Carbohydrate Research, 68 (1979) 151–154

Note

A simple method for the synthesis of benzyl 4-*O*-benzylhexopyranosides

ANDRÁS LIPTÁK, PÉTER FUGEDI, AND PÁL NÁNÁSI
Institute of Biochemistry, L. Kossuth University, H-4010 Debrecen (Hungary)
(Received December 29th, 1977; accepted for publication, January 13th, 1978)

We have found[1] that hydrogenolysis of 2,3-di-*O*-benzyl-4,6-*O*-benzylidenehexopyranosides containing a *trans*-fused ring system yields the 4-benzyl ethers, whereas the *cis*-fused analogues yield both 4- and 6-*O*-benzyl derivatives. We now report that the hydrogenolytic ring-cleavage of 2,3-di-*O*-allyl-4,6-*O*-benzylidenehexopyranosides offers a simple route to 4-*O*-benzylhexopyranosides.

Allylation of benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside[2] and hydrogenolysis of the 2,3-di-*O*-allyl derivative with the $LiAlH_4$–$AlCl_3$ reagent gave benzyl 2,3-di-*O*-allyl-4-*O*-benzyl-β-D-glucopyranoside which, upon removal of the allyl groups[3], gave benzyl 4-*O*-benzyl-β-D-glucopyranoside. Likewise, benzyl 4,6-*O*-benzylidene-α-D-mannopyranoside[4] was converted into benzyl 4-*O*-benzyl-α-D-mannopyranoside.

Conversion of benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside[5] into the 2,3-di-*O*-allyl derivative followed by reduction with the $LiAlH_4$–$AlCl_3$ reagent yielded an 81:19 mixture (g.l.c.) of benzyl 2,3-di-*O*-allyl-4-*O*-benzyl- and benzyl 2,3-di-*O*-allyl-6-*O*-benzyl-β-D-galactopyranoside. Removal of the allyl groups from the former compound gave benzyl 4-*O*-benzyl-β-D-galactopyranoside.

The foregoing benzyl 4-*O*-benzylhexopyranosides, each of which consumed ~1 mol. of periodate[6] without liberation of formic acid, were synthesised from the corresponding benzyl 4,6-*O*-benzylidenehexopyranosides in three steps in good yields. The synthesis of methyl 4-*O*-benzyl-α-D-glucopyranoside by the conventional tritylation procedure required eight steps[7].

EXPERIMENTAL

Melting points (uncorrected) were determined with a Kofler apparatus. T.l.c. and column chromatography were performed on Kieselgel G; detection was effected in t.l.c. by charring with 50% sulphuric acid. G.l.c. was carried out on a Hewlett–Packard 5830A instrument fitted with a helical stainless-steel column (2ft × 0.4 mm i.d.) packed with 10% of UCW-982 Chromosorb WAW/DMCS (80–100 mesh). The temperature programme was started from 250° at 5°/min. The carrier gas was

nitrogen at 20 ml/min. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter. ^{1}H-N.m.r. spectra were recorded with a Jeol MH-100 spectrometer.

*Benzyl 2,3-di-*O*-allyl-4,6-*O*-benzylidene-β-*D*-glucopyranoside.* — Sodium hydride (6 g) was added portionwise to a solution of benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside[2] (9 g) in dry *N,N*-dimethylformamide (50 ml) with stirring. The mixture was kept at 25° for 30 min and then cooled to 0°. Allyl bromide (22 ml) was then added dropwise followed by stirring at room temperature for 20 h. Excess of NaH was decomposed with methanol, and the mixture was concentrated, and then treated with chloroform (200 ml) and water (100 ml). The chloroform layer was washed with water (5 × 100 ml), dried (Na_2SO_4), and concentrated. Crystallisation of the residue from hexane (230 ml) gave the title compound (9.91 g, 90%), m.p. 110–111°, $[\alpha]_D$ −63° (*c* 0.61, chloroform), R_F 0.76 (benzene–methanol, 96:4).

Anal. Calc. for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.18; H, 6.95.

