Carbohydrate Research, 200 (1990) 287–305
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

O-Alkylation at the anomeric centre for the stereoselective synthesis of Kdo-α-glycosides*

Angelika Esswein, Hansjörg Rembold, and Richard R. Schmidt†
Fakultät für Chemie, Universität Konstanz, Postfach 5560, D-7750 Konstanz (F.R.G.)

(Received June 5th, 1989; accepted for publication, September 29th, 1989)

ABSTRACT

O-Alkylation at the anomeric centre of the dianion of 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-*N*-methyl-α-D-*manno*-octulopyranosonamide (**1**) with several triflates led diastereoselectively to the α-glycosides. In this way, lipopolysaccharide building-blocks containing α-Kdo-(2→6)-GlcN and α-Kdo-(2→6)-β-GlcN-(1→6)-GlcN moieties were obtained and deployed in the synthesis of decyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-*N*-methyl-α-D-*manno*-2-octulopyranosidonamide (**18**), 2,3-di-*O*-tetradecanoyl-D-glycer-1-yl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-*N*-methyl-α-D-*manno*-2-octulopyranosid-onamide (**22**), methyl 2,3,4-tri-*O*-acetyl-6-*O*-(methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-α-D-glucopyranoside (**28**), 1-*O*-acetyl-2-deoxy-6-*O*-(methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-2-tetradecanoylamino-α-D-glucopyranose (**33**), *tert*-butyldimethylsilyl *O*-(methyl 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-(2→6)-*O*-(3,4-di-*O*-benzyl-2-deoxy-2-tetradecanoylamino-β-D-glucopyranosyl)-(1→6)-3,4-di-*O*-benzyl-2-deoxy-2-tetradecanoylamino-α-D-glucopyranoside (**36**).

INTRODUCTION

Lipopolysaccharides (LPS) are important components of the outer membrane of Gram-negative bacteria[1,2]. The lipophilic portion of LPS, lipid A, is responsible for anchoring the lipid in the membrane; it determines the toxic and immunostimulatory properties of LPS. Lipid A consists essentially of a β-(1→6)-linked 2-amino-2-deoxy-D-glucose disaccharide that carries phosphate groups at positions 1 and 4′ as well as long-chain fatty acid moieties on the nitrogen and on some of the other hydroxyl groups. The hydrophilic portion of LPS consists of a complex oligosaccharide chain, in which Kdo (3-deoxy-D-*manno*-2-octulosonic acid) is α-(2→6)-linked to the GlcN disaccharide[1,3].

The application of the Koenigs–Knorr method for α-glycosylation, using Kdo glycosyl halides, has often given unsatisfactory results due to elimination of hydrogen halide and, in part, to the formation of β-glycosides[4]. Good results have been reported using the glycosyl fluoride[5]. *O*-Alkylation at the anomeric centre offers a simple procedure for the synthesis of glycosides[6,7] and we now report the application of this method for the stereoselective formation of α-glycosides of Kdo[8].

* Anomeric *O*-Alkylation, Part 7. For Part 6, see ref. 8.
† Author for correspondence.

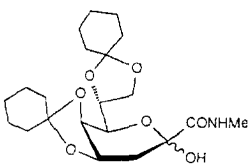
0008-6215/90/$ 03.50

RESULTS AND DISCUSSION

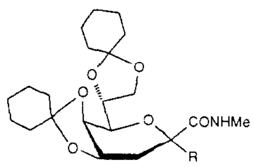
O-Alkylation at the anomeric centre of carbohydrates is based on the selective deprotonation of the anomeric hydroxyl group and nucleophilic attack of the resulting anion[7] on alkylating agents, such as trifluoromethanesulfonates (triflates)[6,7]. Decomposition reactions, particularly of the acyclic form of the sugar anion, must be avoided and it is necessary that the anomeric oxygen anion is sufficiently nucleophilic. Due to the irreversibility of the reaction, stereocontrol must be based on the differences in nucleophilicity of the α- and β-oxygen anions and/or differences in their rates of interconversion. The observation that an equatorial oxygen anion is the more nucleophilic, owing to a kinetic anomeric effect[7,9], led to excellent results in terms of α- and β-stereocontrol[6,7].

On the basis of these results, the methyl 4,5,7,8-tetra-*O*-acetyl ester derivative of Kdo, commonly used in glycoside syntheses, appeared not to be suitable for *O*-alkylation at the anomeric centre. Therefore, the 4,5:7,8-di-*O*-cyclohexylidene derivative **1** (ref. 10) was employed which, according to the ^{1}H-n.m.r data, exists in a boat conformation (a corresponding conformation was observed for a 4,5:7,8-di-*O*-isopropylidene derivative[4]). Thus, HO-2 in the α anomer of **1** is in the quasi-equatorial position required for increased nucleophilicity of the oxygen anion. The nucleophilicity should be increased further by deprotonation of the carboxamide group, thus providing a dianion species $\mathbf{1}^{2-}$ in which, according to stereomodels, the conformation should be stabilized by tetradentate complexation with a metal ion[8]. These considerations were supported by the fact that the addition of 2 equiv. of sodium hydride to **1** in tetrahydrofuran at $-30°$ followed by the addition of 1 equiv. of decyl triflate gave 83% of the α-glycoside **2** and no β isomer was detected. Likewise, 2,3-di-*O*-benzyl-1-*O*-triflyl-D-glycerol gave 80% of the α-glycoside **3**, and methyl 2,3,4-tri-*O*-benzyl-6-*O*-triflyl-α-D-glucopyranoside **6** gave 69% of the α-linked disaccharide derivative **4**. The latter reaction was carried out in dichloromethane at $-10°$ to room temperature and no β isomer was detected.

In order to generate an α-(2→6) linkage to 2-amino-2-deoxy-D-glucose, the triflate **11** was synthesized from D-glucal. 6-*O*-Tritylation of D-glucal gave **6** which was

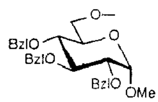


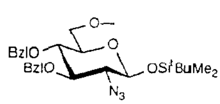
1

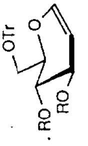


2 R = $CH_3(CH_2)_9O$—

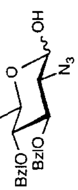
3 R = CHO—
CHOBzl
CH_2OBzl

4 R = 

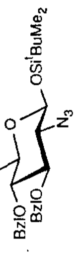
5 R = 



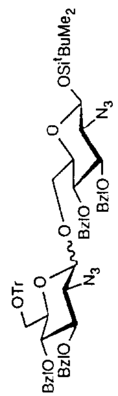
6 R = H
7 R = Bzl



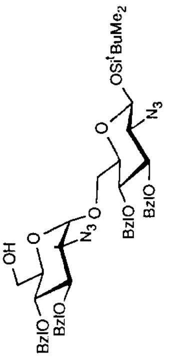
8



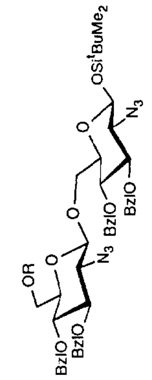
9 R = Tr
10 R = H
11 R = Tf



12



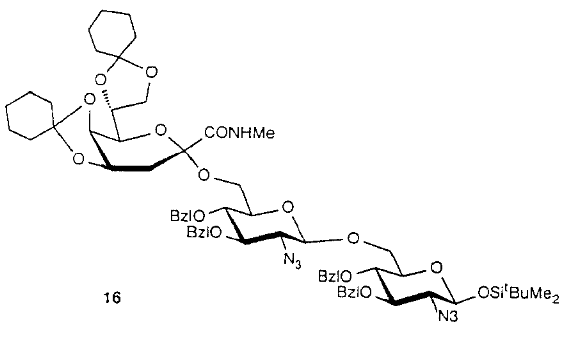
13



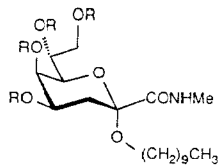
14 R = H
15 R = Tf

O-benzylated to provide **7**. Azidonitration[11] of **7** gave **8** which, with *tert*-butyldimethylsilyl chloride in the presence of pyridine, afforded the *β* derivative **9**. Detritylation of **9** with aqueous trifluoroacetic acid gave **10** which, with triflic anhydride in pyridine, furnished crystalline **11**. Reaction of **11** with the Kdo derivative **1** in tetrahydrofuran at −30° in the presence of 2 equiv. of sodium hydride gave 60% of the desired *α*-linked disaccharide derivative **5**.

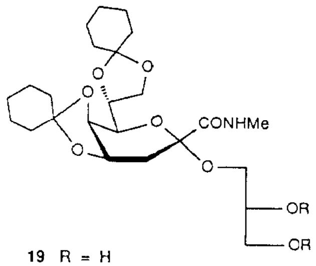
This result encouraged the synthesis of the *α*-Kdo-(2→6)-*β*-GlcN-(1→6)-GlcN



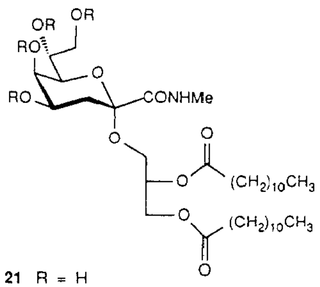
16



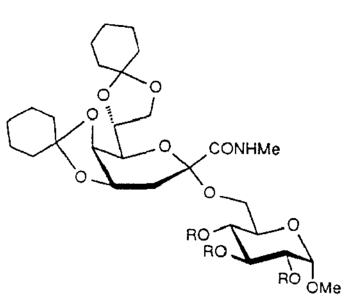
17 R = H
18 R = Ac



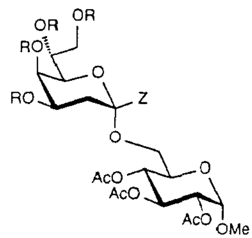
19 R = H
20 R = Myristoyl



21 R = H
22 R = Ac



23 R = H
24 R = Ac



25 R = H, Z = CONHMe
26 R = Ac, Z = CONHMe
27 R = Ac, Z = COOH
28 R = Ac, Z = COOMe

building-block **16** required for connection of lipid A to the inner core structure. The required alkylating agent **15** was obtained readily as follows. Condensation of **8** and **11** gave **12** as a 2:1 αβ-mixture which was detritylated with aqueous trifluoroacetic acid to give **13** (α anomer, 28%) and **14** (β anomer, 55%). Treatment of **14** with triflic anhydride in pyridine then gave **15** in quantitative yield. Reaction of **15** with **1** under the conditions described above gave 48% of the desired α-linked trisaccharide derivative **16**; although no β isomer was obtained, a minor proportion of another isomer was isolated which, presumably, was derived from opening of the pyranose ring.

The syntheses were concluded as follows. Treatment of **2** with aqueous 80% trifluoroacetic acid removed the cyclohexylidene groups to give **17**, which was converted into the tetra-acetate **18**. Hydrogenolysis of **3** removed the benzyl groups to give **19** which, with myristoyl chloride in pyridine, afforded **20**. Removal of the cyclohexylidene groups, as described above, gave **21** which was converted into the tetra-acetate **22**.

