Studies on O→N Acyl Migration in *O*-Acyl-2-deoxystreptamines

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(Received August 4, 1975)

Preparations of mono-*N*-protected 2-deoxystreptamines (racemates of **5, 8, 9, 10, 11, 12**) from 4(and 6)-*O*-acyl-1,3-di-*N*-benzyloxycarbonyl-2-deoxystreptamines by O→N acyl migration were described. O→N Acyl migration of 2-deoxy-tri-*O*-ethoxycarbonylstreptamine (**15**) led to several protected derivatives (racemates of **16, 17, 18**) which also should serve for the preparation of glycosides and other derivatives of 2-deoxystreptamine.

In the course of our synthetic studies of aminoglycoside antibiotics, it was often necessary to protect selectively some of the amino and hydroxyl groups of 2-deoxystreptamine to effect a chemical reaction solely at other sites of the molecule remained intact. In this paper we describe the synthesis of a number of 2-deoxystreptamine derivatives that should serve for the preparation of their glycosides and other derivatives. The syntheses were achieved by way of O→N acyl migration.

The mono-*N*-di-*O*-protected derivatives (**5,8,9**) were prepared as follows: 1,3-Di-*N*-benzyloxycarbonyl-2-deoxystreptamine[1] was converted to a racemic mixture of 4,5-*O*- and 5,6-*O*-cyclohexylidene derivatives (**1**) by the acetal exchange reaction[2] with 1,1-dimethoxycyclohexane and *p*-toluenesulfonic acid in dimethylformamide. Acetylation or benzoylation or ethoxycarbonylation of **1** gave the corresponding racemic mixture of 6- and 4-*O*-acyl derivatives (**2,3,4**), respectively.

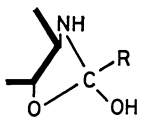
Deblocking of the *N*-protecting groups of the acetyl derivative (**2**) by catalytic hydrogenation with palladium resulted in the formation of 1 (and 3)-*N*-acetyl-4,5(and 5,6)-*O*-cyclohexylidene derivative (**5**, a racemate), which formed a monohydrochloride. This result showed that deblocking was followed by O→N migration.

In the case of similar hydrogenolysis of the benzoyl derivative (**3**), no O→N migration occurred, giving the racemic mixture of 6 (and 4)-*O*-benzoyl-4,5(and 5,6)-*O*-cyclohexylidene-2-deoxystreptamine (**6**), which formed a dihydrochloride. However, when the diacetate of **6** was treated with pyridine[3] at 50 °C for 2 days, migration occurred to give the *N*-benzoyl derivative (**8**), which formed a monohydrochloride.

Similar hydrogenolysis of the ethoxycarbonyl derivative (**4**) also was not followed by O→N migration and gave the racemic mixture of 4,5(and 5,6)-*O*-cyclohexylidene-2-deoxy-6(and 4)-*O*-ethoxycarbonylstreptamine (**7**), whereas similar treatment of **7** with pyridine gave, by way of O→N migration, the *N*-ethoxycarbonyl derivative (**9**), which formed a monohydrochloride.

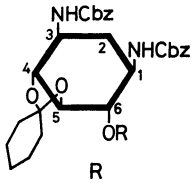
Removal of the cycloxylidene group from **5**, **8**, and **9** with acid gave mono-*N*-protected 2-deoxystreptamines (**10, 11, 12**), respectively.

Next, we investigated the O→N migration of tri-*O*-ethoxycarbonyl derivative (**15**) of 2-deoxystreptamine. Di-*N*-(*p*-methylbenzylidene)-2-deoxystreptamine (**13**) was prepared and made to react with ethyl chloroformate in pyridine to give the tri-*O*-ethoxycarbonyl derivative (**14**), which was treated with 50% acetic acid to give **15**.

