Aminocyclitols. 36. Chlorination and Dechlorination of Aminocyclitol and Inositol Derivatives. Preparation of Dideoxy- and Trideoxystreptamines[1a,b]

Seiichiro Ogawa,* Yuji Hongo, Hitoshi Fujimori, Keiji Iwata,
Akira Kasuga, and Tetsuo Suami
Department of Applied Chemistry, Faculty of Engineering, Keio University, Hiyoshi, Yokohama 223

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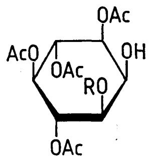
Chlorination of four aminocyclitol and six inositol derivatives with sulfuryl chloride gave the chloro substitution products, which were then dechlorinated by hydrogenolysis with Raney nickel or by treatment with tributyltin(IV) hydride giving the corresponding deoxy compounds. Several useful aminocyclitols, including 2,4-dideoxy- and 2,4,5-trideoxystreptamines, were prepared from 2-deoxystreptamine derivatives by these procedures.

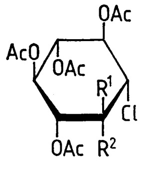
The reaction of sulfuryl chloride with hexopyranoses and hexopyranosides had been extensively studied by Jones *et al.*[2] The mechanism and selectivity of the nucleophilic substitution of sulfate esters by chloride ions have been well established by both steric and electronic effects.[3] In the present paper, the reactions of aminocyclitol and inositol derivatives with sulfuryl chloride, and the preparation of dideoxy- and trideoxystreptamines by dechlorination of the corresponding chloro deoxy compounds are reported.

Inositol Derivatives. Treatment of 1,4,5,6-tetra-*O*-acetyl-*myo*-inositol (**1**)[4] with 3 mol equiv of sulfuryl chloride in pyridine at −10 °C for 0.5 h and subsequently at 5 °C overnight gave tetra-*O*-acetyl-2,3-dichloro-2,3-dideoxy-*myo*-inositol (**5**) in 45% yield. The structure of **5** was confirmed on the basis of the following evidence. In the ^{1}H NMR spectrum of **5** in deuteriochloroform ($CDCl_3$), the signals due to H-2 and H-3 were coupled and appeared as a triplet (δ 4.66) and a double doublet (δ 4.28) having 3-Hz splitting, and 3- and 10-Hz splitting, respectively. Hydrogenolysis of **5** with Raney nickel T-4[5] in ethanol in the presence of Amberlite IR-45 (OH$^-$) gave the known tetra-*O*-acetyl-1,3/2,4-cyclohexanetetrol (**9**)[6] in 67% yield.

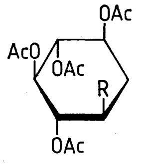
Under similar conditions, the 3-*O*-benzoyl (**2**),[7] 3-*O*-mesyl (**3**),[7] and 3-*O*-tosyl derivatives (**4**)[8] of **1** were readily chlorinated to give the corresponding chloro deoxy compounds (**6**, **7**, and **8**) with inversion of configuration. Compound **6** could be hydrogenolyzed with Raney nickel analogously as described above to give the deoxy derivative (**10**) in 80% yield. Compounds **7** and **8** however gave **9** as the main product, together with a trace of the deoxy compounds (**11** and **12**), resulting from a cleavage of both the chlorine and sulfonyloxyl groups under these reduction conditions. Removal of only the chlorine atom of **8** was effected by treatment with tributyltin(IV) hydride in toluene in the presence of α,α'-azobisisobutyronitrile[9] and **12** was obtained in 87% yield.



1 R=H
2 R=Bz
3 R=Ms
4 R=Ts



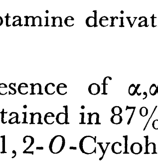
5 R^1=H, R^2=Cl
6 R^1=OBz, R^2=H
7 R^1=OMs, R^2=H
8 R^1=OTs, R^2=H



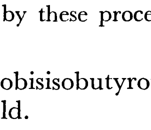
9 R=H
10 R=OBz
11 R=OMs
12 R=OTs

1,2-*O*-Cyclohexylidene-3,4,6-tri-*O*-tosyl-*myo*-inositol (**13**)[10] was similarly chlorinated to give the known chloro deoxy compound (**14**)[11] in 76% yield, which was subsequently reduced with tributyltin(IV) hydride to give the deoxy compound (**15**) in 55% yield.

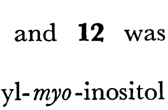
1,4-Di-*O*-benzoyl-2,3-*O*-cyclohexylidene-*myo*-inositol (**16**),[11] when treated with sulfuryl chloride, gave the monochloro substitution product (**17**) in 62% yield. The acetyl derivative (**18**) of **17** was obtained by the conventional way. Acid hydrolysis of **17** followed by acetylation gave the penta-*O*-acetyl-chlorodeoxyinositol (**19**), which was reduced with tributyltin(IV) hydride to the known penta-*O*-acetyl-1,5/2,3,4-cyclohexanepentol (**20**)[12] in 77% yield. These results indicated that the C-5 hydroxyl group of **16** was selectively displaced by a chloride ion *via* the sulfate ester, establishing the structure of **17** as 1,4-di-*O*-benzoyl-5-chloro-2,3-*O*-cyclohexylidene-5-deoxy-*neo*-inositol.



13 R^1=OH, R^2=H
14 R^1=H, R^2=Cl
15 R^1=R^2=H



16 R^1=OH, R^2=R^3=H
17 R^1=R^3=H, R^2=Cl
18 R^1=H, R^2=Cl, R^3=Ac



19 R=Cl
20 R=H

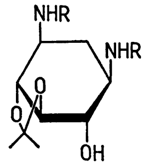
According to the above results, it was noted that an isolated hydroxyl group and both of the vicinal hydroxyl groups in the *cis*-relationship were easily displaced by chloride ions with inversion of configuration, but only one of the vicinal hydroxyl groups in the *trans* position was able to be displaced.

Aminocyclitol Derivatives. Deoxygenation of streptamine and 2-deoxystreptamine has been undertaken to prepare the deoxy derivatives of biological importance. Readily available 2-deoxystreptamine derivatives (**21**, **22**, **23**, and **33**) and streptamine derivative (**38**) were used as the starting materials.

