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Silver Oxide as a Novel Catalyst for Carbon–Carbon Bond-forming Reactions in Aqueous Media

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Silver oxide was found to be an excellent catalyst for allylation reactions of allyltributyltins with aldehydes in aqueous media. Despite the very low solubility of silver oxide in the media, the reactions proceeded smoothly, and the catalyst was recovered and reused. When α-methyl-substituted allyltributyltin was used as the nucleophile, the corresponding α-adducts were obtained exclusively in high yields with good *anti*-selectivity. A reaction mechanism including transmetalation from tin to silver is proposed.

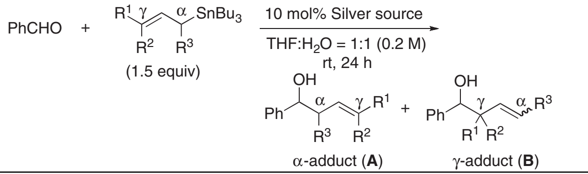
Organic reactions in water are now of great interest. Water is an inexpensive, safe, and environmentally benign solvent.[1] However, the use of water in organic synthesis is limited because most organic materials are hydrophobic, and thus are not soluble in water. In addition, many active catalysts are not stable in water; rather, they decompose even in the presence of a small amount of water. To address these issues, we have searched for efficient catalysts, that can work in aqueous media.[2]

In the course of our investigations, we found that silver oxide (Ag_2O)[3] was an excellent catalyst for the reaction of allyltins with aldehydes in aqueous media. For example, allyltributyltin (**1**) reacted with benzaldehyde in the presence of 10 mol % of Ag_2O in THF/H_2O (1/1) at room temperature to afford the corresponding homoallylic alcohol in 87% yield (Table 1, Entry 1). While silver carbonate (Ag_2CO_3)[4] also showed a high yield (86%, Entry 2), AgOAc and AgF were less effective (38 and 48% yields, respectively using 20 mol % of the catalyst), and only trace amounts of the product were obtained using AgCl and AgOTf. It should be noted that more acidic silver salts gave lower yields.[5] Moreover, the use of water was found to be essential for the silver catalysis, because the allylation reaction proceeded sluggishly in absolute THF.

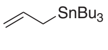
We next examined the reactions with α-methyl-substituted allyltributyltin **2**.[6] Very interestingly, the reaction of **2** with benzaldehyde proceeded faster than that of **1**, and the corresponding α-adduct[7–10] was obtained exclusively in high yields using Ag_2O and Ag_2CO_3 (Table 1, Entries 3 and 4). As for the relative stereochemistry, the *anti*-adduct was obtained preferentially.[11] We further tested the reactions of (*Z*)- and (*E*)-crotyltributyltin (**3*Z*** and **3*E***) with benzaldehyde. In these cases, although Ag_2O gave the γ-adducts (**B**) selectively, the reactions proceeded sluggishly in the presence of Ag_2CO_3.

We were very interested in the unique catalytic activities of the silver salts and the selectivities of the allylations in aqueous media, and further examined the reaction course carefully. The profiles of the reactions of **1**, **2**, and **3*Z*** with benzaldehyde and isomerization of **2** to **3** in the presence of Ag_2O are shown in Figure 1. In the allylations of **1** and **2**, the reactions completed within 1 h in the presence of 3 mol % of Ag_2O. On the other hand, when we used (*Z*)-crotyltributyltin (**3*Z***) as the nucleophile, less than 10% yield of the product was obtained in 1 h. It is known that α-methyl-substituted allyltributyltin **2** is gradually isomerized to the corresponding crotyltributyltin **3**.[6] We carefully examined the isomerization rate from **2** to **3**, which was found to be much slower than the rate of the allylation reaction **2** with benzaldehyde. It was concluded that the allylation reaction

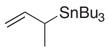
Table 1. Allylation reactions of benzaldehyde with allyltins in the presence of a catalytic amount of silver source in aqueous media



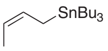
Entry	Allyltin	Silver source	Yield /%	A/B	*syn*/*anti*
1	**1**	Ag_2O	87	—	—
2	**1**	Ag_2CO_3	86	—	—
3	**2**	Ag_2O	84	>99/1	18/82 (**A**)
4	**2**	Ag_2CO_3	73	>99/1	18/82 (**A**)
5	**3*Z***	Ag_2O	86	14/86[a]	18/82 (**B**)
6	**3*Z***	Ag_2CO_3	<5	48/52	—
7	**3*E***	Ag_2O	20	16/84[b]	17/83 (**B**)
8	**3*E***	Ag_2CO_3	6	76/24	16/84 (**B**)



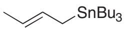
1



2



3*Z* (*E*/*Z* = 1/99)



3*E* (*E*/*Z* = 95/5)

[a] *E*/*Z* ratio of α-adduct(**A**) = 10/1. [b] *E*/*Z* ratio of α-adduct (**A**) = 6/1.

