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Note

Silyl migration and formation of an anhydro derivative on attempted benzylation of 3-*O*-*tert*-butyldimethylsilyl-6-*O*-tosyl-D-glucal

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In a study[1] concerned with the synthesis of the di- and tri-saccharide chains of the antitumor antibiotic olivomycin A, a derivative of 6-deoxy-D-glucal was required in which the two types of protecting groups were stable under the conditions required for further transformations. The recent report[2] on the regioselective 3,6-di-*O*-silylation of D-glucal and subsequent 4-*O*-benzylation prompted an investigation of the sequential mono-*tert*-butyldimethylsilylation and benzylation of 6-*O*-tosyl-D-glucal[3] (**1**).

Treament of **1** with 1.1 equiv. of *tert*-butyldimethylsilyl chloride and 2.2 equiv. of imidazole in *N,N*-dimethylformamide overnight gave 22% of the required 3-*O*-*tert*-butyldimethylsilyl-6-*O*-tosyl-D-glucal (**2**) as a colourless oil. That selective 3-substitution had occurred was confirmed by acetylation, which gave 98% of crystalline 4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-6-*O*-tosyl-D-glucal (**3**).

Attempted benzylation of **2** by sequential treatment with sodium hydride (1.1 equiv., 30 min) and benzyl chloride (1.1 equiv., 3.5 h) in tetrahydrofuran gave 43% of 3,6-anhydro-4-*O*-*tert*-butyldimethylsilyl-D-glucal (**4**) as a colourless oil.

Evidently, deprotonation with sodium hydride provoked 3→4 silyl migration followed by ring closure. Formation of an anhydroglucal on attempted benzylation of **1** has been observed[3], but it was anticipated, in accordance with the work[2] of Kinzy and Schmidt, that this would be prevented by 3-*O*-*tert*-butyldimethylsilylation. Silyl migration in monosilylated glycols has been recorded under various conditions[4], including those employed here[5], but has not previously been reported in the glucal series. The situation is exacerbated by the irreversible formation of an anhydro derivative, however careful attention should be paid to the location of silyl protecting groups in further manipulations of the derivatives reported[2] by Kinzy and Schmidt.

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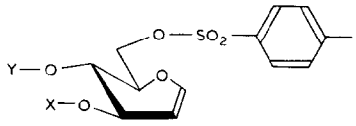
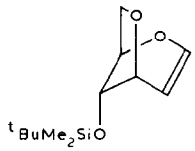


1 X = Y = H
2 X = $SiMe_2{}^tBu$, Y = H
3 X = $SiMe_2{}^tBu$, Y = Ac



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EXPERIMENTAL

General. — Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were recorded with an Optical Activity AA-10 polarimeter. ^{1}H-N.m.r. spectra, for solutions in $CDCl_3$ (internal Me_4Si), were recorded at 200 MHz with a Varian XL 200 instrument. I.r. spectra were recorded with a Perkin–Elmer 983 spectrophotometer. Microanalyses were determined by the University College London microanalytical service.

3-O-tert-*Butyldimethylsilyl-6*-O-*tosyl*-D-*glucal* (**2**). — A solution of crude 6-*O*-tosyl-D-glucal[3] (1.302 g, 4.34 mmol) in dry *N,N*-dimethylformamide (8 mL) was treated, at room temperature under nitrogen, with *tert*-butyldimethylsilyl chloride (0.719 g, 4.77 mmol) and then imidazole (0.65 g, 9.54 mmol), and stirred overnight. The mixture was then poured into water and extracted with ether (3 × 40 mL) and the combined extracts were washed with 2M HCl, water, and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Column chromatography on silica gel [2:3 ether–light petroleum (b.p. 40–60°)] gave **2**, isolated as a colourles syrup (0.387 g, 22%), $[\alpha]_D^{24}$ +7° (*c* 1, chloroform); ν_{max}^{film} 3526, 2950, 2925, 2885, 2852, 1644, 1598, 1461, 1361, 1254, 1175, 1094, 1064, 967, 934, 837, 779, and 671 cm^{-1}. ^{1}H-N.m.r. data: δ 7.79 and 7.33 (4 H, ArH), 6.16 (dd, 1 H, *J* 6.2 and 1.3 Hz, H-1), 4.63 (dd, 1 H, *J* 6.2 and 2.8 Hz, H-2), 4.40 (m, 1 H, H-6), 4.20 (m, 1 H, H-6), 4.11 (m, 1 H, H-3), 3.99 (m, 1 H, H-5), 3.68 (m, 1 H, H-4), 2.43 (s, 3 H, Ar*Me*), 2.31 (d, 1 H, *J* 5.4 Hz, OH), 0.86 (s, 9 H, CMe_3), 0.07 (s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{19}H_{30}O_6SSi$: C, 55.05; H, 7.29. Found: C, 54.78; H, 7.60%.

