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SYNTHESIS OF 1,4:5,8-DIANHYDRO-OCTITOL DERIVATIVES

JÁNOS KUSZMANN*, GÁBOR MEDGYES, AND PÉTER DVORTSÁK
Institute for Drug Research, P.O. Box 82, H-1325 Budapest 4 (Hungary)
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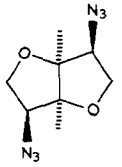
ABSTRACT

The carbon chain of 1,6-dibromo-1,6-dideoxy-3,4-*O*-isopropylidene-D-mannitol was elongated *via* reaction with sodium cyanide to give the 1,6-dicyanide. Hydrolysis and esterification then gave dimethyl 2,7-dideoxy-4,5-*O*-isopropylidene-D-*manno*-octarate, treatment of which with 2,2-dimethoxypropane and an acid catalyst gave dimethyl 2,7-dideoxy-3,6:4,5-di-*O*-isopropylidene-D-*manno*-octarate. Reduction of the terminal methoxycarbonyl groups then gave 2,7-dideoxy-3,6:4,5-di-*O*-isopropylidene-D-*manno*-octitol, which was converted into 1,4:5,8-dianhydro-3,6-diazido-2,3,6,7-tetradeoxy-L-*manno*- and -L-*ido*-octitol.

INTRODUCTION

1,4:3,6-Dianhydro-2,5-diazido-2,5-dideoxy-L-mannitol[1] (**1**), containing two fused tetrahydrofuran rings, is a highly effective hypnotic agent[2], but none of its stereoisomers possessed similar activity. In establishing the structure–activity relationship, the synthesis of compounds containing two isolated tetrahydrofuran rings, *i.e.*, the 1,4:5,8-dianhydro-3,6-diazido-2,3,6,7-tetradeoxyoctitols (**2**) was undertaken.



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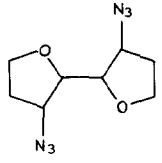

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RESULTS AND DISCUSSION

Treatment of 1,6-dibromo-1,6-dideoxy-3,4-*O*-isopropylidene-D-mannitol[3] (**3**) with potassium cyanide in aqueous ethanol at 80° afforded the dicyano derivative **4**, which was hydrolysed with aqueous sodium hydroxide to give the disodium salt

*To whom correspondence should be addressed.

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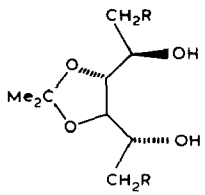
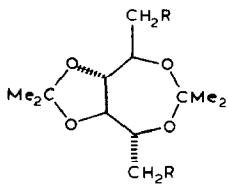
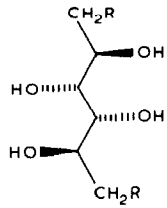
of the corresponding saccharic acid **5**. Reaction of **5** with methyl iodide in methyl sulfoxide gave a low yield (32%) of the diester **6** which, on treatment with boiling 2,2-dimethoxypropane containing toluene-*p*-sulfonic acid as catalyst[4] but no solvent[5–7], gave an equilibrium mixture (t.l.c.) of the monoacetal **6** and the diacetal **7** in the ratio 6:4. The equilibrium could be shifted towards **7** (ratio → 4:6) by distillation of the methanol generated in the reaction. The diacetal **7** crystallised from the cooled reaction mixture; on repeating the acetalation procedure with the products in the mother liquor, **6** could be completely converted into **7**. The presence of a dioxolane and a dioxepane ring in **7** was proved by ^{13}C-n.m.r. spectroscopy, since the signals of the acetal carbon atoms appeared at 111.2 and 102.8 p.p.m., respectively[8]. A similar diacetal was obtained by Buchanan[9] on treating 1,6-dichloro-1,6-dideoxy-D-mannitol with 2,2-dimethoxypropane.



