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Note

Synthesis of 4-*O*-(1-deoxy-D-alditol-1-yl)-D-alditols from disaccharide derivatives

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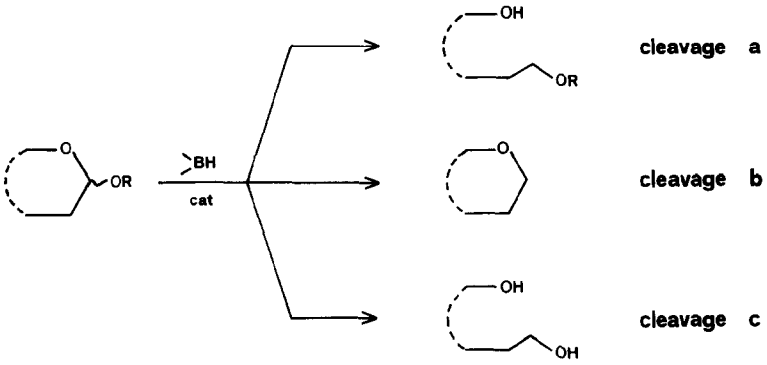
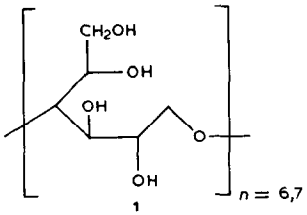
The reduction of glycosides and disaccharides with ethyldiborane and 9-borabicyclo[3.3.1]non-9-yl mesylate (9-BBN mesylate) as catalyst[1] can proceed by cleavage of the *endo*-acetal bond (Scheme 1, cleavage a) to give 1-*O*-substituted alditols or cleavage of the *exo*-acetal bond (cleavage b) to give 1,5-anhydroalditols. In some instances, a third type of cleavage was found between O-1 and the aglycon carbon (cleavage c) to give alditols. We have observed[2] that treatment of cyclomalto-hexaose and -heptaose (α- and β-cyclodextrin) with this reagent gives, *inter alia*, the new, chiral, macrocyclic polyhydroxy-ether **1**.



Scheme 1



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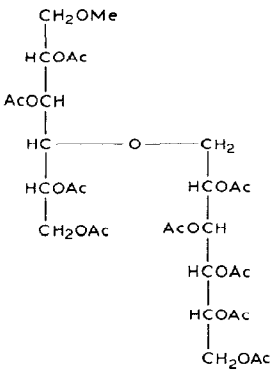
The reduction of per-*O*-diethylboryl-disaccharides gives alditol-(1→*n*)-alditols. These compounds, conveniently substituted, may be considered as synthons for the preparation of other cyclic polyhydroxy-ethers in which the nature and number of the alditol-(1→*n*)-alditol components can be varied at will. Such units as ethylene glycol, diamines, *etc.* could also be introduced into the cyclic molecule.

We now report the preparation of several substituted 4-*O*-(1-deoxy-D-alditol-1-yl)-D-alditols for use in exploring the synthesis of macrocyclic polyhydroxy-ethers.

Treatment of methyl hepta-*O*-diethylboryl-β-maltoside[3,4] (**2**) with ethyldiborane and 9-BBN mesylate at 110° gave, after deboronation and acetylation, a mixture containing mainly 2,3,5,6-tetra-*O*-acetyl-1-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-glucitol-1-yl)-D-glucitol (**3**, 36%) together with 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol (**4**, 17%), hexa-*O*-acetyl-D-glucitol (**5**, 8%), and 2,3,4,5,6-penta-*O*-acetyl-1-*O*-methyl-D-glucitol (**6**, 17%). The yields were determined by g.l.c.



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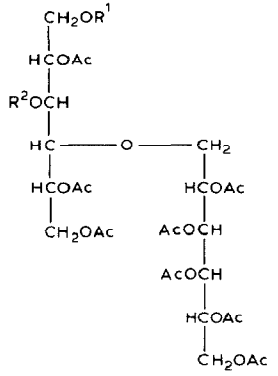


8 R^1 = Me, R^2 = Ac
11 R^1 = Bn, R^2 = Ac
12 R^1 = R^2 = Ac
15 R^1 = Ac, R^2 = Me

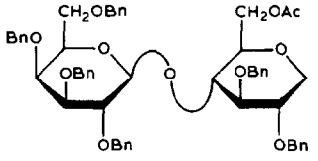
Similar treatment of methyl hepta-*O*-diethylboryl-β-lactoside[3,5] (**7**) gave 2,3,5,6-tetra-*O*-acetyl-1-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-galactitol-1-yl)-D-glucitol (**8**, 70%) and a mixture (5%) of 2,3,4,5,6-penta-*O*-acetyl-1-*O*-methyl-D-glucitol (**6**) and 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-galactitol (**9**).

