

Three-Component Synthesis of Homoallylamines by Scandium(III) Triflate-Mediated Allylation with Allylgermane: A Highly Imine Selective Allylation Reaction

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Abstract: Investigated is a three-component synthesis of homoallylamines by scandium(III) triflate catalyzed allylation of imines, generated *in situ* from aldehyde and amine, with allyltriethylgermane. Imines were allylated exclusively in the presence of aldehydes.

The allylation of imines with allyl organometallics is an important reaction in the preparation of homoallylamines and has been extensively studied.¹ Allylic metals bearing group 14 elements such as allylsilane and allylstannane have been established as useful allyl anion equivalents.² Although allylsilanes reacted sluggishly with imines, allyltrialkylstannanes reacted smoothly with imine under the influence of conventional Lewis acids, affording homoallylamines in good yields. Although more than 1 equivalent of Lewis acid used to be required,³ catalytic allylation of imines promoted by lanthanide triflate has been reported.⁴ Quite recently, Kobayashi et al. disclosed lanthanide triflate catalyzed aldimine selective allylation with allylstannanes⁵ and group 4 metal triflate catalyzed one pot allylation of imines.⁶ Sc(OTf)₃-catalyzed three-component reactions of aldehyde, amine, and allyltributylstannane in micellar system leading to homoallylamines has emerged from the same author.⁷ Yamamoto et al. also reported transition metal-catalyzed allylation of aldehydes and imines with allyltrialkylstannanes.⁸

In sharp contrast to organotin and organosilicon compounds, organogermanium compounds have attracted less attention of synthetic organic chemists.^{9,10} In terms of it having lower toxicity than organotin compounds, elaboration of synthetic utility of organogermanium compounds is of importance. Recently, we have reported that tetraallylgermane reacted readily with aldehydes by means of scandium(III) triflate in aqueous nitromethane to afford homoallyl alcohols in high yields.¹¹ It is noted that the allylation reaction showed high chemical selectivity toward aldehyde in preference to ketone. It was found that allyltriethylgermane turned out to work effectively as an allyl anion equivalent in the reaction with imines. We wish to disclose herein a three-component synthesis of homoallylamines by scandium(III) triflate-promoted allylation of imines with allyltriethylgermane.

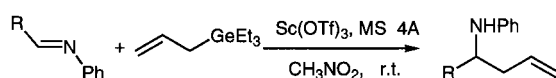


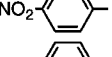
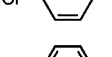
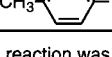


Table 1. Results of the allylation of imines

Entry	R	Amount of Sc(OTf) ₃	Reaction time	Yield/%
1		0.10	20 min	85
2		0.10	30 min	78 ^{a)}
3		0.10	13 min	91
4		0.15	15 min	87
5		0.10	1.5 h	81

a) The reaction was conducted without MS 4A

On treatment of *N*-benzylideneaniline with allyltriethylgermane (1.5 equiv) in the presence of scandium(III) triflate¹² (10 mol%) and MS 4A in nitromethane,¹³ the allylation reaction was complete in 20 min at room temperature to afford a homoallylamine in 85% yield (Table 1, Entry 1). Although use of MS 4A is not mandatory for the present reaction, addition of MS 4A slightly improved the yield of the adduct (Entry 2). Other aromatic imines were also allylated smoothly to furnish homoallylamines in excellent yields (Entries 3-5). When tetraallylgermane was employed as a nucleophile under the identical reaction conditions, the yields of the homoallylamines were much lower. Although other lanthanide triflates such as ytterbium triflate and samarium triflates also promoted the allylation reactions of imines similarly, they generally afforded the homoallylamines in slightly lower yields.

With regard to the reactions of imines, their instability is an inherent drawback. It is desirable, from a synthetic point of view, to generate imine *in situ* and to react with a nucleophile immediately. A three component reaction of aldehyde, amine, and allylgermane was thus tested.^{6,7,14} Gratifyingly, the one-pot synthesis of homoallylamines was successfully achieved. Treatment of benzaldehyde (1.0 eq.), aniline (1.0 eq.), and allyltriethylgermane (1.5 eq.) under the influence of scandium(III) triflate in CH₃NO₂ at room temperature afforded the desired homoallylamine in 81% yield (Table 2, Entry 1).¹⁵ An imine, generated *in situ* from benzaldehyde and *o*-methoxyaniline also furnished a homoallylamine in a good yield (Entry 2). Imines derived from aliphatic aldehydes also produced the corresponding homoallylamines in good yields (Entry 6 and 7). Formation of the homoallyl alcohols was not observed. It should be noted that present three-component reaction proceeded smoothly by mixing an aldehyde, an amine, and an allylgermane in the suspension of Sc(OTf)₃ in nitromethane; generation of imines before the addition of allylgermane is not necessary.

