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Note

A convenient method for the syntheses of 4,5-glycals†

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Pyridinium chlorochromate mediated oxidation of methyl 2,3,4-tri- O-acetyl-α-D-hexoses **1,2,** and **3** constitutes a new and convenient method for synthesizing 4,5-glycals.

Unsaturated hexoses have been used as chiral synthons for the syntheses of natural products like olivin[1], actinobolin[2], carbomycin and related antibiotics[3] and other complex organic compounds[4]. The position of double bond in these sugars (1,2-, 2,3- ,3,4- and 4,5- glycals) is of concern for designing the synthetic strategy for obtaining these molecules. The reported procedures for the preparation of 4,5-glycals involve the use of oxidants like dimethylsulfoxide (DMSO) activated by sulfur trioxide- pyridine-triethylamine complex[5] and oxalyl chloride in DMSO in the presence of triethylamine[6]. This communication describes a convenient method for obtaining 4,5- glycals of some hexoses in excellent yields using pyridinium chlorochromate (PCC) as oxidant.

Partially protected derivatives of hexoses, viz. methyl α-D-glucopyranoside **1**, methyl α-D-galactopyranoside **2** and methyl α-D-mannopyranoside **3** were prepared by following the reported procedures[7]. Oxidation of the protected alcohols **1** and **2** with PCC in dry toluene at reflux temperature for 8-10 hrs yielded the unsaturated aldehyde **4** whereas alcohol **3** under similar condition gave the aldehyde **5** (cf Scheme I) in 70-75% yields as syrupy liquids. Reduction of these aldehydes (**4** and **5**) with sodium borohydride in methanol in the presence of Amberlite IR-120 (H^+) ion exchange resin gave the protected glycals **6** and **7** in excellent yields (80-85%).

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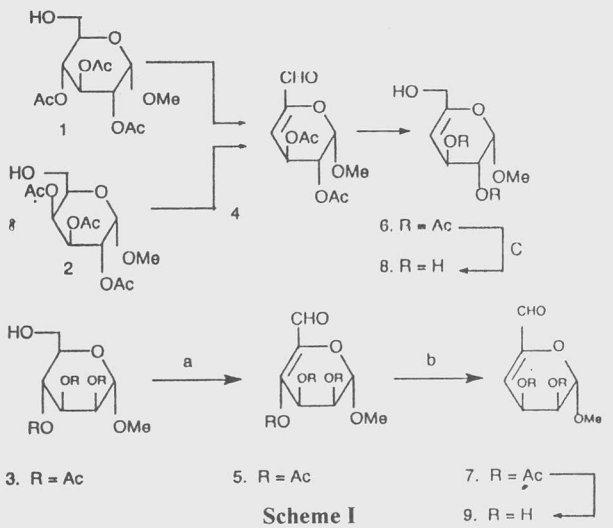

Scheme I

Deprotection of these glycals with sodium methoxide in methanol furnished the 4,5-glycals **8** and **9** (Scheme I) in 70-75% yields. The structures of all the compounds were characterised by FAB MS, ^1H NMR and ^{13}C NMR spectroscopic techniques.

Experimental Section

IR Spectra were recorded on a Perkin-Elmer PE 557 spectrometer (ν_{max} in cm^{-1}). FAB mass spectra were recorded on a JOEL SX 102/DA 6000 mass spectrometer using Argon/Xenon (6kV, 10mA) as the FAB gas. ^1H and ^{13}C NMR spectra were recorded on the Bruker WM-400 FT instrument using TMS as internal reference (chemical shifts in δ, ppm).

Syntheses of 4,5-unsaturated aldehydes 4 and 5: General procedure. PCC (0.32g, 1.5 mmole) was added portionwise to a stirred solution of desired candidate from the compounds **1-3** (0.32g, 1 mmole) in dry toluene (20 mL) and the mixture was refluxed (110°C) for 8-10 hrs. It was then cooled to room temperature (25°C) and filtered through Celite. The residue obtained was then washed with toluene (3× 10mL) and the combined organic extract was concentrated under vaccum to yield a crude residue which was purified by column chromatography over silica gel. Elution with methanol-chloroform (1:99, v/v) gave the aldehydes **4** or **5** as a semisolid.

