and was detected clearly on a t.l.c. plate by exposure to iodine vapor. An analytical sample was obtained as a syrup by chromatography in a column of silica gel with 20:1 carbon tetrachloride–ethyl acetate; $[\alpha]_D^{24}$ −2° (*c* 1, chloroform); ν_{max}^{film} 2100 and 1725 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.51 and 1.52 (each s. 3 H, CMe), 3.27 (dd, 1 H, H-1), 3.43 (t, 1 H, H-3), 3.57 (dd, 1 H, H-1′), 3.94 (ddd, 1 H, H-5), 4.02 (ddd, 1 H, H-2), 4.06 (dd, 1 H, H-4), 4.21 (dd, 1 H, H-6), 4.30 (dd, 1 H, H-6′), 4.74 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 7.26–7.42 (5 H, $CH_2C_6H_5$), and 7.48, 7.61, and 8.03 (2, 1, and 2 H resp.; COC_6H_5), $J_{1,2}$ 6, $J_{1',2}$ 7, $J_{1,1'}$ 12, $J_{2,3} = J_{3,4}$ 1.5, $J_{4,5}$ 8, $J_{5,6}$ 5.5, $J_{5,6'}$ 3, and $J_{6,6'}$ 12 Hz.

Anal. Calc for $C_{23}H_{26}N_6O_5$: C, 59.22; H, 5.62; N, 18.01. Found: C, 59.34; H, 5.62; N, 18.21.

*1,5-Diazido-3-*O*-benzyl-1,5-dideoxy-2,4-*O*-isopropylidene-*L*-iditol* (**9**). — To a solution of **8** (6.81 g) in dry methanol (70 mL) was added 2M sodium methoxide in methanol (0.4 mL), and the solution was kept for 2 h at room temperature. Neutralization with carbon dioxide followed by concentration gave a syrup which was extracted with chloroform. The solution was washed with water, dried (sodium sulfate), and evaporated to give a syrup that was passed through a short column of silica gel with 5:1 toluene–ethyl acetate to give **9** as a syrup, yield 5.03 g (95%); $[\alpha]_D^{25}$ +14° (*c* 1, chloroform); ν_{max}^{film} 2100 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.52 (s, 6 H, CMe_2), 1.89 (dd. 1 H, OH), 3.31 (dd, 1 H, H-1), 3.33 (ddd, 1 H, H-6), 3.40 (t, 1 H, H-3), 3.54 (ddd, 1 H, H-6′), 3.58 (dd, 1 H, H-1′), 3.75 (ddd, 1 H, H-5), 4.04 (ddd, 1 H, H-2), 4.10 (dd, 1 H, H-4), 4.72 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), and 7.37 (5 H, $CH_2C_6H_5$), $J_{1,2}$ 6, $J_{1',2}$ 7.5, $J_{1,1'}$ 12, $J_{2,3} = J_{3,4}$ 1.5, $J_{4,5}$ 8.5, $J_{5,6}$ 4.5, $J_{5,6'}$ 3, $J_{6,OH}$ 7.5, $J_{6',OH}$ 5, and $J_{6,6'}$ 11.5 Hz.

Anal. Calc for $C_{16}H_{22}N_6O_4$: C, 53.03; H, 6.12; N, 23.19. Found: C, 53.17; H, 6.14; N, 23.03.

*2,6-Diazido-4-*O*-benzyl-2,6-dideoxy-*L*-idopyranose* (**10**). — To a mixture of **9** (5.15 g), pyridine (0.57 mL), and pyridinium trifluoroacetate (1.37 g) in dry dimethyl sulfoxide (16 mL) was added a solution of dicyclohexylcarbodiimide (8.89 g) in benzene (50 mL), and the mixture was kept for 1 h at room temperature. T.l.c. (5:1 toluene–ethyl acetate) then showed one major spot having R_F 0.6 (*cf.* **9**: R_F 0.2). The mixture was poured into a solution of oxalic acid dihydrate (3.6 g) in 1,4-dioxane (15 mL), and the resulting precipitate filtered off. Benzene (200 mL)

