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SYNTHESIS OF 1,5-LACTONES OF 3-DEOXY-D-*manno*-2-OCTULOPYRANOSONIC ACID (KDO)*†

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ABSTRACT

An unambiguous synthesis of methyl 3-deoxy-α-D-*manno*-2-octulopyranosidono-1,5-lactone from methyl (methyl 3-deoxy-α-D-*manno*-octulopyranosid)onate *via* the 7,8-*O*-isopropylidene derivative is described. Treatment of the 4,5-stannylene derivative of this acetal with benzyl bromide gave the 1,5-lactone from which the protecting groups were removed. The acetylated 1,5-lactone was produced by acetylation of ammonium 3-deoxy-D-*manno*-2-octulosonate or treatment of the pyridinium salt with dicyclohexylcarbodi-imide and acetylation. No lactone was produced when only HO-7 was unsubstituted. When treated with an excess of 2-methoxypropene, methyl (methyl 3-deoxy-α-D-*manno*-2-octulopyranosid)onate afforded the 4,5:7,8-di-*O*-isopropylidene derivative, from which the 7,8-acetal group could be removed selectively.

INTRODUCTION

3-Deoxy-D-*manno*-2-octulosonic acid ("KDO", **1**) is an important constituent of endotoxins where it is invariably present at the junction of the hydrophilic (sugar chain) and hydrophobic ("Lipid A") regions[1]. It is also a constituent of the capsular polysaccharides of certain *E. coli*[2] and *Neisseria*[3] strains, and occurs in plant cell-walls[4]. As with other α-keto acids, carboxyl esterification takes place readily under mild conditions[5]. Lactone formation occurs on treatment of **1** with acetic anhydride–sodium acetate[6]. In connection with studies of the *Bordetella pertussis* endotoxin, we now report on the formation, structure, and stability of KDO-lactones.

*Dedicated to Professor Bengt Lindberg.
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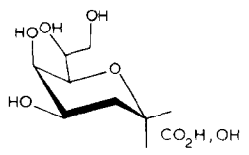
RESULTS AND DISCUSSION

The formation of small amounts of a lactone of KDO was observed[7] when the ammonium salt of KDO was treated with acetic anhydride–pyridine–4-dimethylaminopyridine; after treatment of the crude, acetylated product with diazomethane, the acetylated methyl ester **2** could be separated by chromatography from the lactone. The lactone structure was suggested by the ^{1}H-n.m.r. spectrum in which signals for four OAc groups but no OMe group were found, and by the i.r. carbonyl band at 1775 cm^{-1}. Analysis[7] of the available ^{1}H- and ^{13}C-n.m.r. data indicated a probable 1,5-lactone structure (**3**), but the alternative 1,7-lactone structure could not be excluded. Accordingly, an attempt was made to synthesize unambiguously a compound having the 3-deoxy-α-D-*manno*-2-octulopyranosidono-1,5-lactone structure.

Thus, methyl (methyl 3-deoxy-α-D-*manno*-2-octulopyranosid)onate[3,8–10] (**4**) was converted into the 7,8-isopropylidene acetal **5**. Attempted benzylation of HO-4 of **5** by treatment first with dibutyltin oxide and then, under catalysis with tetrabutylammonium bromide[11], with benzyl bromide gave methyl 4-*O*-benzyl-3-deoxy-7,8-*O*-isopropylidene-α-D-*manno*-2-octulopyranosidono-1,5-lactone (**6**) isolated in 73% yield. The structure of **6** followed from the finding that the compound obtained after removal of the isopropylidene acetal reduced 1 molar equivalent of periodate and produced 1 molar equivalent of formaldehyde. The ^{1}H-n.m.r. spectrum of **6** served to discriminate between the 1,4- and 1,5-lactone structures, the only alternatives possible. As the chemical shift (δ 5.0) of the signal for H-5 was close to that (δ 5.33) observed for H-5 of methyl (methyl 4,5,7,8-tetra-*O*-acetyl-α-D-*manno*-2-octulopyranosid)onate and remote from the value (δ 3.94) measured for the H-5 resonance of methyl (methyl 5-*O*-benzyl-α-D-*manno*-2-octulopyranosid)onate[8], and as in stannylene derivatives of galactopyranosides[11], with which KDO-pyranosides are homomorphous, equatorial hydroxyl groups are preferentially substituted, it was concluded that the 1,5-lactone structure was present in **6**. The conclusion was confirmed by the ^{1}H-n.m.r. data of the triol **7** formed from **6** upon removal of the isopropylidene and benzyl groups. Acetylation (acetic anhydride–pyridine) of **7** afforded a triacetate (**8**), the ^{1}H-n.m.r. data of which were, within experimental error, identical to those measured[6] for a lactone formed upon acetylation (acetic anhydride–sodium acetate) of methyl 3-deoxy-α-D-*manno*-pyranosidonic acid, mistakenly thought to be a 1,7-lactone.

Acid-catalysed condensation of methyl (methyl 3-deoxy-α-D-*manno*-2-octulopyranosid)onate (**4**) with 2-methoxypropene occurred readily: the mono- (**5**), and di-*O*-isopropylidene (**9**) derivatives were formed depending upon the amount of reagent used. Hydrolysis of **9** at 20° with 0.16M trifluoroacetic acid selectively removed the 7,8-*O*-isopropylidene group to give the crystalline 4,5-*O*-isopropylidene derivative **10**. Treatment of **10** with dibutyltin oxide and 2 mol. equiv. of benzyl bromide, in conditions identical to those that led to the formation of the 4-*O*-benzylated lactone (**6**), afforded 80% of methyl (methyl 8-*O*-benzyl-4,5-*O*-isopropyl-



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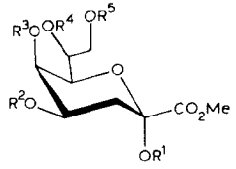
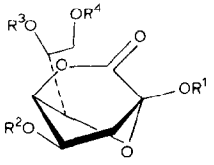
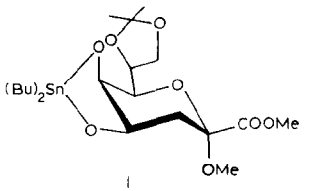


2 $R^1 = R^2 = R^3 = R^4 = R^5 = Ac$
4 $R^1 = Me$, $R^2 = R^3 = R^4 = R^5 = H$
5 $R^1 = Me$, $R^2 = R^3 = H$, R^4, $R^5 = CMe_2$
9 $R^1 = Me$, R^2, $R^3 = R^4$, $R^5 = CMe_2$
10 $R^1 = Me$, R^2, $R^3 = CMe_2$, $R^4 = R^5 = H$
11 $R^1 = Me$, R^2, $R^3 = CMe_2$, $R^4 = H$, $R^5 = Bn$
12 $R^1 = Me$, R^2, $R^3 = CMe_2$, $R^4 = Ac$, $R^5 = Bn$



