Preliminary communication

Cleavage of sugar 1,2-(ortho esters) with dichloromethyl methyl ether

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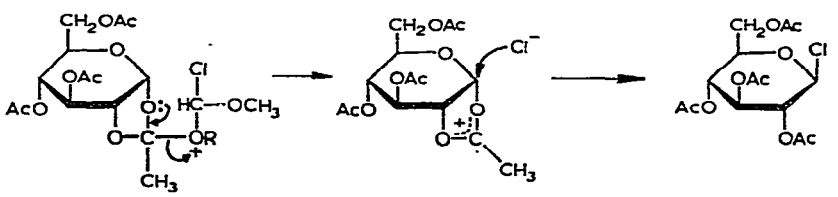
It is well known that the acetates of aldose 1,2-(ortho esters) react with anhydrous hydrochloric acid[1] or titanous chloride[2] to give the acetylated glycosyl chlorides. With the former reagent, the acetylated glycosyl halide usually cannot be isolated in crystalline form, whereas with the latter reagent only the more-stable anomers can be obtained[3].

Our previously developed method for the cleavage of glycosides[4] has now been successfully extended to aldose 1,2-(ortho esters). Thus, 3,4,6-tri-*O*-acetyl-β-D-mannose 1,2-(methyl orthoacetate) (**1**) and 3,4,6-tri-*O*-acetyl-α-D-glucose 1,2-(ethyl orthoacetate) (**2**), when heated with dichloromethyl methyl ether (**3**), gave tetra-*O*-acetyl-α-D-mannopyranosyl chloride (**4**) and tetra-*O*-acetyl-β-D-glucopyranosyl chloride (**5**), respectively, in yields of 50–60%. For example, when **2** (1 g) was heated with **3** (1 ml) for 1h, **5** (0.6 g, 60%) was obtained having m.p. 97–98°, $[\alpha]_D$ −20.8° (*c* 2, chloroform); lit.[5] m.p. 96°, 98°, 101°, $[\alpha]_D$ −22° (chloroform). In the presence of 10% anhydrous zinc chloride, the reaction is faster, and, for example, **1** (1 g), heated for 10 min at 40–45° with **3** (1 ml), was converted into **4** (0.9 g, 90%), m.p. 80–81°, $[\alpha]_D$ +91.5° (*c* 0.4, chloroform); lit.[6] m.p. 81°, $[\alpha]_D$ +90.6° (chloroform). In this way, tetra-*O*-acetyl-α-D-glucopyranosyl chloride (**6**) can be obtained in 72% yield from **2**, as a result of anomerisation of **5**. The identities of compounds **4**–**6** were confirmed by chromatographic analysis, and by determination of mixture melting points.

The acetoxonium ion shown in Scheme 1 is a possible reaction intermediate. Preferential attack of the reagent at the alkoxyl oxygen atom might result from its greater steric accessibility, especially in the *exo*-diastereoisomer.



SCHEME 1

TABLE I

CHARGES ON THE ATOMS OF THE TRI-*O*-ACETYLHEXOPYRANOSE 1,2-(ALKYL ORTHOACETATES) (IN FRACTIONS OF AN ELECTRONIC CHARGE) CALCULATED BY THE DEL RE METHOD[8]

R	O-7	O-1	O-2	O-3	O-4	O-5	O-6	C-1	C-2	C-3	C-4	C-5	C-6	C-7
Me	−0.2531	−0.2458	−0.2662	−0.2688	−0.2617	−0.2657	−0.2589	0.1700	0.1082	0.1141	0.0849	0.0909	0.0851	0.3132
Et	−0.2572	−0.2445	−0.2558	−0.2606	−0.2607	−0.2644	−0.2589	0.1775	0.1005	0.0919	0.0909	0.0918	0.0852	0.3138
i-Pr	−0.2605	−0.2445	−0.2558	−0.2606	−0.2607	−0.2644	−0.2589	0.1776	0.1005	0.0919	0.0909	0.0918	0.0852	0.3135
t-Bu	−0.2630	−0.2446	−0.2560	−0.2611	−0.2656	−0.2650	−0.2590	0.1777	0.1000	0.0883	0.0604	0.0882	0.0848	0.3133

In order to study the possible role of electronic factors in this reaction, Del Re's method[8] has been used to calculate the σ-charge density distribution of several acetylated 1,2-(ortho esters). This method has recently been applied[9-11] to other carbohydrates. The calculated charge densities of the carbon atoms of the pyranose ring are in good agreement with the literature data[10]. As shown in Table I, the σ-charge densities are higher on the alkoxyl oxygen atom (O-7) than on O-1 or O-2, except when R=CH_3; in all four cases, however, the alkoxyl oxygen atom is more negatively charged than O-1. The calculated data thus support the mechanism shown in Scheme 1, involving a cyclic acetoxonium ion stabilised by mesomerism[7], which yields products having the 1,2-*trans* configuration. O-5, the oxygen atom having the strongest negative charge, is apparently not involved in the reaction, presumably because of unfavourable steric and kinetic factors.

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