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SYNTHESES OF 3′,4′,5,6-TETRADEOXYNEAMINE AND 5,6-DIDEOXYNEAMINE

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ABSTRACT

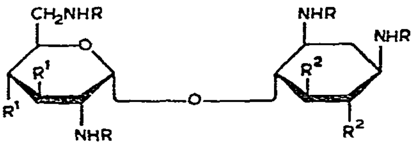
3′,4′,5,6-Tetradeoxyneamine (7) was synthesized from neamine by the reaction sequence *N*-acetylation, *O*-mesylation, treatment with sodium iodide–zinc dust, hydrogenation, and base hydrolysis Alternatively, 7 was obtained by treatment of tetra-(*N*-methoxycarbonyl)neamine with sulphuryl chloride, followed by hydrogenation in the presence of palladium-on-charcoal and triethylamine, and removal of the *N*-protecting groups 5,6-Dideoxyneamine (**11**) was synthesized from known 5,6-*O*-cyclohexylidene-tetra-(*N*-methoxycarbonyl)neamine by the reaction sequence 3′,4′-*O*-acetylation, removal of the 5,6-*O*-cyclohexylidene group, 5,6-di-*O*-mesylation, treatment with sodium iodide–zinc dust, hydrogenation, and base hydrolysis An alternative route involved treatment of 3′,4′-di-*O*-acetyl-tetra-(*N*-methoxycarbonyl)-neamine (**8**) with sulphuryl chloride, hydrogenation of the product, and removal of the protecting groups to give **11**

INTRODUCTION

Neamine, a component of the Neomycin complex of antibiotics, inhibits the growth of many Gram-negative and Gram-positive bacteria As 3′,4′-dideoxyneamine has improved antibacterial activity, especially against those resistant organisms that inactivate neamine by transphosphorylation to HO-3′, we have investigated the role of the other hydroxyl functions in relation to antibacterial activity, and we now report the preparation of 3′,4′,5,6-tetradeoxyneamine and 5,6-dideoxyneamine Both compounds possess biological activity similar to that of neamine

RESULTS AND DISCUSSION

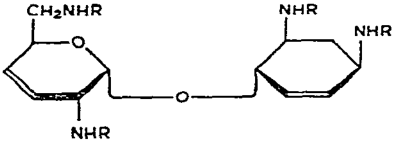
Preparation of 3′,4′,5,6-tetradeoxyneamine (7) was achieved *via* two routes Tetra-(*N*-methoxycarbonyl)neamine[1] (2) was transformed into the tetramesylate **4**, which was then heated with sodium iodide–zinc dust in *N*,*N*-dimethylformamide (Tipson–Cohen conditions[2]) to yield the diene **12** Similarly, tetra-(*N*-benzyloxy-carbonyl)neamine (3) was transformed into the tetramesylate **5** and thence into the diene **13** Hydrogenation of **12** yielded **6**, which was hydrolysed with barium hydroxide to give tetradeoxyneamine (**7**) The same product **7** was prepared, omitting one step, by hydrogenation and hydrogenolysis of **13**



1 R = H R^1 = R^2 = OH, Neamine
2 R = COOMe R^1 = R^2 = OH
3 R = Cbz R^1 = R^2 = OH
4 R = COOMe, R^1 = R^2 = OMs
5 R = Cbz, R^1 = R^2 = OMs
6 R = COOMe, R^1 = R^2 = H

7 R = R^1 = R^2 = H
8 R = COOMe, R^1 = OAc, R^2 = OH
9 R = COOMe, R^1 = OAc R^2 = OMs
10 R = COOMe R^1 = OAc R^2 = H
11 R = R^2 = H R^1 = OH

