

Tin(II) chloride mediated allylation of aldimines generated *in situ* with allylstannane in water

Takahiko Akiyama* and Yuji Onuma

1-5-1, Mejiro, Toshima-ku, Tokyo 171-8588, Japan.

E-mail: takahiko.akiyama@gakushuin.ac.jp; Fax: +81-3-5992-1029; Tel: +81-3-3986-0221

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Three-component synthesis of homoallylic amines starting from aldehyde, amine, and allyltributylstannane were realized by means of tin(II) chloride dihydrate in water in the presence of SDS.

Lewis acid mediated nucleophilic addition of allylic organometallics to carbon–nitrogen double bond constitutes an important reaction for the synthesis of homoallylic amines.¹ Allylic metals bearing group 14 elements, such as allylstannane,^{2,3} allylgermane,⁴ and allylsilane,⁵ have been extensively studied. Numerous kinds of activators of imines have been developed. It is synthetically highly convenient if one could allylate imines generated *in situ* from aldehyde and amine. The chemoselectivity between aldehyde and aldimine has also been studied and imine selective activators have been developed.^{6,7} Three-component synthesis of homoallylic amines starting from aldehyde, amine, and allylic metals thus have been realized.^{3–5} Organic reactions in aqueous media have attracted the attention of synthetic organic chemists⁸ lately, not only because water is a cheap and safe solvent in comparison with conventional organic solvents, but also because water exerts a unique reactivity. Because Lewis acids are generally highly sensitive to moisture, Lewis acid catalyzed nucleophilic addition of organometallics to carbon–nitrogen double bonds normally requires strictly anhydrous conditions in organic solvent. Recently, water-tolerant Lewis acids, such as lanthanide triflate^{9†} and indium(III) chloride,¹⁰ have been developed. We have recently reported that Brønsted acids efficiently activate aldimines in aqueous media and Mannich-type reactions of silyl enolates to aldimine take place smoothly by means of a catalytic amount of HBF₄ in aqueous organic solvent¹¹ or in water with a surfactant.¹² Hetero Diels–Alder reaction also proceeded smoothly in either aqueous organic solvent or in water with a surfactant.¹³

Although Sc(OTf)₃ catalyzed allylation of aldimines with allyltributylstannane¹⁴ and Barbier-type nucleophilic addition of allylic indium compounds¹⁵ to aldimine in water have been reported, there are only a few reports on the allylation of imines in water.¹⁶ As part of our continued interest in the allylation of imines,⁴ we tried to find a new effective catalyst for the allylation of aldimines in water. We focused on conventional Lewis acids. Our idea is that the hydrated form of Lewis acids would be more resistant to water than anhydrous Lewis acids and thus would function as a Lewis acid in aqueous media.^{17,18} It was found that SnCl₂·2H₂O, which is a conventional Lewis acid, is effective for the allylation of aldimines in water (Scheme 1).

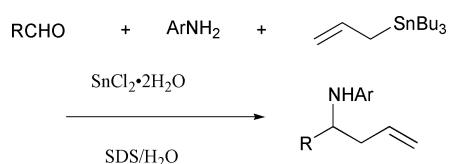


Table 1 Effect of Lewis acid

Entry	Lewis acid	Time/min	Yield (%)
1	SnCl ₂ ·2H ₂ O	10	80
2	SnCl ₂	30	63
3	AlCl ₃ ·6H ₂ O	40	47
4	CuCl ₂ ·2H ₂ O	30	18
5	BF ₃ ·OEt ₂	90	0
6	HCl	20	18

At the outset, we studied three-component synthesis of homoallylic amines starting from benzaldehyde, aniline (1.5 equiv.), and allyltributylstannane (1.5 equiv.) in water in the presence of SDS (sodium dodecyl sulfate) (0.4 equiv.). The effect of several Lewis acids is shown in Table 1. Tin(II) chloride dihydrate turned out to be the most effective among the acids examined. The allylation reaction was complete in 10 min to afford a homoallylic amine (**1**) in 80% yield (entry 1). Interestingly, anhydrous tin(II) chloride gave slightly inferior result (entry 2). AlCl₃·6H₂O was also effective (entry 3) but CuCl₂·2H₂O gave the adduct in a low yield (entry 4). BF₃·OEt₂ was not effective presumably because BF₃·OEt₂ decomposed under the reaction conditions. The fact that HCl was less effective implies that the HCl, generated by decomposition of SnCl₂, is not the real active species. It is noted that a homoallylic alcohol was not obtained at all under the reaction conditions.