3 R = Br
4 R = CN
5 R = COONa
6 R = COOMe



7 R = COOMe
8 R = CH_2OH
9 R = CH_2OBz
10 R = CH_2OMs



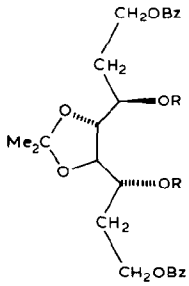
11 R = CH_2OH
12 R = CH_2OBz

The ester groups of **7** were reduced with lithium aluminum hydride to afford the diol **8**, which was rather unstable at room temperature and was used immediately. Hydrolysis of **8** with M sulfuric acid in methanol gave the crystalline and stable 2,7-dideoxy-D-*manno*-octitol (**11**).

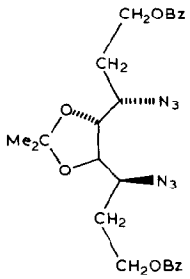
The acid-sensitivity of the two acetal rings in **9** (the dibenzoate of **8**) differed significantly and the dioxepane ring could be hydrolysed selectively with aqueous acetic acid at room temperature within 5 min, to give 81% of the crystalline monoacetal **13**. When the temperature of the hydrolysis was 90°, both isopropylidene groups were removed, giving the crystalline dibenzoate **12**.

The dimesylate (**14**) of **13** was treated with sodium azide in *N,N*-dimethylformamide to give, *via* inversion of configuration at C-3,6, the L-*ido*-diazide **15**. Treatment of **15** with 5:1 acetic acid–M hydrochloric acid at 90° removed the isopropylidene group to give diol **16**, which was isolated crystalline after column chromatography. Mesylation of **16** afforded **17**, which was treated with aqueous sodium hydroxide in methanol. Following loss of the benzoyl groups (→**18**), the anhydro rings were formed *via* elimination of methanesulfonic acid and inversion of the configuration at C-4,5. Since 5- or 6-membered anhydro rings could have been formed, proof of the structure of the L-*manno*-dianhydride **19** was required. Since the ^{1}H- and ^{13}C-n.m.r. spectra were inconclusive, **19** was hydrogenated over

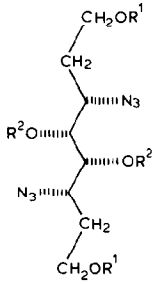
Pd/C, and the resulting diamine **20** was converted into its crystalline bis(acetamido) derivative **21**. The mass spectrum of **21** proved unambigously the presence of the two separated oxolane rings, as the major fragment had *m/z* 128, corresponding to $M^+/2$, a fragmentation which would not be expected for the 1,5:4,8-dianhydro isomer **22**.



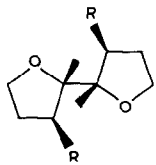
13 R = H
14 R = Ms



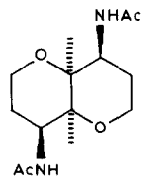
15



16 R^1 = Bz, R^2 = H
17 R^1 = Bz, R^2 = Ms
18 R^1 = H, R^2 = Ms



19 R = N_3
20 R = NH_2
21 R = NHAc



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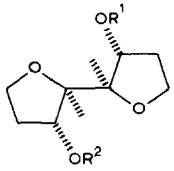
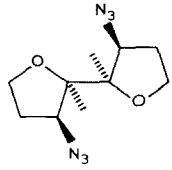
The L-*ido* isomer (**27**) of **19** was synthesised from the diol **8**. Mesylation of **8** afforded the crystalline dimesylate **10**, which was unstable at room temperature and was therefore immediately treated with aqueous acetic acid at 90° to remove the acetal groups. T.l.c. showed that two products were formed, the ratio of which became constant after 5 h. These products were isolated by column chromatography and proved to be the mono- (**23**) and di-acetylated 1,4:5,8-dianhydro-octitol derivatives (**24**). The formation of the tetrahydrofuran rings is not surprising, since, for example, 1,6-di-*O*-tosyl-D-mannitol derivatives gave the corresponding 1,4-anhydro compounds at room temperature[10], and partial acetylation of hydroxyl groups during removal of *O*-isopropylidene groups with aqueous acetic acid has been reported[11]. The base peak in the mass spectrum of **24** was at *m/z* corresponding to $M^+/2$, thereby confirming the structure.