Likewise, benzyl hepta-*O*-diethylboryl-β-lactoside[3,6] (**10**) gave 2,3,5,6-tetra-*O*-acetyl-1-*O*-benzyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-galactitol-1-yl)-D-glucitol (**11**, 43%), 1,2,3,5,6-penta-*O*-acetyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-galactitol-1-yl)-D-glucitol (**12**, 17%), and a mixture (40%) of **4**, **5**, and **9**. Compound **12** was also obtained (70%) by reduction of per-*O*-diethylboryl-D-lactose[3].

Treatment of 1,2,6,2′,3′,4′,6′-hepta-*O*-diethylboryl-3-*O*-methyl-lactose[3,7]

(**14**) under similar conditions gave 1,2,5,6-tetra-*O*-acetyl-3-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-D-galactitol-1-yl)-D-glucitol (**15**, 60%).

Reduction of 1,6-anhydrohexa-*O*-benzyl-β-lactose[8] (**16**) under mild conditions (27% catalyst, 3 h) gave only 6-*O*-acetyl-1,5-anhydro-2,3-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranosyl)-D-glucitol (**17**, 74%).



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EXPERIMENTAL

General methods. — All experiments were carried out under argon. T.l.c. was performed on silica gel GF_{254} (Merck) with detection by charring with sulfuric acid. Column chromatography was performed on Merck silica gel (70–230 mesh). ^1H- and ^{13}C-n.m.r. spectra were recorded for solutions in C_6D_6 using a Varian XL-300 and a Bruker VP-80 (20.2 MHz) spectrometer, respectively. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. G.l.c. was performed on a Perkin–Elmer 3920 gas chromatograph equipped with an SE-30 capillary column.

Ethyldiborane (15.8 mol of H^-/1000 g) and 9-BBN mesylate were prepared as reported in the literature[9].

*2,3,5,6-Tetra-*O*-acetyl-1-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-*D*-glucitol-1-yl)-*D*-glucitol* (**3**). — A stirred mixture of methyl hepta-*O*-diethylboryl-β-maltoside (**2**; 1.16 g, 1.40 mmol), ethyldiborane (1.28 g, 20.2 mmol), and 9-BBN mesylate (85 mg, 0.39 mmol) was heated at 120° for 9 h. The solution was cooled to room temperature, the volatile components were removed *in vacuo*, and the residue was treated first with boiling methanol (3 mL), which was evaporated, and then with ethane-1,2-diol (2 mL), which was evaporated at 70°/10^{-3} Torr. The treatment with ethane-1,2-diol was repeated until a boron-free residue was obtained. The residue was conventionally acetylated with acetic anhydride (2 mL) and pyridine (5 mL), and the mixture was concentrated. G.l.c. of the residue revealed a main product and three by-products [identified as 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol (**4**), hexa-*O*-acetyl-D-glucitol (**5**), and 2,3,4,5,6-penta-*O*-acetyl-1-*O*-methyl-D-glucitol (**6**) by comparison with authentic samples]. The mixture was fractionated by column chromatography (chloroform–ethyl acetate, 2:1) to afford **3** (300 mg, 30%) as a syrup, $[\alpha]_D^{20}$ +35° (*c* 0.9, chloroform). N.m.r. data (C_6D_6): ^1H, δ 5.91 (dd, 1 H, $J_{2',3'}$ 8.0, $J_{3',4'}$ 2.6 Hz, H-3'), 5.77 (m, 1 H, H-2), 5.74 (dd, 1 H, $J_{4',5'}$ 8.4 Hz, H-4'), 5.68 (m, 1 H, H-3), 5.46 (m, 1 H, H-5'), 5.40 (m, 1 H, H-5), 5.32 (m, 1 H, H-2'), 4.81 (dd, 1 H, $J_{6a,5}$ 3.7, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.40 (dd, 1 H, $J_{6'a,6'b}$ 12.4, $J_{6'a,5'}$ 2.8 Hz, H-6'a), 4.32 (dd, 1 H, $J_{6b,5}$ 6.5 Hz, H-6b), 4.22 (dd, 1 H,

