Carbohydrate Research, 247 (1993) 145–158
Elsevier Science Publishers B.V., Amsterdam

Synthesis of 3-deoxy-2-octulosonic acid derivatives and characterization of their 3-deoxyoctitols

Thomas Krülle [a], Otto Holst [b], Helmut Brade [b] and Richard R. Schmidt [a,*]

[a] *Fakultät für Chemie, Universität Konstanz, D-7750 Konstanz (Germany)*
[b] *Forschungsinstitut Borstel, Institut für Experimentelle Biologie und Medizin, Parkallee 22, W-2061 Borstel (Germany)*

(Received August 20th, 1992; accepted March 19th, 1993)

ABSTRACT

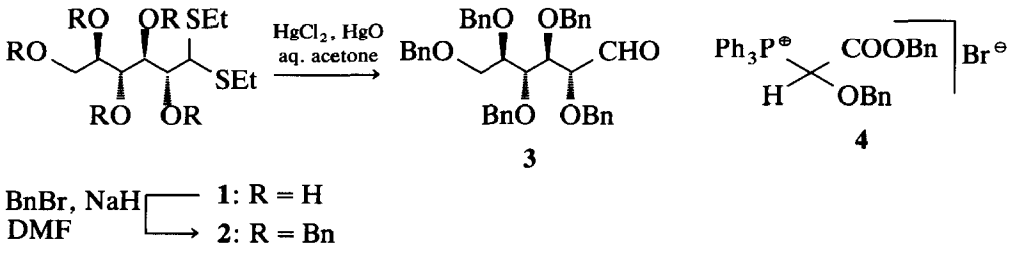
O-Benzyl-protected D-allose, D-galactose, D-glucose, and D-mannose were used to synthesize 3-deoxy-D-*glycero*-D-*allo* / *altro*-, 3-deoxy-D-*glycero*-L-*manno* / *gluco*-, 3-deoxy-D-*glycero*-D-*gulo* / *ido*-, and 3-deoxy-D-*glycero*-D-*galacto* / *talo*-octonate derivatives, respectively, which were transformed by reduction and then deprotection into their 3-deoxyoctitols. The 3-deoxyoctitols were characterized by GLC and GLC–MS in the acetylated and methylated form.

INTRODUCTION

3-Deoxy-D-*manno*-2-octulosonic acid[1] (Kdo), which was first described[2] in 1959, has been reported as a characteristic constituent of the core region[3] of lipopolysaccharides (LPS) and capsular polysaccharides[4] from Gram-negative bacteria. The D-*manno* configuration was determined by Heath et al.[5,6] for Kdo derived from LPS of *Escherichia coli* O111-B4 and its UDP-galactose-4-epimerase-less mutant J-5. The first synthesis of Kdo was reported[5,6] by the same authors. The presence of Kdo has been described for all LPS investigated so far, but in many cases the D-*manno* configuration was suggested by analogy.

Usually, the D-*manno* configuration of isolated Kdo is determined after reduction, followed by methylation, carboxyl-group reduction, and methylation, and comparison by GLC and GLC–MS of the resulting methylated 3-deoxy-D-*glycero*-D-*galacto* / *talo*-octitols with those derived from synthetic Kdo of D-*manno* configuration. However, since it has not been shown that all pairs of octitol isomers obtained from the seven other possible configurations of 3-deoxy-2-octulosonic acid can be separated in GLC, a co-elution of the 3-deoxy-D-*glycero*-D-*galacto* /

* Corresponding author.



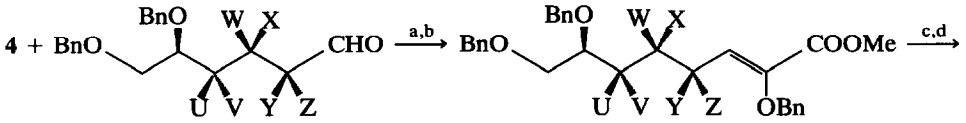
Scheme 1.

talo-octitols with other isomers could not be excluded. Consequently, we decided to synthesize the different octitols, and to characterize their acetylated and methylated derivatives by GLC and GLC–MS.

An efficient Kdo synthesis has recently been described by us[7], based on the Wittig reaction of an *O*-protected-*aldehydo*-D-mannose with the ylid derived from [(benzyloxy)(benzyloxycarbonyl)methyl]triphenylphosphonium bromide. This reaction has now been extended to *O*-benzyl-protected *aldehydo* derivatives of D-allose, D-galactose, and D-glucose. The resulting 3-deoxy-2-octulosonic acid derivatives, including that from D-mannose, were for analytical reasons transformed into the 3-deoxyoctitols which were used for the GLC and GLC–MS analyses.

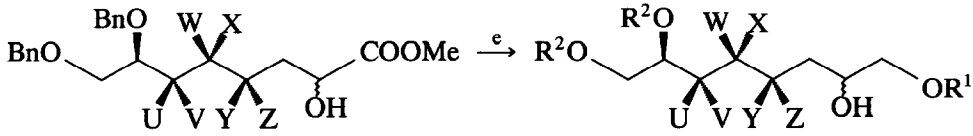
RESULTS AND DISCUSSION

The *aldehydo*-D-allose derivative **3** was prepared in two steps from D-allose diethyl dithioacetal[8] (**1**). Perbenzylation with NaH and benzyl bromide (BnBr) led to the protected acetal **2**, which was hydrolyzed in aqueous acetone in the presence of mercuric chloride–mercuric oxide (Scheme 1). The corresponding *aldehydo*-D-galactose, -D-glucose, and -D-mannose derivatives (**12**, **20**, and **28**, respectively) were obtained in the same way[9]. The chain elongation, for building up the Kdo-skeleton, was achieved by a Wittig reaction[7] using the ylid derived from [(benzyloxy)(benzyloxycarbonyl)methyl]triphenylphosphonium bromide[7] (**4**). For easy separation by flash chromatography, it was necessary to transform the products into the methyl esters **5**, **13**, **21**, and **29**, and to reduce unreacted aldehydic starting material. In each case, only one of the two possible geometric isomers was obtained. ^{1}H NMR chemical shifts at δ 6.32–6.37 for the alkene protons indicated that the ester groups and the protons were on the same side of the double bond. Hydrogenolytic *O*-debenzylation on Pd–$CaCO_3$ in THF permitted the selective cleavage of the enol ether functions in the compounds **5**, **13**, **21**, and **29**. The liberated, acyclic Kdo methyl esters were immediately reduced with $NaBH_4$ to obtain the more stable products **6a,b**, **14a,b**, **22a,b**, and **30a,b** as mixtures of diastereomers which could not be separated by chromatography. Owing to the activation of the esters by the α-hydroxy groups, complete reduction to the penta-*O*-benzyl-3-deoxyoctitols **7a,b**, **15a,b**, **23a,b**, and **31a,b** could be carried out easily with sodium borohydride in ethanol. The structures of the



	U	V	W	X	Y	Z
3	H	OBn	OBn	H	H	OBn
12	OBn	H	H	OBn	H	OBn
20	H	OBn	H	OBn	H	OBn
28	H	OBn	H	OBn	OBn	H

	U	V	W	X	Y	Z
5	H	OBn	OBn	H	H	OBn
13	OBn	H	H	OBn	H	OBn
21	H	OBn	H	OBn	H	OBn
29	H	OBn	H	OBn	OBn	H



	U	V	W	X	Y	Z
6a,b	H	OBn	OBn	H	H	OBn
14a,b	OBn	H	H	OBn	H	OBn
22a,b	H	OBn	H	OBn	H	OBn
30a,b	H	OBn	H	OBn	OBn	H