3 $R^1 = R^2 = R^3 = R^4 = Ac$
6 $R^1 = Me$, $R^2 = Bn$, R^3, $R^4 = CMe_2$
7 $R^1 = Me$, $R^2 = R^3 = R^4 = H$
8 $R^1 = Me$, $R^2 = R^3 = R^4 = Ac$
13 $R^1 = Me$, $R^2 = R^4 = Bn$, $R^3 = H$
22 $R^1 = R^2 = R^3 = R^4 = Bz$



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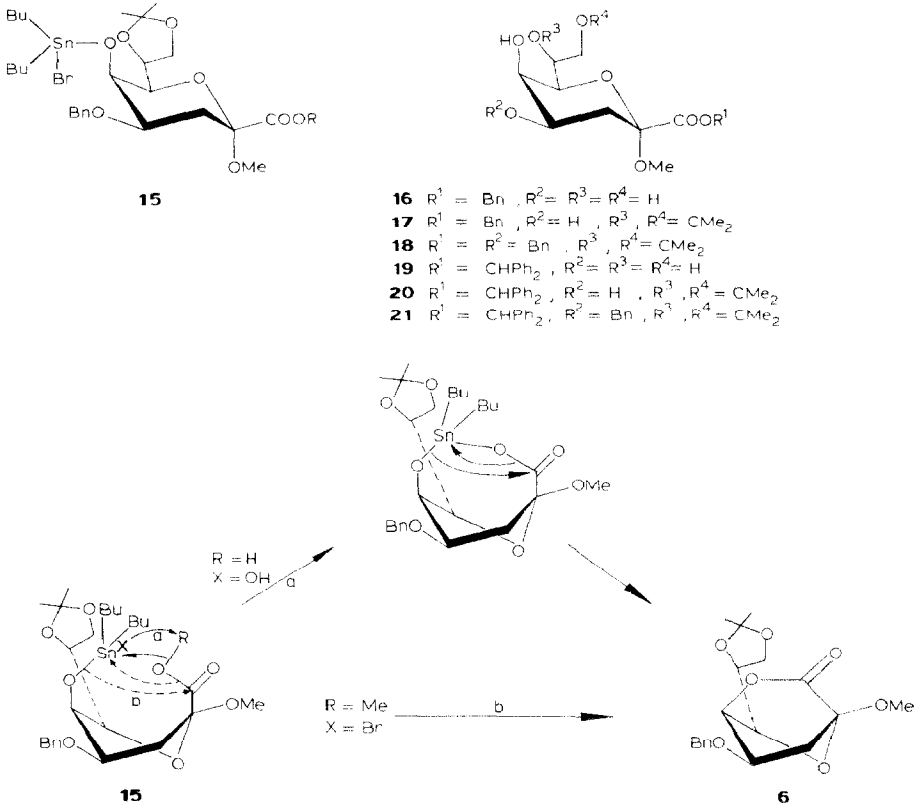
idene-α-D-*manno*-2-octulopyranosid)onate (**11**), the structure of which was determined unequivocally from its ^{1}H-n.m.r. spectrum and that of its acetylated derivative **12**. Although HO-7 is unsubstituted in **11**, a 1,7-lactone was apparently not formed, nor was this type of lactone seen when **4** was treated with dibutyltin oxide and 4 mol. equiv. of benzyl bromide: the main product (though formed in a yield of 25% only) was methyl 4,8-di-*O*-benzyl-3-deoxy-α-D-*manno*-2-octulopyranosidono-1,5-lactone (**13**), the structure of which was established by its ^{1}H-n.m.r. spectrum.

The formation of esters and lactones from acids in reactions involving use of dibutyltin oxide is well known[12], but transesterifications leading to lactones do not seem to have been observed. During the reaction of the stannylene acetal **14** with benzyl bromide, a rapidly formed and persistent intermediate was observed which was eventually transformed into **6**. In keeping with known reactions of stannylene acetals[14], this intermediate was probably **15**. The mechanism by which the lactone **6** is formed from the ester **5** should be different from that proposed[12,13] for ω-hydroxy-carboxylic acids (*cf.* Scheme 1, X = OH, R = H): by the mechanism proposed, a proton is released from acids while a methoxy (alkoxy) group appears to be released from esters (Scheme 1, X = Br, R = Me). It was observed concurrently that, while the lactone **6** was the only product isolated (73% yield) when the methyl ester **5** was benzylated, a 7:1 mixture (total yield, 91%) of **6** and the 4-*O*-benzyl benzyl ester **18** was produced from the benzyl ester **17**, and no lactone

was formed from the diphenylmethyl ester **20**, the product (88% yield) being the 4-*O*-benzyl diphenylmethyl ester **21** with the HO-5 group unsubstituted. The observed propensity to lactonise, namely, **5** (–COOMe) > **17** ($-COOCH_2Ph$) > **20** ($-COOCHPh_2$) could be related to either steric hindrance or the character of the leaving group [$MeO^- > PhCH_2O^- > (Ph)_2CHO^-$].

On acetylation of the ammonium salt of **1** with acetic anhydride, only a small proportion of the acetylated lactone **3** was formed, but benzoylation with benzoyl chloride and pyridine afforded 40% of the benzoylated lactone **22**. This result suggests that, during acetylation, a mixed anhydride is formed from the sugar acid and the acylating agent. If the latter is the weaker acid, *O*-acylation should prevail, if it is stronger, lactone formation should be favoured: this is in fact observed.



Scheme 1. Stannylate-promoted lactonisation of ω-hydroxy acids (a, refs. 12 and 13) and esters (b).

The acetylated 1,5-lactone **3** can be prepared readily, albeit in moderate yield (29%), if the pyridinium salt of **1** is treated first with dicyclohexylcarbodi-imide and then with acetic anhydride.

Although molecular models indicated that the 1,7- and 1,8-lactones can form as easily as the 1,5-lactone, only the last type was isolated in the above-described

reactions. When only HO-7 was available, lactone formation did not occur. This phenomenon remains to be rationalized.

In aqueous acid, the 7,8-*O*-isopropylidene group can be removed relatively selectively from the diacetal **9** to yield the 4,5-monoacetal **10**, but the latter readily undergoes acetal migration in n.m.r.-grade $CDCl_3$ if the solution is stored for a few hours at ≈20°, as shown by the ^{1}H-n.m.r. spectrum. For preparative purposes, the use of the isopropylidene group is, therefore, not recommended.