4-O-*Acetyl-3*-O-tert-*butyldimethylsilyl-6*-O-*tosyl*-D-*glucal* (**3**). — To a solution of **2** (0.10 g, 0.24 mmol) in pyridine (1 mL) and dichloromethane (1 mL) at room temperature was added acetic anhydride (0.1 mL) and 4-dimethylaminopyridine (5 mg). After 1 h, the mixture was poured into water and worked-up conventionally to give **3** as a white crystalline solid (0.107 g, 98%), m.p. 77–80° (from ether–light petroleum), $[\alpha]_D^{24}$ +1° (*c* 1, chloroform); $\nu_{max}^{CHCl_3}$ 2945, 2925, 2885, 2852, 1738, 1645, 1598, 1461, 1364, 1174, 1097, 1067, 977, 960, and 837 cm^{-1}. ^{1}H-N.m.r. data: δ 7.77 and 7.32 (4 H, ArH), 6.19 (d, 1 H, *J* 5.1 Hz, H-1), 4.83 (m, 1 H, H-4), 4.72 (m, 1 H, H-2), 4.38 (m, 1 H, H-6), 4.30 (m, 1 H, H-5), 4.03 (m, 1 H, H-6), 3.98 (m, 1 H, H-3), 2.43 (s, 3 H, Ar*Me*), 2.05 (s, 1 H, Ac), 0.82 (s, 9 H, CMe_3), 0.03 (2 s, 6 H, $SiMe_2$).

Anal. Calc. for $C_{21}H_{32}O_7SSi$: C, 55.24; H, 7.06. Found: C, 55.28; H, 7.15%.

*3,6-Anhydro-4-*O-tert-*butyldimethylsilyl-*D-*glucal* (**4**). — A solution of **2** (0.405 g, 0.978 mmol) in tetrahydrofuran (5 mL) was stirred at room temperature with sodium hydride (80% in oil; 0.032 g, 1.08 mmol) under nitrogen for 30 min. Benzyl chloride (0.124 mL, 1.08 mmol) was added dropwise and, after 3.5 h, the mixture was poured into water and extracted with ether (3 × 15 mL). The combined extracts were washed successively with water and brine, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (1:10 ether–light petroleum) of the residue gave **4**, isolated as a colourless oil (0.102 g, 43%), $[\alpha]_D^{24}$ −41.5° (*c* 0.6, chloroform); ν_{max}^{film} 2945, 2932, 2852, 1621, 1461, 1254, 1224, 1211, 1164, 1081, 1007, 952, 873, 837, and 777 cm^{-1}. ^{1}H-N.m.r. data: δ 6.41 (dd, 1 H, *J* 5.7 and 0.8 Hz, H-1), 4.90 (m, 1 H, H-2), 4.27–4.08 (m, 4 H), 3.89 (m, 1 H), 0.89 (s, 9 H, CMe_3), 0.10 (s, 3 H, SiMe), 0.08 (s, 3 H, SiMe). Mass spectrum: *m/z* 242.1352 (calc. for $C_{12}H_{22}O_3Si$: *m/z* 242.1338).

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