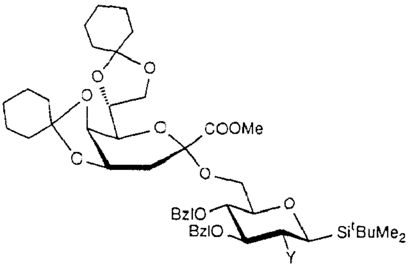
Hydrogenolysis of **4** furnished **23** and thence the triacetate **24**. Decyclohexylidenation of **23** gave **25**, *O*-acetylation of which afforded the hepta-acetate **26**. The transformation of the amide **26** into the acid **27** was effected readily by treatment[12] with sodium nitrite in acetic anhydride–acetic acid. The expected *N*-nitroso derivative of **26** was sufficiently labile for the immediate formation of the acid **27** (presumably due to reaction with acetic acid and subsequent hydrolysis) together with a small proportion of the methyl ester **28**; the yield of **28** was increased to 81% after the addition of diazomethane to the mixture of products.

The *N*-methylamides **5** and **16** were transformed into the esters **29** and **34**, respectively, by the procedure described above. In these reactions, some *N*-nitroso compound was obtained, which, on heating, was converted into the ester. Reduction of the azide groups in **29** and **34** with hydrogen sulfide in pyridine–water gave the amines **30** and **35**, respectively, which were acylated immediately with myristoyl chloride in pyridine to furnish **31** and **36**, respectively. Decyclohexylidenation of the disaccharide derivative **31** with aqueous trifluoroacetic acid also removed the Si^tBuMe_2 group, and *O*-acetylation of the product furnished **32**. Hydrogenolysis of **32** gave the α-linked disaccharide derivative **33**.

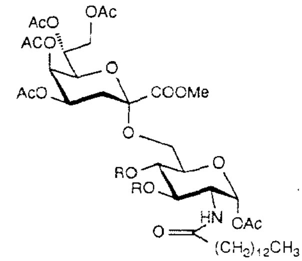
The ^{1}H-n.m.r. data of the Kdo portion of **28** and **33** accorded with the data for other *O*-acetylated Kdo α-glycosides[4] and satisfied the rule stated by Unger and co-workers[13,14], thus confirming the structural assignments.

EXPERIMENTAL

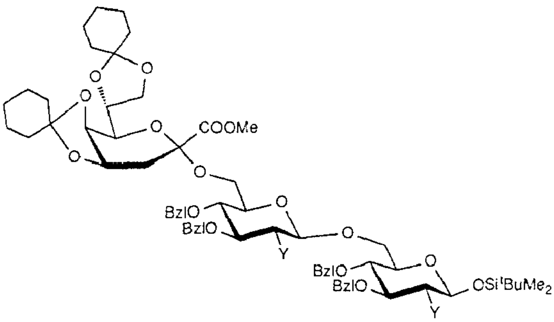
General methods. — Melting points are uncorrected. ^{1}H-N.m.r. spectra (internal Me_4Si) were recorded with Bruker WM 250 Cryospec and Jeol JNM-GX 400 instruments. R_F values refer to t.l.c. on silica gel (Merck). Column chromatography was carried out on silica gel (Merck, 70–230 mesh ASTM, 230–400 mesh ASTM for flash chromatography under normal pressure, and Lichroprep Si 60, 40–60 μm, for medium pressure operation). Light petroleum refers to the fraction b.p. 35–60°. Optical rotations were determined with a Perkin–Elmer 241 MC polarimeter.



29 Y = N_3
30 Y = NH_2
31 Y = $N(H)-C(=O)-(CH_2)_{12}-CH_3$



32 R = Bzl
33 R = H



34 Y = N_3
35 Y = NH_2
36 Y = $N(H)-C(=O)-(CH_2)_{12}-CH_2$

Decyl trifluoromethanesulfonate[15]. — To a solution of 1-decanol (1 g, 6.32 mmol) and triethylamine (0.91 g, 9.03 mmol) in dry toluene (70 mL) was added triflic anhydride (1.96 g, 6.95 mmol). The mixture was stirred at room temperature for 15 min, and the upper phase was separated and then concentrated under reduced pressure. Flash chromatography (9:1 light petroleum–ethyl acetate) of the residue yielded the title compound (1.42 g, 77%), isolated as a colourless oil, R_F 0.67 (9:1 light petroleum–ethyl acetate). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 4.56–4.51 (t, 2 H, OCH_2), 1.88–1.77 (q, 2 H, OCH_2CH_2), 1.27 (bs, 14 H, 7 CH_2), 0.91–0.86 (t, 3 H, CH_3).

*2,3-Di-O-benzyl-1-O-trifluoromethanesulfonyl-*D*-glycerol.* — To a solution of 1,2-di-*O*-benzyl-L-glycerol[16] (780 mg, 2.86 mmol) in dry dichloromethane (20 mL) was added pyridine (340 mg, 4.3 mmol) at −20° followed dropwise by a solution of triflic anhydride (890 mg, 3.15 mmol) in dichloromethane (10 mL). The mixture was stirred for 20 min at −20°, then concentrated. Short-column chromatography (7:3 light petroleum–ethyl acetate) of the residue yielded the title compound (890 mg, 77%), isolated as a colourless oil, R_F 0.76 (7:3 light petroleum–ethyl acetate), that was used immediately.

tert-*Butyldimethylsilyl 2-azido-3,4-di-O-benzyl-2-deoxy-6-O-trifluoromethanesulfonyl-β-D-glucopyranoside* (**11**). — To a solution of **10** (1.81 g, 3.62 mmol) in dry dichloromethane (30 mL) under argon at −20° was added dry pyridine (0.38 mL, 4.7 mmol) followed dropwise by triflic anhydride (0.66 mL, 3.99 mmol). Stirring was continued for 1 h, the solvents were evaporated, and column chromatography (7:1 light petroleum–ethyl acetate) of the residue yielded **11** (2.20 g, 96%), m.p. 49°, $[\alpha]^{22}_{578}$ + 17° (*c* 1, chloroform); R_F 0.66. ^{1}H-N.m.r data (250 MHz, $CDCl_3$): δ 7.38–7.22 (m, 10 H, 2 Ph), 4.94 (d, 1 H, J_{gem} 11.0 Hz, $PhCH_2$), 4.88 (d, 1 H, J_{gem} 11.3 Hz, $PhCH_2$), 4.78 (d, 1 H, J_{gem} 11.0 Hz, $PhCH_2$), 4.56 (d, 1 H, J_{gem} 11.3 Hz, $PhCH_2$), 4.53 (d, 1 H, $J_{1,2}$ 7.0 Hz, H-1), 4.49 (dd, 1 H, $J_{6a,6b}$ 10.7, $J_{5,6b}$ 1.5 Hz, H-6b), 4.29 (dd, 1 H, $J_{5,6a}$ 6.1 Hz, H-6a), 3.57–3.31 (m, 4 H, H-2,3,4,5), 0.92 (s, 9 H, ^{t}Bu), 0.15, 0.14 (2 s, 6 H, 2 $SiMe_2$).

Anal. Calc. for $C_{27}H_{36}F_3N_3O_7SSi$ (631.7): C, 51.33; H, 5.74; N, 6.73. Found: C, 51.59; H, 5.74; N, 6.73.

tert-*Butyldimethylsilyl 2-azido-6-O-(2-azido-3,4-di-O-benzyl-2-deoxy-6-O-trifluoromethanesulfonyl-β-D-glucopyranosyl)-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranoside* (**15**). — To a solution of **14** (570 mg, 0.66 mmol) in dry dichloromethane (40 mL) and dry pyridine (0.08 mL, 0.1 mmol) under argon at −20° was added triflic anhydride (0.13 mL, 0.78 mmol) dropwise. The mixture was stirred for 1 h, then concentrated. Column chromatography (5:1 light petroleum–ethyl acetate) of the residue yielded **15** (650 mg, 98%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +0.8° (*c* 1, chloroform); R_F 0.44. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.51–7.20 (m, 20 H, 4 Ph), 4.93–4.70 (m, 6 H, 3 $PhCH_2$), 4.62–4.54 (m, 3 H, $PhCH_2$, H-6′b), 4.52 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 4.34 (dd, 1 H, $J_{6'a,6'b}$ 10.7 $J_{5',6'a}$ 4.9 Hz, H-6′a), 4.25 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.01 (dd, 1 H, $J_{5,6b}$ 9.7, $J_{6a,6b}$ 11.3 Hz, H-6b), 3.67 (dd, 1 H, $J_{5,6a}$ 5.6 Hz, H-6a), 3.52–3.29 (m, 8 H, H-2,2′,3,3′,4,4′,5,5′), 0.94 (s, 9 H, ^{t}Bu), 0.17 (s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{47}H_{57}F_3N_6O_{11}SSi$ (999.1): C, 56.56; H, 5.75; N, 8.41. Found: C, 56.68; H, 5.80; N, 8.50.

*Decyl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-N-methyl-α-D-*manno*-2-octulopyranosidonamide* (**2**). — To a solution of **1** (470 mg, 1.14 mmol) in dry tetrahydrofuran (50 mL) under nitrogen at −30° was added sodium hydride (40 mg, 1.6 mmol) followed, after 20 min, by a solution of 1-decyl triflate (580 mg, 2 mmol) in tetrahydrofuran (10 mL). The mixture was stirred for 12 h at −30°, then filtered through Celite, and concentrated under reduced pressure. Flash chromatography (7:3 light petroleum–ethyl acetate) of the residue yielded **2** (530 mg, 84%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +28° (*c* 1, chloroform); R_F 0.29. ^{1}H-N.m.r. data (400 MHz $CDCl_3$): δ 6.68 (bq, 1 H, *J* 4.9 Hz, N-H), 4.43 (ddd, 1 H, $J_{4,5}$ 8.0, $J_{3e,4}$ 4.3; $J_{3a,4}$ 3.7 Hz, H-4), 4.33 (ddd, 1 H, $J_{6,7}$ 6.2, $J_{7,8ab}$ 5.2 Hz, H-7), 4.19 (dd, 1 H, $J_{5,6}$ 1.8, $J_{4,5}$ 8.0 Hz, H-5), 4.08 (dd, 1 H, J_{gem} 8.6, $J_{7,8a}$ 6.4 Hz, H-8a), 3.96 (dd, 1 H, J_{gem} 8.6, $J_{7,8b}$ 5.2 Hz, H-8b, 3.71 (dd, 1 H, $J_{6,7}$ 6.2, $J_{5,6}$ 1.8, H-6), 3.40 (dd, 1 H, J_{gem} 15.7, $J_{1'a,2'}$ 7.3 Hz, H-1′a), 3.20 (dd, 1 H, J_{gem} 15.2, $J_{1'b,2'}$ 6.6 Hz, H-1′b), 2.80

(d, 3 H, J 5.9 Hz, NMe), 2.55 (dd, 1 H, $J_{3a,3e}$ 15.4, $J_{3e,4}$ 4.3 Hz, H-3e), 1.86 (dd, 1 H, $J_{3a,3e}$ 15.4, $J_{3a,4}$ 3.7 Hz, H-3a), 1.70–1.12 (m, 36 H, H-2'/9', 2 C_6H_{10}), 0.89 (t, 3 H, J 6.8 Hz, 3 H-10').

Anal. Calc. for $C_{31}H_{53}NO_7$ (551.76): C, 67.48; H, 9.68; N, 2.53; Found: C, 67.38; H, 9.66; N, 2.50.

