

Short communication

Improved synthesis of 3-*O*-acetyl-2,4,6-tri-*O*-benzyl- α -D-glucopyranosyl chloride from allyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-D-glucopyranoside

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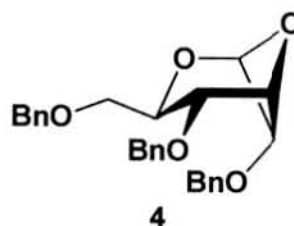
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3-*O*-Acetyl-2,4,6-tri-*O*-benzyl- α -D-glucopyranosyl chloride (**3** in scheme 1) is an important precursor of 1,3-anhydro-2,4,6-tri-*O*-benzyl- β -D-glucopyranose (**4**), which is polymerized by a triisobutylaluminum-water-acetylacetone (1:0.4:0.8) ternary catalyst system to yield a 2,4,6-tri-*O*-benzyl-(1 $\rightarrow$ 3)- β -D-glucopyranan (Okada et al., 1991).

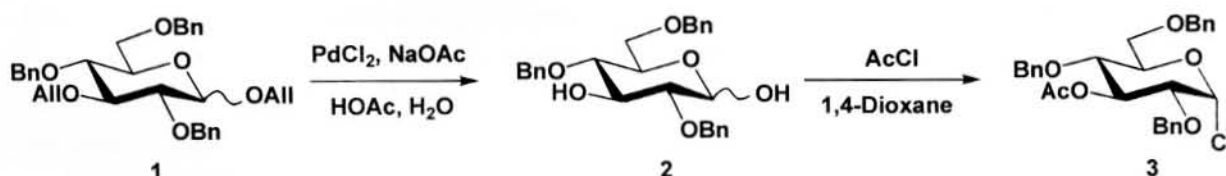
The focus on branched (1 $\rightarrow$ 3)- β -D-glucopyranans has increased considerably as biological immunostimulators for viral, bacterial, fungal, and parasitic infections (Rasmussen et al., 1991) and tumor (Mansell et al., 1975) among others (Patchen et al., 1987; Browder et al., 1988; Williams et al., 1989) in recent years. Those are the primary constituents of bacterial and fungal cell walls (Mueller et al., 2000) and derived from medical mushrooms (such as *Sclerotium glaucum*, *Lentinus edodes*, and *Schizophyllum commune*) and baker's yeast (*Saccharomyces cerevisiae*). Two types of side chains have been identified on such polysaccharides, although others may also exist. Some researches suggested that the preferred and most biologically relevant type of side chain contains (1 $\rightarrow$ 3)- β -linked glucopyranosyl units and that the branching frequency is

also an important factor (Poutsika et al., 1993; Engstad et al., 1995; Michalek et al., 1998).

Although many polysaccharides with well-defined structures have been obtained by ring-opening polymerization of anhydro sugar derivatives (Schuerch, 1981; Sumitomo et al., 1984; Uryu, 1989), only one communication concerning the synthesis of (1 $\rightarrow$ 3)- β -linked polysaccharides has been reported to date (Okada et al., 1991). The author will study the polymerization behavior in detail and synthesize artificial branched (1 $\rightarrow$ 3)- β -D-glucopyranans at Chubu University. There are several difficulties in the synthesis. One of them is the preparation of 1,3-anhydro sugar derivatives as monomers, which are synthesized by an eight-step reaction sequence according to the procedures described by Good et al. (Good et al., 1984). The title compound **3** is the key precursor to monomer **4**.



Scheme 1



In the present paper, a new strategy from allyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-D-glucopyranoside (**1**) to **3** was investigated as shown in scheme 1. Deallylation of **1** was performed by palladium(II) chloride and sodium acetate in acetic acid containing small amount water. Treatment of **2** with acetyl chloride in 1,4-dioxane gave the target compound **3**.

Materials and Methods

Materials

Allyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-D-glucopyranoside (**1**) was synthesized from D-glucose by a four-step reaction sequence according to the previous papers (Good, 1984). 1,4-Dioxane was dried over molecular sieves 3A. Other reagents were used without purification.

Measurements

¹H and ¹³C NMR spectra were recorded on a JEOL JNM EX-400 NMR spectrometer. IR spectra were measured with a Jasco FT/IR 660 plus spectrophotometer.

Deallylation of allyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-D-glucopyranoside (**1**) with palladium(II) chloride

To a suspension of palladium(II) chloride (4.43 g, 25.0 mmol) and sodium acetate (4.92 g, 60.0 mmol) in acetic acid (100 mL) was added 50.0 mL of a solution of **1** in 1,4-dioxane (0.200 mol/L) [**1** (5.31 g, 10.0 mmol)] and water (10 mL). The reaction mixture was stirred at room temperature. After 26 hours, the reaction mixture was filtrated and then concentrated in vacuo. Flash chromatography, with ethyl acetate-hexane (1:2, then 1:1) as eluent, afforded 3.61 g (80.2% yield) of **2** as syrup. Compound **2** gave spectra the same as those recorded in the literature (Good et al., 1984).