Zemplén deacetylation of **23** and **24** gave the dianhydride **25**, the dimesylate (**26**) of which, on treatment with sodium azide in *N,N*-dimethylformamide, afforded the L-*ido*-3,6-diazide **27**.



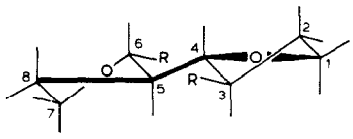
23 R^1 = Ac, R^2 = H
24 R^1 = R^2 = Ac
25 R^1 = R^2 = H
26 R^1 = R^2 = Ms



27

The $J_{H,H}$ values of the L-*manno*-dianhydride **19** indicate that both tetrahydrofuran rings adopt the same twist conformation (**28**; $^2T_3$, $^6T_7$) in which the torsion angles H-2*e*/H-3*a* and H-1*a*/H-2*e* are 150–160°, and that of H-1*e*/H-2*e* is 20–30°, since H-2*e* has three ^3J couplings of the same magnitude (7.2 Hz). The same holds for H-7*a* of the other tetrahydrofuran ring, proving the symmetry of the molecule. In the D-*manno* series, the tetrahydrofuran ring in the monoacetate **23** adopts a similar twist conformation, but, in the diacetate **24** and the dimesylate **26**, the bulky substituents at C-3,6 shift the structure towards the ^1T_o, ^8T_o conformation.

The diazides **19** and **27** were inactive as hypnotic agents.



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EXPERIMENTAL

General methods. — Organic solutions were dried over Na_2SO_4 and concentrated under diminished pressure. Melting points are uncorrected. Light petroleum had b.p. 40–70°. Optical rotations were determined in chloroform (*c* 1) if not stated otherwise. T.l.c. was performed on Kieselgel G with ethyl acetate (*A*); ethyl acetate–carbon tetrachloride 1:1 (*B*), 1:3 (*C*), 1:5 (*D*); ethyl acetate–chloroform 1:1 (*E*), 1:2 (*F*); and ethyl acetate–ethanol 9:1 (*G*), 5:1 (*H*), and 1:1 (*I*). For detection, 1:1 0.1M potassium permanganate–M sulfuric acid was used at 105°. Column chromatography was performed on Kieselgel 40 (62–200 μm). ^{1}H-N.m.r. spectra (90 MHz) were recorded at room temperature with a Varian EM-390 spectrometer, and ^{13}C-n.m.r. spectra with a Varian XL-100 F.t.-spectrometer for solutions in $CDCl_3$ (internal Me_4Si).

*1,6-Dicyano-1,6-dideoxy-3,4-*O*-isopropylidene-*D*-mannitol* (**4**). — A solution of **3**[3] (348 g) and sodium cyanide (120 g) in aqueous 90% ethanol (2 L) was heated at 80° for 30 min, filtered, and concentrated. The residue was extracted with

chloroform (1 L), and the extract was filtered and concentrated to give **4**. Recrystallisation from water gave material (144 g, 60%) having m.p. 108–110°, $[\alpha]_D^{20}$ +24°, R_F 0.4 (solvent *B*). ^{1}H-N.m.r. data: δ 5.8 (bd, OH), 3.9–3.7 (m, H-2,3,4,5), 2.8–2.5 (m, H-1,2), and 1.34 (s, CMe_2).

Anal. Calc. for $C_{11}H_{16}N_2O_4$: C, 54.99; H, 6.71; N, 11.66. Found: C, 54.81; H, 6.88; N, 11.52.

