

## STEREOSPECIFIC CHIRAL RESOLUTION OF TRANS 2-PHENYLCYCLOHEXANOL VIA INDIUM-INDUCED GLYCOSYLATION

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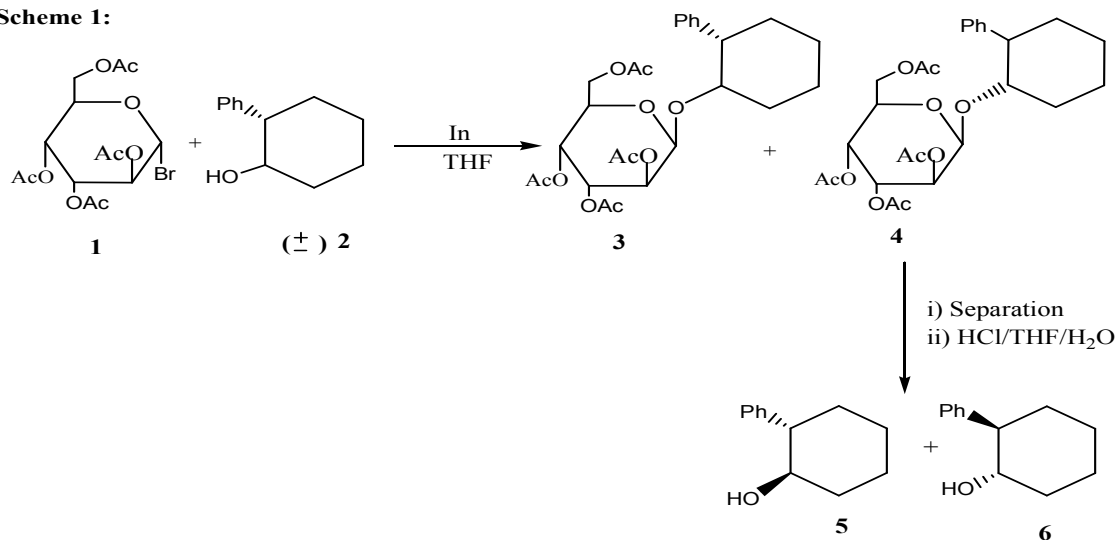
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**Abstract:** Chiral resolution of 2-phenylcyclohexanol has been accomplished starting from bromo peracetylated glucose via indium-induced reaction and acid-induced cleavage of the glycosides.

**Keywords:** Indium, Resolution, Stereospecific

**Introduction:** Glycosylation of alcohols is an attractive area of research because this method can be used to improve the water solubility of drug candidates and resolution of racemic substrates.<sup>1</sup> Many efficient methods of glycosylation have been developed.<sup>2</sup> The glycosyl fluoride<sup>3a</sup> and Ferrier rearrangement<sup>3b</sup> are very effective. Lewis acids<sup>4</sup> and acidic support<sup>5</sup> have also been used with much success. However, most of the reactions are not stereoselective. Improvement of the stereoselectivity of these processes has also been reported.<sup>6,7</sup> Our research in this field resulted in a simple method of stereoselective synthesis of  $\beta$ -glycosides via reaction of alcohol with  $\beta$ -D-bromoglucose derivative mediated by indium metal.<sup>8</sup> The cyclic glycoside can be cleaved to optically active alcohol by mild acid-induced reaction.

**Results and Discussion:** Some of these methods for O-glycosylation have proved to be effective; however, they have limitations that include non-stereoselectivity of the products, lengthy synthesis of the donor or the acceptor and the use of toxic reagents. In this paper, we report a stereospecific synthesis of  $\beta$ -D-O-glycosides with indium metal. Reaction of racemic 2-phenylcyclohexanol (**2**) and with 2,3,4,5,6-penta-*O*-acetyl- $\alpha$ -D-glucopyranosyl acetate (**1**) in the presence of indium metal using tetrahydrofuran as the solvent produced glycosides **3** and **4** in 75% yield (**Scheme 1**). The stereochemistry of the anomeric center is found to be  $\beta$ . The diastereomers **3** and **4** were separated by column chromatography. The anomeric bond in these glycosides was then cleaved very easily with mild acid to produce optically active alcohol **5** and **6**. The absolute stereochemistry of **5** and **6** was determined by comparison with known commercially available compounds with respect to optical rotation and NMR data.

**Scheme 1:**

**Conclusion:** Indium-induced O-glycosylation of *trans*-phenylcyclohexanol has produced highly stereospecific O-glycosides in good yields. These glycosides have been converted to optically active compounds via acid-mediated reaction. Considering the simplicity, this method will find a wide range of applications in organic chemistry.

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