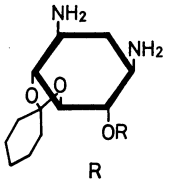


I: R=OC_2H_5
II: R=CH_3

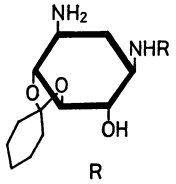
Preliminary analysis for the reaction products of **15** with pyridine at various reaction temperatures and periods was made by tlc analysis of the fractions of reaction mixtures, and it was found that the first O→N migration giving mono-*N*-ethoxycarbonyl-di-*O*-ethoxycarbonyl derivative (**16**) was accompanied by the second O→N migration that is much slower to give di-*N*-ethoxycarbonyl-5-*O*-ethoxycarbonyl derivative (**17**). (See Preliminary Experiment on Treatment of **15** with Pyridine in the Experimental Section). However, when **16** was treated with pyridine similarly, it was readily converted to **17**. These results suggested that the migration of ethoxycarbonyl group probably proceeded through an unstable orthoester-amide structure (I) which may retard the second migration for some stereochemical reason. Although the orthoester-amide intermediate could not be isolated in the present work,



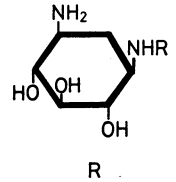
	R
2	Ac
3	Bz
4	Cbe



	R
6	Bz
7	Cbe



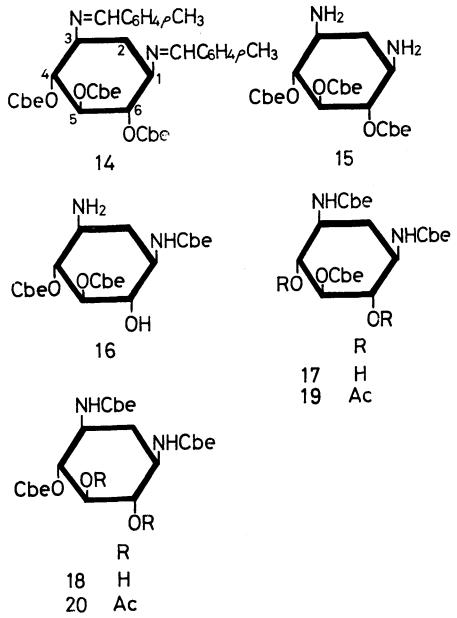
	R
5	Ac
8	Bz
9	Cbe



	R
10	Ac
11	Bz
12	Cbe

Cbe: $CO_2CH_2CH_3$
Cbz: $CO_2CH_2C_6H_5$

Only one isomer was shown in each compound.



Only one isomer was shown in each compound.

formation of a related structure (II) has been reported by G. Fodor *et al.*,[4] who showed it by IR and PMR spectroscopy.

Furthermore, O→O migration was found to occur at higher temperature (100 °C) and prolonged reaction to give the racemic mixture of 2-deoxy-1,3-di-*N*-ethoxycarbonyl-4(and 6)-*O*-ethoxycarbonylstreptamine (**18**).

Confirmation of the structures of **17** and **18** was carried out by PMR spectral studies of their di-*O*-acetyl derivatives (**19**, **20**). The compound **19** showed a 6-proton singlet of acetyls in each of the $CDCl_3$ and pyridine-d_5, whereas another compound **20** showed two 3-proton singlets of acetyls in each of the above media, indicating that **20** (and also **18**) has an unsymmetrical structure. Periodate oxidation studies of **17** and **18** also afforded the same conclusion.

Experimental

*Racemic Mixture of 1,3-Di-*N*-benzyloxycarbonyl-4,5-*O*-cyclohexylidene-2-deoxystreptamine (1).* To a solution of 1,3-di-*N*-benzyloxycarbonyl-2-deoxystreptamine[1] (14.0 g) in dry DMF (280 ml), *p*-toluenesulfonic acid (0.54 g) and 1,1-dimethoxycyclohexane (9.4 ml) were added and the solution was heated at 50 °C under reduced pressure (~40 Torr). After 5 hr, the same amounts of both reagents were added and the solution was treated similarly. On tlc with benzene–methanol (6: 1), the starting material (R_f 0.33) disappeared and **1** (R_f 0.8) appeared as a single spot. The solution was neutralized with Amberlite IRA 400 (OH form, 25 ml), filtered, and concentrated under reduced pressure to approximately 100 ml, and the concentrate was poured into 0.1% sodium hydrogen carbonate solution (2 l) to deposit an amorphous powder, which was purified by reprecipitation with acetone–water, 15.8 g (95%), mp 149—151 °C.