$J_{6'b,5'}$ 5.3 Hz, H-6'b), 4.08 (dd, 1 H, $J_{1'b,2'}$ 3.9 Hz, H-1'b), 4.01 (t, 1 H, $J_{3,4} \simeq J_{4,5} \simeq$ 5.3 Hz, H-4), 3.87 (dd, 1 H, $J_{1'a,1'b}$ 10.8, $J_{1'a,2'}$ 2.8 Hz, H-1'a), 3.59 (dd, 1 H, $J_{1b,2}$ 5.2 Hz, H-1b), 3.45 (dd, 1 H, $J_{1a,1b}$ 10.5, $J_{1a,2}$ 5.2 Hz, H-1a), 3.12 (s, 3 H, OMe), and 2.00–1.66 (s, 27 H, 9 Ac); ^{13}C, 170.0–169.5 (C=O), 78.77 (C-4), 71.45, 71.20 (triple intensity), 70.9, 70.5, 69.2, 68.9, 68.7, 62.4, 62.0 (C-6,6'), 58.9 (OMe), and 20.6–20.2 (CH_3CO).

Anal. Calc. for $C_{31}H_{46}O_{20}$: C, 50.41; H, 6.23. Found: C, 50.36; H, 6.15.

*2,3,5,6-Tetra-*O*-acetyl-1-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-*D*-galactitol-1-yl)-*D*-glucitol* (**8**). — A mixture of methyl hepta-*O*-diethylboryl-β-lactoside (**7**; 1.16 g, 1.40 mmol), ethyldiborane (1.22 g, 19.2 mmol), and 9-BBN mesylate (132.2 mg, 0.61 mmol) was treated as described for **2**. Column chromatography (chloroform–ethyl acetate, 2:1) of the product mixture gave **8** (526 mg, 60%) as a syrup, $[\alpha]_D^{20}$ +24° (*c* 1, chloroform). N.m.r. data (C_6D_6): ^{1}H, δ 5.69–5.59 (m, 5 H, H-2,3,3',4',5'), 5.43–5.39 (m, 2 H, H-2',5), 4.69 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{6a,5}$ 3.1 Hz, H-6a), 4.45 (dd, 1 H, $J_{6'a,6'b}$ 11.7, $J_{6'a,5'}$ 5.0 Hz, H-6'a), 4.24 (dd, 1 H, $J_{6b,5}$ 5.9 Hz, H-6b), 3.94 (dd, 1 H, $J_{6'b,5'}$ 7.4 Hz, H-6'b), 3.83–3.81 (m, 2 H, H-1'a,1'b), 3.50 (dd, 1 H, $J_{1a,1b}$ 10.5, $J_{1a,2}$ 4.6 Hz, H-1a), 3.37 (dd, 1 H, $J_{1b,2}$ 4.7 Hz, H-1b), 3.06 (s, 3 H, OMe), and 1.95–1.70 (s, 27 H, 9 Ac); ^{13}C, 170.0–169.7 (C=O), 78.3 (C-4), 71.4, 71.1 (double intensity), 70.8, 70.4, 69.0, 68.4, 68.2 (double intensity), 62.5 (double intensity, C-6,6'), 58.9 (OMe), and 20.6–20.2 (CH_3CO).

Anal. Calc. for $C_{31}H_{46}O_{20}$: C, 50.41; H, 6.23. Found: C, 50.52; H, 6.57.