4: Yield 72.3%; IR(KBr): 1718(CH=O), 1660(C=C); MS:m/z 259(M^++1), 281(M^++Na); ^{1}H NMR ($CDCl_3$): 9.25(s, 1H, CHO), 5.91(d, *J*=3Hz, 1H, H-4) 5.72 (dd, *J*=12, 4 Hz, 1H, H-3), 5.20(m, 2H, H-1 and H-2), 3.45(s, 3H, OMe), 2.12 and 2.14(2s, 3Heach, 2xOCOC*H*$_3$); ^{13}C NMR ($CDCl_3$): 185.31(CHO), 169.80$_e$* (e, denotes overlapping with other signals); (2xOCOCH$_3$), 148.82(C-5), 116.83 (C-4), 98.19 (C-1), 68.58(C-3), 66.26(C-2), 56.73 (OCH_3), 20.56 (2xOCO*C*H$_3$). [Spectra of the 4,5-unsaturated derivatives **4** of methyl 2,3,4-tri-O-acetyl-α-D-glucopyranoside **1** and methyl 2,3,4-tri-O-acetyl-α-D-galactopyranoside **2** were superimposable with each other]

5: Yield 73.0%; IR(KBr): 1720(CH=O), 1660 (C=C); MS:m/z 259 (M^+ + 1), 281 (M^+ + Na); ^{1}H NMR ($CDCl_3$): 9.25 (s, 1H, CHO), 5.86 (d, *J*=2Hz, 1H, H- 4), 5.80 (dd, *J*=4Hz, 1H, H-3), 5.32 (dd, *J*=4Hz, 1H, H-2), 5.14(d, *J*=4Hz, 1H, H-1), 3.52 (s, 3H, OCH_3), 2.12$_e$ (s, 6H, 2xOCOC*H*$_3$); ^{13}C NMR($CDCl_3$): 185.63 (CHO), 169.78 and 169.67 (2xO*C*OCH$_3$), 149.10 (C-5), 117.69 (C-4), 98.96(C-1), 64.26(C-3), 63.34 (C-2), 56.59 (OCH_3), 20.48$_e$ (2xOCO*C*H$_3$)

Syntheses of 2,3-di-*O*-acetyl-α-D-methyl 4,5-glycals 6 and 7: General procedure. To a stirred solution of the desired compound **4** or **5** (0.25g, 1 mmole) in dry methanol (15 mL) in the presence of Amberlite IR-120 (H^+) ion exchange resin (0.20g) was added $NaBH_4$ (0.012g, 0.33 mmole) in portions. The reaction mixture was then allowed to stir at room temperature (25°C) for 1 hr, filtered through glass wool into a round bottomed flask containing a drop of acetic acid and was evaporated *in vaccuo*. Water (20 mL) was then added to it and extracted with chloroform (3x30 mL). Usual work-up of the organic layer furnished a crude residue which was purified by column chromatography over silica gel. Elution with methanol-chloroform (1:49, v/v) gave pure alcohol **6** or **7** as a semisolid.

6: Yield. 84%; MS; m/z 261 (M^+ + 1), 283 (M^+ + Na); ^{1}H NMR ($CDCl_3$): 5.42 (dd, *J*=3Hz, 1H, H-3), 5.14 (dd, *J*- 3Hz, 1H, H-2), 5.02 (m$_e$, 2H, H-4 and H-1), 4.08 (bs, 2H, H-6), 3.54 (s, 3H, OCH_3), 2.12 and 2.06 (2s, 3H, 2xOCOC*H*$_3$); ^{13}C NMR ($CDCl_3$): 170.28 and 170.19 (2xO*C*OCH$_3$), 152.64 (C-5), 97.26 (C-4), 95.69 (C-1), 69.19 (C-3), 66.89(C-2), 61.67(C-6), 56.61(OCH_3, 20.95 and 20.74 (2 x OCO*C*H$_3$).

7: Yield 85%; MS: m/z 261 (M^+ + 1), 283 (M^+ + Na); ^{1}H NMR ($CDCl_3$): 5.55 (t, *J*=3Hz, 1H, H-3), 5.16 (t, *J*=4.5Hz, 1H, H- 2), 5.00 (d, *J*=6Hz, 1H, H-1), 4.95 (d, *J*=0.6Hz, 1H, H-4), 4.08 (dd, *J*=3Hz, 2H, H-6), 3.52 (s, 3H, OCH_3), 2.10 and 2.09 (2s, 3H each, 2 x $OCOCH_3$) : ^{13}C NMR ($CDCl_3$): 170.33 and 170.18 (2 x O*C*OCH$_3$) 152.71 (C-5), 97.28 (C-4), 96.19 (C- 1), 69.21 (C-3), 66.90 (C-2), 61.67 (C-6), 57.05(OCH_3), 20.98 & 20.81 (2xOCO*C*H$_3$).

Syntheses of 4,5-glycals 8 and 9: General procedure NaOMe (0.05 g, 1 mmole) was added to a stirred solution of **6** or **7** (0.26 g, 1 mmole) in dry methanol (10 mL) and the mixture was stirred at room temperature (25° C) for 1 hr. It was then passed through band of Amberlite IR-120 (H^+) ion exchange resin and the eluent evaporated *in vaccuo* to yield a crude residue. Purification by column chromatography over silica gel using methanol-chloroform (1:9 v/v) as eluent gave pure **8** or **9** as a semisolid.

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*Where e denotes overlapping with other signals