Novel Modes for Selective Protection of Ketose Sugars and Oligosaccharides of Biological and Industrial Importance

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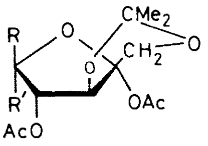
Summary 2-Methoxypropene converts carbohydrates into cyclic isopropylidene acetals under exclusively kinetic control, affording novel, partially protected sugars of value in synthesis; such disaccharides as maltose and lactose react without glycosidic cleavage to give 4′,6′-acetals (on the non-reducing extremity), and lactose also undergoes inter-residue acetonation between O-2′ and O-6.

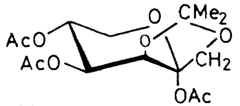
Acetonation of aldohexoses[1] and aldopentoses[2] under kinetic control may be achieved by use of 2-alkoxypropenes. The substitution mode of the products is markedly different from those shown in the products of classical acetonation under thermodynamic control. The potential utility of this kinetic method for oligosaccharides[3] prompted the present evaluation of ketose sugars and of selected oligosaccharides of major importance.

L-Sorbose in *NN*-dimethylformamide containing a trace of toluene-*p*-sulphonic acid was treated under anhydrous conditions at 0 °C with 2-methoxypropene (2 mol equiv.). The water-soluble portion of the product was lyophilized and the resulting syrup acetylated to afford 35% of 2,4,6-tri-*O*-acetyl-1,3-*O*-isopropylidene-*β*-L-sorbofuranose (**1**), syrup, $[\alpha]_D^{20}$ −6° ($CHCl_3$), n.m.r. data *inter alia* δ ($CDCl_3$) 5·32 (d, $J_{4,5}$ 5·2 Hz, H-4), 4·80 (m, H-5), and 4·63 (s, $J_{3,4}$ <0·5 Hz, H-3) plus a minor proportion of the known 3,4,5-tri-*O*-acetyl-1,2-*O*-isopropylidene-*α*-L-sorbopyranose. The same reaction applied to D-fructose gave (after acetylation and purification) 55% of 2,4,6-tri-*O*-acetyl-1,3-*O*-isopropylidene-*α*-D-fructofuranose (**2**), syrup, $[\alpha]_D^{20}$ + 1°



(1) R = H, R′ = CH_2OAc (L-Sorbose series)

(2) R = CH_2OAc, R′ = H (D-Fructrose series)



(3) (D-Tagatose series)

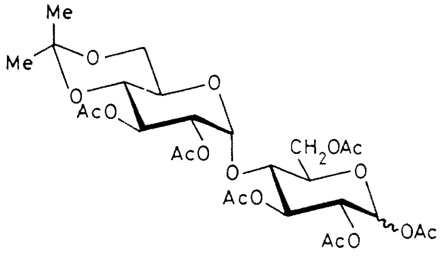
($CHCl_3$), n.m.r. data *inter alia* δ ($CDCl_3$) 4·60 (s, $J_{3,4} < 0·5$ Hz, H-3), 4·92 (d, $J_{4,5}$ *ca.* 1·5 Hz, H-4). Similar treatment of D-tagatose gave almost exclusively 2,4,5-tri-*O*-acetyl-1,3-*O*-isopropylidene-α-D-tagatopyranose (**3**) m.p. 139—141 °C, $[\alpha]_D^{20}$ −49° ($CHCl_3$); n.m.r. spectrum (C_6D_6) shows all coupling constants in accord with the ${}^5C_2$ (D) pyranoid-ring form (particularly $J_{3,4}$ 3·5 and $J_{4,5}$ 10·6 Hz).

As conventional acetonation of L-sorbose, D-fructose, and D-tagatose leads to protected sugars[5] of completely different constitution from compounds (**1**), (**2**), and (**3**), the novel synthetic utility of the kinetic method is thus demonstrated, and opens a route for a range of useful structural modifications.

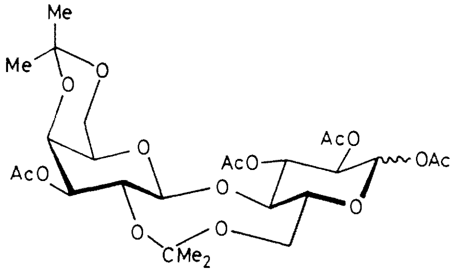
Until very recently[6] there has been no method available for the acetonation of oligosaccharides, mainly because of the lability of the glycosidic linkage to conventional reagents. The kinetic method reported here is, however, mild enough to permit the acetonation of α,α-trehalose.[3] The generality of the procedure has been tested on three important disaccharides, namely, sucrose, maltose, and lactose.

The reaction of 2-methoxypropene with sucrose gave mainly a monoacetal (4,6-*O*-isopropylidene sucrose) and a diacetal (4,6:2,1′-di-*O*-isopropylidene sucrose), isolated after acetylation as their peracetates. They are identical to those reported recently by Khan *et al.*[6]

Maltose gave the 4,6-monoacetal, isolated as a peracetylated mixture of α and β anomers (**4**); m.p. 88—90 °C, $[\alpha]_D^{20}$ −75° ($CHCl_3$), yield 40—50%.



(4)(Maltose series)



(5)(Lactose series)

Lactose gave mainly (30—35%) a diacetal, purified as the peracetylated mixture of α and β anomers, m.p. 99—101 °C, $[\alpha]_D^{20}$ +32° ($CHCl_3$). The bridged structure (**5**) is assigned to this di-*O*-isopropylidene lactose on the basis of its 250-MHz n.m.r. spectrum. The ability of 2-methoxypropene to give medium-sized cyclic acetals previously shown in the D-ribose series[2] is reinforced here. This new protected derivative of lactose has considerable potential synthetic utility for structural modifications and coupling reactions of lactose.

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