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Allylation of Carbonyl Compounds Mediated by Germanium(II) Iodide

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Abstract: Germanium(II) iodide reacts with allyl bromide in the presence of zinc iodide to afford allylgermanium(IV), which adds to carbonyl compounds to give the corresponding homoallylic alcohols in good yields.

Allylation of carbonyl compounds with allylic organometallic reagents is one of the most important carbon-carbon bond forming reactions in organic synthesis, and a number of useful methods have been developed.[1] It is known that the chemo-, regio-, and stereoselectivity are highly dependent on the metal of allylic metals. For the reaction of allylic metals of group 14 elements, the Lewis acid mediated reaction of allylic silanes[2] and stannanes[3] is well-established. Along with this reaction, the Barbier-type allylation, an *in situ* method for preparing allylic organometallic reagents in the presence of carbonyl compounds, is an attractive alternative from the viewpoint of convenience since it is not necessary to isolate the allylic metals. Tin(II) halide is a popular reagent for the Barbier-type allylation of carbonyl compounds.[4] On the other hand, compared with allylic silane or allylic stannane reagents, there are a very few synthetic reactions using allylic germanium reagents.[5] Furthermore, there is no example of allylation reaction mediated by germanium(II) compounds[6] utilizing its reducing property. In this communication, we would like to report the Barbier-type allylation of carbonyl compounds using allylgermanium(IV) reagents, which were formed *in situ* from germanium(II) iodide[7] and allyl halides.

At first, the reaction of benzaldehyde with allyl iodide was tried in *N,N*-dimethylformamide (DMF) in the presence of germanium(II) iodide. As a result, it was found that the reaction proceeded smoothly at room temperature to give the corresponding homoallylic alcohol in 86% yield. Allyl bromide, on the other hand, was less reactive than allyl iodide under the same conditions, and the desired reaction proceeded only very sluggishly. Since the iodide is less favorable than the bromide in respect of stability and availability, we examined the effect of addition of iodide salts to generate allyl iodide from allyl bromide in the reaction system.[4c,8] The results are shown in Table I. Sodium iodide, the most common reagent for the interconversion of bromide to iodide, could not give a satisfactory result, although improvement was observed to some extent. After screening various iodides, we found that zinc iodide is the most effective in this reaction.

A typical procedure is as follows (Table I, Run 8). To a mixture of benzaldehyde (106 mg, 1.0 mmol) and allyl bromide (145 mg, 1.2 mmol) in DMF (4 ml) were added successively germanium(II) iodide (489 mg, 1.5 mmol) and zinc iodide (479 mg, 1.5 mmol) at room temperature under an argon atmosphere. After stirring for 15 h, ether (10 ml) and 30% aq NH_4F (5 ml) were added. The aqueous layer was extracted with ether, and the combined ether layers were washed with brine, dried with sodium sulfate, and concentrated. The crude

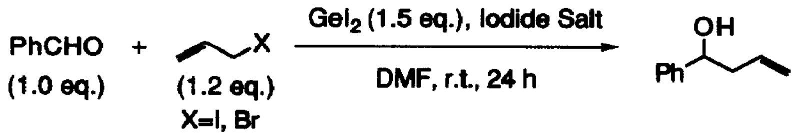


Table I. The Effect of Iodide Salts in the Reaction of Benzaldehyde with Allyl Halides.

Run	X	Iodide Salt		Yield/%
1	I	none		86
2	Br			29
3		NaI	(1.5 eq.)	46
4			(3.0 eq.)	51
5		LiI	(1.5 eq.)	48
6		GeI_4	(0.75 eq.)	61
7		ZnI_2	(0.75 eq.)	79
8[a]			(1.5 eq.)	85

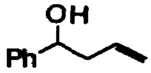
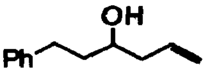
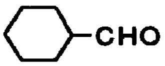
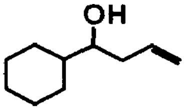
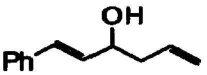
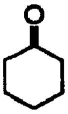
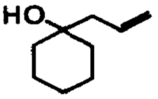
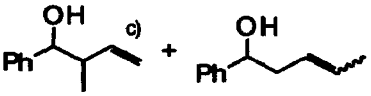
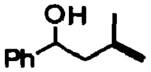
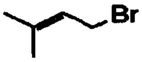
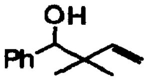
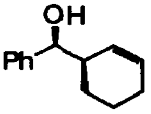
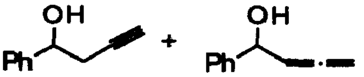
a) Reaction time; 15 h.

product was purified by TLC (silica gel) to afford the corresponding homoallylic alcohol (126 mg, 85% yield). The results of the reaction of carbonyl compounds with allylic bromides are summarized in Table II.

As can be see from Table II, both aromatic and aliphatic aldehydes smoothly reacted with allyl bromide, while cyclohexanone was less reactive and required excess reagents and long reaction time. Cinnamaldehyde exclusively gave a 1,2-adduct. Crotylation and prenylation of benzaldehyde proceeded with excellent regioselectivity to give the adducts arising from the coupling at the most hindered site. In the former case, the stereochemical information of the starting crotyl bromide was not transmitted completely to the product; some *E* to *Z* isomerization probably took place at the stage of the formation of allylgermanium reagent. When 3-bromocyclohexene, in which the stereochemistry of the double bond is fixed to be *cis*, was allowed to react with benzaldehyde, the *erythro* alcohol was formed with complete selectivity. Taking into account the above results, the stereoselectivity may be explained by a chair form, six-membered cyclic transition state. It is noteworthy that in the reaction of benzaldehyde and propargyl bromide, an acetylenic alcohol was obtained with high regioselectivity. This selectivity reveals a sharp contrast to the allylation reaction using $SnCl_2$[8] or $SnCl_2 \cdot 2H_2O$[4c] (allenic alcohol : acetylenic alcohol = 48 : 52 and 69 : 31, respectively).

The precise reaction mechanism has not yet been clear. However, the reaction is assumed to proceed as follows. Germanium(II) iodide reacts with allyl iodide, formed from allyl bromide by the action of zinc iodide, to afford an allylgermanium(IV) reagent regioconvergently, in which germanium atom places at the least hindered termini. The allylgermanium species adds to carbonyl compounds in a fashion of γ-addition to give the corresponding homoallylic alcohols.

Table II. Allylation of Carbonyl Compounds Mediated by Germanium(II) Iodide.

Run	Carbonyl Compound	Allylic Bromide	Reaction Time/h	Product	Yield/%
1	PhCHO		15		85
2			1		85
3			4		88
4			5		82
5[a]			110		76
6[a]	PhCHO		19	 98 : 2	88
7			1		83
8[a]			86		80
9[a]			48		78[d]
10[e]			72	 > 99 : 1	82

a) Molar ratio; carbonyl compound : allyl halide : germanium(II) iodide : zinc iodide = 1 : 3 : 3 : 3.

b) A mixture containing three isomeric species in the ratio of *trans* : *cis* : 3-bromo-1-butene = 70 : 15 : 15 was used.

c) *Erythro* : *threo* = 31 : 69.[9]

d) The stereochemistry was determined by comparison with the data in literature.[10]

e) Molar ratio; benzaldehyde : propargyl bromide : germanium(II) iodide : zinc iodide = 1 : 2 : 2 : 2.

In conclusion, we have found the first example of the germanium(II) iodide-mediated allylation of carbonyl compounds under mild conditions. A further investigation of the synthetic application of this reaction and the reaction mechanism are now in progress.

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