Complete Regiospecificity in the Benzylation of a *cis*-Diol by the Stannylidene Procedure

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Summary While conventional monobenzylation of benzyl 6-*O*-allyl-2-*O*-benzyl-α-D-galactopyranoside (**1**) gives a four component mixture, treatment of the *OO'*-dibutylstannylidene derivative of (**1**) with benzyl bromide provides only the 3-*O*-benzyl ether (**2**) in 66% isolated yield.

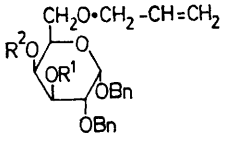
BENZYL ethers are increasingly used as protecting groups in oligosaccharide synthesis, often in conjunction with allyl ethers.[1] However, differences in reactivity of secondary hydroxy-groups generally are small, and attempts at selective etherification by Williamson-type procedure may give mixtures of four components. Wagner *et al.*[2] showed that the 2'3'-*O*-dibutylstannylidene derivative of uridine could be monobenzylated, even in the presence of a free primary hydroxy-group, but the product was a mixture of 2'-*O*- and 3'-*O*-benzyl ethers, in nearly equal amounts (31 and 26%). We report that this kind of activation can lead to completely regiospecific benzylation in good yield of a pyranose vicinal diol function.

The partially protected benzyl glycoside (**1**) was obtained by mild, acidic hydrolysis of the corresponding acetal.[3] Treatment of the diol (**1**) in dimethylformamide with 1·1 equiv. of NaH and benzyl bromide for 3 h at room temperature gave compound (**7**)[3] (9%), unchanged (**1**) (20%), and a mixture of monobenzylation products, (**2**) and (**4**) (60%), which could not be resolved by t.l.c. or column chromatography. The corresponding acetates (**3**) and (**5**) could be separated on a silica gel column (although in an unsatisfactory yield owing to overlapping bands), or estimated in the crude reaction mixture by g.l.c.†

Structural identification was based on n.m.r. spectral data: minor acetate (**3**) (16%): $[\alpha]_D^{20}$ + 90°, ν_{max} 1755 cm^{-1} (CO); δ 2·14 (s, 3H, axial $MeCO_2$), 3·85 (1H, q, $J_{2,3}$ 9·5, $J_{3,4}$

† All new compounds were syrups, characterized by thin-layer or silica gel column chromatography (ether–light petroleum, 1 : 1), g.l.c., optical rotations in $CHCl_3$ (*c ca.* 1), and 240 MHz n.m.r. spectroscopy in $CDCl_3$ with Me_4Si as reference. They gave elemental analytical results within 0·1% of the calculated figures.

3·5 Hz, 3-H) and 5·71br (1H, d, J 3·5, $J_{3,4} + J_{4,5}$ 6·5 Hz, 4-H); major acetate (**5**) (43%): $[\alpha]_D^{20}$ + 109·5°, ν_{max} 1735 cm^{-1} (CO), δ 2·01 (3H, s, equatorial $MeCO_2$) and 5·38 (1H, q, $J_{2,3}$ *ca.* 10, $J_{3,4}$ 3·5 Hz, 3-H). Hydrolysis of the acetate (**5**) (aqueous alcoholic triethylamine) gave the pure galactoside (**4**) [b.p. 230—240 °C at 0·01 mmHg, $[\alpha]_D^{20}$ + 99°, ν_{max} 3500 cm^{-1} (OH)].



Bn = $PhCH_2$

(**1**) $R^1 = R^2 = H$
(**2**) R^1 = Bn, $R^2 = H$
(**3**) R^1 = Bn, R^2 = Ac
(**4**) $R^1 = H$, R^2 = Bn
(**5**) R^1 = Ac, R^2 = Bn
(**6**) R^1, $R^2 = Bu_2Sn$
(**7**) $R^1 = R^2$ = Bn

Azeotropic removal of water from a mixture of the diol (**1**) and polymeric dibutyltin oxide (1·1 equiv.) in benzene for 3·5 h presumably gives, as with other carbohydrate vicinal diols,[4] the acetal analogue (**6**). After evaporation to dryness, the crude syrup (no OH ir absorption) was directly treated with 2·2 equiv. of benzyl bromide in dimethylformamide for 2 h at 100 °C. T.l.c. then indicated the absence of both compounds (**1**) or (**7**), and the presence of only one monobenzylation product. After acetylation, only the 4-*O*-acetate was found by t.l.c. and g.l.c., so the only benzylation product was compound (**2**). This was isolated in 66% yield as a pure syrup {b.p. 210—225 °C at 0·01 mmHg, $[\alpha]_D^{20}$ + 85°, ν_{max} 3500 cm^{-1} (OH)}.

It is noteworthy that by selective benzylation in dimethylformamide, preferential attack at O(4) occurs, in this and other[5] cases, while treatment of the stannylidene derivative in the same solvent leads to the exclusive substitution at O(3). Compound (**2**), now easily accessible, may prove a valuable starting material for the preparation of oligosaccharides with different substituents at positions 4 and 6 of galactose.

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[3] P. A. Gent and R. Gigg, *J.C.S. Perkin I*, 1974, 1446.
[4] S. David and A. Thieffry, *Compt. rend.*, 1974, **279**, 1045.
[5] H. M. Flowers, *Carbohydrate Res.*, 1975, **39**, 245, and references therein.