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-benzyloxyxycarbonyl (Cbz) protected trichloracetimidates 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.

Fig. 1 Structures of allosamidin 1.

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 PPh₃, 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-diodopropane in DMF under the alkaline condition, and then directly was reduced with NaBH₄ 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 Cs₂CO₃ to provide the conjugate 7 in 91% yield based on mass gain of the polymer. Chlorination of compound 7 with Ph₃P/CCl₄ obtained the chloride 8 in 86% yield.

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

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