EXPERIMENTAL

Evaporations were carried out under water-pump vacuum at 40°. Products were dried *in vacuo*; solutions in organic solvents were dried with Na_2SO_4. Melting points were determined on a Kofler hot-plate and are uncorrected. Optical rotations were measured at 19–22°. T.l.c. was performed on Silica Gel 60 F_{254} on aluminium foil (Merck) with detection by charring with sulphuric acid (10% in ethanol). Column chromatography was performed on Silica Gel 60 (70–230 mesh, Merck). Chemical shifts of ^{1}H resonances were measured at room temperature and are given as p.p.m. with respect to internal Me_4Si.

*Methyl (methyl 3-deoxy-α-*D-manno-*2-octulopyranosid)onate* (**4**). — Methanolic 2.55M HCl (35 mL) was added, dropwise, to a stirred solution of methyl (2,4,5,7,8-penta-*O*-acetyl-3-deoxy-α-D-*manno*-2-octulopyranosid)onate[3,9] (4 g, 8.8 mmol) in anhydrous methanol (55 mL), and the mixture was boiled under reflux for 3 h. T.l.c. (7:1:1 ethyl acetate–benzene–methanol) then showed the reaction to be complete (product R_F 0.39). Amberlite IR-45 (HO^-) resin was added to neutralize the cooled mixture, which was then filtered and concentrated. Column (20 × 3.5 cm) chromatography (8:2 chloroform–methanol) of the dry residue gave **4**, isolated as a colourless syrup (2 g, 84%; R_F 0.51), which was pure according to its ^{1}H-n.m.r. spectrum and was further characterized as the tetra-acetate (1:1 acetic anhydride–pyridine, 20°, 24 h), m.p. 110°, $[\alpha]_D$ +91.5° (*c* 1, chloroform); lit.[9] m.p. 110°, $[\alpha]_D$ +77° (*c* 0.6, chloroform).

*Methyl (methyl 3-deoxy-7,8-*O*-isoproplidene-α-*D*-manno-2-octulopyranosid)-onate* (**5**). — 2-Methoxypropene (1.65 mL, 2 mol. equiv.) was added portionwise (0.3 mL) within 4 h to a stirred solution of glycoside **4** (2.09 g, 7.86 mmol) in anhydrous 1,4-dioxane (80 mL) and *N,N*-dimethylformamide (40 mL) containing toluene-*p*-sulphonic acid (200 mg), the temperature of the mixture being maintained at 0–5°. The mixture was stirred overnight at room temperature, diluted with 1:1 ethyl acetate–ether (150 mL), washed with aqueous (2%) sodium hydrogencarbonate (2 × 50 mL) and saturated aqueous NaCl (2 × 50 mL), dried, and concentrated. Column (15 × 3.5 cm) chromatography (4:1 ethyl acetate–hexane) of the syrupy residue gave **5** (1.73 g, 72%) isolated as a colourless oil (R_F 0.3, same solvent) having $[\alpha]_D$ +51.5° (*c* 1, chloroform) (Found: C, 50.7; H, 7.40. $C_{13}H_{22}O_8$ calc.: C, 51.0; H, 7.2%). ^{1}H-N.m.r. data (360 MHz, $CDCl_3$): δ 1.38 and 1.43 (2 s, each 3 H, CMe_2), 1.88 (dd, 1 H, $J_{3a,3e}$ 13, $J_{3a,4}$ 11.5 Hz, H-3*a*), 2.15 (dd, 1 H, $J_{3a,3e}$

13, $J_{3e,4}$ 5 Hz, H-3*e*), 3.24 (s, 3 H, OMe), 3.53 (dd, 1 H, $J_{6,5}$ 1, $J_{6,7}$ 9 Hz, H-6), 3.81 (s, 3 H, CO_2Me), 4.00 (dd, 1 H, $J_{8,8'}$ 9, $J_{8,7}$ 4.5 Hz, H-8), 4.02 (m, 1 H, $J_{5,6}$ 1 Hz, H-5), 4.05 (m, 1 H, $J_{4,3e}$ 5, $J_{4,3a}$ 11.5 Hz, H-4), 4.19 (dd, 1 H, $J_{8,8'}$ 9, $J_{7,8'}$ 6 Hz, H-8'), 4.42 (ddd, 1 H, $J_{6,7}$ 9, $J_{7,8}$ 4.5, $J_{7,8'}$ 6 Hz, H-7).

*Methyl (methyl 3-deoxy-4,5:7,8-di-*O*-isopropylidene-*α-D-manno-*2-octulopyranosid)onate* (**9**). — The glycoside **4** (2 g, 7.52 mmol) was treated as described for the preparation of **5**, but using an excess of 2-methoxypropene (3.6 mL, 5 mol. equiv.) and 6:4 ethyl acetate–hexane for column chromatography, to give **9** (1.79 g, 70%), m.p. 120–123°, $[\alpha]_D$ +43° (*c* 1, chloroform) (Found: C, 55.4; H, 7.55. $C_{16}H_{26}O_8$ calc.: C, 55.5, H, 7.5%). ^{1}H-N.m.r. data (360 MHz, $CDCl_3$): δ 1.32, 1.38, 1.42, 1.44 (4 s, each 3 H, 2 CMe_2), 1.86 (dd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 3 Hz, H-3), 2.79 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 4 Hz, H-3'), 3.23 (s, 3 H, OMe), 3.57 (dd, 1 H, $J_{6,5}$ 2, $J_{6,7}$ 8.0 Hz, H-6), 3.80 (s, 3 H, CO_2Me), 4.02 (dd, 1 H, $J_{8,8'}$ 9, $J_{8,7}$ 4.5 Hz, H-8), 4.17 (dd, 1 H, $J_{8,8'}$ 9, $J_{8',7}$ 6 Hz, H-8'), 4.31 (dd, 1 H, $J_{5,4}$ 7.5, $J_{5,6}$ 2 Hz, H-5), 4.42 (m, 1 H, $J_{7,6}$ 8, $J_{7,8}$ 4.5, $J_{7,8'}$ 6 Hz, H-7), 4.52 (m, 1 H, $J_{3',4}$ 4, $J_{3,4}$ 3, $J_{4,5}$ 7.5 Hz, H-4).