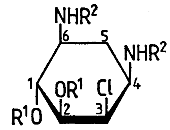
Chlorination of 1,2-*O*-isopropylidene-(1,3/2,4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3-cyclohexanetriol (**22**)[13] with 3 mol equiv of sulfuryl chloride in pyridine gave 1,2-*O*-isopropylidene-(1/2,3,4,6)-3-chloro-4,6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol (**24**) in 63%

yield. The structure was confirmed by ^1H NMR, which revealed a narrow triplet at δ 4.69 attributable to H-3, indicating an inversion of the configuration at C-3. On treatment with 50% aqueous acetic acid at 80 °C followed by acetylation, **24** gave the di-*O*-acetyl derivative (**26**) in 83% yield. Similarly, the *N,N'*-diacetyl (**21**)[14] and *N,N'*-bis(benzyloxycarbonyl) derivatives (**23**)[14] of *O*-isopropylidene-2-deoxystreptamine were treated with sulfuryl chloride followed by mild acid hydrolysis and acetylation which gave the corresponding chloro deoxy compounds (**25** and **27**) in 48 and 34% yields, respectively.

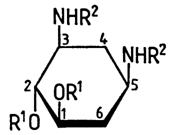
Hydrogenolysis of **25** and **27** with Raney nickel in ethanol gave the deoxy compounds (**28** and **32**) in 56 and 89% yields, respectively. Compound **28** was shown to be identical with an authentic sample of tetra-*N,O*-acetyl-(1,3,5/2)-3,5-diamino-1,2-cyclohexanediol (2,4-dideoxystreptamine).[15] Hydrolysis of **28** with boiling 6 M hydrochloric acid gave the crystalline dihydrochloride (**29**) in 74% yield, which was further characterized by conversion into the *N,N'*-bis(ethoxycarbonyl) (**30**) and *N,N'*-bis(benzyloxycarbonyl) derivatives (**31**). Compound **30** was identical with the compound derived from **24** by mild acid hydrolysis and hydrogenolysis.



21 R=Ac
22 R=Cbe
23 R=Cbz



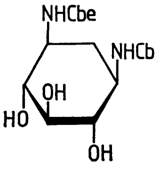
24 R^1, R^1=$C(CH_3)_2$ R^2=Cbe
25 R^1=R^2=Ac
26 R^1=Ac, R^2=Cbe
27 R^1=Ac, R^2=Cbz



28 R^1=R^2=Ac
29 R^1=R^2=H dihydrochloride
30 R^1=H, R^2=Cbe
31 R^1=H, R^2=Cbz
32 R^1=Ac, R^2=Cbz

The chlorination of *N,N'*-bis(ethoxycarbonyl)-2-deoxystreptamine (**33**)[13] was attempted to obtain the other chloro deoxy compounds. However, **33** gave, after acetylation, the cyclic sulfate ester (**34**, 28%) as the major product, together with **26** (17%). Thus, on chlorination, successive treatment with methanolic ammonia, and acetylation, **33** gave **26** in 61% yield.

In addition, the introduction of an amino function into 2-deoxystreptamine was carried out by reacting **26** with an azide ion. Treatment of **26** with an excess of sodium azide in *N,N*-dimethylformamide gave the azido deoxy compound (**35**) in 34% yield, which was reduced with Raney nickel to the 4-amino-4-deoxy derivative of 2-deoxystreptamine characterized as the *N*-acetyl derivative (**36**). Hydrolysis of **36** with boiling 48% hydrobromic acid followed by acetylation gave penta-*N,O*-acetyl-(1,3/2,4,6)-3,4,6-triamino-1,2-cyclohexanediol (**37**) whose ^1H NMR spectrum in dimethyl-d_6 sulfoxide revealed the presence of three equatorial acetamido groups [δ 1.76 (1) and 1.78 (2)] and two equatorial acetoxyl groups [δ 1.91 (1) and 1.92 (1)], establishing the proposed structure.



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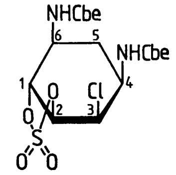

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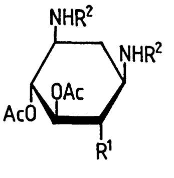
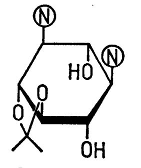


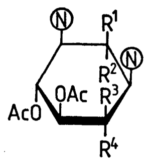
35 R^1=N_3, R^2=Cbe
36 R^1=NHAc, R^2=Cbe
37 R^1=NHAc, R^2=Ac

1,2-*O*-Isopropylidene-(1,3,5/2,4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol (**38**), when treated with sulfuryl chloride, gave two monochlorides (**39** and **40**) and one dichloride (**41**), which after separation by silica-gel chromatography gave yields of 19, 31, and 4%, respectively. Differentiation of **39** from **40** has been done by comparison of the ^1H NMR spectra. Thus, **39** showed two peaks of 2: 1 ratio attributable to the three acetyl groups, while **40** showed three peaks for three individual acetyl groups. Finally, **40** was found to be identical with an authentic sample.[1a]

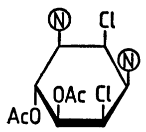


Ⓝ = NHCbe

38



39 R^1=Cl, R^2=R^3=H, R^4=OAc
40 R^1=R^4=H, R^2=OAc, R^3=Cl



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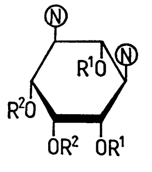
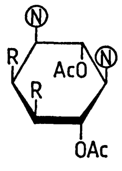
(1,2,3,5/4,6)-4,6-Bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol (**42**) prepared from hexa-*N,O*-acetyl-*myo*-inosadiamine-4,6[16] by hydrolysis and subsequent ethoxycarbonylation was treated with 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of an acid catalyst to give the 1,2-*O*-isopropylidene derivative, which was converted into 1,5-di-*O*-acetyl-2,3-*O*-isopropylidene-(1,2,3,5/4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol (**43**) in 25% overall yield. Chlorination of the hydroxy compound derived from **43** by *O*-deisopropylidenation gave the dichloro dideoxy compound (**44**) in 41% yield. The ^1H NMR spectrum of **44** was shown to be very similar to that of **5**, the protons attached to the carbon atoms bearing chlorine atoms. Dechlorination of **44** gave di-*O*-acetyl-(1,3/2,4)-2,4-bis(ethoxycarbonylamino)-1,3-cyclohexanediol (**45**) in 71% yield. The ^1H NMR spectrum supported the proposed structure.

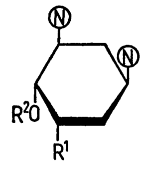
Chlorination of **30** gave one monochloro substitution product (**46**) in 44% yield. The presence of the chlorine atom on C-1 was demonstrated by the appearance of the double doublet (δ 4.89) having 3.5- and 10-Hz



42 R^1=R^2=H
43 R^1=Ac R^2=$C(CH_3)_2$



44 R=Cl
45 R=H



46 R^1=Cl, R^2=Ac
47 R^1=H, R^2=Ac
48 R^1=R^2=H

splitting due to H-2. Dechlorination of **46** gave (1/2, 4)-1-acetoxy-2,4-bis(ethoxycarbonylamino)cyclohexane (**47**) in 63% yield, which was *O*-deacetylated to give *N*,*N'*-bis(ethoxycarbonyl)-2,4,5-trideoxystreptamine (**48**).