*2,3-Di-O-benzyl-*D*-glycer-1-yl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-*N*-methyl-α-*D-manno-*2-octulopyranosidonamide,* (**3**). — To a solution of **1** (300 mg, 0.73 mmol) in dry tetrahydrofuran (50 mL) at −30° under nitrogen was added sodium hydride (25 mg, 1 mmol) followed, after 20 min, by a solution of 2,3-di-*O*-benzyl-1-*O*-triflyl-D-glycerol (440 mg, 1 mmol) in tetrahydrofuran (10 mL). Stirring was continued for 18 h, and the mixture was filtered through Celite and concentrated. Flash chromatography (1:1 light petroleum–ethyl acetate) of the residue yielded **3** (380 mg, 78%), isolated as a colourless oil, $[\alpha]_{578}$ +31° (c 1, chloroform); R_F 0.38. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.23–7.25 (m, 10 H, 2 Ph), 6.71 (bq, 1 H, J 4.9 Hz, NH), 4.66 (bs, 2 H, 2 PhCH_2), 4.58 (d, 1 H, J_{gem} 12.3 Hz, PhCH_2), 4.53 (d, 1 H, J_{gem} 12.3 Hz, PhCH_2), 4.43 (ddd, 1 H, $J_{3a,4}$ 3.7, $J_{3e,4}$ 4.4, $J_{4,5}$ 7.3 Hz, H-4), 4.32 (dd, 1 H, $J_{7,8a} = J_{7,8b} = 6.1$, $J_{6,7} < 1$ Hz, H-7), 4.17 (dd, 1 H, $J_{4,5}$ 7.3, $J_{6,5}$ 1.8 Hz, H-5), 4.08–3.99 (m, 2 H, H-8a,8b), 3.82–3.72 (m, 1 H, H-2'); 3.71 (dd, 1 H, $J_{6,5}$ 1.8, $J_{7,6} < 1$ Hz, H-6), 3.63–3.59 (m, 3 H, H-1',3'), 3.40 (dd, 1 H, J_{gem} 9.5, $J_{1',2'}$ 4.6 Hz, H-1'), 2.80 (d, 3 H, J 4.9 Hz, NMe), 2.57 (dd, 1 H, $J_{3a,3e}$ 15.3, $J_{3e,4}$ 4.4 Hz, H-3e), 1.89 (dd, 1 H, $J_{3a,3e}$ 15.3, $J_{3a,4}$ 3.7 Hz, H-3a), 1.71–1.31 (m, 20 H, 2 C_6H_{10}).

Anal. Calc. for $C_{38}H_{51}NO_9$ (665.7): C, 68.56; H, 7.71; N, 2.10. Found: C, 68.18; H, 7.74; N, 2.23.

*Methyl 2,3,4-tri-O-benzyl-6-O-(4,5:7,8-di-O-cyclohexylidene-3-deoxy-*N*-methyl-α-*D-manno-2-octulopyranosylonamide)*-α-*D*-glucopyranoside* (**4**). — To a solution of **1** (1.74 g, 4 mmol) in dry dichloromethane (100 mL) at −10° under nitrogen was added sodium hydride (200 mg, 8.3 mmol). After 20 min, a solution of methyl 2,3,4-tri-*O*-benzyl-6-*O*-triflyl-α-D-glucopyranoside[6] (2.45 g, 4.5 mmol) in dichloromethane (20 mL) was added dropwise. The mixture was stirred for 10 h at −10° and 48 h at room temperature, then filtered through Celite, and concentrated. The residue was extracted with dichloromethane several times, and the combined extracts were concentrated under reduced pressure. Column chromatography (1:1 light petroleum–ethyl acetate) of the residue yielded **4** (2.36 g, 69%), isolated as a colourless oil, $[\alpha]_{578}^{22}$ −4.1° (c 4, chloroform), R_F 0.41. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.39–7.23 (m, 15 H, 3 Ph), 6.64 (d, 1 H, J 4.9 Hz, NH), 4.94 (d, 1 H, J_{gem} 10.7 Hz, PhCH_2), 4.82 (d, 1 H, J_{gem} 11.2 Hz, PhCH_2), 4.77 (d, 1 H, J_{gem} 12.2 Hz, PhCH_2), 4.74 (d, 1 H, J_{gem} 10.7 Hz, PhCH_2), 4.65 (d, 1 H, J_{gem} 12.2 Hz, PhCH_2), 4.63 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.57 (d, 1 H, J_{gem} 11.2 Hz, PhCH_2), 4.42 (ddd, 1 H, $J_{3'e,4'}$ 3.9, $J_{3'a,4'}$ 4.6, $J_{4',5'}$ 7.3 Hz, H-4'), 4.30 (ddd, 1 H, $J_{6',7'}$ 6.6, $J_{7',8'a}$ 6.3, $J_{7',8'b}$ 4.9 Hz, H-7'), 4.17 (dd, 1 H, $J_{5',6'}$ 1.9 Hz, H-5'), 4.05 (dd, 1 H, $J_{8'a,8'b}$ 8.8 Hz, H-8'b), 4.00 (dd, 1 H, H-8'a), 3.97 (dd, 1 H, $J_{4,5}$ 9.0, $J_{3,4}$ 9.3 Hz, H-4), 3.83 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.75 (dd, 1 H, H-6'), 3.59 (dd, 1 H, $J_{6a,6b}$ 10.0, $J_{5,6b}$ 1.9 Hz, H-6b), 3.50 (dd, 1 H, H-2), 3.44 (dd, 1 H, $J_{5,6a}$ 10.0 Hz, H-6a), 3.37 (s, 3 H, OMe), 3.26 (ddd, 1 H, H-5), 2.76 (d, 3 H, NMe), 2.54 (dd, 1 H, $J_{3'a,3'e}$ 15.4 Hz, H-3'a), 1.90 (dd, 1 H, H-3'e), 1.70–1.25 (m, 20 H, 2 C_6H_{10}).

Anal. Calc. for $C_{49}H_{63}NO_{12}$ (858.0): C, 68.59; H, 7.40; N, 1.63. Found: C, 68.46; H, 7.46; N, 1.59).

tert-*Butyldimethylsilyl 2-azido-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-*N*-methyl-α-*D-manno-*2-octulopyranosylonamide)-β-*D-*glucopyranoside* (**5**). — To a solution of **1** (870 mg, 2 mmol) in dry tetrahydrofuran (40 mL) under nitrogen at −30° was added sodium hydride (101 mg, 4.2 mmol) followed, after 20 min, by a solution of **11** (1.38 g, 2.2 mmol) in tetrahydrofuran (30 mL). The mixture was stirred at −30° for 3 h then at 0° for 15 h, filtered through Celite, and concentrated to dryness. Column chromatography (2:1 light petroleum–ethyl acetate) of the residue yielded **5** (1.08 g, 61%), m.p. 158–159°, $[\alpha]_{578}^{22}$ +35° (*c* 1, chloroform); R_F 0.6. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.34–7.22 (m, 10 H, 2 Ph), 6.64 (q, 1 H, *J* 5.1 Hz, NH), 4.86 (d, 1 H, J_{gem} 11.0 Hz, PhCH_2), 4.76 (d, 1 H, J_{gem} 11.2 Hz, PhCH_2), 4.73 (d, 1 H, J_{gem} 11.0 Hz, PhCH_2), 4.51 (d, 1 H, J_{gem} 11.2 Hz, PhCH_2), 4.49 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.43 (ddd, 1 H, H-4′), 4.31 (ddd, 1 H, $J_{6',7'}$ 6.3 Hz, H-7′), 4.16 (dd, 1 H, $J_{5',6'}$ 1.9, $J_{4',5'}$ 7.1 Hz, H-5′), 4.07 (dd, 1 H, $J_{8'a,8'b}$ 8.6, $J_{7',8'b}$ 6.4 Hz, H-8′b), 3.94 (dd, 1 H, $J_{7',8'a}$ 5.1 Hz, H-8′a), 3.74 (dd, 1 H, H-6′), 3.58–3.35 (m, 4 H, H-3,4,6a,6,b), 3.29 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 3.21 (dd, 1 H, $J_{4,5}$ 8.5, $J_{5,6a}$ 9.8, $J_{5,6b}$ 9.8 Hz, H-5), 2.75 (d, 3 H, NMe), 2.46 (dd, 1 H, $J_{3'a,3'e}$ 15.1, $J_{3'a,4'}$ 5.1 Hz, H-3′), 1.91 (dd, 1 H, $J_{3'e,4'}$ 3.9 Hz, H-3′*e*), 1.61–1.34 (m, 20 H, 2 C_6H_{10}), 0.93 (s, 9 H, ^{t}Bu), 0.16 (s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{47}H_{68}N_4O_{11}Si$ (893.16): C, 63.20; H, 7.67; N, 6.27. Found: C, 62.95; H, 7.52; N, 6.28.

tert-*Butyldimethylsilyl* O-*(4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-*N*-methyl-α-*D-manno-*2-octulopyranosylonamide)-(2→6)-*O*-(2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl-(1→6)-2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**16**). — To a solution of **1** (495 mg, 1.14 mmol) in dry tetrahedrofuran (80 mL) under nitrogen at −30° was added sodium hydride (70 mg, 2.9 mmol) followed, after 20 min, by a solution of **15** (650 mg, 0.65 mmol) in dry tetrahydrofuran (20 mL). The mixture was stirred for 3 h at −30° and for 72 h at −10°, then filtered through Celite, and concentrated *in vacuo*. Column chromatography (2:1 light petroleum–ethyl acetate) of the residue yielded **16** (390 mg, 48%), m.p. 61–62°, $[\alpha]_{578}^{22}$ +8.4° (*c* 1, chloroform); R_F 0.48. ^{1}H-H.m.r. data (400 MHz, $CDCl_3$): δ 7.36–7.26 (m, 20 H, 4 Ph), 6.62 (q, 1 H, *J* 4.9 Hz, NH), 4.87–4.55 (m, 8 H, 4 PhCH_2), 4.54 (d, 1 h, $J_{1',2'}$ 7.3 Hz, H-1′), 4.30–4.27 (m, 2 H, H-4″,7″), 4.26 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.07–4.03 (m, 2 H), 4.02 (dd, 1 H, $J_{5'',6''}$ 2.0 Hz, H-5″), 3.94 (dd, 1 H, $J_{8''a,8''b}$ 8.55, $J_{7'',8'a}$ 5.4 Hz, H-8″a), 3.75 (dd, 1 H, $J_{6'',7''}$ 5.6 Hz, H-6″); 3.68–3.23 (m, 11 H), 2.71 (d, 3 H, NMe), 2.46 (dd, 1 H, $J_{3''a,3''e}$ 15.4, $J_{3''a,4''}$ 4.9 Hz, H-3″*a*), 1.82 (dd, 1 H, $J_{3''e,4''}$ 3.7 Hz, H-3″*e*), 1.58–1.26 (m, 20 H, 2 C_6H_{10}), 0.94 (s, 9 H, ^{t}Bu), 0.18 (s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{67}H_{89}N_7O_{15}Si$ (1260.6): C, 63.84; H, 7.12; N, 7.78. Found: C, 63.66; H, 7.03; N, 7.64.

