Synthesis of Dihydrostreptobiosamine[1)]

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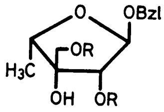
The isopropylidene derivative (**4**) of benzyl dihydrostreptoside and 3,4,6-tri-*O*-acetyl-2-amino-*N*-anisylidene-2-deoxy-α-L-glucopyranosyl bromide (**7**) were prepared, and they were coupled by a modified Koenigs-Knorr condensation. After hydrolysis of the *N*-anisylidene group of the product, *N*-methoxycarbonylation followed by *N*-methylation was accomplished to afford the fully protected derivative (**9**) of dihydrostreptobiosamine, which was, after deblocking, led to benzyl dihydrostreptobiosaminide and dihydrostreptobiosamine.

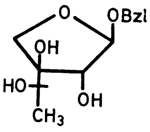
Dihydrostreptobiosamine is the disaccharide portion of dihydrostreptomycin and obtained[2)] by acid hydrolysis of dihydrostreptomycin. In our synthesis of dihydrostreptomycin,[1)] the initial objective was the synthesis of dihydrostreptobiosamine, that will be described here in detail.

The syntheses of the individual components of dihydrostreptomycin have been reported by 1965. Dihydrostreptose has been synthesized by Dyer *et al.*[3)] and 2-deoxy-2-methylamino-L-glucose, by Folkers and his associates.[4)]

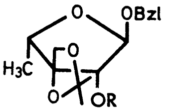
Glycosidation of dihydrostreptose[3)] or transglycosidation of methyl dihydrostreptosides with benzyl alcohol and hydrogen chloride gave a syrup of benzyl α-dihydrostreptoside (**1**) respectively. Its structure was confirmed by the NMR spectral studies of its diacetyl derivative (**2**), thus excluding a potential rearrangement which may result in the formation of another furanoid compound (**1′**) having the C-3′ oxygen atom as a ring oxygen.



1 R=H
2 R=Ac



1′



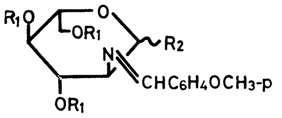
3 R=Ac
4 R=H

Bzl: $CH_2C_6H_5$

The glycosidic linkage between dihydrostreptose and 2-deoxy-2-methylamino-L-glucose is known to be resistant to acid-hydrolysis, however, we found that methanolysis of methyl *N*-methoxycarbonyldihydrostreptobiosaminide, prepared from methyl dihydrostreptobiosaminide[2),5)] and methyl chloroformate, was smooth to give methyl α- and β-dihydrostreptoside together with methyl 2-deoxy-2-methoxycarbonylamino-*N*-methyl-L-glucopyranosides.

The glycoside (**1**) was treated with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide (DMF) in the presence of *p*-toluenesulfonic acid, and the resulting isopropylidene derivative was acetylated with acetic anhydride in pyridine to give the 2-*O*-acetyl-3,3′-*O*-isopropylidene derivative (**3**) in a 50% yield. Isopropylidenation was, therefore, found to occur between hydroxyl groups at C-3 and C-3′ in preference to those at C-2 and C-3. The NMR spectrum of **3** revealed the presence of an *O*-acetyl group at C-2. Deacetylation of **3** with sodium methoxide gave **4**. An alternative protection of the hydroxyl groups at C-3 and C-3′ with a carbonate group was also found to be successful.[6)]

Another key compound for the synthesis of dihydrostreptobiosamine was a fully blocked glycosyl halide of 2-amino-2-deoxy-L-glucose. The 2-amino-2-deoxy-L-glucose has been synthesized from L-arabinose by Kuhn and Kirschenlohr.[7)] Incidentally, we have previously reported an improved synthesis[8)] of paromamine which is an α-glycoside of 2-amino-2-deoxy-D-glucose. The synthesis of this structurally rather simple antibiotic is characterized by some interesting points such as the formation of α-D-glycosidic linkage and a suitable blocking method for the coupling materials. The Koenigs-Knorr condensation of 3,4,6-tri-*O*-acetyl-2-amino-*N*-anisylidene-2-deoxy-α-D-glucopyranosyl bromide[9)] with a protected 2-deoxystreptamine has already been found to give an 85% yield of a mixture of two α-glycosides.