Experimental[17]

*1,4,5,6-Tetra-*O*-acetyl-2,3-dichloro-2,3-dideoxy-*myo*-inositol (5).* To a solution of 1,4,5,6-tetra-*O*-acetyl-*myo*-inositol (**1**)[4] (1 g) in dry pyridine (30 ml) was added sulfuryl chloride (0.7 ml, 3 molar equiv) at −15 °C with agitation. After stirring at the same temperature for 1 h, the reaction mixture was kept at 5 °C overnight. An insoluble matter was filtered off and washed with pyridine. The filtrate and washings were combined and evaporated to dryness, the residue dissolved in chloroform (30 ml), and the solution washed successively with aqueous sodium hydrogencarbonate and water, dried over anhydrous sodium sulfate and evaporated to dryness. The residue was crystallized from ethanol to give 0.48 g (45%) of **5**: mp 159—161 °C. Recrystallization from ethanol gave a pure sample: mp 160—160.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.00 (s, 6), 2.07 (s, 3), and 2.11 (s, 3) (OAc), 4.28 (dd, 1, $J_{2,3}=3$ Hz, $J_{3,4}=10$ Hz, H-3), 4.66 (t, 1, $J_{1,2}=3$ Hz, H-2), 5.05 (dd, 1, $J_{1,6}=10$ Hz, H-1), 5.25 (t, 1, $J_{4,5}=J_{5,6}=8$ Hz, H-5), 5.50 (dd, 1) and 5.65 (dd, 1) (H-4 and H-6).

Found: Cl, 18.64%. Calcd for $C_{14}H_{18}O_8Cl_2$: Cl, 18.41%.

*1,2,3,4-Tetra-*O*-acetyl-5-*O*-benzoyl-6-chloro-6-deoxy-*scyllo*-inositol (6).* To a solution of 1,4,5,6-tetra-*O*-acetyl-3-*O*-benzoyl-*myo*-inositol (**2**)[7] (2 g) in dry pyridine (40 ml) was added sulfuryl chloride (1.3 ml, 3.5 molar equiv) at −10 °C with agitation. After 1 h at this temperature, the solution was stirred for a further 2.5 h at 5 °C. Then the reaction mixture was processed as described for the preparation of **5**. The product was crystallized from chloroform–ethanol to give 1.2 g (55%) of **6**: mp 241—244 °C; ^{1}H NMR ($CDCl_3$) δ 1.90 (s, 3), 2.04 (s, 3), 2.06 (s, 3), and 2.13 (s, 3) (OAc), 4.21 (t, 1, $J_{1,6}=J_{5,6}=9$ Hz, H-6).

Found: C, 53.27; H, 4.87; Cl, 7.70%. Calcd for $C_{21}H_{23}O_{10}Cl$: C, 53.57; H, 4.92; Cl, 7.53%.

*1,2,3,4-Tetra-*O*-acetyl-6-chloro-6-deoxy-5-*O*-mesyl-*scyllo*-inositol (7).* 1,4,5,6-Tetra-*O*-acetyl-3-*O*-mesyl-*myo*-inositol (**3**)[7] (0.51 g) was treated with sulfuryl chloride (0.4 ml, 2 molar equiv) in pyridine (15 ml) as described for the preparation of **5**. The crude product was crystallized from ethanol to give 0.26 g (49%) of **7**: mp 187.5—189 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.98 (s, 3), 2.05 (s, 3), and 2.07 (s, 3) (OAc), 3.18 (s, 3, mesyl CH_3).

Found: C, 40.40; H, 4.65%. Calcd for $C_{15}H_{21}O_{11}SCl$: C, 40.49; H, 4.76%.

*1,2,3,4-Tetra-*O*-acetyl-6-chloro-6-deoxy-5-*O*-tosyl-*scyllo*-inositol (8).* 1,4,5,6-Tetra-*O*-acetyl-3-*O*-tosyl-*myo*-inositol (**4**)[8] (5 g) was treated with sulfuryl chloride (2.4 ml, 3 molar equiv) in pyridine (150 ml) as described for the preparation of **5**. The crystalline product was recrystallized from chloroform–ethanol to give 4.1 g (79%) of **8**: mp 200—201 °C; ^{1}H NMR ($CDCl_3$) δ 2.01 (s, 6), 2.06 (s, 3), and 2.08 (s, 3) (OAc), 2.47 (s, 3, tosyl CH_3), 4.00 (t, 1, $J_{1,6}=J_{5,6}=10$ Hz, H-6).

Found: C, 48.53; H, 4.88%. Calcd for $C_{26}H_{25}O_{11}SCl$: C, 48.42; H, 4.84%.

*Tetra-*O*-acetyl-1,3/2,4-cyclohexanetetrol (9).* A solution of **5** (0.1 g) in dioxane (10 ml) was hydrogenated in a Parr shaker apparatus in the presence of Raney nickel T-4[5] and Amberlite IR-45 (2 ml) under pressure (3.4 kg/cm^2) at room temperature for 2 days. The catalyst and resin were filtered off and the filtrate evaporated to dryness. The product was recrystallized from ethanol to give 0.06 g (67%) of **9**: mp 124.5—127 °C (lit,[6] 125.5—127 °C), identical with an authentic sample in all respects.

Dechlorination of **6**. a) A solution of **6** (0.2 g) in ethanol (60 ml) was hydrogenated with Raney nickel catalyst as described above at room temperature overnight. The crude product was crystallized from ethanol to give 0.1 g (52%) of 1,2,3,4-tetra-*O*-acetyl-5-*O*-benzoyl-1,3,5/2,4-cyclohexanepentol (**10**): mp 168—169 °C; ^{1}H NMR ($CDCl_3$) δ 1.96 (s, 3) and 2.04 (s, 9) (OAc).

Found: C, 57.82; H, 5.52%. Calcd for $C_{21}H_{24}O_{10}$: C, 57.78; H, 5.55%.

b) Compound **6** (1 g) was treated with tributyltin(IV) hydride (1 ml) in toluene (30 ml) in the presence of α,α'-azobisisobutyronitrile (10 mg) at 80—90 °C under a stream of nitrogen for 3 h. The solution was evaporated to give a crystalline residue that was pulverized with ethanol and the crude crystals were collected by filtration. Recrystallization from ethanol gave 0.74 g (80%) of **10**: mp 168—170 °C.