*Methyl (methyl 3-deoxy-4,5-*O*-isopropylidene-*α-D-manno-*2-octulopyranosid)onate* (**10**). — 0.33M Trifluoroacetic acid in methanol–water (1:3, 40 mL) was added to a stirred solution of **9** (1.65 g, 4.77 mmol) in methanol (40 mL); the reaction was monitored by t.l.c. (70:15:15 ethyl acetate–benzene–methanol; R_F of **10** 0.61) and allowed to proceed for 2 h at room temperature. The acid was neutralized with Amberlite IR-45 (HO^-) resin, and the mixture was filtered and brought to dryness. Column (15 × 3.5 cm) chromatography (9:1 ethyl acetate–hexane) of the residue and crystallization from ethyl acetate–hexane gave **10** (620 mg, 42%), m.p. 139–142°, $[\alpha]_D$ +56° (*c* 1, chloroform) (Found: C, 51.1; H, 7.4. $C_{13}H_{22}O_8$ calc.: C, 51.0; H, 7.2%). ^{1}H-N.m.r. data (360 MHz, $CDCl_3$): δ 1.33, 1.43 (2 s, each 3 H, CMe_2), 1.92 (dd, 1 H, $J_{3,3'}$ 15.5, $J_{3,4}$ 3.5 Hz, H-3), 2.63 (dd, 1 H, $J_{3',3}$ 15.5, $J_{3',4}$ 4.5 Hz, H-3'), 3.23 (s, 3 H, OMe), 3.75 (dd, 1 H, $J_{6,5}$ 2, $J_{6,7}$ 7.5 Hz, H-6), 3.8–3.9 (m, 2 H, H-8,8'), 3.81 (s, 3 H, CO_2Me), 4.03 (m, 1 H, $J_{7,6}$ 7.5 Hz, H-7), 4.35 (m, 1 H, $J_{5,6}$ 2, $J_{5,4}$ 7.5 Hz, H-5), 4.53 (m, 1 H, $J_{4,3'}$ 4.5, $J_{4,3}$ 3.5, $J_{4,5}$ 7.5 Hz, H-4).

Besides **10**, **9** (340 mg, 20%) and **4** (350 mg, 27%) were recovered.

*Methyl 4-*O*-benzyl-3-deoxy-7,8-*O*-isopropylidene-*α-D-manno-*2-octulopyranosidono-1,5-lactone* (**6**). — A mixture of dibutyltin oxide (1.45 g, 1 mol. equiv.) and **5** (1.73 g, 5.65 mmol) in anhydrous benzene (170 mL) was heated to reflux for 4 h, using a Dean–Stark water separator. Tetrabutylammonium bromide (1.82 g, 1 mol. equiv.), sodium iodide (850 mg, 1 mol. equiv.), and benzyl bromide (1.7 mL, 2 mol. equiv.) were added to the clear solution and boiling under reflux was continued for 19 h. The cooled, diluted (toluene, 50 mL) solution was washed successively with cold, saturated aqueous $NaHCO_3$ (100 mL) and water (2 × 50 mL), dried, and concentrated. Following column (15 × 3.5 cm) chromatography (3:7 ethyl acetate–cyclohexane; t.l.c., R_F 0.40), appropriate fractions were combined and brought to dryness. The residue was taken up in benzene, the solvent was removed by lyophilization, and the solid residue (1.5 g, 73%) was crystallized from ether, to give **6**, m.p. 92–94°, $[\alpha]_D$ −13° (*c* 1, chloroform) (Found: C, 62.55; H, 6.7.

$C_{19}H_{24}O_7$ calc.: C, 62.6; H, 6.6%). ^{1}H-N.m.r. data (360 MHz, $CDCl_3$): δ 1.36, 1.43 (2 s, each 3 H, CMe_2), 2.02 (dd, 1 H, $J_{3',3}$ 15, $J_{3,4}$ 2 Hz, H-3), 2.55 (dd, 1 H, $J_{3,3'}$ 15, $J_{3',4}$ 9 Hz, H-3'), 3.55 (s, 3 H, OMe), 3.69 (d, 1 H, $J_{6,7}$ 7 Hz, H-6), 3.98 [m, 2 H, H-4 and H-8 (or 8')], 4.13 [m, 2 H, H-7 and H-8 (or 8')], 4.6 (q, 2 H, OCH_2 Ph), 5.00 (d, 1 H, $J_{5,4}$ 1.5, $J_{5,6}$ 0 Hz, H-5), 7.32 (m, 5 H, Ph).

*Methyl (methyl 8-*O*-benzyl-3-deoxy-4,5-*O*-isopropylidene-α-*D*-manno-2-octulopyranosid)onate* (**11**). — Benzylation of **10** (0.57 g, 1.86 mmol), under conditions identical to those described for **5**, gave, after column chromatography, **11** (0.60 g, 81%) as a colourless oil, $[\alpha]_D$ +41° (*c* 1, chloroform) (Found: C, 60.55; H, 7.2. $C_{20}H_{28}O_8$ calc.: C, 60.6; H, 7.1%). ^{1}H-N.m.r. data (360 MHz, $CDCl_3$): δ 1.32, 1.43 (2 s, each 3 H, CMe_2), 1.89 (dd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 3.5 Hz, H-3), 2.67 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 4.5 Hz, H-3'), 3.14 (s, 3 H, OMe), 3.69–3.89 (m, 3 H, H-6,8,8'), 3.77 (s, 3 H, CO_2Me), 4.18 (m, 1 H, H-7), 4.40 (1 H, dd, $J_{5,4}$ 7, $J_{5,6}$ 2 Hz, H-5), 4.50 (1 H, m, $J_{4,3'}$ 4.5, $J_{4,3}$ 3.5, $J_{4,6}$ 7.0 Hz, H-4), 4.60 (2 H, q, OCH_2Ph), 7.30 (m, 5 H, Ph).

*Methyl (methyl 7-*O*-acetyl-8-*O*-benzyl-3-deoxy-4,5-*O*-isopropylidene-α-*D*-manno-2-octulopyranosid)onate* (**12**). — Compound **11** (49 mg, 0.12 mmol) was treated with 1:1 pyridine and acetic anhydride (800 μL) for 12 h at room temperature. Toluene (2 mL) was added and volatile material was evaporated off. Column (70 × 5 mm) chromatography (3:7 ethyl acetate–toluene; t.l.c., R_F 0.51) of the residue gave **12** (43 mg, 79%) as a colourless oil. ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 1.23, 1.31 (2 s, each 3 H, CMe_2), 1.92 (dd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 3.7 Hz, H-3), 2.07 (s, 3 H, Ac), 2.58 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 5 Hz, H-3'), 3.15 (s, 3 H, OMe), 3.78 (s, 3 H, CO_2Me), 3.8–3.9 (m, 2 H, H-8,8'), 4.09 (dd, 1 H, $J_{6,5}$ 2, $J_{6,7}$ 8.3 Hz, H-6), 4.18 (dd, 1 H, $J_{5,4}$ 7, $J_{5,6}$ 2 Hz, H-5), 4.48 (m, 1 H, $J_{4,3}$ 3.7, $J_{4,3'}$ 5, $J_{4,5}$ 7 Hz, H-4), 4.55 (s, 2 H, OCH_2Ph), 5.27 (dt, 1 H, $J_{7,6}$ 8.3, $J_{7,8}$ ≃3.3, $J_{7,8'}$ ≃3.3 Hz, H-7), 7.2–7.35 (m, 5 H, Ph). Other physical constants were not determined.