*1,5-Anhydro-2-deoxy-6-*O*-trityl-*D-arabino-*hex-1-enitol* (**6**). — To a solution of commercial 1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (19.4 g, 0.132 mol) in dry dichloromethane–pyridine (1:1, 300 mL) was added trityl chloride (48 g, 0.172 mol). After 16 h, the mixture was concentrated under reduced pressure, and a solution of the residue in chloroform was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated to dryness. Column chromatography (1:2 light petroleum–ethyl acetate) of the residue yielded amorphous **6** (37.2 g, 73%), $[\alpha]_{578}^{22}$ +31° (*c* 1, chloroform); R_F 0.57. ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 7.48–7.22 (m, 15 H, 3 Ph), 6.40 (d, 1 H, $J_{1,2}$ 5.8 Hz, H-1), 4.75 (dd, 1 H, H-2), 4.24 (bs, 1 H, H-3), 3.92–3.81 (m, 2 H, H-4,5), 3.56 (dd, 1 H, $J_{5,6b}$ 3.1, $J_{6a,6b}$ 10.4 Hz, H-6b), 3.34 (dd, 1 H, $J_{5,6a}$ 3.4 Hz, H-6a), 2.32 (bs, 1 H, OH), 2.16 (bs, 1 H, OH).

Anal. Calc. for $C_{25}H_{24}O_4 \cdot H_2O$ (406.5): C, 73.87; H, 6.45. Found: C, 74.03; H, 6.67.

*1,5-Anhydro-3,4-di-O-benzyl-2-deoxy-6-O-trityl-*D-arabino-*hex-1-enitol* (**7**). — To a solution of **6** (31.9 g, 82.09 mmol) in dry *N,N*-dimethylformamide (400 mL) at −10° was added sodium hydride (4.34 g, 180.6 mmol) followed, after 15 min, by benzyl bromide (19.3 mL, 162.54 mmol). The mixture was stirred at room temperature for 24 h, methanol (20 mL) was added, the mixture was poured onto ice and extracted with chloroform several times, and the combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography of the residue yielded **7** (36.4 g, 78%), m.p. 116°, $[\alpha]_{578}^{22}$ +9.6° (*c* 0.5, chloroform). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 7.49–7.01 (m, 25 H, 3 Ph), 6.49 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 4.86 (dd, 1 H, $J_{2,3}$ 2.4 Hz, H-2), 4.73 (d, 1 H, J_{gem} 11.0 Hz, PhCH_2), 4.62 (d, 1 H, J_{gem} 11.6 Hz, PhCH_2), 4.53 (d, 1 H, J_{gem} 11.6 Hz, PhCH_2),4.49 (d, 1 H, J_{gem} 11.0 Hz, PhCH_2), 4.17 (bs, 1 H, H-3), 4.00–3.97 (m, 2 H, H-4,5), 3.52 (dd, 1 H, $J_{5,6b}$ 1.8, $J_{6a,6b}$ 10.4 Hz, H-6b), 3.39 (dd, 1 H, $J_{5,6a}$ 3.7 Hz, H-6a).

Anal. Calc. for $C_{39}H_{36}O_4$ (568.7): C, 82.37; H, 6.38. Found: C, 82.20; H, 6.49.

*2-Azido-3,4-di-O-benzyl-2-deoxy-6-O-trityl-α,β-*D-*glucopyranose* (**8**). — To a solution of **7** (3 g, 5.28 mmol) in dry acetonitrile (130 mL) at −30° under argon was added a mixture of dry powdered ceric ammonium nitrate (11.16 g, 21.12 mmol) and sodium azide (0.55 g, 8.36 mmol). The suspension was stirred vigorously for 48 h at −20°, then filtered, and diluted with ether–water (2:1, 150 mL). The organic layer was separated, neutralized, dried ($MgSO_4$), and concentrated to dryness. The residue was eluted from a short column of silica gel with 5:1 light petroleum–ethyl acetate. The eluate was concentrated and to a solution of the residue in 1,4-dioxane (30 mL) was added a solution of $NaNO_2$ (1.2 g) in water (1.5 mL). The mixture was heated to 80° for 12 h, then poured on to ice, and extracted several times with ether. The combined extracts were washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. Medium pressure l.c. (5:1 light petroleum–ethyl acetate) of the residue yielded amorphous **8** (1.85 g, 56%), $[\alpha]_{578}^{22}$ −8° (*c* 0.7, chloroform); R_F 0.36. ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 7.48–6.55 (m, 25 H, 5 Ph), 5.43 (dd, 0.5 H, $J_{1,2}$ 3.0 Hz, H-1*α*), 4.88–4.77 (m, 1.5 H, 1.5 PhCH_2), 4.67 (dd, 1 H, $J_{5,6b}$ 2.1, $J_{6a,6b}$ 10.4 Hz, H-6b), 4.60 (dd, 0.5 H, $J_{1,2}$ 7.0 Hz, H-1*β*), 4.34 (d, 1 H, PhCH_2) 4.03–3.77 (m, 2.5 H), 3.59–3.19 (m, 4.5 H), 2.79 (bs, 0.5 H, OH).

Anal. Calc. for $C_{39}H_{37}N_3O_5$ (627.7): C, 74.62; H, 5.94; N, 6.69. Found: C, 74.46; H, 5.92; N, 6.41.

tert-*Butyldimethylsilyl 2-azido-3,4-di-O-benzyl-2-deoxy-6-O-trityl-β-*D-*glucopyranoside* (**9**). — To a solution of **8** (8.45 g, 13.47 mmol) in dry dichloromethane (150 mL) at 0° were added imidazole (1.84 g, 26.95 mmol) and *tert*-butylchlorodimethylsilane

(2.54 g, 16.84 mmol). The mixture was stirred for 24 h at room temperature, then diluted with chloroform, poured into ice–water, and extracted several times with chloroform. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography (9:1 light petroleum–ethyl acetate) of the residue yielded **9** (7.62 g, 76%), isolated as a colourless oil, $[\alpha]_{578}^{22}$ −14° (*c* 1, chloroform); R_F 0.64. ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 7.52–6.82 (m, 25 H, 5 Ph), 4.85 (d, 1 H, J_{gem} 10.7 Hz, PhCH_2), 4.74 (d, 1 H, J_{gem} 10.7 Hz, PhCH_2), 4.63 (d, 1 H, J_{gem} 10.4 Hz, PhCH_2), 4.54 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.26 (d, 1 H, J_{gem} 10.4 Hz, PhCH_2), 3.68–3.34 (m, 5 H, H-2,3,4,6a,6b), 3.23 (ddd, 1 H, $J_{5,6a}$ 5.2, $J_{5,6b}$ 4.3, $J_{4,5}$ 9.5 Hz, H-5), 0.99 (s, 9 H, ^{t}Bu), 0.26, 0.23 (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{45}H_{51}N_3O_5Si$ (742.0): C, 72.84; H, 6.93; N, 5.66. Found: C, 73.03; H, 6.97; N, 5.83.

tert-*Butyldimethylsilyl 2-azido-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**10**). — To a solution of **9** (6.2 g, 8.36 mmol) in dry dichloromethane (150 mL) was added aqueous 10% trifluoroacetic acid (60 mL). The mixture was stirred for 20 h, then poured into saturated aqueous $NaHCO_3$, and extracted several times with chloroform. The combined extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Column chromatography (5:1 light petroleum–ethyl acetate) of the residue yielded **10** (3.05 g, 73%), isolated as a colourless oil. The physical data were in good agreement with those reported[17].

tert-*Butyldimethylsilyl 2-azido-6-*O*-(2-azido-3,4-di-*O*-benzyl-2-deoxy-6-*O*-trityl-α,β-*D*-glucopyranosyl)-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**12β**). — To a solution of **8** (1.62 g, 2.59 mmol) in dry tetrahydrofuran (150 mL) under nitrogen at −30° was added sodium hydride (72 mg, 3 mmol) followed, after 20 min, by a solution of **11** (1.8 g, 2.85 mmol) in dry tetrahydrofuran (30 mL). The mixture was stirred for 3 h at −30°, for 20 h at −10°, and for 20 h at ambient temperature, then filtered through Celite, and concentrated. Column chromatography (97.5:2.5 toluene–ethyl acetate) of the residue yielded **12β** (2.42 g, 84%), isolated as a colourless oil, $[\alpha]_{578}^{22}$ +6.1° (*c* 1.2, chloroform); R_F 0.59 (5:1 light petroleum–ethyl acetate). ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.51–6.85 (m, 35 H, 7 Ph), 5.04 (d, 0.34 H, $J_{1',2'}$ 3.4 Hz, H-1′α), 4.92–4.57 (m, 6.7 H), 4.55 (d, 0.3 H, $J_{1,2}$ 7.6 Hz, H-1α), 4.51 (d, 0.7 H, $J_{1,2}$ 7.3 Hz, H-1β), 4.36–4.18 (m, 2 H), 3.96–3.13 (m, 12 H), 0.92, 0.86 (2 s, 9 H, ^{t}Bu), 0.16, 0.14, 0.10 (3 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{65}H_{72}N_6O_9Si$ (1109.41): C, 70.37; H, 6.54; N, 7.66. Found: C, 70.58; H, 6.60; N, 7.26.

tert-*Butyldimethylsilyl 2-azido-6-*O*-(2-azido-3,4-di-*O*-benzyl-2-deoxy-α- and -β-*D*-glucopyranosyl)-3,4-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**13** *and* **14**). — To a solution of **12** (800 mg, 0.72 mmol) in dichloromethane (30 mL) was added aqueous 10% trifluoroacetic acid (15 mL). The mixture was stirred overnight, then neutralized with saturated aqueous $NaHCO_3$, and extracted with dichloromethane. The extract was dried ($MgSO_4$) and concentrated. Medium pressure l.c. (2:1 light petroleum–ethyl acetate) of the residue yielded **14β** (344 mg, 55%), m.p. 85–86°, $[\alpha]_{578}^{22}$ −25° (*c* 1, chloroform). ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.38–7.25 (m, 20 H, 4 Ph), 4.90–4.61 (m, 8 H, 4 PhCH_2), 4.51 (d, 1 H, $J_{1',2'}$ 7.3 Hz, H-1′), 4.27 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 3.96 (dd, 1 H, $J_{5,6b}$ 1.5, $J_{6a,6b}$ 11.2 Hz, H-6b), 3.82 (dd, 1 H, $J_{5',6'b}$ 2.5, $J_{6'a,6'b}$ 12.0 Hz, H-6'b), 3.72 (dd, 1 H, $J_{5,6a}$ 5.13 Hz, H-6a), 3.67 (dd, 1 H, $J_{5',6'a}$ 4.6 Hz, H-6'a), 3.57–3.25 (m, 8 H), 1.6 (bs, 1 H, OH), 0.94 (s, 9 H, ^{t}Bu), 0.17 (s, 6 H, $SiMe_2$).

