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# Indium Mediated Allylation of $\beta$ -Chloro-/ $\beta$ -Alkoxy Vinylaldehyde: A Facile One Pot Synthesis of 1-Chloro-/1-Alkoxy Hexa-1,5-diene-3-ol Derivatives

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### Indium Mediated Allylation of β-Chloro-/β-Alkoxy Vinylaldehyde: A Facile One Pot Synthesis of 1-Chloro-/1-Alkoxy Hexa-1,5-diene-3-ol Derivatives

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#### ABSTRACT

Indium mediated allylation of  $\beta$ -chloro- or  $\beta$ -alkoxy vinylaldehydes in the presence of sodium iodide produce homoallylic alcohol derivatives (1-chloro-/1-alkoxy hexa-1,5-diene-3-ol derivatives) in good yields.

The synthesis of homoallyl alcohol by reaction of allylic organometallic compounds has received wide spread attention.<sup>[1]</sup> In the last few years indium has emerged as most attractive metal for allyl group

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transfer.<sup>[2]</sup> In the context of our general interest in the chemistry of  $\beta$ -chlorovinylaldehydes<sup>[3]</sup> and exploration of indium mediated allylation of such compounds, we studied to develop a general method for 1-chloro-/1-alkoxy hexa-1,5-diene-3-ol derivatives.

We have found that an allyl indium reagent generated in situ readily undergoes regioselective addition to the carbonyl group of the  $\beta$ -chloro-/ $\beta$ -alkoxy vinylaldehydes in DMF solvent at ambient temperature (Sch. 1).

Thus when 1-chloro-3,4-dihydronaphthalene-2-aldehyde (1a) was treated in DMF, with indium and allyl bromide in presence of NaI, it produced 15a as a white solid in 64% yield (Entry no. 1). Various other alkoxy/chloroaldehydes<sup>[4]</sup> have been subjected to the same allylation protocol<sup>[5]</sup> in order to assess the generality of our method. The results are summarised in Table 1.

In all these cases, the chloroaldehydes (2–11) (Entry nos. 4–15) and alkoxy aldehydes (12-14) (Entry nos. 16-18) undergo facile allylation when subjected to similar reaction condition. Alkoxy aldehydes (12/14)could be easily synthesised from  $\beta$ -chloro vinyl aldehydes by treating it with the corresponding alkoxides (MeO<sup>-</sup>/allyl-O<sup>-</sup>).<sup>[4]</sup> In a similar way,  $\beta$ allyloxy-2,3-diphenyl-2-propenal (14) on reaction with allyl indium iodide afforded 28 in 61% yield (Entry no. 18). Compound 25 (Entry no. 13) is obtained in about 4:1 (E:Z) diastereomeric mixture in 72%yield starting from compound 10a. Compound 26 (Entry no. 14) exists in 1:5 (E:Z) inseparable diastereometric mixture as indicated by  $^{1}HNMR$ spectra. Interestingly we found that this reaction provides a very effective access to novel bis homoallyl alcohols 20-23 (Entry no. 8-11) starting from appropriate bis chlorovinylaldehydes in moderate to high yield. All the compounds gave satisfactory <sup>1</sup>H NMR, <sup>13</sup>C NMR, DEPT, and elemental analysis data.<sup>[6]</sup> Studies are in progress to exploit these compounds for the synthesis of some novel receptor molecule by ring closure metathesis reaction.

We have also studied the behavior of propargyl bromide in this reaction. It has been observed that chloroaldehydes under the same

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Representative <sup>1</sup>H-NMR data of compound 20

condition on reaction with propargyl indium iodide afforded a mixture of homopropargyl alcohols and allenyl alcohols (Sch. 2).

Thus compound 5 under the same reaction condition produced compound 31 and 32 in 1:1.5 ratio in 67% overall yield. Similarly 10a produced 33 and 34 in overall 67% yield as 1:1 mixture.

Compound **27** has been further silylated to the *bis* silyl derivatives in 62% yield with  $Et_3SiH$  in presence of Spier's catalyst<sup>[7]</sup> (H<sub>2</sub>PtCl<sub>6</sub>) (Sch. 3). Further investigation towards the extension of this method to the synthesis of novel sol-gel glass by treating allyloxy homoallyl alcohols with triethoxy silanes [HSi(OEt)<sub>3</sub>] is underway in our laboratory.