Dechlorination of **7**. A solution of **7** (1 g) in dioxane (20 ml) was hydrogenated with Raney nickel at room temperature overnight as described in the preparation of **9**. The product was crystallized from ethanol to give a crystalline mixture, which was fractionated on a silica gel column (40 g) with 1 : 5 2-butanone–toluene. The main fraction was evaporated to give a syrup that crystallized from chloroform–ethanol to give 0.28 g (39%) of **9**: mp 124—126 °C. The minor component was crystallized from ethanol to give 0.04 g (4%) of 1,2,3,4-tetra-*O*-acetyl-5-*O*-mesyl-1,3,5/2,4-cyclohexanepentol (**11**): mp 218.5—219 °C; ^{1}H NMR ($CDCl_3$) δ 2.04 (broad s, 12, four OAc), 3.08 (s, 3, mesyl CH_3).

Found: C, 44.08; H, 5.36; S, 8.06%. Calcd for $C_{15}H_{22}O_{11}S$: C, 43.90; H, 5.40; S, 7.81%.

Dechlorination of **8**. a) Compound **8** (0.2 g) was hydrogenated in dioxane (5 ml) in the presence of Raney nickel and Amberlite IR-45 (OH^-) (4 ml) at room temperature overnight. The product was crystallized from ethanol–ether to give 0.07 g (57%) of **9**: mp 134—135 °C, identical with an authentic sample[6] in all respects.

b) Compound **8** (3 g) was treated with tributyltin(IV) hydride (3 ml) in toluene (60 ml) in the presence of α,α'-azobisisobutyronitrile (30 mg) at 80—90 °C under a stream of nitrogen for 2 h. The reaction mixture was processed as described in the preparation of **10** to give crude crystals, which were recrystallized from chloroform–ethanol to give 2.34g (87%) of 1,2,3,4-tetra-*O*-acetyl-5-*O*-tosyl-1,3,5/2,4-cyclohexanepentol (**12**): mp 157.5—158.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.84 (s, 3), 2.00 (s, 3), 2.02 (s, 3), and 2.05 (s, 3) (OAc), 2.50 (s, 3, tosyl CH_3).

Found: C, 51.85; H, 5.40; S, 6.43%. Calcd for $C_{21}H_{26}O_{11}S$: C, 51.84; H, 5.39; S, 6.59%.

*5-Chloro-1,2-*O*-cyclohexylidene-5-deoxy-3,4,6-tri-*O*-tosyl-*neo*-inositol (14).* To a solution of 1,2-*O*-cyclohexylidene-3,4,6-tri-*O*-tosyl-*myo*-inositol (**13**)[10] (0.5 g) in dry pyridine (15 ml) was added sulfuryl chloride (0.18 ml, 3 molar equiv) at −15 °C and the reaction mixture allowed to stand at this temperature for 1 h. The brown mixture was then poured into ice water and the solution evaporated to dryness. The residue was crystallized from ethanol to give 0.38 g (76%) of **14**: mp 182—183.5 °C (lit,[11] 182—183.5 °C). The IR spectrum was imposable with that of an authentic sample.

*1,2-*O*-Cyclohexylidene-5-deoxy-3,4,6-tri-*O*-tosyl-*myo*-inositol (15).* Compound **14** (0.2 g) was dechlorinated with tributyltin(IV) hydride in toluene as described in the preparation of **10**. The crude product was crystallized from chloroform–ethanol to give 0.11 g (55%) of **15**: mp 171—174 °C; ^{1}H NMR ($CDCl_3$) δ 2.48 (s, 9, three tosyl CH_3).

Found: C, 56.22; H, 5.41; S, 13.46%. Calcd for $C_{33}H_{38}$-

$O_{11}S_3$: C, 56.07; H, 5.42; S, 13.61%.

*1,4-Di-*O*-benzoyl-5-chloro-2,3-*O*-cyclohexylidene-5-deoxy-*neo*-inositol (17).* To a solution of 1,4-di-*O*-benzoyl-2,3-*O*-cyclohexylidene-*myo*-inositol (**16**)[11] (1 g) in dry pyridine (30 ml) was added sulfuryl chloride (1.04 ml, 6 molar equiv) at −15 °C and the mixture stirred at this temperature for 1 h and subsequently at 5 °C for 3 h. The reaction mixture was processed as described in the preparation of **5**, crude product being crystallized from ethanol to give 0.65 g (62%) of **17**: mp 194—196 °C.

Found: C, 63.89; H, 5.52; Cl, 7.51%. Calcd for $C_{26}H_{27}O_7Cl$: C, 64.13; H, 5.59; Cl, 7.28%.

Compound **17** (0.2 g) was treated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature overnight. The reaction mixture was evaporated and the residue crystallized from ethanol to give 0.19 g (87%) of the acetyl derivative (**18**): mp 180—181°C.

Found: C, 63.64; H, 5.50; Cl, 6.83%. Calcd for $C_{28}H_{29}O_8Cl$: C, 63.57; H, 5.53; Cl, 6.70%.

*Penta-*O*-acetyl-5-chloro-5-deoxy-*neo*-inositol (19).* A mixture of **18** (0.53 g), 12 M hydrochloric acid (30 ml), and ethanol (30 ml) was refluxed overnight, and then evaporated to give a crystalline product (0.16 g): mp 240—250 °C. Without further purification, the product was treated with acetic anhydride (10 ml) and pyridine (15 ml) at 60 °C for 2 h. The reaction mixture was evaporated and the residue crystallized from ethanol to give 0.14 g (82%) of **19**: mp 180—183 °C; ^{1}H NMR ($CDCl_3$) δ 1.99 (s, 6), 2.10 (s, 6), and 2.17 (s, 3) (OAc).

Found: C, 46.77; H, 5.08; Cl, 8.96%. Calcd for $C_{16}H_{21}O_{10}Cl$: C, 47.01; H, 5.18; Cl, 8.67%.

*Penta-*O*-acetyl-1,5/2,3,4-cyclohexanepentol (20).* Compound **19** (0.1 g) was dechlorinated with tributyltin(IV) hydride (0.3 ml) as described in the preparation of **10**. The product was crystallized from ethanol to give 0.07 g (77%) of **20**: mp 186—187 °C (lit,[12] 182 °C); ^{1}H NMR ($CDCl_3$) δ 1.45 (broad dd, 1, $J_{1,6ax\ (5,6ax)}=10$ Hz, $J_{6gem}=12$ Hz, H-6ax), 2.01 (s, 6), 2.03 (s, 6), and 2.18 (s, 3) (OAc), 2.50 (td, 1, $J_{1,6eq\ (5,6eq)}=5$ Hz, H-6eq), 4.99 (dd, 2, $J_{1,2\ (4,5)}=10$ Hz, $J_{2,3\ (3,4)}=2.5$ Hz, H-2 and H-4), 5.33 (dt, 2, H-1 and H-5), 5.65 (t, 1, H-3). (Found: C, 50.95; H, 5.74%).