Eluted second was **13** (175 mg, 28%), isolated as a colourless oil, $[\alpha]_{578}$ +58° (*c* 1, chloroform); R_F 0.24 (3:1 light petroleum–ethyl acetate). ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.37–7.27 (m, 20 H, 4 Ph), 4.93 (d, 1 H, $J_{1',2'}$ 3.4 Hz, H-1'), 4.91–4.84 (m, 5 H, 2.5 $PhCH_2$), 4.78 (d, 1 H, J_{gem} 11.0 Hz, $PhCH_2$), 4.66 (d, 1 H, J_{gem} 11.2 Hz, $PhCH_2$), 4.58 (d, 1 H, J_{gem} 11.2 Hz, $PhCH_2$), 4.52 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.00–3.38 (m, 10 H), 3.33 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 3.26 (dd, 1 H, $J_{2',3'}$ 10.3 Hz, H-2'), 1.56 (bs, 1 H, OH), 0.92 (s, 9 H, ^{t}Bu), 0.17, 0.16 (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{46}H_{58}N_6O_9Si$ (867.1): C, 63.72; H, 6.74; N, 9.69. Found: for **15**, C, 63.62; H, 6.76; N, 9.62; for **14**, C, 63.51; H, 6.73; N, 9.50.

*Decyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-*N*-methyl-α-*D-manno*-2-octulopyranosidonamide* (**18**). — To a solution of **2** (75 mg, 0.13 mmol) in dichloromethane (5 mL) was added aqueous 80% trifluoroacetic acid (0.5 mL). The mixture was stirred for 36 h, then concentrated, and water was removed by repeated evaporation of toluene from the residue (**17**). Pyridine (2 mL) and acetic anhydride (0.25 mL) were added to the residue, and the mixture was stirred at room temperature for 2 h and then concentrated. Medium pressure l.c. (1:1 light petroleum–ethyl acetate) of the residue yielded **18** (49 mg, 64%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +67° (*c* 1, chloroform); R_F 0.31. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.63 (q, 1 H, NH), 5.38 (bs, 1 H, H-5), 5.33 (ddd, 1 H, $J_{3e,4}$ 4.1, $J_{3a,4}$ < 1 Hz, $J_{4,5}$ < 1 Hz, H-4), 5.20 (ddd, 1 H, $J_{7,8a}$ 2.2, $J_{7,8b}$ 4.4, $J_{6,7}$ 9.8 Hz, H-7), 4.57 (dd, 1 H, $J_{8a,8b}$ 12.4, $J_{7,8a}$ 2.2 Hz, H-8a), 4.12 (dd, 1 H, $J_{5,6}$ 1.2, $J_{6,7}$ 9.8 Hz, H-6), 4.07 (dd, 1 H, $J_{8a,8b}$ 12.4, $J_{7,8b}$ 4.4 Hz, H-8b), 3.29 (ddd, 2 H, 2 H-1'), 2.88 (d, 3 H, *J* 5.1 Hz, NMe), 2.27 (dd, 1 H, $J_{3a,3e}$ 12.7, $J_{3e',4}$ 4.1 Hz, H-3*e*), 2.08, 2.07, 2.02, 1.97 (s, 4 H, 4 Ac), 1.87 (dd, 1 H, $J_{3a,3e}$ 12.7 Hz, H-3*a*), 1.71–1.52 (m, 2 H, 2 H-2'), 1.42–1.21 (bs, 14 H, decyl 7 CH_2), 0.88 (t, 3 H, *J* 6.8 Hz, decyl CH_3).

Anal. Calc. for $C_{27}H_{45}NO_{11}$ (559.51): C, 57.96; H, 8.08; N, 2.50. Found: C, 57.54; H, 8.20; N, 2.50.

D-*Glycer-1-yl 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-*N*-methyl-α-*D-manno*-2-octulopyranosidonamide* (**19**). — To a solution of **3** (450 mg, 0.67 mmol) in ethyl acetate (4 mL) was added 10% Pd–C (70 mg). After hydrogenolysis for 2 h, the mixture was filtered, and concentrated *in vacuo*. Flash chromatography (9:1 chloroform–methanol) of the residue yielded amorphous **19** (320 mg, 97%), $[\alpha]^{22}_{578}$ +20° (*c* 1, chloroform); R_F 0.51. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.87 (q, 1 H, *J* 4.9 Hz, NH), 4.48 (ddd, 1 H, $J_{3a,4}$ 3.8, $J_{3e,4}$ 3.6, $J_{4,5}$ 7.4 Hz, H-4), 4.36 (ddd, 1 H, $J_{6,7}$ 5.9 Hz, H-7), 4.25 (dd, 1 H, $J_{5,6}$ 2.0, $J_{4,5}$ 7.3 Hz, H-5), 4.11 (dd, 1 H, $J_{8a,8b}$ 8.8, $J_{7,8a}$ 6.4 Hz, H-8a), 4.00 (dd, 1 H, $J_{8a,8b}$ 8.8, $J_{7,8b}$ 5.5 Hz, H-8b), 3.82–3.87 (m, 1 H, H-2'), 3.80 (dd, 1 H, $J_{5,6}$ 1.96, $J_{6,7}$ 5.9 Hz, H-6), 3.70 (dd, 1 H, J_{gem} 11.7, $J_{2',3'}$ 4.6 Hz, H-3'), 3.64 (dd, 1 H, J_{gem} 10.5, $J_{1',2'}$ 2.4 Hz, H-1'), 3.55 (dd, 1 H, J_{gem} 11,5, $J_{2',3'}$ 4.6 Hz, H-3'), 3.37 (dd, 1 H, J_{gem} 10.3, $J_{1',2'}$ 6.7 Hz, H-1'), 2.94 (bs, 2 H, 20 H), 2.84 (d, 3 H, *J* 4.9 Hz, NMe), 2.60 (dd, 1 H, $J_{3a,3e}$ 15.9, $J_{3e,4}$ 3.8 Hz, H-3*e*), 1.90 (dd, 1 H, $J_{3a,3e}$ 15.9, $J_{3a,4}$ 3.7 Hz, H-3*a*), 1.63–1.36 (m, 2 H, 2 C_6H_{10}).

Anal. Calc. for $C_{24}H_{39}NO_9{\cdot}H_2O$ (503.59): C, 57.24; H, 8.20; N, 2.78. Found: C, 57.30; H, 8.09; N, 2.86.

2,3-Di-O-tetradecanoyl-D-glycer-1-yl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-N-methyl-α-D-manno-2-octulopyranosidonamide (**20**). — To a solution of **19** (320 mg, 0.48 mmol) in dry dichloromethane (6 mL) was added pyridine (1 mL) and tetradecanoyl chloride (380 mg, 1.4 mmol). The mixture was stirred for 56 h at room temperature, then concentrated. Flash chromatography (7:3 light petroleum–ethyl acetate) of the residue yielded **20** (330 mg, 76%), m.p. 48–49°, $[\alpha]^{22}_{578}$ +26° (*c* 1, chloroform); R_F 0.29. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.71 (q, 1 H, *J* 4.9 Hz, NH), 5.24–5.17 (m, 1 H, H-2′), 4.49–4.43 (m, 1 H, H-4), 4.35–4.30 (m, 2 H, H-3′a,7), 4.24–4.16 (m, 2 H, H-3′b,5), 4.08 (dd, 1 H, J_{gem} 8.6, $J_{7,8a}$ 6.3 Hz, H-8a), 3.96 (dd, 1 H, J_{gem} 8.6, $J_{7,8b}$ 5.1 Hz, H-8b), 3.76 (dd, 1 H, $J_{6,7}$ 6.3, $J_{5,6}$ < 1 Hz, H-6), 3.62 (dd, 1 H, J_{gem} 10.1, $J_{1'a,2'}$ 4.9 Hz, H-1′a), 3.44 (dd, 1 H, J_{gem} 10.1, $J_{1'b,2'}$ 5.1 Hz, H-1′b), 2.83 (d, 3 H, *J* 4.9 Hz, NMe), 2.63 (dd, 1 H, $J_{3a,3e}$ 15.6, $J_{3e,4}$ 4.0 Hz, H-3*e*), 2.36–2.28 (m, 4 H, 2 $OCO.CH_2$), 1.87 (dd, 1 H, $J_{3e,3a}$ 15.6, $J_{3a,4}$ 3.4 Hz, H-3*a*), 1.74–1.42 (m, 24 H, 2 C_6H_{10} and $OCO.CH_2CH_2$), 1.40–1.15 (bs, 40 H, 20 CH_2), 0.88 (t, 6 H, *J* 6.8 Hz, CH_3).

Anal. Calc. for $C_{52}H_{91}NO_{11}$ (906.02): C, 68.94; H, 10.09; N, 1.55. Found: C, 68.57; H, 10.05; N, 1.50.

2,3-Di-O-tetradecanoyl-D-glycer-1-yl 4,5,7,8-tetra-O-acetyl-3-deoxy-N-methyl-α-D-manno-2-octulopyranosidonamide (**22**). — To a solution of **20** (101 mg, 0.11 mmol) in dichloromethane (15 mL) was added trifluoroacetic acid (80%, 0.5 mL). The mixture was stirred for 8 h at room temperature, then concentrated, and toluene was evaporated several times from the residue to yield **21**; R_F 0.59 (8:2 chloroform–methanol). The residue was dissolved immediately in dry pyridine (2 mL), and acetic anhydride (0.25 mL) was added. The mixture was stirred for 2 h, then concentrated under reduced pressure, and toluene was evaporated repeatedly from the residue. Medium pressure l.c. (1:1 light petroleum–ethyl acetate) of the residue yielded **22** (66 mg, 66%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +94° (*c* 0.5, chloroform); R_F 0.38. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.67 (q, 1 H, *J* 4.9 Hz, NH), 5.38 (bs, 1 H, H-5), 5.29–5.25 (m, 1 H, H-4), 5.23–5.19 (m, 2 H, H-2′,7), 4.58 (dd, 1 H, J_{gem} 12.9, $J_{7,8b}$ 2.2 Hz, H-8b), 4.36 (dd, 1 H, J_{gem} 11.7, $J_{1'a,2'}$ 3.7 Hz, H-1′a), 4.18 (dd, 1 H, J_{gem} 11.7, $J_{1'b,2'}$ 6.6 Hz, H-1′b), 4.11 (dd, 1 H, $J_{6,7}$ 9.8, $J_{5,6}$ 1.3 Hz, H-6), 4.04 (dd, 1 H, J_{gem} 12.3, $J_{7,8a}$ 5.5 Hz, H-8a), 3.53 (dd, 1 H, J_{gem} 10.1, $J_{2',3'a}$ 5.1 Hz, H-3′a), 3.47 (dd, 1 H, J_{gem} 10.1, $J_{2',3'b}$ 4.7 Hz, H-3′b) 2.90 (d, 3 H, *J* 4.9 Hz, NMe), 2.36–2.13 (m, 5 H, 2 $OCO.CH_2$, H-3*e*), 2.09, 2.08, 2.06, 2.00 (4 s, 12 H, 4 Ac), 1.88 (dd, 1 H, $J_{3a,3e}$ 12.8, $J_{3a,4}$ 12.8 Hz, H-3*a*), 1.63–1.60 (m, 4 H, 2 $OCO.CH_2CH_2$), 1.30–1.14 (bs, 40 H, 20 CH_2), 0.88 (t, 6 H, *J* 7.6 Hz, CH_3).

Anal. Calc. for $C_{48}H_{83}NO_{15}$ (931.93): C, 63.05; H, 9.13; N, 1.50. Found: C, 62.94; H, 9.38; N, 1.50.

