Synthesis of 6-Amino-6-deoxy-L-idopyranosides

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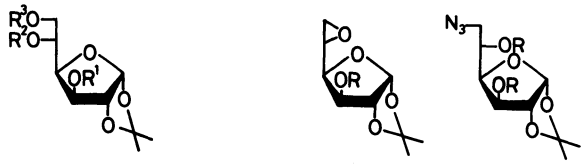
Methyl 6-amino-6-deoxy-α- and -β-L-idopyranosides have been prepared from 3-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose via 5,6-anhydro-1,2-*O*-isopropylidene-L-idofuranose and the azide product derived from it. Isopropyl 6-amino-6-deoxy-α- and -β-L-idopyranosides were prepared from 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-α-L-idopyranosyl chloride and 2-propanol. Nonprotected α- and β-L-idopyranosides were distinguished by their $J_{1,2}$ proton couplings.

In the course of our synthetic studies on the analogs of aminoglycoside antibiotics containing 2,6-diamino-2,6-dideoxy-L-idopyranose, such as neomycin B, lividomycins, and paromomycin I, we needed to know the characteristics of the most basic 6-amino-6-deoxy-L-idopyranosides. In this paper we describe the syntheses of methyl and isopropyl 6-amino-6-deoxy-α-and-β-L-idopyranosides.

Sorkin and Reichstein[1] prepared methyl α-and β-D-idopyranosides from methyl 4,6-*O*-benzylidene-D-galactopyranosides by alkaline hydrolysis of the corresponding 2,3-anhydro-D-gulo- and -talo derivatives. In the synthesis of 3,6-diamino-3,6-dideoxy-D-idose, Hanessian and Haskell[2] used this kind of procedure. To prepare 6-deoxy-L-idosides, 5,6-unsaturated D-*xylo* compounds such as methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*xylo*-hex-5-enopyranoside[3] were usually reduced catalytically. In the synthesis of 3-*O*-acetyl-2,6-diazido-4-*O*-benzyl-2,6-dideoxy-L-idopyranosyl chloride,[4] a precursor for the 2,6-diamino-2,6-dideoxy-L-idoside portion of neomycin B, we applied a head-to-tail inversion technique for a D-glucose derivative. Meyer and Reichstein[5] prepared L-idopyranose from 1,2-*O*-isopropylidene-5-*O*-tosyl-D-glucofuranose derivatives through hydrolysis of the 5,6-anhydro-L-idofuranoses derived from the D-glucofuranose. Since then most investigators used 5,6-anhydro compounds or similar methods using 5,6-epimine[6] or oxazoline[7,8] to prepare L-ido derivatives. In our present synthesis, the 6-amino-6-deoxy-L-idopyranosides (**13** and **14**) were also prepared by way of a 5,6-anhydro compound.



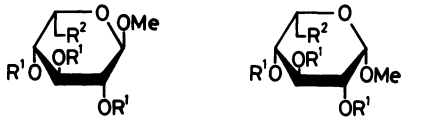
	R^1	R^2	R^3
1	Ac	H	H
2	Ac	H	$COC_6H_4NO_2(p)$
3	Ac	SO_2CH_3	$COC_6H_4NO_2(p)$
4	H	SO_2CH_3	H

	R
5	H
6	Ac

	R
7	H
8	Ac

Chart 1.

3-*O*-Acetyl-1,2-*O*-isopropylidene-D-glucofuranose[9] (**1**) was treated with *p*-nitrobenzoyl chloride in pyridine at −40 °C, when crystalline 6-*O*-(*p*-nitrobenzoyl) derivative **2** was obtained in high yield. No acetyl migration suggested[5] was observed. After mesylation of **2** (to give the 5-*O*-mesyl derivative,**3**) two acyl groups were removed by methanolic ammonia to give the diol **4**. Attempts to selectively remove the 6-*O*-(*p*-nitrobenzoyl) group by controlled reaction conditions were unsuccessful giving a mixture including a migration product, 6-*O*-acetyl derivative. Treatment of **4** with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in oxolane gave the 5,6-anhydro derivative **5** of L-ido structure in a moderate yield. If methanolic ammonia or methanolic sodium methoxide was used instead of DBU, no pure **5** was obtained possibly by contamination of a 3,5-oxetane derivative as suggested by Buchanan and Oakes.[10] The structure of **5** was proved by the acetyl derivative **6** of **5**. From the ^1H NMR spectrum, it was clarified that the acetyl group was introduced at C-3, not at C-6, precluding the oxetane structure of **5**. Opening the 5,6-anhydro ring with a mixture[11] of sodium azide-ammonium chloride gave the 6-azido-L-idofuranose **7**. Reaction without the use of ammonium chloride gave **7** in only poor yield. Structure of **7** was proved by inspection of the ^1H NMR spectrum of the di-*O*-acetyl derivative **8**. Refluxing **7** with methanolic hydrochloric acid gave



