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Gadolinium(III) chloride: a novel and an efficient reagent for the synthesis of homoallylic alcohols☆

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Abstract—Carbonyl compounds efficiently undergo nucleophilic addition reactions with allylstannanes in the presence of $GdCl_3 \cdot 6H_2O$ in acetonitrile under extremely mild reaction conditions to give the corresponding homoallylic alcohols in excellent yields and with high chemoselectivity.

In recent years the synthesis of homoallylic alcohols has been an intense research area.[1] Homoallylic alcohols are useful tools for the construction of complex molecules and can be easily converted into many important building blocks for natural products synthesis.[2] Lewis acid catalyzed C–C bond forming reactions have gained much importance in organic synthesis because of their mild reaction conditions and high selectivity.[3] Lewis acid promoted nucleophilic addition of allyltin reagents to carbonyl compounds is one of the straightforward methods for the synthesis of homoallylic alcohols.[4–6] Lewis acids such as $Et_2O \cdot BF_3$, $TiCl_4$, $SnCl_4$, etc. are extremely moisture sensitive, which causes inconvenience in handling and manipulating. Thus, there is an interest in development of a new catalyst which has advantages with respect to mild reaction conditions, cleaner reactions, shorter reaction times, high yields of products, lower catalytic loading and simple isolation procedures.[7] Consequently, several methods have been reported for the allylation of carbonyl compounds. Generally, strong Lewis acids[8–10] are required to promote the addition of allyltributylstannane to a carbonyl function. Recently, $GdCl_3 \cdot 6H_2O$ has become an attractive candidate as a powerful Lewis acid in C–C bond forming transformations,[11] which would extend the scope and generality of these allylation reactions.

In continuation of our studies aimed to develop new methodologies for organic transformations,[12,13] here we report $GdCl_3 \cdot 6H_2O$ as a mild and efficient catalyst for the allylation of carbonyl compounds with allyl stannanes under mild and neutral conditions.

We chose allyltributylstannane, which is inexpensive, readily available and does not require rigorously dry conditions or an inert atmosphere in comparison with most metal reagents, as our allyl reagent. We first examined the reaction of allyltributylstannane with benzaldehyde using 5 mol % of $GdCl_3 \cdot 6H_2O$ in acetonitrile by TLC monitoring and observed the total disappearance of starting material after 3 h. It was found that $GdCl_3 \cdot 6H_2O$ acts as an excellent promoter leading to the formation of 1-phenyl-3-buten-1-ol in excellent yield (95%) after extractive work-up and purification. This methodology was extended to a variety of aldehydes to determine the scope and reactivity of the procedure and the results are summarized in Table 1. The results suggest that $GdCl_3 \cdot 6H_2O$ is an efficient promoter for the allylation of aldehydes and can be extended to a broad range of aldehydes (Scheme 1). In all cases, the reaction proceeded efficiently at ambient temperature with high chemoselectivity. Enolizable aldehydes also produced the corresponding homoallylic alcohols in good yield. No bis-allylated products were obtained with 3,4,5-trimethoxybenzaldehyde, which are normally observed in allylation reactions using allyltrimethylsilane.[14] Acid sensitive aldehydes such as furfural and cinnamaldehydes also smoothly reacted to afford the corresponding homoallylic alcohols in excellent yields. Encouraged by these results we extended our method to ketones and

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Keywords: Gadolinium chloride; Allylstannanes; Allylation; Carbonyl compounds; Homoallylic alcohols.