*Disodium 2,7-dideoxy-4,5-*O*-isopropylidene-*D-manno-*octarate* (**5**). — A solution of **4** (108 g) and sodium hydroxide (72 g) in water (250 mL) was boiled for 4 h, cooled, diluted with ethanol (2.5 L), and filtered to give **5** (121 g, 83.5%), m.p. >240°. ^{1}H-N.m.r. data (D_2O): δ 4.2–3.9 (m, H-3,4,5,6), 2.52 (dd, *J* 15 and 3 Hz, H-2,7), 2.25 (dd, *J* 9 Hz, H-2′,7′), and 1.42 (s, CMe_2).

Anal. Calc. for $C_{11}H_{16}Na_2O_8$: C, 41.00; H, 5.01; Na, 14.27. Found: C, 40.75; H, 5.30; Na, 14.03.

*Dimethyl 2,7-dideoxy-4,5-*O*-isopropylidene-*D-manno-*octarate* (**6**). — To a stirred suspension of **5** (92 g) in methyl sulfoxide (500 mL) was added methyl iodide (75 mL) during 1.5 h at 30–35°. Thereafter, the cooled mixture was diluted with water and extracted with chloroform, and the extract was washed with water, dried, and concentrated. The residue contained **6** (R_F 0.4, solvent *E*) and another component (R_F 0.6, solvent *E*) in almost equal concentration. Column chromatography (solvent *E*) gave, after recrystallisation from ether–light petroleum, **6** (23 g, 32%), m.p. 59–61°, $[\alpha]_D^{20}$ +33°. ^{1}H-N.m.r. data: δ 4.4 (bd, OH), 4.3–3.6 (m, H-3,4,5,6), 3.70 (s, OMe), 2.75 (dd, *J* 15 and 3 Hz, H-2,7), 2.50 (dd, *J* 8 Hz, H-2′,7′), and 1.38 (s, CMe_2).

Anal. Calc. for $C_{13}H_{22}O_8$: C, 50.97; H, 7.24. Found: C, 50.83; H, 7.30.

*Dimethyl 2,7-dideoxy-3,6:4,5-di-*O*-isopropylidene-*D-manno-*octarate* (**7**). — A solution of **6** (10 g) in 2,2-dimethoxypropane (20 mL) was boiled for 1 h in the presence of a catalytic amount of toluene-*p*-sulfonic acid. The solvent was then slowly distilled off through a column (30 cm) and 2,2-dimethoxypropane was added to maintain the volume. After 5 h, when ~50 mL of distillate had been collected, the residual solution was kept at 5° overnight and the product (7 g, 62%) was filtered off. The mother liquor was submitted to the same procedure to give more (3 g) product. Recrystallisation from acetone afforded **7** (9.1 g, 80%), m.p. 150–152°, $[\alpha]_D^{20}$ +23°, R_F 0.9 (solvent *F*). N.m.r. data: ^{1}H, δ 4.70 (m, H-3,6), 3.64 (s, OMe), 3.33 (dd, *J* 6 and 2 Hz, H-4,5), 2.70 (dd, *J* 15 and 3 Hz, H-2,7), 2.43 (dd, *J* 9 Hz, H-2′,7′), and 1.37 and 1.30 (s, 2 CMe_2); ^{13}C, δ 171.0, 111.2, 102.8, 83.5, 67.2, 51.0, 37.5, 26.5, and 25.9.

Anal. Calc. for $C_{16}H_{26}O_8$: C, 55.49; H, 7.57. Found: C, 55.32; H, 7.40.

*1,8-Di-*O*-benzoyl-2,7-dideoxy-3,6:4,5-di-*O*-isopropylidene-*D-manno-*octitol* (**9**). — To a stirred solution of **7** (10 g) in dry ether (200 mL) was added lithium aluminum hydride (6 g) gradually below 10°. Thereafter, stirring was continued at 20° for 2 h. The excess of hydride was then decomposed by adding ethyl acetate (20 mL), water (6 mL), 15% aqueous sodium hydroxide (6 mL), and water (18 mL) to the stirred and cooled slurry. The precipitate was collected and washed with ether,

the combined filtrate and washings were concentrated, and benzene was twice evaporated from the residue to remove traces of water. The resulting, colorless syrup (8 g, 95.5%) contained (t.l.c., solvent *H*) pure **8**, R_F 0.7, which was unstable and was used immediately.