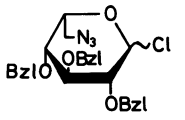
	R^1	R^2
9	Ac	N_3
11	H	N_3
13	H	NH_2

	R^1	R^2
10	Ac	N_3
12	H	N_3
14	H	NH_2

Chart 2.

a mixture of several products. Separation of them by usual silica-gel or resin column chromatography was found difficult; however, the portion of the anomeric mixture of 6-azidoglycopyranosides **11** and **12** was successfully isolated by a borate-form resin column chromatography using a borate buffer as the eluent.

The anomeric mixture was then acetylated and the tri-*O*-acetyl-6-azido-6-deoxy-α- (**9**) and -β-L-idopyranosides (**10**) were separated by silica-gel column chromatography. Removal of the acetyl groups from **9** and **10** gave pure methyl 6-azido-6-deoxy-α- (**11**) and -β-L-idopyranosides (**12**). Catalytic reduction of **11** and **12** gave the corresponding 6-amino-6-deoxy-α- (**13**) and -β-L-idopyranosides (**14**).



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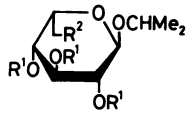

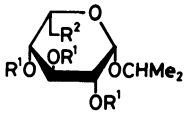

	R¹	R²		R¹	R²
16	$CH_2C_6H_5$	N_3	**17**	$CH_2C_6H_5$	N_3
18	H	NH_2	**19**	H	NH_2
20	H	$NHCO_2CH_2C_6H_5$	**21**	H	$NHCO_2CH_2C_6H_5$

Chart 3.

Isopropyl 6-amino-6-deoxy-α-L-idopyranosides (**18** and **19**) were prepared from 6-azido-2,3,4-tri-*O*-benzyl-6-deoxy-L-idopyranosyl chloride[12] (**15**). Condensation of **15** with 2-propanol in the presence of mercury(II) cyanide in dichloromethane gave the isopropyl α- and -β-L-idopyranoside derivatives **16** and **17** in 1:4 ratio after chromatography. Reduction of the azido and removal of the benzyl groups of **16** and **17** with sodium in liquid ammonia gave the glycosides **18** and **19**. To confirm their structures, *N*-benzyloxycarbonyl derivatives **20** and **21** were prepared. Periodate oxidation of the both compounds gave one molar equivalent of formic acid, respectively, proving the presence of contiguous three hydroxyl groups.

One of the purposes of our syntheses was to examine the possibility to distinguish the anomers from their ^{1}H NMR spectra, especially from the $J_{1,2}$ values. Since hydrogens at C-1 and C-2 of both anomers (**9**, **10**, **11**, **12**, **13**, **14**, **18**, and **19**) are supposed to be situated in gauche relationship except for the $^4C_1$ conformation of the α-L-isomers, small $J_{1,2}$ proton coupling constants of all compounds are expected (see Fig. 1). Indeed, in the β-L-idosides **10**, **12**, **14**, and **19**, the $J_{1,2}$ proton coupling constants were all small (1—2 Hz) and, in **10**, **12**, and **19**, the

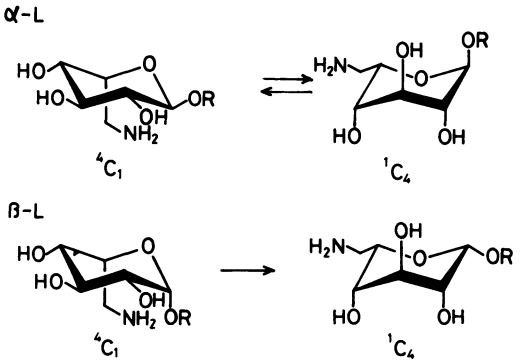

Fig. 1.

