

# A new type of allylation: synthesis of $\beta,\gamma$ -unsaturated ketones from $\alpha$ -halogenated aryl ketones using an allyltributyltin(IV)–tin(II) dichloride–acetonitrile system

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**Allylation of  $\alpha$ -halogenated aryl ketones with an allyltributyltin–tin dichloride–acetonitrile system gave  $\beta,\gamma$ -unsaturated ketones in high yields via selective aryl rearrangement.**

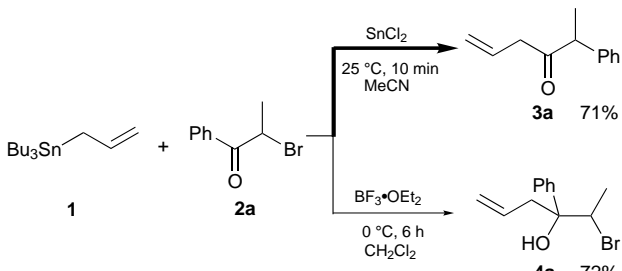
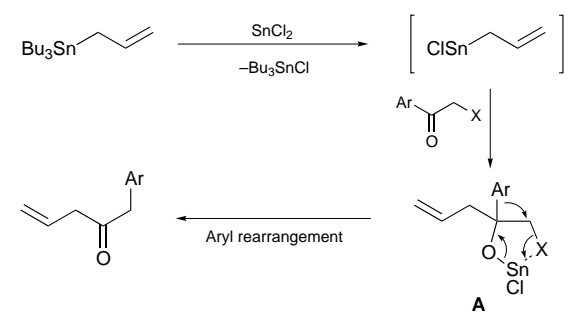
Allylation of carbonyl compounds has been intensively studied for carbon–carbon bond formation, affording homoallylic alcohols.<sup>1</sup> We have recently reported an allylic tin(II) species as powerful allylation reagents toward aldehydes, ketones or imines in preference to the corresponding tin(IV) species.<sup>2</sup> The tin(II) species, which have vacant orbitals to accept electrons, contribute to the selective carbonyl allylation via a cyclic transition state owing to the strong affinity between the tin(II) atom and the carbonyl oxygen.<sup>2</sup> The tin(II) center would be expected to interact even with a halogen atom because the latter bears unshared electron pairs for coordination to tin(II). Herein, we report a new type of allylation system for  $\alpha$ -halogenated aryl ketones.<sup>3</sup> This reaction proceeds via carbonyl allylation and subsequent aryl rearrangement to give  $\beta,\gamma$ -unsaturated ketone derivatives in high yields, in which reaction the tin(II) species characteristically effects the rearrangement.

A mixture of tin dichloride ( $\text{SnCl}_2$ ) and 2-bromopropiophenone **2a** in MeCN was treated with allyltributyltin **1** at room temperature for 10 min to afford, unexpectedly, the  $\beta,\gamma$ -unsaturated ketone **3a**, whereas general activation by a Lewis acid, boron trifluoride–diethyl ether,<sup>1,4</sup> gave the homoallylic alcohol **4a** exclusively (Scheme 1). In the allyltributyltin– $\text{SnCl}_2$  system, migration of the phenyl group takes place as shown in Scheme 2. The homoallylic tin alkoxide **A** is a key intermediate

in which the interaction between the tin(II) atom and the halogen directs the aryl rearrangement.<sup>5</sup> This type of interaction is unlikely to occur using allyltin(IV) reagents, which have a weaker affinity for halogen than the tin(II) species. Allylation using tin(IV) reagents of  $\alpha$ -halo ketones proceeds via cyclization of the intermediate tin alkoxides to give oxiranes exclusively, and no rearrangement is observed.<sup>6–8</sup> Other solvents examined (THF, toluene,  $\text{CH}_2\text{Cl}_2$ ,  $\text{CHCl}_3$ ) in the presence of  $\text{SnCl}_2$  gave low yields of **3a** (0–24% yield) at room temperature for 1 h. These facts strongly support the participation of the allylic tin(II) species in the rearrangement, because our previous report<sup>2</sup> has already shown the efficiency of MeCN as the solvent of choice for transmetalation of allyltributyltin **1** with  $\text{SnCl}_2$ . Allylation of **2a** in MeCN for 24 h without  $\text{SnCl}_2$  did not proceed at all. Considering these results, we suppose that this new type of allylation system giving the  $\beta,\gamma$ -unsaturated ketone evolves from the unique character of the tin(II) reagents.

