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Preliminary communication

Synthesis of a trisaccharide of the inner core region of *Citrobacter PCM* 187 lipopolysaccharide that contains L-*glycero*-α-D-*manno*-heptopyranosyl* units

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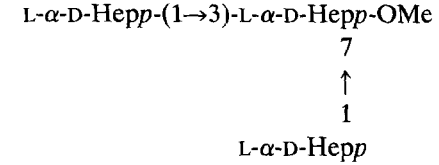
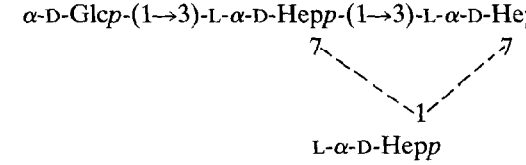
We recently published[1] a new stereoselective hydroxymethylation method for the preparation of L-*glycero*-D-*manno*-heptopyranosides. In this approach the *anti*-diastereogenic addition of (dimethylphenylsilyl)methylmagnesium chloride **2** to a D-*manno*-hexadialdo-1,5-pyranoside (*e.g.*, **1**) constitutes the key carbon bond-forming step: the resulting α-hydroxysilane adduct (*e.g.*, **3**) is then converted to the homologous L-*glycero*-D-*manno*-heptopyranose (*e.g.*, **6**) by generating the hydroxy group from the silyl moiety. Herein we report the successful extension of this concept to the assembly of the branched trisaccharide,



which (see **17**) has been proposed[2] to be part of the inner core region of *Citrobacter PCM* 187 lipopolysaccharide**, as shown here:



*Abbreviated L-α-D-Hepp.
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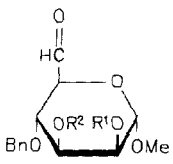
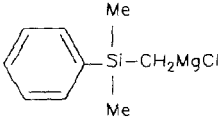
**Alternative locations of the branch terminal heptose are marked by dashed lines.

The key step in the synthesis of acceptor and donor L-D-Hep*p* units **6** and **14**, respectively, could be realized by exploiting the above-referenced stereoselective hydroxymethylene extension method. Thus addition (0°) of **2** in 1,3-dioxolane to 3-*O*-allyl-2,4-di-*O*-benzyl-α-D-*manno*-hexodialdo-1,5-pyranoside[3] (**1**) in the same solvent occurred with high diastereofacial selectivity to afford **3** (d.p. ≥95%) in a yield of 72%; **3** $[\alpha]_D$ +25° (*c* 0.8)†. R_F 0.5 (2:1 pet. ether–ether); ^{1}H-n.m.r. data ($CDCl_3$): δ 4.65 (s, H-1), 1.38 (dd, H-7a), 0.97 (dd, H-7b) and 0.46 [s, $(CH_3)_2Si$]; ^{13}C-n.m.r. data: δ 99.5 (C-1), 21.8 (C-7), −2.0 and −2.4 [$(CH_3)_2Si$]. Benzylation of **3** according to Czernecki *et al.*[4] gave **4** in 97% yield; $[\alpha]_D$ +26.0° (*c* 0.9); R_F 0.7 (2:1 pet. ether–ether). Deallylation[5] of **4** in the presence of 10% Pd–C and *p*-toluenesulfonic acid in 5:1 MeOH–H_2O for 8 h at 70° afforded **5** in 70% yield; $[\alpha]_D$ +21.6° (*c* 1); R_F 0.3 (2:1 pet. ether–ether). Removal of the allyl ether of **4** was accompanied by the formation of a small amount (6%) of the Peterson[6] elimination product **7**; $[\alpha]_D$ +13.7° (*c* 1); R_F 0.25 (2:1 pet. ether–ether); ^{13}C-n.m.r. data ($CDCl_3$): δ 135.7 (C-7), 118.1 (C-6) and 98.0 (C-1). Generating the hydroxy group from the silyl moiety in **5** according to Fleming *et al.*[7] with peroxyacetic acid and potassium bromide in AcOH-NaOAc in the dark for 1.5 h at 25° furnished glycosyl acceptor **6** in 82% yield; $[\alpha]_D$ +37.0° (*c* 1); R_F 0.2 (97:3 CH_2Cl_2–acetone); ^{1}H-n.m.r. data ($CDCl_3$): δ 4.56 (d, *J* 2 Hz, H-1), 3.94 (m, H-7a and 7b); ^{13}C-n.m.r. data: δ 97.7 (C-1) and 61.3 (C-7).

