Synthesis of a Masked Derivative of 3′-Deoxydihydrostreptobiosamine, a Precursor for the Synthesis of 3″-Deoxydihydrostreptomycin

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(Received October 8, 1976)

2′-*N*-Acetyl-4′,6′-di-*O*-acetyl-3,3a-*O*-carbonyl-3′-deoxydihydrostreptobiosamine (**15**), a precursor in the synthesis of 3″-deoxydihydrostreptomycin, was prepared from benzyl α-dihydrostreptobiosaminide. The synthesis involves formation of L-allo compound (**5**) with inversion of the 3′-hydroxyl group of L-gluco derivative (**2**) in order to facilitate 3′-chlorination, dechlorination, of the 3′-chloro-L-gluco derivative (**7** or **11**) with tributyltin hydride, and utilization of cyclic 3,3a-*O*-carbonyl group instead of 3,3a-*O*-isopropylidene group which was unstable in the later reactions.

Recent studies have clarified that streptomycin is inactivated by resistant bacteria carrying R factor and resistant *Pseudomonas* producing enzymes which adenylylate[1] or phosphorylate[2] the 3″-hydroxyl group of the antibiotic. Removal of the 3″-hydroxyl group from dihydrostreptomycin is expected, therefore, to afford a dihydrostreptomycin derivative active against the resistant organisms. In this paper the synthesis of a key intermediate for the synthesis of 3″-deoxydihydrostreptomycin, namely, 4′,6′-di-*O*-acetyl-3′-deoxy-3,3a-*O*-carbonyldihydrostreptobiosamine** (**15**) starting from benzyl α-dihydrostreptobiosaminide is reported. The glycosyl chloride of **15** was successfully condensed with di-*N*-acetyl-di-*N*-benzyloxycarbonyl-4,5(5,6)-*O*-cyclohexylidenestreptidine[3] to give a condensation product which was led to 3″-deoxydihydrostreptomycin.[4]

Benzyl α-dihydrostreptobiosaminide[10] was treated with benzyl chloroformate to give the *N*-benzyloxycarbonyl derivative (**1**), which was converted to the di-*O*-isopropylidene derivative (**2**) by treatment with 2,2-dimethoxypropane in the presence of acidic catalyst. Thereafter, the free hydroxyl group at C-3′ of **2** was mesylated. Treatment of the 3′-*O*-mesyl derivative (**3**) with sodium iodide in *N*,*N*-dimethylformamide (DMF) afforded the *N*,*O*-carbonyl-L-allo derivative (**4**). It should be noted that, in the synthesis[5] of tobramycin, similar treatment of a structurally related compound having a 2,6-bis(ethoxycarbonylamino)-2,6-dideoxy-3-*O*-tosyl-α-D-glucopyranosyl moiety with sodium iodide in DMF gave a 3′-iodo derivative as a major product possibly with participation of the neighbouring ethoxycarbonyl group. It was further found that the derivative (**4**) was more easily obtained by alkaline treatment of **3** (86% yield). The L-allo structure of **4** was confirmed by the PMR spectra of **4** and **5** in which the $J_{2',3'}$ and $J_{3',4'}$ had suitable values (3—6 Hz) for *1C* L-allopyranoside.

Hydrolysis of the carbamate (**4**) with barium hydroxide gave **5**, which was acetylated to give **6**. It should also be noted that treatment of the 3′-*O*-mesyl derivative of **5** with sodium iodide in DMF gave no definite product. This result is unusual because, in a separate experiment,[6] we found that a 3-*O*-mesyl-D-allo compound, namely benzyl 4,6-*O*-benzylidene-2-benzyloxycarbonylamino-2-deoxy-3-*O*-mesyl-2-*N*-methyl-α-D-allopyranoside gave the corresponding 3-iodo derivative on treatment with 50% sodium iodide in DMF (100 °C, 48 h) in good yield.

