A Facile and Stereospecific Synthesis of L-*glycero*-D-*manno*-Heptose and some Derivatives

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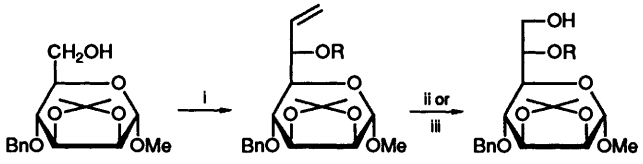
The stereospecific condensation of vinylmagnesium bromide with the readily available aldehyde **2**, gave the olefin **3** which was further elaborated into L-*glycero*-D-*manno*-heptose and some derivatives thereof, through oxidative cleavage of the double bond followed by reductive work up.

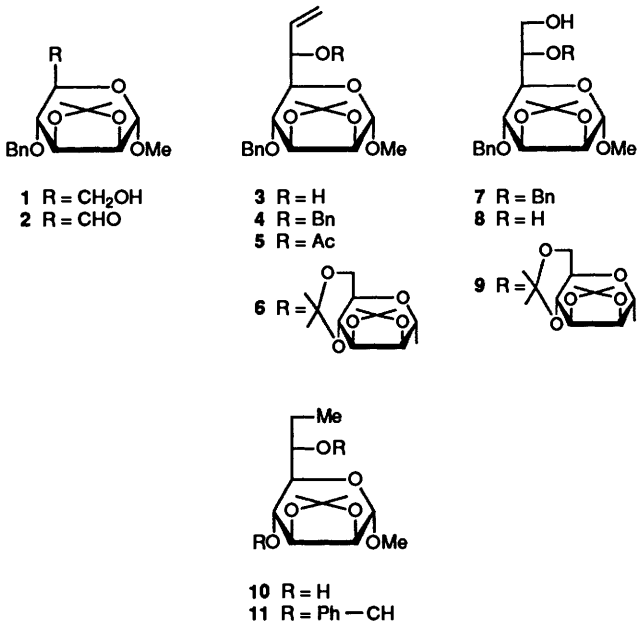
L-*glycero*-D-*manno*-Heptose **17** (LD-Hepp) containing trisaccharides linked to 3-deoxy-D-*manno*-octylulosonic acid (KDO), have been found in the core region of lipopolysaccharides of certain Gram negative bacteria.[1] This core region has been proposed as an immunogen,[2] and therefore there is a particular interest in the synthesis of suitably protected derivatives of LD-Hepp utilizable in oligosaccharide building blocks.[3] Several preparations of this monosaccharide have been reported recently, yielding a mixture of isomers,[4] or requiring a number of steps[5] or using complex reagents.[6,7] We describe here a concise synthesis of the title heptose and some derivatives thereof which starts from the readily available alcohol **1** (see Scheme 1).

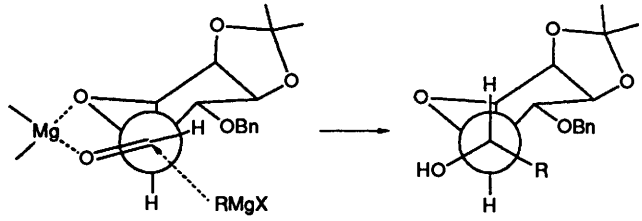


Scheme 1. *Reagents and conditions:* i, DMSO, $(COCl)_2$, NEt_3, THF, −60 °C, then CH_2=CHMgBr, 5 equiv., THF, −60 °C; ii, (*a*) O_3, CH_2Cl_2, −40 °C, (*b*) $NaBH_4$, H_2O, MeOH, room temp.; iii, (*a*) OsO_4, $NaIO_4$, ether, H_2O, room temp., (*b*) as in ii.

Swern oxidation[8] of the alcohol **1**[9] gave the corresponding aldehyde **2** which was immediately condensed with commercially available vinylmagnesium bromide in tetrahydrofuran at −78 °C according to the Ireland procedure for the use of sensitive carbonyl compounds,[10] to afford *a single alcohol* **3** in 83% isolated yield. The stereochemistry at the new chiral centre was confirmed by the two-step conversion of the allylic alcohol **3** into the bis acetal **11** *via* the diol **10**. The ^1H NMR spectrum of compound **11** exhibited a coupling constant ($J_{5,6}$ 6 Hz) supporting an equatorial orientation of 6-H, and the 6*S* configuration for the alcohol **3**. This was expected, in agreement with already reported results,[6,7] according to the Cram chelated model[11] for the attack of the Grignard reagent on the aldehyde **2**. The oxygen ring and the oxygen of the aldehyde are assumed to be chelated with magnesium as depicted in Scheme 2, the approach of the Grignard reagent then occurring from the less hindered side. It is worthy of note that the vinylation of the aldehyde **2** is stereospecific,[12] without the use of complex reagents and/or additives,[13] whereas analogous vinylation of related aldehydes[14] proceeds with only modest stereoselectivity if any.