*1,2-*O*-Isopropylidene-(1/2,3,4,6)-3-chloro-4,6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol (24).* To a solution of 1,2-*O*-isopropylidene-(1,3/2,4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3-cyclohexanetriol (**22**)[13] (0.57 g) in chloroform (5 ml) and pyridine (10 ml) was added sulfuryl chloride (0.4 ml, 3 molar equiv) at −15 °C, and the reaction mixture kept at 4 °C overnight. The mixture was processed as described in the preparation of **5**. The product was crystallized from ethyl acetate–ether to give 0.38 g (63%) of **24**: mp 189—190 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 6, $J=7.5$ Hz, two ethoxycarbonyl CH_3), 1.46 (s, 6, two isopropylidene CH_3), 4.16 (q, 4, two ethoxycarbonyl CH_2), 4.69 (t, 1, $J_{2,3}=J_{3,4}=3$ Hz, H-3).

Found: C, 49.15; H, 6.71; N, 7.46; Cl, 9.92%. Calcd for $C_{15}H_{25}N_2O_6Cl$: C, 49.38; H, 6.91; N, 7.68; Cl, 9.72%.

*Di-*O*-acetyl-(1/2,3,4,6)-3-chloro-4,6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol (26).* A mixture of **24** (1 g) in 50% aqueous acetic acid (80 ml) was heated at 70—80 °C for 2 h. The reaction mixture was evaporated to give a crystalline product that was directly treated with acetic anhydride and pyridine in the usual manner. The product was crystallized from ethyl acetate–ether to give 0.93 g (83%) of **26**: mp 154—155 °C; ^{1}H NMR ($CDCl_3$) δ 1.24 (t, 3) and 1.26 (t, 3) ($J=7$ Hz, ethoxycarbonyl CH_3), 2.07 (s, 3) and 2.11 (s, 3) (OAc), 4.15 (q, 2) and 4.18 (q, 2) (ethoxycarbonyl CH_2), 4.71 (m, 1, H-3).

Found: C, 47.05; H, 6.08; N, 6.77; Cl, 8.53%. Calcd for $C_{16}H_{25}N_2O_8Cl$: C, 47.00; H, 6.16; N, 6.85; Cl, 8.67%.

*Di-*O*-acetyl-(1/2,3,4,6)-4,6-diacetamido-3-chloro-1,2-cyclohexanediol (25).* 1,2-*O*-Isopropylidene-(1,3/2,4,6)-4,6-diacetamido-1,2,3-cyclohexanetriol (**21**)[14] (1 g) was treated with sulfuryl chloride in chloroform and pyridine as described in the preparation of **24**. The product was heated with 1 M hydrochloric acid (20 ml) at 70 °C for 20 min. The mixture was evaporated and the residual product acetylated in the usual manner to give, after crystallization from ethanol, 0.58 g (48%) of **25**: mp 223—224 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.76 (s, 3), 1.85 (s, 3), 1.95 (s, 3), and 2.03 (s, 3) (OAc), 4.75 (broad s, 1, H-3), 5.14—5.25 (m, 2, H-1 and H-2).

Found: C, 48.09; H, 5.94; N, 7.84; Cl, 10.09%. Calcd for $C_{14}H_{21}N_2O_6Cl$: C, 48.21; H, 6.07; N, 8.03; Cl, 10.16%.

*1,2-Di-*O*-acetyl-(1/2,3,4,6)-4,6-bis(benzyloxycarbonylamino)-3-chloro-1,2-cyclohexanediol (27).* 1,2-*O*-Isopropylidene-(1,3/2,4,6)-4,6-bis(benzyloxycarbonylamino)-1,2,3-cyclohexanetriol (**23**)[13] (0.8 g) was chlorinated as described in the preparation of **24**. The product was treated with acid and acetylated as described above. Purification using a silica gel column (40 g) with 1:10 2-butanone–toluene gave 0.31 g (34%) of **27**: mp 128.5—129.5 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.90 (s, 3) and 2.06 (s, 3) (OAc), 4.89 (m, 1, H-3), 5.17 (broad s, 4, two benzyloxycarbonyl CH_2).

Found: C, 58.78; H, 5.28; N, 5.08; Cl, 6.77%. Calcd for $C_{26}H_{29}N_2O_8Cl$: C, 58.59; H, 5.48; N, 5.26; Cl, 6.65%.

(1,3,5/2)-3,5-Bis(ethoxycarbonylamino)-1,2-cyclohexanediol [N,N′*-Bis(ethoxycarbonyl)-2,4-dideoxystreptamine*] *(30).* A mixture of **24** (0.16 g) in dioxane (5 ml) and 50% aqueous acetic acid (20 ml) was heated at 70 °C for 2 h, and then evaporated to dryness. The residue was crystallized from ethyl acetate to give 0.14 g (96%) of the dihydroxy compound: mp 120—123 °C. This compound was hydrogenated in ethanol (10 ml) as described in the preparation of **9** at room temperature for 27 h. The product was crystallized from ethanol to give 0.068 g (54%) of **30**: mp 185—186 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.11 (t, 6, $J=7$ Hz, two ethoxycarbonyl CH_3), 3.78—4.15 (m, 4, two ethoxycarbonyl CH_2).

Found: C, 49.26; H, 7.39; N, 9.42%. Calcd for $C_{12}H_{22}N_2O_6$: C, 49.64; H, 7.64; N, 9.65%.

*Di-*O*-acetyl-(1,3,5/2)-3,5-diacetamido-1,2-cyclohexanediol (*N,N′*-Diacetyl-2,4-dideoxystreptamine) (28).* Compound **25** (0.4 g) was hydrogenated in ethanol (20 ml) as described in the preparation of **9** at room temeprature overnight. The product was crystallized from ethanol–ether to give 0.21 g (65%) of **28**: mp 247—249 °C (lit,[15] 231.5—233 °C). This compound was identified with an authentic sample[15] by comparison with IR and ^{1}H NMR spectra, and shown to be more homogeneous.

*Di-*O*-acetyl-(1,3,5/2)-3,5-bis(benzyloxycarbonylamino)-1,2-cyclohexanediol (32).* Compound **27** (0.075 g) was dechlorinated with tributyltin(IV) hydride (0.3 ml) as described in the preparation of **10**. The crude crystals were recrystallized from chloroform–petroleum ether to give 0.062 g (89%) of **32**: mp 180—182 °C; ^{1}H NMR ($CDCl_3$) δ 1.94 (s, 3) and 2.00 (s, 3) (OAc), 5.10 (broad s, 4, two benzyloxycarbonyl CH_2).

Found: C, 62.26; H, 6.04; N, 5.68%. Calcd for $C_{26}H_{30}N_2O_8$: C, 62.64; H, 6.07; N, 5.62%.