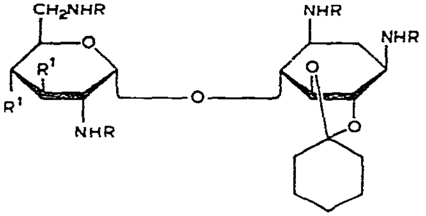
Cbz = $C_6H_5CH_2OCO$



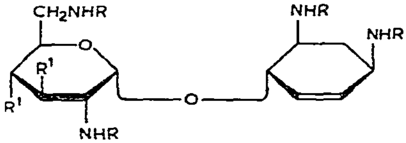
12 R = COOMe
13 R = Cbz

In an alternative route, **2** was treated with sulphuryl chloride [3], and the resulting tetrachloro derivative was hydrogenated in the presence of palladium-on-charcoal and triethylamine, followed by hydrolysis with barium hydroxide to give tetradeoxyneamine (**7**)

For the synthesis of 5,6-dideoxyneamine (**11**), the known[1] 5,6-*O*-cyclohexylidene derivative **14**, purified by crystallization and not by column chromatography as published[1], was treated with acetic anhydride–pyridine, followed by careful acid hydrolysis of the *O*-cyclohexylidene group from the product to give the diol **8** The dimesylate **9** of **8** was treated at 100° with sodium iodide–zinc dust in *N*,*N*-dimethylformamide to give the unsaturated derivative **16** Hydrogenation of **16**, followed by alkaline hydrolysis of the protecting groups, gave **11** When **16** was hydrolysed with barium hydroxide, 5,6-dideoxyneamine-5-ene (**17**) was obtained Replacement of the hydroxyl groups of 3′,4′-di-*O*-acetyl-tetra-(*N*-methoxycarbonyl)neamine (**8**) by chlorine, using sulphuryl chloride, followed by catalytic hydrogenation of the product in the presence of triethylamine, gave 3′,4′-di-*O*-acetyl-5,6-dideoxy-tetra-(*N*-methoxycarbonyl)neamine (**10**), which was readily converted into **11**



14 R = COOMe R^1 = OH
15 R = COOMe R^1 = OAc



16 R = COOMe R^1 = OAc
17 R = H, R^1 = OH

EXPERIMENTAL

General methods — Melting points are uncorrected Solutions were dried with anhydrous sodium sulphate and concentrated under diminished pressure <40° Identification of products was based on mixture m p , comparison of i r and p m r spectra, and chromatographic mobilities T l c was performed on silica gel HF_{254} with detection by ninhydrin, by charring with sulphuric acid, or by exposure to u v light of 254 nm $[\alpha]_D$ values were measured with a Bellingham and Stanley polarimeter, and i r. spectra with a Perkin–Elmer 621 spectrophotometer P m r spectra (90 MHz) were recorded (internal Me_4Si) with a Perkin–Elmer R-32 spectrometer

*3′,4′,5,6-Tetra-*O*-methanesulphonyl-tetra-(*N*-methoxycarbonyl)neamine* (**4**) — A solution of tetra-(*N*-methoxycarbonyl)neamine[1] (**2**, *5* g, *9* mmol) in dry pyridine (50 ml) was treated with methanesulphonyl chloride (4 ml) at 30° overnight, and then at 45° for 3 h The mixture was poured into cold, saturated, aqueous $NaHCO_3$, and extracted with chloroform, and the extract was worked-up in the usual way Recrystallisation of the product from chloroform gave **4** (6 g, 77%), m p 180 5–182 5°, $[\alpha]_D^{25}$ +43° (*c* 1, *N,N*-dimethylformamide), R_F 0 35 (ethyl acetate) P m r data (methyl sulphoxide-d_6) δ 1 35–2 10 (bm, 2 H, H-2), 3 21 (m, 12 H, 4 OMs), 3 60 (s, 12 H, 4 COOMe), 5 28 (m, 1 H, H-1′α), and 7 20 (bm, 4 H, 4 NH)

Anal Calc for $C_{24}H_{42}N_4O_{22}S_4$ C, 33 26, H, 4 88; N, 6 46, S, 14 77 Found C, 33 11, H, 4 96, N, 6 41, S, 14 84

