A Reinvestigation of Partial Benzoylation of 1,5-Anhydro-4,6-*O*-benzylidene-D-glucitol

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Monobenzoylation of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (**1**) with benzoyl chloride in pyridine was first reported by Newth,¹⁾ giving the 2,3-di-*O*- (**2**) and the 2-*O*- (**3**) benzoates in yields of 18.5 and 17%, respectively. It was concluded that the benzoylation of **1** occurred preferentially at the C-2 hydroxyl group in view of the isolation of **3**. However, the yield of **3** is too low to discuss the relative reactivity of the hydroxyl groups in **1**. In the previous study,²⁾ monobenzoylation of **1** with benzoic anhydride in chloroform in the presence of sodium benzoate gave **3** in 63% yield along with the 3-*O*-benzoate (**4**) in 17% yield. This prompted us to perform some detailed study on the benzoylation of **1** with benzoyl chloride in pyridine.

Partial benzoylation of **1** was performed by the method of Newth.¹⁾ Treatment of **1** with one molar equivalent of benzoyl chloride in pyridine at 0°C for 3 h gave the 2,3-di-*O*- (**2**) (10.9%), the 2-*O*- (**3**) (27.5%), the 3-*O*- (**4**) (39.9%) benzoates, and the starting material (21.7%), which were quantitatively determined by thin-layer chromatography. Prolonged treatment of **1** with benzoyl chloride at 0°C for 24 h gave the 2,3-di-*O*- (**2**) (16.6%), the 2-*O*- (**3**) (27.6%), the 3-*O*- (**4**) (42.3%) benzoates, and the starting material (13.5%).

- 1 R=R'=H
- 2 R=R'=Bz
- 3 R=Bz, R'=H
- 4 R=H, R'=Bz

According to the above product-distribution analysis, it is clear that the hydroxyl group at C-3 is more reactive towards benzoyl chloride in pyridine than the hydroxyl group at C-2, while the reverse is true for the benzoylation of **1** with benzoic anhydride in chloroform.²⁾ This is in contrast with the view¹⁾ of Newth that the 2-*O*-benzoate **3** was the preponderant isomer and therefore the hydroxyl group at C-2 was more

readily benzoylated. Isolation of the components by fractional crystallization and no research of the remaining components in the mother liquor may have led to this erroneous conclusion. The difference in reactivity of **1** in the benzoylation experiments may be explained by using different benzoylating reagents. It is of interest to note that the reactivity of the hydroxyl group at C-2 towards benzoyl chloride in pyridine is decreased in spite of that the hydroxyl group at C-2 is less sterically hindered. The lower reactivity of the hydroxyl group at C-2 may be due to lack of hydrogen bond formation. This result is consistent with those obtained for methyl 4,6-*O*-benzylidene-β-D-glucopyranoside³⁾ and methyl 6-deoxy-β-D-glucopyranoside.⁴⁾ This suggests that intramolecular hydrogen bonding is a responsible, main influence for the greater reactivity of the hydroxyl group at C-2 in methyl 4,6-*O*-benzylidene-α-D-glucopyranoside⁵⁾ and methyl α-D-glucopyranoside.⁶⁾

EXPERIMENTAL

Quantitative thin-layer chromatography was performed on quartz rods sintered with silica gel H (Merck) and glass powder (1:2). A benzene-ethyl acetate (9:1) solvent system completely resolved mixtures containing compounds **1**, **2**, **3** and **4** (*R_f* 0.05, 0.62, 0.44 and 0.31, respectively) and the bands were detected with a Iatron chromatoscanner TH-10 equipped with a hydrogen flame ionization detector. Authentic samples **2**, **3** and **4** were prepared by the procedure reported previously.²⁾

Benzoylation

A solution of **1**⁷⁾ (252 mg) in pyridine (2 ml) was cooled to -10°C and treated with benzoyl chloride (0.116 ml, 1.0 molar equiv.). The mixture was kept at 0°C for 3 h (or 24 h) and then extracted with chloroform. The extract was washed successively with 1 N hydrochloric acid, aqueous sodium bicarbonate and water, dried (Na₂SO₄), and then evaporated to dryness. The residue was subjected to quantitative analysis.

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