

# Novel Carbonyl Allylation Mediated by SnCl<sub>2</sub>/TiCl<sub>3</sub> in Water

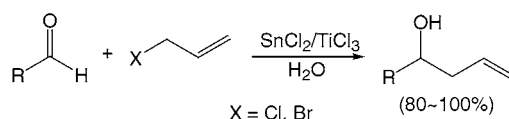
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## ABSTRACT



Under the Lewis acid catalysis offered by TiCl<sub>3</sub>, SnCl<sub>2</sub> can efficiently mediate the aqueous Barbier reactions between aldehydes and allyl chloride or bromide.

Recently, the study of organic reactions occurring in aqueous media has developed into a very important field.<sup>1</sup> In particular, by virtue of its synthetic potential, mechanistic intrigue, and operational simplicity, the Barbier coupling reaction between allyl halide and carbonyl compounds in aqueous media has attracted considerable attention recently.<sup>2</sup> Use of this elegant method allows homoallylic alcohols to be synthesized in a highly efficient and environmentally benign way.

Numerous metals have been reported to be effective in mediating the aqueous Barbier reaction. Examples include aluminum,<sup>3</sup> magnesium,<sup>4</sup> manganese,<sup>5</sup> cadmium,<sup>6</sup> indium,<sup>7</sup> antimony,<sup>8</sup> bismuth,<sup>9</sup> lead,<sup>10</sup> gallium,<sup>11</sup> zinc,<sup>12</sup> and tin.<sup>13</sup> Although good yields can often be obtained in these reactions, the use of zero-valent metals unavoidably causes

some operational problems. For instance, it is often difficult to stir the reaction mixture when a large amount of metal is used. Furthermore, metal oxide or hydroxide precipitation on the surface of metal may slow or stop the reaction.

Water-soluble reductive metal salts such as SnCl<sub>2</sub>, if applicable to the aqueous Barbier reaction, may solve the above operational problems. However, it was reported that SnCl<sub>2</sub> cannot mediate the coupling between allyl halide and a carbonyl compound in water, unless some Pd(II)<sup>14</sup> or

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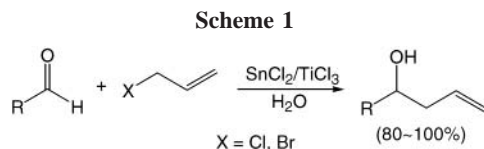
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Cu(I)<sup>15,16</sup> catalyst is introduced to the reaction. In the present study, we report our recent finding that TiCl<sub>3</sub> can also efficiently catalyze the SnCl<sub>2</sub>-mediated Barbier reaction (Scheme 1).



The experimental results are summarized in Table 1.<sup>17</sup> All of the homoallylic alcohols listed in Table 1 were confirmed by IR and 300 MHz <sup>1</sup>H NMR analyses.<sup>18</sup>

From Table 1, it can be seen that carbonyl allylation mediated by SnCl<sub>2</sub>/TiCl<sub>3</sub> in fully aqueous media usually has a high yield (80~100%). Compared to the previously reported allylation mediated by zero-valent metals,<sup>4–13</sup> there is no need to use any organic cosolvent or ultrasonic irradiation under the present conditions. In addition, since SnCl<sub>2</sub> and TiCl<sub>3</sub> are both soluble in water, it is fairly easy to stir the reaction mixture.

Allyl chloride and bromide provide similar yields in SnCl<sub>2</sub>/TiCl<sub>3</sub>-mediated allylation, although for allyl chloride a longer reaction time is needed in some cases. In a comparison, zero-valent metals usually cannot mediate the coupling between carbonyl compounds and allyl chloride in aqueous media.<sup>4–13</sup>

Both aliphatic and aromatic aldehydes can be efficiently allylated under the present reaction conditions. For unsaturated aldehydes (entry 4), only the 1,2-addition takes place. Nevertheless, the SnCl<sub>2</sub>/TiCl<sub>3</sub>-mediated allylation does not work efficiently for ketones (entry 15).

Little allylation product (<5%) was observed when only SnCl<sub>2</sub> was employed in the reaction. No allylation product was found when only TiCl<sub>3</sub> was employed in the reaction. Therefore, both SnCl<sub>2</sub> and TiCl<sub>3</sub> are essential for the allylation. Since the violet color of TiCl<sub>3</sub> remains and no TiO<sub>2</sub> can be found after the reaction, we propose that SnCl<sub>2</sub> should be the reductant and TiCl<sub>3</sub> should be the catalyst.

Interestingly, it was found that TiCl<sub>3</sub> can be reused many times as the catalyst in the allylation reaction. As shown in Figure 1, we allylated benzaldehyde five times using the same load of TiCl<sub>3</sub> catalyst. In the five allylation reactions,

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(17) Typical procedures for the SnCl<sub>2</sub>/TiCl<sub>3</sub>-mediated aqueous allylation are as follows. To a mixture of carbonyl compound (10 mmol) and allyl halide (18 mmol) in water (20 mL) were added aqueous TiCl<sub>3</sub> solution (15%, 1.5 mL) and SnCl<sub>2</sub> (20 mmol). The mixture was vigorously stirred at room temperature for several hours. Then, the mixture was extracted with ether (3 × 30 mL). The combined organic layers were dried over anhydrous MgSO<sub>4</sub> and filtered and evaporated. The residue, in most cases, afforded the corresponding homoallylic alcohols of sufficient purity as judged by TLC and <sup>1</sup>H NMR without the need for further purification. If necessary (entries 6, 7, 11, 12, and 13), purification was performed by flash column chromatography over silica gel.