$J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ were so small (2—4 Hz) as those typical for the $^1C_4$(L) conformation of idopyranosides reported.[13,14] It should be stressed that both tri-*O*-acetyl-6-azido-6-deoxy-β-L-idoside (**10**) and the corresponding deacetylated idoside **12** had almost equal *J* values ($J_{1,2}$—$J_{4,5}$) suggesting that the presence of the *O*-acetyl groups of **10** did not necessarily contribute[15] the stability of the $^1C_4$(L) conformation. In the 6-amino-6-deoxy-β-L-idosides (**14** and **19**), although the *J* values of **14** except for $J_{1,2}$ could not be measured by overlapping with other signals, $^1C_4$ (L) conformations were presumed. Therefore it is concluded that all β-L-idosides described here take the $^1C_4$ (L) conformation exclusively. In the α-L-idosides **9**, **11**, **13**, and **18**, the $J_{1,2}$ values (3.5—6 Hz) of **11**, **13**, and **18** were larger than those (0.5—2 Hz) of the tri-*O*-acetyl-6-azido-6-deoxy-α-L-idoside (**9**), which, judging from the other *J* values (see Experimental), was suggested to take the ideal $^1C_4$ (L) conformation, stabilized[15] by the presence of the *O*-acetyl groups. Other nonprotected derivatives **11**, **18**, and possibly **13** will take a conformation equilibrated by two chair conformations ($^1C_4 \rightleftarrows {}^4C_1$), in NMR time-scale. It was further assumed that the isopropyl α-L-idopyranoside (**18**) took more $^4C_1$ (L) conformation than the methyl α-L-idosides **11**, **13**, the fact being ascribed to the tendency of the bulky isopropoxy group of **18** to take an equatrial position. Since $J_{2,3}$ and $J_{3,4}$ of **11** and **18** were almost equal,[16] respectively, contribution of a skew conformation will be negligible. In conclusion, α- and β-L-idopyranosides, so far described, can be distinguished by the $J_{1,2}$ values (α-L: 3.5—6 Hz, β-L: 1—2 Hz) if the protecting groups of the idopyranosides are absent. This affords a useful method for the discrimination of the anomers of nonprotected idopyranosides.

Experimental

General. ^{1}H NMR spectra were recorded at 90 MHz with a Varian EM-390 spectrometer unless otherwise stated.

The 250 MHz spectra were measured in the FT mode with a Bruker WM 250 spectrometer. IR spectra were recorded with a Hitachi 285 infrared spectrophotometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. Thin-layer chromatography (TLC) was performed on precoated kieselgel 60, Merck. For column chromatography, silica gel (Wakogel C-200) was used.

3-*O*-Acetyl-1,2-*O*-isopropylidene-6-*O*-(*p*-nitrobenzoyl)-D-glucofuranose (2). A mixture of 3-*O*-acetyl-1,2-*O*-isopropylidene-D-glucofuranose[9] (**1**, 36.4 g) and *p*-nitrobenzoyl chloride (30.7 g) in pyridine (600 ml) was kept at −40 °C overnight. Addition of water (3 ml) followed by evaporation gave a residue, that was extracted with chloroform. The organic solution was washed with aqueous saturated potassium hydrogensulfate and aqueous saturated sodium hydrogencarbonate, dried (Na_2SO_4), and concentrated to give a solid. Recrystallization from chloroform–hexane gave pale-yellow crystals, 53.0 g (93%), mp 132—133 °C, $[\alpha]_D^{20}$ −14 ° (*c* 1, chloroform); IR (KBr): 1735 (ester); 1540 and 1350 cm^{-1}(nitro); ^1H NMR ($CDCl_3$): δ=1.37 and 1.54 (Me_2C), 2.20 (3H, s, Ac), 3.08 (1H, br m, OH), 3.98 (1H, dq, H-5), 4.32 (1H, dd, $J_{3,4}$=2.5, $J_{4,5}$=9 Hz, H-4), 4.48 (1H, dd, $J_{5,6}$=6, $J_{6,6'}$=12.5 Hz, H-6), 4.65 (1H, d, $J_{1,2}$=4, $J_{2,3}$=0 Hz, H-2), 4.80 [1H, dd, *J*=2.5 (=$J_{5,6'}$) and 12.5 Hz, H-6'], 5.33 (1H, d, *J*=2.5 Hz, H-3), 5.95 (1H, d, H-1), 8.32 (4H, s, phenyl).

Found: C, 52.43; H, 5.20; N, 3.36%. Calcd for $C_{18}H_{21}NO_{10}$: C, 52.56; H, 5.15; N, 3.40%.

3-*O*-Acetyl-1,2-*O*-isopropylidene-5-*O*-methylsulfonyl-6-*O*-(*p*-nitrobenzoyl)-D-glucofuranose (3). A solution of **2** (5.2 g) and methanesulfonyl chloride (2.94 ml) in pyridine (100 ml) was kept for 3 h at room temperature. Work-up as described above gave a solid of **3**, 5.8 g (94%), $[\alpha]_D^{20}$ −4 ° (*c* 1, chloroform); ^1H NMR ($CDCl_3$): δ=3.08 (3H, s, Ms), 5.32 (1H, dq, H-5), 5.42 (1H, d, H-3), 5.98 (1H, d, H-1).