*Methyl 4,8-di-*O*-benzyl-3-deoxy-α-*D*-manno-2-octulopyranosidono-1,5-lactone* (**13**). — A mixture of **4** (850 mg, 3.2 mmol) and dibutyltin oxide (1.6 g, 2 mol. equiv.) in dry toluene (60 mL) was boiled under reflux, using a Dean–Stark water separator. After 8 h, tetrabutylammonium bromide (2.06 g, 2 mol. equiv.), sodium iodide (950 mg, 2 mol. equiv.), and benzyl bromide (2 mL, 4 mol. equiv.) were added and boiling under reflux was continued for 15 h. The reaction was monitored by t.l.c. (4:6 ethyl acetate–cyclohexane, R_F of **13** 0.56). The cooled mixture was diluted with toluene (50 mL), washed with saturated, aqueous $NaHCO_3$ (50 mL), then with water (2 × 50 mL). The combined aqueous washings were extracted with ether (50 mL), and the combined organic layers were dried and concentrated. Column (18.5 × 2.5 cm) chromatography (25:75 ethyl acetate–cyclohexane; t.l.c., R_F 0.20) of the residue gave **13** as a colourless oil (300 mg, 23%), $[\alpha]_D$ +6.1° (*c* 1, chloroform) (Found: C, 66.4; H, 6.4. $C_{23}H_{26}O_7$ calc.: C, 66.7; H, 6.3%). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 1.93 (ddd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 2.25, $J_{3,5}$ 1 Hz, H-3), 2.47 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 8.8 Hz, H-3'), 3.48 (s, 3 H, OMe), 3.55 (ddd, 1 H, $J_{7,6}$ 10, $J_{7,8}$ or $J_{7,8'}$ 2, $J_{7,8}$ or $J_{7,8'}$ 2.5 Hz, H-7), 3.64 (d, 1 H, $J_{6,7}$ 10, $J_{6,5}$ ≃0 Hz, H-6), 3.74 (m, 2 H, H-8,8'), 3.87 (dt, 1 H, $J_{4,3}$ 2.25, $J_{4,3'}$ 8.8, $J_{4,5}$ 2.5 Hz, H-4), 4.50 (q, 4 H, OCH_2Ph), 5.05 (dd, 1 H, $J_{5,4}$ 2.5, $J_{5,6}$ 0, $J_{5,3}$ 1 Hz, H-5), 7.26 (m, 10 H, 2 Ph).

*Methyl 3-deoxy-α-*D-manno*-2-octulopyranosidono-1,5-lactone* (**7**). — A solution of **6** (56 mg, 0.153 mmol) in aqueous 90% acetic acid (1 mL) was kept for 30 min at 100°, 10% Pd/C (50 mg) was added to the cooled solution, and the stirred mixture was treated with H_2 for 30 min, then filtered, and concentrated. Column (6.2 × 2.4 cm) chromatography (8:2 chloroform–methanol; t.l.c., R_F 0.48) gave **7** as a colourless oil (23 mg, 63%). The $[\alpha]_D$ was not determined (material insufficient). ^{1}H-N.m.r. data (250 MHz, CD_3OD): δ 1.75 (ddd, 1 H, $J_{3,3'}$ 14.5, $J_{3,4}$ 2, $J_{3,5}$ 1 Hz, H-3), 2.67 (dd, 1 H, $J_{3',3}$ 14.5, $J_{3',4}$ 9 Hz, H-3'), 3.55 (s, 3 H, OMe), 3.56 (dd, 1 H, $J_{7,6}$ 9.5, $J_{7,8}$ 5, $J_{7,8'}$ 2.5 Hz, H-7), 3.65 (dd, 1 H, $J_{8,8'}$ 11.5, $J_{8,7}$ 5 Hz, H-8), 3.80 (dd, 1 H, $J_{8,8'}$ 11.5, $J_{8',7}$ 2.5 Hz, H-8'), 3.92 (d, 1 H, $J_{6,5}$ 0, $J_{6,7}$ 9.5 Hz, H-6), 4.29 (dt, 1 H, $J_{3',4}$ 9, $J_{3,4}$ 2, $J_{4,5}$ 2 Hz, H-4), 4.88 (dd, 1 H, $J_{5,4}$ 2, $J_{5,6}$ 0, $J_{5,3}$ 1 Hz, H-5).

*Methyl 4,7,8-tri-*O*-acetyl-3-deoxy-α-*D-manno*-2-octulopyranosidono-1,5-lactone* (**8**). — The isopropylidene and benzyl groups were removed from **6** (77.2 mg) as described for the preparation of **7**. Anhydrous pyridine (2 mL) and acetic anhydride (2 mL) were added to the filtered solution obtained after hydrogenation, the solvents were removed, and dry toluene was evaporated from the residue which was then treated with 1:1 anhydrous pyridine–acetic anhydride (2 mL) containing 4-dimethylaminopyridine (20 mg). The mixture stood for 24 h at room temperature, and was then concentrated. Column (7 × 2 cm) chromatography (1:1 ethyl acetate–cyclohexane; t.l.c., R_F 0.55) gave **8** as a colourless oil (25 mg, 78%), $[\alpha]_D$ −2.6° (*c* 1, chloroform) (Found: C, 49.9; H, 5.7. $C_{15}H_{20}O_{10}$ calc.: C, 50.0; H, 5.6%). ^{1}H-N.m.r. data (400 MHz, C_6D_6): δ 1.49, 1.62, 1.70 (3 s, each 3 H, 3 Ac), 1.81 (ddd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 2.5, $J_{3,5}$ 0.8 Hz, H-3), 2.35 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 9.5 Hz, H-3'), 3.50 (s, 3 H, OMe), 3.85 (d, 1 H, $J_{6,7}$ 9.0 Hz, H-6), 4.00 (dd, 1 H, $J_{8,8'}$ 12.5, $J_{8,7}$ 4.1 Hz, H-8), 4.62 (dd, 1 H, $J_{8',8}$ 12.5, $J_{8',7}$ 2.5 Hz, H-8'), 4.63 (dt, 1 H, $J_{4,3'}$ 9.5, $J_{4,3}$ 2.5, $J_{4,5}$ 2.3 Hz, H-4), 4.70 (dd, 1 H, $J_{5,4}$ 2.3, $J_{5,6}$ 0, $J_{5,3}$ 0.8 Hz, H-5), 5.24 (ddd, 1 H, $J_{7,6}$ 9.0, $J_{7,8}$ 4.1, $J_{7,8'}$ 2.5 Hz, H-7).