	U	V	W	X	Y	Z	R^1	R^2
7a,b	H	OBn	OBn	H	H	OBn	H	Bn
8a,b	H	OAc	OAc	H	H	OAc	Ac	Ac
9a,b	H	OBn	OBn	H	H	OBn	Ac	Bn
10a,b	H	OH	OH	H	H	OH	H	H
11a,b	H	OMe	OMe	H	H	OMe	Me	Me

f,g → 8a,b; b → 10a,b; g ← 9a,b; h ← 11a,b

	U	V	W	X	Y	Z	R^1	R^2
15a,b	OBn	H	H	OBn	H	OBn	H	Bn
16a,b	OAc	H	H	OAc	H	OAc	Ac	Ac
17a,b	OBn	H	H	OBn	H	OBn	Ac	Bn
18a,b	OH	H	H	OH	H	OH	H	H
19a,b	OMe	H	H	OMe	H	OMe	Me	Me

f,g → 16a,b; b → 18a,b; g ← 17a,b; h ← 19a,b

	U	V	W	X	Y	Z	R^1	R^2
23a,b	H	OBn	H	OBn	H	OBn	H	Bn
24a,b	H	OAc	H	OAc	H	OAc	Ac	Ac
25a,b	H	OBn	H	OBn	H	OBn	Ac	Bn
26a,b	H	OH	H	OH	H	OH	H	H
27a,b	H	OMe	H	OMe	H	OMe	Me	Me

f,g → 24a,b; b → 26a,b; g ← 25a,b; h ← 27a,b

	U	V	W	X	Y	Z	R^1	R^2
31a,b	H	OBn	H	OBn	OBn	H	H	Bn
32a,b	H	OAc	H	OAc	OAc	H	Ac	Ac
33a,b	H	OBn	H	OBn	OBn	H	Ac	Bn
34a,b	H	OH	H	OH	OH	H	H	H
35a,b	H	OMe	H	OMe	OMe	H	Me	Me

f,g → 32a,b; b → 34a,b; g ← 33a,b; h ← 35a,b

a) n-BuLi; THF; −78°–40°C
b) NaOMe; MeOH
c) $Pd/CaCO_3$; H_2; THF
d) $NaBH_4$; MeOH; −10°C
e) $NaBH_4$; EtOH
f) Pd/C; H_2; MeOH
g) Ac_2O; Py
h) MeI; NaOH

Scheme 2.

TABLE I

Retention times (t_R) in GLC of **8a,b, 11a,b 16a,b, 19a,b, 24a,b, 27a,b, 32a,b**, and **35a,b** (relative to α-D-glucopyranose pentaacetate, t_R 1.00).

Compound	Separating phase	
	SE-54	SP-2380
Acetylated compounds [a]		
8a,b	2.70/2.75	1.40 [c]
16a,b	2.80/2.92	1.44/1.47
24a,b	2.88 [c]	1.53 [c]
32a,b	2.87 [c]	1.44/1.45
Methylated compounds [b]		
11a,b	0.26/0.27	0.11 [c]
19a,b	0.36/0.38	0.19/0.20
27a,b	0.33/0.35	0.17/0.18
35a,b	0.31/0.33	0.16/0.17

[a] Temperature programs: SE-54, 140°C for 3 min, then 3°C min^{-1} to 250°C; SP-2380, 200°C for 5 min, then 5°C min^{-1} to 270°C. [b] SE-54, 130°C for 5 min, then 5°C min^{-1} to 250°C; SP-2380, 180°C for 5 min, then 5°C min^{-1} to 250°C. [c] Isomers not separated.

products were established by the ^1H NMR data of their di-*O*-acetyl derivatives **9a,b, 17a,b, 25a,b**, and **33a,b** obtained by conventional acetylation. Hydrogenolytic debenzylation of the penta-*O*-benzyl-3-deoxyoctitols over palladium-on-carbon and subsequent *O*-acetylation of the crude products led to the hepta-*O*-acetyl-3-deoxyoctitols **8a,b, 16a,b, 24a,b**, and **32a,b**. After treatment of the hepta-*O*-acetyl-3-deoxyoctitols with sodium methoxide, the completely deprotected 3-deoxyoctitols **10a,b, 18a,b, 26a,b**, and **34a,b** were obtained. *O*-Acetylation of the deprotected compounds yielded again the hepta-*O*-acetyl-3-deoxyoctitols. Methylation of the 3-deoxyoctitols gave, after purification, the 3-deoxy-hepta-*O*-methyloctitols **11a,b, 19a,b, 27a,b**, and **35a,b** (Scheme 2).

The relative retention times in GLC of the acetylated derivatives **8a,b, 16a,b, 24a,b**, and **32a,b** are listed in Table I. The isomers of **24a,b** and **32a,b** were not separated on SE-54, and those of **8a,b** and **24a,b** not on SP-2380. On SP-2380, derivatives **16a,b** and **32a,b** had similar relative retention times which in analyses may lead to an incorrect assignment of peaks. The mol wt of 520 was determined in CI(ammonia)-MS [m/z 538, $(M + 18)^+$]. The EIMS data are listed in Table II, and the general fragmentation pattern is shown in Fig. 1. Primary ions originated from C-4–C-5, C-5–C-6, C-6–C-7, and C-7–C-8 cleavages, and the secondary ions were derived from the loss of ketene (−42) and acetic acid (−60). The EI-mass spectra were similar; however, the ion at m/z 123 was the base peak in the spectra of **16a,b**, and **32a,b**, and that at m/z 129 was the base peak in the spectra of **8a,b** and **24a,b**, respectively. Furthermore, the ions at m/z 141, 175, 285, and 303 were absent from the spectrum of **32a,b** and the ion at m/z 175 was absent from the spectrum of **24a,b**. There were some differences in the intensities of the ions, but these may not be sufficient for a reliable differentiation of the respective derivatives.

TABLE II

EIMS data of **8a,b**, **16a,b**, **24a,b**, and **32a,b** after GLC–MS (SE-54)

Compound	*m/z* (% of base peak)
8a,b	55 (7.5/6.6), 69 (77.2/86.3), 73 (19.9/26.3), 81 (15.9/18.7), 82 (15.7/20.3), 85 (19.3/24.0), 86 (20.0/23.8), 95 (14.2/14.0), 97 (9.8/15.0), 103 (48.8/54.2), 111 (16.0/21.9), 115 (61.2/70.0), 123 (69.1/76.0), 127 (18.0/25.7), 128 (65.6/86.3), 129 (100.0/100.0), 136 (28.2/31.8), 137 (15.8/19.9), 141 (15.0/17.7), 145 (23.0/31.8), 153 (13.4/15.3), 157 (34.5/39.8), 165 (25.7/25.7), 170 (56.3/70.3), 171 (25.5/27.5), 175 (6.2/9.7), 178 (16.0/18.1), 179 (12.6/15.7), 183 (13.5/18.1), 187 (15.7/21.9), 196 (11.6/16.3), 201 (49.3/68.4), 213 (10.0/15.2), 217 (27.1/39.2), 225 (22.8/23.9), 231 (96.7/93.2), 243 (2.8/4.1), 273 (7.4/10.0), 285 (3.4/3.9), 289 (3.6/6.0), 303 (9.0/12.6), 345 (6.6/9.0), 447 (3.4/5.4).
16a,b	55 (8.1/9.4), 69 (69.5/79.8), 73 (41.3/33.3), 81 (25.9/22.8), 82 (21.3/19.5), 85 (28.7/25.1), 86 (26.5/23.8), 95 (21.0/20.7), 97 (18.5/17.0), 103 (56.0/49.4), 111 (32.8/26.4), 115 (73.6/73.5), 123 (100.0/100.0), 127 (44.4/34.2), 128 (62.5/61.5), 129 (71.4/91.8), 136 (45.9/35.2), 137 (30.0/26.1), 141 (24.5/20.2), 145 (33.1/24.8), 153 (31.4/22.8), 157 (38.9/31.5), 165 (35.6/32.7), 170 (41.7/46.9), 171 (27.3/23.9), 175 (6.0/4.9), 178 (43.1/25.8), 179 (22.6/17.8), 183 (26.4/25.6), 187 (51.3/41.8), 196 (24.9/16.1), 201 (52.7/49.7), 213 (36.4/22.3), 217 (22.0/18.3), 225 (31.0/28.4), 231 (58.8/92.7), 243 (8.7/7.2), 273 (23.2/11.5), 285 (11.1/10.4), 289 (23.8/18.9), 303 (9.6/9.1), 345 (19.4/20.8), 447 (9.3/13.8).
24a,b	55 (10.0), 69 (89.9), 73 (38.1), 81 (22.6), 82 (19.5), 85 (32.1), 86 (32.8), 95 (19.4), 97 (15.4), 103 (62.5), 111 (29.4), 115 (74.4), 123 (96.8), 127 (34.3), 128 (76.1), 129 (100.0), 136 (41.6), 137 (24.8), 141 (24.6), 145 (32.8), 153 (21.7), 157 (37.8), 165 (36.0), 170 (59.6), 171 (21.3), 178 (30.1), 179 (22.1), 183 (25.7), 187 (32.6), 196 (19.9), 201 (46.0), 213 (13.6), 217 (19.7), 225 (34.1), 231 (79.6), 243 (6.1), 273 (9.9), 285 (4.7), 289 (9.5), 303 (6.6), 345 (13.0), 447 (9.8).
32a,b	55 (5.7), 69 (88.4), 73 (55.6), 81 (27.7), 82 (17.8), 85 (27.8), 86 (33.3), 95 (19.7), 97 (15.7), 103 (59.1), 111 (31.2), 115 (80.6), 123 (100.0), 127 (35.8), 128 (69.4), 129 (85.2), 136 (41.2), 137 (22.8), 145 (22.7), 153 (20.0), 157 (33.9), 165 (46.4), 170 (48.4), 171 (20.6), 178 (31.9), 179 (22.0), 183 (27.2), 187 (48.3), 196 (19.1), 201 (40.0), 213 (14.5), 217 (19.5), 225 (35.7), 231 (69.9), 243 (8.6), 273 (13.5), 289 (15.5), 345 (14.1), 447 (5.2).