In order to investigate the reason why the present allylation reaction gave rise to imine adducts exclusively, chemoselectivity of the present

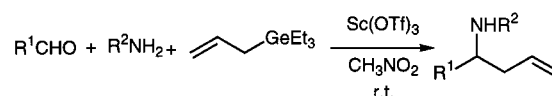


Table 2. Results of the three-component synthesis of homoallylamines

Entry	R ¹	R ²	Amount of Sc(OTf) ₃	Reaction time	Yield/%
1	Ph	Ph	0.10	45 min	81
2	Ph	<i>o</i> -MeO-Ph	0.10	60 min	80
3	<i>p</i> -NO ₂ -Ph	Ph	0.10	30 min	87 ^{a)}
4	<i>p</i> -Cl-Ph	Ph	0.15	45 min	81
5	<i>p</i> -CH ₃ -Ph	Ph	0.10	70 min	86
6	<i>o</i> -C ₆ H ₁₁	Ph	0.10	10 min	87 ^{a)}
7	<i>t</i> -Bu	Ph	0.10	75 min	75

a) The reaction was conducted in the presence of MS 4A

allylation was studied. In the coexistence of aldehyde and imine derived from the same aldehyde (1:1 / mol : mol), allyltriethylgermane (1.5 equiv) was treated with scandium(III) triflate and the results are shown in Table 3. Homoallylamines were obtained exclusively in high yields and the corresponding homoallyl alcohols were not observed at all. Allyltriethylgermane turned out to show no reactivity toward aldehyde. Indeed, treatment of benzaldehyde and allyltriethylgermane in the presence of $\text{Sc}(\text{OTf})_3$ (10 mol%) in nitromethane at room temperature for 7 days, the desired homoallyl alcohol was obtained in less than 5% yield.

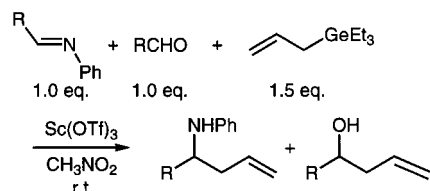


Table 3. Results of the chemoselective allylation

Entry	R	Amount of $\text{Sc}(\text{OTf})_3$	Yield of amine/%	Yield of alcohol/%
1		0.10	86	<1
2		0.10	93	<1
3		0.15	87	<1
4		0.10	81	<1

It turned out that the present reaction system exhibited excellent chemoselectivity toward imines in preference to aldehydes. In general, the reactivity of allylmetal to aldehydes is higher than that to imines under the conventional Lewis acid-promoted conditions.⁸ Recently, Kobayashi elucidated that ytterbium(III) triflate coordinated more strongly toward imines than to aldehydes by ^{13}C NMR analysis.^{8,16} The unique reactivity of the present allylation reaction would also be ascribed to the stronger activation of imines by scandium(III) triflate in comparison to that of aldehydes. Furthermore, the overall difference in the reactivity towards aldehydes between tetraallylgermane and allyltriethylgermane is of great interest; tetraallylgermane showed high reactivity toward aldehydes¹¹ whereas allyltriethylgermane showed no reactivity.¹⁷ In general, the reactivity order of allylmetals bearing a 14 group metal is $\text{Sn} > \text{Ge} > \text{Si}$.¹⁸ The present chemoselectivity is ascribed to the moderate reactivity of germanium compounds in comparison to organotin compounds.

Although one-pot synthesis of homoallylamines from aldehyde and amine utilizing allylsilane¹⁴ as well as allylstannanes^{6,7} have been already reported, present protocol will provide us with a novel and simple method for the preparation of homoallylamines.

In summary, we have developed a novel allylation reaction of imines utilizing allylgermane. Salient features of the present allylation reaction are: 1) allylation of imine proceeded smoothly by use of catalytic amount of Lewis acid under mild conditions, 2) allylation of imine proceeded efficiently by three component synthesis from aldehyde, amine, and allylgermane by one-pot procedure, 3) allylation exhibited excellent selectivity toward imine in the presence of aldehyde, 4) the less toxic organogermanium compound has been employed as an allylmetal.

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