(1,3,5/2)-3,5-Diamino-1,2-cyclohexanediol Dihydrochloride (2,4-Dideoxystreptamine Dihydrochloride) (29). Compound **28** (0.46 g) was refluxed with 6 M hydrochloric acid (20 ml) for 3.5 h. The reaction mixture was evaporated and the residual syrup crystallized from ethanol–methanol–water to give 0.24 g (74%) of **29**: mp 247—249 °C (dec.).

Found: C, 32.69; H, 7.18; N, 12.72; Cl, 32.20%. Calcd for $C_6H_{16}N_2O_2Cl_2$: C, 32.89; H, 7.36; N, 12.78; Cl, 32.36%.

Compound **29** (0.44 g) was treated with ethyl chloroformate (0.76 ml) in acetone (12 ml) and water (12 ml) containing sodium carbonate (2.2 g) under vigorous agitation at room temeprature overnight. The mixture was neutralized with 1 M hydrochloric acid and evaporated to dryness. The residue was extracted with hot dioxane (20 ml), the extract evaporated and crystallized from ethanol to give 0.45 g (78%) of **30**: mp 185—186 °C, identical with the compound obtained before.

(1, 3, 5/2)-3, 5-Bis(benzyloxycarbonylamino)-1, 2-cyclohexanediol [N,N′*-Bis(benzyloxycarbonyl)-2,4-dideoxystreptamine*] *(31).* The crude **29** obtained from **28** (0.16 g) was treated with 30% toluene solution of carbobenzyloxy chloride (1.1 ml) in acetone (4 ml) and water (2 ml) in the presence of sodium hydrogencarbonate (0.19 g) at 5 °C overnight. The resulting crystals were collected and recrystallized from ethanol to give 0.15 g (73%) of **31**: mp 204—205 °C.

Found: C, 63.45; H, 6.46; N, 6.39%. Calcd for $C_{22}H_{26}N_2O_6$: C, 63.75; H, 6.32; N, 6.76%.

Chlorination of (1,3/2,4,6)-4,6-Bis(ethoxycarbonylamino)-1,2,3-cyclohexanetriol (33).[13] a) To a solution of **33** (1 g) in pyridine (40 ml) was added sulfuryl chloride (1.1 ml, 4 molar equiv) at −15 °C with stirring, and the mixture was kept at 4 °C for 4 h. TLC indicated the formation of two components (R_f 0.81 and 0.51, in 5: 1 benzene–ethanol). The reaction mixture was processed as described in the preparation of **5** and the product acetylated in the usual manner. The mixture of two components (R_f 0.56 and 0.51, in 2: 1 benzene–ethyl acetate) was fractionated using a silica-gel column (100 g) with 3: 1 and 5: 1 benzene–ethyl acetate as the eluate. The first fraction (R_f 0.56) was evaporated and crystallized from chloroform–ethyl acetate to give 0.33 g (28%) of (1/2,3,4,6)-3-chloro-4,6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol 1,2-cyclic sulfate (**34**): mp 183 °C (dec) after melting and resolidification at 105—110 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.19 (t, 6, J=7.5 Hz, two ethoxycarbonyl CH_3), 4.06 (q, 4, two ethoxycarbonyl CH_2), 5.06 (t, 1, $J_{1,2}=J_{1,6}=10$ Hz, H-1), 5.64 (dd, 1, $J_{2,3}=3$ Hz, H-2); IR 3300 (NH), 1700 and 1540 (amide), 1390 cm^{-1} (sulfate).

Found: C, 36.96; H, 4.79; N, 7.19%. Calcd for $C_{12}H_{14}N_2O_8SCl$: C, 37.24; H, 4.95; N, 7.24%.

The second fraction (R_f 0.51) was evaporated and crystallized from ethyl acetate–petroleum ether to give 0.23 g (17%) of **26**: mp 154—155 °C, identical with the compound obtained before.

b) Compound **33** (3 g) was treated with sulfuryl chloride (3.3 ml) in pyridine (100 ml) as described above. The syrupy mixture thus obtained was treated with methanol (100 ml) saturated with ammonia at 5 °C at room temperature for 4 days. The reaction mixture evaporated to dryness and the residue treated with 1 M hydrochloric acid (50 ml) at 80 °C for 15 h. Then the mixture was neutralized with sodium carbonate (2.6 g) and evaporated to give solid residue, which was extracted with hot dioxane (50 ml). The extract was evaporated and the residual product acetylated in the usual manner. The product was purified by passage through a short alumina column with chloroform and crystallized from ethyl acetate–petroleum ether to give 2.46 g (61%) of **26**: mp 153—155 °C.

Di-O-acetyl-(1, 3/2, 4, 6)-3-azido-4, 6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol (35). A mixture of **26** (2 g), sodium azide (3.65 g), and *N*,*N*-dimethylformamide (30 ml) was heated at 100 °C under stirring overnight. An insoluble matter was filtered off and the filtrate evaporated to dryness. The residue was treated with acetic anhydride (20 ml) and pyridine (20 ml) at room temperature overnight. The reaction mixture was evaporated, and the residual product dissolved in chloroform and filtered through a short alumina column. The filtrate was evaporated and crystallized from chloroform– ether to give 0.86 g (34%) of **35**: mp 155—156 °C; ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 3) and 1.27 (t, 3) (J=7 Hz, ethoxycarbonyl CH_3), 2.07 (s, 3) and 2.13 (s, 3) (OAc), 4.12 (q, 2) and 4.18 (q, 2) (ethoxycarbonyl CH_2).

Found: C, 46.14; H, 6.01; N, 16.84%. Calcd for $C_{16}H_{25}N_5O_8$: C, 46.26; H, 6.07; N, 16.86%.

Di-O-acetyl-(1,3/2,4, 6)-3-acetamido-4, 6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol (36). Compound **35** (0.76 g) was treated with methanolic ammonia (20 ml) at room temperature overnight. The mixture was evaporated to give a white powder, which was hydrogenated in ethanol (20 ml) with Raney nickel as described in the preparation of **9**. The product was acetylated in the usual manner and crystallized from ethanol to give 0.42 g (54%) of **36**: mp 267—268 °C.

Found: C, 49.97; H, 6.56; N, 9.83%. Calcd for $C_{18}H_{29}N_3O_9$: C, 50.11; H, 6.77; N, 9.74%.

*Penta-*N,O*-acetyl-(1,3/2,4, 6)-3,4, 6-triamino-1,2-cyclohexanediol (37).* Compound **36** (0.045 g) was refluxed with 48% hydrobromic acid (2 ml) for 3 h. The reaction mixture was evaporated and the residue dissolved in water. The solution was passed through a short column of Dowex 1×2 (OH^-) and the eluate was evaporated to give the free base, which on acetylation gave 0.032 g (83%) of **37**: mp 298—303 °C (dec); ^{1}H NMR (Me_2SO-d_6), see text.