*Benzyl 2,3-di-*O*-allyl-4-*O*-benzyl-β-*D*-glucopyranoside.* — To a solution of the foregoing compound (6.6 g) in dichloromethane (50 ml) and ether (30 ml) was added $LiAlH_4$ (0.86 g) with stirring, and the mixture was heated to reflux. A solution of $AlCl_3$ (3 g) in ether (20 ml) was then added during 5 min, and boiling was continued for 2 h. After cooling, the excess of reagent was decomposed with ethyl acetate, and $Al(OH)_3$ was precipitated with water. The reaction mixture was diluted with ether (100 ml), the organic layer was decanted, and the precipitate was washed with ether (3 × 50 ml). The combined ethereal solutions were washed with water (3 × 50 ml), dried (Na_2SO_4), and concentrated, to give the title compound (6.2 g, 94%) which was used for the next steps without any further purification. Recrystallisation from ethanol afforded material having m.p. 78–80°, $[\alpha]_D$ −25° (*c* 1.67, chloroform), R_F 0.44 (benzene–methanol, 96:4), *T* 3.70 min.

Anal. Calc. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 70.75; H, 7.28.

*Benzyl 4-*O*-benzyl-β-*D*-glucopyranoside.* — A mixture of the foregoing compound (4.7 g), dry methyl sulphoxide (50 ml), and potassium *tert*-butoxide (4.7 g) was stirred at 100° for 2 h, cooled, diluted with water (200 ml), and extracted with chloroform (3 × 50 ml). The combined extracts were washed with water (5 × 50 ml), dried (Na_2SO_4), and concentrated. The crystalline residue was stirred with HgO (1.86 g) in acetone–water (10:1, 100 ml), and a solution of $HgCl_2$ (2.33 g) in acetone–water (10:1, 25 ml) was added dropwise. Stirring was continued for 30 min and then the reaction mixture was filtered through Celite and concentrated. A solution of the residue in chloroform (100 ml) was washed successively with aqueous 5% KI (3 × 50 ml) and water (3 × 50 ml), dried (Na_2SO_4), and concentrated. Crystallisation of the residue from ethyl acetate–hexane gave the title compound (1.90 g, 52%), m.p. 103–104°, $[\alpha]_D$ −25.5° (*c* 0.83, chloroform), R_F 0.28 (benzene–methanol, 9:1). N.m.r. data (Me_2SO-d_6): δ 7.25–7.00 (m, 10 H, aromatic), 5.08 (d, 2 H, HO-2,3), 4.61 (q, 2 H, PhCH_2), 4.59 (q, 2 H, PhCH_2), 4.57 (t, 1 H, HO-6), 4.19 (d, 1 H, H-1), and 3.70–2.90 (m, 6 H, H-2,3,4,5,6,6′).

Anal. Calc. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.61; H, 6.74.

Benzyl 2,3-di-O-allyl-4,6-O-benzylidene-α-D-mannopyranoside. — Allylation of benzyl 4,6-*O*-benzylidene-α-D-mannopyranoside[4] (2.1 g), as described for the β-D-*gluco* analogue, gave the title compound as a syrup (2.35 g, 91%), $[\alpha]_D$ +53.5° (*c* 1.33, chloroform), R_F 0.72 (benzene–methanol, 96:4).

Anal. Calc. for $C_{26}H_{30}O_6$: C, 71.21; H, 6.89. Found: C, 71.12; H, 6.83.

Benzyl 2,3-di-O-allyl-4-O-benzyl-α-D-mannopyranoside. — Treatment of the foregoing compound (2.2 g) with $LiAlH_4$–$AlCl_3$, as described for the β-D-*gluco* analogue, gave the title compound as a syrup (2.04 g, 92%), $[\alpha]_D$ +50° (*c* 1, chloroform), R_F 0.37 (benzene–methanol, 96:4).

Anal. Calc. for $C_{26}H_{32}O_6$: C, 70 89; H, 7.32. Found: C, 70.64; H, 7.41.