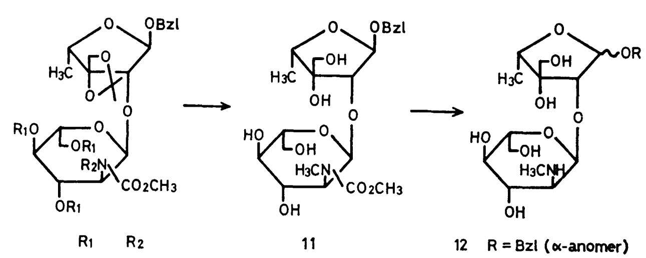
	R_1	R_2
5	H	OH
6	Ac	OAc(β-anorner)
7	Ac	Br (α-anomer)

In analogy to this synthesis, 2-amino-2-deoxy-L-glucose was converted into a Schiff base (**5**) by treatment with anisaldehyde in aqueous ethanol, and, acetylation of the anisylidene derivative with acetic anhydride in pyridine gave the 1,3,4,6-tetra-*O*-acetyl derivative (**6**), which, on treatment with hydrogen bromide–acetic acid in methylene chloride, gave the desired α-glycosyl bromide (**7**). The structure was well defined by the NMR spectrum.

Condensation of **4** with the glycosyl bromide (**7**) in benzene in the presence of mercuric cyanide and Drierite at room temperature was followed by treatment with a mixture of 50% acetic acid and methanol and the crude deanisylidenated product was treated with methyl chloroformate and sodium carbonate in aqueous acetone to give the *N*-methoxycarbonyl disaccharide (**8**) in 42% overall yield from **4**. The NMR spectrum clearly showed that the two components were successfully coupled, and the IR spectrum showed that there occurred no O→N acetyl migration which is sometimes experienced between adjacent amino and acetoxy groups.

Treatment of **8** with methyl iodide and silver oxide in DMF gave the corresponding *N*-methyl derivative (**9**) in a 72% yield. In the NMR spectrum the coupling constant (*J* 3.3 Hz) indicated an equatorial-axial H-1-H-2 relationship and thus the α-configuration for the 2-amino-2-deoxy-L-glucose moiety.

Deacetylation of **9** with sodium methoxide gave **10**,



R1 R2
8 Ac H
9 Ac CH3
10 H CH3

11

12 R = Bzl (α-anomer)
13 R = H

and, deisopropylidenation with 2 M hydrochloric acid–methanol (1 : 1) at room temperature gave the benzyl *N*-methoxycarbonyl-α-dihydrostreptobiosaminide (**11**). It was identified with the authentic specimen, which was prepared from benzyl α-dihydrostreptobiosaminide.[10)] Treatment of the benzyl α-dihydrostreptobiosaminide with methyl chloroformate readily gave the natural specimen.

Hydrolysis of **11** with aqueous barium hydroxide, followed by neutralization with dilute hydrochloric acid, gave the hydrochloride of benzyl α-dihydrostreptobiosaminide (**12**) in a 48% overall yield from **9**. Finally, hydrogenolysis of the benzyl glycoside (**12**) over palladium black gave dihydrostreptobiosamine (**13**). The IR and NMR spectra of these synthetic benzyl dihydrostreptobiosaminide and dihydrostreptobiosamine were identical with those of the natural specimens,[2,10)] respectively, in every respect.

Experimental

Thin layer (tlc) and column chromatography were carried out on silica gel of Silica Rider 5B (Daiichi Pure Chemicals Co., Ltd., Tokyo) and Wakogel C-200 (Wako Pure Chemicals Co., Ltd., Osaka) unless otherwise stated, respectively, and the spots on tlc were visualized with sulfuric acid.

*Benzyl α-Dihydrostreptoside (**1**).* *a) From Dihydrostreptose*: A solution of well dried dihydrostreptose (78 mg) in 2 M hydrogen chloride in benzyl alcohol (4.4 ml) was heated at 50 °C for 40 hr. Basic lead carbonate (1.37 g) was then added and the mixture was stirred for 3 hr. The mixture was filtered and the solid was washed with chloroform. The filtrate and the washings were combined and evaporated to give a yellow oil, which was chromatographed on a column of the silica gel with benzene–ethanol (8 : 1). A colorless syrup (62 mg, 52%) was obtained, $[\alpha]^{25}_{D}$ −100° (*c* 1, $CHCl_3$).