*3′,4′,5,6-Tetradeoxy-tetra-(*N*-methoxycarbonyl)neamine-3′,5-diene* (**12**) — A mixture of **4** (2.3 g, 41 mmol), dry *N,N*-dimethylformamide (70 ml), anhydrous sodium iodide (30 g), and zinc dust (15 g) was heated at 105–110° for 2 h with vigorous stirring and then cooled Chloroform (100 ml) was added, the mixture was filtered, and the solids were washed with chloroform The combined organic liquids were washed successively with aqueous $NaHCO_3$ (50 ml), aqueous $Na_2S_2O_3$ (50 ml), and water (3 × 50 ml), dried, and concentrated A solution of the syrupy product in toluene was concentrated to dryness, and the residue was recrystallized from hot ethyl acetate to give **12** (1 g, 78%), m p 218–220° (sinters at 176°), $[\alpha]_D^{27}$ +114° (*c* 0 5, methanol), R_F 0 42 (3 1 butanone–chloroform), $\nu_{max}^{CHCl_3}$ 3320 (NH), 1690 (N-COOMe), and 1530 cm^{-1} (Amide II) P m r data (methyl sulphoxide-d_6, 60°) δ 1 25 (bm, 1 H, H-2ax), 1 96 (bm, 1 H, H-2eq), 3 56 (s, 12 H, 4 COOMe), 5 10 (m, 1 H, H-1′α), 5 63 (m, 4 H, H-3′,4′,5,6), and 6 30–7 20 (b, 4 H, 4 NH)

Anal Calc for $C_{20}H_{30}N_4O_{10}$ C, 49 37, H, 6 21, N, 11 51 Found C, 49 50, H, 6 13, N, 11 72

*3′,4′,5,6-Tetradeoxy-tetra-(*N*-methoxycarbonyl)neamine* (**6**) — A mixture of **12** (0 6 g, 1 2 mmol), ethanol (25 ml), and 10% Pd/C (0 03 g) was hydrogenated at 3 atmos for 3 h (20°) The filtered solution was concentrated to give an amorphous solid that was recrystallized from water to yield **6** (0 55 g, 90%), m p 185–187°, $[\alpha]_D^{27}$ +84° (*c* 0 5, methanol), + 97° (*c* 1, chloroform), R_F 0 50 (10 1 ethyl acetate–ethanol), $\nu_{max}^{CHCl_3}$ 3210 (NH), 1700 (N-COOMe), and 1520 cm^{-1} (Amide II) P m r data ($CDCl_3$, 80°) δ 3 65 (s, 12 H, 4 COOMe) and 4.95 (m, 1 H, H-1′α)

Anal Calc for $C_{20}H_{34}N_4O_{10}$ C, 48 97, H, 6 98, N, 11 42 Found C, 49 10, H, 7 05, N, 11 21

*Tetra-(*N*-benzyloxycarbonyl)neamine* (**3**) — To a solution of neamine hydrochloride (**1**, 5 g, 10 7 mmol) and anhydrous Na_2CO_3 (10 g) in 60% aqueous acetone (150 ml), benzyl chloroformate (10 ml, 58 mmol) was added, and stirring was continued for 3 h at 20° The mixture was concentrated, the residue was extracted with acetone (2 × 100 ml), the combined extracts were concentrated, and the residue was recrystallized from *N,N*-dimethylformamide–water to give **3** (7 6 g, 85%), m p 230–234°, $[\alpha]_D^{25}$ +39° (*c* 1, *N,N*-dimethylformamide), R_F 0 7 (4 1 ethyl acetate–methanol), $\nu_{max}^{CHCl_3}$ 3500 (OH), 3320 (NH), 1700 (N-COOMe), and 1545 cm^{-1} (Amide II)