was added to the filtrate, which was successively washed with a large amount of water, and 10% aqueous sodium chloride, dried (sodium sulfate), and evaporated to give an unstable aldehyde as a syrup. The ^{1}H-n.m.r. spectrum (90 MHz, in $CDCl_3$) of this syrup showed a singlet at δ 9.85 for an aldehyde proton. A mixture of the syrup in 80mM sulfuric acid in 1:5.5 water–1,4-dioxane (65 mL) was heated for 1.5 h at 70°. Neutralization with sodium hydrogencarbonate, followed by evaporation gave a residue that was extracted with chloroform. The solution was washed successively with saturated aqueous sodium hydrogencarbonate and 10% aqueous sodium chloride, dried (sodium sulfate), and evaporated. The syrupy residue was chromatographed on a column of silica gel with 3:1 toluene–ethyl acetate to give **10** as a syrup that crystallized spontaneously after 3 days, yield 3.3 g (72%); m.p. 91–95° (chloroform–hexane), $[\alpha]_D^{23}$ −10 (10 min)→ −15° (100 h) (*c* 0.7, chloroform); ν_{max}^{KBr} 2100 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$–D_2O) of major anomer: δ 3.27 (dd, 0.65 H, H-6), 3.46 (dd, 0.65 H, H-2), 3.53 (dd, 0.65 H, H-4), 3.62 (dd, 0.65 H, H-6′), 3.91 (apparent t, 0.65 H, H-3), 4.28 (dt, 0.65 H, H-5), 4.64 (AB q, 1.3 H, *J* 12 Hz, CH_2C$_6$H$_5$), 5.04 (d, 0.65 H, H-1), and 7.36 (5 H, Ph of both anomers), $J_{1,2}$ 4.5, $J_{2,3}$ 6.5, $J_{3,4}$ 5.5, $J_{4,5} = J_{5,6}$ 4, $J_{5,6'}$ 9, and $J_{6,6'}$ 13 Hz; of minor anomer: δ 3.30 (dd, 0.35 H, H-6), 3.41 (dd, 0.35 H, H-4), 3.47 (dd, 0.35 H, H-2), 3.77 (dd, 0.35 H, H-6′), 4.06 (ddd, 0.35 H, H-5), 4.22 (apparent t, 0.35 H, H-3), 4.62 (AB q, 0.7 H, *J* 12 Hz, CH_2C$_6$H$_5$), and 5.17 (d, 0.35 H, H-1), $J_{1,2}$ 2.6, $J_{2,3}$ 5.5, $J_{3,4}$ 5.2, $J_{4,5}$ 3.6, $J_{5,6}$ 5, $J_{5,6'}$ 9, and $J_{6,6'}$ 13 Hz.

Anal. Calc. for $C_{13}H_{16}N_6O_4$: C, 48.75; H, 5.04; N, 26.24. Found: C, 48.58; H, 5.07; N, 25.97.

*1,3-Di-*O*-acetyl-2,6-diazido-4-*O*-benzyl-2,6-dideoxy-*L*-idopyranose* (**11**). — A solution of **10** (95 mg) in acetic anhydride (0.1 mL)–pyridine (0.5 mL) was kept for 2.5 h at room temperature. Usual processing gave **11** as a syrup, yield 114 mg (95%); $[\alpha]_D^{25}$ +12° (*c* 0.8, chloroform); ν_{max}^{film} 2100 and 1750 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.12, 2.13, and 2.19 (each s, 6 H in total, Ac of both anomers); major anomer: 3.23 (dd, 0.8 H, H-6), 3.52 (apparent t, 0.8 H, H-4), 3.61 (dd, 0.8 H, H-2), 3.64 (dd, 0.8 H, H-6′), 4.18 (ddd, 0.8 H, H-5), 4.66 (AB q, 1.6 H, *J* 11.5 Hz, CH_2C$_6$H$_5$), 5.24 (t, 0.8 H, H-3), and 6.06 (d, 0.8 H, H-1), $J_{1,2}$ 3.5, $J_{2,3} = J_{3,4}$ 4.5, $J_{4,5}$ 3, $J_{5,6}$ 5, $J_{5,6'}$ 8, and $J_{6,6'}$ 13 Hz; minor anomer: δ 3.23 (dd, 0.2 H, H-6), 3.40 (dd, 0.2 H, H-4), 3.57 (dd, 0.2 H, H-2), 3.70 (dd, 0.2 H, H-6′), 4.05 (ddd, 0.2 H, H-5), 4.67 (AB q, 0.4 H, *J* 11.5 Hz, CH_2C$_6$H$_5$), 5.40 (t, 0.2 H, H-3), and 6.09 (d, 0.2 H, H-1), $J_{1,2}$ 2.5, $J_{2,3} = J_{3,4}$ 4.5, $J_{4,5}$ 3, $J_{5,6}$ 5, $J_{5,6'}$ 8, and $J_{6,6'}$ 13 Hz.

Anal. Calc. for $C_{17}H_{20}N_6O_6$: C, 50.49; H, 4.99; N, 20.78. Found: C, 50.49; H, 5.02; N, 21.00.