To a solution of **8** (8 g) in dry pyridine (45 mL) was added benzoyl chloride (9 mL) at room temperature, and the mixture was processed after 1 h in the usual way to give **9** as a colorless syrup (13 g, 94.5%), $[\alpha]_D^{20}$ +19°, R_F 0.9 (solvent *B*). ^{1}H-N.m.r. data: δ 8.00 (dd, 4 H, aromatic), 7.6–7.3 (m, 6 H, aromatic), 4.40 (m, H-1,8), 3.90 (m, H-4,5), 3.38 (dd, *J* 6 and 2 Hz, H-3,6), 2.4–1.6 (m, H-2,7), 1.40 and 1.30 (s, 2 CMe_2).

Anal. Calc. for $C_{28}H_{34}O_8$: C, 67.45; H, 6.87. Found: C, 67.24; H, 6.90.

*2,7-Dideoxy-3,6:4,5-di-*O*-isopropylidene-1,8-di-*O*-methanesulfonyl-*D-manno-*octitol* (**10**). — To a solution of **8** (8 g) in dry pyridine (30 mL) was gradually added mesyl chloride (6 mL) while keeping the temperature below 20°. Thereafter, the solution was kept at room temperature for 1 h and then poured into water, and the aqueous solution was decanted from the precipitated oil. The oil crystallised on treatment with ethanol to give **10** (10 g, 81%), R_F 0.5 (solvent *B*), which decomposed on storage overnight at room temperature.

Anal. Calc. for $C_{16}H_{30}O_{10}S_2$: S, 14.36. Found: S, 14.15.

*2,7-Dideoxy-*D-manno-*octitol* (**11**). — A solution of **8** (8 g) in methanol (10 mL) and 0.5M sulfuric acid (10 mL) was kept at 60° for 4 h and then stored overnight at 5°. The crystals were collected and washed with methanol to give **11** (4.5 g, 78%), m.p. 172–174°, $[\alpha]_D^{20}$ +26° (water). ^{1}H-N.m.r. data (D_2O): δ 3.9–3.6 (m, H-1,3,4,5,6,8) and 2.2–1.5 (m, H-2,7).

Anal. Calc. for $C_8H_{18}O_6$: C, 45.70; H, 8.36. Found: C, 45.68; H, 8.30.

*1,8-Di-*O*-benzoyl-2,7-dideoxy-*D-manno-*octitol* (**12**). — A solution of **9** (2 g) in 3:1 acetic acid–water (20 mL) was kept at 90° for 2 h. The crystals formed on cooling were collected, and washed with water to give **12** (1.35 g, 80%), m.p. 131–133°, $[\alpha]_D^{20}$ +28° (methyl sulfoxide), R_F 0.7 (solvent *A*). ^{1}H-N.m.r. data (Me_2SO-d_6): δ 8.00 (dd, 4 H, aromatic)), 7.7–7.4 (m, 6 H, aromatic), 4.8 (bd, OH), 4.48 (t, H-1,8), 4.4 (bd, OH), 4.0–3.4 (m, H-3,4,5,6), 2.6–1.6 (m, H-2,7).

Anal. Calc. for $C_{22}H_{26}O_8$: C, 63.15; H, 6.26. Found: C, 63.09; H, 6.30.

