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$SnCl_2$-mediated carbonyl allylation in fully aqueous media

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Abstract—Systematic studies were performed on $SnCl_2$-mediated carbonyl allylation reaction between aldehydes and allyl halides in fully aqueous media. Totally three valuable reaction systems were discovered, which were $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, and $SnCl_2/PdCl_2$. They all provided good to excellent yields in the allylation of aliphatic and aromatic aldehydes under very mild and convenient conditions. $SnCl_2$, by itself, was also found to be effective for the allylation reaction when allyl bromide was employed. However, the $SnCl_2$-only reaction could only tolerate very small amount of water as the solvent. The $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, and $SnCl_2/PdCl_2$-mediated reactions exhibited good regioselectivity favoring the γ-adduct when cinnamyl halides were employed as the allylation reagent. The same reactions with cinnamyl halides also showed good diastereoselectivity favoring the *anti*-product. Mechanistic studies using proton NMR techniques suggested that the additive (i.e., $CuCl_2$, $TiCl_3$, $PdCl_2$) could accelerate the formation of allyltin intermediate, but this step was shown not to be the most important for the allylation. Thus we proposed that the Lewis acid catalysis effect exerted by the additive was the main reason for the observed reactivity enhancement.

1. Introduction

Carbonyl allylation is a highly important synthetic transformation in organic and pharmaceutical chemistry, because the homoallylic alcohol product is a versatile subunit in synthesis that can easily be converted to a number of other useful functions.[1] Until now, many methods have been developed to accomplish carbonyl allylation, which usually involve the synthesis of a certain allylic organometallic reagent and the addition of the organometallic reagent to the carbonyl compound in anhydrous organic solvents. However, because of the high reactivity and moisture-sensitivity of most allylic organometallic reagents, this synthetic approach is neither operationally simple nor safe to scale up.

An alternative and attractive approach to achieve carbonyl allylation is to use the Barbier reaction,[2] which refers to the metal-mediated coupling between a carbonyl compound and an organic halide in a one-pot fashion. Operational simplicity is an obvious advantage of the Barbier reaction, because no reaction intermediate needs to be isolated. Moreover, it was found recently that the Barbier reaction could be conducted in partially or even fully aqueous media.[3] This 'surprising' discovery attracts considerable attention because of the increasing public interest in Green Chemistry.[4]

So far, numerous metals have been reported to be effective in mediating the aqueous Barbier reaction. Examples include aluminum,[5] magnesium,[6] manganese,[7] indium,[8] antimony,[9] bismuth,[10] lead,[11] gallium,[12] zinc,[13] and tin.[14] 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. Metal oxide or hydroxide precipitation on the surface of metal may slow or stop the reaction, so that organic co-solvent or ultrasonic radiation has to be utilized in some of the above reactions. Furthermore, some zero-valent metals are too reactive and significant byproducts (e.g., pinacol reaction product, carbonyl reduction product, and Wurtz reaction product) can be produced in the reaction.

We thought that water-soluble reductive metal salts such as $SnCl_2$, if applicable to the aqueous Barbier reaction, might solve some of the above problems associated with the zero-valent metals. Thus we recently investigated the possible use of $SnCl_2$ in aqueous Barbier reaction. We found that a combination of $SnCl_2$ and Cu could efficiently mediate the aqueous carbonyl allylation reactions.[15] We also found that $TiCl_3$ could dramatically catalyze the $SnCl_2$-mediated carbonyl allylation reactions in fully aqueous media.[16] It is worth mentioning that Roy et al. recently found that SnO/Cu_2O and $SnCl_2/CuCl_2$ could also mediate the carbonyl allylation reactions.[17] However, in their reactions the use of organic co-solvent such as THF was necessary. Furthermore, Samoshin[18] and Yuan[19] reported very recently that $SnCl_2$/KI and $SnCl_2$/untrasonication could mediate the carbonyl allylation reactions in water.

Keywords: Allylation; $SnCl_2$; Aqueous medium; Green chemistry; Barbier reaction.
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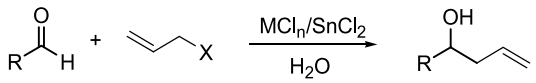
All the above findings suggest that $SnCl_2$-mediated allylation in aqueous media might be developed into a valuable reaction for organic synthesis. However, a lot of details about this reaction still remain poorly understood at present. For instance, the mechanism of the reaction is not fully clear and the role of the additive (e.g., Cu, $TiCl_3$) in the reaction is quite ambiguous. Secondly, the scope of the reaction has not been adequately studied and the reaction condition may require more optimization. Thirdly, most studies reported so far only put emphasis on un-substituted allyl halides, while the regio- and diastereo-chemistry associated with substituted allyl halides has received little attention.