*3-*O*-Acetyl-2,6-diazido-4-*O*-benzyl-2,6-dideoxy-*L*-idopyranosyl chloride* (**12**). — A solution of **11** (56 mg) in dry ether saturated with hydrogen chloride (2 mL) was kept overnight at room temperature. A small amount of pale brown gum had precipitated. T.l.c. (1,2-dichloroethane) of the solution then showed one major product having R_F 0.5. Evaporation gave a residue that was extracted with dichloromethane. The solution was, without delay, washed successively with cold

water, cold saturated aqueous sodium hydrogencarbonate, and cold water again, dried (sodium sulfate), and evaporated to give **12** as a pale brown syrup, yield 42 mg (80%); $[\alpha]_D^{21}$ −42° (*c* 0.9, chloroform); ν_{max}^{film} 2120 and 1750 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$) of major anomer: δ 2.14 (s, 2.6 H, Ac), 3.21 (dd, 0.85 H, H-6), 3.49 (m, 0.85 H, H-4), 3.64 (dd, 0.85 H, H-6'), 3.85 (ddd, 0.85 H, H-2), 4.38 (broad ddd, sharpened by irradiation at δ 6.08, 0.85 H, H-5), 4.67 (AB q, 1.7 H, *J* 11.5 Hz, $CH_2C_6H_5$), 5.22 (dt, 0.85 H, H-3), 6.08 (broad s, 0.85 H, H-1), and 7.36 (5 H, Ph of both anomers), $J_{1,2}$ 1.5, $J_{1,3}$ 1, $J_{2,3}$ 3, $J_{2,4} \leqq 1$, $J_{3,4}$ 3, $J_{4,5}$ 2, $J_{5,6}$ 5, $J_{5,6'}$ 7.5, and $J_{6,6'}$ 13 Hz; of minor anomer: δ 2.12 (s, 0.45 H, Ac), 3.22 (dd, 0.15 H, H-6), 3.39 (ddd, 0.15 H, H-4), 3.56 (ddd, 0.15 H, H-2), 3.78 (dd, 0.15 H, H-6'), 3.99 (ddd, 0.15 H, H-5), 4.69 (AB q, 0.3 H, *J* 12 Hz, $CH_2C_6H_5$), 5.44 (t, 0.15 H, H-3), and 5.79 (d, 0.15 H, H-1), $J_{1,2}$ 2, $J_{2,3}$ 4, $J_{2,4} \leqq 1$, $J_{3,4}$ 4, $J_{4,5}$ 2.5, $J_{5,6}$ 5, $J_{5,6'}$ 8, and $J_{6,6'}$ 13 Hz.

Anal. Calc. for $C_{15}H_{17}ClN_6O_4$: C, 47.31; H, 4.50; Cl, 9.31; N, 22.07. Found: C, 47.30; H, 4.52; Cl, 9.03; N, 21.80.

*2,6-Diamino-2,6-dideoxy-*L*-idose (neosamine B) (pyranose* **13** *and furanose) dipicrate.* — A solution of **10** (147 mg) in 1,4-dioxane (2 mL) containing 2M aqueous hydrochloric acid (0.5 mL) was hydrogenated in the presence of palladium black for 20 h under pressure of 0.3 MPa. The palladium black was replaced with fresh, and the reaction was continued for another 20 h. T.l.c. (6:4:3:1 1-butanol–pyridine–water–acetic acid; Avicel SF plate) showed a major (R_F 0.15) and a minor component (R_F 0.12). The major component could be detected by spraying the t.l.c. plate with a solution of silver nitrate in aqueous ammonia, but the latter not. The catalyst was filtered off, and the filtrate was evaporated with several additions of toluene to give a syrup that was dissolved in a small volume of methanol. Addition of acetone afforded a syrup (97 mg), which solidified. It was chromatographed on a column of Dowex 50W-X2 (H^+) resin (33 mL) with aqueous hydrochloric acid (0 to 1M, gradually changed). The fractions containing the major product were collected and evaporated to give a hygroscopic solid of neosamine B (as dihydrochloride); yield 64 mg (56%). The dihydrochloride was converted into the dipicrate according to the procedure reported by Rinehart *et al.*[17], m.p. 126–128° (dec.) [authentic sample obtained from lividomycin B according to the procedure reported by Oda *et al.*[18], 125.5–127.5° (dec.); lit.[18] 126–128° (dec.), lit.[17] 125–126.5°], $[\alpha]_D^{21}$ +7° (*c* 1, water) [authentic sample from lividomycin B, +7° (*c* 1, water); lit.[18] +8° (*c* 1, water), lit.[17] +13° (*c* 0.94, water)]; ν_{max}^{KBr} 3300 (broad), 3075, 1630, 1560, 1490. 1430, 1370, 1330, 1270, 1155, 1075, 1050, 935, 905, 795, 745, 710, 545, and 520 cm^{-1}; ^{1}H-n.m.r. (D_2O at 50°) of major anomer: δ 3.31–3.47 (m, 1.6 H, H-6,6'), 3.50 (ddd, 0.8 H, H-2), 3.84 (ddd, 0.8 H, H-4), 4.27 (t, 0.8 H, H-3), 4.32 (ddd, 0.8 H. H-5), 5.43 (d, 0.8 H, H-1), and 8.88 (s, 4 H, aromatic protons of all anomers), $J_{1,2}$ 2, $J_{2,3}$ 3.5, $J_{2,4}$ ~1, $J_{3,4}$ 3.5, $J_{4,5}$ 1.8, $J_{5,6}$ 4, and $J_{5,6'}$ 7.5 Hz; of one of the minor anomers: δ 3.88 (dd, 0.1 H, H-2), and 5.69 (d, 0.1 H, H-1), $J_{1,2}$ 5, and $J_{2,3}$ 7.5 Hz; and of another minor anomer: δ ~3.4 (0.1 H, H-2), 4.06 (broad t, 0.1 H, H-3), and 5.39 (broad d, 0.1 H, H-1), $J_{1,2}$ ~3, $J_{2,3}$ ~5, and $J_{3,4}$ ~5 Hz.

