Simple Synthetic Method of Allyl- and Vinyl-Epoxides by Allylation of Carbonyl Groups with Allylic Tins Catalyzed by PbI_2-HMPA

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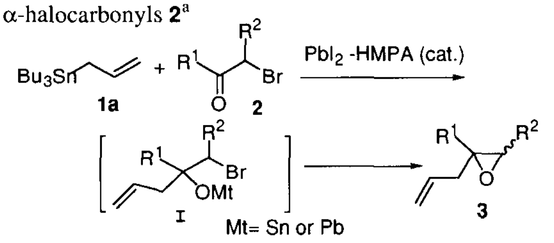
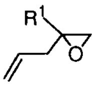
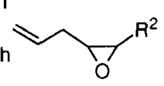
Allyl epoxides were prepared by the chemoseletive allylation at the carbonyl groups of α-bromo ketones with allylic tin, where PbI_2-HMPA effected as a chemoselective catalyst. Moreover, vinyl epoxides were obtained in one pot procedure by the PbI_2-HMPA catalyzed reaction of γ-chloroallyltri-*n*-butyltin with aldehydes. Because of the mildness of the catalyst, the formed epoxide functionalities were not decomposed.

Allylic tins are good candidates for the carbonyl-selective allylations because of its easy handling, and moderate reactivity.[1] However, allyltri-*n*-butyltin generally requires strong Lewis acids such as $SnCl_4$, and BF_3·OEt to perform effective allylations of carbonyl compounds.[2] Recently, milder activators such as Bu_2SnCl_2[3] and $InCl_3$[4] have been developed. However, these conventional activators requires stoichiometric amounts and can not be used yet for the bifunctional carbonyl compounds such as epoxy ketones because of the further transformation and decomposition of the products.[5] Based on these background, we have reported PbI_2-HMPA as a novel catalyst for the allylation of α,β–epoxy ketones.[6] The characteristic feature of PbI_2-HMPA is its mild and neutral catalytic activity. Namely, highly chemoselective reaction toward the carbonyls was established without decomposing epoxides. Beside the above competitive reaction, PbI_2-HMPA would be a good catalyst to generate labile epoxides. We present here the PbI_2-HMPA catalyzed carbonyl-allylation in α-halo ketones without affecting reactive halides to achieve one-pot preparation of allyl epoxides. Moreover, we could found a simple and effective method to prepare vinyl epoxides by the reaction using γ-chloroallyltin.

Table 1. Synthesis of allyl epoxides **3** from **1a** and α-halocarbonyls **2**[a]

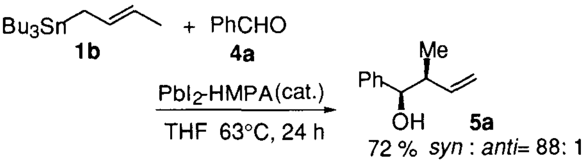


Entry	R^1	R^2		Conditions	Product **3**		Yield /%
1	Ph	H	**2a**	40°C, 24 h		**3a**	96
2	*p*-Tol	H	**2b**	"		**3b**	66
3	*p*-ClC_6H_4	H	**2c**	"		**3c**	67
4	*p*-$NO_2C_6H_4$	H	**2d**	rt, 24 h		**3d**	77
5	Me	H	**2e**	40°C, 24 h		**3e**	43
6	H	C_5H_{11}	**2f**	63°C, 24 h		**3f**	63[b]

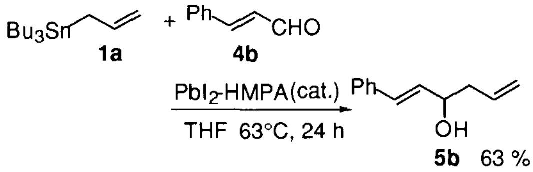
[a] **1** 1 mmol, **2** 1 mmol, PbI_2 0.1 mmol, HMPA 0.2 mmol, THF 1 mL, 40°C, 24 h, [b] *cis*:*trans*= 19:81.