Found: C, 66.02; H, 6.46; N, 5.39%. Calcd for $C_{28}H_{34}N_2O_7$: C, 65.86; H, 6.71; N, 5.49%.

*Racemic Mixture of 4-O-Acetyl-1,3-di-*N*-benzyloxycarbonyl-5,6-O-cyclohexylidene-2-deoxystreptamine (2).* A sample of **1** was treated in a usual manner with acetic anhydride in pyridine. Reprecipitation from cyclohexane gave **2** in 97% yield, mp 162—163 °C; PMR (in $CDCl_3$) δ: 1.97 (3H, s, OAc).

Found: C, 65.19; H, 6.58; N, 5.07%. Calcd for $C_{30}H_{36}N_2O_8$: C, 65.20; H, 6.57; N, 5.07%.

*Racemic Mixture of 4-O-Benzoyl-1,3-di-*N*-benzyloxycarbonyl-5,6-O-cyclohexylidene-2-deoxystreptamine (3).* A sample of **1** was treated with benzoyl chloride in pyridine in a usual manner to give **3** in 95% yield; Recrystallization from hot ether, mp 182—183 °C; IR (KBr): 1700, 1735 cm^{-1}.

Found: C, 68.49; H, 6.23; N, 4.58%. Calcd for $C_{35}H_{38}N_2O_8$: C, 68.39; H, 6.23; N, 4.56%.

*Racemic Mixture of 1,3-Di-*N*-benzyloxycarbonyl-4,5-O-cyclohexylidene-2-deoxy-6-O-ethoxycarbonylstreptamine (4).* To a solution of **1** (4.99 g) in pyridine (30 ml), ethyl chloroformate (3.1 ml) was added and the solution was allowed to stand at 5 °C overnight. On tlc with benzene–ethanol (20: 1), **1** (R_f 0.43) disappeared and **4** (R_f 0.66) appeared as a single spot. The solution was poured into ice-water and the precipitate was reprecipitated from ether, 5.36 g (94%), mp 150 °C; IR (KBr): 1765 (ν_{CO} of OCbe), 1690 (ν_{CO} of NCbe), 1535 cm^{-1}; PMR (in $CDCl_3$) δ: 1.26 (3H, t, $OCO_2CH_2C\underline{H}_3$).

Found: C, 64.04; H, 6.66; N, 4.83%. Calcd for $C_{31}H_{38}N_2O_9$: C, 63.90; H, 6.57; N, 4.81%.

*Racemic Mixture of 1-*N*-Acetyl-4,5-*O*-cyclohexylidene-2-deoxystreptamine (5).* A solution of **2** (5.22 g) in aqueous dioxane (1: 5, 25 ml), acetic acid (0.2 ml) was added and the solution was hydrogenated over palladium black at 40 °C overnight. On tlc with benzene–methanol (1: 1), **2** (R_f 1.0) disappeared and **5** (R_f 0.6) appeared as a single spot. The reaction mixture was filtered and the filtrate was evaporated. To the resulting syrup, 0.01 M hydrochloric acid was added until the mixture became weak acidic (pH~4.5) and the solution was evaporated to give a syrup. Addition of acetone gave precipitates, 2.62 g (82%), mp 112—113 °C; IR (KBr): 1635, 1550 cm^{-1}; PMR (in pyridine-d_5+D_2O) δ: 2.13 (3H, s, NAc).

Found: C, 49.67; H, 8.04; N, 7.95; Cl, 10.65%. Calcd for $C_{14}H_{24}N_2O_4\cdot HCl\cdot H_2O$: C, 49.62; H, 8.03; N, 8.27; Cl, 10.4%.

Racemic Mixture of 4-O-Benzoyl-5,6-O-cyclohexylidene-2-deoxystreptamine (6). A sample of **3** (5.70 g) was hydrogenated in a similar manner as above. On tlc with benzene–methanol (1: 1), **3** (R_f 1.0) disappeared and **6** (R_f 0.3) appeared as a single spot. The reaction mixture was similarly treated as described above, 3.66 g (100%); IR (KBr): 1725 cm^{-1}; no peaks between 1650—1700 cm^{-1}.

