A New Type of Catalysis by Copper(I) Salts in the Barbier-type Aldehyde Allylation with Tin(II) Chloride. Short Syntheses of (±)-Lavandulol and its γ, δ-Dihydro Derivative

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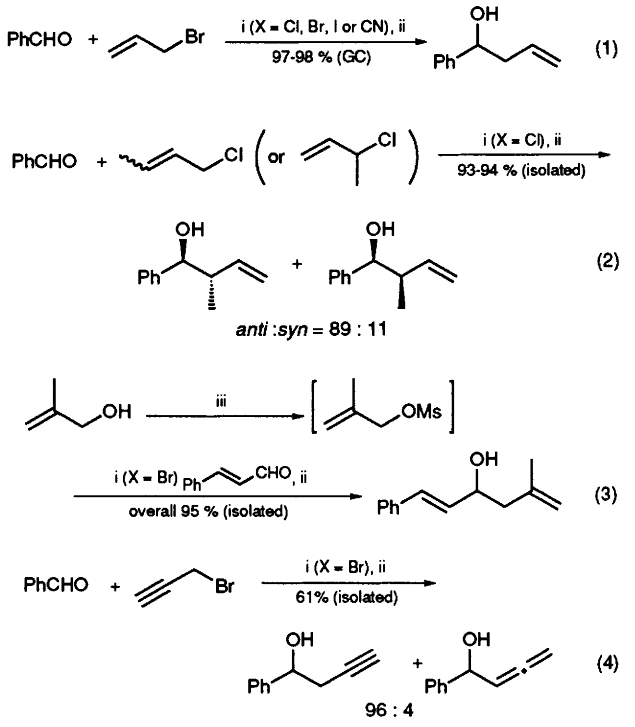
Copper(I) halides and cyanide catalyse the Barbier-type aldehyde allylation with allylic bromides, chlorides or sulfonates and tin(II) chloride enabling the reaction to take place under very mild conditions with high efficiency.

It is well known that tin(II) halides and alkali metal or ammonium halides form anionic halogeno tin complex salts.[1] These nucleophilic tin species, however, have hardly been utilized in organic synthesis except for one case, in which $LiSnBr_2Cl$ generated *in situ* from $SnCl_2$ and LiBr has been used for converting *tert*-butyl chloromethyl ether to the (*tert*-butoxymethyl)trihalogenotin compound.[2]

We have studied the possibility of such nucleophilic assistance in the stanylation of allylic halides and reported recently on the effect of alkali metal halides which do indeed promote the reaction, with varying efficiency. The major factor was, however, attributed to *in situ* generation of allylic iodides because of the pronounced effect of the iodide salts.[3]

Here, we report a new type of catalysis by copper(I) salts[4] which seems to have the predicted effect, *i.e.* nucleophilic activation of the divalent tin species, presumably through the formation of tin–copper complex salts $CuSnCl_2X$.[†] Thus, benzaldehyde (5 mmol) was allylated smoothly at room temperature with allyl bromide and tin(II) chloride dihydrate (7.5 mmol each) in THF (10 ml) in the presence of copper(I) chloride (0.5 mmol) to give a 98% yield of 1-phenylbut-3-en-1-ol [eqn. (1)]. In the absence of the copper salt, the allylation proceeded in only 6% yield under otherwise identical conditions. Noteworthy is that the catalytic effect is independent of the counter anion: copper(I) chloride, bromide, iodide and cyanide are all equally effective in promoting reaction (1). This is in sharp contrast to what was observed for alkali metal salts.[3]



Scheme 1 *Reagents and conditions*: i, $SnCl_2.2H_2O$ (1.5 equiv.), CuX (0.1 equiv.), THF, room temp., 20–24 h; ii, 30% aq. NH_4F; iii, $MeSO_2Cl$, Et_3N, THF, room temp., 15 min

The iodide ion-promoted reaction has opened a route to the use of otherwise practically unreactive allylic chlorides in these transformations. The present reaction also enables these chlorides to be used even under milder conditions [eqn. (2)]. Furthermore, allyl sulfonates could also be used [eqn. (3)], as expected from their reactivity in nucleophilic substitution. These derivatives can be readily prepared from allylic alcohols and methanesulfonyl chloride in the presence of triethylamine and immediately used for the allylation in one pot since the byproduct ammonium salt does not affect the subsequent transformation. This procedure, thus, makes these alcohols a convenient and practical source of allylating agents.

Another difference between these systems is in the solvent; while the iodide ion-promoted reaction proceeds more smoothly in a highly polar solvent like DMF, the copper(I)-catalysed reaction prefers ethereal solvents. In some cases, this may be of synthetic merit [for example, higher diastereoselectivity was observed in the reactions of eqn. (2) (*anti* : *syn* = 89 : 11 in THF and 92 : 8 diethyl ether) than in the previous reaction in DMF (53 : 47), and higher and even reversed regioselectivity was observed in the reaction of prop-2-ynyl bromide, eqn. (4), homopropynyl : allenyl alcohol = 96 : 4) compared to the previous example (31 : 69)].

Although internal chlorides such as 3-chlorobut-1-ene were practically unreactive in the previous system,[3] they react as smoothly as terminal allylic chlorides under the present conditions [eqn. (2)]. By exploiting this advantage, the monoterpene lavandulol **3a**[5] and its γ,δ-dihydro derivative **3b**[6] were prepared in short synthesis from simple commercial chemicals (Scheme 2). The required main chain framework and the allylic chloride functionality were prepared in one step by the known procedure.[7] The subsequent hydroxymethylations were conveniently performed by mild heating with formalin (2 equiv.) in isopropyl alcohol. Treatment of the crude product with acidic methanol was required since the desired alcohols had been partially converted to the corresponding isopropoxymethyl ethers under the reaction conditions.

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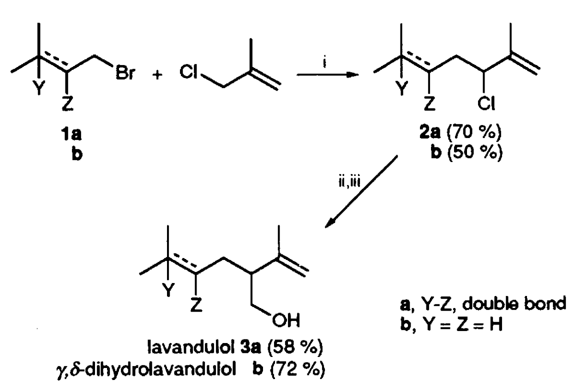

Scheme 2 *Reagents and conditions*: i, $LiNPr^i_2$, THF, −78 °C, 15 min; ii, 37% aq. HCHO, $SnCl_2{\cdot}2H_2O$, cat. CuCl, Pr^iOH, 50 °C, 15 h; iii, cat. $HClO_4$, MeOH, room temp., 40 h

Footnote

† Formation of such a stannate(II) species is supported by ^{119}Sn NMR spectroscopy; the chemical shift of −772 ppm measured for an equimolar mixture of $SnCl_2$ and CuCl in DMF (0.5 mol dm^{-3} each) indicated considerable shielding of the tin nuclear compared with that of $SnCl_2$ (−359 ppm).

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