We then explored the generality of the reaction by varying the aryl halo ketones. As shown in Table 1,  $\beta,\gamma$ -unsaturated ketones

**Table 1** Synthesis of  $\beta,\gamma$ -unsaturated ketones **3**

Entry	Halo ketone <b>2</b>			Yield (%)			
	Ar	R	X	$t_1$ /h	$t_2$ /h	<b>3</b>	<b>4</b>
1	4-MeOC <sub>6</sub> H <sub>4</sub>	H	Br	1	0	98	0
2	4-MeC <sub>6</sub> H <sub>4</sub>	H	Br	1	0.5	81	0
3	4-PhC <sub>6</sub> H <sub>4</sub>	H	Br	1	0.5	65	0
4	4-PhC <sub>6</sub> H <sub>4</sub>	H	Br	1	0	0	89
5	Ph	H	Br	1	0.5	60	0
6	4-ClC <sub>6</sub> H <sub>4</sub>	H	Br	1	0.5	26	27 <sup>a</sup>
7	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	H	Br	1	0.5	0	16
8	2-naphthyl	H	Br	1	1	74	0
9	2-naphthyl	H	Br	1	0	0	95
10	2-thienyl	H	Br	0.25	0.5 <sup>b</sup>	72	0
11	2-thienyl	H	Br	1	0	0	76
12	3-thienyl	H	Br	1	0.5	61	0
13	3-thienyl	H	Br	1	0	0	83
14	Ph	Me	Br	24	0	98	0
15	Ph	Me	Cl	1	0.5	71	0
16	Ph	Me	Cl	0.25	0	0	90 <sup>c</sup>
17	Ph	Ph	Cl	1	0	86	0

<sup>a</sup> 2-(*p*-Chlorophenyl)pent-4-enal (ca. 10% yield) was obtained as a side product (see ¶). <sup>b</sup> 50 °C. <sup>c</sup> Isomeric ratio = 61 : 39.

**3** were effectively obtained.‡ The aryl rearrangement often required high temperature conditions (80 °C) because homoallyl alcohols **4** were formed exclusively at 25 °C (entries 4, 9, 11, 13 and 16). This result suggests that the reaction includes the intermediate **A** illustrated in Scheme 2. The effect of different aromatic substituents was interesting. Generally, the allylation of aryl-substituted carbonyls is enhanced by an electron-withdrawing group on the aromatic substituents since the electrophilicity of the carbonyl group is increased. The opposite effect was observed in entries 1–3 and 5–7 in regard to the synthesis of **3**. The unrearranged products **4** were observed in the reaction with the substrates bearing chloro or nitro groups (entries 6 and 7). These substituent effects are explainable by the rate-determining migration of the aryl groups,<sup>9</sup> as the allyltin(II) species have an adequate ability to promote carbonyl allylation.<sup>2</sup> The thienyl ring is tolerated in this reaction system (entries 10–13), in which sulfur did not reduce the activity of the tin(II) reagent at all. The secondary bromo or chloro ketones also gave **3** exclusively (entries 14, 15 and 17). The rearrangement took place readily without the need for high temperatures (entries 14 and 17). The interaction of tin(II) with the halogen (in **A**) would generate cationic halide carbon species, which are more stable for secondary substrates.

On the other hand,  $\alpha$ -halogenated alkyl ketones showed a different reaction course, without any rearrangement; allyloxazolines were formed by the addition of solvent nitriles to the tin alkoxide intermediate, albeit in low yields.§

This work describes a new allylation system for the synthesis of  $\beta,\gamma$ -unsaturated carbonyl compounds, in which an unusual reaction course, including aryl rearrangement, is proposed. The selective rearrangement is promoted by the properties of the tin(II) species. Further investigation of allylic tin(II) species is in progress.

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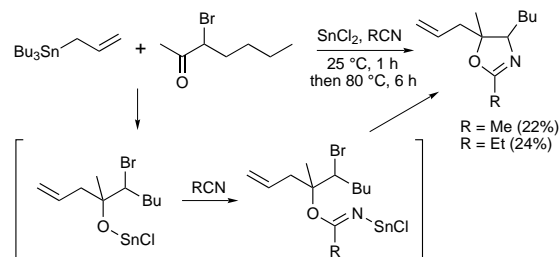
## Notes and References

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‡ Typical experimental procedure: Allyltributyltin **1** (1.0 mmol) was added to a stirred suspension of SnCl<sub>2</sub> (1.0 mmol) and  $\alpha$ -halo ketone **2** (1.0 mmol)

in dry MeCN (1.0 ml), and the mixture was stirred under the conditions noted in the text. Et<sub>2</sub>O (100 ml) and aq. NH<sub>4</sub>F (15%; 40 ml) were added, the organic layer was separated and washed with water (50 ml  $\times$  2), dried (MgSO<sub>4</sub>) and evaporated to give  $\beta,\gamma$ -unsaturated ketone **3**. The crude product was further purified by flash chromatography on silica gel.

§ Since the alkyl group has a low aptitude for migration, reaction of the intermediate with the solvent nitrile occurred.



¶ The aldehyde, 2-(*p*-chlorophenyl)pent-4-enal, was formed *via* 2-allyl-2-(*p*-chlorophenyl)oxirane. The transformation of oxirane to aldehyde commonly proceeds in acidic conditions.

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