ChemComm

Chemoselective allylation of aldimine with allyltriethylgermane by the combined use of BF_3•OEt_2 and AcOH

Takahiko Akiyama,* Junko Iwai, Yuji Onuma and Hirotaka Kagoshima

Department of Chemistry, Faculty of Science, Gakushuin University, 1-5-1, Mejiro, Toshima-ku, Tokyo 171, Japan. E-mail: takahiko.akiyama@gakushuin.ac.jp

Received (in Cambridge, UK) 17th September 1999, Accepted 28th September 1999

Allyltriethylgermane reacts with aldimines in preference to aldehydes by means of BF_3•OEt_2 and AcOH to afford homoallylic amines in high yields; three component syntheses of homoallytic amines starting from aldehyde, aniline and allylgermane were successfully achieved.

Lewis acid promoted nucleophilic addition of allylic organometallics to imines constitutes an important reaction for the preparation of homoallylic amines.[1] Although numerous kinds of activator of aldimines have been reported, the addition toward aldimines has been less extensively explored due to its inherent lower reactivity in comparison with that toward aldehydes.[2] Recently, several groups have developed imine selective activators.[3] For instance, Yamamoto and co-workers reported Pd^{II} catalyzed chemoselective allylation of aldimines with allylstannanes.[4] Kobayashi and co-workers found that lanthanide or scandium triflate[5] mediated allylation reactions proceeded smoothly toward aldimines in preference to aldehydes.[6] BF_3•OEt_2 catalyzed chemoselective allylation of aldimines, generated from aldehydes and carbamates[7] or sulfonamides,[8] with allylsilane has been realized. We have also reported that $Sc(OTf)_3$ catalyzed allylation with allylgermane took place highly chemoselectively toward aldimines in preference to aldehydes.[9]

We have recently shown that Brønsted acids activate imines chemoselectively in the presence of aldehydes in aqueous media.[10] Thus, upon reaction of aldimines and silyl enolates in the presence of a catalytic amount of HBF_4, Mannich-type reactions proceeded smoothly in aqueous media to afford β-amino carbonyl compounds in high yields. Three component syntheses of β-amino carbonyl compounds starting from aldehydes and anilines have been also successfully achieved. Furthermore, the Brønsted acid catalyzed Mannich-type reaction proceeded smoothly in water without organic solvent in the presence of surfactants such as SDS.[11]

We report herein that aldimines underwent allylation with allylgermane highly chemoselectively in preference to aldehydes by the combined use of BF_3•OEt_2 and AcOH and that three-component syntheses utilizing aldehydes, amines and allylgermanes furnished homoallylic amines in high yields.

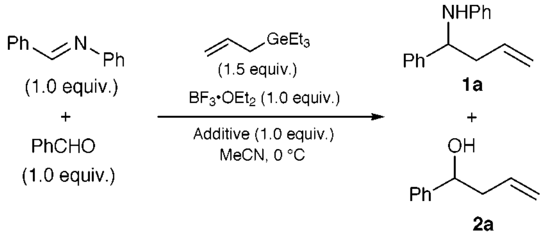
In the first place, the chemoselectivity of the allylation with allylgermane was studied and the results are shown in Table 1. On reaction of an equimolar amount of benzaldehyde and *N*-benzylideneaniline in the presence of allyltriethylgermane (1.5 equiv.) and BF_3•OEt_2 (1.0 equiv.) in MeCN at room temperature, allylation proceeded towards aldehyde to afford a homoallylic alcohol **1a** in a good yield accompanied by a homoallylic amine **2a**. Interestingly, addition of a proton source changed the reaction course dramatically and the aldimine underwent allylation exclusively. As an additive, AcOH gave the best result. It is noted that the present allylation did not proceed at all with the aldimine derived from benzaldehyde and benzylamine. The presence of the *N*-aryl group is mandatory.

After screening the reaction conditions, use of 1.0 equiv. of BF_3•OEt_2 and 0.5 equiv. of AcOH gave the best results.[12,13] It is noted that allylation did not proceed at all with AcOH alone without BF_3•OEt_2. Results for the chemoselective allylation with several aromatic aldimines are shown in Table 2. Allylation of the aldimines proceeded smoothly and showed high chemoselectively in preference to the aldehyde.

Since aldimines are not always stable, it would be synthetically quite useful if the allylation of imines could be achieved *via* reaction with aldimines generated *in situ* from aldehydes and amines. The three component synthesis of homoallylic amines starting from aldehyde, amine and allylgermane took place smoothly in the presence of BF_3•OEt_2 (0.5 equiv.), AcOH (1.0 equiv.) and MS 3A in MeCN to afford homoallylic amines in high yields; the results are shown in Table 3. Not only aldimines derived from aromatic aldehydes but also those derived from aliphatic and α-keto aldehydes worked reasonably well to afford the corresponding homoallylic amines in high yields.