Another advantage of this study is the generation of a tetrahedral carbon, which could be made chiral under appropriate reaction condition in presence of chiral ligands such as (–) sparteine or (–) cinchonidine. An initial study shows that reaction of compound **5** with 2 equiv. of indium, and 3 equiv. of allylbromide in presence of 2 equiv. of (–) sparteine, produced respective homoallyl alcohol derivative and the specific rotation of the compound  $[\alpha]_d^{25}$  was found to be +35 (c=0.2, CHCl<sub>3</sub>). However this result is not yet optimised and systematic studies on the enantiose-lective indium mediated allylation of  $\beta$ -chlorovinylaldehydes is under progress in our laboratory. Furthermore homoallyl alcohols could be dehydrated by using PTSA in dry benzene to produce novel hexatriene derivatives. (Sch. 4) It is worthy of mention that hexatriene derivatives are very important class of organic molecules.

For a specific example, compound 1c when refluxed with *p*-toluene sulphonic acid in dry benzene as a solvent afforded 36 as a yellow solid in 78% yield.

So, in general we have developed a simple and efficient method for the synthesis of *mono-* and *bis*-homoallyl alcohols (1-chloro-/1-alkoxy-

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Scheme 5.

hexa-1,5-diene-3-ol derivatives) which could be further functionalised to synthesise some interesting designed molecules like macrocyclic oxaheterocycles (via ring closure metathesis reaction) or sol-gel glass (via triethoxysilanes) (Sch. 5).

Our method also opens up the possibility of enantioselective indium-mediated allylation reaction of  $\beta$ -substituted vinylaldehydes by performing the reaction in presence of chiral ligands and also provide a facile entry into the novel substituted hexatriene system.

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#### ACKNOWLEDGMENT

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- Typical experimental procedure: A mixture of β-chlorovinylaldehyde (1 mmol), allyl bromide (3 mmol), indium metal (Sisco Research Laboratory, India) (2 mmol), sodium iodide (3 mmol) in dimethyl formamide (4–5 mL) was stirred at 25°C until completion of the reaction (checked by TLC). The reaction mixture was quenched with a

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#### 1-Chloro-/1-Alkoxy Hexa-1,5-diene-3-ol Derivatives

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few drops of 1N HCl, diluted with water and extracted with diethyl ether. After usual work up, the crude product obtained was purified by column chromatography (silica gel).

- 6. (a) All compounds gave satisfactory elemental and spectroscopic data; (b) Data of the product 15c. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.9 (brs, 1H), 2.26–2.53 (m, 4H), 2.53–2.74 (m, 2H), 5.04–5.20 (m, 3H), 5.71–5.92 (m, 1H), 6.96 (d, 1H, J=8.0 Hz), 7.28 (dd, 1H, J=2.0 & 8.0 Hz), 7.71 (d, 1H, J=2.0 Hz) ppm; <sup>13</sup>C NMR 23.09, 27.12, 39.26, 70.32, 118.39, 120.23, 124.34, 127.42, 128.46, 130.64, 133.58, 134.67, 135.01, 139.27; DEPT 135: 23.09, 27.13, 39.27, 70.31, 118.41, 127.42, 128.48, 130.64, 133.57. DEPT 90: 70.31, 127.41, 128.48, 130.65, 133.57. CHN calcd: C (53.59), H (4.47). Observed: C (53.35), H (4.27). Data of the product 20. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 1.85 (br, 1H), 2.37–2.50 (m, 4H), 4.81 (m, 2H), 5.16–5.24 (m, 4H), 5.87–5.95 (m, 2H), 6.13 (d, 2H, J=7.6 Hz), 7.00 (dd, 4H, J=2.2 & 6.8 Hz), 7.55 (dd, 4H, J=2.2 & 6.8 Hz) ppm. <sup>13</sup>C NMR 40.81, 68.88, 109.90, 118.58, 118.73, 128.13, 128.69, 133.51. CHN calcd: C (66.82), H (5.57). Observed: C (66.57), H (5.31).
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