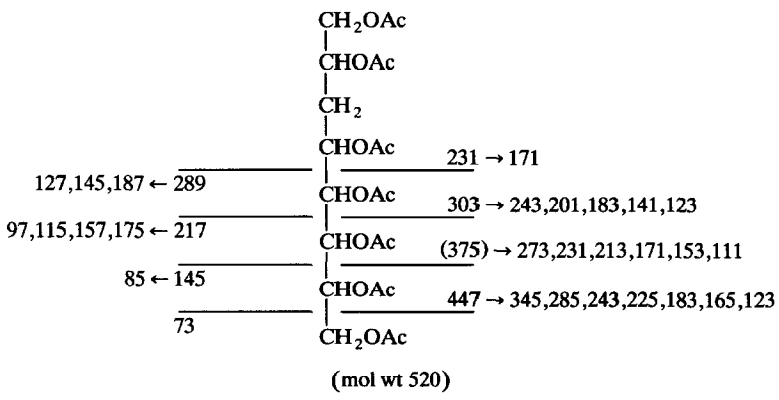


Fig. 1. Fragmentation pattern of **8a,b**, **16a,b**, **24a,b**, and **32a,b**.

TABLE III

EIMS data of **11a,b**, **19a,b**, **27a,b**, and **35a,b** after GLC–MS (SE-54)

Compound	*m/z* (% of base peak)
11a,b	59 (55.3/50.7), 71 (20.1/18.1), 73 (16.0/12.6), 75 (27.7/22.8), 88 (22.1/18.6), 89 (100.0/100.0), 95 (2.5/2.6), 101 (99.9/99.6), 115 (84.5/882.), 127 (22.7/18.0), 133 (8.6/7.9), 145 (17.9/20.7), 147 (10.3/10.3), 159 (5.1/3.3), 177 (2.5/3.5), 183 (5.4/4.8), 191 (9.6/5.9), 215 (3.0/3.6), 247 (0.9)/1.0), 279 (2.1/2.3).
19a,b	59 (52.8/49.8), 71 (19.6/17.8), 73 (16.0/13.2), 75 (23.4/22.5), 88 (22.6/18.6), 89 (88.0/93.0), 95 (2.4/2.4), 101 (100.0/100.0), 115 (76.8/78.5), 127 (18.5/17.8), 133 (6.0/5.4), 145 (10.7/12.2), 147 (8.7/9.5), 159 (3.7/3.4), 177 (2.7/3.7), 183 (2.8/2.9), 191 (4.6/4.5), 215 (2.1/1.8), 247 (0.6/0.7), 279 (1.0/1.3).
27a,b	59 (59.0/50.4), 71 (20.3/19.8), 73 (15.7/14.9), 75 (26.1/23.3), 88 (22.1/19.5), 89 (100.0/100.0), 95 (2.3/2.3), 101 (85.8/84.2), 115 (77.8/70.6), 127 (29.4/30.7), 133 (6.8/6.3), 145 (19.3/21.1), 147 (11.4/9.3), 159 (6.5/7.4), 177 (2.3/3.1), 183 (4.2/3.0), 191 (12.4/12.3), 215 (1.7/1.7), 247 (-/1.0), 279 (1.4/1.1).
35a,b	59 (61.8/59.4), 71 (24.4/22.5), 73 (15.7/17.8), 75 (26.4/27.3), 88 (21.3/24.2), 89 (100.0/100.0), 95 (2.4/2.7), 101 (87.1/83.3), 115 (75.6/73.5), 127 (23.6/25.4), 133 (8.5/73), 145 (20.7/15.4), 147 (9.5/8.1), 159 (5.3/5.1), 177 (3.3/2.0), 183 (5.2/3.6), 191 (7.6/9.7), 215 (2.7/1.9), 247 (1.0/0.5), 279 (1.7/0.8).

The relative retention times of the methylated derivatives **11a,b**, **19a,b**, **27a,b**, and **35a,b** are also listed in Table I. The derivatives could be differentiated on both columns used. All isomers were separated, except those of **11a,b**, using SP-2380. The mol wt of 324 was determined in CI(ammonia)-MS [*m/z* 325 $(M + 1)^+$, 342 $(M + 18)^+$]. The EIMS data (Table III, fragmentation pattern in Fig. 2) of the derivatives were very similar and, therefore, may not be used for the differentiation of the compounds. The ion at *m/z* 101 was the base peak in the spectra of **27a,b**, and the ion at *m/z* 89 was the base peak in the other spectra.

In summary, we have synthesized 3-deoxy-D-*glycero*-D-*allo* / *altro*-, 3-deoxy-D-*glycero*-L-*manno* / *gluco*-, 3-deoxy-D-*glycero*-D-*gulo* / *ido*-, and 3-deoxy-D-*glycero*-D-

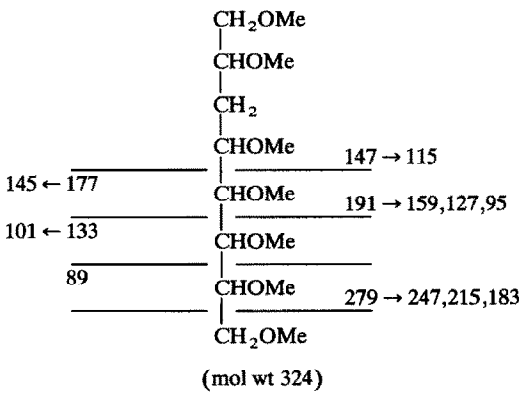


Fig. 2. Fragmentation pattern of **11b**, **19a,b**, **27a,b**, and **35a,b**.

galacto / *talo*-octonate derivatives, and have shown that their 3-deoxyoctitols could be differentiated by GLC, preferably as methylated derivatives. We are currently synthesizing the 3-deoxy-D-*altro*,3-deoxy-D-*gulo*-, 3-deoxy-D-*ido*-, and 3-deoxy-D-*talo*-2-octulosonates, and their 3-deoxyoctitol derivatives, in order to complete the series.