Anal Calc for $C_{44}H_{50}N_4O_{14}$ C, 61 53, H, 5 82, N, 6 52 Found C, 61 87, H, 5 96, N, 6 80

*Tetra-(*N*-benzyloxycarbonyl)-3′,4′,5,6-tetra-*O*-methanesulphonylneamine* (**5**) — Conventional mesylation of **3** (1 g, 1 1 mmol) in pyridine (20 ml) with mesyl chloride (1 ml) at 20° for 12 h gave **5** (1 2 g, 90%), m p 182–185° (from xylene), $[\alpha]_D^{25}$ +18° (*c* 1, chloroform), R_F 0 65 (8 1 ethyl acetate–ethanol), 0 30 (3 1 chloroform–ethyl acetate) P m r data (chloroform-*d*) δ 2 08 (bm, 2 H, H-2), 2 77 and 2 82 (2 s, 6 H, 2 OMs), 3 10 (s, 6 H, 2 OMs), 5 05 (m 8 H, 4 CH_2-Ph), 5 77 (m, 1 H, H-1′α), and 7 29 (m, 20 H, 4 Ph)

Anal Calc for $C_{48}H_{58}N_4O_{22}S_4$ C, 49 23, H, 4 95 N, 4 78, S, 10 94 Found C, 49 53 H, 5 27 N, 4 55 S, 10 96

*Tetra-(*N*-benzyloxycarbonyl)-3′,4,′5,6-tetradeoxyneamine-3′,5-diene* (**13**) — A mixture of **5** (1 g, 0 85 mmol), dry *N,N*-dimethylformamide (40 ml), anhydrous NaI (25 g), and zinc dust (12 g) was heated at 90° for 1 5 h with vigorous stirring Chloroform (100 ml) was added, and the mixture was filtered and then worked-up as described above for **12** The crude product was crystallized from 1-butanol to give **13** (0 35 g, 51%), m p 223–225°, $[\alpha]_D^{22}$ +59° (*c* 1, *N,N*-dimethylformamide), R_F 0 7 (8 1 ethyl acetate–ethanol), ν_{max}^{Nujol} 3345 (NH), 1695 (N-COOMe), and 1545 cm^{-1} (Amide II) P m r data (methyl sulphoxide-d_6) δ 1 55 (bm, 2 H, H-2), 5 08 (bm, 9 H, H-1′a and 4 CH_2-Ph), 5 60 (bm, 4 H, H-3′,4′,5,6), 7 00 (b, 4 H, 4 NH), and 7 38 (bm, 20 H, 4 Ph)

Anal Calc for $C_{44}H_{46}N_4O_{10}$ C, 66 83, H, 5 82, N, 7 08 Found C, 66 77, H, 5 98, N, 7 05

3′,4′,5,6-Tetradeoxyneamine (**7**) — (*a*) A mixture of **6** (0 486 g, 1 mmol), $Ba(OH)_2$ $8H_2O$ (5 g) water (10 ml), and *p*-dioxane (3 ml) was boiled under reflux for 24–36 h, and then neutralized with solid CO_2, filtered, and concentrated A solution of the residue in water (2 ml) was centrifuged, and acidified to pH ~3 with 10% aqueous H_2SO_4, and methanol (3 5 ml) was then added The precipitate was collected, dissolved in water (1 5 ml), and reprecipitated with methanol (2 5 ml) to give **7** as the sulphate (0 30 g, 66%), m p 253–265°, $[\alpha]_D^{27}$ +80° (*c* 1, water), R_F 0 35 (2 1 methanol–35% NH_4OH)

(*b*) A solution of **13** (0 79 g, 1 mmol) in ethanol (20 ml) containing 10% Pd/C (60 mg) was hydrogenated at 4 atmos for 6 h The solution was filtered and concentrated to give a glassy product that was dissolved in water (2 ml) and neutralized with 10% aqueous H_2SO_4 The addition of methanol (3 ml) precipitated **7** as the sulphate (0 386 g, 85%), m p 264–265°, $[\alpha]_D^{27}$ +80 5° (*c* 1, water), R_F 0 35 (2 1 methanol–35% NH_4OH)