Found: C, 54.67; H, 6.98; N, 6.44; Cl, 16.49%. Calcd for $C_{19}H_{26}N_2O_4\cdot 2HCl$: C, 54.41; H, 6.73; N, 6.68; Cl, 16.91%.

Diacetate of **6** was obtained by using acetic acid instead of hydrochloric acid in the preparation described above, mp 92—93 °C.

Found: C, 59.49; H, 7.39; N, 6.19%. Calcd for $C_{19}H_{26}N_2O_4\cdot 2CH_3CO_2H$: C, 59.21; H, 7.35; N, 6.01%.

Racemic Mixture of 4,5-O-Cyclohexylidene-2-deoxy-6-O-ethoxycarbonylstreptamine (7). A sample of **4** (5.36 g) was hydrogenated in a similar manner as described in the preparation of **5**. The crude product was recrystallized from acetone containing acetic acid to give **7**, 3.06 g (77%), mp 116—117 °C; tlc: R_f 0.2 (benzene–methanol 2: 1); IR (KBr): 1760 cm^{-1}; PMR (in D_2O) δ: 1.28 (3H, t, $OCO_2CH_2C\underline{H}_3$), 1.90 (6H s, AcOH).

Found: C, 52.72; H, 7.76; N, 6.29%. Calcd for $C_{15}H_{26}N_2O_5\cdot 2CH_3CO_2H$: C, 52.52; H, 7.89; N, 6.45%.

*Racemic Mixture of 1-*N*-Benzoyl-4,5-O-cyclohexylidene-2-deoxystreptamine (8).* A solution of diacetate (3.66 g) of **6** in pyridine (73 ml) was maintained at 50 °C for 2 days. On tlc with benzene–methanol (3: 1), **6** (R_f 0.16) disappeared and **8** (R_f 0.56) appeared as a single spot. The solution was evaporated and then coevaporated with toluene to leave a residue, which was dissolved in aqueous methanol (1: 1). Addition of

0.01 M hydrochloric acid (pH~4.5) followed by evaporation gave a syrup. The procedure was repeated twice more. The methanol solution of the syrup was treated with charcoal to give the hydrochloride of **8**, 2.49 g (91%), mp 139—140 °C; IR (KBr): 1640, 1535 cm^{-1}.

Found: C, 57.16; H, 6.90; N, 6.47; Cl, 8.95%. Calcd for $C_{19}H_{26}N_2O_4 \cdot HCl \cdot H_2O$: C, 56.92; H, 7.29; N, 6.99; Cl, 8.84%.

Racemic Mixture of 4,5-O-Cyclohexylidene-2-deoxy-1-N-ethoxycarbonylstreptamine (9). The diacetate (3.06 g) of **7** was similarly treated in pyridine as described above. On tlc with benzene–methanol (1: 1), **7** (R_f 0.32) disappeared and **9** (R_f 0.74) appeared as a single spot. The solution was evaporated and then coevaporated with toluene. The residue was dissolved in aqueous methanol (1: 1) containing acetic acid (0.5 ml), treated with charcoal, and the solution was evaporated to give a solid, 2.99 g (82%); IR (KBr): 1690, 1620, 1540 cm^{-1}; PMR (in pyridine-d_5) δ: 1.13 (3H, t, $NCO_2CH_2C\underline{H}_3$), 2.12 (3H, s, AcOH).

Found: C, 54.20; H, 8.41; N, 7.79%. Calcd for $C_{15}H_{26}N_2O_5 \cdot CH_3CO_2H$: C, 54.53; H, 8.08; N, 7.48%.

Removal of Cyclohexylidene Group from 5, 8, and 9. The solution of 0.3 mmol of the starting material in 1M hydrochloric acid (2 ml) was allowed to stand at room temperature overnight. The product was purified by precipitation with acetone.