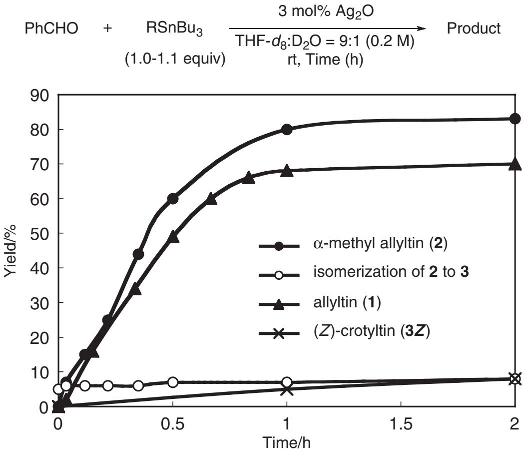
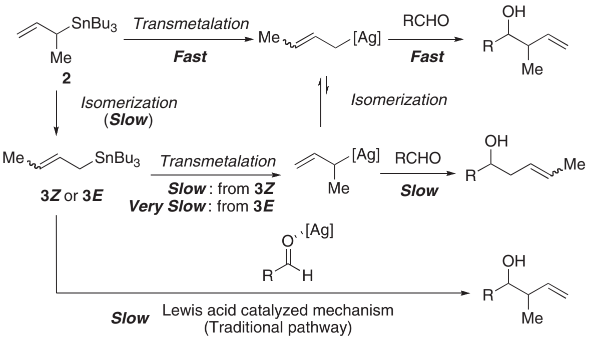


Figure 1. Reaction profiles of **1**, **2**, and **3*Z*** with benzaldehyde and isomerization of **2** to **3**.



Scheme 1. Assumed reaction pathway.

of **2** with benzaldehyde did not proceed via the corresponding isomerized crotyltin **3**.

Based on these experiments, we assume the overall reaction pathway as shown in Scheme 1. It is likely that the key step is transmetalation from **2** to a crotylsilver species, which rapidly reacts with an aldehyde to afford the formal α-addition product. Thus, two γ-additions could result in providing the α-addition product. It is noted that the transmetalation of **2** seems to be much faster than the isomerization from **2** to **3*Z*** or **3*E***. In contrast, transmetalation of crotyltin **3*Z*** or **3*E*** is supposed to be slow, probably because of steric hindrance at the γ-position of **3*Z*** or **3*E***. In addition, conventional addition of **3*Z*** or **3*E*** to an aldehyde in the presence of a silver salt also seems to be slow because of the low Lewis acidity of the silver salt.

We then surveyed the substrate scope of this allylation (Table 2). Not only aromatic aldehydes (Entries 1–5), α,β-unsaturated aldehyde (Entry 6), but also aliphatic aldehyde (Entry 7) reacted smoothly in the presence of a catalytic amount of silver oxide to afford the desired compounds in good to excellent yields. It is noted that in all cases only α-adducts were obtained in high yields when α-methyl-substituted allyltributyltin **2** was used (Entries 8–14). In addition, it was found that the reactions of **2** with aldehydes proceeded faster than those of **1**, and the corresponding α-adducts were obtained exclusively with good *anti*-selectivity.

In conclusion, we have found that allylation reactions of allyltins with aldehydes proceed smoothly in the presence of a catalytic amount of silver oxide in aqueous media. The use of silver oxide as a catalyst in organic synthesis is rare, and particularly interesting is the use of aqueous media for the reactions. In addition, it is unique that the α-addition adducts were obtained exclusively in high yields with good *anti*-selectivity when α-methyl-substituted allyltributyltin was used as the nucleophile. Further investigations to clarify the detailed mechanism of this reaction, including the role of water, are now in progress.

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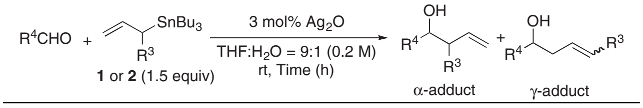
Table 2. Substrate scope of aldehydes with allyltins in aqueous media



Entry	R^4	R^3	Time /h	Yield /%	α/γ	*syn/anti* (α)
1	1-Naphthyl	H	5	79	—	—
2	2-Furyl	H	24	87	—	—
3	4-Pyridyl	H	24	quant[g]	—	—
4	Ph	H	5	74	—	—
5	$(4\text{-Br})C_6H_4$	H	24	76	—	—
6	PhCH=CH	H	5	76	—	—
7[a]	$PhCH_2CH_2$	H	12	67	—	—
8[b]	1-Naphthyl	Me	4	99	>99/1	13/87
9[b,c]	2-Furyl	Me	4	78	>99/1	14/86
10[b]	4-Pyridyl	Me	4	89	>99/1	14/86
11[b]	Ph	Me	3	84	>99/1	10/90
12[d,e]	$(4\text{-MeO})C_6H_4$	Me	4	62	>99/1	11/89
13[f]	$(4\text{-Br})C_6H_4$	Me	4	96	>99/1	13/87
14[c]	$PhCH_2CH_2$	Me	4	66	>99/1	14/86

[a] 3.0 equiv allyltin **1** was used. [b] $MeOH{:}H_2O = 9{:}1$ was used as solvent. [c] 5 mol % Ag_2CO_3 was used instead of Ag_2O. [d] *i*-$PrOH{:}H_2O = 9{:}1$ was used as solvent. [e] 7 mol % 1,10-phenanthroline was added. [f] $MeCN{:}H_2O = 9{:}1$ was used as solvent. [g] 84% yield in 5 h.

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