(*c*) A solution of **2** (1 g, 1 8 mmol) in pyridine (10 ml) was treated with SO_2Cl_2 (2 16 g, 16 mmol) at 60° for 16 h, and then concentrated A solution of the syrupy residue in chloroform (25 ml) was washed successively with 20% aqueous KI, 10% aqueous $KHSO_4$, saturated, aqueous $NaHCO_3$, and water, dried, and concentrated The syrupy product was dissolved in ethanol (50 ml) and hydrogenated in the presence of 10% Pd/C (0 1 g) and triethylamine (1 ml) at 4 atmos for 10 h The filtered solution was concentrated, and the residue was treated with SO_2Cl_2 and hydrogenated as described above The crude product was heated for 24 h at 80° in 50% aqueous MeOH (10 ml) containing $Ba(OH)_2$ $8H_2O$ (3 g) The mixture was neutralized with CO_2, centrifuged, concentrated, neutralized with 10% H_2SO_4, and treated with methanol to yield **7** as the sulphate (0 236 g, 29%) m p 263–265°, $[\alpha]_D^{27}$ +80 5° (*c* 1, water), R_F 0 35 (2 1 methanol–35% NH_4OH)

Anal Calc for $C_{12}H_{26}N_4O_2$ $2H_2SO_4$ C, 31 71, H, 6 65, N 12 33 Found C, 31 40, H, 6 79, N, 12 50

3',4'-Di-O-acetyl-5,6-O-cyclohexylidene-tetra-(N-methoxycarbonyl)neamine (**15**) — A solution of 5,6-*O*-cyclohexylidene-tetra-(*N*-methoxycarbonyl)neamine[1] (**14**, 1 g, 1 5 mmol, readily purified by crystallisation from tetrahydrofuran–water, m p 221–229°) was conventionally acetylated with pyridine (30 ml) and acetic anhydride (1 ml) for 24 h at 25° The crude product was recrystallized from benzene–light petroleum to give **15** (1 g, 90%), m p 139–141°, $[\alpha]_D^{30}$ +45° (*c* 0 92, chloroform), R_F 0 3 (ethyl acetate), 0 65 (10 1 ethyl acetate–ethanol) P m r data (chloroform-*d*) δ 1 26 (m, 2 H, H-2), 1 60 (m, 10 H, cyclohexylidene protons), 1 99 and 2 03 (2 s, 6 H, 2 OAc), 3 66 (m, 12 H, 4 COOMe), and 5 20 (m, 1 H, H-1'α)

Anal Calc for $C_{30}H_{46}N_4O_{16}$ C, 50 13, H, 6 45, N, 7 79 Found C, 50 21, H, 6 55, N, 8 01

3',4'-Di-O-acetyl-tetra-(N-methoxycarbonyl)neamine (**8**) — A solution of **15** (3 2 g, 4 4 mmol) in chloroform (50 ml) was stirred with toluene-*p*-sulphonic acid (0 1 g) in methanol (10 ml) at 50° for 3 h, and then neutralized with NEt_3 (1 ml) and concentrated A solution of the residue in chloroform (40 ml) was washed with water, dried, and concentrated to give **8** (2 55 g, 90%) which, after recrystallization from water, had m p 154–156 5°, $[\alpha]_D^{20}$ +69° (*c* 1, methanol), R_F 0 3 (10 1 ethyl acetate–ethanol), $\nu_{max}^{CHCl_3}$ 3300 (broad, NH, OH), 1730 (OAc), 1695 (N-COOMe), and 1530 cm^{-1} (Amide II) P m r data (methyl sulphoxide-d_6) δ 1 28 (s, 1 H, H-2ax), 1 91 and 1 95 (2 s, 6 H, 2 OAc), 3 57 (m, 12 H, 4 COOMe), 5 10–5 20 (bm, 2 H, 2 OH), 5 22 (d, 1 H, H-1'α), and 6 95 (bm, 4 H, 4 NH)

