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Allylation reactions of carbonyl compounds using an organosilicon reagent in aqueous media

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Allylation reactions of carbonyl compounds such as aldehydes and reactive ketones using allyltrimethoxysilane in aqueous media proceeded smoothly in the presence of 5 mol% of a CdF_2–terpyridine complex; the presence of the ligand plays an important role for the catalytic activity; the catalyst was easily recovered and reused without loss of activity.

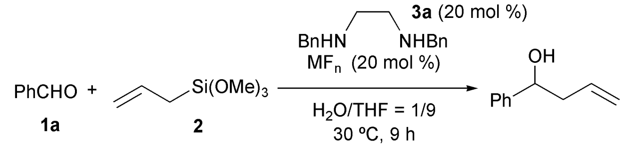
Allylation reactions of carbonyl compounds, which afford synthetically useful homoallylic alcohols, have been a subject of extensive investigations.[1] Recently, development of allylation reactions in aqueous media has attracted great attention, because dehydrative drying of the substrates and solvents is not required, and unique reactivity and selectivity are often observed.[2] In the allylations in aqueous media, highly reactive allyltins have been often used in many cases.[3] On the other hand, allylsilanes are generally preferable reagents compared to allyltins due to their low toxicity and simple removal of silicon by-products. However, as far as we know, there is no report on allylation reactions of simple carbonyl compounds in aqueous media using allylsilanes,[4] because allylsilanes are generally less reactive than allyltins. To solve this problem, we decided to develop ligand-accelerated catalysts. Quite recently, we have reported that some ligands accelerate metal-catalyzed allylation reactions using allyltributyltin in aqueous media to realize high reactivity and even enantioselectivity.[5] Herein, we report allylation reactions using allyltrimethoxysilane in aqueous media. This is the first example of allylation reaction of simple carbonyl compounds using an organosilicon reagent in aqueous media. In this reaction system, remarkable acceleration by ligands is observed, and allylation of aldehydes and reactive ketones proceeds smoothly.

At first, we selected allyltrimethoxysilane as an allylating agent[6] because it would be activated by the fluoride anion more easily than allyltrimethysilane. In fact, two groups reported allylation reactions using a combination of the fluoride anion and allyltrimethoxysilane in organic solvents.[7] We aimed at ligand-acceleration and chose *N*,*N*′-dibenzylethylenediamine (**3a**) as a representative ligand, and various metal fluorides were screened under mild conditions (H_2O/THF = 1 : 9, 30 °C) (Table 1). As a result, the metal fluorides of soft metal cations such as CdF_2, CuF_2, CuF, and AgF gave the allylated product in moderate yields. Among these metal fluorides, CdF_2 gave the best yield. Other metal fluorides (MgF_2, SrF_2, ScF_3, LaF_3, TiF_4, ZrF_4, HfF_4, FeF_3, and NiF_2) and other cadmium salts ($CdCl_2$, $Cd(ClO_4)_2$) did not work at all. These results suggest that both the cadmium cation and the fluoride anion are crucial for the catalysis.

Next, we examined the effect of ligands in the allylation reaction catalyzed by 5 mol% of CdF_2 (Table 2). The reaction was found to be remarkably accelerated by **3a**; the reaction without **3a** gave only 5% yield (entry 1). We tested the ligands which worked effectively in the case of allyltributyltin (entries 2–4).[5] Among them, 2,9-dimethyl-1,10-phenanthroline (**3c**) gave higher yield compared with **3a** or *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (**3b**). Interestingly, 1,10-phenanthroline (**3d**) and 6,6′-dimethyl-2,2′-bipyridine (**3e**) were not effective (entries 5, 6). After further investigations, 2,2′:6′,2″-terpyridine (**3f**) was found to be the best ligand (entry 7). We then examined the effect of water. The reaction catalyzed by CdF_2–**3f** in anhydrous THF gave only a trace amount of the product. This result shows that water is essential for this catalytic system.

With the optimized reaction conditions, this catalyst was applied to allylation of various aldehydes and ketones (Table 3).† In most aldehydes, their allylated adducts were obtained in

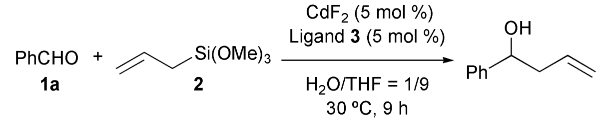
Table 1 Metal fluorides-catalyzed allylation reactions using allyltrimethoxysilane in the presence of **3a**[a]

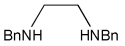
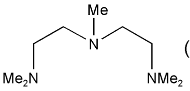
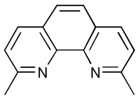
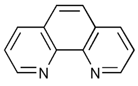
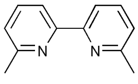
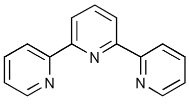


Entry	MF$_n$	Yield (%)	Entry	MF$_n$	Yield (%)
1	BiF_3	5	5	CdF_2	51
2	SnF_2	10	6[b]	CuF	23
3	InF_3	7	7	CuF_2	48
4	ZnF_2	trace	8	AgF	44

[a] All reactions were carried out with aldehyde **1** (1 equiv.) and allyltrimethoxysilane **2** (1.5 equiv.). [b] CuF was prepared by mixing CuCl and TBAF in THF at rt, for 30 min.