Racemic Mixture of 1-N-Acetyl-2-deoxystreptamine Hydrochloride (10): yield 82%, mp 171—172 °C. Found: C, 37.63; H, 7.11; N, 10.48, Cl, 13.56%. Calcd for $C_8H_{16}N_2O_4 \cdot HCl \cdot H_2O$: C, 37.14; N, 7.40; N, 10.83; Cl, 13.71%.

Racemic Mixture of 1-N-Benzoyl-2-deoxystreptamine Hydrochloride (11): yield 82%, mp 214—215 °C. Found: C, 50.28; H, 6.18; N, 8.55; Cl, 11.60%. Calcd for $C_{13}H_{18}N_2O_4 \cdot HCl \cdot 1/2H_2O$: C, 50.08; H, 6.47; N, 8.99; Cl, 11.37%.

Racemic Mixture of 2-Deoxy-1-N-ethoxycarbonylstreptamine Hydrochloride (12): yield 89%, mp 207—208 °C. Found: C, 40.06; H, 7.21; N, 10.52; Cl, 13.25%. Calcd for $C_9H_{18}N_2O_5 \cdot HCl$: C, 39.93; H, 7.07; N, 10.35; Cl, 13.10%.

1,3-Di-N-(p-methylbenzylidene)-2-deoxystreptamine (13). To a mixture of 2-deoxystreptamine dihydrochloride (1.02 g) and anhydrous potassium carbonate (6.9 g) in methanol (12 ml), *p*-methylbenzaldehyde (1.3 ml) was added under the atmosphere of nitrogen and the mixture was stirred at room temperature overnight. Evaporation gave a residue, which was extracted with chloroform. The solution was washed with water, dried over sodium sulfate and concentrated to give a syrup. Addition of hexane gave a solid, 1.09 g (63%); IR (KBr): 1630, 1605, 1100, 1030, 815, 500 cm^{-1}; PMR (in $CDCl_3$) δ: 2.31 (6H, s, $C\underline{H}_3C_6H_4$), 8.31 (2H, s, =CH-N).

Found: C, 68.35; H, 7.14; N, 6.96%. Calcd for $C_{22}H_{26}N_2O_3 \cdot H_2O$: C, 68.72; H, 7.34; N, 7.29%.

2-Deoxy-4,5,6-tri-O-ethoxycarbonyl-1,3-di-N-(p-methylbenzylidene)streptamine (14). To a solution of **13** (1.86 g, dried at 80 °C under reduced pressure) in pyridine (19 ml), a small amount of calcium hydride (to remove a trace of moisture) and ethyl chloroformate (2.9 ml) were added and the mixture was stirred at 50 °C overnight. Another ethyl chloroformate (0.8 ml) was added and the mixture was stirred for 1 hr. On tlc with benzene–ethyl acetate–triethylamine (6: 1: 0.01), **13** (R_f 0.2) disappeared and **14** (R_f 0.38) appeared. The mixture was poured into saturated sodium hydrogen carbonate solution (150 ml) and the mixture was stirred for 1 hr. The lower layer separated was extracted with chloroform and the solution was washed with water, dried over sodium sulfate and evaporated to give a syrup. Addition of hexane gave a solid, 2.45 g (85%); IR (KBr): 1750, 1710, 1640, 1610, 1370, 1290—1240 (s), 1010, 880, 820, 790, 510 cm^{-1}; PMR (in $CDCl_3$) δ: 1.08 (6H, t, $OCO_2CH_2C\underline{H}_3$), 1.29 (3H, t, $OCO_2CH_2C\underline{H}_3$), 2.40 (6H, s, $C\underline{H}_3C_6H_4$), 4.08 (4H, q, $OCO_2C\underline{H}_2CH_3$), 4.26 (2H, q, $OCO_2C\underline{H}_2CH_3$), 8.40 (2H, s, =CH-N).

Found: C, 63.50; H, 6.47; N, 4.68%. Calcd for $C_{31}H_{33}N_2O_9$: C, 63.90; H, 6.57; N, 4.81%.

