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Note

Boron trifluoride etherate-induced glycosidation: formation of alkyl glycosides and thioglycosides of 2-deoxy-2-phthalimidoglycopyranoses

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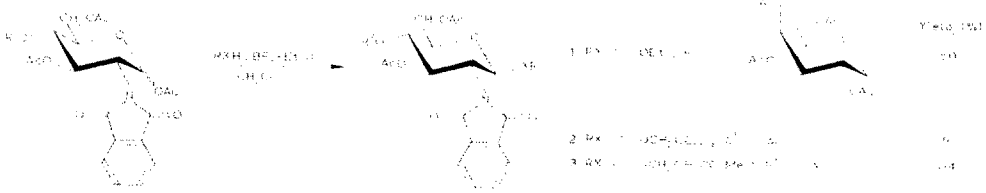
Glycosides can be formed directly from the corresponding acetylated sugar by the use of boron trifluoride etherate[1], which has also been used to effect anomerisation[2] and for the preparation of thioglycosides[3]. With acetylated 2-amino-2-deoxy sugars, only low yields (<20%) of the desired glycosides were obtained[4].

We now report the preparation of alkyl glycosides and thioglycosides of 2-deoxy-2-phthalimido-β-D-glycopyranoses (**1**–**3**) from an anomeric mixture of the corresponding acetylated sugar by the boron trifluoride etherate method. The procedure is simple and the reaction is highly stereoselective: only traces of α-glycosides are formed.

Phthalimido protection is well established[5] for 2-amino-2-deoxy sugars, which makes the present procedure a good alternative to other methods of glycosidation.



EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. N.m.r. spectra were recorded with a Varian XL-200 spectrometer.

Ethyl 3,6-di-O-acetyl-2-deoxy-2-phthalimido-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**1**). — A solution of 1,3,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α,β-D-gluco-

pyranose[6]* (1 mmol, $\alpha\beta$-ratio 5:95) in ethanol (2.3 mmol) and dry dichloromethane (10 mL) was cooled (ice-bath) and boron trifluoride etherate (18 mmol) was added dropwise with stirring. The mixture was kept for 1 h at 0° and 2 h at room temperature, and the reaction was monitored by t.l.c. (SiO_2; ethyl acetate–iso-octane, 2:1). The mixture was washed with aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and concentrated. The residue was subjected to chromatography on silica gel (ethyl acetate–iso-octane, 2:1) to give **1** (297 mg, 60%). Recrystallisation from ethanol gave material having m.p. 239–240°, $[\alpha]_D^{27}$ +12° (*c* 0.2, chloroform). N.m.r. data ($CDCl_3$, Me_4Si): ^1H, δ 7.88–7.72 (m, 4 H, aromatic H), 5.74 (dd, 1 H, *J* 10.5 and 7.9 Hz, H-3), 5.38 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1), 5.34 (d, 1 H, $J_{3',4'}$ 3.3 Hz, H-4'), 5.13 (dd, 1 H, $J_{1',2'}$ 7.7, $J_{2',3'}$ 10.4 Hz, H-2'), 4.96 (dd, 1 H, H-3'), 4.54 (d, 1 H, H-1'), 4.52 (bd, 1 H, $J_{4,5}$ 12.7 Hz, H-5), 4.24–4.05 (m, 4 H), 3.92–3.75 (m, 4 H), 3.6–3.4 (m, 1 H, O-CH_2-CH_3), 2.15, 2.14, 2.07, 2.04, 1.96, 1.91 (6 s, each 3 H, 6 AcO), and 1.06 (t, 3 H, *J* 7.0 Hz, O-CH_2-CH_3); ^{13}C, δ 170.4, 170.3, 170.2, 170.1, 169.8, 169.1 (Me*C*O), 167.0, 166.5 (phthaloyl-*C*O), 134.2, 131.4, 123.5 (aromatic C), 101.1 (C-1'), 97.6 (C-1), 77.0 (C-4), 72.5, 71.3, 71.0, 70.5, 69.0, 66.5, 65.5 (C-3,4,5, C-2',3',4',5', O-CH_2-CH_3), 62.2, 60.6 (C-6,6'), 55.0 (C-2), 20.9, 20.61, 20.56, 20.51 (CH_3CO), and 15.0 (OCH_2-CH_3).

Anal. Calc. for $C_{28}H_{41}NO_{17}$: C, 54.33; H, 5.50. Found: C, 54.00; H, 5.45.

*2,2,2-Trichloroethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**2**). — 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose[5] (1 mmol, $\alpha\beta$-ratio 1:1) and 2,2,2-trichloroethanol (1.2 mmol) were treated, as described above, with boron trifluoride etherate (5.8 mmol) for 1 + 24 h. The crude product was subjected to chromatography on silica gel (ethyl acetate–iso-octane, 2:1), to give pure **2** (416 mg, 76%). Recrystallisation from ether gave material having m.p. 175–176°, $[\alpha]_D^{23}$ +4° (*c* 0.4, chloroform); lit.[5,7] m.p. 176–177° and 188–189°, $[\alpha]_D^{23}$ +4.4° (*c* 0.5, chloroform) and +5.6° (*c* 0.68).

*2-Methoxycarbonylethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-*D*-glucopyranoside* (**3**). — 1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-phthalimido-α,β-D-glucopyranose[5] (1 mmol, $\alpha\beta$-ratio 1:1) and methyl 3-mercaptopropionate (1.2 mmol) were treated, as described above, with boron trifluoride etherate (5 mmol) for 1 + 48 h. The crude product was subjected to chromatography on silica gel (trichlorotrifluoroethane–ether, 5:14), to give **3** (290 mg, 54%) as a syrup, $[\alpha]_D^{27}$ +34° (*c* 0.6, chloroform). N.m.r. data ($CDCl_3$, Me_4Si): ^1H, δ 7.90–7.28 (m, 4 H, aromatic H), 5.83 (dd, 1 H, $J_{2,3}$ 10.0, $J_{3,4}$ 9.3 Hz, H-3), 5.52 (d, 1 H, $J_{1,2}$ 10.6 Hz, H-1), 5.18 (dd, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 4.39 (dd, 1 H, H-2), 4.32 (dd, 1 H, $J_{6,6'}$ 12.5, $J_{5,6'}$ 5.0 Hz, H-6'), 4.19 (dd, 1 H, $J_{5,6}$ 2.3 Hz, H-6), 3.93 (m, 1 H, H-5), 3.62 (s, 3 H, MeO), 2.89 (m, 2 H, SCH_2), 2.65 (t, 2 H, CH_2CO), 2.12, 2.04, and 1.87 (3 s, each 3 H, 3 AcO);

*A modification of the procedure gave a higher yield: the hydrogenation step should be carried out in the presence of phthalic anhydride for *in situ* protection of the amino group formed (J. Lönngren, personal communication).

^{13}C, δ 171.9, 170.7, 170.0, 169.4 (CO), 168.8, 168.1 (phthaloyl-CO), 134.4, 131.5, 131.1, 123.7 (aromatic C), 81.5 (C-1), 75.9, 71.4, 68.8 (C-3,4,5), 62.2 (C-6), 53.5 (C-2), 51.7 (OCH_3), 35.1 ($S\text{-}CH_2$), 25.5 ($CH_2\text{-}CO$), 20.7, 20.6, and 20.4 ($CH_3\text{-}CO$).

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