The next problem to be addressed was the transformation of the double bond into a hydroxymethyl group without destruction of the different protecting groups. The allylic alcohol **3** was then protected as the benzyl ether **4** in 90% yield or acetylated to give quantitatively the acetate **5**. The double

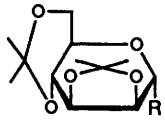


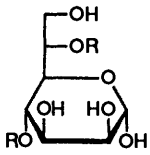


Scheme 2.

bond of **4** was oxidatively cleaved by ozone at low temperature, followed by reductive work-up with sodium borohydride to give the expected heptose **7** in 70% isolated yield. The same transformation was attempted on the olefins **4** and **5** using sodium periodate in the presence of osmium tetroxide in aqueous ether. In both cases the intermediate aldehyde was immediately reduced with sodium borohydride. Thus, the alcohol **7** was obtained in 73% yield from **4**, whereas the olefin **5** yielded directly the diol **8** (67%) owing to concomitant removal of the acetyl group during the reduction step. Subsequent deprotection of the alcohol **7** in acidic medium gave the dibenzyl ether **16** which was then submitted to catalytic hydrogenation, with palladium on charcoal in methanol to afford LD-Hepp **17** in 38% overall yield.

The alcohols **3** and **7** are suitable building blocks for the synthesis of disaccharides including one or two LD-Hepp units, which are of interest as potential antigenic substances. In order to check the stability of such a glycosidic bond in the above oxidative conditions, we prepared a model disaccharide by coupling the glycosyl acceptor **3** with a mannosyl residue. The readily available derivative **12**[15] was chosen as the mannosyl donor. We have developed some years ago a method for the





12 R = OH
13 R = $O\overset{+}{P}(NMe_2)_3$, Cl^-
14 R = $O\overset{+}{P}(NMe_2)_3$, TsO^-
15 R = Cl

16 R = Bn
17 R = H

activation of a hemiacetal hydroxy group *via* alkoxyphosphonium salts. This approach allowed the synthesis of glycosyl chlorides, glycosides, thioglycosides and of some disaccharides.[16] We took advantage of this methodology to activate the alcohol **12** in order to achieve the synthesis of the disaccharide **9**. In a first attempt, the alkoxyphosphonium chloride **13** was treated at −40 °C with silver tosylate and the resulting alkoxyphosphonium tosylate **14** was then treated with the alcohol **3** in refluxing dichloromethane. The disaccharide **6** was isolated in only 35% yield as the single α anomer. A more efficient alternate route was explored. Upon warming to the room temperature, the alkoxyphosphonium salt **13** was allowed to form the mannosyl chloride **15** which was used in a one-pot reaction. The treatment of the glycosyl halide **15** with silver triflate[17] and the alcohol **3** in the presence of 4 Å molecular sieves, gave the α disaccharide **6**, isolated in 66% yield.

Cleavage of the double bond of the olefin **6**, followed by reduction of the intermediate aldehyde, were done according to both previously described methods. Ozonolysis or the osmium tetroxide–sodium periodate method, allowed the formation of the disaccharide **9** in 43 and 55% yields respectively. It is interesting to note that this particular disaccharide itself, could be further elaborated to L-αD-Hepp-(1,6)-LD-Hepp. Indeed, further functional manipulation of the mannose moiety would allow the formation of an aldehyde function at C-6 and the same sequence of vinylation-oxidation-reduction would afford the second LD-Hepp moiety.

These results demonstrate that the stereospecific vinylation of the aldehyde **2** opens a new easy route to LD-Hepp, and to some protected derivatives of interest in the synthesis of oligosaccharides of biological importance. The two-step transformation of the olefin into a hydroxymethyl group is compatible with the presence of different protecting groups and a neighbouring glycosidic linkage. The origin of the observed high stereospecificity and further synthetic use of this reaction are now under investigation.

