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Novel carbonyl allylation mediated by $SnCl_2$/Cu in water

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Abstract—Copper metal was found to be able to catalyze $SnCl_2$-mediated coupling between carbonyl compounds and allyl halides to give the corresponding homoallylic alcohols in high yields. © 2002 Elsevier Science Ltd. All rights reserved.

Allylation of carbonyl compounds to produce homoallylic alcohols is a very important reaction in synthetic organic and pharmaceutical chemistry. Therefore, numerous reagents and methods have been developed to accomplish this transformation.[1]

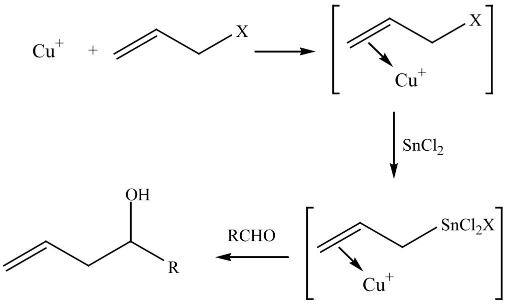
Since the 1980s, it has been gradually realized that carbonyl allylation can even be achieved in aqueous media through a Barbier-type reaction.[2] This discovery attracts considerable attention because of the increasing public interest in Green Chemistry.[3]

So far many metals have been reported to be effective in mediating the coupling between allyl halides and carbonyl compounds to give the corresponding homoallylic alcohols in aqueous media. Examples include indium,[4] antimony,[5] bismuth,[6] lead,[7] manganese,[8] magnesium,[9] zinc,[10] and tin.[11] However, because the metal-mediated allylation is a heterogeneous reaction, high conversion of starting materials is often hard to achieve. In order to improve the reaction yield, use of inorganic salt (e.g. NH_4Cl), organic cosolvent and ultrasonic irradiation is often recommended.

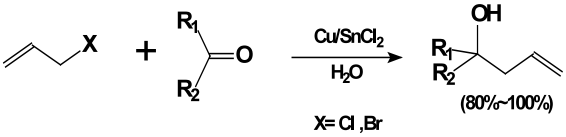
Reductive metal salts (e.g. stannous chloride, $SnCl_2$) provide an alternative way to mediate the carbonyl allylation reaction.[12] They do not have the solubility problem zerovalent metals possess and therefore, appear promising for large scale application. However, it was found that unless some catalyst is employed, metal salts cannot efficiently mediate the coupling between carbonyl compounds and organic halides.

An interesting recent discovery is that cupric chloride ($CuCl_2$) is able to catalyze $SnCl_2$-mediated coupling reaction between aldehydes and allyl bromide in a water–dichloromethane (1:1) solution.[13] It was proposed that Cu^+ produced by $SnCl_2$ reduction of $CuCl_2$ forms a cation-π complex with allyl bromide. This cation-π interaction activates allyl bromide toward $SnCl_2$ displacement, catalyzing the allylation (Scheme 1).[14,15]

As part of our recently initiated program to explore novel Green Chemistry reactions for industrial application, we are interested in finding a cheap and environmentally-benign catalyst for the metal salt-mediated carbonyl allylation. Interestingly, we found that zerovalent Cu metal is a very good catalyst for $SnCl_2$-mediated coupling between allyl halide and carbonyl compounds in completely aqueous media[16] (Scheme 2).



Scheme 1.



Scheme 2.

Keywords: carbonyl compound; allylation; stannous chloride; copper.

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Typical procedures for the allylation are as follows: To a mixture of carbonyl compound (10 mmol) and allyl halide (15 mmol) in water (20 ml), copper powder (20 mmol) and $SnCl_2$ (20 mmol) were added in one portion. The mixture was vigorously stirred at room temperature for approximately 3 h. The mixture was extracted with ether (3×30 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and were filtered and evaporated. The residue, in most cases, afforded the corresponding homoallylic alcohols of sufficient purity as judged by TLC and ^{1}H NMR without the need for further purification. If necessary, purification was performed by flash column chromatography over silica gel.