Methyl 6-O-(4,5:7,8-di-O-cyclohexylidene-3-deoxy-N-methyl-α-D-manno-2-octulopyranosylonamide)-α-D-glucopyranoside (**23**). — To a solution of **4** (2.03 g, 2.36 mmol) in dry ethyl acetate (40 mL) was added 10% Pd–C (1 g). After hydrogenolysis for 2 h, the mixture was filtered and concentrated *in vacuo*. Column chromatography (9:1 chloroform–methanol) of the residue yielded **23** (1.18 g, 80%), m.p. 118–119°, $[\alpha]^{22}_{578}$ +60° (*c* 3, methanol); R_F 0.37. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.79 (q, 1 H, *J* 4.8 Hz, NH), 4.75 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.88 (ddd, 1 H, $J_{3'e,4'}$ 3.2, $J_{3'a,4'}$ 3.7, $J_{4',5'}$ 7.3 Hz, H-4′), 4.36 (ddd, 1 H, $J_{7',8'a}$ = $J_{7',8'b}$ = 5.9, $J_{6',7'}$ 5.6 Hz, H-7′), 4.49–3.39 (bs, 3 H, 3 OH), 4.23 (dd, 1 H, $J_{5',6'}$ <1 Hz, H-5′), 4.10 (dd, 2 H, $J_{8'a,8'b}$ 5.9 Hz, H-8′a, 8′b), 3.83 (dd, 1 H, H-6′), 3.76–3.71 (m, 2 H, H-3,4), 3.64 (ddd, 1 H, $J_{4,5}$ 9.3, $J_{5,6a}$ 3.7, $J_{5,6b}$ 9.5 Hz, H-5), 3.54 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2); 3.50–3.44 (m, 2 H, H-6a,6b), 3.39 (s, 3 H, OMe), 2.85 (d, 3 H, CH_3), 2.68 (dd, 1 H, $J_{3'e,3'a}$ 15.9 Hz, H-3′*e*), 1.90 (dd, 1 H, H-3′*a*), 1.64–1.32 (m, 20 H; 2 C_6H_{10}).

Anal. Calc. for $C_{28}H_{45}NO_{12}\cdot H_2O$ (605.7): C, 55.53; H, 7.82; N, 2.31. Found: C, 55.69; H, 7.98; N, 2.17.

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-(4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-*N*-methyl-α-*D*-*manno*-2-octulopyranosylonamide)-α-*D*-glucopyranoside* (**24**). — To a solution of **23** (1.03 g, 1.75 mmol) in dry pyridine (15 mL) was added acetic anhydride (15 mL) at 0°. The mixture was stirred for 24 h at room temperature, then concentrated, and toluene was evaporated repeatedly from the residue. Column chromatography (1:2 light petroleum–ethyl acetate) then yielded **24** (1.21 g, 97%), isolated as a colourless oil, $[\alpha]_{578}^{22}$ +94° (*c* 0.5, chloroform); R_F 0.56. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.72 (q, 1 H, *J* 4.9 Hz, NH), 5.43 (dd, 1 H, $J_{3,4}$ 9.8, $J_{2,3}$ 9.5 Hz, H-3), 4.98 (dd, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.94 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.90 (dd, 1 H, H-2), 4.45 (ddd, 1 H, $J_{3'e,4'}$ 3.7, $J_{3'a,4'}$ 4.4, $J_{4',5'}$ 7.6 Hz, H-4′), 4.33 (ddd, 1 H, $J_{6',7'}$ 6.4, $J_{7',8'b}$ 4.6, $J_{7',8'a}$ 6.1 Hz, H-7′), 4.21 (dd, 1 H, $J_{5',6'}$ <1 Hz, H-5′), 4.14–4.04 (m, 2 H, H-8′b,8′a), 3.95 (ddd, 1 H, $J_{5,6a}$ 6.5 Hz, H-5), 3.72 (dd, 1 H, H-6′), 3.56 (dd, 1 H, $J_{6a,6b}$ 10.0 Hz, H-6b), 3.39 (s, 3 H, OMe), 3.34 (dd, 1 H, H-6a), 2.83 (d, 3 H, CH_3), 2.58 (dd, 1 H, $J_{3'a,3'e}$ 15.4 Hz, H-3′*a*), 2.06, 2.03, 1.99 (3 S, 9 H, 3 Ac), 1.93 (dd, 1 H, H-3′*e*), 1.59–1.26 (m, 20 H, 2 C_6H_{10}).

Anal. Calc. for $C_{34}H_{51}NO_{15}$ (713.7): C, 57.21; H, 7.20; N, 1.96. Found: C, 57.06; H, 7.27; N, 1.84.

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-(3-deoxy-*N*-methyl-α-*D*-*manno*-2-octulopyranosylomanide)-α-*D*-glucopyranoside* (**25**). — To a solution of **23** (740 mg, 1.04 mmol) in dichloromethane (20 mL) was added trifluoroacetic acid (50%). The mixture was stirred at room temperature for 3 h then concentrated under reduced pressure, and toluene was evaporated several times from the residue. Column chromatography (8:2 chloroform–methanol) then yielded **25** (350 mg, 61%), isolated as a colourless oil, $[\alpha]_{578}^{22}$ +114° (*c* 1.3 methanol); R_F 0.31. ^{1}H-N.m.r. data (400 MHz, CD_3OD): δ 5.39 (dd, 1 H, $J_{3,4}$ 9.5, $J_{2,3}$ 10.0 Hz, H-3), 5.03 (dd, 1 H, $J_{4,5}$ 10.3 Hz, H-4), 4.94 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.83 (dd, 1 H, H-2), 4.03–3.92 (m, 4 H, H-4′,5,5′,7′), 3.78 (dd, 1 H, $J_{8'a,8'b}$ 11.2, $J_{7',8'b}$) 4.2 Hz, H-8′b), 3.72 (dd, 1 H, $J_{6',7'}$ 8.1, $J_{5',6'}$ <1 Hz, H-6′), 3.66 (dd, 1 H, $J_{7',8'a}$ 5.4 Hz, H-8′a), 3.52 (dd, 1 H, $J_{5,6b}$ 5.9, $J_{6a,6b}$ 10.7 Hz, H-6b), 3.41 (s, 3 H, OMe), 3.35 (dd, 1 H, $J_{5,6a}$ 1.7 Hz, H-6a), 2.78 (s, 3 H, CH_3), 2.05 (dd, 1 H, $J_{3'e,4'}$ 5.1 Hz, H-3′*e*), 2.03, 2.02, 1.97 (3 s, 9 H, 3 Ac), 1.81 (dd, 1 H, $J_{3'a,4'}$ 11.7, $J_{3'e,3'a}$ 12.7 Hz, H-3′*a*).

A correct elemental analysis could not be obtained and the compound was used immediately in the next step.

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-(4,5,7,8-tetra-*O*-acetyl-3-deoxy-*N*-methyl-α-*D*-*manno*-2-octulopyranosylonamide)-α-*D*-glucopyranoside* (**26**). — To a solution of **25** (350 mg, 0.63 mmol) in dry pyridine (10 mL) was added acetic anhydride (5 mL) at 0°. The mixture was stirred for 24 h at room temperature, then concentrated, and toluene was evaporated repeatedly from the residue. Column chromatography (1:3 light petroleum–ethyl acetate) then yielded **26** (330 mg, 73%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +132° (*c* 1, chloroform); R_F 0.34. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.72 (q, 1 H, *J* 4.9 Hz, NH), 5.47 (dd, 1 H, $J_{3,4}$ 10.3, $J_{2,3}$ 9.3 Hz, H-3), 5.35 (dd, 1 H, $J_{4',5'}$ 2.9, $J_{5',6'}$ <1 Hz, H-5'), 5.32 (ddd, 1 H, $J_{3'e,4'}$ 3.27 Hz, H-4'), 5.21 (ddd, 1 H, $J_{6',7'}$ 9.5, $J_{7',8'a}$ 5.9, $J_{7',8'b}$ 2.2 Hz, H-7'), 4.96 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.84 (dd, 1 H, H-4), 4.81 (dd, 1 H, H-2), 4.62 (dd, 1 H, $J_{8'a,8'b}$ 12.2, H-8'b), 4.27 (dd, 1 H, H-6'), 4.06 (ddd, 1 H, $J_{4,5}$ 8.5, $J_{5,6a}$ 8.3 Hz, H-5), 3.99 (dd, 1 H, H-8'a), 3.46 (s, 3 H, OMe), 3.43 (dd, 1 H, $J_{6a,6b}$ 9.8 Hz, H-6b), 3.35 (dd, 1 H, H-6a), 2.89 (d, 3 H, CH_3), 2.24 (dd, 1 H, $J_{3'e,3'a}$ 11.7 Hz, H-3'*e*), 2.11, 2.08, 2.04, 2.03, 2.00, 1.95 (7 s, 21 H, 7 Ac), 1.95 (dd, 1 H, $J_{4',3'a}$ 12.9 Hz, H-3'*a*).

Anal. Calc. for $C_{30}H_{43}NO_{19}$ (721.7): C, 49.93; H, 6.00; N, 1.94. Found: C, 49.51; H, 6.17; N, 1.82.

*Methyl 2,3,4-tri-*O*-acetyl-6-*O*-(4,5,7,8-tetra-*O*-acetyl-3-deoxy-α-*D-manno*-2-octulopyranosylonic acid)-α-*D*-glucopyranoside* (**27**) *and methyl 2,3,4-tri-*O*-acetyl-6-*O*-(methyl 4,5,7,8-tetra-*O*-acetyl-3-deoxy-α-*D-manno*-2-octulopyranosylonate)-α-*D*-glucopyranoside* (**28**). — To a solution of **26** (190 mg, 0.26 mmol) in acetic acid (1 mL) and acetic anhydride (5.3 mL) was added sodium nitrite (395 mg) during 5 h. The mixture was stirred for 16 h at 0°, then poured into ice, and extracted with chloroform several times. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated to dryness. Column chromatography (1:2 light petroleum–ethyl acetate or 8:2 chloroform–methanol) of the residue yielded **28** (25 mg) and then **27** (130 mg, 70%), m.p. 48–49°, $[\alpha]^{22}_{578}$ +86° (*c* 0.5, methanol); R_F 0.34. ^{1}H-N.m.r. data (400 MHz, CD_3OD): δ 5.36 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 9.3 Hz, H-3), 5.34 (ddd, 1 H, $J_{3a,4'}$ 8.15, $J_{3'e,4'}$ 4.9, $J_{4,5'}$ <1 Hz, H-4'), 5.29 (bs, 1 H, H-5'), 5.19 (ddd, 1 H, $J_{7',8'b}$ 2.4, $J_{7,8'a}$ 4.9, $J_{6',7'}$ 9.5 Hz, H-7'), 4.99 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.96–4.82 (m, 2 H, H-2,4); 4.58 (dd, 1 H, $J_{8'a,8'b}$ 12.2 Hz, H-8'b), 4.26–4.22 (m, 2 H, H-6',8'a), 4.03 (ddd, 1 H, $J_{4,5}$ 8.3, $J_{5,6a}$ = $J_{5,6b}$ = 8.0 Hz, H-5), 3.59–3.50 (m, 2 H, H-6a,6b), 3.47 (s, 3 H, OMe), 2.17 (dd, 1 H, $J_{3'e,3'a}$ 12.4 Hz, H-3'*e*), 2.08–1.93 (m, 22 H, H-3'*a*, 7 Ac).