Anal. Calc. for $C_6H_{14}N_2O_4 \cdot 2C_6H_3N_3O_7 \cdot 0.5\ H_2O$: C, 33.50; H, 3.28; N, 17.36. Found: C, 33.40; H, 3.32; N, 17.28.

Methyl 2,6-diazido-4-O-benzyl-2,6-dideoxy-α-L-idopyranoside (**14**) *and methyl 2,6-diazido-4-O-benzyl-2,6-dideoxy-β-L-idopyranoside* (**15**). — A mixture of **10** (505 mg) and Amberlite CG-120 (H^+) cation-exchange resin (2.5 g; the water-swollen resin was washed thoroughly with methanol, kept in methanol for 1 day, and dried for 3 h at 60° *in vacuo*) in dry methanol (15 mL) was boiled for 2.5 h. T.l.c. (7:1 toluene–ethyl acetate) showed a major (R_F 0.4) and a minor component (R_F 0.25). The resin was filtered off, and the filtrate was evaporated to give a syrup that was chromatographed on a silica gel column in 12:1 toluene–ethyl acetate. Compound **14** was obtained as a syrup from the earlier fractions, yield 275 mg (52%); $[\alpha]_D^{23}$ −17° (*c* 0.9, chloroform); ν_{max}^{film} 2100 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.96 (d, 1 H, *J* 7 Hz, OH; disappeared on deuteration), 3.15 (dd, 1 H, H-6), 3.47–3.54 (m, 2 H, H-2,4), 3.50 (s, 3 H, OMe), 3.68 (dd, 1 H, H-6'), 3.95 (dddd; collapsed to broad t on deuteration, 1 H, H-3), 4.14 (apparent dt, 1 H, H-5), 4.66 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 4.72 (d, 1 H, H-1), and 7.36 (5 H, Ph); $J_{1,2}$ 3.5, $J_{1,3} \leqq 1$, $J_{2,3}$ and $J_{3,4}$ 5.5 or 4.5, $J_{4,5}$ 3.2, $J_{5,6}$ 3.8, $J_{5,6'}$ 8.5, and $J_{6,6'}$ 13.5 Hz.

Anal. Calc. for $C_{14}H_{18}N_6O_4$: C, 50.29; H, 5.43; N, 25.14. Found: C, 50.16; H, 5.43; N, 24.88.

Evaporation of the later fractions afforded compound **15** as crystals, yield 143 mg (27%); m.p. 98.5–100° (chloroform–hexane), $[\alpha]_D^{23}$ +59° (*c* 0.8, chloroform); ν_{max}^{KBr} 2120 and 2100 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.41 (d, 1 H, *J* 3 Hz, OH; disappeared on deuteration), 3.34 (dd, 1 H, H-2), 3.45 (dd, 1 H, H-6), 3.50 (dd, 1 H, H-4), 3.57 (s, 3 H, OMe), 3.75 (dd, 1 H, H-6'), 4.10 (dt, 1 H, H-5), 4.15 (dt, collapsed to t on deuteration, 1 H, H-3), 4.65 (AB q, 2 H, *J* 11.5 Hz, $CH_2C_6H_5$), 4.79 (d, 1 H, H-1), and 7.36 (5 H, Ph); $J_{1,2}$ 3, $J_{2,3} = J_{3,4}$ 7.5, $J_{4,5}$ 5, $J_{5,6}$ 4.5, $J_{5,6'}$ 9, and $J_{6,6'}$ 13 Hz.

