Communications

Lead Iodide−HMPA as a Novel Catalyst for Chemo- and Diastereoselective Carbonyl Allylation of α,*β*-Epoxy Ketones with Allylic Stannanes

Ikuya Shibata, Shoji Fukuoka, Naritoshi Yoshimura,
Haruo Matsuda,[†] and Akio Baba*

Department of Applied Chemistry, Faculty of Engineering,
Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan

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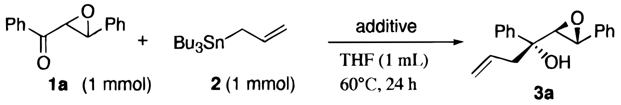
Chemo- and stereoselective allylation of multifunctional compounds is one of the most fundamental subjects for the construction of complex molecules. Allyltri-*n*-butyltin is a good candidate for the purpose because of easy handling and moderate reactivity compared with conventional allylmetals such as Grignard and lithium reagents.[1] In general, allyltri-*n*-butyltin requires some activation methods to perform effective allylations of carbonyl compounds. In some cases, stereoselective reactions are established in the presence of strong Lewis acids such as titanium chlorides, $SnCl_4$, and $BF_3{\cdot}OEt$.[2] Recently, milder activators such as Bu_2SnCl_2[3] and $InCl_3$[4] have been developed. However, these conventional Lewis acids cannot be used yet in the chemoselective allylation of carbonyl compounds bearing other reactive functional groups because of the further transformation and decomposition of the products.

Little attention has been paid to the chemoselective Lewis acid-promoted carbonyl allylation of α,*β*-epoxy ketones because epoxides are susceptible to acidic conditions. In fact, the reaction of **1a** with allyltributyltin (**2**) in the presence of $BF_3{\cdot}OEt_2$ at −78 °C afforded a complex mixture, where the desirable products allylated at carbonyl moiety were not detected at all. Here we found that a lead(II) iodide system is a good catalyst for the allylation of α,*β*-epoxy ketones only at the carbonyl group under mild and neutral conditions. This is the first chemo- and diastereoselective allylation of α,*β*-epoxy ketones.

The efficiency of lead iodide systems is indicated in Table 1. In the reaction of chalcone oxide **1a** with allyltributyltin (**2**) at 60 °C for 24 h, no addition proceeded without any additives, where both substrates, **1a** and **2**, were recovered quantitatively (Table 1, entry 1). In contrast, under the same conditions, a high yield of allylated product **3a** was obtained when PbI_2 and HMPA were added to the reaction mixture (Table 1, entry 4). Of importance is the necessity of combination of PbI_2 and HMPA. The sole use of PbI_2 or HMPA did not promote the reaction at all (Table 1, entries 2 and 3). It is noted that the reaction proceeded with only a catalytic amount of PbI_2 (0.1 equiv)−HMPA (0.2 equiv).[5] HMPA was the additive of choice since DMF, DMSO, or diphenylphosphinoethane (DPPE) gave lower yields (Table 1, entries 5−7). Instead of PbI_2, the use of $PbCl_2$ did not exhibit catalytic activity at all (Table 1, entry 8). Although organolead(IV) iodides, Ph_3PbI and Ph_2PbI_2, also afforded **3a** selectively, the yields were not as good compared with PbI_2 (Table 1, entries 9 and 10). In this way, the PbI_2−HMPA complex was employed as a most effective catalyst for the chemoselective allylation of epoxy ketones **1**.[6]

Table 1. Carbonyl Selective Allylation of 1a



entry	additive (equiv)	yield of **3a** (%)	entry	additive (equiv)	yield of **3a** (%)
1	none	0	6	PbI_2 (0.1), DMSO (0.2)	78
2	HMPA (0.2)	0	7	PbI_2 (0.1), DPPE (0.1)	57
3	PbI_2 (0.1)	trace	8	$PbCl_2$ (0.1), HMPA (0.2)	0
4	PbI_2 (0.1), HMPA (0.2)	100	9	Ph_3PbI (0.1), HMPA (0.2)	79
5	PbI_2 (0.1), DMF (0.2)	34	10	Ph_2PbI_2 (0.1), HMPA (0.2)	28

By using PbI_2−HMPA as a catalyst, various epoxy ketones could be allylated at the carbonyl group as shown in Table 2. Similar to **1a**, aromatic epoxy ketone **1b** also gave **3b** in a quantitative yield (Table 2, entry 1). Although alkyl ketones **1c** and **1d** showed only moderate reactivity at 60 °C, the reaction proceeded carbonyl selectively to give **3c** and **3d** (Table 2, entries 2 and 4).[7] The use of diallyldi-*n*-butyltin (**4**) instead of **2** increased the yield of **3c** and **3d** up to 77% and 73% yield, respectively, even at room temperature (Table 2, entries 3 and 5). In particular, the carbonyl-selective allylation of **1e** is remarkable because terminal epoxide ring is much more readily opened (Table 2, entry 6).[8]

Another noteworthy feature of PbI_2−HMPA-catalyzed allylation is that the reactions proceeded with a high

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[†] Present address: Department of Applied Chemistry, Osaka Institute of Technology, 5-16-1 Omiya, Asahi, Osaka 535, Japan.