*Benzyl (methyl 3-deoxy-α-*D-manno*-2-octulopyranosid)onate* (**16**). — A solution of **4** (416 mg, 1.56 mmol) in 0.1M NaOH (25 mL) was stirred for 2 h at room temperature, then decationized with IR-77 (H^+) resin, and filtered. Methanol (70 mL) was added followed by a solution of phenyldiazomethane in ether until the solution remained neutral. After removal of the solvents, a solution of the residue in water (30 mL) was extracted with ether (2 × 10 mL), and the water was evaporated. Column (20 × 2.3 cm) chromatography (9:1 chloroform–methanol; t.l.c., R_F 0.24) then gave **16** as a crystalline solid (350 mg, 66%). Recrystallization (yield, 50%) from dichloromethane–carbon tetrachloride gave material having m.p. 46–49°. Although reproducible, this value is probably that of a solvate. Compound **16** and the diphenylmethyl ester **19** are very hygroscopic compounds that deliquesce even in a desiccator. Neither a satisfactory elementary analysis nor a reliable $[\alpha]_D$ value could be obtained. The compound was characterized both by its ^{1}H-n.m.r. spectrum and as its 7,8-isopropylidene acetal **17**. ^{1}H-N.m.r. data (60 MHz, $CDCl_3$): δ 2–2.2 (m, 2 H, H-3*a*,3*e*), 3.2 (s, 3 H, OMe), 3.6–4.1 (m, 6 H, H-4,5,6,7,8,8'), 5.3 (s, 2 H, OCH_2Ph), 7.2–7.4 (m, 5 H, Ph).

*Benzyl (methyl 3-deoxy-7,8-*O*-isopropylidene-α-*D*-manno-2-octulopyranosid)onate* (**17**). — 2-methoxypropene (500 μL, 2.5 mol. equiv.) was added dropwise during 5 h to a stirred, cold (−5°) solution of **16** (700 mg, 2.08 mmol) in *N,N*-dimethylformamide and 1,4-dioxane (2:1, 30 mL), containing toluene-*p*-sulphonic acid (100 mg). The condensation was monitored by t.l.c. (8:2 ethyl acetate–cyclohexane). After 2 h, the mixture was diluted with dichloromethane (20 mL), solid $NaHCO_3$ was added, the neutral suspension was filtered, the solids were washed with 8:2 chloroform–methanol, and the combined organic layers were washed with aqueous 2% $NaHCO_3$ (30 mL) and then water (2 × 30 mL), dried, and concentrated. Column (15 × 3.5 cm) chromatography (1:1 ethyl acetate–cyclohexane; t.l.c., R_F 0.23) of the residue gave **17** (550 mg, 70%) as a colourless liquid, $[\alpha]_D$ +51° (*c* 1, chloroform) (Found: C, 59.8; H, 7.0. $C_{19}H_{26}O_8$ calc.: C, 59.7; H, 6.8%). ^{1}H-N.m.r. data (60 MHz, $CDCl_3$): δ 2.02–2.2 (m, 2 H, H-3*a*,3*e*), 3.2 (s, 3 H, OMe), 3.6–4.5 (m, 6 H, H-4,5,6,7,8,8′), 5.2 (s, 2 H, OCH_2Ph), 7.2–7.3 (m, 5 H, Ph).

Upon treatment with dibutyltin oxide and benzyl bromide under conditions used to benzylate **5, 17** afforded **6** and a small amount of benzyl (methyl 4-*O*-benzyl-7,8-*O*-isopropylidene-α-*D*-*manno*-2-octulopyranosid)onate (**18**), $[\alpha]_D$ +39° (*c* 0.8, chloroform). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 1.34 and 1.37 (2 s, each 3 H, CMe_2), 1.95 (dd, 1 H, $J_{3,3'}$ 12, $J_{3,4}$ 11.9 Hz, H-3), 2.17 (dd, 1 H, $J_{3',3}$ 12, $J_{3',4}$ 5 Hz, H-3′), 3.14 (s, 3 H, OMe), 3.46 (dd, 1 H, $J_{6,5}$ 1.6, $J_{6,7}$ 8 Hz, H-6), 3.86 (dq, 1 H, $J_{4,3}$ 11.9, $J_{4,3'}$ 5, $J_{4,5}$ 2.8 Hz, H-4), 3.97 (dd, 1 H, $J_{8,8'}$ 8, $J_{8,7}$ 5 Hz, H-8), 4.08 (m, 1 H, $J_{5,3}$ 0.8, $J_{5,4}$ 2.8, $J_{5,6}$ 1.6 Hz, H-5), 4.14 (dd, 1 H, $J_{8',8}$ 8, $J_{8',7}$ 6 Hz, H-8′), 4.42 (m, 1 H, $J_{7,6}$ 8, $J_{7,8}$ 5, $J_{7,8'}$ 6 Hz, H-7), 4.54 (m, 2 H, OCH_2Ph), 5.16 (m, 2 H, CO_2CH_2Ph), 7.25–7.35 (m, 10 H, 2 Ph).

*2,4,7,8-Tetra-*O*-acetyl-3-deoxy-α-*D*-manno-2-octulopyranosono-1,5-lactone* (**3**). — (*a*) Acetic anhydride (35 mL) was added to a cold (0°), stirred solution of ammonium 3-deoxy-α-*D*-*manno*-2-octulopyranosonate monohydrate (4 g, 14.6 mmol) in anhydrous pyridine (35 mL) containing 4-dimethylaminopyridine (300 mg). The stirred mixture was allowed to reach room temperature overnight. Methanol (10 mL) and, after 1 h, dichloromethane (100 mL) were added, and the solution was washed with 0.9M sulphuric acid (250 mL) and then water (2 × 150 mL), dried, and concentrated. To a solution of the residue in methanol (100 mL) ethereal diazomethane was added until neutrality. Upon t.l.c. (6:4 ethyl acetate–cyclohexane), the main component had R_F 0.5. Column (23 × 4.5 cm) chromatography (1:1 ethyl acetate–cyclohexane) of the material remaining after removal of the solvent gave methyl 2,4,5,7,8-penta-*O*-acetyl-3-deoxy-α-*D*-*manno*-2-octulopyranosonate (6.77 g, 51.5%), m.p. 157–159° (from ether), R_F 0.5 (6:4 ethyl acetate–cyclohexane), followed by **3** (R_F 0.46). The appropriate fractions were combined and concentrated, and the residue was crystallized from ether to give **3** (240 mg, 4.5%), m.p. 123–125°, $[\alpha]_D$ +4.3° (*c* 1, chloroform) (Found: C, 49.6; H, 5.3. $C_{16}H_{20}O_{11}$ calc.: C, 49.5; H, 5.15%). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 2.05–2.25 (4 s + 1 m, 13 H, 4 Ac and H-3), 2.80 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 9 Hz, H-3′), 4.15 (dd, 1 H, $J_{8,8'}$ 12.5, $J_{8,7}$ 4 Hz, H-8), 4.45 (d, 1 H, $J_{6,7}$ 9, $J_{6,5}$ 0 Hz, H-6), 4.59