When the loading of tin(II) chloride dihydrate was decreased, the yield dropped. Furthermore, when the reaction was run under N₂ conditions in distilled and degassed water, highly reproducible results were obtained. Presumably, tin(II) chloride is oxidized by O₂ in water, resulting in the deterioration of the catalytic activity.

Next, three component synthesis of homoallylic amines was studied. *p*-Chloroaniline was found to be highly effective as an amine component (entry 2 Table 2). The results of the allylation with various kinds of aldehydes are shown in Table 2.¹⁹ Aromatic, hetero-aromatic, and aliphatic aldehydes worked well to afford the adducts in good yields. It is noted that the allylation reaction is very fast and most of the reactions were completed in less than half an hour.

We have developed a simple procedure for the preparation of homoallylic amines in high yields in water. Salient features of the present reaction are: 1) high chemoselectivity towards aldimine in preference to aldehyde, 2) use of a conventional Lewis acid, 3) extremely short reaction time.

Table 2 Results of the allylation with various aldimines

$$\text{RCHO} + \text{ArNH}_2 + \text{CH}_2=\text{CH}-\text{CH}_2-\text{SnBu}_3$$

$$\xrightarrow[\text{20-30 min}]{\text{SnCl}_2 \cdot 2\text{H}_2\text{O} (0.5 \text{ equiv})} \text{R}-\text{CH}(\text{NHAr})-\text{CH}_2-\text{CH}=\text{CH}_2$$

$$\text{SDS/H}_2\text{O}^a \text{ under N}_2$$

Entry	R	Ar	Yield (%)
1	Ph	Ph	85
2	Ph	<i>p</i> -ClC ₆ H ₄	86
3	<i>p</i> -ClC ₆ H ₄	<i>p</i> -ClC ₆ H ₄	83
4	<i>p</i> -MeOC ₆ H ₄	<i>p</i> -ClC ₆ H ₄	87
5	<i>p</i> -MeC ₆ H ₄	<i>p</i> -ClC ₆ H ₄	82
6	2-Thienyl	<i>p</i> -ClC ₆ H ₄	69
7	2-Furyl	<i>p</i> -ClC ₆ H ₄	69
8	Cyclohex	<i>p</i> -ClC ₆ H ₄	82
9	<i>i</i> -Pr	<i>p</i> -ClC ₆ H ₄	69
10	PhCH(CH ₃)	<i>p</i> -ClC ₆ H ₄	68 ^b
11	PhCH(CH ₃)	<i>p</i> -ClC ₆ H ₄	84 ^c
12	BnOCH(CH ₃)	<i>p</i> -ClC ₆ H ₄	72 ^d

^a Distilled water was employed. ^b *syn-anti* = 85 : 15. ^c *syn-anti* = 83 : 17. ^d *syn-anti* = 55 : 45.

References and notes

† The IUPAC name for triflate is trifluoromethanesulfonate.

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- Recent example of the use of Lewis acid with water of crystallization, see W. Zhuang, R. G. Hazell and K. A. Jørgensen, *Chem. Commun.*, 2001, 1240.
- A typical experimental procedure for entry 1 of Table 2. Benzaldehyde (16 μ l, 0.158 mmol) and aniline (22 μ l, 0.241 mmol) were mixed in degassed water (9.6 ml) under a N₂ atmosphere for 1 h at room temperature. SDS (18.0 mg, 0.064 mmol) and an aqueous solution of tin(II) chloride dihydrate (18.0 mg, 0.080 mmol) in water (0.5 ml), and allyltributylstannane (75 μ l, 0.242 mmol) were added successively into the mixture. After being stirred at the temperature for 20 min, DOWEX1-X8 (100–200 mesh, Cl form), and sat. NaHCO₃ solution KF solution were added to stop the reaction, and the mixture was stirred for 5 min. The resultant solution was filtered to remove the resin and the filtrate was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated to dryness. Purification of the crude mixture by preparative TLC (SiO₂, hexane–ethyl acetate = 12 : 1, v/v) gave a homoallylic amine (29.8 mg) in 85% yield.