Found: C, 46.35; H, 4.71; N, 2.63; S, 6.66%. Calcd for $C_{19}H_{23}NO_{12}S$: C, 46.63; H, 4.74; N, 2.86; S, 6.55%.

1,2-*O*-Isopropylidene-5-*O*-methylsulfonyl-D-glucofranose (4). A mixture of **3** (38 g) and 1 M† methanolic ammonia (680 ml) was stirred until the mixture became clear and the solution was kept at room temperature (totally 6 h). Neutralization with 1 M aqueous hydrochloric acid followed by evaporation gave a residue, that showed, on TLC with benzene–ethyl acetate (2:1), spots at R_f 0.38 (minor), 0.27 (**5**, minor) and 0.16 (**4**, major) (cf. **3**: R_f 0.63). The residue was extracted with chloroform and the soution washed with aqueous saturated sodium sulfate, dried (Na_2SO_4), and concentrated. Silica-gel (1 kg) column chromatography of the residue with benzene–ethyl acetate (1:2) gave an unknown product (R_f 0.38, 3.6 g), the 5,6-epoxy compound (**5**, 2.2 g) and a solid of **4**, 14.1 g (61%); **4**: $[\alpha]_D^{20}$ −3 ° (*c* 1, chloroform); ^1H NMR ($CDCl_3$; measured after shaking with slight D_2O): δ=1.34 and 1.55 (each s, Me_2C), 3.22 (3H, s, Ms), 3.85 (1H, dd, $J_{5,6}$=5.5, $J_{6,6'}$=12.5 Hz, H-6), 4.10 (1H, dd, $J_{5,6'}$=3 Hz, H-6'), 4.15—4.4 (2H, H-3, 4), 4.58 (1H, d, $J_{1,2}$=4 Hz, H-2), 4.95 (1H, H-5), 5.96 (1H, d, H-1).

Found: C, 39.94; H, 6.35; S, 10.37%. Calcd for $C_{10}H_{18}O_8S$: C, 40.26; H, 6.08; S, 10.75.

5,6-Anhydro-1,2-*O*-isopropylidene-L-idofuranose (5). To a solution of **4** (14.0 g) in oxolane (300 ml) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (20 ml) and the solution was kept at room temperature overnight, then another DBU (8 ml) was added and kept likewise for further 24 h. TLC of the solution with benzene–ethyl acetate (1:2) showed spots at R_f 0.55 (**5**) and 0.45 (slight, **4**). After concentration to a small valume, chloroform was added and the organic solution was washed with 0.2 M phosphate buffer (pH 6) (a part of **5** was lost by dissolving in the solution), then aqueous saturated sodium sulfate, dried (Na_2SO_4), and concentrated. Silica-gel (250 g) column chromatography of the residue with benzene–ethyl acetate (1:2) gave **5** as crystals, 5.9 g (62%) and **4** recovered (0.9 g); mp 74—75 °C, $[\alpha]_D^{20}$ −26 ° (*c* 1, chloroform); ^1H NMR ($CDCl_3$): δ=1.35 and 1.52 (each s, Me_2C), 2.87 (2H, narrow m, H-6,6'), 3.02 (1H, d, *J*=5 Hz, OH-3; disappeared on deuteration), 3.35 (1H, q, $J_{5,6}$=$J_{5,6'}$=$J_{4,5}$=3.5 Hz, H-5), 4.22 [1H, dd, *J*=3 (=$J_{3,4}$) and 3.5 Hz, H-4], 4.38 (1H, dd, *J*= 3 and 5 Hz, H-3; on irradiation at δ 3.02 or on deuteration, the dd collapsed to a d), 4.56 (1H, d, $J_{1,2}$=3.5 Hz, H-2), 5.96 (1H, d, H-1).

Found: C, 53.18; H, 6.85%. Calcd for $C_9H_{14}O_5$: C, 53.46; H, 6.98%.

3-*O*-Acetyl-5,6-anhydro-1,2-*O*-isopropylidene-L-idofuranose (6). Compound **5** (490 mg) was treated with acetic anhydride (0.26 ml) in pyridine (15 ml) at 0 °C for 20 h. Usual work up gave amorphous powder of **6**, 496 mg (84%), $[\alpha]_D^{20}$ +15 ° (*c* 1, chloroform); ^1H NMR ($CDCl_3$): δ=1.36 and 1.55 (each s, Me_2C), 2.17 (3H, s, Ac), 5.38 (1H, d, *J*=3 Hz, H-3).