EXPERIMENTAL

General methods.—Solvents were purified in the usual way; the petroleum ether (PE) used had a boiling range of 30–70°C. ^{1}H NMR spectra: Bruker AC 250 Cryospec; internal standard, tetramethylsilane. Flash chromatography: Silica Gel 60 (Merck; 40–60 μm). Medium-pressure liquid chromatography (MPLC): silica gel LiChroPrep RP 8 (Merck; 40–60 μm). Thin-layer chromatography (TLC): Foil plates, Silica Gel 60 F_{254} (Merck; layer thickness, 0.2 mm). Optical rotations: Perkin–Elmer polarimeter 241/MS, 1-dm cell.

Methylation was performed according to the method of Ciucanu and Kerek[10], and methylated products were purified[11] on a SEP-PAK C_{18} cartridge.

GLC was performed on a Varian model 3700 gas chromatograph equipped with a flame-ionisation detector. For analysis of the acetylated and methylated 3-deoxyoctitols, fused-silica columns with chemically bonded SE-54 (25 m × 0.32 mm, 0.25-μm film thickness, Weeke Mühlheim). at 0.15 MPa H_2, and SP-2380 (30 m × 0.25 mm, 0.20 μm, Supelco, Inc.) at 0.15 MPa H_2, were used. The temperature programs are given in Table I. GLC–MS was carried out on a Hewlett–Packard 5985 instrument, equipped with an SE-54 capillary column and an HP-1000 data system. EI-mass spectra were recorded at 70 eV, and CI-mass spectra were obtained with ammonia as reactant gas.

2,3,4,5,6-Penta-O-benzyl-D-allose diethyl dithioacetal (**2**).—To a solution of D-allose diethyl dithioacetal[8] (**1**; 1.8 g, 6.3 mmol) and benzyl bromide (7.2 g, 42 mmol) in dry DMF (30 mL) was added sodium hydride (1.2 g, 50 mmol) in 3 portions during 1 h; the reaction temperature should not exceed 30°C. After 2 h, the reaction mixture was poured on to ice (100 g) and extracted with ether (3 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated. After purification of the residue by flash chromatography (11:1 PE–EtOAc), **2** was obtained as a colourless oil (4.0 g, 86%); TLC (6:1 PE–EtOAc): R_f 0.47; $[\alpha]_D^{20}$ + 24.4° (*c* 0.97, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 1.12–1.20 (m, 6 H, 2 SCH_2CH_3), 2.46–2.67 (m, 4 H, 2 SCH_2CH_3), 3.63 (dd, 1 H, $J_{5,6a}$ 4.7, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.70 (dd, 1 H, $J_{5,6b}$ 2.4 Hz, H-6b), 3.93 (ddd, 1 H, $J_{4,5}$ 8.1 Hz, H-5), 4.06 (dd, 1 H, $J_{1,2}$ 2.6, $J_{2,3}$ 8.2 Hz, H-2), 4.23 (d, 1 H, H-1), 4.28 (dd, 1 H, H-3), 4.47–4.93 (m, 10 H, 5 OCH_2Ph), 7.23–7.32 (m, 25 H, 5 Ph). Anal. Calcd for $C_{45}H_{52}O_5S_2$ (737.04): C, 73.33; H, 7.11. Found: C, 73.30; H, 7.06.

2,3,4,5,6-Penta-O-benzyl-D-allose (**3**).—To a solution of **2** (4.0 g, 5.4 mmol) in acetone (50 mL) and water (5 mL) was added HgO (4 g). To this mixture was added dropwise a solution of $HgCl_2$ (4 g) in acetone (20 mL) with vigorous stirring.

After 12 h, the suspension was filtered through Celite and concentrated in vacuo. A solution of the residue in $CHCl_3$ (100 mL) was washed with warm water (4 × 50 mL) and aq KI (30%, 3 × 30 mL), dried ($MgSO_4$), and evaporated to dryness. The crude product was purified by flash chromatography (6:1 PE–EtOAc), to yield aldehyde **3** (3.2 g, 94%); TLC (6:1 PE–EtOAc): R_f 0.30; $[\alpha]_D^{20}$ + 11.7° (*c* 0.53, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.65–3.67 (m, 2 H, H-6a,6b), 3.97–4.07 (m, 4 H, H-2,3,4,5), 4.46–4.79 (m, 10 H, 5 OCH_2Ph), 7.19–7.34 (m, 25 H, 5 Ph), 9.41 (d, 1 H, $J_{1,2}$ 0.5 Hz, CHO). Anal. Calcd for $C_{41}H_{42}O_6$ (630.79): C, 78.07; H, 6.71. Found: C, 78.02; H, 6.83.

*Methyl (Z)-2,4,5,6,7,8-Hexa-O-benzyl-3-deoxy-*D-allo*-oct-2-enosonate* (**5**).—To a suspension of [(benzyloxy)(benzyloxycarbonyl)methyl]triphenylphosphonium bromide[7] (**4**; 5 g, 8.4 mmol) in dry THF was added dropwise 1.6 M butyllithium in hexane (4.4 mL) at −78°C under N_2. After 20 min, **3** (3.2 g, 5.1 mmol) in dry THF (15 mL) was added, and the cooling bath was removed. The mixture was stirred for an additional 12 h at 40°C, and then partitioned between ether and water (100 mL, 1:1). The aqueous layer was extracted three times with 30 mL of ether. The combined ethereal extracts were dried ($MgSO_4$), concentrated in vacuo, and filtered through a short column of silica gel (3:1 PE–EtOAc). The solvent was evaporated and the residue was dissolved in toluene–methanol (100 mL, 1:4). $NaBH_4$ (100 mg) was added with vigorous stirring for reduction of unreacted aldehyde. After 1 h, sodium (50 mg) was added to complete the transesterification (monitored by TLC). The solution was diluted with water (100 mL), neutralized with 1 M HCl, and extracted with ether (3 × 70 mL). The organic layer was dried ($MgSO_4$) and concentrated. Purification of the residue by flash chromatography (5:1 PE–EtOAc) yielded **5** (2.2 g, 55%); TLC (6:1 PE–EtOAc): R_f 0.37; $[\alpha]_D^{20}$ + 18.2° (*c* 1.29, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.65–3.67 (m, 2 H, H-8a,8b), 3.78 (s, 3 H, $COOCH_3$), 3.86, 3.98 (2 m, 3 H, H-5,6,7), 4.14, 4.33 (2 d, 2 H, *J* 11.9 Hz, OCH_2Ph), 4.44–4.75 (m, 11 H, 5 OCH_2Ph, H-4), 6.32 (d, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 7.16–7.27 (m, 30 H, 6 Ph). Anal. Calcd for $C_{51}H_{52}O_8$ (792.98): C, 77.25; H, 6.61. Found: C, 77.00; H, 6.71.

