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Allylation of ketones with allylstannanes catalyzed by Lewis acid–Lewis base combined reagents

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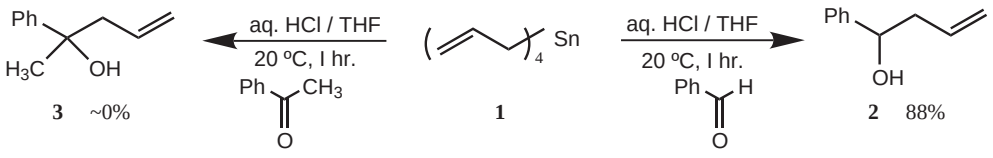
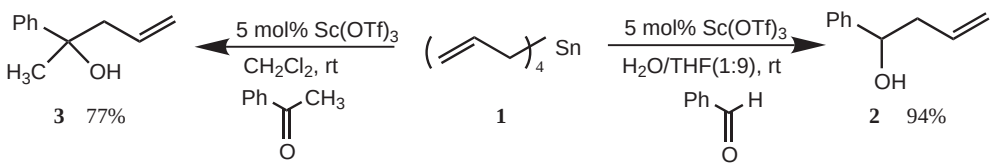
Abstract

Although the Lewis acid promoted allylation of ketones with allylstannanes gives the corresponding *tert*-homoallyl alcohols in lower yields in comparison with those of aldehydes, the use of Lewis acid–Lewis base combined catalysts such as $Zn(OTf)_2$–2,6-lutidine and $Zn(OTf)_2$–pyridine dramatically enhances the yield of the *tert*-alcohols. © 2000 Published by Elsevier Science Ltd.

The Lewis acid promoted allylation of aldehydes with allylstannanes is a useful method for synthesizing homoallyl alcohols.[1] Diastereoselective and enantioselective allylation with allylstannanes has been studied mostly for *aldehydes*.[2] However, allylation of *ketones* has been scarcely reported. Perhaps, this is due to the lower reactivity of ketones, compared to aldehydes, towards allylstannanes. For example, the reaction of benzaldehyde with tetraallylstannane **1** in the presence of catalytic amounts of aq. HCl gave the corresponding homoallyl alcohol **2** in 88% yield,[3] whereas the reaction of acetophenone with **1** under the same conditions did not give the corresponding allylation product **3** at all (Eq. (1)).[3] The $Sc(OTf)_3$ catalyzed reaction of **1** with benzaldehyde in THF/H_2O gave **2** in 94% yield, whereas the $Sc(OTf)_3$ catalyzed reaction of **1**



(1)



(2)

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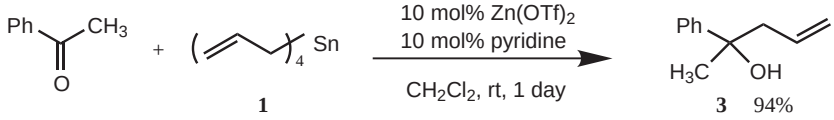
with acetophenone proceeded only in *dry* CH_2Cl_2 affording **3** in 77% yield[4] (Eq. (2)); the Lewis acidity of $Sc(OTf)_3$ in a non-coordinative solvent such as CH_2Cl_2 seems to be stronger than that in a coordinative solvent such as THF. As can be seen from the above examples, the reactivity of simple ketones in the Lewis acid (or protic acid) promoted allylation with allylstannanes is significantly lower than that of simple aldehydes, primarily due to both steric and electronic effects.[5]

We also observed lower reactivity of acetophenone in the $Zn(OTf)_2$ catalyzed (10 mol%) allylation with **1**: only 16% of **3** was formed after 1 day in CH_2Cl_2 at room temperature. The lower chemical yield (16%) in this case, in comparison with 77% in Eq. (2), is understandable since the Lewis acidity of $Zn(OTf)_2$ is weaker than that of $Sc(OTf)_3$. However, we have discovered that a *Zn(OTf)$_2$–pyridine* combined reagent system[6] enhances dramatically the chemical yield in the allylation of acetophenone with **1**; **3** was obtained in 94% yield in the presence of 10 mol% $Zn(OTf)_2$–10 mol% pyridine after 1 day in CH_2Cl_2 at room temperature (Eq. (3)).