(1) A recent review: (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (b) Pereyre, M.; Quintard J. P; Rahm, A. *Tin in Organic Synthesis*; Butterworth, London, 1987. (c) Wardell, J. I. In *Chemistry of Tin*; Harrison, P. G., Ed.; Blackie: Glasgow, 1989; pp 315−358. (d) Omae, I. *Organotin Chemistry*; Elsevier: Amsterdam, 1989.

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

(3) Yano, K.; Baba, A.; Matsuda, H. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 66.

(4) (a) Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *36*, 9497. (b) Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1996**, *61*, 105. (c) Yasuda, M.; Miyai, T.; Shibata, I.; Baba, A.; Nomura, R.; Matsuda, H. *Tetrahedron Lett.* **1995**, *36*, 9497.

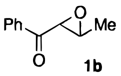
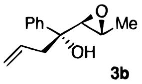
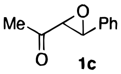
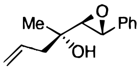
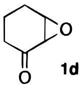
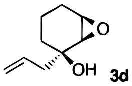
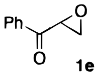
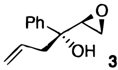
(5) The use of PbI_2 (0.1 equiv)−HMPA (0.1 equiv) gave **3a** in lower yield (63%).

(6) Representative procedure for the reaction between **1a** and allyltributyltin (**2**) 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 the mixture was stirred for 10 min, the yellow solid of PbI_2 was dissolved to give a pale yellow solution. To the mixture was added **1a** and **2**. The mixture was stirred under reflux conditions for 24 h. After the mixture was quenched with MeOH (5 mL), 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 of **3a** was performed by TLC, eluting with hexane−Et_2O (9:1). Care must be taken in the handling of tin, lead reagents, and HMPA because of their toxity.

(7) Instead of the lead iodide, a tin halide did not afford carbonyl-selective reaction. Thus, an equimolar amount of Bu_2SnI_2-HMPA caused double allylation at the carbonyl and epoxide groups of **1d**. This is because of the nucleophilicity of the Sn−I bond toward epoxide rings. Shibata, I.; Baba, A.; Iwasaki, H., Matsuda, H. *J. Org. Chem.* **1986**. *51*, 2177.

S0022-3263(97)00242-9 CCC: $14.00

Table 2. Chemo- and Diastereoselective Allylation of Epoxy Ketones

entry	substrate (**1**)	allylic tin	product (**3**)	yield (%)
1	 **1b**	**2**	 **3b**	99[a), c)]
2	 **1c**	**2**	 **3c**	32[d)]
3		**4**		77[b),d)]
4	 **1d**	**2**	 **3d**	18[a)]
5		**4**		73[b), c)]
6	 **1e**	**4**	 **3e**	56[b), c)]

[a] Conditions: **1** (1 mmol), allyltributyltin (**2**) (1 mmol), PbI_2 (0.1 mmol), HMPA (0.2 mmol), THF (1 mL), 60 °C, 24 h. [b] Conditions: **1** (1 mmol), diallyldibutyltin (**4**) (1 mmol), PbI_2 (0.1 mmol), HMPA (0.2 mmol), THF 1 mL, rt, 24 h. [c] Diastereomer ratio = >99:<1. [d] Diastereomer ratio = 87:13.

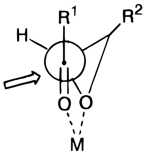


Figure 1.

diastereoselectivity. Almost all products except **3c** were obtained as single diastereoisomers with the *anti* relationship between the hydroxy and epoxy groups.[9] From this stereochemical outcome, it is assumed that the reaction proceeds *via* Cram's chelation model (Figure 1). Although the correct mechanism of how lead iodide complex works is not yet clear, it seems that the catalyst acts as a mild Lewis acid or the metal exchange occurred with allylic tins.

In summary, PbI_2−HMPA is an effective catalyst for the allylation with allylic tins. This catalyst can be used under mild conditions; hence, carbonyl-selective allylation can be performed in various epoxy ketones. Further use of this catalyst and detailed mechanism is under investigation.

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Supporting Information Available: Experimental procedures and ^1H and ^{13}C NMR data of products **3a**−**e** (12 pages).

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(8) The structures of crystalline products **3a** and **3b** were indicated by X-ray analysis. The author has deposited atomic coordinates for **3a**,**b** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(9) For example: (a) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323. (b) Smith, J. G. *Synthesis* **1984**, 629.