*Methyl 4,5,6,7,8-Penta-O-benzyl-3-deoxy-*D-glycero-D-allo*-octonate and methyl 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-altro*-octonate* (**6a,b**).—Pd–$CaCO_3$ (5%, 250 mg) in dry THF (20 mL) was activated for 6 h under H_2. A solution of **5** (1.5 g, 1.9 mmol) in THF (10 mL) was added. Debenzylation was carried out until compound **5** disappeared in TLC. The suspension was filtered through Celite and washed several times with THF. The filtrate was evaporated to dryness and the residue redissolved in MeOH (50 mL). After cooling to −10°C, $NaBH_4$ (100 mg) was added with vigorous stirring. After 1.5 h, the solution was neutralized with 1 M HCl, diluted with water (50 mL), and extracted with ether (3 × 75 mL). The ethereal extracts were dried ($MgSO_4$) and concentrated. After purification of the residue by flash chromatography (3:1 PE–EtOAc), **6a,b** (800 mg, 59%) was obtained as a colourless oil (diastereomer ratio 2.1:1); TLC (5:1 PE–EtOAc): R_f 0.27; ^1H NMR ($CDCl_3$): major product, δ 2.07, 2.21 (2 m, 2 H, H-3a,3b), 3.32 (d, 1

H, *J* 3.7 Hz, OH), 3.51 (s, 3 H, $COOCH_3$), 3.74, 3.95, 4.04, 4.13 (4 m, 6 H, H-4,5,6,7,8a,8b), 4.27–4.81 (m, 11 H, 5 OCH_2Ph, H-2), 7.22–7.35 (m, 25 H, 5 Ph); minor product, δ 1.76, 2.21 (2 m, 2 H, H-3a,3b), 2.98 (d, 1 H, *J* 6.8 Hz, OH), 3.67 (s, 3 H, $COOCH_3$), 3.74, 3.95, 4.04, 4.13 (4 m, 6 H, H-4,5,6,7,8a,8b), 4.27–4.81 (m, 11 H, 5 OCH_2Ph, H-2), 7.22–7.35 (m, 25 H, 5 Ph). Anal. Calcd for $C_{44}H_{48}O_8$ (704.86): C, 74.98; H, 6.86. Found: C, 74.94; H, 6.90.

*4,5,6,7,8-Penta-*O*-benzyl-3-deoxy-*D-glycero-D-allo-*octitol*, *4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-altro-*octitol* (**7a,b**); *and 1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-allo-*octitol*, *1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-altro-*octitol* (**9a,b**).—To a solution of **6a,b** (570 mg, 0.81 mmol) in EtOH (50 mL) was added $NaBH_4$ (340 mg). After 6 h, the solution was neutralized with 1 M HCl and concentrated to half of the original volume. The solution was diluted with water (50 mL) and extracted with ether (3 × 70 mL). The organic layer was dried ($MgSO_4$) and evaporated to dryness. After purification of the residue by flash chromatography (1:1 PE–EtOAc), **7a,b** (460 mg, 86%) was obtained as an oil; TLC (1:1 PE–EtOAc): R_f 0.51.

A sample of **7a,b** (50 mg) was acetylated with pyridine (10 mL) and acetic anhydride (10 mL). After the usual workup, the syrupy acetate was purified by flash chromatography (3:1 PE–EtOAc); **9a,b** was obtained quantitatively; TLC (3:1 PE–EtOAc): R_f 0.46; ^1H NMR ($CDCl_3$): major product, δ 1.79–2.09 (m, 2 H, H-3a,3b), 1.90 and 1.95 (2 s, 6 H, 2 OAc), 3.69–4.05 (m, 7 H, H-1a,4,5,6,7,8a,8b), 4.10 (dd, 1 H, $J_{1b,2}$ 2.8, $J_{1a,1b}$ 12.1 Hz, H-1b), 4.30–4.80 (m, 10 H, 5 OCH_2Ph), 5.23 (m, 1 H, H-2), 7.23–7.34 (m, 25 H, 5 Ph); minor product, δ 1.79–2.09 (m, 2 H, H-3a,3b), 1.83 and 2.01 (2 s, 6 H, 2 OAc), 3.69–4.05 (m, 7 H, H-1a,4,5,6,7,8a,8b), 4.26 (dd, 1 H, $J_{1b,2}$ 3.4, $J_{1a,1b}$ 11.9 Hz, H-1b), 4.30–4.80 (m, 10 H, 5 OCH_2Ph), 5.33 (m, 1 H, H-2), 7.23–7.34 (m, 25 H, 5 Ph). Anal. Calcd for $C_{47}H_{52}O_9$ (acetylated compounds): C, 74.19; H, 6.89. Found: C, 73.90; H 6.93.

*1,2,4,5,6,7,8-Hepta-*O*-acetyl-3-deoxy-*D-glycero-D-allo-*octitol* and *1,2,4,5,6,7,8-hepta-*O*-acetyl-3-deoxy-*D-glycero-D-altro-*octitol* (**8a,b**).—Mixture **7a,b** (460 mg, 0.68 mmol) in MeOH (20 mL) was hydrogenated in presence of palladium-on-carbon (10%, 68 mg). After 12 h, the suspension was filtered through Celite and washed several times with MeOH. The filtrate was evaporated to dryness and the residue was acetylated with pyridine (10 mL) and acetic anhydride (10 mL). After 1 day at room temperature, the mixture was concentrated under high vacuum with a rotary evaporator, and the residue was purified by flash chromatography (1:1.5 PE–EtOAc) to yield **8a,b** (279 mg, 79%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.33; ^1H NMR ($CDCl_3$): major product, δ 1.93–1.97 (m, 2 H, H-3a,3b), 2.04–2.12 (m, 21 H, 7 OAc), 3.94 (dd, 1 H, $J_{1a,2}$ 5.6, $J_{1a,1b}$ 12.2 Hz, H-1a), 4.07 (dd, 1 H, $J_{7,8a}$ 6.8, $J_{8a,8b}$ 12.2 Hz, H-8a), 4.20 (dd, 1 H, $J_{1b,2}$ 3.5 Hz, H-1b), 4.29 (dd, 1 H, $J_{7,8b}$ 3.2 Hz, H-8b), 5.00–5.37 (3 m, 5 H, H-2,4,5,6,7); minor product, δ 1.84–1.97 (m, 2 H, H-3a,3b), 2.02–2.13 (m, 21 H, 7 OAc), 3.96 (dd, 1 H, $J_{1a,2}$ 5.9, $J_{1a,1b}$ 11.7 Hz, H-1a), 4.08 (dd, 1 H, $J_{7,8a}$ 7.8, $J_{8a,8b}$ 12.2 Hz, H-8a), 4.23 (dd, 1 H, $J_{1b,2}$ 3.4 Hz, H-1b),

4.29 (dd, 1 H, $J_{7,8b}$ 3.2 Hz, H-8b), 5.00–5.37 (3 m, 5 H, H-2,4,5,6,7). Anal. Calcd. for $C_{22}H_{32}O_{14}$ (520.49): C, 50.77; H, 6.20. Found: C, 50.96; H, 6.09.

3-Deoxy-D-glycero-D-allo-*octitol and 3-deoxy*-D-glycero-D-altro-*octitol* (**10a,b**).—A solution of **8a,b** (230 mg, 0.44 mmol) in MeOH (25 mL) was treated with sodium methoxide (100 μL, M solution in dry MeOH). After 6 h, the solution was neutralized with Amberlite IR-120 (H^+). Then the resin was removed by filtration. The filtrate was concentrated in vacuo to a syrup which was purified by MPLC (1:20 acetone–water). The aqueous solution was concentrated and freeze-dried to give **10a,b** (78 mg, 77%); TLC (5:4:1 $CHCl_3$–MeOH–water): R_f 0.30. Acetylation of **10a,b** under the usual conditions gave **8a,b** in quantitative yield.

Methyl (Z)-*2,4,5,6,7,8-Hexa*-O-*benzyl-3-deoxy*-D-galacto-*oct-2-enosonate* (**13**).—Bromide **4** (25g, 42 mmol), butyllithium (20 mL of a 1.6 M solution in hexane), and 2,3,4,5,6-penta-*O*-benzyl-D-galactose[3] (**12**; 10 g, 15.9 mmol) were used as described for compound **5**, to yield **13** (7.1 g, 57%) as a colourless oil; TLC (3:1 PE–EtOAc): R_f 0.58; $[\alpha]_D^{20}$ + 9.3° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.57–3.80 (m, 3 H, H-7,8a,8b), 3.76 (s, 3 H, $COOCH_3$), 3.98–4.50 (2 m, 10 H, 4 OCH_2Ph, H-5,6), 4.55 and 4.75 (2 d, 2 H, *J* 11.9 Hz, OCH_2Ph), 4.71 (dd, 1 H, $J_{4,5}$ 2.9, $J_{3,4}$ 9.2 Hz, H-4), 4.84 and 4.87 (2 d, 2 H, *J* 11.2 Hz, C=COCH_2Ph), 6.37 (d, 1 H, H-3), 7.17–7.33 (m, 30 H, 6 Ph). Anal. Calcd for $C_{51}H_{52}O_8$ (792.98): C, 77.25; H, 6.61. Found: C, 77.13; H, 6.70.