Found: C, 61.40; H, 7.24%. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14%.

NMR (in $CDCl_3$ containing D_2O): τ 8.78 (3H d, *J* 6.6 Hz, CH_3), 6.47 (2H s, CH_2 at C-3′), 5.88 (1H d, 2 Hz, H-2), 5.40 (AB q centered at τ 5.40, *J* 12 Hz, $OC\underline{H_2}C_6H_5$), 4.98 (1H d, *J* 2 Hz, H-1), 2.68 (5H s).

b) From Methyl α-Didydrostreptoside and Methyl β-Dihydrosteptoside: Methyl α- or β-dihydrostreptoside was treated with benzyl alcohol and hydrogen chloride in a similar manner as described above to give **1** in yields of 50—60%.

Methyl N-*Methoxycarbonyldihydrostreptobiosaminide.* A solution of methyl dihydrostreptobiosaminide hydrochloride[2,5)] (5.20 g) and anhydrous sodium carbonate (1.84 g) in aqueous acetone (1 : 1, 100 ml) was treated with methyl chloroformate (2.65 ml) in a usual manner to give a syrup, 5.15 g (94%), $[\alpha]^{24}_{D}$ −121° (*c* 1, MeOH).

Found: C, 46.36; H, 7.42; N, 3.17%. Calcd for $C_{16}H_{29}NO_{11}$: C, 46.71; H, 7.11; N, 3.40%.

NMR (in D_2O): τ 8.80 (3H d, CCH_3), 6.98 (3H s, NCH_3), 6.58 (3H s, OCH_3), 6.49 (2H s, CH_2 at C-3′), 6.27 (3H s, CO_2CH_3), 4.95 (2H m, H-1,1′).

Methyl Dihydrostreptosides. A solution of methyl *N*-methoxycarbonyldihydrostreptobiosaminide (44.3 g) in 2 M methanolic hydrogen chloride (720 ml) was refluxed for 64 hr. Basic lead carbonate (223 g) was added and the mixture was stirred for several hours to give pH about 4. Filtration was followed by evaporation under reduced pressure to give an oil, which was chromatographed on a short column of Dowex 50W-X4 (K form) to remove the color impurities accompanied, and then again chromatographed on Dowex 50W-X4 (K form, 6000 ml) with water as eluent to give five fractions. Evaporation of the fractions in turn gave the starting material, methyl α-dihydrostreptoside, methyl 2-deoxy-2-methoxycarbonylamino-*N*-methyl-β-L-glucopyranoside, methyl β-dihydrostreptoside and methyl 2-deoxy-2-methoxycarbonylamino-*N*-methyl-α-L-glucopyranoside, respectively (cited in the order of elution).

Methyl α-Dihydrostreptoside. A syrup, 9.62 g (53%), $[\alpha]^{25}_{D}$ −111° (*c* 2, $CHCl_3$), R_f 0.39 (tlc with benzene–ethanol 4 : 1); NMR ($CDCl_3$): τ 8.78 (3H d, CCH_3), 6.58 (3H s, OCH_3), 6.44 (2H s, CH_2), 5.10 (1H d, *J* 4.0 Hz, H-1). Found: C, 47.14; H, 7.92%. Calcd for $C_7H_{14}O_5$: C, 47.18; H, 7.92%.

Methyl β-Dihydrostreptoside. A syrup, 1.80 g (10%), $[\alpha]^{20}_{D}$ +100° (*c* 2, $CHCl_3$), R_f 0.20 (tlc with benzene–ethanol 4 : 1); NMR ($CDCl_3$): τ 8.72 (3H d, CCH_3), 6.53 (3H s, OCH_3), 6.36 (2H s, CH_2), 5.14 (1H d, *J* 4.6 Hz, H-1). Found: C, 46.89; H, 7.84%.