Initially, we prepared allyl epoxides by the PbI_2-HMPA catalyzed allylation of bifunctional substrates such as α-bromo ketones **2** (Table 1). The reaction of **1a** with α-bromoacetophenone **2a** proceeded in good yield (entry 1).[7] Allyl epoxide **3a** was formed by the cyclization of the adduct I. Namely, the allylation took place chemoselectively at the carbonyl group without affecting the bromide moiety. Under the same conditions, aryl, allyl-substituted epoxides **3b**-**3d** were obtained selectively (entries 2-4). Epoxides were formed in one pot reaction. The bromohydrines derived from I were not isolated. Aliphatic ketone **2e** was also reactive to give **3e** (entry 5). In the case of α-halo aldehyde **2f**, internal epoxide **3f** was obtained (entry 6). The carbonyl-selectivity of PbI_2-HMPA catalyzed allylation is sharp contrast to the reaction under radical conditions where the allylation at halide moiety of **2** takes place.[8] As to the allylation to carbonyls, it has been carried out by using palladium catalyst.[8,9] PbI_2-HMPA was employed as an effective catalyst in place of expensive transition metals.

The reaction of γ-halo allyltin **1c** with aldehydes is suitable for the preparation of epoxides because remaining halogen functionality played a role for the cyclization. For the purpose, it is necessary that the C-C bond formation must take place at the halogen bonded carbon of **1c** to form halohydrin derivatives. Prior to use this tin reagent, we examined the basic reactivity of PbI_2-HMPA catalyzed allylation. (*E*)-Crotyl tributyltin **1b** afforded S_E2' allylation with PhCHO **4a** to give α-methyl homoallyl alcohol **5a** with high *syn*-selectivity. (eq. 1). This *syn*-selectivity suggests that the allylation proceeded *via* acyclic antiperiplanar transition state.[2b] In the reaction of allyltributyltin **1a** with unsaturated aldehyde **4b**, regioselective 1, 2-addition took place to give **5b** (eq. 2)



(1)

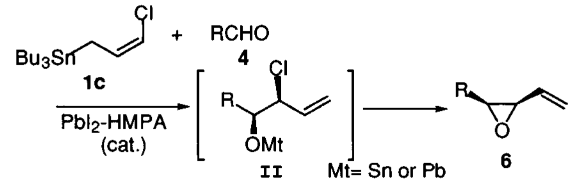


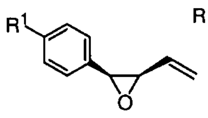
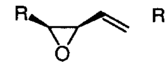
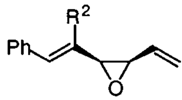
(2)

These high regio- and stereoselective reactions could be applied to the preparation of functionalized epoxides using γ-chloro allylic tin **1c** (Table 2).[10] For example, the reaction with **4a** gave *cis*-vinyl phenyl epoxide **6a** selectively (entry 1). Similar to the case of crotyltin **1b**, the reaction proceeded by S_E2' reaction.

Subsequently, the formed chlorohydrin intermediate II resulted in the immediate cyclization to give **6a**. The formed epoxide ring was not decomposed by the catalyst.

Table 2. Synthesis of vinyl epoxides **6** from γ-chloro allyltin **1c** and aldehydes **4**[a]

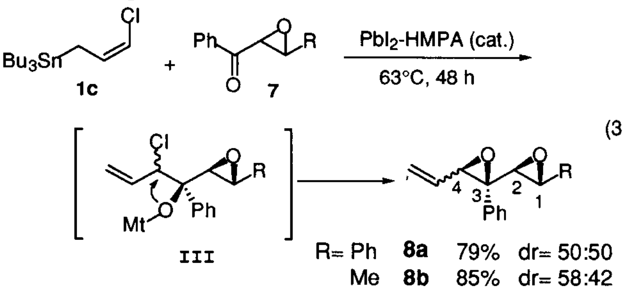


Entry	Aldehyde 4 R		Product 6			Yield /%
1	Ph	**4a**		R^1= H	**6a**	58
2	*p*-ClC$_6$H$_4$	**4c**		Cl	**6b**	65
3	*p*-NO$_2$C$_6$H$_4$	**4d**		NO$_2$	**6c**	67
4	*p*-CNC$_6$H$_4$	**4e**		CN	**6d**	69
5	*n*-C$_6$H$_{13}$	**4f**		R= *n*-C$_6$H$_{13}$	**6e**	27
6	c-Hexyl	**4g**		c-Hexyl	**6f**	14
7	PhCH=CCl	**4h**		R^2= Cl	**6g**	67
8	PhCH=CBr	**4i**		Br	**6h**	59

[a] **1c** 1 mmol, **4** 1 mmol, PbI$_2$ 0.1 mmol, HMPA 0.2 mmol, THF 1mL, 63°C, 24 h.