In the present paper we wish to report some new findings concerning the aqueous $SnCl_2$-mediated carbonyl allylation reactions. We screened many Lewis acid additives for the reaction and we studied the role of the additive in the reaction. For the Lewis acid additives that were found to be effective, we optimized the reaction conditions and investigated the scope of the reaction. We also studied the allylation reactions involving cinnamyl halides, where some interesting regio- and diastereo-selectivities were observed. Furthermore, we performed some NMR studies on the reaction intermediates, from which we obtained some novel insights into the reaction mechanism.

2. $SnCl_2/MCl_n$-mediated carbonyl allylation

In the previous studies Cu, $CuCl_2$, Cu_2O, and $TiCl_3$ additives were found to be able to catalyze the $SnCl_2$-mediated carbonyl allylation reactions in water.[15–19] Herein, we examined a variety of water-soluble metal chlorides as the additive for the aqueous $SnCl_2$-mediated allylation reaction (Scheme 1). It is worth mentioning that we did not examine the water-insoluble Lewis acids, because the water-insoluble Lewis acids (usually solids) might cause serious operational trouble for large scale reactions.



Scheme 1.

Our results (Table 1) show that $TiCl_3$, $CuCl_2$, and $PdCl_2$ can effectively catalyze the $SnCl_2$-mediated allylation reaction (yields >95%). $LaCl_3$, $CrCl_3$, $MnCl_2$, $FeCl_2$, $CoCl_2$, and $NiCl_2$ show some but fairly low catalytic effects (yields= 6–40%). Other Lewis acids, for example, $MgCl_2$, $ZnCl_2$, $CdCl_2$, $InCl_3$, $PbCl_2$, and $BiCl_3$ exhibit almost no effects as very little product can be detected.

Interestingly, the trend of the catalytic activities of different Lewis acids in our allylation reaction is not fully consistent with that observed by Kobayashi et al. in their aqueous aldol reactions.[20] In their cases, Ln(III), Fe(II), Cu(II), Zn(II), Cd(II), and Pb(II) were found to afford the desired aldol adduct in high yields in aqueous solvents, whereas Pd(II) was found to be much less active. In our aqueous allylation reaction, however, $PdCl_2$ is found to be the most effective. Moreover, we found that Ti(III) could be used as an interesting water-compatible Lewis acid. This application of Ti(III) has received very little attention before.

Table 1. Carbonyl allylation between benzaldehyde and allyl bromide mediated by $SnCl_2/MCl_n$[a]

Entry	MCl_n[a]	Yield (%)[b]
1	$MgCl_2$	Trace
2	$LaCl_3$	6
3	$TiCl_3$	99
4	$CrCl_3$	22
5	$MnCl_2$	27
6	$FeCl_2$	32
7	$CoCl_2$	40
8	$NiCl_2$	27
9	$PdCl_2$	99
10	$CuCl_2$	95
11	$ZnCl_2$	Trace
12	$CdCl_2$	Trace
13	$InCl_3$	Trace
14	$PbCl_2$	Trace
15	$BiCl_3$	Trace

[a] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of allyl bromide, 10 mmol of $SnCl_2$, 5 mmol of MCl_n (for $PdCl_2$ this amount is reduced to 0.5 mmol), 25 mL of water.
[b] Yields were calculated using ^1H NMR (300 MHz) after the reaction was stirred for 24 h.

Using the $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, and $SnCl_2/PdCl_2$ methods we examined the scope of the aqueous allylation reactions (Table 2). It is found that both aliphatic and aromatic aldehydes can be efficiently allylated using any one of these three methods. Using allyl bromide as the allylation reagent the reaction yields are mostly over 90%. The yields are slightly lower (>80%) when allyl chloride is used in the reaction.

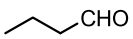
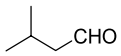
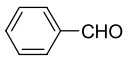
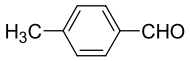
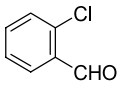
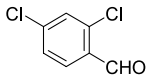
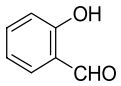
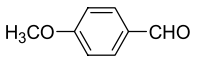
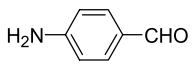
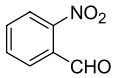
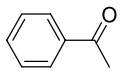
It is worth noting that 2-nitrobenzyldehyde (entry 10 in Table 2) cannot be effectively allylated using $SnCl_2/TiCl_3$, because the NO_2 group is considerably reduced in the reaction. Similar NO_2 reduction problem was noted before in many zero-valent metal mediated carbonyl allylation reactions.[5–14] Nevertheless, $SnCl_2/CuCl_2$ and $SnCl_2/PdCl_2$ do not have this problem as their allylation yields for 2-nitrobenzaldehyde are about 80–90%.