Benzyl 4-O-benzyl-α-D-mannopyranoside. — The foregoing compound (1.5 g) was de-allylated, as described for the β-D-*gluco* analogue, to give the title compound as a syrup (0.6 g, 49%), $[\alpha]_D$ +51° (*c* 3.14, chloroform), R_F 0.30 (benzene–methanol, 9:1). N.m r. data ($CDCl_3$): δ 7.30–7.10 (m, 10 H, aromatic), 4.85 (s, 1 H, H-1), 4.72 (q, 2 H, PhCH_2), 4.45 (q, 2 H, PhCH_2), and 4.20–3.20 (m, 9 H, H-2,3,4,5,6,6′ and HO-2,3,6).

Anal. Calc. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.47; H, 6.70.

Benzyl 2,3-di-O-allyl-4,6-O-benzylidene-β-D-galactopyranoside. — Benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside[5] (6 g) was allylated, as described for the β-D-*gluco* analogue, to give the title compound (6.05 g, 82%), m.p. 140–141° (from ethanol), $[\alpha]_D$ −0.3° (*c* 1.1, chloroform), R_F 0 64 (benzene–methanol, 96:4).

Anal. Calc. for $C_{26}H_{30}O_6$: C, 71.21; H. 6.89. Found: C, 71 24; H, 6.95.

Benzyl 2,3-di-O-allyl-4-O-benzyl- and benzyl 2,3-di-O-allyl-6-O-benzyl-β-D-galactopyranoside. — The foregoing compound (5.5 g) was treated with $LiAlH_4$–$AlCl_3$, as described for the β-D-*gluco* analogue, to give a crude product (5.2 g, 94%), which was shown by t.l.c. (benzene–methanol, 96:4) to consist of a major [R_F 0.33, *T* 3.56 min (81%)] and a minor component [R_F 0.48, *T* 3.86 mın (19%)]. Crystallisation of the crude product from cyclohexane (15 ml) gave the title 4-*O*-benzyl derivative (2.13 g, 39%), m p. 63–64°, $[\alpha]_D$ −54° (*c* 1.26, chloroform), R_F 0.33 (benzene–methanol, 96:4).

Anal. Calc. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32. Found: C, 70.70; H, 7.36.

The mother liquor was concentrated, and the residue was eluted from Kieselgel G (180 g) with benzene–methanol (96:4), to give, first, the title 6-*O*-benzyl compound as a syrup (0.7 g, 13%), $[\alpha]_D$ −27.5° (*c* 2.32, chloroform), R_F 0.48 (benzene–methanol, 96:4).

Anal. Found: C, 70.96; H, 7.45.

Subsequent elution gave the 4-*O*-benzyl derivative (0.95 g; total yield, 65%).

Benzyl 4-O-benzyl-β-D-galactopyranoside. — The foregoing 4-*O*-benzyl derivative (1 g) was de-allylated, as described for the β-D-*gluco* analogue, to give the title compound (0.36 g, 44%), m.p. 128–129°, $[\alpha]_D$ −50° (*c* 1.1, chloroform), R_F 0.27 (benzene–methanol, 9:1). N.m.r. data ($CDCl_3$ + Me_2SO-d_6): δ 7.54–7.10 (m, 10 H, aromatic), 4.98–4.55 (2 q, 4 H, 2 PhCH_2), 4.31 (d, 1 H, H-1), and 4.10–3.30 (m, 9 H, H-2,3,4,5,6,6′ and HO-2,3,6).

Anal. Calc. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.52; H, 6.73.

REFERENCES

1 A. Lipták, I. Jodál, and P. Nánási, *Carbohydr. Res.*, 44 (1975) 1–11.
2 A. Klemer, *Chem. Ber.*, 92 (1959) 218–226.
3 R. Gigg and C. D. Warren, *J. Chem. Soc., C*, (1968) 1903–1911.
4 G. Alfredsson, H. B. Boren, and P. J. Garegg, *Acta Chem. Scand.*, 26 (1972) 3431–3434.
5 J. R. Turvey and T. P. Williams, *J. Chem. Soc.*, (1962) 2119–2122.
6 G. W. Hay, B. A. Lewis, and F. Smith, *Methods Carbohydr. Chem.*, 5 (1965) 357–361.
7 J. W. Van Cleve and C. R. Russell, *Carbohydr. Res.*, 25 (1972) 465–473.