Anal. Calc. for $C_{29}H_{40}O_{20}\cdot H_2O$ (726.7): C, 47.93; H, 5.83. Found: C, 47.52; H, 5.73.

To a solution of **27** (130 mg, 0.18 mmol) in ether (15 mL) was added an excess of diazomethane. The mixture was stirred for 2 h at room temperature and then concentrated. Column chromatography (1:2 light petroleum–ethyl acetate) of the residue yielded **28** (129 mg, total yield, 154 mg, 81%), m.p. 66–67°, $[\alpha]^{22}_{578}$ +109.5° (*c* 0.34, chloroform); R_F 0.58. ^{1}H-N.m.r. data (400 MHz, C_6D_6): δ 5.92 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.5 Hz, H-3), 5.77 (bs, 1 H, H-5'), 5.68 (ddd, 1 H, $J_{3'e,4'}$ 5.1, $J_{3'a,4'}$ 12.2, $J_{4',5'}$ 2.9 Hz, H-4'), 5.54 (ddd, 1 H, $J_{7',8'a}$ 4.4, $J_{7',8'b}$ 2.4, $J_{6',7'}$ 9.3 Hz, H-7'), 5.22 (dd, 1 H, $J_{4,5}$ 10.3 Hz, H-4), 5.08 (dd, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 4.87 (d, 1 H, H-1), 4.81 (dd, 1 H, $J_{8'a,8'b}$ 12.4 Hz, H-8'b), 4.51 (dd, 1 H, $J_{5,6}$ 1 Hz, H-6'), 4.23 (dd, 1 H, H-8'a), 4.15 (ddd, 1 H, $J_{5,6a}$ 8.1, $J_{5,6b}$ 2.2 Hz, H-5), 3.93 (dd, 1 H, $J_{6a,6b}$ 10.5 Hz, H-6b), 3.89 (dd, 1 H, H-6a), 3.26 (s, 3 H, COOMe), 3.25 (s, 3 H, OMe), 2.40 (dd, 1 H, $J_{3'a,3'e}$ 12.7 Hz, H-3'*a*), 2.32 (dd, 1 H, H-3'*e*), 1.86, 1.80, 1.72, 1.71, 1.65, 1.59 (7 s, 21 H, 7 Ac).

Anal. Calc. for $C_{30}H_{42}O_{20}$ (722.6): C, 49.86; H, 5.86. Found: C, 50.15; H, 5.86.

tert-*Butyldimethylsilyl 2-azido-3,4-di-*O*-benzyl-2-deoxy-6-*O*-(methyl 4,5:7,8-di-*

*O-cyclohexylidene-3-deoxy-α-*D-manno*-2-octulopyranosylonate)-β-*D*-glucopyranoside* (**29**). — To a solution of **5** (1.41 g, 1.57 mmol) in acetic acid (7.85 mL) and acetic anhydride (39.25 mL) at 0° was added sodium nitrite (2.35 g, 34 mmol) during 5 h. The mixture was stirred for 16 h at 0°, then poured on to ice, and extracted with chloroform several times. The combined extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated. Column chromatography (8:2 or 1:3 light petroleum–ethyl acetate) of the residue yielded the *N*-nitroso derivative (700 mg, 48%), isolated as a yellow oil, R_F 0.56 (8:2 light petroleum–ethyl acetate). Eluted second was the acid (660 mg, 48%), isolated as a colourless oil, R_F 0.46 (1:3 light petroleum–ethyl acetate).

A solution of the *N*-nitroso derivative (700 mg, 0.79 mmol) in dry hexane (30 mL) was boiled under reflux for 12 h, then concentrated. Medium pressure l.c. (8:2 light petroleum–ethyl acetate) of the residue yielded **29** (500 mg).

To a solution of the acid (660 mg, 0.75 mmol) in ether (40 mL) was added an excess of diazomethane at 0°. The mixture was stirred for 2 h at room temperature and then concentrated under reduced pressure. Column chromatography (8:2 light petroleum–ethyl acetate) of the residue yielded **29** (540 mg; total yield, 1.04 g, 75%), m.p. 100–102°, $[\alpha]^{22}_{578}$ +15° (*c* 1, chloroform); R_F 0.52. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.34–7.21 (m, 10 H, 2 Ph), 4.87 (d, 1 H, J_{gem} 10.7 Hz, $PhCH_2$), 4.80 (d, 1 H, J_{gem} 10.7 Hz, $PhCH_2$), 4.74 (d, 1 H, J_{gem} 10.7 Hz, $PhCH_2$), 4.52 (d, 1 H, J_{gem} 10.7 Hz, $PhCH_2$), 4.48 (d, 1 H, $J_{1,2}$ 7.11 Hz, H-1), 4.44 (ddd, 1 H, $J_{4',5'}$ 7.3, $J_{3'a,4'}$ 4.4, $J_{3'e,4'}$ 3.2 Hz, H-4'), 4.36 (ddd, 1 H, H-7'), 4.22 (dd, 1 H, $J_{5',6'}$ 1.7 Hz, H-5'), 4.10 (dd, 1 H, $J_{7',8'b}$ 6.1, $J_{8'a,8'b}$ 8.6 Hz, H-8'b), 3.98 (dd, 1 H, $J_{7',8'a}$ 5.6 Hz, H-8'a) 3.70–3.60 (m, 5 H, COOMe, H-6b,6'), 3.54 (dd, 1 H, $J_{5,6a}$ 2.0, $J_{3'a,3'e}$ 15.0 Hz, H-3'*a*), 1.85 (dd, 1 H, H-3'*e*), 1.62–1.32 (m, 20 H, 2 C_6H_{10}), 0.94 (s, 9 H, ^{t}Bu), 0.17, 0.16, (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{47}H_{67}N_3O_{12}Si$ (894.1): C, 63.13; H, 7.55; N, 4.70. Found: C, 62.95; H, 7.55; N, 4.70.

tert-*Butyldimethylsilyl 3,4-di-O-benzyl-2-deoxy-6-O-(methyl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-α-*D-manno*-2-octulopyranosylonate)-2-tetradecanoylamino-β-*D*-glucopyranoside* (**31**). — A solution of **29** (300 mg, 0.33 mmol) in 2:1 pyridine–water (30 mL) was saturated with hydrogen sulphide, then stirred at room temperature for 24 h. The mixture was then concentrated and toluene was evaporated several times from the residue (**30**), to a solution of which in dry pyridine (15 mL) at 0° was added tetradecanoyl chloride (0.7 mL, 0.67 mmol). The mixture was stirred for 16 h at room temperature, then concentrated, and toluene was evaporated repeatedly from the oily residue. Medium pressure l.c. (3:1 light petroleum–ethyl acetate) then yielded amorphous **31** (270 mg, 76%), $[\alpha]^{22}_{578}$ +25° (*c* 1, chloroform); R_F 0.52. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.51–7.22 (m, 10 H, 2 Ph), 5.46 (q, 1 H, *J* 8.1 Hz, NH), 4.98 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.78 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.74 (d, 1 H, J_{gem} 11.0 Hz, $PhCH_2$), 4.63 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.54 (d, 1 H, J_{gem} 11.0 Hz, $PhCH_2$), 4.45 (ddd, 1 H, $J_{3'a,4'}$ 4.25; $J_{3'e,4'}$ 3.2, $J_{4',5'}$ 7.3 Hz, H-4'), 4.36 (ddd, 1 H, $J_{7',8'b}$ 5.9 Hz, H-7'), 4.22 (dd, 1 H, $J_{5',6'}$ 2.0 Hz, H-5'), 4.13–4.09 (m, 2 H, H-2,8b), 4.06 (dd, 1 H, $J_{8'a,8'b}$ 8.6, $J_{7',8'a}$ 5.6 Hz, H-8'a), 3.71 (dd, 1 H, $J_{6a,6b}$ 10.3, $J_{5,6b}$ 7.3 Hz, H-6b), 3.64–3.55 (m, 6 H, H-5,6a,6', COOMe), 3.44–3.22 (m, 2 H, H-3,4), 2.70 (dd, 1 H, $J_{3'a,3'e}$ 15.1 Hz, H-3'*a*), 2.04–2.00 (m, 2 H, CH_2), 1.86 (dd, 1 H, H-3'*e*), 1.63–1.02 (m, 42 H, 2 C_6H_{10}, 11 CH_2), 0.87 (t, 3 H, CH_3), 0.86 (s, 9 H, ${}^tBu$), 0.10, 0.08, (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{61}H_{95}NO_{13}Si$ (1078.5): C, 67.93; H, 8.88; N, 1.30. Found: C, 67.64; H, 8.90; N, 1.37.

*1-O-Acetyl-3,4-di-O-benzyl-2-deoxy-6-O-(methyl 4,5:7,8-tetra-O-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-2-tetradecanoylamino-α-D-glucopyranose* (**32**). — To a solution of **31** (130 mg, 0.11 mmol) in dichloromethane (10 mL) was added aqueous 80% trifluoroacetic acid (2 mL). The mixture was stirred for 18 h at room temperature, then concentrated, and toluene was evaporated repeatedly from the residue, to a solution of which in dry pyridine (10 mL) was added acetic anhydride (5 mL) at 0°. The mixture was stirred for 24 h at room temperature, then concentrated, and toluene was evaporated repeatedly from the residue. Column chromatography (1:1 light petroleum–ethyl acetate) then yielded **32** (50 mg, 45%), isolated as a colourless oil, $[\alpha]^{22}_{578}$ +86° (*c* 1.4, chloroform); R_F 0.36. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.38–7.29 (m, 10 H, 2 Ph), 6.05 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.30 (bs, 1 H, H-5'), 5.26–5.18 (m, 2 H, H-4',7'), 4.94 (d, 1 H, *J* 9.3 Hz, NH), 4.93–4.60 (4 d, 4 H, J_{gem} 11.5 Hz, 2 $PhCH_2$), 4.56 (dd, 1 H, $J_{8'a,8'b}$ 12.2, $J_{7',8'b}$ 2.4 Hz, H-8'b), 4.30 (ddd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.14 (dd, 1 H, $J_{5',6'}$ 1.5, $J_{6',7'}$ 9.5 Hz, H-6'), 4.04 (dd, 1 H, $J_{7',8'a}$ 5.1 Hz, H-8'a), 3.81 (ddd, 1 H, H-5), 3.76–3.65 (m, 5 H, COOMe, H-6a,6b), 3.55–3.51 (m, 2 H, H-3,4), 2.17 (dd, 1 H, $J_{3'a,3'e}$ 12.7, $J_{3'a,4'}$ 4.9 Hz, H-3'*a*), 2.12, 2.07 (2 s, 6 H, 2 Ac), 2.04 (dd, 1 H, $J_{3'e,4'}$ 3.7 Hz, H-3'*e*), 2.02, 2.00, 1.97 (3 s, 9 H, 3 Ac), 1.55–1.46 (m, 2 H, CH_2), 1.32–1.22 (m, 22 H, 11 CH_2), 0.88 (t, 3 H, CH_3).

Anal. Calc. for $C_{53}H_{75}NO_{18}$ (1014.2): C, 62.77; H, 7.45; N, 1.38. Found: C, 63.16; H, 7.54; N, 1.43.