Methyl 2-Deoxy-2-methoxycarbonylamino- N- *methyl-α-L-glucopyranoside.* A solid, 9.39 g (35%), $[\alpha]^{22}_{D}$ −143° (*c* 2, MeOH), R_f 0.30 (tlc with benzene–ethanol 4 : 1); NMR (D_2O): τ 7.02 (3H s, NCH_3), 6.58 (3H s, OCH_3), 6.23 (3H s, CO_2CH_3), 5.14 (1H d, *J* 2.1 Hz, H-1). Found: C, 45.18; H, 7.15; N, 5.24%. Calcd for $C_{10}H_{19}NO_7$: C, 45.28; H, 7.22; N, 5.28%.

*Methyl 2-Deoxy-2-methoxycarbonylamino-*N*-methyl-β-L-glucopyranoside.* A crystal (from ethanol–ether), 3.59 g (13%), mp 184—185 °C, $[\alpha]^{22}_{D}$ +19° (*c* 2, MeOH), R_f 0.14 (tlc with benzene–ethanol 4 : 1); NMR (D_2O): τ 7.06 (3H s, NCH_3), 6.43 (3H s, OCH_3), 6.23 (3H s, CO_2CH_3), 5.23 (1H d, *J* 8.0 Hz, H-1). Found: C, 44.90; H, 7.10; N, 5.12%.

Both of the 2-deoxy-2-methylamino-α- and β-L-glucoside derivatives obtained above could be transformed to 2-deoxy-2-methylamino-L-glucose hydrochloride[4)] by refluxing them in 6 M hydrochloric acid for 2 hr, respectively, in yield of ~80%, mp 156—161 °C (decomp) (from ethanol).

*Benzyl 2,3′-Di-O-acetyl-α-dihydrostreptoside (**2**).* Compound **1** (178 mg) was treated with acetic anhydride in pyridine in a usual manner to give a syrup, 156 mg (66%), $[\alpha]^{21}_{D}$ −107° (*c* 2, $CHCl_3$).

Found: C, 60.39; H, 6.33%. Calcd for $C_{17}H_{22}O_7$: C, 60.35; H, 6.55%.

NMR (in $CDCl_3$): τ 8.70 (3H d, CCH_3), 7.92 and 7.87 (each 3H s, Ac), 5.75 (AB q centered at 5.75, *J* 12 Hz, CH_2 at C-3′), 4.87 and 4.78 (each 1H d, H-1 and H-2).

*Benzyl 2-*O*-Acetyl-3,3′-*O*-isopropylidene-α-dihydrostreptoside (**3**).* To a solution of **1** (1.26 g) and anhydrous *p*-toluenesulfonic acid (46 mg) in dry DMF (21 ml), 2,2-dimethoxypropane (4.2 ml) was added and the solution was heated at 60 °C for 2.5 hr. The solution was poured into a mixture of saturated sodium hydrogen carbonate solution (100 ml) and benzene (65 ml) under stirring. The aqueous layer was separated and extracted with benzene (65 ml × 2). The combined benzene layer was dried with sodium sulfate, and evaporated to give a syrup (1.4 g). To a solution of the syrup in pyridine (27 ml), acetic anhydride (1.7 ml) was added and the solution was allowed to stand overnight at room temperature. Water (0.3 ml) was added and the solution was poured into water. The mixture was extracted with benzene (70 ml × 3). The combined benzene layer was dried over sodium sulfate and evaporated. Chromatography of the resulting syrup on a short column of silica gel with benzene–methyl ethyl ketone (MEK) (30 : 1) gave a syrup, 841 mg (50%), $[\alpha]_D^{25}$ −110° (*c* 2, $CHCl_3$).

Found: C, 64.28; H, 7.22%. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19%.

NMR (in $CDCl_3$): τ 8.70 (3H d, CCH_3), 8.64 and 8.59 (each 3H s, isopropylidene), 7.89 (3H s, Ac), 6.13 and 5.69 (each 1H d, *J* 9.2 Hz, CH_2 at C–3′), 4.93 and 4.82 (each 1H d, *J* 1.6 Hz, H–1 and H–2).

*Benzyl 3,3′-*O*-Isopropylidene-α-dihydrostreptoside (**4**).* To a solution of **3** (203 mg), sodium methoxide in methanol was added and the mixture was allowed to stand for 2 hr. After evaporation, the residue was dissolved in benzene (12 ml) and the solution was washed with water, dried over sodium sulfate, and the solvent was removed to give an oil (165 mg, 94%). Tlc with benzene–MEK (20 : 1) gave R_f 0.26, $[\alpha]_D^{18}$ −85° (*c* 1, $CHCl_3$).