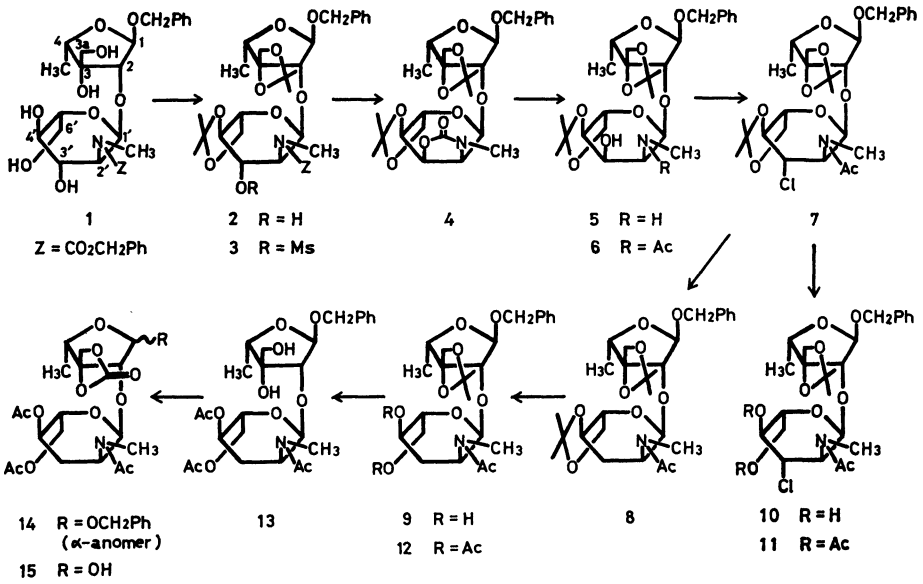
Treatment of **6** with sulfuryl chloride successfully gave 3′-chloro-L-gluco derivative (**7**) with inversion of the configuration at C-3′. The L-gluco configuration of **7** was confirmed by its PMR spectrum, in which the $J_{2',3'}$, gave 11.5 Hz, an indication that the 3′-chlorine is equatorial. At this stage, we have to mention that treatment of **2** with sulfuryl chloride gave no 3′-chloro derivative.

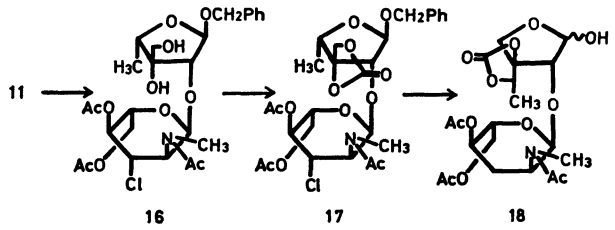
Catalytic hydrogenolysis of **7** with platinum oxide only recovered the starting material. Hydrogenolysis of **7** with palladium black gave a debenzylated product, while treatment with Raney nickel with addition of potassium hydroxide or triethylamine gave a dechlorodebenzylated product, both products being useless for the present synthesis. Reduction with tributyltin hydride[7] in the presence of α,α′-azobisisobutyronitrile successfully gave the 3′-deoxy compound (**8**) quantitatively. Its structure was confirmed by its PMR spectrum.

The deoxy derivative was modified to a derivative suitable for glycosylation. In the first place the 4′,6′-*O*-isopropylidene group of **8** was selectively removed to give **9**, which was then acetylated to give 4′,6′-di-*O*-acetyl derivative (**12**). This requirement originated from our experience in the synthesis of dihydrostreptomycin,[3,8,9] in which similar replacement of an isopropylidene group by two acyl groups gave a successful result. Alternatively, compound **12** was prepared from **7** by acid hydrolysis of **7** (which selectively removed the isopropylidene group at C-4′ and 6′ to give **10**) followed by acetylation to give **11** and dechlorination with tributyltin hydride.

The 3,3a-*O*-isopropylidene group of **12** was unstable for later treatment with thionyl chloride to prepare a glycosyl chloride; transketalization[8] was expected to occur in the dihydrostreptose moiety. The 3,3a-*O*-isopropylidene group of **12** was therefore removed by treatment with 75% acetic acid and the resulting diol

** In this paper, the dihydrostreptose moiety is taken as a parent monosaccharide and numbers of the carbon atoms of the 2-deoxy-2-methylamino-L-glucose moiety, the second monosaccharide, are primed and the hydroxymethyl carbon of dihydrostreptose moiety is numbered 3a.





