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Note

Corrected order in the simultaneous debenzylation–acetolysis of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside

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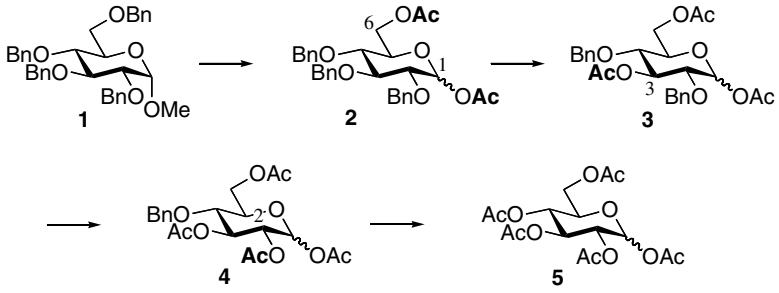
Abstract—The benzyl groups of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside were cleaved in the order of 6-*O*-Bn > 3-*O*-Bn > 4-*O*-Bn > 2-*O*-Bn under acid-mediated conditions in acetic anhydride. The order is a correction of that previously reported.

Keywords: Order of debenzylation; Acid mediation; Acetolysis; D-Glucopyranose

The benzyl group is one of the most practical protecting groups in synthetic organic chemistry. In synthetic sugar chemistry, full benzylation of carbohydrate hydroxy groups is generally effortless.[1] In contrast, the regioselective partial benzylation of carbohydrate hydroxy groups is still a problem that has been the subject of numerous researches.[2–8] Among them, debenzylation of polybenzylated sugars is one of the practical answer to this problem.[8]

The debenzylation of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**1**) occurs stepwise. Sakai et al. reported that when **1** is acetolyzed in acetic anhydride containing 1% (v/v) sulfuric acid, the anomeric methyl and 6-*O*-benzyl groups are first replaced by acetyl groups, and then the 3-, 2-, and 4-*O*-benzyl groups are replaced in this order to afford the 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-D-glucopyranose (**2**), 1,3,6-tri-*O*-acetyl-2,4-di-*O*-benzyl-D-glucopyranose (**3**), 1,2,3,6-tetra-*O*-acetyl-4-*O*-benzyl-D-glucopyranose (**4**), then eventually penta-*O*-acetyl-D-glucopyranose (**5**) (Scheme 1).[8a]

By following Sakai's procedure, we could not find **4** as the mono-benzylated compound. We confirmed that each tri-, di-, and mono-O-benzylated derivative was generated as a single product without considering the anomeric stereochemistry, and the tri- and di-O-benzylated ones were definitely **2** and **3**, respectively.[8a,9,10]



Scheme 1. Reported simultaneous debenzylation–acetolysis sequence of **1** by Sakai et al.[8a]

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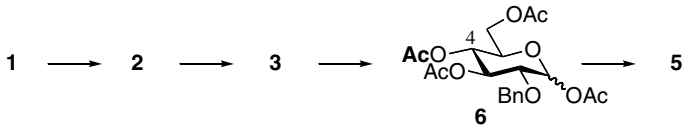

Scheme 2. Corrected simultaneous debenzylation–acetolysis sequence of **1**. Reagents and conditions: Ac_2O, 1% (v/v) H_2SO_4, rt.

However, the isolated mono-O-benzylated product was not the tetraacetate of the 4-O-benzylated glucose **4** as reported, but the 2-O-benzylated tetraacetate **6** (Scheme 2). The structure of **6** was confirmed by comparing the NMR data to that reported in the literature after HPLC separation of the anomeric mixture into the pure α and β anomers (**6a** and **6b**, respectively).[11] Comparison of Sakai's ^{13}C NMR data with ours revealed that the compound we isolated as **6a** was identical with the compound they isolated as **4** (α anomer).[8a] Consequently, the sequence of the simultaneous debenzylation–acetolysis should be corrected as 6-*O*-Bn > 3-*O*-Bn > 4-*O*-Bn > 2-*O*-Bn.

In summary, the benzyl groups of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**1**) were stepwise cleaved in the order of 6-*O*-Bn > 3-*O*-Bn > 4-*O*-Bn > 2-*O*-Bn under acid-mediated acetolysis conditions in acetic anhydride. This should serve as basic knowledge for preparation of partly benzylated sugar compounds that are known or potential building blocks, not only for more complex sugar compounds, but also for optically active natural products.[12]

1. Experimental

1.1. Sulfuric acid-mediated debenzylation–acetolysis of 1

A sulfuric acid solution in Ac_2O (2% v/v) (2.0 mL, 0.75 mmol as H_2SO_4) was added to a solution of methyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (**1**) (373 mg, 0.673 mmol) in Ac_2O (2 mL) in one portion. The solution was stirred at room temperature for 5 min, then poured into ice water. The mixture was successively extracted with EtOAc. The organic layer was washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated under reduced pressure. The resulting residue was purified by column chromatography using Silica Gel 60 (70–230 mesh, 60 g) and eluting with a gradient of 10:1 → 4:1 hexane/EtOAc to afford **2** (202 mg, 56%, α:β = 1:0.15), **3** (98 mg, 30%, α:β = 1:0.2), and **6** (19 mg, 6%, α:β = 1:0.2), each as a colorless syrup. The NMR spectra of these compounds were identical to the literature data[9–11] (for details, see Supplementary data).

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Supplementary data

Supplementary data is available for this paper: Characterization data and copies of ^1H and ^{13}C NMR spectra for both α and β isomers of compounds **2**, **3**, and **6**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.02.018.

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