Found: C, 65.24; H, 7.28%. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53%.

NMR (in $CDCl_3$): τ 8.54 (6H s, isopropylidene), 4.95 (1H d, *J*∼1 Hz, H–1).

*2-Amino-*N*-anisylidene-2-deoxy-*L*-glucose (**5**).* To a solution of 2-amino-2-deoxy-L-glucose hydrochloride (3.21 g) in 1 M sodium hydroxide (15 ml), a solution of anisaldehyde (1.87 ml) in ethanol (3.8 ml) was added and the mixture was stirred at room temperature for 40 min. On seeding, **5** was precipitated as crystals. After storage in a refrigerator overnight, the crystals were filtered and washed with cold water and with a mixture of ethanol–ether (1 : 2), 3.19 g (72%), mp 181—182 °C, $[\alpha]_D^{20}$ −33° (*c* 1, pyridine); IR (KBr): 1610, 1645 cm^{-1}.

Found: C, 56.85; H, 6.43; N, 4.87%. Calcd for $C_{14}H_{19}NO_6$: C, 56.56; H, 6.44; N, 4.71%.

*1,3,4,6-Tetra-*O*-acetyl-2-amino-*N*-anisylidene-2-deoxy-β-*L*-glucopyranose (**6**).* To a suspension of **5** (2.85 g) in ice cold pyridine (14 ml), acetic anhydride (7.46 ml) was added and the mixture was stirred for 1 hr at the temperature. The resulting clear solution was allowed to stand overnight at room temperature and poured into ice-water. Precipitates occurred were filtered and washed with cold water to give a solid of **6**, 3.85 g (86%), mp 187—189 °C, $[\alpha]_D^{24}$ −100° (*c* 1, $CHCl_3$).

Found: C, 56.56; H, 5.77; N, 3.13%. Calcd for $C_{22}H_{27}NO_{10}$: C, 56.77; H, 5.85; N, 3.01%.

NMR (in $CDCl_3$): τ 8.12, 7.98, 7.97, 7.90 (each 3H s, Ac), 6.15 (3H s, OCH_3), 4.02 (1H d, *J* 8.0 Hz, H–1), 1.81 (1H s, =CH–).

*3,4,6-Tri-*O*-acetyl-2-amino-*N*-anisylidene-2-deoxy-α-*L*-glucopyranosyl Bromide (**7**).* To a suspension of **6** (1.50 g) in dichloromethane (0.7 ml), a saturated solution (2.6 ml) of hydrogen bromide in glacial acetic acid containing 5% acetic anhydride was added and the solution was allowed to stand for 3 hr at room temperature in the dark. A mixture of dry ether (6 ml) and petroleum ether (6 ml) was added to precipitate an oil, which was triturated with the above mixture to give a solid. The solid was dissolved in dichloromethane and washed with an aqueous phosphate buffer (pH 6.8) and then with cold water. After drying over sodium sulfate and then over molecular sieves (3A, Wako Pure Chemicals Co., Ltd., Osaka), the solution was concentrated. Addition of ether deposited some amorphous impurities, which was removed by filtration. Subsequent addition of petroleum ether gave needles, 705 mg (45%), mp 110—111 °C, $[\alpha]_D^{20}$ −194° (*c* 1, $CHCl_3$).

Found: C, 49.35; H, 5.02; N, 2.79, Br, 16.42%. Calcd for $C_{20}H_{24}NO_8Br$: C, 49.40; H, 4.97; N, 2.88, Br, 16.44%.

NMR (in $CDCl_3$): τ 8.12, 7.94, 7.89 (each 3H s, Ac), 3.64 (1H d, *J* 3.5 Hz, H–1), 1.69 (1H s, =CH–).