Found: C, 54.31; H, 6.58%. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60%.

6-Azido-6-deoxy-1,2-*O*-isopropylidene-L-idofuranose (7). A mixture of sodium azide (3.8 g) and ammonium chloride (3.6 g) in dry *N*, *N*-dimethylformamide (300 ml) was stirred at 100 °C for 1 h, then **5** (5.8 g) was added and further heated at the temperature for 1.2 h. TLC of the solution with chloroform–methanol (10:1) showed spots at R_f 0.5 (**5**, slight), 0.45 (**7**) and 0.4 (trace). After addition of chloroform (500 ml) the organic solution was washed with aqueous saturated sodium sulfate, dried (Na_2SO_4), and concentrated. Chromatography (silica gel, 260 g) of the residue with chloroform (300 ml), then chloroform–methanol (10:1) gave crystals of **7**, 4.7 g (68%) and **5** recovered (1.1 g, 19%); **7**: mp 97—99 °C, $[\alpha]_D^{20}$ −24 ° (*c* 1, chloroform); IR (KBr) 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$; measured after shaking with slight D_2O): δ=1.36 and 1.50 (Me_2C), 3.53 (2H, double ABq, H-6,6'), 4.31 (1H, d, $J_{3,4}$=3 Hz; t before deuteration; H-3), 4.55 (1H, d, $J_{1,2}$=4 Hz, H-2), 6.01 (1H, d, H-1).

Found: C, 44.09; H, 5.99; N, 16.88%. Calcd for $C_9H_{15}N_3O_5$: C, 44.08; H, 6.16; N, 17.13%.

3,5-Di-*O*-acetyl-6-azido-6-deoxy-1,2-*O*-isopropylidene-L-idofuranose (8). Compound **7** (70 mg) was treated with acetic anhydride (0.08 ml) in pyridine (1.5 ml) in a usual manner to give a syrup, 80 mg (85%), $[\alpha]_D^{20}$ −26 ° (*c* 1, chloroform); *m/z* 330 $(M+1)^+$; ^1H NMR (benzene-d_6): δ=1.08 and 1.40 (Me_2C), 1.60 and 1.72 (each 3H, s, Ac), 5.28 (1H, d, H-3), 5.45 [1H, ddd, *J*=8 (=$J_{4,5}$), 4, and 5.5 Hz, H-5].

Methyl 6-Azido-6-deoxy-L-idopyranosides (11+12). A solution of **7** (100 mg) in 1.4 M methanolic hydrochloric acid (5 ml) was refluxed for 1.5 h. TLC of the solution

† 1M=1 mol dm^{-3}.

with chloroform–methanol (10:1) showed spots at R_f 0.38, 0.33, 0.27 (minor), and 0.15 (trace) (cf. **7**: R_f 0.52). The solution was neutralized with Dowex 1×2 resin (OH^- form), filtered, and concentrated. The residue was chromatographed on a column of Dowex 1×2 (borate form, 15 ml) with 0.0025 M aqueous $K_2B_4O_7$ solution (elution speed: 0.25 ml min^{-1}). The eluate (16—26 ml) containing the pyranosides (R_f 0.38 and 0.33) was passed through a column of Dowex 50W ×2 resin (H^+ form, 5ml) with water and concentrated. The residue was repeatedly concentrated with additions of methanol (until boric acid was undetected) to afford a syrup of a mixture of **11** and **12**, 55 mg (6%).

Methyl 2,3,4-Tri-*O*-acetyl-6-azido-6-deoxy-α- (9) and -β-L-idopyranosides (10). A solution of a mixture of **11** and **12** (54.8 mg) in pyridine (1.5 ml) was treated with acetic anhydride (0.2 ml) at room temperature overnight. TLC of the solution with benzene–ethyl acetate (3:1), showed spots of R_f 0.54 (**9**) and 0.48 (**10**). After addition of water (0.1 ml), the solution was concentrated. The chloroform solution of the residue was washed with water, dried (Na_2SO_4), and concentrated. The residue was chromatographed with benzene–ethyl acetate (5:1) to give a syrup (from the earlier fractions) of **9**, 43.4 mg (50%) and crystals of **10**, 30.8 mg (36%).