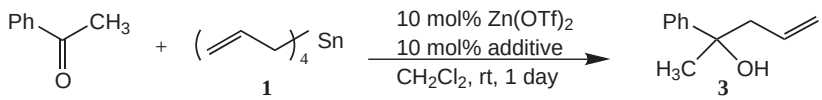


(3)

A detailed investigation on the effect of bases was carried out using acetophenone (1 equiv.), **1** (1 equiv.), base (10 mol%), and 10 mol% $Zn(OTf)_2$. The results are summarized in Table 1.

The use of $Zn(OTf)_2$ alone is ineffective (entry 1), as stated above. Pyridine, $PhNMe_2$, 2,6-lutidine and 2,6-di-*tert*-butylpyridine are quite effective (entries 2–5). Et_3N, Dabco, DBU and 2,2′-dipyridyl are not effective (entries 6–9). Only a trace amount of the allylation product was obtained in the presence of *i*-Pr_2NEt (entry 10). Additives other than the above nitrogen bases were tested; 10 mol% $Zn(OTf)_2$–10 mol% PPh_3 and 10 mol% $Zn(OTf)_2$–10 mol% HCl in Et_2O were examined but the results were unsatisfactory. Next, we examined the effect of the

Table 1
Effect of additive on catalytic allylation of acetophenone with tetraallylstannane



Entry	Additive	Yield (%)[a]	Recovery (%)[a]
1	–	16	84
2	Pyridine	94	–
3	$PhNMe_2$	Quant.	–
4	2,6-Lutidine	Quant.	–
5	2,6-Di-*tert*-butylpyridine	Quant.	–
6	Et_3N	48	52
7	Dabco	Trace	89
8	DBU	14	86
9	2,2′-Dipyridyl	21	79
10	*i*-Pr_2NEt	Trace	83

[a] Yields of **3** and recovery of acetophenone were determined by ^{1}H NMR using an internal standard (1,4-dioxane).

allylstannane (1 equiv.) on the reaction of acetophenone (1 equiv.) in the presence of 10 mol% $Zn(OTf)_2$ and 10 mol% pyridine in CH_2Cl_2 at room temperature for 1 day: 94% of **3** was obtained with **1**, 59% of **3** with $(CH_2{=}CHCH_2)_2SnBu_2$, and 19% of **3** with $(CH_2{=}CHCH_2)SnBu_3$; acetophenone was recovered in the last two cases. It may be said that the use of **1** is not necessarily desirable since only one of the four allyl groups can be utilized and the remaining three allyl groups have to be discarded. Fortunately, the use of 2,6-lutidine, instead of pyridine, enhanced the yield of **3** even in the reaction of $(CH_2{=}CHCH_2)SnBu_3$: 79% of **3** was obtained along with 20% of the recovered acetophenone. This result should be compared with that of the $Sc(OTf)_3$ catalyzed allylation with $(CH_2{=}CHCH_2)SnBu_3$: only 54% of **3** was obtained even using the much stronger and expensive $Sc(OTf)_3$. Then we searched for the optimized reaction conditions in the $Zn(OTf)_2$–2,6-lutidine promoted reaction of acetophenone (1 equiv.) with **1** (1 equiv.). The following three conditions (amount of $Zn(OTf)_2$, amount of 2,6-lutidine, reaction time) gave **3** in quantitative yield; (10 mol%, 1 mol%, 1 day), (1 mol%, 10 mol%, 1 day), (1 mol%, 1 mol%, 1 day). If we used 10 mol% $Zn(OTf)_2$ and 10 mol% 2,6-lutidine, 94% of **3** was obtained even after 1 h.