In comparison with aldehydes, neither aliphatic nor aromatic ketones can be efficiently allylated using any one of the three methods (entries 11 and 12 in Table 2). In particular, when the $SnCl_2/PdCl_2$ method is employed and allyl chloride is used as the allylation reagent, only trace amount of allylation product can be detected for both the aliphatic and aromatic ketones. Therefore, one can use the $SnCl_2/PdCl_2$ method to selectively allylate aldehyde groups in the presence of ketone groups.

3. $SnCl_2$-mediated carbonyl allylation

Yuan et al. reported very recently that $SnCl_2$ can mediate aqueous carbonyl allylation reactions under ultrasonic condition without using any other additive.[19] This report immediately called upon our attention as we were interested in the role of the additive in the allylation reaction. Thus we carefully studied the aqueous allylation reactions using $SnCl_2$ alone.

Table 2. Carbonyl allylation mediated by $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, $SnCl_2/PdCl_2$, and $SnCl_2$

Entry	Substrates	X[a]	Yield (%)[b]			
			$SnCl_2/CuCl_2$[c]	$SnCl_2/TiCl_3$[c]	$SnCl_2/PdCl_2$[c]	$SnCl_2$ only[d]
1		Br	92	95	92[b]	85
		Cl	85	88	90	21
2		Br	95	98	99	95
		Cl	90	94	99	25
3		Br	96	99	99	99
		Cl	98	99	99	51
4		Br	93	99	99	99
		Cl	90	91	99	36
5		Br	91	99	99	75
		Cl	87	99	99	25
6		Br	96	99	99	87
		Cl	88	93	99	22
7		Br	94	90	99	92
		Cl	83	85	90	41
8		Br	92	93	94	87
		Cl	79	90	92	30
9		Br	90	96	80	65
		Cl	84	96	95	15
10		Br	88	51	88	49
		Cl	79	Trace	80	Trace
11		Br	43	25	Trace	Trace
		Cl	41	17	Trace	Trace
12		Br	23	9	17	Trace
		Cl	11	Trace	Trace	Trace

[a] X indicates whether the allylation reagent is allyl bromide (X=Br) or allyl chloride (X=Cl).
[b] All the reactions were run for 24 h at room temperature.
[c] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of allyl bromide, 10 mmol of $SnCl_2$, 5 mmol of MCl_n (for $PdCl_2$ this amount is reduced to 0.5 mmol), 25 mL of water.
[d] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of allyl bromide, 10 mmol of $SnCl_2$, 2–5 mL of water.

We found that $SnCl_2$ indeed could mediate the carbonyl allylation reactions in water without using any additive (Table 2). However, only allyl bromide can be used in these reactions as allyl chloride provides very poor yields. Moreover, we observed a very interesting water effect on $SnCl_2$-mediated allylation reactions (Fig. 1).

As shown in Figure 1, the yield of the aqueous $SnCl_2$-mediated carbonyl allylation reaction is highly sensitive to the amount of water used in the reaction. When less than 30 equiv. of water (compared to $SnCl_2$) is used in the reaction, the allylation yield is over 98%. When 55 equiv. of water is used, the yield drops to 75%. When over 100 equiv. of water is used, the yield is lower than 10%. Therefore, the key for the $SnCl_2$-mediated allylation reaction without any additive is to use very little amount of water. That is, for 1 g of $SnCl_2$ one can only add less than 3 g of water as solvent. Indeed, in Yuan's work only 10 mL of water was used as solvent for a reaction involving 3.8 g of $SnCl_2$ (20 mmol).[19]

Interestingly, the dramatic water effect on the $SnCl_2$-mediated allylation reaction is not exhibited by the $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, or $SnCl_2/PdCl_2$-mediated reactions (Fig. 1). For these three reactions, increasing the amount of water from 30 equiv. to over 200 equiv. only reduces the allylation yield from 99% to about 94%. Therefore, $CuCl_2$, $TiCl_3$, and $PdCl_2$ truly have some positive effects on the $SnCl_2$-mediated allylation reactions. The positive effects of $CuCl_2$, $TiCl_3$, and $PdCl_2$ are also revealed by the fact that allyl chloride can be successfully used in these allylation reactions.

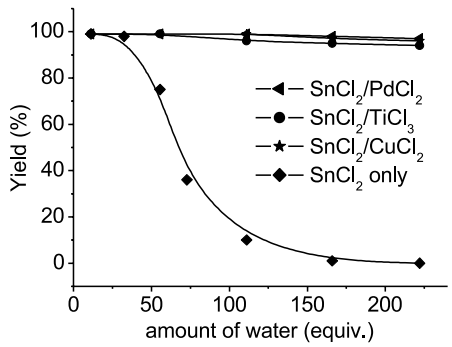
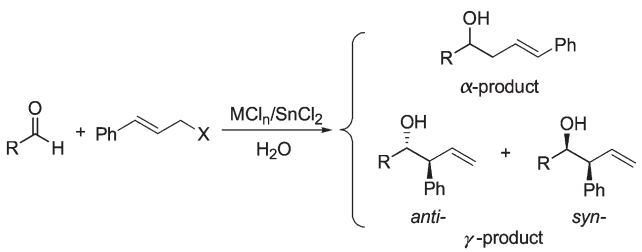


Figure 1. Yields of benzaldehyde allylation mediated by $SnCl_2$ and $MCl_x/SnCl_2$ in different amount of water.