Anal Calc for $C_{24}H_{38}N_4O_{16}$ C, 45 14, H, 5 99, N, 8 77 Found C, 45 22, H, 6 10, N, 8 95

3',4'-Di-O-acetyl-5,6-di-O-methanesulphonyl-tetra-(N-methoxycarbonyl)neamine (**9**) — Conventional mesylation of **8** (2 g, 3 13 mmol) with dry pyridine (40 ml) and mesyl chloride (1 g) at 30° overnight, followed by 2 h at 50°, with recrystallization of the crude product from benzene, gave **9** (2 4 g, 92%), m p 215–216°, $[\alpha]_D^{29}$ +36° (*c* 1, chloroform), R_F 0 5 (10 1 ethyl acetate–ethanol) P m r data (methyl sulphoxide-d_6) δ 1 15–1 80 (bm, 2 H, H-2), 1 88 and 1 95 (2 s, 6 H, 2 OAc), 3 18 and 3 28 (2 s, 6 H, 2 OMs), 3 56 (m, 12 H, 4 COOMe , 5 22 (d, 1 H, H-1′α), and 6 80–7 50 (bm, 4 H, 4 NH)

Anal Calc for $C_{26}H_{42}N_4O_{20}S_2$ C, 39 29, H, 5 32, N, 7 05, S, 8 05 Found C, 39 51; H, 5 49, N, 7 16, S, 7 89.

*3′,4′-Di-O-acetyl-5,6-dideoxy-tetra-(*N*-methoxycarbonyl)neamine-5-ene* (**16**) — A mixture of **9** (0 5 g, 0 63 mmol), dry *N,N*-dimethylformamide (30 ml), anhydrous sodium iodide (10 g), and zinc dust (5 g) was vigorously stirred at 100° for 2 h, and then worked-up as described above for **12** The crude product (0 37 g, 92%) was eluted with ethyl acetate from silica gel to give **16**, m p 213–215°, $[\alpha]_D^{23}$ +150° (*c* 1, chloroform), R_F 0 3 (ethyl acetate), $\nu_{max}^{CHCl_3}$ 3310 (NH), 1740 (OAc), 1695 (N-COOMe), and 1515 cm^{-1} (Amide II) P m r. data (methyl sulphoxide-d_6) δ 1 17 (s, 1 H, H-2ax), 1 50–1 70 (bm, 1 H, H-2eq), 1 90 and 1 95 (2 s, 6 H, 2 OAc), 3 58 (m, 12 H, 4 COOMe), 5 02 (d, 1 H, H-1′α), and 5 67 (bm, 2 H, H-5,6)

Anal Calc for $C_{24}H_{36}N_4O_{14}$ C, 47 68, H, 6 00, N, 9 29 Found C, 47 63, H, 5 94, N, 9 44

5,6-Dideoxyneamine-5-ene (**17**) — A mixture of **16** (0 37 g, 0 61 mmol), barium hydroxide octahydrate (1 1 g), and 50% aqueous *p*-dioxane (10 ml) was boiled under reflux for 18 h, and then neutralized with CO_2, centrifuged, and concentrated The residue (0 13 g, 70%) was eluted from silica gel with methanol–35% ammonia (2 1) to give **17**, m p 233° (dec), $[\alpha]_D^{25}$ +70° (*c* 0 75, water), R_F 0 3 (8 1 methanol–35% ammonia), 0 5 (2 1 methanol–35% ammonia) P m r data (D_2O) δ 2 17 (t, 2 H, H-2), 5 68 (d, 1 H, H-1′α), and 6 17 (q, 2 H, H-5,6)

