Carbohydrate Research, 74 (1979) C5–C7

Preliminary communication

Selective monobenzylation of methyl 4-*O*-benzyl-α-L-rhamnopyranoside*

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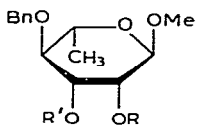
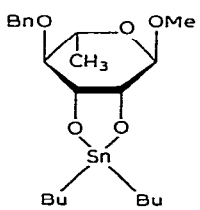
(Received June 1st, 1979; accepted for publication, June 16th, 1979)

Large amounts of methyl 2,4-di-*O*-benzyl-α-L-rhamnopyranoside (2) and methyl 3,4-di-*O*-benzyl-α-L-rhamnopyranoside (3) were needed in our laboratory for the preparation of deoxyfluoro sugars[2]. According to Lipták *et al.*[3], compounds 2 and 3 can be obtained by hydrogenolysis of methyl 4-*O*-benzyl-*endo*-2,3-*O*-benzylidene-α-L-rhamnopyranoside and methyl 4-*O*-benzyl-*exo*-2,3-*O*-benzylidene-α-L-rhamnopyranoside, respectively. Alternatively, in this Communication, we report that the desired compounds can be readily prepared by selective monobenzylation[4] of methyl 4-*O*-benzyl-α-L-rhamnopyranoside (1).



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

Bn = $PhCH_2$, Tr = Ph_3C



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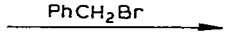

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*Synthetic Studies in Carbohydrates, Part VII. For Part VI of the series, see ref. 1.
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In one of the approaches, we have taken advantage of the phase-transfer catalysis technique for the monobenzylation of diols, introduced by Garegg *et al.*[5]. Thus, in a typical experiment, a mixture of **1** (1.88 g, 7 mmol) in dichloromethane (120 mL), 5% sodium hydroxide (10 mL), and benzyl bromide (1.44 mL, 12 mmol) was refluxed for 4 days in the presence of tetrabutylammonium hydrogensulfate (0.8 g, 1.4 mmol), and cooled, and the two layers were separated. The dichloromethane layer was washed with water (3 X 50 mL), dried (Na_2SO_4), and evaporated. The syrupy material, containing **2** as the major and **3** as the minor (< 5%) component, was conveniently purified by chromatography on a column of silica gel to give **2**, 1.2 g (48%), $[\alpha]_D^{23}$ –15° (*c* 1, $CHCl_3$); lit.[3] –15.4° ($CHCl_3$).

In another experiment, a mixture of the starting material **1** (2.68 g, 10 mmol) and bis(tributylstannyl) oxide (4.47 g, 7.5 mmol) in toluene (50 mL) was refluxed at 140° with continuous removal of water (6 h), to give, after evaporation of the toluene, an oily, intermediate, stannylated product[6] that was heated with benzyl bromide (15 mL) under nitrogen for 20 h at 90°. The mixture was cooled, and co-evaporated several times with water, and finally with toluene, to give a syrup. Column chromatography of the crude material provided pure compound **3** in 56% yield (2 g), $[\alpha]_D^{23}$ –45.4° (*c* 1, $CHCl_3$); lit.[2] –46.4°.

According to Nashed *et al.*[7], a *cis*-diol can be effectively monobenzylated by employing the dibutylstannylene derivative as a key intermediate. Thus, a suspension of compound **1** (1.3 g, 5 mmol) and dibutyltin oxide (1 g, 4 mmol) in absolute methanol was refluxed for 3 h, and then the solvent was removed under diminished pressure. The resulting methyl 4-*O*-benzyl-2,3-*O*-(dibutylstannylene)-α-L-rhamnopyranoside (**6**) was dried, and heated with benzyl bromide (0.72 mL, 6 mmol) in *N*,*N*-dimethylformamide (15 mL) for 2 h at 100°. The solvent was removed under diminished pressure, and column chromatography on silica gel gave, in 52% yield (0.9 g), a pure compound that was identical to compound **3** on the basis of optical rotation and i.r. and n.m.r. spectra.

The reaction of diol **1** (1.6 g, 6 mmol), trityl chloride (1.8 g), and triethylamine (1.5 mL) in dichloromethane (100 mL) in the presence of 4-(dimethylamino)pyridine[8] (0.058 g, 0.5 mmol) for 18 h at 60°, followed by the usual processing, provided methyl 4-*O*-benzyl-3-*O*-trityl-α-L-rhamnopyranoside (**4**), $[\alpha]_D^{23}$ –71.1° (*c* 1, $CHCl_3$), in 20% yield after column chromatography. The structure of compound **4** was based on the observation that, under these conditions[8], an equatorial hydroxyl group is the more reactive towards trityl chloride. The structure is further supported by the fact that benzylation of compound **4** under the usual conditions, to give **5**, followed by removal of the trityl group from **5**, gave compound **2**, suggesting that monotritylation of diol **1** occurred at the 3-hydroxyl group. The i.r. and n.m.r. spectra of the material obtained were identical to those of compound **2** prepared by the aforementioned method*.

Thus, we have attempted the benzylation of compound **1** by four different proce-

*The structure of these compounds was confirmed by n.m.r. studies. The ^{13}C-n.m.r. spectra of compounds **2** and **3** were in agreement with the data reported by Lipták *et al.*[3].

dures. Phase-transfer catalysis, and tritylation (followed by benzylation, with subsequent removal of the trityl group), lead to benzylation of the 2-hydroxyl group, whereas, for monobenzylation of the 3-hydroxyl group in **1**, use of the tin derivatives mentioned is recommended. It has been observed that synthesis involving the *O*-(dibutylstannylene) derivative is simple and not time-consuming. Compounds **2** and **3** were conveniently purified by column chromatography on Mallinckrodt CC-7 silica gel as the support, with 9 : 1 chloroform–ethyl acetate or 4 : 1 hexane–ethyl acetate as the eluant.

The phase-transfer method† was also employed for monobenzylation of methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[10], to give crystalline methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside[11] (60%) and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (syrup, 8%); these were readily separated by column chromatography, using 3 : 2 hexane–ethyl acetate as the eluant. The two compounds were found to be identical with authentic samples thereof, prepared by other procedures[7,11].

ACKNOWLEDGMENTS

We thank Nancy Pyszczynski for her excellent, technical assistance and Onda Simmons for performing the n.m.r.-spectral studies. This investigation was supported by Grant Number R01-CA 24051-01, awarded by the National Cancer Institute, DHEW.

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†After this work was completed, Pozsgay reported the alkylation of compound **1** and related compounds by the phase-transfer technique[9].