(dd, 1 H, $J_{8',8}$ 12.5, $J_{8',7}$ 2.5 Hz, H-8'), 4.98 (d, 1 H, $J_{5,4}$ 2, $J_{5,6}$ ≈0 Hz, H-5), 5.15 (ddd, 1 H, $J_{7,6}$ 9, $J_{7,8}$ 4, $J_{7,8'}$ 2.5 Hz, H-7), 5.32 (dt, 1 H, $J_{4,3'}$ 9, $J_{4,3}$ 2.5, $J_{4,5}$ 2 Hz, H-4).

(*b*) Amberlite IR-77 (pyridinium) resin (10 mL) was added to an aqueous solution (20 mL) of ammonium 3-deoxy-α-D-*manno*-2-octulopyranosonate (1.1 g, 4 mmol) at 0° to remove ammonium ions. Some pyridine was added to the filtered solution, the solvents were removed, and anhydrous pyridine (5 × 50 mL) was evaporated from the residue which was then dissolved in anhydrous pyridine (50 mL) containing dicyclohexylcarbodi-imide (1 g, 1.1 mol. equiv.) and 4-dimethylaminopyridine (250 mg, 0.55 mol. equiv.). The mixture was stirred for 48 h at room temperature, the appearance of a major product (R_F 0.5) being detected by t.l.c. (60:30:0.5 chloroform–methanol–formic acid). Acetic anhydride (3.5 mL, 8 mol. equiv.) was added dropwise to the cooled (2°), stirred mixture, and stirring was continued for 24 h. The mixture was concentrated. Column (17.1 × 4.6 cm) chromatography (1:1 ethyl acetate–cyclohexane; t.l.c., R_F 0.46) of the residue gave **3** (450 mg, 29%), m.p. 123–125° alone and in admixture with the material obtained in (*a*). The ^{1}H-n.m.r. spectrum was identical to that described for the material obtained under (*a*).

*Diphenylmethyl (methyl 3-deoxy-α-*D-manno-*2-octulopyranosid)onate* (**19**). — A stirred solution of **4** (1.5 g, 5.7 mmol) in 2:8 water–methanol (80 mL), 0.1M with respect to NaOH, was kept for 4 h at 20°, then diluted with methanol (50 mL), and neutralized with Dowex 50 (H^+) resin, and solids were filtered off. Diphenyldiazomethane (4 g, 3.5 mol. equiv.) in ether (20 mL) was added to the stirred filtrate during 1 h. The reaction was monitored by t.l.c. (9:1 chloroform–methanol; R_F 0.33). During the next 24 h, portions of solid diphenyldiazomethane (3 g) were added to obtain a neutral solution. Solvents were evaporated off and column (17.5 × 5.5 cm) chromatography (9:1 chloroform–methanol) of the residue gave **19** (1.1 g, 50%) as a colourless oil. ^{1}H-N.m.r. data (90 MHz, $CDCl_3/CD_3OD$): δ 2.0 (t, 1 H, $J_{3a,3e}$ 12, $J_{3a,4}$ 12 Hz, H-3*a*), 2.20 (dd, 1 H, $J_{3a,3e}$ 12, $J_{3e,4}$ 4.5 Hz, H-3*e*), 3.08 (s, 3 H, OMe), 3.4–4.0 (6 H, m, H-4,5,6,7,8,8'), 6.85 (1 H, C*H*Ph$_2$), 7.3 (s, 10 H, 2 Ph).

*Diphenylmethyl (methyl 3-deoxy-7,8-*O*-isopropylidene-α-*D-manno-*2-octulopyranosid)onate* (**20**). — 2-Methoxypropene (220 μL, 1.2 mol. equiv.) was added to a stirred mixture of **19** (947 mg, 2.265 mmol), toluene-*p*-sulphonic acid (50 mg), and anhydrous copper sulphate (200 mg) in 1,4-dioxane (35 mL) kept at +4°. The mixture was allowed to reach room temperature and stirring was continued for 2 h. Solid sodium hydrogencarbonate was added, the neutral mixture was filtered, and the solids were washed first with dichloromethane (50 mL) and then with chloroform–methanol (8:2, 50 mL). The filtrate and washings were combined, washed with saturated aqueous sodium hydrogencarbonate (40 mL) and water (2 × 40 mL), dried, and concentrated. Column (15 × 2.5 cm) chromatography [1:1 ethyl acetate–cyclohexane (250 mL), then 8:2 chloroform–methanol (300 mL)] of the residue gave, first, the crystalline 4,5:7,8-di-isopropylidene acetal (280 mg,

25%), m.p. 117–118°, $[\alpha]_D$ +23° (*c* 0.8, chloroform), R_F 0.55 (t.l.c., 3:7 ethyl acetate–cyclohexane) (Found: C, 67.4; H, 6.9. $C_{28}H_{34}O_8$ calc.: C, 67.5; H, 6.8%). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 1.15, 1.20, 1.31, 1.37 (4 s, each 3 H, 2 CMe_2), 1.84 (dd, 1 H, $J_{3,3'}$ 15.8, $J_{3,4}$ 3 Hz, H-3), 2.77 (dd, 1 H, $J_{3',3}$ 15.8, $J_{3',4}$ 4.2 Hz, H-3′), 3.00 (s, 3 H, OMe), 3.54 (dd, 1 H, $J_{6,7}$ 7.8, $J_{6,5}$ 2 Hz, H-6), 3.99 (dd, 1 H, $J_{8,8'}$ 8.4, $J_{8,7}$ 4.8 Hz, H-8), 4.11 (dd, 1 H, $J_{8',8}$ 8.4, $J_{8',7}$ 6 Hz, H-8′), 4.21 (dd, 1 H, $J_{5,4}$ 7.8, $J_{5,6}$ 2 Hz, H-5), 4.34 (m, 1 H, $J_{7,6}$ 7.8, $J_{7,8}$ 4.8, $J_{7,8'}$ 6 Hz, H-7), 4.44 (m, 1 H, $J_{4,3}$ 3, $J_{4,3'}$ 4.2, $J_{4,5}$ 7.8 Hz, H-4), 6.88 (s, 1 H, C*H*Ph_2), 7.3–7.4 (m, 10 H, 2 Ph).