Other aromatic aldehydes, **4c**-**4e**, were also reactive to give aryl vinyl epoxides **6b**-**6d** (entries 2-4). These reactions proceeded with high stereoselectivity because epoxides obtained were *cis*-isomers. Aliphatic aldehydes, **4f** and **4g**, also gave vinyl epoxides, **6e** and **6f**, although these substrates were less reactive compared with aromatic ones (entries 5 and 6). Divinyl substituted epoxides, **6g** and **6h**, were obtained selectively by the initial 1, 2-addition of unsaturated aldehydes, **4h** and **4i** (entries 7 and 8).

From the results of Table 1 and 2, PbI$_2$-HMPA act as a effective catalyst for the allylation of carbonyl groups without decomposition of the generated epoxide functionalities. Probably, only carbonyl groups were activated because of the relatively low activity of the catalyst. PbI$_2$-HMPA was the best choice in the case to form labile functionalities such as epoxide rings. The high chemoselective reaction enabled the preparation of diepoxides, **8a** and **8b**, by the reaction between **1c** and epoxy ketones **7** (eq. 3).



(3)

In the products **8**, the relationship between C2 and C3 was stereoselective because the chelation controlled reaction proceeded,[6] however the selectivity between C3 and C4 was not so good compared with the reaction of aldehydes.[11]

Although the correct mechanism how lead iodide complex works is not clear as yet, it seems that the catalyst acts as a mild Lewis acid or the tansmetallation occurred with allyltins.

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References and Notes

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2 For example, a) G. E. Keck, S. Castellio, and M. B. Andrus, "Selectivities in Lewis Acid Promoted Reactions," Kluwer Acad. Pub., Dordrecht (1988), p. 73. b) Y. Nishigaichi, A. Takuwa, Y. Naruta, and K. Maruyama, *Tetrahedron*, **49**, 7395 (1993). c) J. A. Marshall, *Chem. Rev.*, **96**, 31 (1996). d) J. S. Carey, T. S. Coulter, D. J. Hallett, R. J. Maguire, A. H. McNeill, S. J. Stanway, A. Teerawutgulrag, and E. J. Thomas, *Pure & Appl. Chem.*, **68**, 707 (1996).

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5 For example, tin halide complexes bears high nucleophilicity toward epoxide rings. a) I. Shibata, A. Baba, H. Iwasaki, and H. Matsuda, *J. Org. Chem.*, **51**, 2177 (1986). b) I. Shibata, A. Baba, and H. Matsuda, *Tetrahedron Lett.*, **26**, 3021 (1986).

6 I. Shibata, S. Fukuoka, and A. Baba*J. Org. Chem.*, **62**, 3790 (1997).

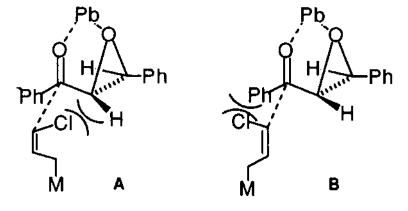
7 Representative procedure for the reaction between **1a** and **2a** in the presence of PbI$_2$-HMPA is as follows. In THF (1 mL) solution, PbI$_2$ (0.1 mmol) and HMPA (0.2 mmol) were added. After stirring for 10 min, the yellow solid of PbI$_2$ was dissolved to give a pale yellow solution. To the solution were added **1a** and **2a**. The mixture was stirred at 40°C for 24 h. Volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with hexane-EtOAc (9:1) to give almost pure product **3a**. Further purification was performed by TLC eluting with hexane-Et$_2$O (9:1).

8 M. Kosugi, H. Arai, A. Yoshino, and T. Migita, *Chem. Lett.*, **1978**, 795.

9 I. Pri-Bar, P. S. Pearlman, and J. K. Stille, *J. Org. Chem.*, **48**, 4629 (1983).

10 The synthesis of vinyl epoxides from γ-chloro allyltin derived from Sn(II) reagents has been reported, where both *cis* and*trans* isomers were formed. a) J. Auge and S. David, *Tetrahedron Lett.*, **37**, 4009 (1983). b) J. Auge and G. Bourleaux, *J. Organomet. Chem.*, **377**, 205 (1989).

11 In the acyclic antiperiplanar transition state, there would be no difference of steric effects between **A** and **B** (Scheme 1).



Scheme 1.