It is possible that $SnCl_2$ serves as the Lewis acid catalyst in the allylation reaction mediated by $SnCl_2$ alone. However, the fact that only a strictly limited amount of water can be used indicates that $SnCl_2$ is not as effective as $CuCl_2$, $TiCl_3$, or $PdCl_2$. Furthermore, there is one serious operational problem associated with the $SnCl_2$-mediated allylation reaction without using any additive. That is, so little amount of water can be used in the process that the reaction mixture may become too dense to deal with. In comparison, the $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, and $SnCl_2/PdCl_2$ reactions are much easier to stir.

4. Regio- and diastereo-selectivity

In order to investigate the regio- and diastereo-selectivities of the allylation reactions, we used cinnamyl and crotyl halides as the allylation reagent. The allylation reactions involving cinnamyl halides can provide both α-adduct and γ-adduct. The γ-adduct can be either *anti*- or *syn*-product (Scheme 2).



Scheme 2.

It is found that $SnCl_2$, by itself, cannot effectively mediate the allylation reaction in water when cinnamyl chloride is used as reactant. Thus $CuCl_2$, $TiCl_3$, or $PdCl_2$ catalyst has to be added to induce the reaction. The yields under these conditions are usually 80–90%. On the other hand, when cinnamyl bromide is used as reactant, $SnCl_2$ is capable of mediating the aqueous allylation reaction by itself, although in this case a strictly limited amount of water can be used in the reaction. The yields under this condition are around 70–80%. Adding $CuCl_2$, $TiCl_3$, or $PdCl_2$ catalyst increases the yields to 80–95%. It is worth noting that by utilizing $CuCl_2$, $TiCl_3$, or $PdCl_2$ as catalyst, we do not need to restrict the amount of water to be used.

Fairly good regioselectivities are observed for the $SnCl_2/CuCl_2$, $SnCl_2/TiCl_3$, or $SnCl_2/PdCl_2$-mediated allylation reactions, in which the γ-adduct is obtained as the favored isomer. For most cases, the ratio between the γ- and α-adduct is over 95:5. This type of regioselectivity has been well known in literature.

On the other hand, when $SnCl_2$ is used for the allylation reaction without any additive, we observed a significant amount of α-adduct so that the ratio between the γ- and α-adduct decreases to about 60:40. Similar observations about the α-adducts have been reported recently by Loh et al.[21] They proposed that the metal salts formed from the metal-mediated allylation can catalyze the γ-adduct to undergo a bond cleavage to generate the parent aldehyde in situ followed by a concerted rearrangement, perhaps a retroene reaction followed by a 2-oxonia[3,3]-sigmatropic rearrangement to furnish the α-adduct.

Loh et al. found that the α-adduct became important only when very little amount of water was used as solvent.[21] This indicates that the proposed rearrangement may only occur in a highly concentrated solution of metal salts. In our $SnCl_2$-mediated allylation without any additive, we had to use very little water as solvent. Thus the α-adduct observed in the present work may also be explained by Loh's mechanism (Table 3).

The diastereoselectivity of the allylation reaction (i.e., *anti*- vs. *syn*-product) can be studied using both proton NMR and GC–MS techniques.[22] It is found in the present study that the $SnCl_2$-mediated allylation reaction always exhibits the *anti*-selectivity with or without $CuCl_2$, $TiCl_3$, or $PdCl_2$ catalyst for both cinnamyl halides and crotyl bromide (Table 4). The same *anti*-selectivity was also observed before by Masuyama et al.[22] and Roy et al.[17]

5. Mechanism

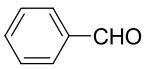
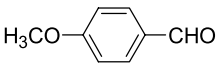
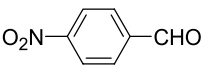
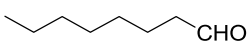
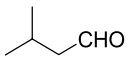
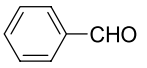
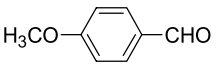
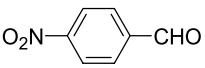
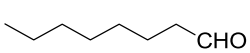
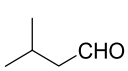
A possible (and crude) mechanism for the $SnCl_2$-mediated allylation reaction is shown in Scheme 3. What remains unclear is the role of $CuCl_2$, $TiCl_3$, or $PdCl_2$ in the reaction. Do they catalyze the first step (umpolung of the allyl species) or the second step (allylation)?