*1,8-Di-*O*-benzoyl-2,7-dideoxy-4,5-*O*-isopropylidene-*D-manno-*octitol* (**13**). — Diacetal **9** (2 g) was dissolved in 3:1 acetic acid–water (20 mL) at room temperature. After complete dissolution (5 min), only **13** could be detected by t.l.c. The solution was diluted with water (20 mL) and extracted with chloroform, and the extract was washed with water, aqueous sodium hydrogencarbonate, and water, dried, and concentrated. The residue was recrystallised from ether–light petroleum to yield **13** (1.5 g, 81.5%), m.p. 87–89°, $[\alpha]_D^{20}$ +14°, R_F 0.3 (solvent *C*). N.m.r. data: ^{1}H, δ 8.00 (dd, 4 H, aroamtic), 7.6–7.2 (m, 6 H, aromatic), 4.7–4.3 (m, H-1,8 and OH), 3.76 (s, H-3,4,5,6), 2.5–1.7 (m, H-2,7) and 1.33 (s, CMe_2); ^{13}C, δ 166.2, 132.5, 129.5, 129.0, 128.2, 108.5, 82.5, 69.5, 60.6, 32.8, and 25.2.

Anal. Calc. for $C_{25}H_{30}O_8$: C, 65.49; H, 6.60. Found: C, 65.55; H, 6.54.

1,8-Di-O-benzoyl-2,7-dideoxy-4,5-O-isopropylidene-3,6-di-O-methanesulfonyl-D-manno-*octitol* (**14**). — A solution of **13** (12 g) in pyridine (30 mL) was treated with mesyl chloride (6 mL), as described for **10**, to give **14** as a colorless syrup (15.3 g, 95.5%), $[\alpha]_D^{20}$ +30°, R_F 0.3 (solvent *C*). ^{1}H-n.m.r. data: δ 7.97 (dd, 4 H, aromatic), 7.5–7.3 (m, 6 H, aromatic), 4.96 (m, H-3,6), 4.46 (t, *J* 6 Hz, H-1,8), 4.27 (d, *J* 4 Hz, H-4,5), 3.03 (s, OMs), 2.4–2.2 (m, H-2,7), and 1.37 (s, CMe_2).

Anal. Calc. for $C_{27}H_{34}O_{12}S_2$: S, 10.43. Found: S, 10.28.

3,6-Diazido-1,8-di-O-benzoyl-2,3,6,7-tetradeoxy-4,5-O-isopropylidene-L-ido-*octitol* (**15**). — To a solution of **14** (15 g) in *N,N*-dimethylformamide (250 mL) was added sodium azide (4.5 g), the mixture was stirred at 120° for 1 h and then concentrated, and the residue was partitioned between ether and water. The organic solution was washed with water, dried, and concentrated to give **15** as a yellow syrup (10 g, 80.5%), $[\alpha]_D^{20}$ +6°, R_F 0.9 (solvent *D*). ^{1}H-N.m.r. data: δ 7.97 (dd, 4 H, aromatic), 7.6–7.2 (m, 6 H, aromatic), 4.50 (m, H-1,8), 4.23 (d, *J* 1 Hz, H-4,5), 3.31 (t, *J* 6 Hz, H-3,6), 2.4–2.0 (m, H-2,7), and 1.47 (s, CMe_2).

Anal. Calc. for $C_{25}H_{28}N_6O_6$: N, 16.53. Found: N, 16.40.

3,6-Diazido-1,8-di-O-benzoyl-2,3,6,7-tetradeoxy-L-ido-*octitol* (**16**). — A solution of **15** (10 g) in 3:1 acetic acid–M hydrochloric acid was heated at 90° for 15 min. The cooled solution was diluted with water and extracted with chloroform, and the extract gave, after the usual processing, a crude residue which was submitted to column chromatography (solvent *C*). The fractions containing the component with R_F 0.35 gave, on concentration and treatment of the solid residue with ether, **16** (4.1 g, 44.5%), m.p. 85–87°, $[\alpha]_D^{20}$ −49°. ^{1}H-N.m.r. data: δ 7.95 (dd, 4 H, aromatic), 7.6–7.2 (m, 6 H, aromatic) 4.43 (t, *J* 7 Hz, H-1,8), 3.75 (d, *J* 2 Hz, H-4,5), 3.6 (m, H-3,6), 3.1 (bd, OH), and 2.3–1.9 (m, H-2,7).