(**13**) was treated with *p*-nitrophenyl chloroformate by a procedure previously described[8] to give the 3,3a-carbonate derivative (**14**). The presence of the cyclic carbonate group was confirmed by the absorption peak at 1810 cm^{-1} in the IR spectrum. Catalytic hydrogenolysis of the benzyl group with palladium black gave a masked derivative (**15**) of 3'-deoxydihydrostreptobiosamine. As separately reported,[4] the C-1 chloride of **15** was prepared and coupled[4] with a protected derivative[3] of streptidine and the condensation product was successfully led to 3"-deoxydihydrostreptomycin.[4]

In an alternative approach to **15** from **11**, deisopropylidenation of **11** gave the corresponding diol (**16**), which was converted into a 3,3a-carbonate (**17**). An attempt to prepare **15** from **17** by simultaneous removal of the 3'-chloro and 1-*O*-benzyl groups by catalytic hydrogenolysis, however, gave an unusual result. Treatment of **17** with Raney nickel and hydrogen gave **18**, an isomer of **15**. Its structure was confirmed by PMR spectroscopy. The methine proton signal at C-4 appeared as a quartet at a low field (δ 5.16), indicating that 4-hydroxyl group is acylated. This observation is another example which shows that the dihydrostreptose moiety is labile and tends to undergo ring-isomerization.

Experimental

General. Infrared spectra were recorded for potassium bromide pellets with a Hitachi Model 285 grating infrared spectrophotometer. PMR spectra were recorded at 60 and 100 MHz with Hitachi R-24A and Varian XL-100 spectrometers. Thin layer chromatography (TLC) was performed on Wakogel B-5 with sulfuric acid spray for detection. For column chromatography, silica gel (Wakogel C-200) was used.

Benzyl 2'-N-Benzyloxycarbonyl-α-dihydrostreptobiosaminide (1). To a mixture of benzyl α-dihydrostreptobiosaminide hydrochloride[10] (6.81 g) and sodium carbonate (3.23 g) in aqueous acetone (1: 1, 180 ml), benzyl chloroformate (4.6 ml) was added and the mixture was stirred at 0 °C for 5 h. The mixture was filtered and the filtrate was concentrated. The residue, after washing with ether, was dissolved in chloroform. Filtration followed by concentration gave a residue. Recrystallization from chloroform–ether gave needles, 5.56 g (67%), mp 152—152.5 °C, $[\alpha]_D^{24}$ −140° (*c* 1, $CHCl_3$).

Found: C, 59.57; H, 6.57; N, 2.54%. Calcd for $C_{28}H_{37}NO_{11}$: C, 59.67; H, 6.62; N, 2.49%.

Benzyl 2'-N-Benzyloxycarbonyl-3,3a: 4',6'-di-O-isopropylidene-α-dihydrostreptobiosaminide (2). To a solution of **1** (6.72 g) in DMF (120 ml), anhydrous *p*-toluenesulfonic acid (960 mg) and 2,2-dimethoxypropane (19.2 ml) were added and the solution was heated at 50 °C for 3 h. The solution was poured into a mixture of aqueous 5% sodium hydrogencarbonate solution (850 ml) and chloroform (850 ml) with vigorous stirring and the organic layer separated was concentrated to a syrup. The chloroform solution of the syrup was washed with water, dried (Na_2SO_4), and concentrated to give a syrup, which was chromatographed over silica gel (benzene–methyl ethyl ketone 9: 1) to give a thick syrup of **2**, 7.28 g (94%), $[\alpha]_D^{24}$ −117° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 1.25 (3H d, CCH_3); 1.23, 1.3, 1.42, and 1.48 (each 3H s, $2C(CH_3)_2$); 3.06 (3H s, NCH_3), 4.56 (2H q, OCH_2Ph) 4.9—5.15 (4H, H-1,1' and CO_2CH_2Ph).

Found: C, 63.14; H, 6.94; N, 1.94%. Calcd for $C_{34}H_{45}NO_{11}$: C, 63.34; H, 7.19; N, 2.17%.

Benzyl 2'-N-Benzyloxycarbonyl-3,3a: 4',6'-di-O-isopropylidene-3'-O-mesyl-α-dihydrostreptobiosaminide (3). Compound **2** was treated with methanesulfonyl chloride in pyridine in a usual manner to give a thick syrup of **3**, 99%, $[\alpha]_D^{24}$ −95° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 3.07 and 3.10 (each 3H s, NCH_3 and SO_2CH_3).

Found: C, 58.03; H, 6.50; N, 1.99; S, 4.66%. Calcd for $C_{35}H_{47}NO_{13}S$: C, 58.24; H, 6.56; N, 1.94; S, 4.44%.