Experimental

The ^1H NMR spectra were recorded with a Bruker Aspect 3000 spectrometer operating at 400 MHz using deuteriochloroform as solvent. Assignments were confirmed by double irradiation. Chemical shifts are reported relative to internal $SiMe_4$. TLC was performed on silica gel (Merck 60 F_{254}). Column chromatography used silica gel (Merck 60 70–23 mesh). Mixtures of ethyl acetate (A) and hexane (H) or methanol (M), or ether (E) and toluene (T) were used as eluants. Optical rotations were measured on a Perkin-Elmer 141 polarimeter at 20 °C. M.p.s were measured in capillary tubes and were uncorrected. The elementary analyses were performed by the Service Central de Microanalyses du CNRS at Vernaison (France).

Methyl 4-O-*Benzyl*-2,3-O-*isopropylidene*-α-D-manno-*hexodialdo*-1,5-*pyranose* **2**.—To a cooled (−60 °C) solution of oxalyl chloride (0.16 ml, 1.8 mmol) in anhydrous tetrahydrofuran (5 ml) was added a solution of dimethyl sulphoxide (0.4 ml, 3.6 mmol) in anhydrous tetrahydrofuran (2 ml). After 5 min, a solution of methyl 4-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannopyranoside **1** (600 mg, 1.6 mmol) in anhydrous tetrahydrofuran (5 ml) was added dropwise at this temperature. After the mixture had been stirred during 15 min, a solution of triethylamine (808 mg) in tetrahydrofuran (2 ml) was added, and the mixture was allowed to warm to room temperature during 5 min. The aldehyde was used directly in the next step without isolation.

Methyl 4-O-*Benzyl*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*oct*-7-*enopyranoside* **3**.—The above solution was recooled to −60 °C. A solution of vinylmagnesium bromide in tetrahydrofuran (1M; 8 mmol) was added and the mixture was stirred during 3 h. Ethanol (1 ml) and saturated aqueous ammonium chloride were successively added. The mixture was extracted with ether (3 × 50 ml) and the combined extracts were washed with water (3 × 10 ml), dried ($MgSO_4$) and evaporated under reduced pressure to give crude **3** which was purified on a silica gel column using A/H 2:8 as eluant (400 mg, 83%), m.p. 56–57 °C, $[\alpha]_D$ +27.5° (*c* 0.3 in $CHCl_3$); R_F 0.31 (A/H 2:8) (Found: C, 64.95; H, 7.5. $C_{19}H_{26}O_6$ requires C, 65.13; H, 7.48%); ν_{max} 3300–3600, 1660 and 1380 cm^{-1}; δ 1.37 (3 H, s, isopropylidene), 1.50 (3 H, s, isopropylidene), 2.23 (1 H, s, OH), 3.34 (3 H, s, OCH_3), 3.56 (1 H, dd, 5-H, $J_{5,6}$ 1.5, $J_{4,5}$ 10 Hz), 3.72 (1 H, dd, 4-H, $J_{3,4}$ 6.5 Hz), 4.12 (1 H, d, 2-H, $J_{2,3}$ 6.5 Hz), 4.33 (1 H, t, 3-H), 4.45 (1 H, m, 6-H), 4.64 (1 H, d, CH_2Ph, *J* 11.5 Hz), 4.91 (1 H, d, CH_2Ph), 4.92 (1 H, s, 1-H), 5.21 (1 H, dd, 8′-H, $J_{7,8'}$ 10.5, $J_{8,8'}$ 1.5 Hz), 5.36 (1 H, dd, 8-H, $J_{7,8}$ 17 Hz), 5.99 (1 H, ddd, 7-H, $J_{6,7}$ 5 Hz) and 7.39 (5 H, m, ArH).