Table 2 Allylation reactions catalyzed by CdF_2–ligand **3** using allyltrimethoxysilane[a]



Entry	Ligand **3**	Yield (%)
1	—	5
2	 BnNH HNBn (**3a**)	36
3	 Me N Me$_2$N NMe$_2$ (**3b**)	42
4	 (**3c**)	82
5	 (**3d**)	16
6	 (**3e**)	2
7	 (**3f**)	93

[a] All reactions were carried out with aldehyde **1** (1 equiv.) and allyltrimethoxysilane **2** (1.5 equiv.).

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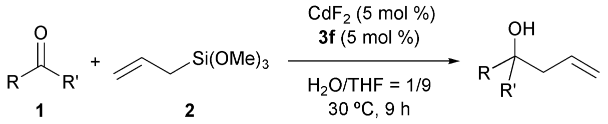
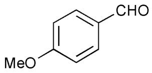
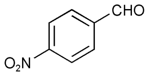
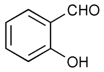
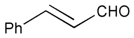
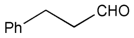
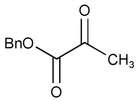
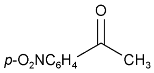
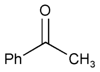
Table 3 Allylation reactions catalyzed by CdF_2–**3f** using allyltrimethoxysilane[a]

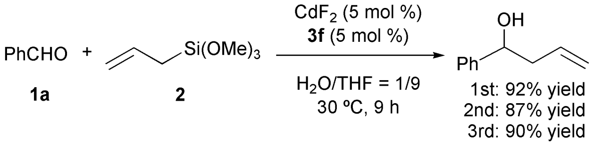


Entry	**1**	Yield (%)
1	 (**1b**)	81
2	 (**1c**)	99
3	 (**1d**)	99
4	 (**1e**)	96
5	 (**1f**)	82
6	 (**1g**)	72
7[b]	 (**1h**)	86
8[b]	 (**1i**)	32

[a] The reactions were carried out with aldehyde **1** (1 equiv.) and allyltrimethoxysilane **2** (1.5 equiv.). [b] Allyltrimethoxysilane **2** (3 equiv.) was used and reaction time was 24 h.

high yields (entries 1–5), and reactive ketones such as benzyl pyruvate and 4′-nitroacetophenone also gave the allylated products in high yields (entries 6, 7). On the other hand, unreactive ketones such as acetophenone afforded the product in lower yield (entry 8).

Considering the toxicity of cadmium compounds, it is desirable to recover and reuse the cadmium catalyst. In the present catalytic system using CdF_2 and **3f**, the recovery and reuse of the cadmium complex was performed by extraction with water (4 times) after diluting the reaction mixture with ether. ICP-MS determination of the cadmium amount in the organic phase showed that more than 99.99% cadmium was extracted with water. After concentrating the aqueous phase, the catalyst was recovered and reused without loss of catalytic activity (Scheme 1).



Scheme 1 Reuse of the catalyst

In conclusion, we have developed allylation reactions catalyzed by CdF_2–terpyridine using allyltrimethoxysilane in aqueous media. This unique ligand-accelerated catalytic system gave the corresponding products of various aldehydes and reactive ketones in high yields. Although the mechanism of the cadmium-catalyzed allylation including the ligand acceleration has not been clarified yet, to the best of our knowledge, this is the first example of an allylation reaction using an allyltrimethoxysilane in aqueous media. It is noteworthy that toxic tin reagents are not needed for the synthesis and that the catalyst was easily recovered and reused without loss of activity. Further investigations on diastereo- and enantioselective allylation reactions of allyltrimethoxysilane in aqueous media using this catalyst and elucidation of the mechanism of the ligand-accelerated allylation are currently in progress in our laboratory.

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Notes and references

† A typical experimental procedure is described for the reaction of benzaldehyde with allyltrimethoxysilane using the CdF_2–**3f** catalyst. To a clear solution of CdF_2 (2.3 mg) and **3f** (3.5 mg) in H_2O (0.15 mL) was added THF (1.35 mL). To this suspension were added benzaldehyde (31.9 mg) and allyltrimethoxysilane (72.2 mg, 1.5 equiv.) successively. The mixture was stirred at 30 °C for 9 h and diluted with water (5 mL). The aqueous layer was extracted with CH_2Cl_2 three times, and the organic layer was washed with satd. NaCl and dried over Na_2SO_4. The solvents were evaporated after filtration. The residual crude product was purified by preparative TLC on silica gel to give the pure product as a colorless oil (42.4 mg, 93% yield).

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