Eluted second was **20** as an oil (480 mg, 47%), R_F 0.28 (t.l.c., 1:1 ethyl acetate–cyclohexane), $[\alpha]_D$ +31° (*c* 1, chloroform) (Found: C, 65.3; H, 6.7. $C_{25}H_{30}O_8$ calc.: C, 65.5; H, 6.55%). ^{1}H-N.m.r. data (90 MHz, $CDCl_3$): δ 1.35, 1.40 (2 s, each 3 H, CMe_2), 1.82 (dd, 1 H, $J_{3a,3e} \simeq 12$, $J_{3a,4} \simeq 10.5$ Hz, H-3*a*), 2.22 (dd, 1 H, $J_{3e,3a} \simeq 12$, $J_{3e,4} \simeq 6$ Hz, H-3*e*), 3.08 (s, 3 H, OMe), 3.40–4.5 (m, 6 H, H-4,5,6,7,8,8′), 6.83 (s, 1 H, C*H*Ph_2), 7.27 (m, 10 H, 2 Ph). Eluted third was **19** (80 mg, 9%), R_F 0.33 (t.l.c., 9:1 chloroform–methanol).

*Diphenylmethyl (methyl 4-*O*-benzyl-3-deoxy-7,8-*O*-isopropylidene-α-*D*-manno-2-octulopyranosid)onate* (**21**) — A mixture of **20** (384 mg, 0.84 mmol) and dibutyltin oxide (230 mg, 1 mol. equiv.) in benzene (35 mL) was boiled under reflux for 3 h, using a Dean–Stark water-separator. Tetrabutylammonium bromide (275 mg, 1 mol. equiv.), sodium iodide (150 mg, 1.2 mol. equiv.), and benzyl bromide (255 mg, 2 mol. equiv.) were added successively, and boiling under reflux was maintained for 4 h. The reaction was monitored by t.l.c. (3:7 ethyl acetate–cyclohexane; R_F 0.44). The cooled mixture was then diluted with toluene (50 mL), filtered, and washed successively with cold, saturated aqueous sodium hydrogencarbonate (20 mL) and water (2 × 20 mL), the aqueous extracts being re-extracted with toluene (2 × 20 mL). The combined organic phases were dried and concentrated. Column (12.5 × 2.5 cm) chromatography (3:7 ethyl acetate–cyclohexane) of the residue gave **21** as a colourless oil (403 mg, 88%), $[\alpha]_D$ +26° (*c* 1, chloroform) (Found: C, 69.9; H, 6.6. $C_{32}H_{36}O_8$ calc.: C, 70.1; H, 6.6%). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 1.40, 1.45 (2 s, each 3 H, CMe_2), 2.00 (t, 1 H, $J_{3e,3a}$ 11, $J_{3a,4}$ 11 Hz, H-3*a*), 2.25 (dd, 1 H, $J_{3e,3a}$ 11, $J_{3e,4}$ 5 Hz, H-3*e*), 3.15 (s, 3 H, OMe), 3.53 (d, 1 H, $J_{6,7}$ 7.0 Hz, H-6), 3.94 (dq, 1 H, $J_{4,3a}$ 11, $J_{4,3e}$ 5, $J_{4,5}$ 2.5 Hz, H-4), 4.06 (dd, 1 H, $J_{8,8'}$ 8.5, $J_{8,7}$ 5.2 Hz, H-8), 4.13 (d, 1 H, $J_{5,4}$ 2.5, $J_{5,6} \simeq 0$ Hz, H-5), 4.19 (dd, 1 H, $J_{8,8'}$ 8.5, $J_{8',7}$ 6 Hz, H-8′), 4.48 (q, 1 H, $J_{7,6}$ 7, $J_{7,8}$ 5.2, $J_{7,8'}$ 6 Hz, H-7), 6.95 (s, 1 H, C*H*Ph_2), 7.35 (s, 15 H, 3 Ph).

*2,4,7,8-Tetra-*O*-benzoyl-3-deoxy-α-*D*-manno-2-octulopyranosono-1,5-lactone* (**22**). — Benzoyl chloride (2.1 mL, 9 mol. equiv.) was added to a stirred solution of ammonium 3-deoxy-α-D-*manno*-2-octulopyranosonate (600 mg, 2 mmol) in pyridine (4 mL) at −40°. The mixture was then allowed to reach room temperature and stored for 24 h at room temperature. After addition of an ice-chip, the solution was added, dropwise, to a stirred mixture of ice and water (200 mL); the aqueous layer was decanted from the insoluble gum that was formed, and the latter was dissolved in diethyl ether (50 mL). The ethereal solution was washed first with

cold, aqueous 0.5M sulphuric acid (20 mL) and then with cold, saturated $NaHCO_3$ (20 mL), dried, and concentrated. Column (20 × 2.5 cm) chromatography (2:1 hexane–ethyl acetate) of the residue and crystallization from diethyl ether gave **22** (509 mg, 40%), m.p. 178°, $[\alpha]_D$ −58° (*c* 1, chloroform) (Found: C, 67.9; H, 4.5. $C_{36}H_{28}O_{11}$ calc.: C, 67.9; H, 4.4%). ^{1}H-N.m.r. data (250 MHz, $CDCl_3$): δ 2.55 (dd, 1 H, $J_{3,3'}$ 15, $J_{3,4}$ 3 Hz, H-3), 3.33 (dd, 1 H, $J_{3',3}$ 15, $J_{3',4}$ 10 Hz, H-3′), 4.70 (dd, 1 H, $J_{8,8'}$ 13, $J_{8,7}$ 3 Hz, H-8), 4.72 (d, 1 H, $J_{6,7}$ 10 Hz, H-6), 5.00 (dd, 1 H, $J_{8',8}$ 13, $J_{8',7}$ 3 Hz, H-8′), 5.15 (d, 1 H, $J_{5,4}$ 2, $J_{5,6}$ 0 Hz, H-5), 5.61 (ddd, 1 H, $J_{4,3'}$ 10, $J_{4,3}$ 3, $J_{4,5}$ 2 Hz, H-4), 5.73 (dt, 1 H, $J_{7,6}$ 10, $J_{7,8}$ 3, $J_{7,8'}$ 3 Hz, H-7), 7.48–8.00 (m, 20 H, 4 Ph).

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