A number of proton NMR experiments were conducted to investigate the first step of the allylation reaction. In the first series of experiments, we mixed $SnCl_2$ (2 mmol) and allyl bromide (1.5 mmol) in 3 mL of D_2O. After the reaction was run for 6 h, we observed a new peak in ^1H NMR corresponding to an allyltin species (δ=2.5 ppm, doublet, J ($^{119}Sn-H$)=155 Hz.) (Fig. 2A). Comparing this new peak with the peak for allyl bromide (δ=4.1 ppm), we determined that the yield of the allyltin species was 57%.

Then we added $PdCl_2$ (0.1 mmol) into the above mixture, and continued the reaction for 18 h. The NMR spectrum of the new mixture (Fig. 2B) is almost identical to that shown in A. This experiment demonstrates that the allyltin species can form without the help of $PdCl_2$. Addition of $PdCl_2$ does not change the nature and yield of the allyltin species, either.

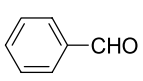
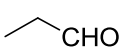
Since the allylation reaction mediated by $SnCl_2$ without any

Table 3. The reactions of cinnamyl halides and aldehydes mediated by $SnCl_2$, $CuCl_2/SnCl_2$, $TiCl_3/SnCl_2$ and $PdCl_2/SnCl_2$

Entry	Condition	Substrates	X[a]	Yield (%)	γ:α[b]	*anti*:*syn*[b]
1	$SnCl_2/CuCl_2$[c]		Cl	88	99:1	90:10
2	$SnCl_2/TiCl_3$[c]			89	98:2	83:17
3	$SnCl_2/PdCl_2$[c]			85	98:2	85:15
4	$SnCl_2/CuCl_2$		Cl	80	94:6	67:33
5	$SnCl_2/TiCl_3$			83	95:5	90:10
6	$SnCl_2/PdCl_2$			91	89:11	75:25
7	$SnCl_2/CuCl_2$		Cl	75	99:1	83:17
8[d]	$SnCl_2/TiCl_3$			—	—	—
9	$SnCl_2/PdCl_2$			93	93:7	89:11
10	$SnCl_2/CuCl_2$		Cl	90	99:1	88:12
11	$SnCl_2/TiCl_3$			94	88:12	75:25
12	$SnCl_2/PdCl_2$			94	97:3	90:10
13	$SnCl_2/CuCl_2$		Cl	81	93:7	75:25
14	$SnCl_2/TiCl_3$			89	95:5	80:20
15	$SnCl_2/PdCl_2$			88	98:2	62:38
16	$SnCl_2$ only[d]		Br	87	85:15	91:9
17	$SnCl_2/CuCl_2$			86	99:1	89:11
18	$SnCl_2/TiCl_3$			93	90:10	87:13
19	$SnCl_2/PdCl_2$			80	99:1	83:17
20	$SnCl_2$ only		Br	71	58:42	62:38
21	$SnCl_2/CuCl_2$			84	98:2	84:16
22	$SnCl_2/TiCl_3$			87	96:4	83:17
23	$SnCl_2/PdCl_2$			92	97:3	75:25
24	$SnCl_2$ only		Br	70	55:45	91:9
25	$SnCl_2/CuCl_2$			77	90:10	96:4
26	$SnCl_2/TiCl_3$			—	—	—
27	$SnCl_2/PdCl_2$			85	94:6	85:15
28	$SnCl_2$ only		Br	81	56:44	85:15
29	$SnCl_2/CuCl_2$			92	87:13	77:23
30	$SnCl_2/TiCl_3$			95	96:4	82:18
31	$SnCl_2/PdCl_2$			92	99:1	86:14
32	$SnCl_2$ only		Br	79	75:25	68:32
33	$SnCl_2/CuCl_2$			87	95:5	78:22
34	$SnCl_2/TiCl_3$			84	96:4	77:23
35	$SnCl_2/PdCl_2$			82	94:6	81:19

[a] X indicates whether the allylation reagent is cinnamyl bromide (X=Br) or cinnamyl chloride (X=Cl). All the reactions were run for 24 h at room temperature.
[b] Determined using GC–MS and 300 MHz ^{1}H NMR.
[c] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of cinnamyl bromide, 10 mmol of $SnCl_2$, 10 mmol of MCl_n (for $PdCl_2$ this amount is reduced to 0.5 mmol), 25 mL of water.
[d] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of cinnamyl chloride or bromide, 10 mmol of $SnCl_2$, 2 mL of water.