Methyl 4,6-*Di*-O-*benzyl*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*oct*-7-*enopyranoside* **4**.—Sodium hydride in oil (65%; 52 mg, 1.4 mmol) was twice washed with anhydrous tetrahydrofuran. To the suspension of sodium hydride in anhydrous dimethylformamide (20 ml) was added the alcohol **3** (400 mg, 1.22 mmol), and after 10 min benzyl bromide (0.2 ml, 1.6 mmol) was added. The mixture was stirred at room temperature for 3 h after which a few drops of pyridine were added and the solvent was evaporated. The residue was extracted with methylene dichloride (3 × 50 ml), and the combined extracts were washed with water until neutral, dried ($MgSO_4$) and evaporated to dryness. Chromatography of the residue (A/H 2:8) gave the pure olefin **4** (450 mg, 90%), $[\alpha]_D$ +57.7° (*c* 0.65 in $CHCl_3$); R_F 0.53 (A/H 2:8) (Found: C, 71.05; H, 7.3. $C_{26}H_{32}O_6$ requires C, 70.89; H, 7.32%); ν_{max} 1640 cm^{-1}; δ 1.36 (3 H, s, isopropylidene), 1.52 (3 H, s, isopropylidene), 3.31 (3 H, s, OCH_3), 3.55 (1 H, dd, 5-H, $J_{5,6}$ 1.5, $J_{4,5}$ 10 Hz), 3.85 (1 H, dd, 4-H, $J_{3,4}$ 7 Hz), 4.10 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.20 (1 H, dd, 6-H, $J_{6,7}$ 8.5 Hz), 4.31 (3 H, m, 3-H + CH_2Ph), 4.65 (1 H, d, CH_2Ph, *J* 11.5 Hz), 4.84 (1 H, d, CH_2Ph), 4.99 (1 H, s, 1-H), 5.33 (2 H, m, 8-H and 8′-H), 6.07 (1 H, m, 7-H, $J_{7,8}$ 17, $J_{7,8'}$ 10 Hz) and 7.25 (10 H, m, ArH).

Methyl 6-O-*Acetyl*-4-O-*benzyl*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*oct*-7-*enopyranoside* **5**.—To a solution of compound **3** (20 mg, 0.57 mmol) in pyridine (10 ml) was added acetic anhyride (0.5 ml). The mixture was stirred overnight at

room temperature. Ethanol was then added (2 ml) and the solvents were evaporated. The residue was extracted with methylene dichloride (3 × 50 ml). The combined extracts were washed with 3M hydrochloric acid (10 ml), water, 3M aqueous sodium hydroxide (10 ml) and water until neutral, dried ($MgSO_4$) and evaporated to dryness. Column chromatography of the residue (A/H 2:8) gave the pure olefin **5** (210 mg, 94%), m.p. 97–98 °C; $[\alpha]_D$ +51.3° (*c* 0.24 in $CHCl_3$) (Found: C, 64.05; H, 7.25. $C_{21}H_{28}O_7$ requires C, 64.27; H, 7.19%); ν_{max} 1750, 1640 and 1380 cm^{-1}; δ 1.37 and 1.49 (2 × 3 H, 2s, isopropylidene), 2.00 (3 H, s, OAc_3), 3.33 (1 H, dd, 4-H, $J_{3,4}$ 6.5, $J_{4,5}$ 10 Hz), 3.66 (1 H, dd, 5-H, $J_{5,6}$ 2 Hz), 4.12 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.33 (1 H, t, 3-H), 4.52 (1 H, d, CH_2Ph, *J* 11 Hz), 4.82 (1 H, d, CH_2Ph), 4.97 (1 H, s, 1-H), 5.26 (1 H, dt, 8′-H, $J_{8',7}$ 10, $J_{8,8'}$ 0.5, $J_{8',6}$ 0.5 Hz), 5.35 (1 H, dt, 8-H, $J_{8,7}$ 18, $J_{8,6}$ 0.5 Hz), 5.65 (1 H, dd, 6-H, $J_{6,7}$ 6.5 Hz), 5.93 (1 H, m, 7-H) and 7.4 (5 H, m, ArH).

Methyl 6-O-[2,3:4,6-*Di*-O-*isopropylidene*-α-D-*mannopyranosyl*]-4-O-*benzyl*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*oct*-7-*enopyranoside* **6**.—*From the tosylate* **14**. To a solution of the alcohol **12** (780 mg, 3 mmol) and carbon tetrachloride (785 mg, 6 mmol) in anhydrous tetrahydrofuran, cooled at −40 °C was added dropwise within 1 h, a solution of tris(dimethylamino)phosphine (624 mg, 4.5 mmol) in anhydrous tetrahydrofuran (10 ml). After the addition was completed, silver tosylate (1.06 g, 4.5 mmol) was poured into the solution of the salt **13**. After the precipitation of silver chloride was complete (15 min), a solution of the alcohol **3** (270 mg, 0.77 mmol) was added. The mixture was allowed to warm to room temperature and then refluxed during 4 h. After dilution with methylene dichloride and filtration over Celite, the organic phase (150 ml) was washed with 3M hydrochloric acid (10 ml) and then water until neutral, and then dried ($MgSO_4$). Evaporation of the solvent afforded crude **6** which was purified by preparative HPLC (E/T 3:7) (165 mg, 35%).