9: $[\alpha]_D^{20}$ −25° (*c* 1, chloroform); IR (KBr) 2100 cm^{-1} (N_3); *m/z* 346 $(M+1)^+$, 314 (M^+-MeO); ^1H NMR ($CDCl_3$): δ=2.15, 2.17 and 2.20 (each 3H, s, Ac), 3.25 (1H, dd, H-6), 3.50 (3H, s, OCH_3), 3.59 (1H, dd, H-6′), 4.37 (1H, ddd, H-5), 4.77 (1H, br s, half-height width was ≈3.5 Hz, H-1), 4.87 (2H, m, H-2,4), 5.02 (incomplete t with small splittings, H-3); $J_{1,2}$ ≈0.5, $J_{2,3}$ ≈3, $J_{3,4}$=3.5, $J_{4,5}$=2, $J_{5,6}$=4, $J_{5,6'}$=8.5 and $J_{6,6'}$=13 Hz.

In C_6D_6 at 250 MHz: δ=1.55, 1.60, and 1.65 (each s, Ac), 2.66 (1H, dd, H-6), 3.14 (3H, s, OCH_3), 3.20 (1H, dd, H-6′), 4.14 (1H, dt, H-5), 4.66 (1H, d, H-1), 4.85 (1H, t, H-4), 5.14 (1H, dd with small splittings, H-2), 5.26 (1H, t with small splittings, H-3); $J_{1,2}$=2, $J_{2,3}$=$J_{3,4}$=4, $J_{4,5}$ ≈3, $J_{5,6}$=8.5, $J_{5,6'}$= 3,5, $J_{1,3}$≈0.5, and $J_{2,4}$≈0.5 Hz.

10: Mp 107—108 °C, $[\alpha]_D^{20}$ +62° (*c* 1, chloroform); IR (KBr) 2100 cm^{-1} (N_3); ^1H NMR ($CDCl_3$) δ=2.18 (9H, s, Ac) (in pyridine-d_5: 2.08, 2.10 and 2.18, each 3H s), 3.30 (1H, dd, H-6), 3.62 (3H, s, OCH_3), 3.70 (1H, dd, H-6′), 4.16 (1H, ddd, H-5), 4.80 (1H, d, H-1), 4.88 [1H, dd with small splittings ($J_{2,4}$ ≈0.5 Hz), H-4], 4.98 [1H, dd with small splittings (≈0.5 Hz), H-2], 5.20 (1H, t, H-3); $J_{1,2}$=2, $J_{2,3}$= $J_{3,4}$=$J_{5,6}$=4, $J_{4,5}$=2.5, $J_{5,6'}$=8, and $J_{6,6'}$=13 Hz.

Found: C, 45.30; H, 5.59; N, 12.03%. Calcd for $C_{13}H_{19}N_3O_8$: C, 45.22; H, 5.55; N, 12.17%.

Methyl 6-Azido-6-deoxy-α- (11) and -β-L-Idopyranosides (12). To a solution of **9** (34.7 mg) in methanol (2 ml), barium hydroxide octahydrate (70 mg) was added and the mixture was stirred for 10 min at room temperature. After bubbling carbon dioxide, the mixture containing barium carbonate was concentrated and the residue was extracted with 1,4-dioxane. The extracted product was chromatographed on a short column of silica gel with chloroform–methanol (10:1) to give a syrup of **11**, 19.4 mg (88%), which crystallized on standing. In a similar manner a syrup of **12**, 15.1 mg (82%) was obtained from **10** (29.1 mg).

11: Mp 62—63 °C, $[\alpha]_D^{20}$ −74° (*c* 0.9, water); IR (KBr) 2100 cm^-; ^1H NMR (pyridine-d_5–D_2O=10:1): δ=3.58 (3H, s, OCH_3), 3.61 (1H, dd, H-6), 3.98 (1H, dd, H-6′), ≈4.13 (1H, H-4), 4.15 (1H, dd, H-2; on irradiation of H-1, the dd collapsed to a d), 4.46 [1H, dd with small splittings ($J_{1,3}$≦0.5 Hz), H-3], 4.62 (1H, ddd, H-5), 5.11 (1H, d with small splittings, H-1); $J_{1,2}$=3.5, $J_{2,3}$=5, $J_{3,4}$=$J_{5,6}$=4, $J_{4,5}$=2.5, $J_{5,6'}$=9, and $J_{6,6'}$=13 Hz.

Found: C, 38.53; H, 5.97; N, 18.85%. Calcd for $C_7H_{13}N_3O_5$: C, 38.36; H, 5.98; N, 19.17%.