Anal. Calc. for $C_{22}H_{24}N_6O_6$: C, 56.40; H, 5.16; N, 17.94. Found: C, 56.28; H, 5.20; N, 17.82.

3,6-Diazido-1,8-di-O-benzoyl-2,3,6,7-tetradeoxy-4,5-di-O-methanesulfonyl-L-ido-*octitol* (**17**). — To a solution of **16** (4.1 g) in dry pyridine (10 mL) was added mesyl chloride (2 mL), and the solution was kept at room temperature for 5 h, to give, after the usual processing, **17** as a syrup (5 g, 91.5%), R_F 0.4 (solvent *C*).

Anal. Calc. for $C_{24}H_{28}N_6O_{10}S_2$: N, 13.46; S, 10.27. Found: N, 13.34; S, 10.30.

1,4:5,8-Dianhydro-3,6-diazido-2,3,6,7-tetradeoxy-L-manno-*octitol* (**19**). — To a stirred solution of **17** (5 g) in methanol (35 mL) was added gradually a solution of sodium hydroxide (3.2 g) in water (9 mL). Stirring was continued for 16 h and the solution was then diluted with water and extracted with chloroform. The extract was washed with water, dried, and concentrated to give **19** as a colorless syrup (1.7 g, 95%), $[\alpha]_D^{20}$ +128°, R_F 0.75 (solvent *C*). ^{1}H-N.m.r. data: δ 4.08 (ddd, *J* 7.2, 4, and 4 Hz, H-3,6), 4.0–3.6 (m, H-1,4,5,8), 2.25 (dddd, *J* 12, 7.2, 7.2, and 7.2 Hz, H-2,7), and 1.95 (dddd, *J* 12, 7.0, 4.5, and 4.5 Hz, H-2′,7′).

Anal. Calc. for $C_8H_{12}N_6O_2$: N, 37.48. Found: N, 37.29.

3,6-Bis(acetamido)-1,4:5,8-dianhydro-2,3,6,7-tetradeoxy-L-manno-*octitol* (**21**). — A solution of **17** (0.5 g) in ethanol (50 mL) was hydrogenated at room

temperature in the presence of 10% Pd/C (1 g) for 2 h. T.l.c. (solvent *I*) then revealed the complete conversion of **17** into diamine **20** (R_F 0.1). The filtered solution was concentrated, the semi-solid residue was dissolved in pyridine (5 mL), and acetic anhydride (0.8 mL) was added. After 30 min, the solution was poured into water and extracted with chloroform to give, after the usual processing and recrystallisation from ethanol, **21** (0.3 g, 52.6%), m.p. 220–225° (dec.), R_F 0.4 (solvent *B*). N.m.r. data: ^{1}H, δ 5.86 (d, NH), 4.45 (m, H-3,6), 3.92 (m, H-1,8), 3.75 (m, H-4,5), 2.35 and 1.75 (m, H-2,7), and 1.97 (s, OAc); ^{13}C, δ 170.7, 85.2, 68.6, 52.9, 34.5, and 24.2. Mass spectrum: *m/z* 256 (0.5%), 197 (67), 138 (61), 128 (100), 86 (85), 57 (43.5), 56 (29), 43 (34), and 28 (20.6).

Anal. Calc. for $C_{12}H_{20}N_2O_4$: C, 56.23; H, 7.87; N, 10.93. Found: C, 56.20; H, 7.66; N, 10.88.