*1-O-Acetyl-2-deoxy-6-O-(methyl 4,5,7,8-tetra-O-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-2-tetradecanoylamino-α-D-glucopyranose* (**33**). — To a solution of **32** (31 mg, 0.03 mmol) in dry ethyl acetate was added 10% Pd–C (20 mg). After hydrogenolysis for 2 h, the mixture was filtered, concentrated *in vacuo*, eluted from a short column of silica gel with 9:1 chloroform–methanol, and then subjected to medium pressure l.c. (1:1 ethyl acetate–acetone), to yield amorphous **33** (20.6 mg, 80%), $[\alpha]^{22}_{578}$ +69° (*c* 0.7, chloroform); R_F 0.58 (9:1 chloroform–methanol). ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 6.11 (d, 1 H, 3.7 Hz, H-1), 5.69 (d, 1 H, *J* 8.1 Hz, NH), 5.35 (bs, 1 H, H-5'), 5.31–5.22 (m, 2 H, H-4', 7'), 4.52 (dd, 1 H, $J_{8'a,8'b}$ 12.2, $J_{7',8'b}$ 2.4 Hz, H-8'b), 4.28 (dd, 1 H, $J_{6',7'}$ 9.5, $J_{5',6'}$ <1 Hz, H-6'), 4.20 (ddd, 1 H, H-2), 4.14 (dd, 1 H, $J_{7',8'a}$ 4.9 Hz, H-8'a), 3.83 (s, 3 H, COOMe), 3.78–3.56 (m, 7 H, H-3,4,5,5a,6b, 2 OH), 2.23–2.11 (m, 17 H, H-3'*e*, 3'*a*, 5 Ac), 1.75 (m, 2 H, CH_2), 1.30–1.20 (m, 22 H, 11 CH_2), 0.87 (t, 3 H, CH_3).

Anal. Calc. for $C_{39}H_{63}NO_{18}\cdot H_2O$ (851.9): C, 54.98; H, 7.69; N, 1.65. Found: C, 54.70; H, 7.50; N, 2.16.

tert-*Butyldimethylsilyl O-(methyl 4,5:7,8-di-O-cyclohexylidene-3-deoxy-α-D-*manno*-2-octulopyranosylonate)-(2→6)-O-(2-azido-3,4-di-O-benzyl-2-deoxy-β-D-gluco-pyranosyl)-(1→6)-2-azido-3,4-di-O-benzyl-2-deoxy-β-D-glucopyranoside* (**34**). — To a solution of **16** (270 mg, 0.2 mmol) in acetic acid (1 mL) and acetic anhydride (5 mL) at

0° was added sodium nitrite during 5 h. The mixture was stirred for 16 h at 0°, then poured on to ice–water, and extracted with chloroform. The extract was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated under reduced pressure. A solution of the residue in dry hexane (30 mL) was boiled under reflux for 12 h, then concentrated, the residue was dissolved in ether, and an excess of diazomethane was added. The mixture was stirred at room temperature for 2 h, then concentrated under reduced pressure. Column chromatography (8:2 light petroleum–ethyl acetate) of the residue yielded **34** (220 mg, 87%), m.p. 51–52°, $[\alpha]_{578}^{22}$ −2.0° (*c* 1.3, chloroform); R_F 0.41. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$): δ 7.27–7.13 (m, 20 H, 4 Ph), 4.82–4.51 (m, 8 H, 4 $PhCH_2$), 4.46 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 4.28–4.25 (m, 2 H, H-4″,7″), 4.13 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.06–3.92 (m, 4 H, H-5″,6″,8″a,8″b), 3.66–3.24 (m, 15 H), 2.65 (dd, 1 H, $J_{3''a,3''e}$ 15.1, $J_{3''a,4''}$ 4.2 Hz, H-3″*a*), 1.71 (dd, 1 H, $J_{3''e,4''}$ 2.9 Hz, H-3″*e*), 1.60–1.18 (m, 20 H, 2 C_6H_{10}), 0.87 (s, 9 H, ^{t}Bu), 0.12, 0.11, (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{67}H_{88}N_6O_{16}Si \cdot H_2O$ (1279.6): C, 62.89; H, 7.16; N, 6.56. Found: C, 62.70; H, 7.06; N, 6.57.

tert-*Butyldimethylsilyl* O-*(methyl 4,5:7,8-di-*O*-cyclohexylidene-3-deoxy-α-*D-manno-*2-octulopyranosylonate)-(2→6)-*O*-(3,4-di-*O*-benzyl-2-deoxy-2-tetradecanoylamino-β-*D*-glucopyranosyl)-(1→6)-3,4-di-*O*-benzyl-2-deoxy-2-tetradecanoylamino-α-*D*-glucopyranoside* (**36**). — A solution of **34** (155 mg, 0.12 mmol) in 2:1 pyridine–water (15 mL) was saturated with hydrogen sulphide and stirred for 24 h at room temperature, then concentrated, and toluene was evaporated from the residue several times to yield **35**, R_F 0.54 (1:2 light petroleum–ethyl acetate, to a solution of which in dry pyridine (10 mL), was added tetradecanoyl chloride (0.19 mL, 0.74 mmol). The mixture was stirred at room temperature for 3 h, then concentrated, and toluene was evaporated several times from the residue. Medium pressure l.c. (2:1 light petroleum–ethyl acetate) then yielded amorphous **36** (140 mg, 70%), $[\alpha]_{578}^{22}$ +19° (*c* 1.8, chloroform); R_F 0.50. ^{1}H-N.m.r. data (400 MHz, $CDCl_3$), δ 7.36–7.21 (m, 20 H, 4 Ph), 5.61 (d, 1 H, *J* 7.6 Hz, NH′), 5.49 (d, 1 H, *J* 8.1 Hz, NH), 5.01 (d, 1 H, $J_{1',2'}$ 7.6 Hz, H-1′), 4.87 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 4.79–4.57 (m, 8 H, 4 $PhCH_2$), 4.36–4.32 (m, 2 H, H-4″,7″), 4.22 (dd, 1 H, $J_{2',3'}$ 8.1, $J_{3',4'}$ 9.0 Hz, H-3′), 4.15 (dd, 1 H, $J_{5'',6''}$ 1.5, $J_{4'',5''}$ 7.3 Hz, H-5″), 4.10–3.99 (m, 4 H, H-3,6″,8″a,8″b), 3.78–3.43 (m, 11 H), 3.36–3.29 (m, 2 H, H-2,2′), 2.72 (dd, 1 H, $J_{3''a,3''e}$ 15.4, $J_{3''a,4''}$ 4.4 Hz, H-3″*a*), 2.33 (t, 1 H, CH_2), 2.17–1.87 (m, 3 H, 3 CH_2), 1.79 (dd, 1 H, $J_{3''e,4''}$ 2.7 Hz, H-3″*e*), 1.60–1.20 (m, 64 H, 2 C_6H_{10} 22 CH_2), 0.89–0.85 (m, 15 H, ^{t}Bu, 2 CH_3), 0.09, 0.07 (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{95}H_{144}N_2O_{18}Si$ (1630.3): C, 70.00; H, 8.90; N, 1.72. Found: C, 69.83; H, 9.22; N, 1.72.

ACKNOWLEDGEMENTS

The Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie are thanked for financial support.

REFERENCES

1 E. T. Rietschel, L. Brade, U. Schade, U. Seydel, V. Zähringer, S. Kusumoto, and H. Brade, in E. Schrinner, M. H. Richmond, G. Seibert, and V. Schwaz (Eds.), *Surface Structures of Microorganisms and Their Interactions with the Mammalian Host, Workshop Conferences Hoechst*, Vol. 18, VCH Verlagsgesellschaft, Weinheim, 1988, pp. 1–41, and references therein.
2 F. M. Unger, *Adv. Carbohydr. Chem. Biochem.*, 38 (1981) 323.
3 M. Imoto, S. Kusumoto, T. Shiba, H. Naoki, T. Iwashita, E. T. Rietchel, H. W. Wollenweber, C. Galanos, and O. Lüderitz, *Tetrahedron Lett.*, 24 (1983) 4017–4020; H. Brade and E. T. Rietschel, *Eur. J. Biochem.*, 145 (1984) 231–236; H. Brade, U. Zähringer, and E. T. Rietschel, *Carbohydr. Res.*, 134 (1984) 157–166; R. Christian, G. Schulz, P. Waldstätten, and F. M. Unger, *Tetrahedron Lett.*, 25 (1984) 3433–3436.
4 H. Paulsen and M. Schüller, *Liebigs Ann. Chem.*, (1987) 249–258; H. Paulsen, M. Stiem, and F. M. Unger, *ibid.*, (1987) 273–281; M. Kiso, M. Fujita, E. Hayashi, A. Hasegawa, and F. M. Unger, *J. Carbohydr. Chem.*, 6 (1987) 691–696; and references therein.
5 M. Imoto, N. Kusunose, Y. Matsuura, S. Kusumoto, and T. Shiba, *Tetrahedron Lett.*, 28 (1987) 6277–6280.
6 R. R. Schmidt and M. Reichrath, *Angew. Chem.*, 91 (1979) 497–499; *Angew. Chem. Int. Ed. Engl.*, 18 (1979) 466–468, R. R. Schmidt, M. Reichrath, and V. Moering, *Tetrahedron Lett.*, 21 (1980) 3561–3564; *J. Carbohydr. Chem.*, 3 (1984) 67–84; R. R Schmidt, U. Moering, and M. Reichrath, *Tetrahedron Lett.*, 21 (1980) 3565–3568; *Chem. Ber.*, 115 (1982) 39–49.
7 R. R. Schmidt, *Angew. Chem.*, 98 (1986) 213–236; *Angew. Chem. Int. Engl.*, 25 (1986) 212–235.
8 R. R. Schmidt and A. Esswein, *Angew. Chem.*, 100 (1988) 1234–1236; *Angew. Chem. Int. Ed. Engl.*, 27 (1988) 1178–1180.
9 R. R. Schmidt and J. Michel, *Tetrahedron Lett.*, 25 (1984) 821–824; R. R. Schmidt, J. Michel, and M. Roos, *Liebigs Ann. Chem.*, (1984) 1343–1357.
10 R. R. Schmidt and R. Betz. *Angew. Chem.*, 96 (1984) 420–421; *Angew. Chem. Int. Ed. Engl.*, 23 (1984) 430–431; A. Esswein, R. Betz, and R. R. Schmidt, *Helv. Chim. Acta*, 72 (1989) 213–223.
11 R. U. Lemieux and R. M. Ratcliffe, *Can. J. Chem.*, 57 (1979) 1244–1251; Ger. Offen. 2,816,340 (1978); *Chem. Abstr.*, 90 (1979) 87846k.
12 E. H. White, *J. Am. Chem. Soc.* 77 (1955) 6008–6022.
13 H. Paulsen, Y. Hayauchi, and F. M. Unger, *Liebigs Ann. Chem.*, (1984) 1270–1287; *ibid.*, 1288–1297.
14 F. M. Unger, D. Stix, and G. Schulz, *Carbohydr. Res.*, 80 (1980) 191–195.
15 H. Wulff, Diplomarbeit, University of Konstanz, 1988.
16 H. F. G. Beving, H. B. Boren, and P. J. Garegg, *Acta Chem. Scand.*, 21 (1967) 2083.
17 W. Kinzy, Dissertation, University of Konstanz, 1986.