Benzyl 2-O-(2,3-N,O-Carbonyl-2-deoxy-4,6-O-isopropylidene-2-methylamino-α-L-allopyranosyl)-3,3a-O-isopropylidene-α-dihydrostreptoside (4). A solution of **3** (8.14 g) and sodium

acetate trihydrate (8.14 g) in 2-methoxyethanol (160 ml) was refluxed for 65 h. Evaporation of the solvent gave a solid, which was dissolved in chloroform. The solution was washed with water, dried (Na_2SO_4), and concentrated to give a solid. Recrystallization from ethanol gave prisms, 5.17 g (86%), mp 170.5—172 °C, $[\alpha]_D^{24}$ −171° (*c* 1, $CHCl_3$); IR: 1760 cm^{-1} (cyclic carbamate); PMR ($CDCl_3$) δ: 1.29 (3H, d J=6.5 Hz, CCH_3; collapsed to a singlet on irradiation at 4.05); 1.40 (6H), 1.45 (3H) and 1.50 (3H) (each s, $2C(CH_3)_2$); 3.00 (3H s, NCH_3), 3.5—3.9 (6H), 4.05 (1H q, J=6.5 Hz, H-4; collapsed to a singlet on irradiation at δ 1.29); 2H AB q centered at δ 4.07 (J=9 Hz, H-3a); 4.54 (1H q, J=3 and 6 Hz, H-3′; collapsed to a singlet on irradiation at δ ≈3.84 (H-2′,4′)); 2H AB q centered at δ 4.54 (OCH_2Ph); 5.04 (1H d, J≈1 Hz, H-1), 5.12 (1H d, J=5 Hz, H-1′), 7.27 (5H s, Ph). The doublets of H-1 and H-1′ were collapsed to singlets, respectively, on irradiation at δ ≈3.84, therefore, the signals at δ ≈3.84 were assigned to H-2, 2′,4′.

Found: C, 60.37; H, 6.87; N, 2.45%. Calcd for $C_{27}H_{37}NO_{10}$: C, 60.55; H, 6.96; N, 2.62%.

Benzyl 2-O-(2-Deoxy-4,6-O-isopropylidene-2-methylamino-α-L-allopyranosyl)-3,3a-O-isopropylidene-α-dihydrostreptoside (5). To a solution of **4** (4.74 g) in methanol (120 ml), 5.5% aqueous barium hydroxide (120 ml) was added and the mixture was stirred at 50 °C for 110 h. Filtration followed by evaporation of the filtrate gave a residue, which was extracted with chloroform. The solution was washed with water, dried (Na_2SO_4), and concentrated to give a thick syrup, which was crystallized from ether to give needles, 3.39 g (75%), mp 110—111 °C, $[\alpha]_D^{24}$ −131° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 1.28 (3H d, CCH_3); 1.42 (3H) and 1.47 (9H) (each s, $2C(CH_3)_2$); 2.46 (3H s, NCH_3), 5.03 (1H d, J=4 Hz, H-1′), 5.05 (1H s, H-1). When measured in $CDCl_3$–D_2O, an 1H triplet ($J_{1',2'}=J_{2',3'}$ ≈3.5 Hz, H-2′) appeared at δ 2.65 and it was collapsed to a doublet on irradiation at δ 5.03.

Found: C, 61.31; H, 7.73; N, 2.66%. Calcd for $C_{26}H_{39}NO_9$: C, 61.28; H, 7.71; N, 2.75%.

Benzyl 2-O-(2-Acetamido-2-deoxy-4,6-O-isopropylidene-2-N-methyl-α-L-allopyranosyl)-3,3a-O-isopropylidene-α-dihydrostreptoside (6). To a solution of **5** (652 mg) in methanol (17.5 ml), acetic anhydride (0.28 ml) was added and the solution was kept at room temperature overnight. Concentration of the solution gave a syrup, which was dissolved in chloroform. The solution was washed with water, dried (Na_2SO_4), and evaporated to give a thick syrup, 659 mg (93%), $[\alpha]_D^{23}$ −132° (*c* 1.3, $CHCl_3$); IR: 1650 cm^{-1}; PMR ($CDCl_3$) δ: 2.12 (3H s, Ac), 3.38 (3H s, NCH_3).

Found: C, 60.75; H, 7.32; N, 2.35%. Calcd for $C_{28}H_{41}NO_{10}$: C, 60.96; H, 7.49; N, 2.54%.