(18) All the products were reported before in ref 16.

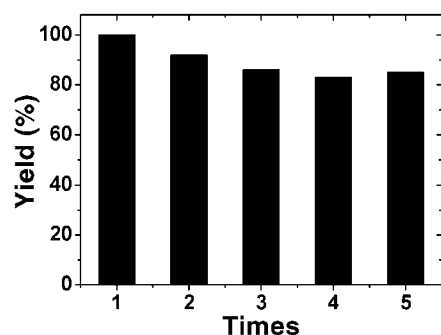
**Table 1.** Carbonyl Allylation Mediated by SnCl<sub>2</sub>/TiCl<sub>3</sub> in Water

entry	substrate	product	X	yield (%) /time (h)
1	(CHO) <sub>2</sub>		Cl Br	88 / 24 <sup>19</sup> 92 / 10
2			Cl Br	85 / 6 95 / 6
3	CCl <sub>3</sub> CHO		Cl Br	82 / 6 91 / 6
4			Cl Br	87 / 6 91 / 6
5			Cl Br	92 / 6 92 / 6
6	i-C <sub>7</sub> H <sub>15</sub> CHO		Cl Br	94 / 6 98 / 6
7	PhCH <sub>2</sub> CHO		Cl Br	87 / 8 92 / 8
8			Cl Br	100 / 8 100 / 8
9			Cl Br	91 / 18 100 / 8
10			Cl Br	100 / 8 100 / 8
11			Cl Br	85 / 8 90 / 8
12			Cl Br	90 / 18 93 / 8
13			Cl Br	95 / 8 95 / 8
14			Cl Br	100 / 8 100 / 8
15			Cl Br	30 / 24 50 / 24

TiCl<sub>3</sub> was added only before the first reaction. After each allylation reaction was accomplished, all the organic materials were extracted out using ether and analyzed. Then, to the remaining water layer was added a certain amount of benzaldehyde and SnCl<sub>2</sub> again to initiate a new round of allylation.<sup>20</sup>

According to Figure 1, the yields of the five allylation reactions are all higher than 80%, indicating that TiCl<sub>3</sub> is a

(19) Ratio of *dl:meso* = 69:31 for allyl chloride. Ratio of *dl:meso* = 70:30 for allyl bromide.

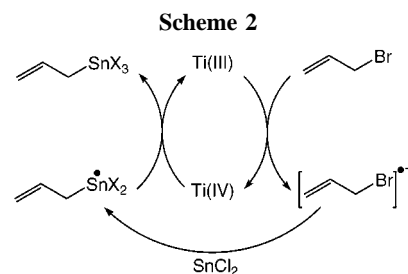


**Figure 1.** Yields of five allylation reactions between benzaldehyde and allyl bromide-catalyzed by reused  $\text{TiCl}_3$ .

reusable catalyst for the allylation. In fact, after the fifth reaction, the color of  $\text{TiCl}_3$  still did not fade away. The slight decrease of the yield over the reactions is possibly due to the loss of  $\text{TiCl}_3$  in the extraction.

The mechanism of the  $\text{SnCl}_2/\text{TiCl}_3$ -mediated allylation is quite intriguing. Although it is known that low-valent titanium may reductively couple carbonyl compounds to olefins,<sup>21</sup> the dimerization product was never found under the  $\text{SnCl}_2/\text{TiCl}_3$  conditions. Clerici et al. found that an aqueous  $\text{TiCl}_3/\text{NH}_3$  system can reduce aldehydes and ketones to alcohols.<sup>22</sup> However, under our conditions, no reduction product was observed, either.

A possible mechanism for the  $\text{TiCl}_3$ -catalyzed allylation is that  $\text{Ti(III)}$  transfers one electron to allyl halide in the first step (Scheme 2).<sup>23</sup> The allyl halide radical anion then reacts with  $\text{SnCl}_2$  to form an allyltin radical, which is oxidized by  $\text{Ti(IV)}$  yielding  $\text{Ti(III)}$  and a neutral allyltin compound. The



allyltin compound adds to the carbonyl group, yielding the homoallylic alcohol.

Another possible mechanism for the  $\text{TiCl}_3$ -catalyzed allylation is that  $\text{Ti(III)}$  activates the carbonyl group because of its Lewis acidity.<sup>24,25</sup> It is also possible that the electron transfer and Lewis acid catalytic effects are both involved in the allylation. A more detailed study on the mechanism of the reaction is underway in our lab.

In conclusion, the present study demonstrated a novel carbonyl allylation reaction mediated by  $\text{SnCl}_2/\text{TiCl}_3$  in water. The reaction is very efficient and simple to run. We expect that the reaction can be easily scaled up for both laboratorial and industrial synthesis.

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**Supporting Information Available:** Experimental procedures and pertinent spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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