Glycals from Glycosyl Chlorides

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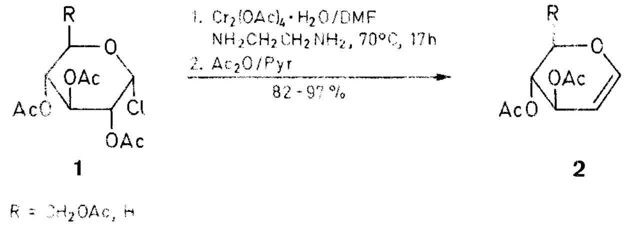
Peracetylated glycosyl chlorides **1** are readily converted into peracetylated glycals **2** by reaction with chromium (II) diacetate dimer in dimethylformamide in the presence of 1,2-ethanediamine.

Glycals are versatile intermediates in synthesis, illustrated by many recent applications.[2–15] In the traditional method of preparation peracetylated glycosyl bromides are reacted with zinc dust in aqueous acetic acid[16] but the yields of peracetylated glycal are variable, products of solvolysis being formed as by-products. Various methods of activation of the zinc have been proposed thought it has also been claimed that such activation failed with some zinc samples.[17] Ireland and coworkers have recently reported lithium in liquid ammonia as a reagent for converting glycosyl chloride derivatives into the corresponding glycal derivatives.[18] These conditions require base-stable protecting groups such as acetals and ethers. Zinc/silver-graphite has also been shown to be an effective reagent for converting *O*-acylated glycosyl chlorides into glycal esters under mild conditions,[19] but the reagent is prepared from C_8K which is pyrophoric.

Since peracetylated glycosyl chlorides **1** can be prepared in one step from aldoses[20,21] and are more stable than glycosyl bromides, we have investigated the conversion of peracetylated glycosyl chlorides into glycal peracetates **2**. Peracetylated glycosyl chlorides were not converted into glycals by the action of zinc dust in aqueous acetic acid; glycosyl chloride was recovered with varying amounts of solvolysis products. Varying the solvent, activating the zinc with acid or copper, and the use of ultrasound to promote this reaction also failed.

The observation that the reducing power of chromium(II) towards alkyl halides was enhanced substantially by the presence of bidentate ligands such as 1,2-ethanediamine,[22] lead us to investigate chromium(II) as a reagent for converting peracetylated glycosyl chlorides **1**, to peracetylated glycals **2**. The reaction of **1** with chromium(II) diacetate dimer monohydrate[23] and 1,2-ethanediamine in dimethylformamide, gave the glycals **2** in good yield. The reaction was slow at room temperature glycal formation being incomplete after 24 hours. The reaction conditions were optimised from the study of glycal formation from the α-pyranosyl chlorides of D-glucose, D-xylose and D-arabinose. The mole ratio of Cr(II)/1,2-ethanediamine/peracetylated glycosyl chloride was 3:6:1 and the reaction mixture was kept at 70 °C for 17 hours. These conditions caused some deacetylation, one glycal by-product of lower R_f value than peracetylated glycal (**2**, R = CH_2OAc) was detected by TLC analysis of the crude product from peracetylated glycosyl chloride (**1**, R = CH_2OAc). Reacetylation converted this crude product into the pure glycal, and a reacetylation step was incorporated into the standard procedure given below to provide optimum yields of glycal.



Optical rotations were measured at the Na-D line at 20 °C using a Perkin-Elmer Model 141 polarimeter. NMR spectra were measured on a Bruker WM250 spectrometer with $CDCl_3$/TMS as solvent/reference. TLC was carried out on Merck silica gel plates.

Per-*O*-acetylated Glycals; General Procedure:

Chromium diacetate dimer monohydrate[23] [5.09 g, 27 mmol of Cr(II)] is added to degassed dry DMF (100 mL) under N_2. 1,2-Ethanediamine (3.6 mL, 54 mmol) is added and the mixture stirred for 15 min. The peracetylated glycosyl chloride (9 mmol) is added, the mixture is stirred for 10 min. and then heated to 70 °C in an oil bath with stirring for 17 h.

The mixture is cooled, acetic anhydride (32 mL) in dry pyridine (25 mL) is added and the mixture stirred a further 5 h. The reaction of mixture is then diluted to 250 mL with water, extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic layers are washed with 2 M HCl (2 × 100 mL), sat. aq. $NaHCO_3$ (100 mL) and water (2 × 100 mL) and dried ($MgSO_4$). Removal of solvent *in vacuo* gives crude product, which is purified by chromatography to remove chromium salts and residual DMF on a silica gel column (25 g) eluting with toluene/EtOAc 1:1. The products are pure by TLC (solvent: EtOAc/toluene 3:2; spray reagent: 20% HCl in EtOH followed by heating) and ^1H-NMR.

3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**2**, R = CH_2OAc) is prepared from 2,3,4,6-tetra-*O*-acetyl-α-D-*gluco*-pyranosyl chloride as a crystalline solid in 93% yield; mp 50-52 °C; $[\alpha]_D^{20} -22°$ ($c = 2.1$, $CHCl_3$) [Lit.[24] mp 54-55 °C; $[\alpha]_D^{22} -16°$ ($c = 8.5$, EtOH)].

3,4-Di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*threo*-pent-1-enitol (2, R = H) is prepared from 2,3,4-tri-O-acetyl-α-D-*xylo*-pyranosyl chloride as a syrup in 82% yield; $[\alpha]_D^{20} -303°$ ($c = 2.3$, $CHCl_3$) [Lit.[25] $[\alpha]_D^{25} -315°$ ($CHCl_3$)].

^1H-NMR: δ = 2.07 (s, 3H, CH_3); 2.10 (s, 3H, CH_3). 3.98 (dd, 1H, J = 1.7, 12.1 Hz, H-5); 4.20 (m, 1H, H-5′); 4.97 (m, 3H); 6.60 (d, 1H, J = 5.6 Hz, H-1).

^{13}C-NMR: δ = 20.8, 21.0, (2q, 2 CH_3); 63.49 (d, C-4), 63.64 (t, C-5); 67.25 (d, C-3); 97.48 (d, C-2); 148.06 (d, C-1); 169.65, 169.74 (2s, 2 C=O).

3,4-Di-*O*-acetyl-1,5-anhydro-2-deoxy-D-*erythro*-pent-1-enitol is prepared from 2,3,4-tri-*O*-acetyl-α-D-*arabino*-pyranosyl chloride as a syrup in 97% yield, $[\alpha]_D^{20} +262°$ ($c = 0.9$, $CHCl_3$) [Lit.[26] $[\alpha]_D^{22} +266°$ ($CHCl_3$)].

^1H-NMR: δ = 2.07 (s, 3H, CH_3); 2.08 (s, 3H, CH_3); 4.00 (m, 2H, H-5); 4.85 (dd, 1H, J = 5.0, 6.0 Hz, H-2): 5.18 (quint, 1H, H-4); 5.44 (m, 1H, H-3); 6.51 (dd, 1H, J = 0.8, 6.0 Hz, H-1).

^{13}C-NMR: δ = 20.65, 20.91 (2q, 2 CH_3); 62.89 (t + d, C-5, C-4); 65.99 (d, C-3); 97.63 (d, C-2); 147.80 (d, C-1); 169.68, 170.26 (2s, 2 C=O).

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