Found: C, 51.65; H, 6.62; N, 11.34%. Calcd for $C_{16}H_{25}N_3O_7$: C, 51.74; H, 6.79; N, 11.34%.

1,2-O-Isopropylidene-(1,3,5/2,4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol (38). 1,5-Di-*O*-acetyl-2,3-*O*-isopropylidene-(1,3,5/2,4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol[18] (1 g) was treated with methanol (50 ml) saturated with ammonia at 5 °C. After standing at room temperature overnight, the reaction mixture was evaporated to dryness and the residue crystallized from ethanol to give 0.64 g (78%) of **38** as tiny needles: mp 228—230 °C, after sintering and resolidifying at 200—203 °C.

Found: C, 49.57; H, 7.03; N, 7.74%. Calcd for $C_{15}H_{26}N_2O_8$: C, 49.72; H, 7.23; N, 7.73%.

Chlorination of **38**. To a solution of **38** (2 g) in pyridine (50 ml) was added sulfuryl chloride (2.7 ml, 4 molar equiv) at −20 °C with stirring, and then the mixture was kept at 4 °C for 6 h. The reaction mixture was diluted with chloroform (100 ml) and the solution washed successively with aqueous sodium hydrogencarbonate and water. After drying over anhydrous sodium sulfate, the organic layer was evaporated to give a syrup, which was dissolved in dioxane (10 ml) and heated with 50% aqueous acetic acid (10 ml) at 80 °C for 2 h. The reaction mixture was evaporated to dryness and the residue treated with acetic anhydride (10 ml) and pyridine (10 ml) at room temperature overnight. TLC indicated the formation of three components (R_f 0.58, 0.37, and 0.25 in 3: 1 benzene–ethyl acetate). The reaction mixture was evaporated and the residual product was chromatographed on silica gel (100 g) with 4: 1 benzene–ethyl acetate as an eluent.

The fraction (R_f 0.58) was evaporated and crystallized from ethanol to give 0.1 g (4%) of di-*O*-acetyl-(1/2,3,4,5,6)-3,5-dichloro-4,6-bis(ethoxycarbonylamino)-1,2-cyclohexanediol(**41**): mp 200—202 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.19 (t, 6, J=7 Hz, two ethoxycarbonyl CH_3), 2.08 (s, 6, two OAc), 4.06 (q, 4, two ethoxycarbonyl CH_2), 4.72 (dd, 1, J=*ca.* 3 Hz, H-3 or H-5), 7.69 (d, 2, J=7 Hz, 2NH).

Found: C, 43.20; H, 5.29; N, 6.19; Cl, 16.00%. Calcd for $C_{16}H_{24}N_2O_8Cl_2$: C, 43.35; H, 5.46; N, 6.32; Cl, 15.99%.

The fraction (R_f 0.37) was evaporated and crystallized from ethanol to give 0.49 g (19%) of tri-*O*-acetyl-(1,3/2,4,5,6)-5-chloro-4,6-bis(ethoxycarbonylamino)-1,2,3-cyclohexanetriol (**39**): mp 195—196 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.18 (t, 6, J=7 Hz, two ethoxycarbonyl CH_3), 1.92 (s, 3) and 1.97 (s, 6) (OAc), 4.07 (q, 4, two ethoxycarbonyl CH_2), 7.26 (d, 2, J=8

Hz, 2NH).

Found: C, 46.59; H, 5.69; N, 6.00; Cl, 7.77%. Calcd for $C_{18}H_{27}N_2O_{10}Cl$: C, 46.31; H, 5.38; N, 6.00; Cl, 7.59%.

The fraction (R_f 0.25) was evaporated and crystallized from ethanol to give 0.81 g (31%) of tri-*O*-acetyl-(1,3,5,6/2,4)-6-chloro-3,5-bis(ethoxycarbonylamino)-1,2,4-cyclohexanetriol (**40**): mp 183—184 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.13 (t, 3) and 1.18 (t, 3) (J=7 Hz, ethoxycarbonyl CH_3), 1.97 (s, 6) and 2.03 (s, 3) (OAc), 3.99 (q, 2) and 4.05 (q, 2) (ethoxycarbonyl CH_2), 6.94 (d, 1) and 7.19 (d, 1) (J=8 Hz, NH). (Found: C, 46.57; H, 5.56; N, 6.06; Cl, 7.76%). This compound was identified with an authentic sample[1a)] (mp 180—182 °C).

(1,2,3,5/4,6)-Bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol [N,N′-*Bis(ethoxycarbonyl)*-myo-*inosadiamine-4,6*] *(**42**)*. Hexa-*N,O*-acetyl-*myo*-inosadiamine-4,6[16)] (1.33 g) was treated with 6 M hydrochloric acid (30 ml) at reflux temperature for 2 h. The reaction mixture was evaporated and the crude dihydrochloride obtained treated with ethyl chloroformate (1.2 ml) in 1 M sodium hydroxide solution (15 ml) at room temperature overnight. After neutralization with 1 M hydrochloric acid, the mixture was evaporated to dryness and the residue extracted with hot dioxane (30 ml). The extract was evaporated and the crystals recrystallized from dioxane to give 0.73 g (80%) of **42**: mp 247.5—248.5 °C.

Found: C, 45.01; H, 6.84; N, 8.39%. Calcd for $C_{12}H_{22}N_2$-O_8: C, 44.71; H, 6.88; N, 8.69%.

Compound **42** was acetylated in the conventional way. The crude product was crystallized from ethanol to give the tetra-*O*-acetyl derivative: mp 247—248.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 6, J=7 Hz, two ethoxycarbonyl CH_3), 2.02 (s, 6), 2.07 (s, 3), and 2.20 (s, 3) (OAc), 4.10 (q, 4, two ethoxycarbonyl CH_2), 4.21 (q, 2, $J_{1,6(3,4)}=J_{4,5(5,6)}=J_{4,NH(6,NH)}$ =10.5 Hz, H-4 and H-6), 5.07 (t, 1, H-5), 5.09 (dd, 2, $J_{1,2(2,3)}$ =2.5 Hz, H-1 and H-3), 5.23 (d, 2, 2NH), 5.62 (t, 1, H-2).

Found: C, 48.92; H, 6.22; N, 5.53%. Calcd for $C_{20}H_{30}N_2$-O_{12}: C, 48.97; H, 6.17; N, 5.71%.