Synthesis of 3-*O*-acetyl-2,4,6-tri-*O*-benzyl- α -D-glucopyranosyl chloride (**3**) from **2** by using acetyl chloride

In a flask with a three-way stopcock was placed 4.00 mL of a solution of **2** in 1,4-dioxane (0.100 mol/L) [**2** (0.180 g, 0.400 mmol)], followed by addition of acetyl chloride 0.280 mL (0.309 g,

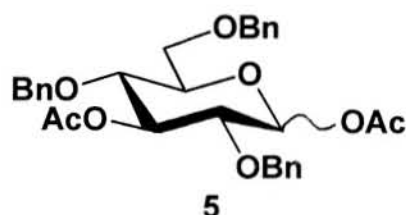
3.94 mmol) at room temperature under nitrogen. After stirring for 17 hours at room temperature, the reaction mixture was diluted with chloroform and the solution was poured onto cracked ice. The mixture was rapidly shaken, the organic layer was run into saturated sodium hydrogen carbonate solution containing cracked ice, and the mixture was stirred at first, and then shaken until the acid was neutralized. The chloroform layer was separated and dried over sodium sulfate. Following concentration in vacuo, the product was purified by flash chromatography, with ethyl acetate-hexane (1:3, then 1:2) as eluent, afforded 0.11 g (54.0% yield) of **3** as a syrup. Compound **3** gave spectra the same as those recorded in the literature (Good et al., 1984).

Results and Discussion

In previous paper (Good et al., 1984), deallylation of **1**, allyl 3-*O*-allyl-2,4,6-tri-*O*-*p*-bromobenzyl-D-glucopyranoside, and allyl 3-*O*-allyl-2,4,6-tri-*O*-*p*-methylbenzyl-D-glucopyranoside were carried out with chlorotris(triphenylphosphine)rhodium in benzene-aqueous ethanol under reflux. Good et al. described that both 2,4,6-tri-*O*-*p*-bromobenzyl-D-glucopyranose and 2,4,6-tri-*O*-*p*-methylbenzyl-D-glucopyranose were obtained in 80% yield, but they did not show detail about deallylation of **1**. Before using palladium(II) chloride, the author checked deallylation of **1** with chlorotris(triphenylphosphine)rhodium and resulted in 73-43% yield (the average yield, 56.5%). Deallylation with palladium(II) chloride was reported in 1983 by Ogawa et al (Ogawa et al., 1983). The allyl group of **1** was selectively removed by treatment with palladium(II) chloride to afford **2** in 80% yield (reproducible). In addition, palladium(II) chloride is lower than chlorotris(triphenylphosphine) rhodium in price. As a result, it was found that deallylation of **1** was improved by employing palladium(II) chloride-mediated deallylation condition.

In the method of Good et al. (Good et al., 1984), **2** was acetylated to 1,3-di-*O*-acetyl-2,4,6-tri-*O*-benzyl-D-glucopyranoside (**5**), and then

converted into **3**. On the other hand, Horton et al. derived 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy- α -D-glucopyranosyl chloride directly from 2-acetamido-2-deoxy- α -D-glucopyranose (**6**) with acetyl chloride (Horton et al., 1962). Acetylation of **6** and substitution of chloride at the anomer carbon were performed in one pot. First, a mixture of **2** and acetyl chloride was stirred overnight without external heating according to the procedure described by Horton et al. But the attempt to convert **2** was completely unsuccessful. Therefore, the procedure of Horton et al. was modified moderately in preparation of **3**. Treatment of **2** with acetyl chloride in 1,4-dioxane at room temperature furnished **3** in 54.0% yield.



Compared with the previous procedure (Good et al., 1984), the improved method from **2** to **3** has only one step instead of two, which is the great advantage. Although the yield of **3** was lower than that by the previous procedure (total yield, 99%), the main by-product was **5** (14.0% yield), which could be converted to **3** with anhydrous hydrogen chloride according to the previous procedure (Good et al., 1984). Optimization of reaction condition was not satisfactory in preparation of **3** from **2** with acetyl chloride. As yet it is not concluded that the improved method was superior to the previous procedure (Good et al., 1984). However, this one-step reaction will be practical after a few modification of reaction condition.

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タイトル：アリル3-O-アリル-2,4,6-トリ-O-ベンジル-D-グルコピラノシドから3-O-アセチル-2,4,6-トリ-O-ベンジル- α -D-グルコピラノシルクロリドの改良合成

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キーワード：塩化パラジウム(II)，化学合成，(1→3)- β -グルカン，脱アリル化，ハロゲン糖