2-Deoxy-4,5,6-tri-O-ethoxycarbonylstreptamine (15) Diacetate. A sample of **14** (3.70 g) was dissolved in 50% acetic acid (60 ml). Monitoring by tlc showed that **14** disappeared immediately, and **15** (R_f 0.5 with the lower layer of chloroform–ethanol–8% aqueous ammonia (2: 1: 1)) appeared. The solution was evaporated to give a syrup. Addition of ether gave a solid, 2.51 g (84%), mp 85—86 °C; IR (KBr): 1760, 1620 (w), 1400, 1280, 1250, 1020, 1000, 880, 780 cm^{-1}.

Found: C, 45.49; H, 6.52; N, 5.25%. Calcd for $C_{15}H_{26}N_2O_9 \cdot 2CH_3CO_2H$: C, 45.78; H, 6.87; N, 5.62%.

Preliminary Experimemt on Treatment of 15 with Pyridine. A solution of **15** (10 mg) in dry pyridine (0.2 ml) was allowed to stand at various temperatures and the change in the reaction was monitored by tlc (Wakogel B5, Wako Pure Chemicals Ind.) with ethyl acetate–ethanol–water (45: 5: 3) (Solvent A) and with chloroform–ethanol–8% aqueous ammonia (6: 1: 1) (lower layer) (Solvent B). Four spots A, B, C, and D appeared: A (R_f 0.1 by Solvent A and 0.1 by Solvent B, **15**), B (R_f 0.35 and 0.38, **16**), C (R_f 0.6 and 0.38, **17**) and D (R_f 0.6 and 0.3, **18**). At 20 °C: after 7 hr: *A* (卅), B(±); 24 hr: A (+), B(卅), C(±); 48 hr; A(±), B(卅), C(+). At 50 °C: 4 hr: A(卄), B(+), C(±); 5.5 hr: A(卄), B(卄), C(±); 7.5 hr: A(±), B(卅), C(+); 10 hr: A(±), B(卄), C(卄); 22 hr: B(卄), C(卄); 46 hr: B(+), C(卅); 50 hr: C(卅), D(+). At 100 °C: 0.5 hr: A(卄), B(+), C(±); 1 hr: A(+), B(卅), C(+); 2 hr: A(±), B(卄), C(卄), D(±); 3 hr: B(+), C(卄), D(卄); 5 hr: C(卄), D(卄).

Racemic Mixture of 2-Deoxy-1-N-ethoxycarbonyl-4,5-di-O-ethoxycarbonylstreptamine (16) and 1,3-Di-N-ethoxycarbonyl-5-O-ethoxycarbonyl-2-deoxystreptamine (17). A solution of **15** (1.18 g) in dry pyridine (21 ml) was allowed to stand at 50 °C for 46 hr. Evaporation of the solution gave a solid, which was charged on a column of silica gel (Wakogel C-200, Wako Pure Chemicals Ind.) and eluted with ethyl acetate–ethanol–water (45: 5: 3). From the earlier fraction, **17** was obtained, 425 mg (47%); Recrystallization from ethyl acetate gave needles, mp 112—113 °C; IR (KBr): 1740 (carbonate), 1700 (carbamate), 1540, 1270 (s), 1040, 880, 780 cm^{-1}; PMR (in $CDCl_3$) δ: 1.25 (6H, t, $NCO_2CH_2C\underline{H}_3$), 1.34 (3H, d, $OCO_2CH_2C\underline{H}_3$), 4.21 (4H, q, $CO_2C\underline{H}_2CH_3$).

Found: C, 47.30; H, 6.70; N, 7.13%. Calcd for $C_{15}H_{26}N_2O_9$: C, 47.61; H, 6.93; N, 7.40%.

From the later fraction, a solid of **16**, 172 mg (free base) (19%) was obtained, IR (KBr): 1750, 1700, 1540, 1270, 1030, 1000, 870, 780 cm^{-1}; PMR (in $CDCl_3$) δ: 1.23 (3H, t, $OCO_2CH_2C\underline{H}_3$), 1.30 (6H, t, $NCO_2CH_2C\underline{H}_3$); no peaks at ~$\delta$ 2 (acetate) was observed.

The hydrochloride of **16**. PMR (in CD_3OD) δ: 1.20 (3H, t, $OCO_2CH_2C\underline{H}_3$), 1.26 and 1.28 (each 3H, t, $NCO_2CH_2C\underline{H}_3$).

