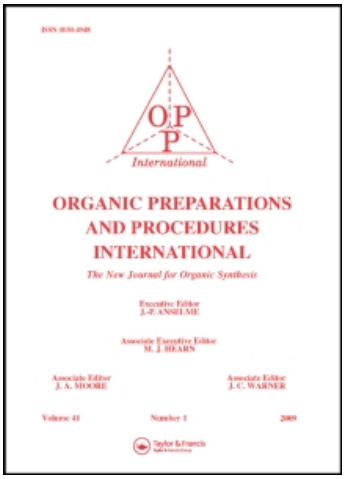

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PARTIAL DEPROTECTION OF 1.2.5.6-DI-O-ISOPROPYLIDENE-D-GLUCOFURANOSES

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PARTIAL DEPROTECTION OF 1,2,5,6-DI-O-ISOPROPYLIDENE-D-GLUCOFURANOSES

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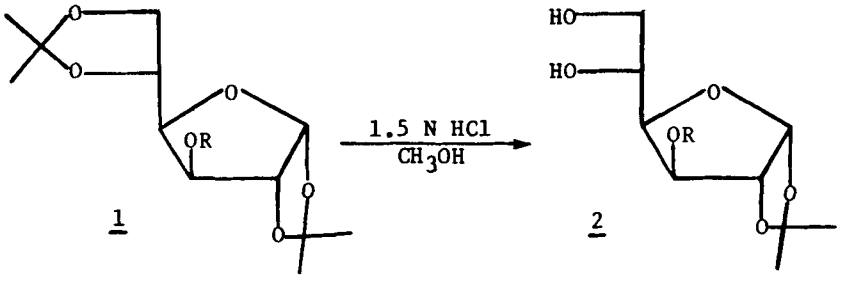
We have been interested in the synthesis of naturally-occurring 1,3,6-O-triacyl-D-glucopyranoses from the readily accessible 3-O-acyl-1,2,5,6-di-O-isopropylidene-D-glucofuranoses (1). Such a substances can be partially deprotected to the 3-O-acyl-1,2-O-isopropylidene-D-glucofuranose (2) which, in turn, can be preferentially acylated to the 6-position. Hence, using this method it is possible to introduce different acyl functions at positions 1, 3 and 6 of the pyranose. Collins[1] has shown that hydrolysis of 1,2,5,6-di-O-isopropylidene-D-glucofuranose (1a) to the 1,2-O-isopropylidene-D-glucofuranose (2a) in HCl is about eighty times faster than hydrolysis of the latter (2a) to D-glucose. Several methods have been reported for the partial hydrolysis of the 5,6-O-isopropylidene group based on this rate difference:[2] a) Stirring for 24 hrs with 0.8% H_2SO_4 in methanol,[3] b) stirring with 30% acetic acid at 50-60° for 13 hrs[4] or 70% acetic acid at room temperature for 6 hrs,[5] c) $LiAlH_4/AlCl_3$ which though a useful method,[6] has a possible limitation whenever an ester function is present at C-3 position.

Although the above methods have proven to be excellent, they are time consuming, taking from 6-24 hrs to be completed. A simpler, more rapid, yet efficient method of monitoring the removal of the 5,6-O-isopropylidene group independent of the C-3 functional group was needed. Using 1.5 N HCl in methanol, we were able to monitor (NMR) the disappearance of the 5,6-O-isopropylidene group in the glucofuranoses (1a-d). Reaction time to

completion was 5-90 minutes depending on the C-3 substituent. Once the sig-



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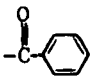
(a) R = H (b) R =  (c) R =  (d) R = 

nals of the 5,6-O-isopropylidene group had disappeared, the mixture was quenched with solid $NaHCO_3$ and the subsequent work-up gave the 3-O-acyl-1,2-O-isopropylidene-D-glucofuranoses (2a-d) in good yields (see Experimental) and of excellent purity (NMR, TLC), free of traces of the glucopyranose (further hydrolysis) and starting material.

EXPERIMENTAL SECTION

The NMR spectra were obtained on a Varian EM-390 (90 MHz) spectrometer. The IR spectra were determined on a Beckman 137 spectrometer.

Preparation of Esters (1b-d).- 1,2,5,6-Di-O-isopropylidene-D-glucofuranose (1a, Aldrich Chemical Co.) was acylated using the appropriate acid chloride in pyridine and after the usual work-up, the 3-O-acyl-1,2,5,6-di-O-isopropylidene-D-glucofuranose (1b-d) were obtained as syrups.