*2,3,5,6-Tetra-*O*-acetyl-1-*O*-benzyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-*D*-galactitol-1-yl)-*D*-glucitol* (**11**) *and 1,2,3,5,6-penta-*O*-acetyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-*D*-galactitol-1-yl)-*D*-glucitol* (**12**). — A mixture of benzyl hepta-*O*-diethylboryl-β-lactoside (**10**; 1.04 g, 1.15 mmol), ethyldiborane (1.35 g, 21.3 mmol), and 9-BBN mesylate (151.7 mg, 0.70 mmol) was treated as for **2**. Column chromatography (hexane–ethyl acetate, 1:1) of the product mixture gave, first, **11** (230 mg, 35%) as a syrup, $[\alpha]_D^{20}$ +30.5° (*c* 0.7, chloroform). N.m.r. data (C_6D_6): ^{1}H, δ 5.80–5.59 (m, 5 H, H-2,3,3',4',5'), 5.44–5.37 (m, 2 H, H-2',5), 4.68 (dd, 1 H, $J_{6a,5}$ 3.3, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.45 (dd, 1 H, $J_{6'a,6'b}$ 11.6, $J_{6'a,5'}$ 5.1 Hz, H-6'a), 4.35 (d, 1 H, *J* 11.8 Hz, CH_2Ph), 4.23 (d, 1 H, CH_2Ph), 4.22 (dd, 1 H, $J_{6b,5}$ 5.2 Hz, H-6b), 3.93 (dd, 1 H, $J_{6'b,5'}$ 7.1 Hz, H-6'b), 3.90 (dd, 1 H, *J* 4.4 and 6.4 Hz, H-4), 3.79 (dd, 1 H, $J_{1'a,1'b}$ 10.1, $J_{1'a,2'}$ 6.2 Hz, H-1'a), 3.69 (dd, 1 H, $J_{1'b,2'}$ 5 Hz, H-1'b), 3.60 (dd, 1 H, $J_{1b,2}$ 4.5 Hz, H-1b), 3.52 (dd, 1 H, $J_{1a,1b}$ 10.5, $J_{1a,2}$ 4.9 Hz, H-1a), and 1.94–1.62 (s, 27 H, 9 Ac); ^{13}C, 170.2–169.7 (C=O), 138.2 (C-ipso), 78.5 (C-4), 73.5, 71.0 (triple intensity), 70.6, 69.1, 68.8, 68.4, 68.3 (double intensity), 62.6 (double intensity, C-6,6') and 20.6–20.3 (CH_3CO).

Anal. Calc. for $C_{37}H_{50}O_{20}$: C, 54.54; H, 6.14. Found: C, 54.27; H, 6.11.

Eluted second was **12** (150 mg) as a syrup, $[\alpha]_D^{20}$ +23.5° (*c* 0.3, chloroform). N.m.r. data (C_6D_6): ^{1}H, δ 5.74 (m, 1 H, H-2), 5.64–5.57 (m, 4 H, H-3,3',4',5'), 5.42 (m, 1 H, H-2'), 5.35 (m, 1 H, H-5), 4.66 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{6a,5}$ 3.7 Hz, H-6a), 4.50 (dd, 1 H, $J_{1a,1b}$ 12.0, $J_{1a,2}$ 4.2 Hz, H-1a), 4.45 (dd, 1 H, $J_{6'a,6'b}$ 11.8, $J_{6'a,5'}$ 5.1 Hz, H-6'a), 4.21 (dd, 1 H, $J_{6b,5}$ 6.1 Hz, H-6b), 4.17 (dd, 1 H, $J_{1b,2}$ 6.0 Hz,

H-1b), 3.93 (dd, 1 H, $J_{6'b,5'}$ 7.3 Hz, H-6'b), 3.89 (t, 1 H, $J_{3,4} \simeq J_{4,5} \simeq 5.1$ Hz, H-4), 3.79 (dd, 1 H, $J_{1'a,1'b}$ 10.2, $J_{1'a,2'}$ 6.4 Hz, H-1'a), 3.73 (dd, 1 H, $J_{1'b,2'}$ 5.3 Hz, H-1'b), and 1.90–1.70 (s, 30 H, 10 Ac); ^{13}C, 170.2–170.0 (C=O), 78.6 (C-4), 71.4, 70.9, 70.6, 70.0, 69.1, 68.3 (triple intensity), 62.5 (triple intensity, C-1,6,6'), and 20.6–20.3 (CH_3CO).

Anal. Calc. for $C_{32}H_{46}O_{21}$: C, 50.13; H, 6.00. Found: C, 50.30; H, 6.10.