Found: C, 43.62; H, 6.44; N, 6.37; Cl, 8.46%. Calcd for $C_{15}H_{26}N_2O_9 \cdot HCl$: C, 43.43; H, 6.56; N, 6.75; Cl, 8.55%.

17 from 16. A solution of **16** (free base, 115 mg) in pyridine (2 ml) was allowed to stand at 35 °C for 12 hr. On tlc, the solution gave a single spot. The solution was evaporated and the residue was similarly purified by chromatography as described above to give **17**, 52 mg (52%).

4,6-Di-O-acetyl-2-deoxy-1,3-di-N-ethoxycarbonyl-5-O-ethoxycarbonylstreptamine (19). A solution of **17** in pyridine was acetylated with acetic anhydride in a usual manner to give **19** almost quantitatively, mp 154—155 °C; IR (KBr): 1760, 1730, 1700, 1530, 1380, 1270, 1230, 1040 cm^{-1}; PMR (in

$CDCl_3$) δ: 1.23 (6H, t, $NCO_2CH_2C\underline{H}_3$), 1.30 (3H, t, $OCO_2CH_2C\underline{H}_3$), 2.07 (6H, s, Ac), 4.15 (6H, q, $CO_2C\underline{H}_2CH_3$).

Found: C, 49.31; H, 6.42; N, 6.01%. Calcd for $C_{19}H_{30}N_2O_{11}$: C, 49.35; H, 6.54; N, 6.05%.

*Racemic Mixture of 2-Deoxy-1,3-di-*N*-ethoxycarbonyl-4-*O*-ethoxycarbonylstreptamine (18).* A solution of the diacetate (1.0 g) of **15** in dry pyridine (20 ml) was heated at 100 °C for 5 hr. Evaporation of the solution gave a solid. The solid was chromatographed on a column of silica gel with ethyl acetate. From the earlier fraction **17** was obtained, 280 mg (37%) and from the later fraction **18**, 258 mg (34%) was obtained; Recrystallization from ethyl acetate gave needles, mp 120—121 °C; IR (KBr): 1740, 1700, 1540, 1270, 1030, 1010, 880, 780 cm^{-1}; PMR (in $CDCl_3$) δ: 1.22 and 1.23 (each 3H, t, $NHCO_2CH_2C\underline{H}_3$), 1.30 (3H, t, $OCO_2CH_2C\underline{H}_3$).

Found: C, 47.66; H, 6.89; N, 7.15%. Calcd for $C_{15}H_{26}N_2O_9$: C, 47.61; H, 6.93; N, 7.40%.

*Racemic Mixture of 4,5-Di-*O*-acetyl-2-deoxy-1,3-di-*N*-ethoxycarbonyl-6-*O*-ethoxycarbonylstreptamine (20).* A sample of **18** was similarly treated as described in the preparation of **19**, mp 169—170 °C. The IR spectrum was substantially similar to that of **19**. PMR (in $CDCl_3$) δ: 1.21 (6H, t, $NHCO_2CH_2C\underline{H}_3$), 1.27 (3H, t, $OCO_2CH_2C\underline{H}_3$), 2.10 and 2.12 (each 3H, s, Ac), 4.05 (6H, q, $CO_2C\underline{H}_2CH_3$).

Found: C, 49.84; H, 6.51; N, 5.98%. Calcd for $C_{19}H_{30}N_2O_{11}$: C, 49.35; H, 6.54; N, 6.05%.

Periodate Oxidation of the Mixture of 17 and 18. The reaction mixture of **17** and **18** described in the preparation of **18** was evaporated. The residue showed two spots at R_f 0.7 (**17**) and 0.55 (**18**) in almost equal strength on tlc with chloroform–ethanol–8% aqueous ammonia (6: 1: 1). To the solution of the residue (20.1 mg) in aqueous dioxane (1: 1, 0.5 ml), periodic acid (6.1 mg) was added and the solution was allowed to stand at room temperature for 1 hr. The reaction mixture showed a clear spot at R_f 0.7, but the spot at R_f 0.55 disappeared completely.

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