Anal. Calc. for $C_{14}H_{18}N_6O_4$: C, 50.29; H, 5.43; N, 25.14. Found: C, 50.41; H, 5.44; N, 24.94.

Methyl 2,6-diamino-2,6-dideoxy-α-L-idopyranoside (**16**). — A solution of **14** (155 mg) in 1,4-dioxane (1.5 mL)–acetic acid (0.5 mL) was hydrogenated in the presence of palladium black for 4 h under a pressure of 0.3 MPa. T.l.c. (6:4:3:1 1-butanol–pyridine–water–acetic acid; Avicel SF plate) showed one major spot (R_F 0.15). Filtration followed by evaporation of the filtrate gave a syrup that was deposited onto a column of CM-Sephadex C-25 (NH_4^+). After washing with water, the column was developed with 0 to 0.1M aqueous ammonia. The fractions containing the major product were collected and freeze-dried to give a hygroscopic solid (as the 0.4 carbonate), yield 64 mg (64%); $[\alpha]_D^{23}$ −89° (*c* 1.7, water); ^{1}H-n.m.r. (20% ND_3 in D_2O): δ 2.75 (dd, sharpened by irradiation at δ 3.71, 1 H, H-2), 2.79 (dd, 1 H, H-6), 2.89 (dd, 1 H, H-6'), 3.45 (s, 3 H, OMe), 3.60 (apparent t, 1 H, H-3), 3.71 (dd, sharpened by irradiation of H-2, 1 H, H-4), 4.00 (apparent dt, 1 H, H-5), and 4.57 (d, 1 H, H-1), $J_{1,2}$ 4.5, $J_{2,3}$ 6.5, $J_{3,4}$ 6, $J_{4,5}$ 3.5, $J_{5,6}$ 4.5, $J_{5,6'}$ 9, and $J_{6,6'}$ 13.5

Hz.; ^{13}C-n.m.r. (20% ND_3 in D_2O): δ 40.4 (C-6), 54.6 (C-2), 56.4 (OMe), 71.4 (C-4), 72.6 (C-5), 72.7 (C-3), and 103.1 (C-1).

Anal. Calc. for $C_7H_{16}N_2O_4 \cdot 0.4\ H_2CO_3$: C, 40.95; H, 7.81; N, 12.91. Found: C, 40.81; H, 8.06; N, 12.69.

Methyl 2,6-diamino-2,6-dideoxy-β-L-idopyranoside (**17**). — A solution of **15** (93 mg) in 1,4-dioxane (1 mL)–acetic acid (0.3 mL) was hydrogenated under the conditions described for **16**, to give a hygroscopic solid (as the 0.6 carbonate), yield 40 mg (63%); t.l.c. (6:4:3:1 1-butanol–pyridine–water–acetic acid; Avicel SF plate) R_F 0.25; $[\alpha]_D^{23}$ +51° (*c* 0.8, water); ^{1}H-n.m.r. (20% ND_3 in D_2O): δ 2.79 (dd, 1 H, H-6), 2.90 (m, collapsed to dd by irradiation at δ 3.60 or δ 4.73, 1 H, H-2), 2.94 (dd, 1 H, H-6'), 3.57 (s, 3 H, OMe), 3.60 (ddd, 1 H, H-4), 3.86 (ddd, 1 H, H-5), 3.95 (t, 1 H, H-3), and 4.73 (d, 1 H, H-1), $J_{1,2}$ 2, $J_{2,3} = J_{3,4}$ 3.5, $J_{2,4} \sim 1$, $J_{4,5}$ 2, $J_{5,6}$ 4.5, $J_{5,6'}$ 8.5, and $J_{6,6'}$ 13.5 Hz; ^{13}C-n.m.r. (20% ND_3 in D_2O): δ 42.1 (C-6), 53.7 (C-2), 57.3 (OMe), 69.7 (C-4), 71.4 (C-3), 76.9 (C-5), and 101.6 (C-1).

Anal. Calc. for $C_7H_{16}N_2O_4 \cdot 0.6\ H_2CO_3$: C, 39.79; H, 7.56; N, 12.21. Found: C, 39.98; H, 7.84; N, 12.08.

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