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Synthesis of di-*N*-acetyl-β-chitobiosyl *N*-glycothiazoline

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The synthesis of di-*N*-acetyl-β-chitobiosyl *N*-glycothiazoline **2** was investigated. The synthesis was processed using the *N*-benzyloxycarbonyl (Cbz) protected trichloroacetimidates **11** and **13** as donors, polystyrene as support, and *o*-nitrobenzyl ether tether as linker. The target compound **2** was efficiently yielded by three glycosylations, catalytic hydrogenolysis, acetylation, deacetylation, and photolysis, respectively.

Keywords: di-*N*-acetyl-β-chitobiosyl *N*-glycothiazoline, synthesis, glycosylation, analogue

INTRODUCTION

The allosamidin **1** (Fig. 1) is a well-known pseudotrisaccharide, and it is a typical chitinase inhibitor. Compound **1** has the important biological activities, for example, acting as insecticide and fungicide [1]. It has been reported about the synthetic methods of allosamidin **1** and its analogues [2-3], and these compounds mostly were synthesized by the liquid-phase synthesis. The methods have multiple steps and the manufacturing costs are high, which prevents allosamidin **1** and its analogues from being widely utilized in agriculture. The compound **1** was synthesized by the solid/liquid phase methods [1]. However, but the allosamidin **1** must be purified to use column chromatography in the final step. Therefore, it doesn't fully utilize the strongpoint of solid-phase synthesis to synthesize compound **1**. Namely, one can distinctly avoid the purification process if the allosamidin **1** is synthesized by total solid-phase method. So, the redundant reactants or outgrowths can be removed by filtrating and washing. For such point of view, the solid-phase synthesis of di-*N*-acetyl-β-chitobiosyl *N*-glycothiazoline **2** was re-studied herein.

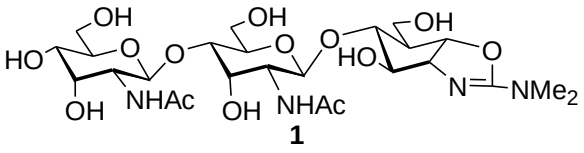

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Fig. 1 Structures of allosamidin **1**.

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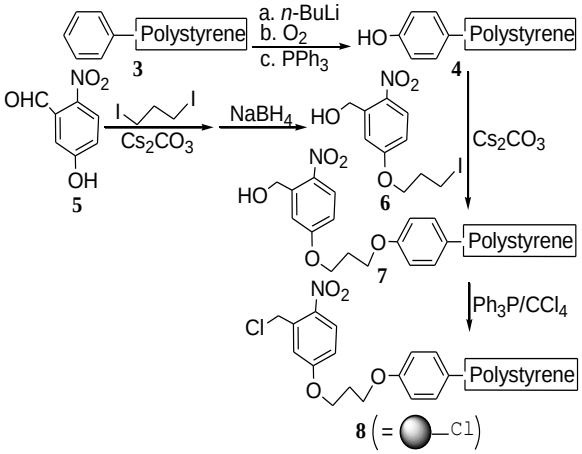

Scheme 1 Preparation of the chlorinated *o*-nitrobenzyl ether polystyrene **8**.

RESULTS AND DISCUSSION

Polystyrene **3** (Scheme 1) was functionalized to phenolic polystyrene **4** by reaction with *n*-BuLi, oxygen, and PPh_3, respectively. The linker, *o*-nitrobenzyl ether tether, was used because it was easy to attach and cleave. So, the available 5-hydroxy-2-nitrobenzaldehyde **5** was reacted with 1,3-diiodopropane in DMF under the alkaline condition, and then directly was reduced with $NaBH_4$ to offer iodobenzyl alcohol **6** in 93% yield for the above two steps. Compound **6** was attached to phenolic polystyrene **4** via its linker with Cs_2CO_3 to provide the conjugate **7** in 91% yield based on mass gain of the polymer. Chlorination of compound **7** with Ph_3P/CCl_4 obtained the chloride **8** in 86% yield.

The *N*-glycothiazoline **9** was obtained according to the reported method [4]. The C-3 hydroxyl group