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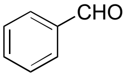
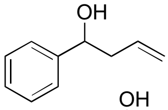
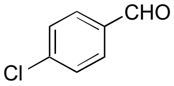
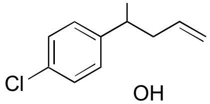
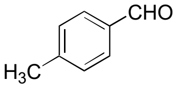
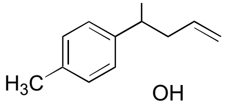
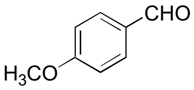
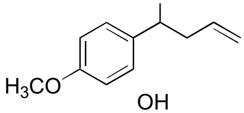
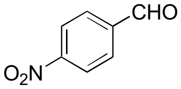
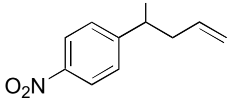
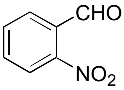
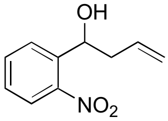
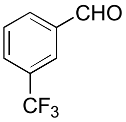
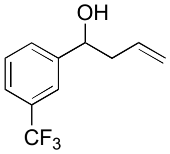
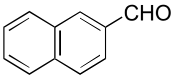
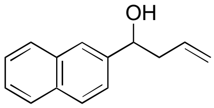
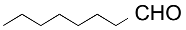
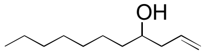
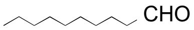
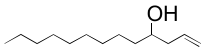
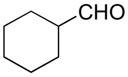
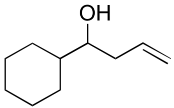
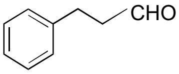
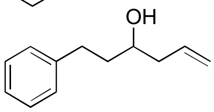
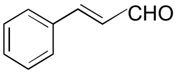
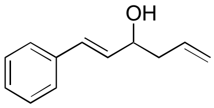
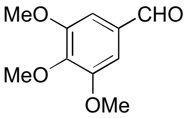
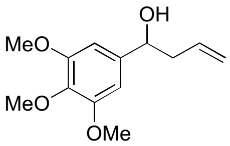
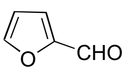
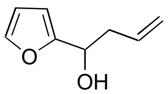
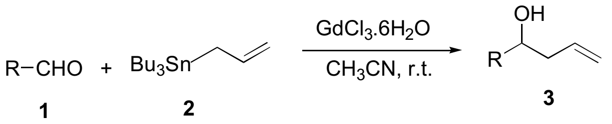
Table 1. Synthesis of homoallylic alcohols from aldehydes

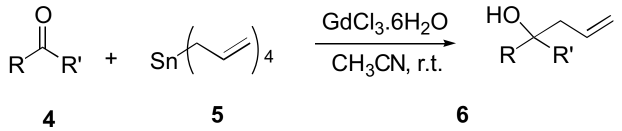
Entry	Aldehyde	Homoallylic alcohol[a]	Time (h)	Yield[b] (%)
a			3.0	95
b			3.0	95
c			2.5	92
d			3.0	94
e			3.0	89
f			3.5	87
g			3.5	87
h			3.0	94
i			2.5	90
j			2.5	92
k			3.0	86
l			3.0	88
m			3.0	92
n			3.5	90
o			3.0	93

[a] All the products were characterized by ^{1}H NMR, IR and mass spectrometry.

[b] Isolated yields.



Scheme 1.



Scheme 2.

carried out the reaction using acetophenone, cyclohexanone and a β-ketoester. None of the ketones gave homoallylic alcohols even after longer reaction times, thus providing a chemoselective allylation of aldehydes in the presence of a ketone. The most interesting result was observed for aryl aldehydes with electron withdrawing and releasing groups which underwent allylation at the same rate, suggesting that the reactivity of the