Benzyl 2′-N-Acetyl-3′-chloro-3′-deoxy-3,3a: 4′,6′-di-O-isopropylidene-α-dihydrostereptobiosaminide (7). To a cold solution (−5 °C) of **6** (487 mg) in dichloromethane (5.3 ml), pyridine (0.9 ml) and sulfuryl chloride (0.35 ml) were added and the solution was kept in the cold for 18 h and then at 5 °C for 25 h. The solution was poured into a mixture of chloroform (90 ml) and saturated sodium hydrogencarbonate solution (90 ml) with vigorous stirring and the organic layer separated was dried (Na_2SO_4). Concentration gave a reddish-brown syrup, which was chromatographed over silica gel (benzene–methyl ethyl ketone 9: 1) and the fractions containing **7** were concentrated to give a reddish syrup (334 mg). Recrystallization from ether gave colorless prisms, 284 mg (56%), mp 170—171.5 °C, $[\alpha]_D^{24}$ −129° (*c* 1, $CHCl_3$). PMR ($CDCl_3$) δ: 1.26 (3H d, J=6.5 Hz, CCH_3); 1.36, 1.38, 1.47, and 1.51 (each 3H s, $2C(CH_3)_2$); 2.13 (3H s, Ac), 3.06 (3H s, NCH_3), 3.80 (1H d, J≈1 Hz, H-2; collapsed to a singlet on irradiation at δ 4.98 (H-1)); 3.83, 3.93, 4.14, and 4.23 (2H, AB q, H-3a); 4.38, 4.50, 4.65, and 4.77 (2H AB q, OCH_2Ph); 4.90 (1H q, J=3.5 and 11.5 Hz, H-2′; collapsed to a doublet (J=3.5 Hz) on irradiation at δ 4.15 (H-3′)), 4.98 (1H s, H-1; on irradiation at δ 3.80 (H-2), the signal sharpened), 5.08 (1H d, J=3.5 Hz, H-1′), 7.30 (5H s, Ph).

Found: C, 58.87; H, 7.00; N, 2.33; Cl, 6.38%. Calcd for $C_{28}H_{40}NO_9Cl$: C, 58.99; H, 7.07; N, 2.46; Cl, 6.22%.

Benzyl 2′-N-Acetyl-3′-deoxy-3,3a: 4′,6′-di-O-isopropylidene-α-dihydrostreptobisaminide (8). To a solution of **7** (1.01 g) in dry toluene (21 ml), tributyltin hydride (1.0 ml) and α,α′-azobisisobutyronitrile (10 mg) were added under the atmosphere of nitrogen and the solution was heated at 80 °C for 2 h. Concentration of the solution gave a syrup, which was chromatographed over silica gel (benzene–methyl ethyl ketone 4: 1). The fraction containing **8** were concentrated to give a thick syrup, 935 mg (99%), $[\alpha]_D^{25}$ −100° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 1.27 (3H d, J=6.5 Hz, CCH_3); 1.36, 1.38, 1.42, and 1.50 (each 3H s, $2C(CH_3)_2$; 1.80 (1H double t, J≈4, ≈4, and 11 Hz, H-3′$_{eq}$; on irradiation at δ 3.8, the sextet collapsed to a quartet (J≈4 and 11 Hz (J_{gem})), 2.09 (3H s, Ac), 3.01 (3H s, NCH_3).

Found: C, 62.47; H, 7.46; N, 2.46%. Calcd for $C_{28}H_{41}NO_9$: C, 62.79; H, 7.72; N, 2.62%.

Benzyl 2′-N-Acetyl-3′-deoxy-3,3a-O-isopropylidene-α-dihydrostreptobiosaminide (9). A solution of **8** (932 mg) in 25% acetic acid in methanol (34 ml) was refluxed for 50 min. Concentration of the solution gave a syrup, which was chromatographed over silica gel (benzene–ethanol 9: 1) to give a thick syrup of **9**, 821 mg (95%), $[\alpha]_D^{25}$ −161° (*c* 1, $CHCl_3$).

Found: C, 60.36; H, 7.31; N, 2.75%. Calcd for $C_{25}H_{37}NO_9$: C, 60.59; H, 7.53; N, 2.83%.

Benzyl 2′-N-Acetyl-3′-chloro-3′-deoxy-3,3a-O-isopropylidene-α-dihydrostreptobiosaminide (10). A solution of **7** (284 mg) in 25% acetic acid in methanol (10 ml) was refluxed for 3 h. Concentration of the solution *in vacuo* gave a syrup. It showed, on TLC (benzene–ethanol 9: 1), spots of R_f 0.15 (very slight), 0.3 (**10**), and 0.45 (very slight, **7**). The syrup was chromatographed over silica gel (benzene–ethanol 12: 1) to give a colorless thick syrup, 253 mg (96%), $[\alpha]_D^{24}$ −148° (*c* 1, $CHCl_3$).