Glycosyl donor **14** was synthesized in an overall yield of 65% starting from **8**



1 R¹ = Bn, R² = All



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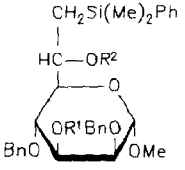
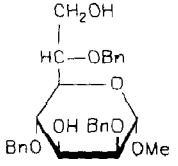


3 R¹ = All, R² = H

4 R¹ = All, R² = Bn

5 R¹ = H, R² = Bn



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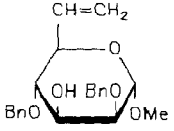

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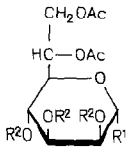
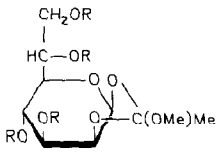
†Unless otherwise noted, optical rotations were determined at 25° in $CHCl_3$ solutions at the indicated concentration.



8 R^1 = OMe, R^2 = Ac

9 R^1 = OAc, R^2 = Ac

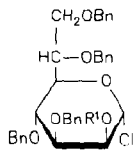
10 R^1 = Br, R^2 = Ac



11 R = Ac

12 R = H

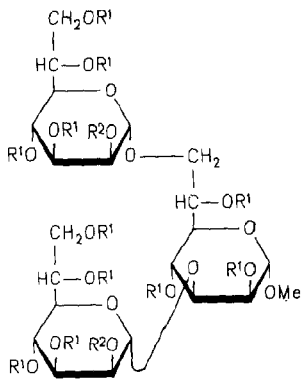
13 R = Bn



14 R^1 = Ac

which was obtained[1] *via* the same hydroxymethylene extension principle. Acetolysis of **8** with HOAc–H_2SO_4 resulted in **9**, which was converted quantitatively with HBr–AcOH in the known[8] α-D-glycosyl bromide **10**. Transformation of **10** into the α-D-glycosyl chloride **14** was executed *via* intermediates **11, 12,** and **13** according to Paulsen and Heitman[8].

Glycosylation of acceptor **6** with donor **14** under the conditions described by Hanessan and Banoub[9] in the absence of 1,1,3,3-tetramethylurea gave a 71% yield of trisaccharide **15**; $[\alpha]_D$ +31.6° (*c* 1); R_F 0.6 (97:3 CH_2Cl_2–acetone); ^{1}H-n.m.r. data ($CDCl_3$): δ 5.42 (t, *J* = 2 Hz, H-2″), 5.26 (t, *J* = 2 Hz, H-2′), 5.17 (bs, H-1″), 4.82 (d, H-1′), and 4.45 (d, H-1). Zemplén deacylation of **15** led to the isolation of **16** in 95% yield; $[\alpha]_D$ +28.2° (*c* 1). Hydrogenolysis of **16** in the presence of 10% Pd–C in EtOH afforded the target methyl *O*-L-*glycero*-α-D-*manno*-heptopyranosyl-(1→3)-*O*-[L-*glycero*-α-D-*manno*-heptopyranosyl-(1→7)]-L-*glycero*-α-D-*manno*-heptopyranoside (**17**) in 85% yield; $[\alpha]_D$ +114.2° (*c* 1, H_2O). The ^{1}H-n.m.r. spectrum in $CDCl_3$ at 20° showed signals for the three anomeric protons at δ 5.11 (d, 1



15 R^1 = Bn, R^2 = Ac

16 R^1 = Bn, R^2 = H

17 R^1 = R^2 = H

H, J = 2 Hz), 4.88 (d, 1 H, J = 2 Hz), and 4.71 (d, 1 H, J = 2 Hz). The stereochemistry at all three anomeric carbon atoms was confirmed by ^{13}C-n.m.r. spectroscopy ($CDCl_3$, at 20°), which showed three signals for anomeric carbon atoms of L-α-D-Hep*p* residues at δ 103.4 ($^1J_{CH}$ = 172.9 Hz), 101.9 ($^1J_{CH}$ = 172.2 Hz), and 101.6 ($^1J_{CH}$ = 171.5 Hz), in excellent agreement with the $^1J_{CH}$ value at anomeric carbon atoms observed by Bock and Pedersen[10].

In conclusion the *anti* addition of (dimethylphenylsilyl)methylmagnesium chloride to a properly protected D-*manno*-hexodialdo-1,5-pyranoside gives easy access to L-α-D-Hep*p* units suitable for the assembly of naturally occurring oligosaccharides. In close connection with our approach to the synthesis of **6** and **14**, it may also be noted that other approaches to these type of compounds have been recently reported by Paulsen *et al.*[11], Brimacombe and Kabir[12], and Dziewiszek and Zamojski[13].

ACKNOWLEDGMENTS

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