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Preliminary communication

Syntheses of partially protected methyl α-D-mannopyranosides*

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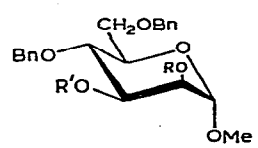
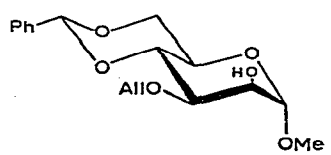
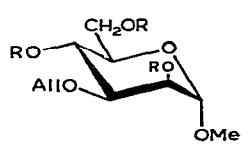
In recent years, much emphasis has been placed on the synthesis of complex saccharides[2,3]. The benzyl group has been used widely as a "persistent" protective group in various aglycon hydroxides suitable for such synthetic investigations in carbohydrate chemistry[4]. Recently, we reported selective monobenzylation of methyl 4-*O*-benzyl-α-L-rhamnopyranoside[1]. Using methyl 4,6-di-*O*-benzyl-α-D-mannopyranoside (**1**) as a model compound, we have studied monobenzylation under the various conditions now described.

In one of the approaches, we employed phase-transfer catalysis, as introduced by Garegg *et al.*[5], for selective monobenzylation of the 2-hydroxyl group. Thus, to a solution of compound **1** (2.6 g), tetrabutylammonium hydrogensulfate (0.48 g), and benzyl bromide (1.44 mL) in dichloromethane (120 mL) was added aqueous sodium hydroxide (10 mL of a 5% solution), and the mixture was boiled under reflux for 40 h. The usual processing gave a syrupy residue that was conveniently purified by chromatography on a column of silica gel, to afford product **2** having $[\alpha]_D^{25}$ +14.4° (*c* 1, $CHCl_3$); this was clearly distinguishable in t.l.c. from the known methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside[6] (**3**) having $[\alpha]_D^{25}$ +54.2° (*c* 1, $CHCl_3$). An







1 R = R′ = H
2 R = Bn, R′ = H
3 R = H, R′ = Bn
4 R = H, R′ = Tr
5 R = Bn, R′ = Ac
6 R = Ac, R′ = Bn

7

8 R = H
9 R = Bn

Bn = benzyl All = allyl

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authentic sample of compound **2** was also obtained as follows. On heating with acetic acid, methyl 3-*O*-allyl-4,6-*O*-benzylidene-α-D-mannopyranoside[7] (**7**) gave methyl 3-*O*-allyl-α-D-mannopyranoside (**8**) as a syrup, $[\alpha]_D^{23}$ +59.7° (*c* 1, $HCONMe_2$), which, on benzylation in the presence of powdered potassium hydroxide in *N*,*N*-dimethylformamide, produced **9** in 49.5% yield; $[\alpha]_D^{24}$ +35.3° (*c* 1, $CHCl_3$). Removal of the 3-*O*-allyl group by treatment with tris(triphenylphosphine)rhodium chloride[8] gave compound **2**. The i.r. and p.m.r. spectra of the two samples prepared by the different methods were respectively superposable.

In another approach, a mixture of diol **1** (1 g), trityl chloride (0.92 g), triethylamine (0.75 mL), 4-(dimethylamino)pyridine[9] (30 mg), and dichloromethane (50 mL) was refluxed under nitrogen for 20 h. The usual processing, and purification by column chromatography, provided pure compound **4** (0.6 g, 38%), which was recrystallized from acetone–pet. ether; m.p. 128–130°, $[\alpha]_D^{23}$ +94.8° (*c* 1, $CHCl_3$). Compound **4** was characterized by conversion, in two steps, into the aforementioned methyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**2**); benzylation of compound **4** under the usual conditions, followed by removal of the trityl group (with CF_3CO_2H–$CHCl_3$), afforded compound **2**, thereby supporting the finding[9] that tritylation of diol **1** occurs at the (equatorial) 3-hydroxyl group. The i.r. and ^{1}H-n.m.r. spectra of the compound obtained were identical to those of compound **2** prepared by the aforementioned routes.

For selective monobenzylation of the 3-hydroxyl group, diol **1** (1.07 g) was treated with bis(tributyltin) oxide (2.2 g) in toluene (30 mL) for 4 h at 140°, with continuous removal of water, to give, after evaporation of toluene, an intermediate, oily, stannylation product which was then heated with benzyl bromide (15 mL) under nitrogen for 30 h at 90°. The mixture was cooled, coevaporated several times with water, and finally with toluene, to give a syrup which, on column chromatography, afforded pure **3** (1.7 g, 73%); identical with an authentic sample of methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside[6] on the basis of optical rotation, and i.r. and ^{1}H-n.m.r. spectroscopy.

The structures assigned to compounds **2** and **3** were confirmed by examination of the ^{1}H-n.m.r. spectra of their acetates (**5** and **6**, respectively). Acetylation (acetic anhydride–pyridine) of **2** gave syrupy **5**, $[\alpha]_D^{24}$ +9.1° (*c* 1, $CHCl_3$); p.m.r. at 100 MHz ($CDCl_3$): τ 4.74 (dd, 1 H, $J_{3,4}$ 9 Hz, $J_{3,2}$ 3 Hz, H-3) and 8.1 (s, 3 H, equatorial OAc). Similar acetylation of **3** furnished syrupy **6**, $[\alpha]_D^{24}$ +29.8° (*c* 1, $CHCl_3$); p.m.r. at 100 MHz ($CDCl_3$): τ 4.54 (dd, 1 H, $J_{2,3}$ 3 Hz, $J_{2,1}$ 2 Hz, H-2) and 7.84 (s, 3 H, axial OAc).

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