Found: C, 56.36; H, 6.92; N, 2.34; Cl, 6.92%. Calcd for $C_{25}H_{36}NO_9Cl$: C, 56.65; H, 6.85; N, 2.64; Cl, 6.69%.

Benzyl 2′-N-Acetyl-4′,6′-di-O-acetyl-3′-chloro-3′-deoxy-3,3a-O-isopropylidene-α-dihydrostreptobiosaminide (11). To a solution of **10** (215 mg) in pyridine (6 ml), acetic anhydride (0.13 ml) was added and the solution was kept at room temperature overnight. Water (0.1 ml) was added and the solution was concentrated. The chloroform solution of the residual syrup was successively washed with aqueous sodium hydrogencarbonate solution, aqueous potassium hydrogensulfate solution, and water, dried (Na_2SO_4), and concentrated to give a syrup of **11**, 236 mg (94%), $[\alpha]_D^{25}$ −84° (*c* 2, $CHCl_3$); PMR ($CDCl_3$) δ: 1.36 (6H s, $C(CH_3)_2$), 2.03 (3H s, Ac), 2.11 (6H s, Ac), 3.00 (3H s, NCH_3).

Found: C, 56.46; H, 6.49; N, 2.16; Cl, 5.86%. Calcd for $C_{29}H_{40}NO_{11}Cl$: C, 56.72; H, 6.57; N, 2.28; Cl, 5.77%.

Benzyl 2′-N-Acetyl-4′,6′-di-O-acetyl-3′-deoxy-3,3a-O-isopropylidene-α-dihydrostreptobisaminide (12). *From 11*: To a solution of **11** (2.04 g) in dry toluene (39 ml), tributyltin hydride (1.9 ml) and α,α′-azobisisobutyronitrile (19 mg) were added and the solution was treated similarly as described for **8**. Column chromatography over silica gel (benzene–methyl ethyl ketone 6: 1) gave an amorphous solid of **12**, 1.81 g (94%), $[\alpha]_D^{25}$ −140° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 1.29 (3H d, CCH_3), 1.40 (6H s, $C(CH_3)_2$), 2.09 (6H s, Ac), 2.11 (3H s, Ac), 3.00 (3H s, NCH_3).

Found: C, 60.27; H, 7.16; N, 2.38%. Calcd for $C_{29}H_{41}$-

NO_{11}: C, 60.09; H, 7.13; N, 2.42%.

From **9**: Compound **9** was treated with acetic anhydride in pyridine to give **12** in a 98% yield.

*Benzyl 2'-*N*-Acetyl-4',6'-di-*O*-acetyl-3'-deoxy-α-dihydrostreptobiosaminide (13).* A solution of **12** (1.73 g) in 75% acetic acid (43 ml) was heated at 80 °C for 3 h. Concentration of the solution gave a syrup, which was chromatographed over silica gel (benzene–ethanol 9: 1) to give **12** (470 mg, 27%) and **13**. The latter was recrystallized from ether to give needles, 811 mg (51%), mp 157—159 °C, $[\alpha]_D^{25}$ −169° (*c* 1, $CHCl_3$); PMR ($CDCl_3$) δ: 2.00, 2.06, and 2.09 (each 3H s, Ac).

Found: C, 57.82; H, 6.87; N, 2.51%. Calcd for $C_{26}H_{37}NO_{11}$: C, 57.87; H, 6.91; N, 2.60%.