The experimental results are summarized in Table 1. Most of the homoallylic alcohol products reported in Table 1 are known compounds.[17] They were confirmed by IR and 400 MHz ^{1}H NMR spectra.

From Table 1 it can be seen that carbonyl allylation mediated by $SnCl_2$/Cu in fully aqueous media usually has a high yield (80–100%). Compared to the previously reported allylation mediated by zerovalent metals,[4–11] there is no need to use any organic cosolvent under the present condition. There is also no necessity to employ ultrasonic irradiation.

Both aldehydes and ketones can be allylated in the $SnCl_2$/Cu-mediated reaction. Also, both aliphatic and aromatic carbonyl compounds are reactive. Therefore, compared to the metal mediated allylation,[4–11] $SnCl_2$/Cu-mediated allylation is applicable to a larger range of carbonyl substrates.

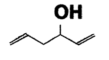
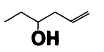
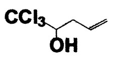
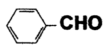
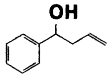
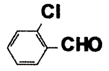
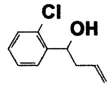
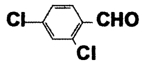
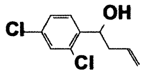
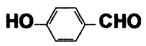
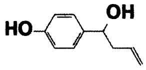
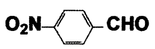
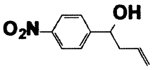
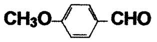
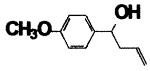
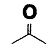
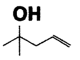
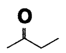
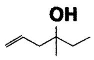
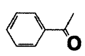
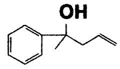
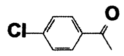
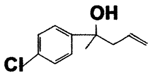
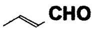
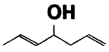
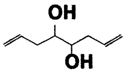
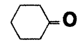
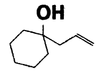
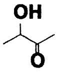
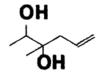
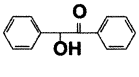
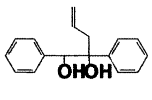
In addition to allyl bromide, allyl chloride was also found to be reactive in $SnCl_2$/Cu-mediated allylation. In comparison, zerovalent metals usually cannot mediate the coupling between carbonyl compounds and allyl chloride in aqueous media.[4–11] Nevertheless, for aromatic ketones it was found that allyl chloride gives a very low yield in $SnCl_2$/Cu-mediated allylation (entry 12).

No pinacol coupling product is produced in the reaction. For α,β-unsaturated aldehydes, only the 1,2-addition product is observed (entries 1 and 14). In addition, there is no need to protect active hydrogen in the substrates (entries 7, 17 and 18).

Interestingly, nitro-containing substrate (entry 8) can also be successfully allylated. In comparison, it is usually hard to turn nitro-containing carbonyl compounds into homoallylic alcohols without reducing the nitro group through the zerovalent metal mediated allylation.

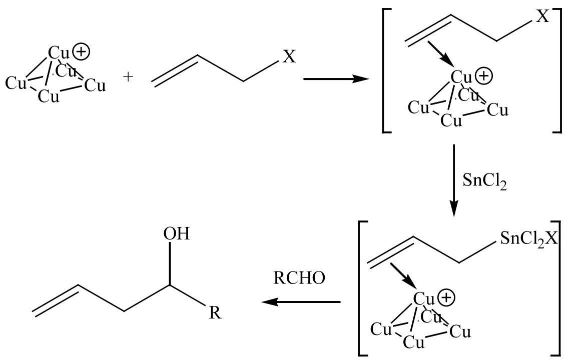
No product was observed when only copper was used in the reaction. Little product (<5%) was observed when only $SnCl_2$ was employed in the reaction. Therefore, both Cu and $SnCl_2$ are essential for the allylation. Since it was found that after the reaction almost all Cu can be easily recovered, we propose that Cu should be a catalyst for the reaction.