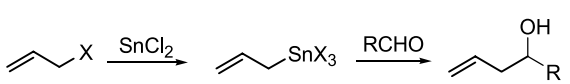
Table 4. The reactions of crotyl bromide and aldehydes mediated by $SnCl_2$, $CuCl_2/SnCl_2$, $TiCl_3/SnCl_2$ and $PdCl_2/SnCl_2$[a]

Entry	Condition	Substrates	X	Yield (%)	γ:α[b]	*anti*:*syn*[b]
1	$SnCl_2$ only[c]		Br	97	95:5	91:9
2	$SnCl_2/CuCl_2$[d]			98	99:1	94:6
3	$SnCl_2/TiCl_3$[d]			99	99:1	93:7
4	$SnCl_2/PdCl_2$[d]			99	99:1	96:4
5	$SnCl_2$ only		Br	68	78:22	62:38
6	$SnCl_2/CuCl_2$			81	82:18	66:34
7	$SnCl_2/TiCl_3$			82	80:20	71:29
8	$SnCl_2/PdCl_2$			88	84:16	69:31

[a] All the reactions were run for 24 h at room temperature.
[b] Determined using GC–MS and 300 MHz ^{1}H NMR.
[c] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of crotyl bromide, 10 mmol of $SnCl_2$, 10 mmol of MCl_n (for $PdCl_2$ this amount is reduced to 0.5 mmol), 25 mL of water.
[d] Reaction condition: 5 mmol of benzaldehyde, 10 mmol of crotyl bromide, 10 mmol of $SnCl_2$, 2 mL of water.

additive has a strong restriction on the amount of water that can be used, we also studied the water effect of the allyltin intermediate formation. We added 10 mmol of $SnCl_2$ and 7.5 mmol of allyl bromide in 3 mL of D_2O. The proton NMR of this reaction mixture (Fig. 2C) is very similar to that in Figure 2A or B. Therefore, the yield of the allyltin species is not dependent on the amount of water as the solvent.

The next question is whether or not the additive increases the rate of allyltin formation. Therefore, we monitored the appearance of the NMR peak at 2.5 ppm in the first 6 h of



Scheme 3.

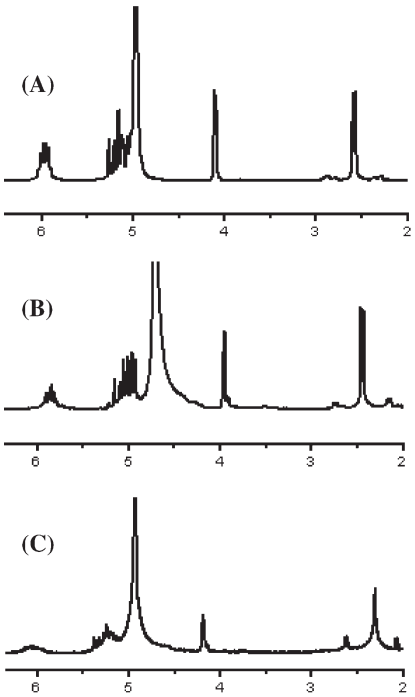


Figure 2. ^{1}H NMR spectra in D_2O (3 mL) for: (A) $SnCl_2$ (2 mmol)/allyl bromide (1.5 mmol), standing for 6 h; (B) the same mixture as in A with 0.1 mmol of $PdCl_2$ added after 6 h, standing for extra 18 h; (C) $SnCl_2$ (10 mmol)/allyl bromide (7.5 mmol), standing for 24 h.

the reaction (Fig. 3). It was found that $PdCl_2$ and $CuCl_2$ indeed could accelerate the formation of the allytin species. Nevertheless, the yield of the allyltin species is always ca. 60% with or without the additive. The maximum yield of the allyltin species can also be achieved in 6 h with or without the additive.

The above experiments show some effects of the additive on the formation of the allyltin intermediate. However, none of the above experimental findings can be used to explain the following observation. That is, without appropriate additive carbonyl allylation reaction does not occur even after 24 h (Table 1), although it is expected that the allyltin intermediate is adequately produced in 6 h.

Thus we have to propose that more important catalytic effects (presumably Lewis acid catalysis) should be exerted by the additives in the allylation step (Scheme 4). There are two possible structures for the transition state. The first is an acyclic one as proposed by Koreeda and Tanaka.[23] They reported that carbonyl allylation by (*E*)-cinnamyltributyltin or (*E*)-cinnamyltriphenyltin catalyzed by $BF_3{\cdot}Et_2O$ in CH_2Cl_2 also exhibited *anti*-diastereoselectivity.[23] The second one, which is more popular, involves a cyclic six-membered ring structure.[1]

Currently we are not certain about which transition state structure is correct. More detailed experiments need to designed and conducted. Meanwhile theoretical studies are required to compare the energies of all the possible transition states. These studies are undergoing at the moment in our lab and we will report the results in due course.