*1,5-Di-O-acetyl-2,3-O-isopropylidene-(1,2,3,5/4,6)-4,6-bis(ethoxycarbonylamino)-1,2,3,5-cyclohexanetetrol (**43**).* Compound **42** (0.4 g) was dissolved in *N,N*-dimethylformamide (20 ml), and 2,2-dimethoxypropane (5 ml) and *p*-toluenesulfonic acid (10 mg) were added. The mixture was heated at 80 °C for 10 min and then treated with Amberlite IRA-400 (OH^-) after cooling. The solution was evaporated and crystallized from ethanol to give 0.15 g (34%) of the *O*-isopropylidene derivative: mp 190—191 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.22 (t, 6, J= 7 Hz, two ethoxycarbonyl CH_3), 1.33 (s, 3) and 1.53 (s, 3) (isopropylidene CH_3), 4.12 (q, 4, two ethoxycarbonyl CH_2).

A 0.1-g portion of the crystals was acetylated in the usual manner and the product crystallized from ethanol to give 0.1 g (74%) of **43**: mp 221—222 °C; ^{1}H NMR ($CDCl_3$) δ 1.22 (t, 6, J=7 Hz, two ethoxycarbonyl CH_3), 1.36 (s, 3) and 1.64 (s, 3) (isopropylidene CH_3), 2.05 (s, 3) and 2.13 (s, 3) (OAc), 4.11 (q, 4, two ethoxycarbonyl CH_2), 4.43 (t, 1, $J_{1,2}=J_{2,3}$=3 Hz, H-2), 4.95 (t, 1, $J_{4,5}=J_{5,6}$=10 Hz, H-5), 5.00 (d, 1, J= 10 Hz) and 5.19 (d, 1, J=9 Hz) (NH), 5.20 (dd, 1, $J_{1,6}$=11 Hz, H-1).

Found: C, 51.38; H, 6.89; N, 6.35%. Calcd for $C_{19}H_{30}N_2$-O_{10}: C, 51.12; H, 6.77; N, 6.27%.

*Di-O-acetyl-(1,3/2,4,5,6)-4,5-dichloro-2,6-bis(ethoxycarbonylamino)-1,3-cyclohexanediol (**44**).* Compound **43** (0.057 g) was heated with 90% aqueous acetic acid (10 ml) at 80 °C for 30 min. The mixture was evaporated to give a syrupy dihydroxy compound. Without further purification, the product was treated with sulfuryl chloride (0.05 ml) in pyridine (5 ml) at 5 °C overnight. The reaction mixture was processed as described in the preparation of **5**. The product was recrystallized from ethanol to give 0.023 g (41%) of **44**: mp 218—219 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 3) and 1.24 (t, 3) (J=7 Hz, ethoxycarbonyl CH_3), 2.07 (s, 3) and 2.10 (s, 3) (OAc), 4.11 (q, 2) and 4.15 (q, 2) (ethoxycarbonyl CH_2), 4.35 (dd, 1, $J_{3,4}$=10 Hz, $J_{4,5}$=3 Hz, H-4), 4.63 (t, 1, $J_{5,6}$=3 Hz, H-5), 5.14 (d, 1) and 5.26 (d, 1) (J=9 Hz, NH), 5.26 (t, 1, $J_{1,2}=J_{1,6}$=10 Hz, H-1), 5.38 (t, 1, $J_{2,3}$=10 Hz, H-3).

Found: C, 43.26; H, 5.41; N, 6.28; Cl, 15.95%. Calcd for $C_{16}H_{24}N_2O_8Cl_2$: C, 43.34; H, 5.46; N, 6.32; Cl, 16.00%.

Di-O-acetyl-(1,3/2,4)-2,4-bis(ethoxycarbonylamino)-1,3-cyclohexanediol [*Di-O-acetyl*-N,N′-*bis(ethoxycarbonyl)-4,5-dideoxystreptamine*] *(**45**).* Compound **44** (0.21 g) was hydrogenated in ethanol (15 ml) as described in the preparation of **9**. The product was crystallized from ethyl acetate–ether to give 0.13 g (71%) of **45**: mp 170 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.15 (t, 6, J=7.5 Hz, two ethoxycarbonyl CH_3), 1.91 (s, 3) and 1.97 (s, 3) (OAc), 4.01 (q, 4, two ethoxycarbonyl CH_2), 4.71 (dd, 1, $J_{2,3}=J_{3,4}$=*ca.* 10 Hz, H-3).

Found: C, 51.33; H, 7.00; N, 7.48%. Calcd for $C_{16}H_{26}N_2$-, O_8: C, 51.13; H, 6.86; N, 7.28%.

*(1,2/3,5)-2-Acetoxy-1-chloro-3,5-bis(ethoxycarbonylamino)cyclohexane (**46**).* Compound **30** (0.09 g) was treated with sulfuryl chloride (0.15 ml) in pyridine (5 ml) at −20 °C for 10 min and then at 5 °C for 6 h. The reaction mixture was processed as described in the preparation of **5**. The product was acetylated in the usual manner and purified through a short column of alumina with chloroform. Recrystallization from chloroform–ether gave 0.047 g (44%) of **46**: mp 162—163 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (t, 6, J=7 Hz, two ethoxycarbonyl CH_3), 2.08 (s, 3, OAc), 4.10 (q, 4, two ethoxycarbonyl CH_2), 4.86 (dd, 1, $J_{1,2}$=3.5 Hz, $J_{2,3}$=10 Hz, H-2).

Found: C, 47.76; H, 6.42; N, 7.80; Cl, 10.07%. Calcd for $C_{14}H_{23}N_2O_6Cl$: C, 47.93; H, 6.61; N, 7.98; Cl, 10.11%.

*(1/2,4)-1-Acetoxy-2,4-bis(ethoxycarbonylamino)cyclohexane (**47**).* A solution of **46** (0.5 g) in ethanol (20 ml) was hydrogenated as described in the preparation of **9**. The product was crystallized from ethanol to give 0.28 g (63%) of **47**: mp 151—152 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.17 (t, 1, J=7 Hz, two ethoxycarbonyl CH_3), 1.97 (s, 3, OAc), 4.03 (q, 4, two ethoxycarbonyl CH_2), 4.53 (ddd, 1, $J_{1,2}=J_{1,6ax}$=9 Hz, $J_{1,6eq}$=4 Hz, H-1).

Found: C, 52.89; H, 7.46; N, 8.99%. Calcd for $C_{14}H_{24}N_2$-O_6: C, 53.15; H, 7.65; N, 8.85%.

(1/2,4)-2,4-Bis(ethoxycarbonylamino)-1-cyclohexanol [N,N′-*Bis(ethoxycarbonyl)-2,4,5-trideoxystreptamine*] *(**48**).* Compound **47** (0.22 g) was treated with methanolic ammonia (20 ml) at room temperature overnight. The reaction mixture was evaporated and recrystallized from ethanol–ether to give 0.17 g (88%) of **48**: mp 133—136 °C.

Found: C, 52.41; H, 7.98; N, 10.15%. Calcd for $C_{12}H_{22}$-N_2O_5: C, 52.54; H, 8.09; N, 10.29%.

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