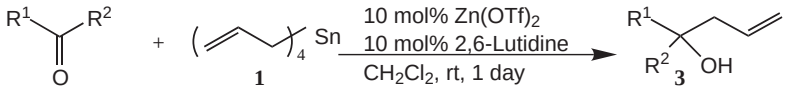
The allylation of several different kinds of ketone with **1** was examined in the presence of 10 mol% $Zn(OTf)_2$–10 mol% 2,6-lutidine in CH_2Cl_2 at room temperature for 1 day, and the results are summarized in Table 2. Arylmethyl ketones bearing an EWG at the *para*-position of the aromatic ring gave the corresponding allylation products in quantitative yield (entries 1–3). Arylmethyl ketones bearing an EDG such as *p*-Me or *p*-MeO gave quantitative or high yields of the allylation products (entries 4 and 5). However, a *p*-Me_2N substituent halted the allylation completely (entry 6), the reason for which is not clear at present. In general, aliphatic ketones and α,β-unsaturated ketones underwent the allylation without problem (entries 7–11). Not only arylmethyl ketones but also phenylethyl ketone and benzophenone afforded the corresponding allylation products in quantitative yield (entries 12 and 13).

It is clear that the $Zn(OTf)_2$–2,6-lutidine catalyst is very effective for the allylation of ketones with **1**. Two remaining questions at this point were (1) whether other metal triflates can be applied or not, and more importantly (2) whether allyltributylstannane is applicable or not.[6] The reaction of acetophenone with allyltributylstannane in 10 mol% catalyst in CH_2Cl_2 at room temperature for 1 day was examined. (Catalyst, yield of **3**, recovery of acetophenone) is shown below. ($Sc(OTf)_3$, 54, 15), ($Sc(OTf)_3$–2,6-lutidine, 93, 7), ($Hf(OTf)_4$–2,6-lutidine, 52, 46), ($Cp_2Ti(OTf)_2$–2,6-lutidine, 23, 49). Accordingly, the $Sc(OTf)_3$–2,6-lutidine catalyst is more effective than the $Zn(OTf)_2$–2,6-lutidine system in the reaction with allyltributylstannane.

A representative procedure is shown for the reaction of acetophenone with tetraallylstannane using a $Zn(OTf)_2$–2,6-lutidine catalyst. To a mixture of $Zn(OTf)_2$ (14.6 mg, 0.04 mmol) and 2,6-lutidine (4.7 μl, 0.04 mmol) in dry CH_2Cl_2 were added acetophenone (48 μl, 0.4 mmol) and tetraallylstannane (110 μl, 0.44 mmol) under an Ar atmosphere. The reaction was carried out at room temperature for 1 day and quenched with sat. aqueous $NaHCO_3$ solution (4 ml). The product was extracted with Et_2O and dried with Na_2SO_4. The solvent was evaporated, and the product was purified by silica gel column chromatography, giving **3** (64.8 mg) in a quantitative yield.

In conclusion, we have found that the Lewis acid–Lewis base catalysts,[7] such as $Zn(OTf)_2$–2,6-lutidine and $Sc(OTf)_3$–2,6-lutidine, are quite effective for converting *ketones* into the corresponding homoallyl alcohols. Further investigation on diastereo- and enantio-selective allylation using the new catalyst system is currently in progress in our laboratories.

Table 2
Allylation of ketones catalyzed by $Zn(OTf)_2$–2,6-lutidine



entry	R^1	R^2	yield (%) [a]	recovery (%) [a]
1	*p*-$NO_2C_6H_4$	CH_3	quant	-
2	*p*-ClC_6H_4	CH_3	quant	-
3	*p*-FC_6H_4	CH_3	quant	-
4	*p*-MeC_6H_4	CH_3	quant	-
5	*p*-$MeOC_6H_4$	CH_3	86	7
6	*p*-$Me_2NC_6H_4$	CH_3	-	92
7	n-C_7H_{15}	CH_3	quant	-
8	PhCH=CH	CH_3	quant	-
9		CH_3	80	trace
10			82	-
11			80	-
12	Ph	Et	quant	-
13	Ph	Ph	quant	-

[a] Isolated yield.

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7. A referee pointed out that the present catalyst system is rather similar to the $TiCl_4$/*N*-methylaniline system for the allylation of allylic alcohols: Saito, T.; Itoh, A.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1979**, *37*, 3519. We appreciate this comment.