Table 1. Carbonyl allylation mediated by Cu/$SnCl_2$ in water

Entry	Substrates	Products	X	Yield(%)*/time(h)
1			Cl Br	88 / 3 94 / 3
2			Cl Br	98 / 3 98 / 3
3	CCl_3CHO		Cl Br	95 / 3 96 / 3
4			Cl Br	100 / 8 100 / 8
5			Cl Br	100 / 3 100 / 3
6			Cl Br	100 / 8 100 / 8
7			Cl Br	92 / 8 94 / 8
8			Cl Br	85 / 8 92 / 8
9			Cl Br	88 / 3 92 / 3
10			Cl Br	91 / 3 95 / 3
11			Cl Br	92 / 3 95 / 3
12			Cl Br	20 / 24 91 / 8
13			Br	100 / 8
14			Br	92 / 3
15	$(CHO)_2$		Br	91 / 3
16			Br	90 / 8
17			Br	95 / 8
18			Br	100 / 8

* Isolated yield

Compared to the previous work,[13] we propose that the likely mechanism for the reaction to be as follows (Scheme 3). First, copper metal loses an electron to an oxidant, which gives a singly-charged copper cluster located on the surface of copper metal.[18,19] Second, the



Scheme 3.

positively charged copper cluster forms a cation-π complex with allyl halide on the surface of copper metal activating the allyl halide. Third, the activated allyl halide reacts with SnCl$_2$, producing an organotin complex. Finally, the organotin complex allylates the carbonyl compound giving homoallylic alcohol.

The key of the above mechanism is that the reaction should occur on the surface of copper metal. Therefore, enlarging the effective surface area should increase the reaction efficiency. To test if this is true, we are now trying to make nanometer copper materials[20] and then use them to catalyze allylation.

In conclusion, this study demonstrated a novel carbonyl allylation reaction mediated by SnCl$_2$/Cu in aqueous media. The reaction is very efficient and applicable to various aliphatic and aromatic aldehydes and ketones. Since copper metal is cheap, easy to handle and fully recoverable after the reaction, we think that this reaction could be valuable for laboratory and industrial synthesis.

Acknowledgements

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17. New compounds include: **3-methyl-hex-5-ene-2,3-diol**: IR (film): 3417, 3079, 3026, 1642 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 1.12 (s, 3H), 1.14–1.19 (m, 3H), 2.0–2.5 (br, 2H), 2.26 (d, $J=6.4$ Hz, 2H), 3.67 (t, $J=6.0$, 1H), 5.11–5.20 (m, 2H), 5.86–5.93 (m, 1H). **1,2-Diphenyl-pent-4-ene-1,2-diol**: IR (film): 3549, 3471, 1633 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$, ppm): δ 2.4–2.7 (br, 2H), 2.68–2.74 (m, 1H), 2.88–2.92 (m, 1H), 4.75 (s, 1H), 5.02–5.14 (m, 2H), 5.50–5.52 (m, 1H), 6.96–7.18 (m, 10H).

18. Copper is metallic. Therefore, it is not hard for a copper cluster to lose an electron to oxidants like O_2 in the air and H^+ in water. Of course this does not mean Cu is oxidized to free Cu^+ or Cu^{2+} ions. All Cu atoms still stay in the cluster.
19. We tried to use CuO to catalyze $SnCl_2$-mediated allylation of benzaldehyde. We found that the yield was low (~50%). Therefore, the catalytic effect of Cu metal is not from CuO.
20. Nanotin material was recently used for carbonyl allylation in aqueous media: Wang, Z. Y.; Zha, Z. G.; Zhou, C. L. *Org. Lett.* **2002**, *4*, 1683.