



Iodine-catalyzed one-pot three-component synthesis of homoallyl benzyl ethers from aldehydes

Dolly Kataki, Prodeep Phukan *

Department of Chemistry, Gauhati University, Guwahati 781 014, Assam, India

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ABSTRACT

Iodine has been found to be an effective catalyst for one-pot synthesis of homoallyl benzyl ethers under mild reaction conditions. Various homoallyl benzyl ethers were synthesized in moderate to high yield by three-component condensation of aldehydes, benzyloxytrimethylsilane, and allyltrimethylsilane in presence of iodine (10 mol %) in dichloromethane at 0 °C.

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The reaction of an allyltrimethylsilane with a carbonyl compound in the presence of Lewis acid, known as the Sakurai–Hosomi reaction,¹ has been extensively studied and successfully applied in organic synthesis.² The allylation of acetals using allyltrimethylsilane³ is a useful method because the resulting homoallyl ethers and homoallyl acetates can be subjected to further synthetic manipulation. Synthesis of homoallyl ethers from aldehydes can also be achieved by using an alkoxy silane and allyltrimethylsilane in presence of a catalytic amount of iodotrimethylsilane.⁴ Seebach had developed another variation of the method for synthesis of homoallyl ethers by treating an aldehyde with dialkoxydichlorotitanium and subsequent addition of allyltrimethylsilane.⁵ Several catalysts such as TiCl_4 ,³ AlCl_3 ,⁶ $\text{BF}_3 \cdot \text{Et}_2\text{O}$,⁶ tritylperchlorate,⁷ diphenylboryl triflate,⁷ montmorillonite,⁸ Pb/Al ,⁹ $(\text{CH}_3)_3\text{SiI}$,¹⁰ TMSOTf ,¹¹ $\text{TiCp}_2(\text{CF}_3\text{SO}_3)_2$,¹² trimethylsilylbis(fluorosulfonyl)imide,¹³ CF_3COOH ,¹⁴ BiBr_3 ,¹⁵ $\text{Sc}(\text{OTf})_3$,¹⁶ indium metal,¹⁷ TMSNTf_2 ,¹⁸ $\text{Bi}(\text{OTf})_3 \cdot x\text{H}_2\text{O}$ ¹⁹ and TMSOF ²⁰ have been used to investigate the reaction of acetals with allyltrimethylsilane. However, these methods have several drawbacks. For example: (1) synthesis of acetals from corresponding benzaldehyde is a prerequisite as most of these acetals are not commercially available and further synthetic manipulation of the homoallylmethyl or ethyl ether is not practicable due to the inactivity of the aliphatic ether linkage; (2) many of these methods use corrosive and moisture sensitive catalysts such as TMS; (3) Metal triflates are expensive and toxic. In most of the organic synthetic methods, benzyl ethers are preferred to their alkyl counterparts as the benzyl group can be easily deprotected.

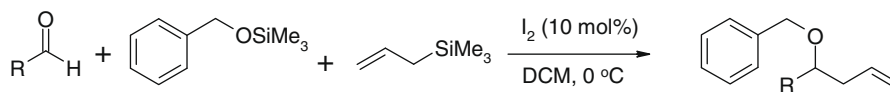
However, the synthesis of homoallyl benzyl ethers has received scant attention in the literature, with only a few methods outlined.^{20–24} Recently, Mohan et. al. developed a three-component procedure for the synthesis of homoallyl benzyl ethers using $\text{Bi}(\text{OTf})_3$ as a catalyst.²⁴ However, bismuth triflate is expensive and toxic. In recent years, iodine is finding extensive applications as a catalyst for organic transformations.²⁵ The advantages in the use of iodine are (i) mild neutral conditions (ii) cost effectiveness and ready availability (iii) no stringent dry conditions required. As a part of our ongoing work on iodine-catalyzed reactions,²⁶ we report herein an one-pot three-component method for the synthesis of homoallyl benzyl ether from aldehydes using iodine as a catalyst (Scheme 1).

Initially, we investigated the allylation reaction under various conditions for benzaldehyde as a model substrate. In order to accomplish the synthesis, allyltrimethyl silane (1.2 mmol) was added to a solution of benzaldehyde (1 mmol), benzyloxytrimethylsilane (1.2 mmol), and iodine (0.1 mmol) in acetonitrile at room temperature. After 24 h of reaction at room temperature, the reaction afforded the corresponding homoallyl benzyl ether in 60% yield (Table 1, entry 1). To optimize the reaction conditions, a screening was performed on several parameters such as solvents, catalyst concentration, and the amount of benzyloxytrimethylsilane and allyltrimethylsilane. Initially, the reaction was examined by taking different solvents (Table 1). Dichloromethane was found to be superior to other solvents.