Anal Calc for $C_{12}H_{24}N_4O_4$ C, 49 98, H, 8 38, N, 19 43 Found C, 50 21, H, 8 17, N, 19.59

*3′,4-Di-O-acetyl-5,6-dideoxy-tetra-(*N*-methoxycarbonyl)neamine* (**10**) — (*a*) A solution of **16** (0 7 g, 1 14 mmol) in methanol (50 ml) containing 10% Pd/C (30 mg) was hydrogenated at 3 atmos for 3 h, and then filtered and concentrated The residue (0 7 g, 100%) was recrystallized from chloroform–ether to give **10**, m p 199–201°, $[\alpha]_D^{26}$ +88° (*c* 1, chloroform), R_F 0 3 (ethyl acetate), 0 4 (3 1 butanone–chloroform), $\nu_{max}^{CHCl_3}$ 3410 and 3310 (NH), 1740 (OAc), 1700 (N-COOMe), and 1520 cm^{-1} (Amide II) P m r data (chloroform-*d*, 80°) δ 1 10–1 70 (bm, 5 H, methylene protons), 1 95 and 1 99 (2 s, 6 H, 2 OAc), 2 31 (bm, 1 H, methylene proton), 3 65 (m, 12 H, 4 COOMe), and 4 60–5 40 (m, 7 H, 4 NH, H-1′α,3′,4′)

Anal Calc for $C_{24}H_{38}N_4O_{14}$ C, 47 52, H, 6 31, N, 9 33 Found C, 47.59, H, 6 54, N, 9 51

(*b*) A mixture of **8** (0 638 g, 1 mmol), pyridine (15 ml), and sulphuryl chloride (3 ml) was kept at 60° overnight and then concentrated A solution of the syrupy residue in chloroform (3 ml) was washed with aqueous KI, aqueous $NaHCO_3$, and water, dried, and concentrated The residue was hydrogenated in ethanol (25 ml) containing 10% Pd/C catalyst (60 mg) and triethylamine (0 7 ml), at 4 atmos and 40° for 12 h After concentration of the filtered solution, the residue was again treated with sulphuryl chloride and hydrogenated, and then worked-up as described above The crude product was recrystallized from chloroform–ether to give pure **10** (0 15 g, 24%), m p 199–201°, $[\alpha]_D^{26}$ +88° (*c* 1, chloroform), R_F 0 4 (3 1 butanone–chloroform) The i r and p m r spectra were identical with those of the compounds prepared in (*a*)

5,6-Dideoxyneamine (**11**) — (*a*) A mixture of **10** (0 29 g, 0 47 mmol), 50% aqueous *p*-dioxane (8 ml), and $Ba(OH)_2$ $8H_2O$ (0 75 g) was boiled under reflux for 15 h, and then neutralized with CO_2, centrifuged, and concentrated. Elution of the residue (0 12 g) from Amberlite CG-50(NH_4^+) resin with 0 1–0 2M NH_4OH gave **11** (98 mg, 73%), m p 255° (dec), $[\alpha]_D^{22}$ +36 5° (*c* 0 5, water), R_F 0 4 (2 1 methanol–35% ammonia)

(*b*) A solution of **17** (0 15 g, 0 52 mmol) in water (5 ml) was hydrogenated with 10% Pd/C catalyst at 3 atmos for 3 h (22°), and then filtered and concentrated to give **11** (0 15 g, 100%), m p 255° (dec), $[\alpha]_D^{22}$ +36° (*c* 1, water), R_F 0 4 (2 1 methanol–35% ammonia) P m r data (D_2O) δ 1 40–2 00 (m, 6 H, H-2,5,6), 5 22 (m, 1 H, H-1'α)

Anal Calc for $C_{12}H_{26}N_4O_4$ C, 49 63, H, 9 02, N, 19 29 Found C, 49 75, H, 9 14, N, 19 11

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