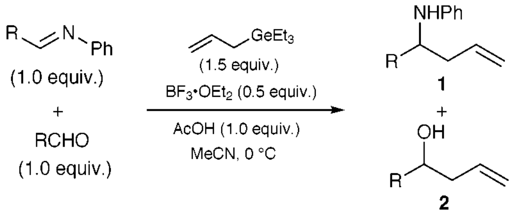
Finally, the chemoselectivity of Si, Ge and Sn reagents was studied. In the presence of equimolar amounts of aldimine and aldehyde, allylic metals were treated with BF_3•OEt_2 (0.5 equiv.) and AcOH (1.0 equiv.) and the results are shown in Table 4. The reaction with allylsilane was sluggish and the corresponding adduct was obtained in a low yield. Although the reactivity of

Table 1 Effect of the additive



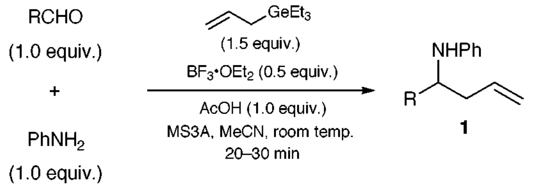
Entry	Additive	Yield of **1a** (%)	Yield of **2a** (%)
1	None	42	88
2	H_2O	72	< 1
3	MeOH	79	< 1
4	AcOH	86	7
5	BzOH	75	< 1

Table 2 Results of the allylation



Entry	R	Yield of **1** (%)	Yield of **2** (%)
1	Ph	90	< 1
2	p-$NO_2C_6H_4$	87	6
3	p-ClC_6H_4	86	< 1
4	p-$CH_3C_6H_4$	75	7
5	p-$MeOC_6H_4$	72	< 1

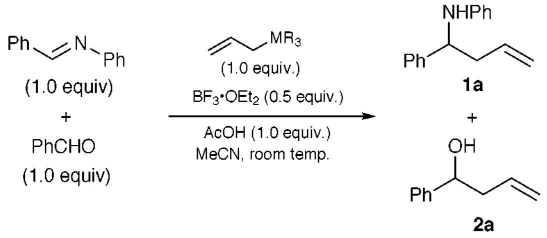
Table 3 Results of the three-component allylation



Entry	R	Yield of **1** (%)
1	Ph	81
2	p-$NO_2C_6H_4$	87
3	p-ClC_6H_4	83
4	c-C_6H_{11}	80
5	Bu^t	80
6	PhCO[a]	88

[a] PhCOCHO•H_2O was employed.

Table 4 Reactivity of 14-group allylic organometallics



Entry	MR_3	Yield of **1a** (%)	Yield of **2a** (%)
1	$SiMe_3$	19	<1
2	$GeEt_3$	79	<1
3	$SnBu_3$	82	9

allylstannane turned out to be higher than that of allylgermane, allylgermane showed the highest chemoselectivity toward aldimines.

In summary, we have found a simple method for the selective allylation of aldimines. Salient features are (i) environmentally benign organogermanium reagents are employed, (ii) the combination of a conventional Lewis acid and a Brønsted acid is found to be an effective activator of aldimines, and (iii) addition of a small amount of protic acid to BF_3•OEt_2 alters the reactivity dramatically.

Partial financial support from the Ministry of Education, Science and Culture of Japan (Grant-in-Aid for Scientific Research) and the Takeda Award in Synthetic Organic Chemistry, Japan, is gratefully acknowledged.

Notes and references

1 E. F. Kleinman and R. A. Volkmann, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 2, p. 975; Y. Yamamoto and N. Asao, *Chem. Rev.*, 1993, **93**, 2207.
2 R. A. Volkmann, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 1, p. 355; R. Bloch, *Chem. Rev.*, 1998, **98**, 1407.
3 Although Grieco and co-workers reported three allylations of aldimines generated *in situ* from aldehyde, only formaldehyde was employed. See: S. D. Larsen, P. A. Grieco and W. F. Fobare, *J. Am. Chem. Soc.*, 1986, **108**, 3512; P. A. Grieco and A. Bahsas, *J. Org. Chem.*, 1987, **52**, 1378.
4 H. Nakamura, N. Asao and Y. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1995, 1273; H. Nakamura, H. Iwama and Y. Yamamoto, *J. Am. Chem. Soc.*, 1996, **118**, 6641.
5 S. Kobayashi, *Synlett*, 1994, 689; S. Kobayashi, *Eur. J. Org. Chem.*, 1999, 15.
6 S. Kobayashi and S. Nagayama, *J. Org. Chem.*, 1997, **62**, 232; S. Kobayashi and S. Nagayama, *J. Am. Chem. Soc.*, 1997, **119**, 10 049.
7 S. J. Veenstra and P. Schmid, *Tetrahedron Lett.*, 1997, **38**, 997.
8 Y. Masuyama, J. Tosa and Y. Kurusu, *Chem. Commun.*, 1999, 1075.
9 T. Akiyama and J. Iwai, *Synlett*, 1998, 273.
10 T. Akiyama, J. Takaya and H. Kagoshima, *Synlett*, 1999, 1045; T. Akiyama, J. Takaya and H. Kagoshima, *Chem. Lett.*, 1999, 947.
11 T. Akiyama, J. Takaya and H. Kagoshima, *Synlett*, 1999, 1426.
12 Use of commercially available BF_3•2AcOH gave comparable results.
13 Brønsted acid, generated from BF_3•OEt_2 and 0.5 equiv. of AcOH, may be the active species. For examples of the intramolecular allylation of imines with allylstannanes wherein protic acids have been employed, see: I. Kadota, J.-Y. Park and Y. Yamamoto, *Chem. Commun.*, 1996, 841; J.-Y. Park, I. Kadota and Y. Yamamoto, *J. Org. Chem.*, 1999, **64**, 4901.

Communication 9/07538K