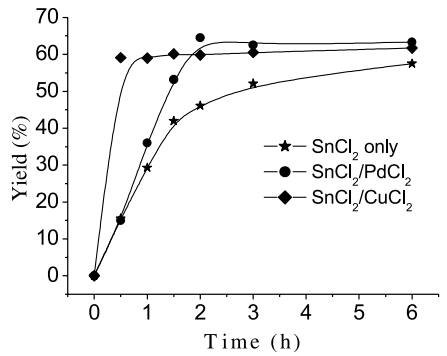
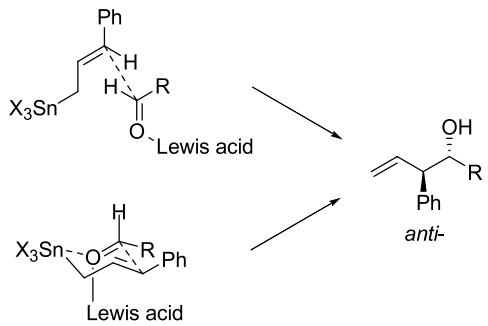


Figure 3. Yields of the allyltin species with or without additive in the first 6 h of the reaction. Conditions: $SnCl_2$ (2 mmol), allyl bromide (1.5 mmol), D_2O (3 mL), $CuCl_2$ (when applicable, 1 mmol), $PdCl_2$ (when applicable, 0.1 mmol).



Scheme 4.

6. Conclusion

In the present paper we reported our systematic studies on $SnCl_2$-mediated carbonyl allylation reaction between aldehydes and allyl halides in fully aqueous media. Totally three valuable reaction systems were found, which were $SnCl_2$/$CuCl_2$, $SnCl_2$/$TiCl_3$, and $SnCl_2$/$PdCl_2$. They all provided good to excellent yields in the allylation of aliphatic and aromatic aldehydes under very mild and convenient conditions. $SnCl_2$, by itself, was also found to be effective for the allylation reaction when allyl bromide was employed. However, the $SnCl_2$-only reaction could only tolerate very small amount of water as the solvent.

The reactions exhibited good regioselectivity favoring the γ-adduct when cinnamyl halides were employed as the allylation reagent. The same reactions with cinnamyl halides also showed good diastereoselectivity favoring the *anti*-product. Mechanistic studies using NMR techniques suggested that the additive (i.e., $CuCl_2$, $TiCl_3$, $PdCl_2$) could accelerate the formation of allyltin intermediate, but this step was shown not to be the most important. Thus we proposed that the Lewis acid catalysis effect exerted by the additive was the main reason for the observed reactivity enhancement.

7. Experimental

All the reactions were carried out in air. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300 or 400 MHz)

instrument using TMS as internal standard and $CDCl_3$ or D_2O as solvent. IR spectra were recorded on an FT/IR/410 JASCO instrument. GC–MS was recorded on a TRACE GC–MS instrument.

The yields reported in Tables 1 and 3 were determined using the ^1H NMR method. We obtained the ^1H NMR spectrum of the crude product from extraction. We integrated the peaks for the aldehyde C–H proton ($\delta\approx10$) of the starting material and for the allylic C–H proton ($\delta\approx4.8$) of the homoallylic alcohol product. Since the aldehyde and homoallylic alcohol in these cases are not volatile and they can be fully extracted into the organic layer, we consider this method to be accurate and convenient for yield determination.

The yields reported in Table 2 were determined as the isolation yields. The α:γ ratio in Table 3 were determined using ^1H NMR peak areas for the allylic C–H protons of the homoallylic alcohol products ($\delta\approx2.5$ for α and $\delta\approx3.4$ for γ). The *anti*:*syn* ratio in Table 3 were determined using the GC–MS method.

7.1. Typical procedure of $SnCl_2$ and $MCl_x/SnCl_2$-mediated carbonyl allylation

To a mixture of carbonyl compound (10 mmol) and allyl halide (15 mmol) in water, $SnCl_2$ (20 mmol) and certain catalyst were added (for the detailed amount of water and catalyst please see Tables 1–3). 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 washed by water (2×20 mL). Then the organic layer was dried over anhydrous $MgSO_4$ and was filtered and evaporated. The residue, for most cases, afforded the corresponding homoallylic alcohols of sufficient purity as judged by TLC and 300 MHz ^1H NMR without the need for further purification. If necessary, purification was performed by flash column chromatography (silica gel: 60–120 mesh; eluent: ethyl acetate–petroleum, 1/5 v/v). The products in Table 2 are known compounds. Some products in Table 3 are new compounds and listed below.