From the chloride **15**. A solution of the alkoxyphosphonium chloride **13**, starting from **12**, was prepared as described above. After the addition of the phosphine was completed, the solution was allowed to warm to room temperature during 3 h to ensure complete formation of the mannosyl chloride **15**. To this solution was added silver triflate (457 mg, 1.78 mmol) and 4 Å molecular sieves (100 mg). After 5 min a solution of the alcohol **3** (270 mg, 0.77 mmol) was added. The mixture was stirred during 18 h at room temperature. The reaction was treated as above to yield the disaccharide **6** (310 mg, 66%), $[\alpha]_D$ +35.1° (*c* 0.39 in $CHCl_3$); R_F 0.3 (A/H 2:8) (Found: C, 62.4; H, 7.5. $C_{31}H_{44}O_{11}$ requires C, 62.82; H, 7.48%); ν_{max} 1645 and 1380 cm^{-1}; δ 1.34–1.58 (18 H, 6 s, isopropylidene), 3.35 (3 H, s, OMe), 3.57 (4 H, m, 5-H, 5′-H, 6-H and 6′-H), 3.78 (2 H, m, 4-H and 4′-H), 4.06 (2 H, m, 2′-H and 3′-H), 4.29 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.35 (1 H, t, 3-H, $J_{3,4}$ 6.5 Hz), 4.47 (1 H, dd, 6-H, $J_{5,6}$ 2, $J_{6,7}$ 9 Hz), 5.00 (1 H, s, 1′-H), 5.02 (1 H, d, CH_2Ph, *J* 13 Hz), 5.17 (1 H, s, 1-H), 5.36 (2 H, m, 8-H and 8′-H), 5.51 (1 H, d, CH_2Ph), 5.90 (1 H, m, 7-H, $J_{7,8}$ 10, $J_{7,8'}$ 18 Hz) and 7.30 (5 H, m, ArH).

General Procedure for Olefin Cleavage.—Method A: ozonolysis. Ozonized oxygen was passed through a solution of the olefin in anhydrous methylene dichloride (20 ml, mmol) at −40 °C until no starting material remained (TLC). The solvent was then evaporated and the residue was taken up in ethanol (15 ml, mmol). To this solution was added a solution of sodium borohydride (2 equiv.) water–ethanol (1:1) at room temperature. After 1 h, a solution of 3M hydrochloric acid was added until the mixture was neutral. The solvents were then evaporated and the residue was extracted with methylene dichloride (3 × 50 ml). The combined extracts were washed with water until neutral, dried ($MgSO_4$) and evaporated to dryness. Column chromatography of the residue gave the pure alcohol.

Method B: sodium periodate–osmium tetroxide cleavage. To a solution of the olefin in an ether–water mixture (1:1; 10 ml, mmol) was added a solution of osmium tetroxide in t-butyl alcohol (1% w/v; 2 ml, mmol) and sodium periodate (5 equiv.). The mixture was stirred until no starting material remained (TLC). The organic solvents were removed under reduced pressure and methanol (20 ml, mmol) was added to the residue. A solution of sodium borohydride (4 equiv.) in water (10 ml, mmol) was added and the mixture stirred at room temperature for 1 h. Work-up as described above gave the pure alcohol.

Methyl 4,6-*Di*-O-*benzyl*-2,3-O-*isopropylidene*-L-glycero-α-D-manno-*heptopyranoside* **7**.—*Method A*. The olefin **4** (70 mg, 0.16 mmol) gave the alcohol **7** (50 mg, 70%). *Method B*. The olefin **4** (150 mg, 0.34 mmol) gave **7** (110 mg, 73%), $[\alpha]_D$ +57.4° (*c* 0.84 in $CHCl_3$); R_F 0.53 (A/H 1:1) (Found: C, 67.55; H, 7.4. $C_{25}H_{32}O_7$ requires C, 67.55; H, 7.26%); ν_{max} 3400–3500 and 1380 cm^{-1}; δ 1.36 (3 H, s, isopropylidene), 1.55 (3 H, s, isopropylidene), 2.10 (1 H, s, OH), 3.4 (3 H, s, OMe), 3.75 (1 H, dd, 5-H, $J_{5,6}$ 5, $J_{4,5}$ 10 Hz), 3.77 (1 H, dd, 4-H, $J_{3,4}$ 6 Hz), 3.85 (2 H, m, 7-H, 7′-H), 3.91 (1 H, dd, 6-H, $J_{6,7}$ 4.5, $J_{6,7'}$ 3 Hz), 4.13 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.33 (1 H, t, 3-H, $J_{3,4}$ 6 Hz), 4.36 (1 H, d, CH_2Ph, *J* 12 Hz), 4.45 (1 H, d, CH_2Ph, *J* 12 Hz), 4.70 (1 H, d, CH_2Ph), 4.90 (1 H, d, CH_2Ph), 4.98 (1 H, s, 1-H) and 7.30 (10 H, m, ArH).