*Benzyl 2-*O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-methoxycarbonylamino-α-*L*-glucopyranosyl)-3,3′-*O*-isopropylidene-α-dihydrostreptoside (**8**).* To a solution of well dried **4** (270 mg) in dry benzene (5.1 ml), freshly prepared Drierite (730 mg) was added and the mixture was stirred for 1 hr at room temperature. The glycosyl bromide **7** (723 mg) and well dried mercuric cyanide (705 mg) were added and the mixture was stirred at room temperature for 45 hr. Chloroform (60 ml) was added and the organic layer was filtered and washed with saturated sodium hydrogen carbonate solution and then with water. After drying over sodium sulfate, evaporation of the solvents gave a syrup (826 mg). On tlc with benzene–MEK (7 : 1), the syrup gave a main spot at R_f 0.43.

The syrup was dissolved in a mixture of methanol (34 ml) and 50% acetic acid (14 ml) and the solution was allowed to stand at room temperature for 5 hr. Sodium carbonate (6.3 g) was added and the mixture was concentrated to a small volume (∼15 ml). Addition of acetone (60 ml) gave precipitates, which were filtered off. The filtrate was evaporated to give a syrup. On tlc with benzene–MEK (1 : 1), the syrup gave a main spot at R_f 0.42.

To a solution of the syrup in aqueous 60% acetone (15 ml), sodium carbonate (130 mg × 3) and methyl chloroformate (0.16 ml × 3) were added at 4 hr intervals with stirring at room temperature. On tlc with benzene–MEK (7 : 1), the mixture gave a main spot at R_f 0.3. The reaction mixture was evaporated, and the resulting syrup was chromatographed on a short column of silica gel with benzene–MEK (7 : 1) to give a syrup of **8**, (248 mg, 42% from **4**); $[\alpha]_D^{24}$ −133° (*c* 0.8, $CHCl_3$); IR (in CH_2Cl_2): 1750, 1725 (shoulder), 1520 cm^{-1}.

Found: C, 56.45; H, 6.21; N, 2.32%. Calcd for $C_{30}H_{41}NO_{14}$: C, 56.32; H, 6.46; N, 2.19%.

NMR (in $CDCl_3$): τ 8.67 (3H d, CCH_3), 8,59 (6H s, isopropylidene), 7.98 and 7.95 (6H s and 3H s, Ac), 6.32 (3H s, CO_2CH_3), 5.36 (AB q, $OC\underline{H}_2C_6H_5$), 2.64 (5H s, C_6H_5).

*Benzyl 2-*O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-methoxycarbonylamino-*N*-methyl-α-*L*-glucopyranosyl)-3,3′-*O*-isopropylidene-α-dihydrostreptoside (**9**).* To a solution of **8** (168 mg) in dry DMF (2.3 ml), methyl iodide (0.066 ml × 4) and silver oxide (80 mg × 4) were added at 10 hr intervals and the mixture was stirred at room temperature. Chloroform was added to the reaction mixture and the mixture was filtered. The solution was washed with 5% aqueous sodium cyanide and then with water, and dried over sodium sulfate. Evaporation gave a syrup (167 mg), which was purified by column chromatography on silica gel with benzene–MEK (9 : 1) to give a syrup of **9** (122 mg, 72%), $[\alpha]_D^{20}$ −133° (*c* 1.2, $CHCl_3$); IR (KBr): 1760, 1710 cm^{-1}. The peak at 1520 cm^{-1} in **8** had disappeared.

Found: C, 57.06; H, 6.41; N, 2.33%. Calcd for $C_{31}H_{43}NO_{14}$: C, 56.96; H, 6.63; N, 2.14%.

NMR (in $CDCl_3$): τ 8.73 (3H d, CCH_3), 8.64 (6H s, isopropylidene); 8.01, 7.98, 7.96 (each 3H s, Ac); 7.13 (s, more intense) and 7.09 (s) (3H in total, NCH_3, rotamers;

in pyridine-d_6, the signals collapsed to a singlet at 50 °C), 6.29 (3H s, CO_2CH_3), 4.94 (1H d, *J* 1 Hz, H-1), 4.86 (1H d, *J* 3.3 Hz, H-1′).

*Benzyl 2-*O*-(2-Deoxy-2-methoxycarbonylamino-*N*-methyl-α-*L*-glucopyranosyl)-3,3′-*O*-isopropylidene-α-dihydrostreptoside (**10**).* Compound **9** was treated with sodium methoxide in methanol in a similar manner as described for the preparation of **4** to give a syrup in a yield of 99%; $[\alpha]_D^{18}$ −121° (*c* 1.7, $CHCl_3$).