3-O-Nicotinoyl-1,2,5,6-di-O-isopropylidene-D-glucofuranose (1b).[7] 82% yield. IR (liq. film): 1750 cm^{-1}; nMR ($CDCl_3$): δ 9.05 (br, s, 1, ArH), 8.65 (m, 1, ArH), 8.15 (m, 1, ArH), 7.30 (m, 1, ArH), 5.85 (d, 1, J = 4 Hz, sugar H), 5.4 (br, s, 1, sugar H), 4.55 (d, 1, J = 4 Hz, sugar H), 4.25 (m, 2, sugar H), 4.05 (m, 2, sugar H), 1.5 and 1.25 (each s and 3, 1,2-$(CH_3)_2$), 1.38 and 1.18 (each s and 3, 5,6-$(CH_3)_2$).

3-O-Benzoyl-1,2,5,6-di-O-isopropylidene-D-glucofuranose (1c), 80% yield. IR (liq. film) 1750 cm^{-1}; NMR ($CDCl_3$): δ 7.6-8.00 (m, 5, ArH), 5.85 (d, 1,

J = 4 Hz, sugar H), 5.45 (br, s, 1, sugar H), 4.55 (d, 1, J = 4 Hz, sugar H), 4.32 (m, 2, sugar H), 4.10 (m, 2, sugar H), 1.55 and 1.32 (each s and 3, 1,2-$(CH_3)_2$), 1.40 and 1.28 (each s and 3, 5,6-$(CH_3)_2$).

3-O-Acetyl-1,2,5,6-di-O-isopropylidene-D-glucofuranose (1d), 75% yield. IR (liq. film) 1750 cm^{-1}; NMR ($CDCl_3$): δ 5.82 (d, 1, J = 4 Hz, sugar H), 5.20 (m, 1, sugar H), 4.45 (d, 1, J = 4 Hz, sugar H), 4.20 (m, 2, sugar H), 4.05 (m, 2, sugar H), 2.10 (s, 3, $-COCH_3$), 1.5 and 1.3 (each s and 3, 1,2-$(CH_3)_2$), 1.4 and 1.3 (each s and 3, 5,6-$(CH_3)_2$).

Deprotection. A Typical Experiment.- The glucofuranose (1b), 100 mg, was dissolved in methanol (10 ml) and stirred with 1.5 N HCl (1 ml) at 20-25°. Aliquots were taken periodically and NMR spectra were taken until one pair of isopropylidene (methyls) group signals had disappeared. The reaction mixture was quenched with solid $NaHCO_3$, filtered, concentrated, and the residue triturated with absolute ethanol. Removal of the ethanol gave 2b as a crystalline solid, mp. 65-69°.

1,2-O-Isopropylidene-D-glucofuranose (2a), 70% yield, as a syrup. NMR (DMSO-d_6): δ 5.65 (d, 1, J = 4 Hz, sugar H), 4.95 (d, 1, J = 4 Hz, sugar H), 4.47 (d, 1, J = 4 Hz, sugar H), 4.25 (m, 2, sugar H), 3.95-3.60 (m, 2, sugar H), 1.35 and 1.25 (each s and 3, 1,2-$(CH_3)_2$).

3-O-Nicotinoyl-1,2-O-isopropylidene-D-glucofuranose (2b), 83% yield, as a solid. NMR (DMSO-d_6): δ 9.00 (d, 1, J = 2 Hz, ArH), 8.75 (dd, 1, J = 3 Hz, 1.5 Hz, ArH) 8.20 (m, 1, ArH), 7.5 (m, 1, ArH), 5.7 (d, 1, J = 4 Hz, sugar H), 4.32 (d, 1, J = 4 Hz, sugar H), 4.00 (d, 2, J = 2 Hz, sugar H), 3.70 (m, 3, sugar H), 1.35 and 1.20 (each s and 3, 1,2-$(CH_3)_2$).

3-O-Benzoyl-1,2-O-isopropylidene-D-glucofuranose (2c), 85% yield, as a syrup. NMR (DMSO-d_6): δ 8.00-7.5 (m, 5, ArH), 5.65 (d, 1, J = 4 Hz, sugar H), 4.29 (d, 1, J = 4 Hz, sugar H), 4.00-3.70 (m, 5, sugar H) 1.32 and 1.18 (each s and 3, 1,2-$(CH_3)_2$).

3-O-Acetyl-1,2-O-isopropylidene-D-glucofuranose (2d): 70% yield, as a syrup. NMR (DMSO-d_6): δ 5.66 (d, 1, J = 4 Hz, sugar H), 5.00 (d, 1, J = 4 Hz, sugar H), 4.49 (d, 1, J = 4 Hz, sugar H), 4.26-3.60 (m, 4 sugar H), 2.11 (s and 3, $COCH_3$), 1.36 and 1.26 (each s and 3, 1,2-$(CH_3)_2$).

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