*1,2,5,6-Tetra-*O*-acetyl-3-*O*-methyl-4-*O*-(2,3,4,5,6-penta-*O*-acetyl-1-deoxy-*D*-galactitol-1-yl)-*D*-glucitol* (**15**). — A mixture of 1,2,6,2',3',4',6'-hepta-*O*-diethylboryl-3-*O*-methyl-lactose (**14**; 208 mg, 0.25 mmol), ethyldiborane (0.29 g, 4.6 mmol), and 9-BBN mesylate (32.8 mg, 0.15 mmol) was treated as described for **2**. Column chromatography (hexane–ethyl acetate, 1:1) of the product mixture gave **15** (83.7 mg, 45%) as a syrup, $[\alpha]_D^{20}$ +15° (*c* 0.4, chloroform). N.m.r. data (C_6D_6): ^{1}H, δ 5.72 (dd, 1 H, $J_{3',4'}$ 10.0 Hz, H-3'), 5.66–5.57 (m, 3 H, H-2,4',5'), 5.50 (dt, 1 H, $J_{2',1'a} \simeq J_{2',1'b} \simeq 5.9$, $J_{2',3'}$ 1.7 Hz, H-2'), 5.39 (dt, 1 H, $J_{5,6b}$ 7.2, $J_{5,6a} \simeq J_{5,4} \simeq 3.6$ Hz, H-5), 4.65 (dd, 1 H, $J_{6a,6b}$ 12.2 Hz, H-6a), 4.56 (dd, 1 H, $J_{1a,1b}$ 11.8, $J_{1a,2}$ 3.8 Hz, H-1a), 4.45 (dd, 1 H, $J_{6'a,6'b}$ 11.4, $J_{6'a,5'}$ 4.9 Hz, H-6'a), 4.39 (dd, 1 H, $J_{1b,2}$ 7.0 Hz, H-1b), 4.36 (dd, 1 H, H-6b), 3.93 (dd, 1 H, $J_{6'b,5'}$ 7.4 Hz, H-6'b), 3.82–3.79 (m, 3 H, H-1'a,1'b,4), 3.46 (dd, 1 H, $J_{2,3}$ 4.5, $J_{3,4}$ 6.2 Hz, H-3), 3.27 (s, 3 H, MeO), and 1.90–1.70 (s, 27 H, 9 Ac); ^{13}C, 170.1–169.9 (C=O), 81.2, 80.8 (C-3,4), 72.7, 71.8, 70.9, 69.1, 68.3 (triple intensity), 63.0, 62.5 (double intensity) (C-1,6,6'), 60.5 (OMe), and 20.6–20.3 (CH_3CO).

Anal. Calc. for $C_{31}H_{46}O_{20}$: C, 50.41; H, 6.23. Found: C, 50.47; H, 6.48.

*6-*O*-Acetyl-1,5-anhydro-2,3-di-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-β-*D*-galactopyranosyl)-*D*-glucitol* (**17**). — A stirred mixture of 1,6-anhydrohexa-*O*-benzyl-β-lactose (**16**; 330 mg, 0.38 mmol), ethyldiborane (1.73 g, 27.3 mmol), and 9-BBN mesylate (22 mg, 0.1 mmol) was heated to 120° for 3 h. The solution was worked up as described for **2**. Column chromatography (hexane–ethyl acetate, 7:4) of the product mixture gave **17** (250 mg, 74%) as a syrup, $[\alpha]_D^{20}$ +9° (*c* 0.5, chloroform). N.m.r. data (C_6D_6): ^{1}H δ 4.71 (dd, 1 H, $J_{6a,6b}$ 11.8, $J_{6a,5}$ 2.0 Hz, H-6a), 4.57 (dd, 1 H, $J_{6b,5}$ 3.5 Hz, H-6b), 4.49 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.03 (dd, 1 H, $J_{2',3'}$ 9.7 Hz, H-2'), 3.90 (dd, 1 H, $J_{1b,2}$ 5.0 Hz, H-1b), 3.89 (t, 1 H, $J_{3,4} \simeq J_{4,5} \simeq 8.4$ Hz, H-4), 3.81 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-4'), 3.64 (dd, 1 H, $J_{2,3}$ 8.2 Hz, H-3), 3.50 (m, 1 H, H-2), 3.34 (m, 2 H, H-3',5), 3.09 (dd, 1 H, $J_{1a,1b}$ 11.0, $J_{1a,2}$ 10.0 Hz, H-1a), and 1.64 (s, 3 H, Ac); ^{13}C, 169.9 (C=O), 140.2–138.9 (C-ipso), 103.8 (C-1'), 84.7, 83.0, 80.6, 78.5, 78.1 (double intensity), 75.4 (double intensity), 75.2, 74.6, 74.1, 73.6, 73.4, 73.0, 68.9, 68.3, 63.5, and 20.5 (CH_3CO).

Anal. Calc. for $C_{56}H_{60}O_{11}$: C, 74.01; H, 6.61. Found: C, 73.69; H, 6.72.

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