Found: C, 56.84; H, 7.07; N, 2.44%. Calcd for $C_{25}H_{37}NO_{11}$: C, 56.92; H, 7.07; N, 2.65%.

*Benzyl 2-*O*-(2-Deoxy-2-methoxycarbonylamino-*N*-methyl-α-*L*-glucopyranosyl)-α-dihydrostreptoside (**11**).* A solution of **10** (64 mg) in 2 M hydrochloric acid–methanol (1 : 1, 3 ml) was allowed to stand at room temperature for 7.5 hr. After neutralization of the solution with Amberlite IRA–900 (OH form), the solution was evaporated to give a syrup. Recrystallization from methanol–chloroform gave needles (38 mg, 67%), mp 184.5—185 °C, $[\alpha]_D^{18}$ −153° (*c* 2, MeOH); IR (KBr): 1675 cm^{-1}.

Found: C, 53.34; H, 6.81; N, 2.83%. Calcd for $C_{21}H_{33}NO_{11}$: C, 53.05; H, 6.99; N, 2.95%.

NMR (in CD_3OD): τ 8.79 (3H d, CCH_3), 6.92 (3H s, NCH_3), 6.48 (2H s, $C\underline{CH_2}OH$), 6.24 (3H s, CO_2CH_3), 4.87 (1H broad s, H-1), 4.78 (1H d, *J* 3 Hz, H-1′).

The melting point of this derivative (**11**) was not depressed by admixture with the specimen derived from natural benzyl dihydrostreptobiosaminide.

*Conversion of Natural Benzyl Dihydrostreptobiosaminide into **11**.* Natural benzyl dihydrostreptobiosaminide hydrochloride[10] was treated with methyl chloroformate and sodium carbonate in a similar manner as described in the preparation of **8** to give **11**; mp 184.5—186 °C, $[\alpha]_D^{22}$ −150° (*c* 1, MeOH).

*Benzyl 2-*O*-(2-Deoxy-2-methylamino-α-*L*-glucopyranosyl)-α-dihydrostreptoside Hydrochloride (Benzyl α-Dihydrostreptobiosaminide Hydrochloride) (**12**).* A mixture of **10** (90 mg) and 10% aqueous barium hydroxide (4.5 ml) was heated at 70 °C for 2 hr. Carbon dioxide was introduced and the precipitates were filtered off. The filtrate was evaporated and the residue was dissolved in methanol. After filtration, the solution was again evaporated. The procedure was repeated twice. Neutralization of the final methanol solution with hydrochloric acid followed by evaporation gave a glassy solid (62 mg, 72%), $[\alpha]_D^{20}$ −140° (*c* 1, H_2O) (lit[10], −110°).

Found: C, 51.12; H, 7.02; N, 3.08%. Calcd for $C_{20}H_{31}NO_9 \cdot HCl$: C, 51.56; H, 6.92; N, 3.00%.

NMR (in D_2O): τ 8.70 (3H d, CCH_3), 7.06 (3H s, NCH_3), 4.64 (1H d, *J* 3 Hz), 4.39 (1H d, *J* 3.5 Hz), 2.46 (5H s, C_6H_5).

*Dihydrostreptobiosamine (**13**).* To a solution of **12** (67 mg) in water (2 ml), 0.05 ml of acetic acid was added and the solution was hydrogenated with palladium black. The solution was filtered and evaporated to give a solid 41 mg (75%), $[\alpha]_D^{21}$ −104° (*c* 1, H_2O).

Found: C, 44.82; H, 7.32; N, 3.40%. Calcd for $C_{13}H_{25}NO_9 \cdot CH_3CO_2H$: C, 45.11; H, 7.32; N, 3.51%.

NMR (in D_2O): τ 8.78 (d, *J* 6.7 Hz, more intense than the other) and 8.73 (d, *J* 6.7 Hz) (3H in total, CCH_3); 8.05 (3H s, Ac), 6.88 (3H, NCH_3), 4.52 (1H d, *J* 3.7 Hz), 4.34 (1H d, *J* 3.2 Hz).

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