Methyl 4,5,6,7,8-penta-O-*benzyl-3-deoxy*-D-glycero-L-manno-*octonate and methyl 4,5,6,7,8-penta*-O-*benzyl-3-deoxy*-D-glycero-L-gluco-*octonate* (**14a,b**).—Debenzylation and reduction of **13** (2 g, 2.5 mmol) were carried out as described for compound **6a,b**; Pd–$CaCO_3$ (5%, 245 mg) and $NaBH_4$ (100 mg) were used. After purification by flash chromatography (3:1 PE–EtOAc), **14a,b** (850 mg, 48%) was obtained as a colourless oil (diastereomer ratio 1.6:1); TLC (3:1 PE–EtOAc): R_f 0.38; ^1H NMR ($CDCl_3$): major product, δ 2.04, 2.26 (2 m, 2 H, H-3a,3b), 3.15 (d, 1 H, *J* 3.9 Hz, OH), 3.68 (s, 3 H, $COOCH_3$), 3.66–3.71 (m, 2 H, H-8a,8b), 3.80–4.07 (m, 4 H, H-4,5,6,7), 4.25 (m, 1 H, H-2), 4.40–4.74 (m, 10 H, 5 OCH_2Ph), 7.19–7.35 (m, 25 H, 5 Ph); minor product, δ 1.87, 2.04 (2 m, 2 H, H-3a,3b), 2.75 (d, 1 H, *J* 6.7 Hz, OH), 3.53 (s, 3 H, $COOCH_3$), 3.66–3.71 (m, 2 H, H-8a,8b), 3.80–4.07 (m, 4 H, H-4,5,6,7), 4.33 (m, 1 H, H-2), 4.40–4.74 (m, 10 H, 5 OCH_2Ph), 7.19–7.35 (m, 25 H, 5 Ph). Anal. Calcd for $C_{44}H_{48}O_8$ (704.86): C, 74.98; H, 6.86. Found: C, 74.73; H, 6.92.

4,5,6,7,8-Penta-O-*benzyl-3-deoxy*-D-glycero-L-manno-*octitol, 4,5,6,7,8-penta*-O-*benzyl-3-deoxy*-D-glycero-L-gluco-*octitol* (**15a,b**); *and 1,2-di*-O-*acetyl-4,5,6,7,8-penta*-O-*benzyl-3-deoxy*-D-glycero-L-manno-*octitol, 1,2-di*-O-*acetyl-4,5,6,7,8-penta*-O-*benzyl-3-deoxy*-D-glycero-L-gluco-*octitol* (**17a,b**).—Treatment of **14a,b** (530 mg, 0.75 mmol) with $NaBH_4$ (300 mg), under the same conditions as described for **7a,b**, yielded **15a,b** (400 mg, 79%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.35.

A sample of **15a,b** (50 mg) was acetylated with pyridine (10 mL) and acetic anhydride (10 mL). After the usual workup, the syrupy acetate was purified by flash chromatography (3:1 PE–EtOAc); **17a,b** was obtained quantitatively; TLC

(1:1 PE–EtOAc): R_f 0.72; ^{1}H NMR ($CDCl_3$): major product, δ 1.83–2.04 (m, 2 H, H-3a,3b), 1.91 and 1.96 (2 s, 6 H, 2 OAc), 3.67–3.69 (m, 2 H, H-8a,8b), 3.74–4.04 (m, 5 H, H-1a,4,5,6,7), 4.08 (dd, 1 H, $J_{1b,2}$ 3.1, $J_{1a,1b}$ 12.1 Hz, H-1b), 4.39–4.77 (m, 10 H, 5 OCH_2Ph), 5.11 (m, 1 H, H-2), 7.20–7.35 (m, 25 H, 5 Ph); minor product, δ 1.78, 1.83–2.04 (m, 2 H, H-3a,3b), 1.92 and 2.00 (2 s, 6 H, 2 OAc), 3.67–3.69 (m, 2 H, H-8a,8b), 3.74–4.04 (m, 5 H, H-1a,4,5,6,7), 4.22 (dd, 1 H, $J_{1b,2}$ 3.5, $J_{1a,1b}$ 11.9 Hz, H-1b), 4.39–4.77 (m, 10 H, 5 OCH_2Ph), 5.33, (m, 1 H, H-2), 7.20–7.35 (m, 25 H, 5 Ph). Anal. Calcd for $C_{47}H_{52}O_9$ (acetylated compounds): C, 74.19; H, 6.89. Found: C, 73.87; H, 7.02.

*1,2,4,5,6,7,8-Hepta-*O*-acetyl-3-deoxy-*D*-glycero-*L*-manno-octitol and 1,2,4,5,6,7,8-hepta-*O*-acetyl-3-deoxy-*D*-glycero-*L*-gluco-octitol* (**16a,b**).—Mixture **15a,b** (300 mg, 0.44 mmol) was debenzylated and acetylated as described for **8a,b**, to give **16a,b** (190 mg, 84%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.33; ^{1}H NMR ($CDCl_3$): major product, δ 1.56–1.86 (m, 2 H, H-3a,3b), 2.02–2.09 (m, 21 H, 7 OAc), 3.80 (dd, 1 H, $J_{1a,2}$ 2.6, $J_{1a,1b}$ 11.7 Hz, H-1a), 4.07 (dd, 1 H, $J_{7,8a}$ 5.2, $J_{8a,8b}$ 12.0 Hz, H-8a), 4.15 (dd, 1 H, $J_{7,8b}$ 3.65 Hz, H-8b), 4.24 (m, 1 H, H-1b), 5.04 (m, 1 H, H-2), 5.23–5.30 (m, 4 H, H-4,5,6,7); minor product, δ 1.56–1.86 (m, 2 H, H-3a,3b), 1.99, 2.01, 2.04, 2.05, 2.10 (5 s, 21 H, 7 OAc), 3.77 (dd, 1 H, $J_{1a,2}$ 2.7, $J_{1a,1b}$ 11.5 Hz, H-1a), 3.92 (dd, 1 H, $J_{7,8a}$ 5.3, $J_{8a,8b}$ 12.0 Hz, H-8a), 4.24 (m, 2 H, H-1b,8b), 4.85 (m, 1 H, H-2), 5.00–5.30 (2 m, 4 H, H-4,5,6,7). Anal. Calcd for $C_{22}H_{32}O_{14}$ (520.49): C, 50.77; H, 6.20. Found: C, 50.79; H, 6.11.

*3-Deoxy-*D*-glycero-*L*-manno-octitol and 3-deoxy-*D*-glycero-*L*-gluco-octitol* (**18a,b**).—Mixture **16a,b** (120 mg, 0.23 mmol) was deprotected and purified as described for **10a,b**, to give **18a,b** (36 mg, 70%); TLC (5:4:1 $CHCl_3$–MeOH–water): R_f 0.30. Acetylation of **18a,b** under the usual conditions gave **16a,b** in quantitative yield.