7.1.1. 1,2-Diphenyl-but-3-en-1-ol. IR (neat, cm^{-1}) 3422, 3078, 3029, 2930, 1643, 1600, 1496, 1450, 744, 699. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.35–7.05 (m, 10H), 6.25 (m, 1H), 5.30 (q, J=8.73 Hz, 2H), 4.85 (m, 1H), 3.55 (t, J=8.21 Hz, 1H), 2.30 (br, 1H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) δ 141.8, 140.6, 140.3, 137.9, 137.7, 128.8, 128.7, 128.4, 127.9, 127.7, 127.4, 127.1, 126.7, 126.6, 118.5, 117.2, 77.5, 77.2, 59.2, 58.5. HRMS (EI) *m*/*z* calcd for $C_{16}H_{16}O$ 224.1201. Found 224.1252. GC (column temp.=250 °C) t_R=8.51 (*anti*), 10.60 (*syn*).

7.1.2. 1-(4-Methoxy-phenyl)-2-phenyl-but-3-en-1-ol. IR (neat, cm^{-1}) 3441, 3029, 2906, 1635, 1611, 1585, 1513, 1453, 1248, 701, 676. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.26–7.00 (m, 7H), 6.73 (d, J=11.49 Hz, 2H), 6.25 (m, 1H), 5.26 (m, 2H), 4.80 (d, J=12.0 Hz, 1H), 3.74 (s, 3H), 3.52 (m, 1H), 2.25 (br, 1H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) 158.8, 140.4, 138.3, 137.9, 134.2, 134.1, 132.1, 128.9, 128.7, 128.0, 127.9, 127.2, 126.6, 126.5, 118.3, 117.3, 116.2, 115.2, 113.7, 113.5, 113.4, 75.5, 74.5, 59.4, 58.6, 55.4, 55.3. HRMS (EI) *m*/*z* calcd for $C_{17}H_{18}O_2$ 254.3280. Found 254.3252. GC (column temp.=250 °C) t_R=10.86 (*anti*), 11.06 (*syn*).

7.1.3. 1-(4-Nitro-phenyl)-2-phenyl-but-3-en-1-ol. IR (neat, cm^{-1}) 3422, 3080, 3028, 1637, 1601, 1518, 1493, 1452, 1346, 759, 700. ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.05 (d, J=7.90 Hz, 2H), 7.30–7.18 (m, 5H), 7.04 (d, J=7.40 Hz, 2H), 6.25 (m, 1H), 5.34 (m, 2H), 4.94 (d, J=7.76 Hz, 1H), 3.50 (t, J=8.54 Hz, 1H), 1.60 (br, 1H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) (*anti*) 149.4, 139.7, 137.0, 128.8, 128.3, 127.6, 127.3, 123.2, 119.5, 76.5, 59.5. HRMS (EI) *m*/*z* calcd for $C_{16}H_{15}NO_3$ 269.2994. Found 269.2911. GC (column temp.=250 °C) t_R=13.12 (*anti*), 13.32 (*syn*).

7.1.4. 3-Phenyl-undec-1-en-4-ol: (*anti*). IR (neat, cm^{-1}) 3380, 3060, 1600. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.41–7.19 (m, 5H), 6.12 (m, 1H), 5.22 (q, J=7.0 Hz, 2H), 3.80 (m, 1H), 3.25 (t, J=8.13 Hz, 1H), 1.78(br, 1H), 1.48–1.21 (m, 12H), 0.88 (t, J=6.6 Hz 3H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) (*anti*) δ 142.0, 138.5, 128.5, 128.4, 126.6, 126.1, 117.2, 74.0, 57.1, 34.6, 31.7, 29.6, 29.5, 25.7, 22.6, 14.0. HRMS (EI) *m*/*z* calcd for $C_{17}H_{26}O$ 246.3918. Found 246.3930. GC (column temp.=250 °C) t_R=8.99 (*anti*), 9.09 (*syn*).

7.1.5. 6-Methyl-3-phenyl-hept-1-en-4-ol: (*anti*). IR (neat, cm^{-1}) 3421, 3078, 3025, 2985, 1640, 1600, 1495, 1450, 1000, 744, 699. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.41–7.19 (m, 5H), 6.05 (m, 1H), 5.18 (q, J=7.0 Hz, 2H), 3.87 (m, 1H), 3.20 (t, J=8.03 Hz, 1H), 1.80 (br, 1H), 1.32 (m, 2H), 1.11 (m, 1H), 0.87 (d, J=5.23 Hz, 6H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm) (*anti*) 141.9, 138.4, 128.8, 128.3, 126.7, 117.7, 72.1, 57.9, 43.9, 24.5, 23.8, 21.6. HRMS (EI) *m*/*z* calcd for $C_{14}H_{20}O$ 204.3114. Found 204.3158. GC (column temp.=250 °C) t_R=5.39 (*anti*), 5.54 (*syn*).

Acknowledgements

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