3-O-Acetyl- (**23**) *and 3,6-di-O-acetyl-1,4:5,8-dianhydro-2,7-dideoxy*-D-manno-*octitol* (**24**). — A solution of **10** (10 g) in 3:1 acetic acid–water (100 mL) was kept at 90° for 5 h and then concentrated, and a solution of the residue in chloroform was washed with a small volume of water, dried, and concentrated. The residue was subjected to column chromatography (solvent *B*). The fractions containing the component having R_F 0.7 gave, on concentration, **24** as a syrup (1.3 g, 22.5%). ^{1}H-N.m.r. data: δ 5.23 (ddd, *J* 6, 2, and 2 Hz, H-3,6), 4.1–3.6 (m, H-1,4,5,8), 2.03 (s, OAc), and 2.4–1.8 (m, H-2,7). Mass spectrum: *m/z* 258 (0%), 138 (21), 129 (100), 99 (7), 70 (31.5), and 43 (70).

Anal. Calc. for $C_{12}H_{18}O_6$: C, 55.80; H, 7.03. Found: C, 55.66; H, 7.12.

The fractions containing the component having R_F 0.2 gave, on concentration, **23** as a syrup (2.3 g, 47.5%). ^{1}H-N.m.r. data: δ 5.17 (ddd, *J* 6, 2, and 2 Hz, H-6), 4.30 (ddd, *J* 6, 3, and 3 Hz, H-3), 4.1–3.6 (m, H-1,4,5,8), 3.4 (s, OH), 2.05 (s, OAc), and 2.4–1.7 (m, H-2,7).

Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.50; H, 7.35.

1,4:5,8-Dianhydro-2,7-dideoxy-D-manno-*octitol* (**25**). — A 3:1 mixture of **23** and **24** was dissolved in dry methanol (30 mL), and 1 drop of methanolic M sodium methoxide was added. The solution was neutralised after 3 h with solid carbon dioxide and then concentrated. A solution of the residue in chloroform was treated with charcoal, filtered, and concentrated to give **25** as a colorless syrup (2.15 g, 94%), $[\alpha]_D^{20}$ −64°, R_F 0.5 (solvent *G*). ^{1}H-N.m.r. data: δ 4.4 (bd, OH), 4.25 (m, H-3,6), 3.85 (t, *J* 7 Hz, H-1,8), 3.60 (s, H-4,5), and 2.4–1.7 (m, H-2,7).

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.08; H, 7.97.

1,4:5,8-Dianhydro-2,7-dideoxy-3,6-di-O-methanesulfonyl-D-manno-*octitol* (**26**). — To a solution of **25** (2.1 g) in dry pyridine (10 mL) was added mesyl chloride (2.5 mL). The mixture was poured into ice–water after 2 h, and the precipitate was collected, washed with water, and recrystallised from ethanol to give **26** (2.4 g, 60%), m.p. 110–112°, $[\alpha]_D^{20}$ −58°, R_F 0.15 (solvent *C*). ^{1}H-N.m.r. data: δ 5.17 (m, H-3,6), 4.15 (s, H-4,5), 4.1–3.6 (m, H-1,8), 3.00 (s, OMs), and 2.4–2.0 (m, H-2,7).

Anal. Calc. for $C_{10}H_{18}O_8S_2$: C, 36.35; H, 5.49; S, 19.41. Found: C, 36.32; H, 5.40; S, 19.36.

1,4:5,8-Dianhydro-3,6-diazido-2,3,6,7-tetradeoxy-L-ido-*octitol* (**27**). — To a stirred solution of **26** (2.1 g) in *N,N*-dimethylformamide (65 mL) was added sodium azide (1.1 g), and stirring was continued at 120° for 1 h. Thereafter, the solution was concentrated and the residue was partitioned between ether and water. The organic solution was washed with water, dried, and concentrated to give **27** as a pale-yellow syrup (0.65 g, 45.5%), $[\alpha]_D^{20}$ +293°, R_F 0.5 (solvent *C*). ^{1}H-N.m.r. data: δ 4.3–3.6 (m, H-1,3,4,5,6,8) and 2.6–2.0 (m, H-2,7).

Anal. Calc. for $C_8H_{12}N_6O_2$: C, 42.85; H, 5.39; N, 37.48. Found: C, 42.62; H, 5.40; N, 37.25.

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