Methyl (Z)*-2,4,5,6,7,8-hexa-*O*-benzyl-3-deoxy-*D*-gluco-oct-2-enosonate* (**21**).—Bromide **4** (25 g, 42 mmol), butyllithium (20 mL of a 1.6 M solution in hexane), and 2,3,4,5,6-penta-*O*-benzyl-D-glucose[12] (**20**; 10 g, 15.9 mmol) were used as described for compound **5**, to yield **21** (10.5 g, 83%) as a colourless oil; TLC (5:1 PE–EtOAc): R_f 0.38; $[\alpha]_D^{20}$ + 21.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.66–3.77 (m, 4 H, H-6,7,8a,8b), 3.79 (s, 3 H, $COOCH_3$), 4.01–4.82 (2 m, 14 H, 6 OCH_2Ph, H-4,5), 6.32 (d, 1 H, $J_{3,4}$ 9.2 Hz, H-3), 7.22–7.35 (m, 30 H, 6 Ph). Anal. Calcd for $C_{51}H_{52}O_8$ (792.98): C, 77.25; H, 6.61. Found: C, 76.82; H, 6.74.

*Methyl 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-gulo-octonate and methyl 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-ido-octonate* (**22a,b**).—Debenzylation and reduction of **21** (2.8 g, 3.5 mmol) were carried out as described for compound **6a,b**; Pd–$CaCO_3$ (5%, 240 mg) and $NaBH_4$ (100 mg) were used. After purification by flash chromatography (3:1 PE–EtOAc), **22a,b** (1.6 g, 64%) was obtained as a colourless oil (diastereomer ratio 2:1); TLC (3:1 PE–EtOAc): R_f 0.36; ^{1}H NMR ($CDCl_3$): major product, δ 1.96 and 2.23 (2 m, 2 H, H-3a,3b), 3.06 (d, 1 H, *J* 4.2 Hz, OH), 3.50 (s, 3 H, $COOCH_3$), 3.71–4.06 (m, 6 H, H-4,5,6,7,8a,H-8b), 4.16 (m, 1 H, H-2), 4.34–4.78 (m, 10 H, 5 OCH_2Ph), 7.20–7.32 (m, 25 H, 5 Ph); minor

product, δ 1.76, 1.96 (2 m, 2 H, H-3a,3b), 2.69 (d, 1 H, *J* 6.4 Hz, OH), 3.67 (s, 3 H, $COOCH_3$), 3.71–4.06 (m, 6 H, H-4,5,6,7,8a,8b), 4.32 (m, 1 H, H-2), 4.34–4.78 (m, 10 H, 5 OCH_2Ph), 7.20–7.32 (m, 25 H, 5 Ph). Anal. Calcd for $C_{44}H_{48}O_8$ (704.86): C, 74.98; H, 6.86. Found: C, 74.98; H, 6.96.

*4,5,6,7,8-Penta-*O*-benzyl-3-deoxy-*D-glycero-D-gulo*-octitol, 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-ido*-octitol* (**23a,b**); *and 1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-gulo*-octitol, 1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D-glycero-D-ido*-octitol* (**25a,b**).—Treatment of **22a,b** (370 mg, 0.52 mmol) with $NaBH_4$ (150 mg), under the same conditions as described for **7a,b**, yielded **23a,b** (270 mg, 77%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.33.

A sample of **23a,b** (50 mg) was acetylated with pyridine (10 mL) and acetic anhydride (10 mL). After the usual workup, the syrupy acetate was purified by flash chromatography (3:1 PE–EtOAc); **25a,b** was obtained quantitatively; TLC (3:1 PE–EtOAc): R_f 0.38; ^1H NMR ($CDCl_3$): major product, δ 1.74–2.01 (m, 2 H, H-3a,3b), 1.88 and 1.96 (2 s, 6 H, 2 OAc), 3.64–4.05 (m, 8 H, H-1a,1b,4,5,6,7,8a,8b), 4.34–4.79 (m, 10 H, 5 OCH_2Ph), 5.05 (m, 1 H, H-2), 7.22–7.32 (m, 25 H, 5 Ph); minor product, δ 1.74–2.01 (m, 2 H, H-3a,3b), 1.90 and 2.00 (2 s, 6 H, 2 OAc), 3.64–4.01 (m, 7 H, H-1a,4,5,6,7,8a,8b), 4.20 (dd, 1 H, $J_{1b,2}$ 3.5, $J_{1a,1b}$ 12.0 Hz, H-1b), 4.34–4.79 (m, 10 H, 5 OCH_2Ph), 5.25 (m, 1 H, H-2), 7.22–7.32 (m, 25 H, 5 Ph). Anal. Calcd for $C_{47}H_{52}O_9$ (acetylated compounds): C, 74.19; H, 6.89. Found: C, 73.74; H, 6.98.

*1,2,4,5,6,7,8-Hepta-*O*-acetyl-3-deoxy-*D-glycero-D-gulo*-octitol and 1,2,4,5,6,7,8-hepta-*O*-acetyl-3-deoxy-*D-glycero-D-ido*-octitol* (**24a,b**).—Mixture **23a,b** (330 mg, 0.49 mmol) was debenzylated and acetylated as described for **8a,b**, to give **24a,b** (190 mg, 76%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.34; ^1H NMR ($CDCl_3$): major product, δ 1.76 and 1.91 (2 m, 2 H, H-3a,3b), 2.01–2.09 (m, 21 H, 7 OAc), 3.94–4.11 and 4.16–4.26 (2 m, 4 H, H-1a,1b,8a,8b), 4.93–5.22 (2 m, 3 H, H-2,4,7), 5.29 (m, 1 H, H-5), 5.40 (dd, 1 H, *J* 3.9, *J* 7.3 Hz, H-6); minor product, δ 1.91 (2 m, 2 H, H-3a,3b), 1.99–2.10 (m, 21 H, 7 OAc), 3.94–4.11 and 4.16–4.26 (2 m, 4 H, H-1a,1b,8a,8b), 4.93–5.08 (m, 3 H-2,4,7), 5.29 (m, 1 H, H-5), 5.35 (dd, 1 H, *J* 3.5, *J* 7.7 Hz, H-6). Anal. Calcd for $C_{22}H_{32}O_{14}$ (520.49): C, 50.77; H, 6.20. Found: C, 50.79; H, 6.00.

*3-Deoxy-*D*-glycero-D-gulo-octitol and 3-deoxy-*D*-glycero-D-ido-octitol* (**26a,b**).—Mixture **24a,b** (170 mg, 0.33 mmol) was deprotected and purified as described for **10a,b**, to give **26a,b** (68 mg, 91%); TLC (5:4:1 $CHCl_3$–MeOH–water): R_f 0.31. Acetylation of **26a,b** under the usual conditions gave **24a,b** in quantitative yield.

Methyl (Z)*-2,4,5,6,7,8-hexa-*O*-benzyl-3-deoxy-*D*-manno-oct-2-enosonate* (**29**).—Bromide **4** (25 g, 42 mmol), butyllithium (20 mL of a 1.6 M solution in hexane), and 2,3,4,5,6-penta-*O*-benzyl-D-mannose[3] (**28**; 10 g, 15.9 mmol) were used as described for compound **5**, to yield **29** (8.2 g, 65%) as a colourless oil; TLC (5:1 PE–EtOAc): R_f 0.44; $[\alpha]_D^{20}$ + 12.1° (*c* 1.27, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.66–3.98 (m, 5 H, H-5,6,7,8a,8b), 3.79 (s, 3 H, $COOCH_3$), 4.04 and 4.33 (2 d, 2 H, *J* 11.8 Hz, OCH_2Ph), 4.38–4.77 (m, 11 H, 5 OCH_2Ph, H-4), 6.34 (d, 1 H, $J_{3,4}$ 9.7 Hz, H-3),

7.13–7.35 (m, 30 H, 6 Ph). Anal. Calcd for $C_{51}H_{52}O_8$ (792.98): C, 77.26; H, 6.61. Found: C, 77.02; H, 6.65.