Methyl 4-O-*Benzyl*-2,3-O-*isopropylidene*-L-glycero-α-D-manno-*heptopyranoside* **8**.—*Method B*. The olefin **5** (140 mg, 0.36 mmol) gave **8** (85 mg, 67%), $[\alpha]_D$ +37.2° (*c* 0.25 in $CHCl_3$); R_F 0.16 (A/H 6:4) (Found: C, 60.55; H, 7.4. $C_{18}H_{26}O_6$ requires C, 61.00; H, 7.39%); ν_{max} 1648 and 1370 cm^{-1}; δ 1.37 and 1.51 (2 × 3 H, 2s, isopropylidene), 2.05 (2 H, m, OH), 3.34 (3 H, s, OMe), 3.61 (1 H, dd, 7′-H, $J_{6,7'}$ 2, $J_{7,7'}$ 10 Hz), 3.70 (1 H, dd, 7-H, $J_{6,7}$ 4.5 Hz), 3.71 (1 H, dd, 4-H, $J_{3,4}$ 6.5, $J_{4,5}$ 10.5 Hz), 3.79 (1 H, dd, 5-H, $J_{5,6}$ 6 Hz), 4.00 (1 H, m, 6-H), 4.20 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.32 (1 H, t, 3-H), 4.65 (1 H, d, CH_2Ph, *J* 12.5 Hz), 4.91 (1 H, d, CH_2Ph), 4.94 (1 H, s, 1-H) and 7.40 (5 H, m, ArH).

Methyl 6-O-[2,3:4,6-*Di*-O-*isopropylidene*-α-D-*mannopyranosyl*]-4-O-*benzyl*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*oct*-7-*enopyranoside* **9**.—*Method A*. The olefin **6** (130 mg, 0.22 mmol) gave the alcohol **9** (56 mg, 43%). *Method B*. The olefin **6** (60 mg, 0.1 mmol) gave the alcohol **9** (34 mg, 55%), $[\alpha]_D$ +41.8° (*c* 0.56 in $CHCl_3$); R_F 0.38 (A/H 1:1) (Found: C, 60.5; H, 7.4. $C_{30}H_{44}O_{12}$ requires C, 60.39; H, 7.43%); ν_{max} 3300–3600 and 1380 cm^{-1}; δ 1.34–1.58 (18 H, 6 s, isopropylidene), 2.20 (1 H, s, OH), 3.40 (3 H, s, OMe), 3.60–4.00 (9 H, m, 7-H, 7′-H, 6-H, 6′-H, 6″-H, 5-H, 5′-H, 4-H and 4′-H), 4.12 (1 H, d, 2′-H, $J_{2',3'}$ 6 Hz), 4.17 (1 H, t, 3′-H, $J_{2',3'}$ 6, $J_{3',4'}$ 6.5 Hz), 4.33 (2 H, m, 2-H and 3-H), 4.56 (1 H, d, CH_2Ph, *J* 11 Hz), 4.96 (1 H, s, 1′-H), 4.98 (1 H, d, CH_2Ph), 5.28 (1 H, d, 1-H, $J_{1,2}$ 2 Hz) and 7.30 (5 H, m, ArH).