Thereafter, the reaction was examined carefully under the influence of different concentrations of the catalyst using dichloromethane as solvent (Table 2). The use of 10 mol % of iodine (based on benzaldehyde) gave the best result with a yield of

* Corresponding author. Tel.: +91 9435111114.

E-mail address: pphukan@yahoo.com (P. Phukan).



Scheme 1.

Table 1

Synthesis of homoallyl benzyl ether in different solvents^a

Entry	Solvent	Time (h)	Yield ^b (%)
1	CH ₃ CN	24	60
2	CH ₂ Cl ₂	24	68
3	CH ₃ OH	24	0
4	Diethyl ether	24	0
5	CH ₃ NO ₂	24	43
6	DMF	24	0
7	THF	24	0

^a Reaction condition: benzaldehyde (1 mmol), benzyloxytrimethylsilane (1.2 mmol), iodine (0.1 mmol), allyltrimethylsilane (1.2 mmol), solvent (2 mL), rt.^b Isolated yield after chromatographic purification.

Table 2

Synthesis of homoallyl benzyl ether in dichloromethane under different conditions

Entry	Benzaldehyde (mmol)	Benzyloxy-trimethylsilane (mM)	Allyltri-methylsilane (mM)	Iodine (mol %)	Temp (°C)	Time (min)	Yield (%)
1	1	1.2	1.2	10	27	210	67
2	1	1.2	1.2	20	27	120	52
3	1	1.2	1.2	5	27	300	45
4	1	1.1	1.2	10	27	210	70
5	1	1.1	1.2	10	0	40	82
6	1	1.2	1.2	10	0	45	86
7	1	1.2	1.5	10	0	30	75

67% after 3 h of reaction. Neither decreasing nor increasing the iodine concentration helped in improving the yield. Although the optimal amount of catalyst was found to be 10 mol %, the yield was not satisfactory. Hence, the reaction was further studied by lowering the temperature to 0 °C. Surprisingly, the reaction worked in a much better way at 0 °C. The reaction was complete in 45 min with 86% yield of the corresponding homoallyl benzyl ether. Finally, the best result was obtained when the ratio of benzaldehyde, benzyloxytrimethylsilane, allyltrimethylsilane, and iodine was 1:1.2:1.2:0.1 at 0 °C in dichloromethane (Table 2, entry 6).

Next, we examined the scope of the reaction using various aldehydes and the results are summarized in Table 3. In general, high yields of homoallyl benzyl ethers were obtained with 10 mol % of iodine at 0 °C in dichloromethane.²⁷ Aromatic substrates bearing functional groups such as –CH₃, –OMe, –Cl, –Br, –NO₂, and –F all reacted successfully to give the corresponding homoallyl benzyl ethers (Table 3) in high yields irrespective of the substituent position on the aromatic ring. This reaction works with aliphatic aldehyde such as cinnamaldehyde but the yield was relatively lower.

In conclusion, we have developed an efficient protocol for the one-pot three-component synthesis of homoallyl benzyl ether starting from aldehyde in the presence of iodine as a catalyst. The merits of this method are (a) very simple, one-pot, and high yielding process which eliminates the need to isolate the intermediate and thus minimizes waste; (b) very cheap and easily available iodine; (c) low amount of catalyst (10%); (d) absence of toxicity; (e) reactions are carried out in air since iodine is not moisture sensitive. This method has wide scope for further applications as the catalyst is cheap and easily available commercially.

Table 3

Synthesis of homoallyl benzyl ethers using iodine as catalyst^a

Entry	Aldehyde	Time (min)	Yield ^b (%)
1		45	86
2		45	76
3		60	74
4		60	78
5		45	85
6		45	80
7		40	76
8		45	77
9		40	82
10		90	65

^a Reaction condition: aldehyde (1 mmol), benzyloxytrimethylsilane (1.2 mmol), iodine (0.1 mmol), allyltrimethylsilane (1.2 mmol), dichloromethane (2 mL), 0 °C.^b Isolated yield after chromatographic purification.

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27. *General procedure for the synthesis of homoallyl benzyl ether*: To a solution of aldehyde (1 mmol) and iodine (0.1 mmol) in dichloromethane (2 mL) at 0 °C, benzyloxytrimethylsilane (1.2 mmol) was added followed by the addition of allyltrimethylsilane (1.2 mmol). The mixture was stirred at 0 °C for appropriate time (TLC). After completion of the reaction, sodium thiosulfate (20 mg approximately) was added and the reaction mixture was stirred for 20 min. It was then extracted with ethylacetate, washed with brine, dried (Na₂SO₄), and concentrated. Purification of the crude product by chromatography on silica gel (60–120 mesh) with petroleum ether–EtOAc (5%) as eluent gave the pure product.