12: $[\alpha]_D^{20}$ +54° (*c* 0.9, water): IR (KBr) 2100 cm^{-1}; ^1H NMR (pyridine-d_5–D_2O=10:1): δ=3.48 (1H, dd, H-6), 3.66 (3H, s, OCH_3), 4.00 (1H, narrow m, H-2), 4.01 (1H, dd, H-6′), 4.28 (1H, dd with small splittings, H-4), 4.53 (1H, ddd, H-5), 4.66 (1H, t, H-3), 5.14 (1H, d, H-1); $J_{1,2}$=1, $J_{2,3}$= $J_{3,4}$=$J_{5,6}$=4, $J_{4,5}$=2.5, $J_{5,6'}$=7.5, and $J_{6,6'}$=13 Hz.

Found: C, 38.27; H, 5.91; N, 18.88%. Calcd for $C_7H_{13}N_3O_5$: C, 38.36; H, 5.98; N, 19.17%.

Metyl 6-Amino-6-deoxy-α- (13) and -β-L-idopyranosides (14). An aqueous solution (1.5 ml) of **11** (16.5 mg) was hydrogenated (3 kg cm^{-2} of hydrogen) for 1 h in the presence of palladium black under shaking. Filtration followed by concentration gave a ninhydrin-positive solid of **13**, that was reprecipitated from methanol solution by addition of ethyl acetate, 13.0 mg (77% as hemicarbonate). In a similar manner **14** was obtained from **12** (12.9 mg) as a solid of hemicarbonate, 10.4 mg (79%).

13: $[\alpha]_D^{20}$ −88° (*c* 1, water): ^1H NMR (D_2O at 60 °C): δ=3.57 (3H, s, OCH_3), 4.75 (1H, d, $J_{1,2}$=4.5 Hz, H-1).

Found: C, 39.84; H, 7.02; N, 5.95%. Calcd for $C_7H_{15}NO_5 \cdot 1/2\ H_2CO_3$: C, 40.17; H, 7.19; N, 6.25%.

14: $[\alpha]_D^{20}$ +52° (*c* 0.9, water); ^1H NMR (D_2O at 60 °C): δ=3.65 (3H, s, OCH_3), 4.83 (1H, d, $J_{1,2}$=2 Hz, H-1).

Found: C, 40.32; H, 7.04; N, 6.08%. Calcd for $C_7H_{15}NO_5 \cdot 1/2H_2CO_3$: C, 40.17; H, 7.19; N, 6.25%.

Isopropyl 6-Azido-2,3,4-tri-*O*-benzyl-6-deoxy-α- (16) and -β-L-idopyranosides (17). A mixture of dry 2-propanol (0.8 ml), mercury(II) cyanide (680 mg) and Drierite ($CaSO_4$, 1.84 g activated at 235 °C for 3 h in vacuo) in dichloromethane (3 ml) was stirred for 1 h at room temperature. The 1-chloride[12] **15** (667 mg) dissolved in dichloromethane (3 ml) was added to the above suspension and the mixture was stirred overnight at room temperature. After addition of chloroform (50 ml), the mixture was filtered, and the solution was washed with aqueous sodium hydrogencarbonate, dried (Na_2SO_4), and concentrated. The residue was chromatographed on a silica-gel column with benzene–ethyl acetate (100:1) to give solids of **16**, 114 mg (16%), R_f 0.6 on TLC with benzene–ethyl acetate=30:1, and **17**, 425 mg (61%), R_f 0.48.

16: $[\alpha]_D^{26}$ −14.5° (*c* 1, chloroform). Found: C, 69.49; H, 6.77; N, 7.91%. Calcd for $C_{30}H_{35}N_3O_5$: C, 69.32; H, 6.77; N, 8.12%.

17: $[\alpha]_D^{26}$ +80° (*c* 1, chloroform). Found: C, 69.40; H, 6.79; N, 8.07%. Calcd for $C_{30}H_{35}N_3O_5$: C, 69.32; H, 6.77; N, 8.12%.

Isopropyl 6-Amino-6-deoxy-α-L-idopyranoside (18). A solution of **16** (76 mg) in oxolane (1.5 ml) was added to a solution of sodium metal (ca. 50 mg) in liquid ammonia (ca. 5 ml, −50 °C) and the deep-blue solution was kept at the temperature for 2 h. After addition of methanol to consume the residual sodium to give a colorless solution, ammonia was evaporated with gradual raise in temperature (finally under diminished pressure). The strongly alkaline