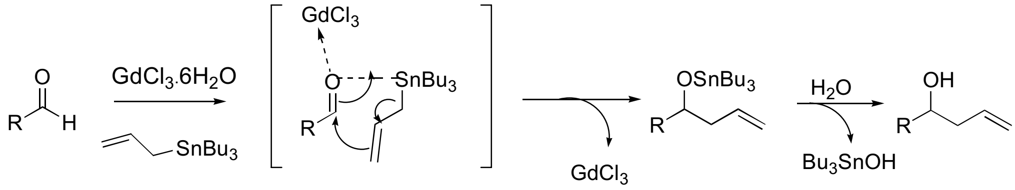
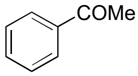
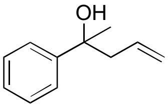
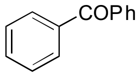
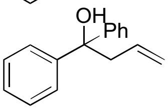
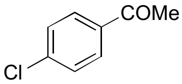
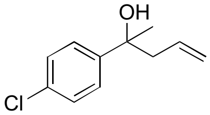
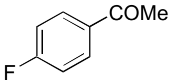
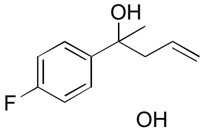
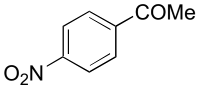
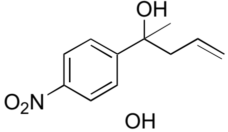
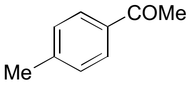
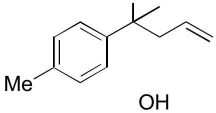
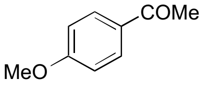
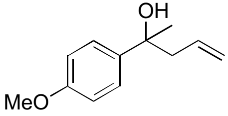
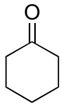
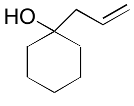
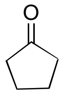
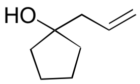


Figure 1.

Table 2. Synthesis of homoallylic alcohols from ketones

Entry	Ketone	Homoallylic alcohol[a]	Time (h)	Yield[b] (%)
a			3.0	94
b			3.0	88
c			3.5	86
d			3.0	90
e			3.0	85
f			3.0	88
g			3.5	90
i			2.5	86
j			2.5	88

The experimental procedure is included in Ref. 16.

[a] All the products were characterized by ^{1}H NMR, IR and mass spectrometry.

[b] Isolated yields.

aldehydes is independent of substituent effects and depends mainly on activation of the carbonyl moiety. The high coordinating ability of gadolinium(III) towards the oxygen of the carbonyl moiety may be responsible for the effective activation of the carbonyl moiety, which drives the reaction towards the product. We propose the mechanism as depicted in Figure 1.

Allylation of ketones is a challenging task due to the lower electrophilicity of the carbonyl group and steric hindrance present in ketones. After successful allylation of aldehydes we studied the allylation of ketones using $GdCl_3{\cdot}6H_2O$ as a catalyst and tetraallyltin as the allylating agent. The reaction of acetophenone proceeded smoothly and gave the corresponding homoallylic alcohol. Encouraged by this result, this method was extended to various ketones such as aryl, alkyl, cyclic heterocyclic and α,β-unsaturated ketones (Scheme 2). In all cases the reaction proceeded smoothly and gave the corresponding homoallylic alcohols in good to excellent yields. The results are summarized in Table 2. The usage of hydrated form of catalyst is having an advantage in reduced reaction timings compared to the reaction carried out in methanol.[15]

In conclusion, we have demonstrated a simple, convenient and efficient protocol for the synthesis of homoallylic alcohols from carbonyl compounds and allylstannanes using $GdCl_3{\cdot}6H_2O$ under mild and neutral conditions. This catalyst offers several advantages including mild conditions, clean reactions, shorter reaction times, high yields of products and lower catalytic loading.

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16. *Experimental procedure:* A mixture of aldehyde (2 mmol), allyltributylstannane (2 mmol) or [1 mmol of tetraallyltin for the allylation of 2 mmol of ketone] and gadolinium chloride hexahydrate (5 mol %) in acetonitrile (2 mL) was stirred at ambient temperature for an appropriate time (see Tables 1 and 2). After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (2 × 15 mL). The combined organic layers was washed with brine, dried over anhydrous Na_2SO_4 and concentrated in vacuo, and the resulting product was purified by column chromatography on silica gel (Merck, 60–120 mesh, ethyl acetate–hexane, 2:8) to afford pure homoallylic alcohol.