Methyl 7,8-*Dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*octopyranoside* **10**.—To a solution of **3** (200 mg, 0.57 mmol) in anhydrous tetrahydrofuran (15 ml) was added, under nitrogen, palladium-on-charcoal (10%; 10 mg). The flask was placed under a hydrogen atmosphere and the mixture stirred during 4 h. The solution was filtered through Celite and evaporated to give crude **10**, which was purified on a silica gel column (A/H 5:5) (120 mg, 80%), m.p. 119–120 °C; $[\alpha]_D$ +31.6° (*c* 0.23 in $CHCl_3$); R_F 0.30 (A/H 5:5) (Found: C, 54.7; H, 8.25. $C_{12}H_{22}O_6$ requires C, 54.95; H, 8.45%); ν_{max} 3600–3200 and 1385 cm^{-1}; δ 1.01 (3 H, t, Me, $J_{Me,7}$ 7 Hz), 1.36 (3 H, s, isopropylidene), 1.54 (3 H, s, isopropylidene), 1.60 (1 H, m, 7′-H), 1.7 (1 H, m, 7-H), 2.10 (1 H, s, OH), 2.30 (1 H, s, OH), 3.40 (3 H, s, OCH_3), 3.47 (1 H, dd, 5-H, $J_{5,6}$ 1.5, $J_{4,5}$ 10 Hz), 3.79 (1 H, m, 6-H, $J_{6,7}$ 5, $J_{6,7'}$ 9 Hz), 3.83

(1 H, dd, 4-H, $J_{3,4}$ 6.5 Hz), 4.14 (2 H, m, 2-H and 3-H) and 4.95 (1 H, s, 1-H).

Methyl 4,6-O-*Benzylidene*-7,8-*dideoxy*-2,3-O-*isopropylidene*-α-D-manno-*octopyranoside* **11**.—To a solution of **10** (100 mg, 0.38 mmol) in anhydrous dimethylformamide (10 ml) was added toluene-*p*-sulphonic acid (10 mg) and α,α-dimethoxytoluene (1 ml). The solution was then concentrated under reduced pressure on a rotary evaporator at 65 °C. Aqueous saturated sodium hydrogen carbonate (10 ml) was added to the residue and the mixture evaporated to dryness. The residue was chromatographed on a silica gel column to yield **11** (85 mg, 64%), $[\alpha]_D$ −50.7° (*c* 0.4 in $CHCl_3$); R_F 0.66 (A/H 3:7) (Found: C, 65.4; H, 7.65. $C_{19}H_{26}O_6$ requires C, 65.13; H, 7.48%); ν_{max} 1380 cm^{-1}; δ 1.09 (3 H, t, Me, $J_{Me,7}$ 7 Hz), 1.36 (3 H, s, isopropylidene), 1.58 (3 H, s, isopropylidene), 1.76 (1 H, m, 7′-H), 2.11 (1 H, m, 7-H), 3.40 (3 H, s, OCH_3), 3.91 (1 H, dd, 4-H, $J_{4,5}$ 11, $J_{3,4}$ 7 Hz), 3.99 (1 H, dd, 5-H, $J_{5,6}$ 6 Hz), 4.12 (1 H, dd, 6-H), 4.18 (1 H, d, 2-H, $J_{2,3}$ 6 Hz), 4.30 (1 H, dd, 3-H), 4.98 (1 H, s, 1-H), 5.80 (1 H, s, PhC-*H*) and 7.40 (5 H, m, ArH).

L-glycero-D-manno-*Heptose* **17**.—To a solution of the alcohol **7** (170 mg, 0.38 mmol) in a mixture of water–dioxane (2:1; 10 ml) was added 12M hydrochloric acid (3 drops), and the solution was stirred overnight at room temperature. The solution was neutralised with 3M aqueous sodium hydroxide and evaporated to dryness. Flash chromatography on silica gel using A/M (95:5) as eluant yielded **16** as an anomeric mixture (70 mg, 66%). To a solution of this compound (70 mg, 0.25 mmol) in methanol (15 ml) was added palladium-on-charcoal (10%; 45 mg) and the flask was placed under hydrogen atmosphere during 3 h at room temperature. After filtration of the solution through Celite, the eluant was evaporated to give the heptose **17** as a hygroscopic foam (31 mg, 59%), $[\alpha]_D$ +13.1° (*c* 0.25 in H_2O); R_F 0.3 ($CHCl_3$, MeOH, H_2O 5:4:1); $CHCl_3$–MeOH–H_2O; {lit.,[4] $[\alpha]_D$ +15.2° (*c* 2.67 in H_2O)}; {lit.,[5] $[\alpha]_D$ +14.1° (*c* 1.23 in H_2O); R_F 0.22–0.29 ($CHCl_3$–MeOH–H_2O, 5:4:1)}. The ^1H NMR spectrum was in full agreement with that described by Paulsen *et al.*[5]

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