*Methyl 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-octonate and methyl 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-talo-octonate* (**30a,b**).—Debenzylation and reduction of **29** (2 g, 2.5 mmol) were carried out as described for compound **6a,b**; Pd–$CaCO_3$ (5%, 245 mg) and $NaBH_4$ (100 mg) were used. After purification by flash chromatography (3:1 PE–EtOAc), **30a,b** (1.15 g, 64%) was obtained as a colourless oil (diastereomer ratio 1.1:1); TLC (5:1 PE–EtOAc): R_f 0.21; ^{1}H NMR ($CDCl_3$): major product, δ 2.13 and 2.24 (2 m, 2 H, H-3a,3b), 3.35 (d, 1 H, J 3.3 Hz, OH), 3.48 (s, 3 H, $COOCH_3$), 3.73–4.06 (2 m, 6 H, H-4,5,6,7,8a,8b), 4.17–4.83 (m, 11 H, 5 OCH_2Ph, H-2), 7.18–7.35 (m, 25 H, 5 Ph); minor product, δ 1.72 and 2.24 (2 m, 2 H, H-3a,3b), 2.82 (d, 1 H, J 6.8 Hz, OH), 3.70 (s, 3 H, $COOCH_3$), 3.73–4.06 (2 m, 6 H, H-4,5,6,7,8a,8b), 4.17–4.83 (m, 11 H, 5 OCH_2Ph, H-2), 7.18–7.35 (m, 25 H, 5 Ph). Anal. Calcd for $C_{44}H_{48}O_8$ (704.86): C, 74.98; H, 6.86. Found: C, 74.85; H, 6.79.

*4,5,6,7,8-Penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-octitol, 4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-talo-octitol* (**31a,b**); *and 1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-galacto-octitol, 1,2-di-*O*-acetyl-4,5,6,7,8-penta-*O*-benzyl-3-deoxy-*D*-glycero-*D*-talo-octitol* (**33a,b**).—Treatment of **30a,b** (580 mg, 0.82 mmol) with $NaBH_4$ (360 mg), under the same conditions as described for **7a,b**, yielded **31a,b** (440 mg, 79%) as an oil; TLC (1:1 PE–EtOAc): R_f 0.55.

A sample of **31a,b** (50 mg) was acetylated under the usual conditions. The syrupy acetate was purified by flash chromatography (3:1 PE–EtOAc); **33a,b** was obtained quantitatively; TLC (3:1 PE–EtOAc): R_f 0.48; ^{1}H NMR ($CDCl_3$): major product, δ 1.85–2.14 (m, 2 H, H-3a,3b), 1.90 and 1.96 (2 s, 6 H, 2 OAc), 3.63–3.89, 3.95–4.02, 4.06–4.13, 4.25 (4 m, 8 H, H-1a,1b,4,5,6,7,8a,8b), 4.29 and 4.41–4.82 (2 m, 10 H, 5 OCH_2Ph), 5.25 (m, 1 H, H-2), 7.25–7.33 (m, 25 H, 5 Ph); minor product, δ 1.85–2.14 (m, 2 H, H-3a,3b), 1.92 and 1.98 (2 s, 6 H, 2 OAc), 3.63–3.89, 3.95–4.02, 4.06–4.13, 4.25 (4 m, 8 H, H-1a,1b,4,5,6,7,8a,8b), 4.29 and 4.41–4.82 (2 m, 10 H, 5 OCH_2Ph), 5.36 (m, 1 H, H-2), 7.25–7.33 (m, 25 H, 5 Ph). Anal. Calcd for $C_{47}H_{52}O_9$ (acetylated compounds): C, 74.19; H, 6.89. Found: C, 74.03; H, 6.75.

*1,2,4,5,6,7,8-Hepta-*O*-acetyl-3-deoxy-*D*-glycero-*D*-galacto-octitol and 1,2,4,5,6,7,8-hepta-*O*-acetyl-3-deoxy-*D*-glycero-*D*-talo-octitol* (**32a,b**).—Mixture **31a,b** (440 mg, 0.65 mmol) was debenzylated and acetylated as described for **8a,b**; **32a,b** (273 mg, 80%) was obtained as an oil; TLC (1:1 PE–EtOAc): R_f 0.29; ^{1}H NMR ($CDCl_3$): major product, δ 1.91 (m, 2 H, H-3a,3b), 2.02–2.11 (m, 21 H, 7 OAc), 4.05 (dd, 1 H, $J_{1a,2}$ 5.7, $J_{1a,1b}$ 12.0 Hz, H-1a), 4.09 (dd, 1 H, $J_{7,8a}$ 5.2, $J_{8a,8b}$ 12.5 Hz, H-8a), 4.22 (dd, 1 H, $J_{7,8b}$ 3.0 Hz, H-8b), 4.25 (dd, 1 H, $J_{1b,2}$ 3.6 Hz, H-1b), 5.01–5.13 (m, 3 H, H-2,4,7), 5.27 (dd, 1 H, $J_{5,6}$ 2.7, $J_{4,5}$ 7.4 Hz, H-5), 5.41 (dd, 1 H, $J_{6,7}$ 8.6 Hz, H-6); minor product, δ 1.73–1.94 (m, 2 H, H-3a,3b), 2.02–2.11 (m, 21 H, 7 OAc), 3.98 (dd, 1 H, $J_{1a,2}$ 5.6, $J_{1a,1b}$ 11.9 Hz, H-1a), 4.11 (dd, 1 H, $J_{7,8a}$ 5.4, $J_{8a,8b}$ 12.3 Hz, H-8a), 4.19–4.25 (m, 2 H, H-1b,8b), 5.01–5.13 (m, 3 H, H-2,4,7), 5.27 (m, 1 H, H-5),

5.43 (dd, 1 H, *J* 3.0, *J* 8.3 Hz, H-6). Anal. Calcd for $C_{22}H_{32}O_{14}$ (520.49): C, 50.77; H, 6.20. Found: C, 50.88; H, 6.04.

3-Deoxy-D-glycero-D-galacto-*octitol and 3-deoxy*-D-glycero-D-talo-*octitol* (**34a,b**). —Mixture **32a,b** (224 mg, 0.43 mmol) was deprotected and purified as described for **10a,b**, to give **34a,b** (75 mg, 77%); TLC (5:4:1 $CHCl_3$–MeOH–water): R_f 0.29. Acetylation of **34a,b** under the usual conditions gave **32a,b** in quantitative yield.

ACKNOWLEDGMENTS

The authors thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support of this work, V. Susott for technical assistance, and H. Moll for recording the mass spectra.

REFERENCES

1 F.M. Unger, *Adv. Carbohydr. Chem. Biochem.*, 122 (1983) 323–388.
2 D.H. Levin and E. Racker, *J. Biol. Chem.*, 234 (1959) 2532–2539.
3 O. Holst and H. Brade, in D.C. Morrison and J.L. Ryan (Eds.), *Bacterial Endotoxic Lipopolysaccharides*, Vol. 1, CRC Press, 1992, in press.
4 B. Jann and K. Jann, *Curr. Top. Microbiol. Immunol.*, 150 (1990) 19–42.
5 E.C. Heath and M.A. Ghalambor, *Biochem. Biophys. Res. Commun.*, 10 (1963) 340–345.
6 M.A. Ghalambor, E.M. Levine, and E.C. Heath, *J. Biol. Chem.*, 241 (1966) 3207–3215.
7 W. Frick, T. Krülle, and R.R. Schmidt, *Liebigs Ann. Chem.*, (1991) 435–438.
8 M. Blanc-Muesser, J. Defaye, and D. Horton, *Carbohydr. Res.*, 87 (1980) 71–86.
9 W. Frick, Thesis, Universität Konstanz, 1989.
10 J. Ciucanu and F. Kerek, *Carbohydr. Res.*, 131 (1984) 209–217.
11 T. Waeghe, A.G. Darvill, M. McNeil, and P. Albersheim, *Carbohydr. Res.*, 123 (1983) 281–304.
12 R.R. Schmidt and W. Frick, *Tetrahedron*, 44 (1988) 7163–7169.