Carbohydrate Research, 69 (1979) C1–C3

Preliminary communication

The selective 2-benzoylation of methyl-4,6-*O*-benzylidene-α-D-glucopyranoside

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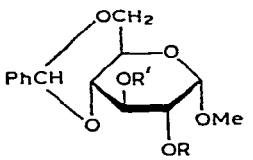
(Received October 31st, 1978; accepted for publication, November 21st, 1978)

Several methods for selective benzoylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (1) have been reported, by using *N*-benzoylimidazole[1], benzoyl cyanide[2], benzoyl chloride–triethylamine[3], benzoyl chloride–pyridine[3], and benzoic anhydride–pyridine[3], and various yields of the 2-benzoate (2) have been obtained. The highest reported yield (78%) of 2 was achieved by using *N*-benzoylimidazole, whereas benzoic anhydride–pyridine gave the 3-benzoate (3) as the major benzoylated product, in low yield.



1 R = R′ = H
2 R = H, R′ = Bz
3 R = H, R′ = Bz

Our research required considerable quantities of compound 2, but attempts to prepare it by using either *N*-benzoylimidazole or benzoyl cyanide afforded only modest yields (~50% after crystallisation) of the desired product[4]. It is possible that our lower yields arose through inadequate control of the reaction conditions, for example, exclusion of moisture, but we decided to attempt to develop a synthetic route to 2 that could be performed with less-stringent attention to reaction conditions and yet produce a high overall yield.

We had noted, with interest, the work of Garegg et al. on the monotosylation of diols using phase-transfer catalysis[5], and attempted to benzoylate 1 under those conditions.

Thus to a solution of 1 (2.50 g) in dichloromethane (250 mL), tetrabutylammonium hydrogensulphate (0.60 g), benzoyl chloride (1.56 g) and 20 mL of 5% aqueous sodium hydroxide were added. The mixture was stirred for 15 min and then processed by separating the phases, washing the organic phase with water, drying it with anhydrous

sodium sulphate, and evaporating it to a solid. The residual benzoyl chloride was then removed by trituration with light petrol, prior to any attempts at recrystallising the solid residue from acetone–water.

The early stages of the reaction indicated only the formation of the 2-benzoate **2**. However when the concentration of **2** became appreciable, then the 3-benzoate (**3**) began to be formed, by hydroxide-catalysed isomerisation[6].

Although we were able to achieve good selectivity and an overall yield of **2** of 50%, after recrystallisation, the reaction was synthetically unsatisfactory for the following reasons: (*a*) the rate of the reaction varied enormously with the efficiency of dispersal of the phases in each other; (*b*) the rate of hydroxide-catalysed isomerisation of **2** to **3** was comparable with the rate of formation of **2**; and (*c*) in order to achieve a good yield of **2**, the reaction had to be terminated while there still remained a significant amount of starting compound (**1**). This reaction promises to be of utility for a diol system or an acyl group that resists base-catalysed acyl migration.

The ability of the "phase-transfer agents" to solubilise anions in non-polar media, such as hydroxide in dichloromethane in the foregoing reaction, the seeming increase in the selectivity of benzoylations on changing from polar to non-polar reaction media, and the apparent trend of increasing selectivity of benzoylations as the group X in Ph–CO–X becomes "softer"[7] led us to attempt to benzoylate **1** in benzene by using benzoyl iodide and crushed, anhydrous potassium carbonate as the base.

The preparation of benzyl iodide has been described[8]. However, we had noted the efficient preparation of benzoyl cyanide from benzoyl chloride and tetrabutylammonium cyanide (generated under phase-transfer conditions from tetrabutylammonium bromide and sodium cyanide)[9], and decided to generate the benzoyl iodide, *in situ*, from benzoyl chloride and tetrabutylammonium iodide.

Stirring a 10% solution of **1** in benzene containing one molar equiv. each of benzoyl chloride and tetrabutylammonium iodide and two molar equiv. of crushed, anhydrous potassium carbonate, for 48 h, at room temperature, followed by removal of the potasssium carbonate by filtration, washing the benzene solution with water, drying (sodium sulphate), concentrating, and finally triturating the residue with light petrol to remove any residual benzoyl chloride, yielded the 2-benzoate **2** in 85% yield, with only a trace of the 3-benzoate **3**.

This reaction did *not* proceed in the absence of the tetrabutylammonium iodide, thus substantiating our view that the acylating agent was benzoyl iodide. Interestingly, the use of tetrabutylammonium hydrogensulphate instead of tetrabutylammonium iodide resulted in the very slow (40% conversion of **1** after 72 h) production of a mixture of **2** and **3**, with **3** being the major product.

The mechanistic aspects of this reaction will be discussed in our full paper, together with the use of benzoyl iodide as an acylating agent for other aldohexopyranosides.

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