aqueous solution of the residue was passed through a column of Dowex 50 W×2 (NH_4^+ form) with water, and the ninhydrin-positive fractions combined were concentrated. The residue was chromatographed on a column of CM-Sephadex C-25 (10 ml) with water (30 ml), then 0.5 M aqueous ammonia to give a solid of **18**, 22 mg (65% as 1/6 carbonate), $[\alpha]_D^{24}$ −73° (*c* 1, water); ^{1}H NMR (in D_2O containing 20% ND_3 at 250 MHz): δ=1.19 and 1.24 (each 3H d, *J*=6 Hz, CH*Me*$_2$), ABq cendered at 2.85 (2H, H-6,6′), 3.35 (1H, dd, H-2), 3.72 (1H, dd, H-4), 3.96 (1H, m, H-5), 4.02 (1H, m, OC*H*Me$_2$), 4.72 (1H, d, H-1); $J_{1,2}$=6, $J_{2,3}$=8.5, $J_{3,4}$=7.5, $J_{4,5}$=4.5 Hz.

Found: C, 47.79; H, 8.22; N, 5.76%. Calcd for $C_9H_{19}NO_5 \cdot 1/6H_2CO_3$:C, 47.55; H, 8.36; N, 6.05%

Isopropyl 6-Amino-6-deoxy-β-L-idopyranoside (19). Compound **17** (160 mg) was treated smilarly as described for **18** to give a solid of **19**, 45 mg (63% as 1/6 carbonate), $[\alpha]_D^{24}$ +42° (*c* 1, water). ^{1}H NMR (in D_2O containing 20% ND_3 at 250 MHz): δ=1.19 and 1.24 (each 3H, d, *J*=6 Hz, CH*Me*$_2$), ABq centered at 2.86 (2H, H-6,6′), 3.58 (1H, dd, H-4), 3.62 (1H, ddd, H-2), 3.85 (1H, m, H-5), 3.99 (1H, t, H-3), 4.11 (1H, m, OC*H*Me$_2$), 4.91 (1H, d, H-1); $J_{1,2}$=1.5, $J_{2,3}$=$J_{3,4}$=4, $J_{4,5}$=2, $J_{2,4}$=1 Hz.

Found: C, 47.38; H, 8.23; N, 6.13%. Calcd for $C_9H_{19}NO_5 \cdot 1/6\ H_2CO_3$: C, 47.55; H, 8.36; N, 6.05%.

Isopropyl 6-Benzyloxycarbonylamino-6-deoxy-α-L-idopyranoside (20). To a solution of **18** (18 mg) in 50% aqueous methanol (2 ml) were added benzyl chloroformate (0.03 ml) and anhydrous sodium carbonate (50 mg), and the mixture was stirred for 2 h under ice-cooling. Concentration gave a residue, that was extracted with hot acetone. The isolated product was purified by silica-gel column chromatography with chloroform–methanol (20:1) to give a solid of **20**, 18 mg (65%). Recrystallization from chloroform–hexane gave needles, mp 157.5—159.5 °C, $[\alpha]_D^{25}$ −93° (*c* 1, chloroform). ^{1}H NMR ($CDCl_3$ containg slight D_2O): δ=1.20 and 1.25 (each 3H, d, CH*Me*$_2$), 5.02 (1H, d, *J*≈1 Hz, H-1), 5.19 (2H, s, PhC*H*$_2$CO$_2$).

Found: C, 57.20; H, 6.93; N, 3.82%. Calcd for $C_{17}H_{25}NO_7$: C, 57.46; H, 7.04; N, 3.94%.

Isopropyl 6-Benzyloxycarbonylamino-6-deoxy-β-L-idopyranoside (21). Compound **19** (55 mg) was treated similarly as described for **20** to give a solid of **21**, 67 mg (79%), $[\alpha]_D^{25}$ +10° (*c* 1, chloroform). ^{1}H NMR ($CDCl_3$ containing slight D_2O): δ=1.18 and 1.26 (each 3H, d, CH*Me*$_2$), 4.88 (1H, apparent s, H-1), 5.14 (2H, s, PhC*H*$_2$CO$_2$).

Found: C, 57.19; H, 7.06; N, 3.86%. Calcd for $C_{17}H_{25}NO_7$: C, 57.46; H, 7.04; N, 3.94%.

Periodate Oxidations of 20 and 21. A mixture of **20** or **21** (4.0 mg, each, 11.27 μM) and sodium periodate (12 mg, 56 μM) in water (1.2 ml) was stirred at 5 °C for 2 days. Analysis of the formic acid liberated by color detection method (at 450 mμ) by 5,5-diethyl-2-thiobarbituric acid[17] showed 14.20 and 14.75 μM (1.26 and 1.31 molar equiv for **20**), and 13.40 and 13.65 μM (1.19 and 1.21 molar equiv for **21**) formic acid.

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