*Benzyl 2'-*N*-Acetyl-4',6'-di-*O*-acetyl-3,3a-*O*-carbonyl-3'-deoxy-α-dihydrostreptobiosaminide (14).* To a solution of **13** (251 mg) in pyridine (7.5 ml), *p*-nitrophenyl chloroformate (115 mg) was added and the mixture was stirred at room temperature. Triethylamine (0.16 ml × 3) and the chloride (230 mg × 3) were added alternately in every 5 h. After 35 h, chloroform (80 ml) was added and the solution was washed with aqueous sodium hydrogencarbonate solution and water throughly, dried (Na_2SO_4), and concentrated to give a yellow syrup. Column chromatography over silica gel (benzene–methyl ethyl ketone 3: 1) gave a thick syrup of **14**, 225 mg (85%), R_f 0.35 (TLC, benzene–ethanol 9: 1), $[\alpha]_D^{25}$ −144° (*c* 1, $CHCl_3$). IR: 1810 (carbonate), 1740 (ester), 1640 (amide) cm^{-1}. PMR ($CDCl_3$) δ: 1.34 (3H d, CCH_3); 2.02, 2.07, 2.12 (each 3H s, Ac), 2.94 (3H s, NCH_3), 4.96 (1H d, J=3 Hz, H-1 or 1'), 5.19 (1H d, J=3 Hz, H-1' or 1; on irradiation at δ 4.24, the doublet collapsed to a singlet).

Found: C, 57.47; H, 6.21; N, 2.29%. Calcd for $C_{27}H_{35}NO_{12}$: C, 57.34; H, 6.24; N, 2.48%.

*2'-*N*-Acetyl-4',6'-di-*O*-acetyl-3,3a-*O*-carbonyl-3'-deoxydihydrostreptobiosamine (15).* Compound **14** was hydrogenated with palladium black in a usual manner to give **14** as a syrup in a yield of 96%, $[\alpha]_D^{25}$ −141°→−127° (*c* 1, $CHCl_3$). IR: 1820, 1740, 1640 cm^{-1}. PMR ($CDCl_3$) δ: 1.30 and 1.40 (totally 3H d in the ratio of ≈3: 1, J=6 Hz, CCH_3), 2.06 (6H s, OAc), 2.13 (3H s, NAc (?)), 2.95 (3H s, NCH_3), 5.39 (≈1H d, J=4 Hz, H-1 (?)).

Found: C, 49.67; H, 6.27; N, 2.51%. Calcd for $C_{20}H_{29}NO_{12}\cdot 0.5H_2O$: C, 49.58; H, 6.24; N, 2.89%.

*Benzyl 2'-*N*-Acetyl-4',6'-di-*O*-acetyl-3'-chloro-3'-deoxy-α-dihydrostreptobiosaminide (16).* Prepared from **11** in a similarn manner as described for **13** to give a thick syrup of **16** in a 77% yield, $[\alpha]_D^{23}$ −144° (*c* 2, $CHCl_3$).

Found: C, 54.34; H, 6.14; N, 2.24; Cl, 6.32%. Calcd for $C_{26}H_{36}NO_{11}Cl$: C, 54.40; H, 6.32; N, 2.44; Cl, 6.18%.

*Benzyl 2'-*N*-Acetyl-4',6'-di-*O*-acetyl-3,3a-*O*-carbonyl-3'-chloro-3'-deoxy-α-dihydrostreptobiosaminide (17).* Prepared from **16** in a similar manner as described for **14** to give a thick syrup of **17** in a 87% yield, $[\alpha]_D^{24}$ −126° (*c* 1, $CHCl_3$).

Found: C, 54.21; H, 5.72; N, 2.16; Cl, 6.00%. Calcd for $C_{27}H_{34}NO_{12}Cl$: C, 54.05; H, 5.71; N, 2.33; Cl, 5.91%.

Hydrogenolysis of 17 with Raney Nickel to 18. A solution of **17** (28 mg) in aqueous dioxane (1: 10, 1 ml) was hydrogenated under pressure (50 lb/in²) with Raney nickel at room temperature for 26 h. Filtration followed by concentration of the filtrate gave colorless needles, which was filtered with aid of benzene to give **18**, 17 mg (66%), mp 188—190 °C, $[\alpha]_D^{25}$ −78° (final value, *c* 0.5, $CHCl_3$); IR: 1810, 1770 (sh), 1740, 1620 cm^{-1}. PMR ($CDCl_3$+CD_3OD) δ: 1.52 (3H d, J=7 Hz, $CHCH_3$); 2.09, 2.10, and 2.13 (each 3H s, Ac); 2.98 (3H s, NCH_3), 5.01 (1H d, J=3.5 Hz, H-1'; it collapsed to a singlet on irradiation at δ 4.61), 5.16 (1H q, J=7 Hz, $CHCH_3$; it collapsed to a singlet on irradiation at δ 1.52).

Found: C, 49.52; H, 6.52; N, 2.89%. Calcd for $C_{20}H_{29}NO_{12}\cdot 0.5H_2O$: C, 49.58; H, 6.24; N, 2.89%.

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