Direct coupling of alcohols with alkenylsilanes catalyzed by indium trichloride or bismuth tribromide†

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Indium halides or bismuth halides catalyzed the coupling of various alcohols with alkenylsilanes to give the corresponding alkenes stereospecifically without any other activators.

Although a carbon–carbon bond formation using an alcohol as a coupling partner might be fascinating in organic chemistry, the system is much more difficult than that using other partners such as organic halides because of the poor leaving ability of the hydroxy group. The use of alcohols, which are plentiful and inexpensive compounds, can have advantages over the use of the corresponding organic halides, and the establishment of this reaction system has been a long-cherished dream of organic chemists. Many groups, including our's, have recently reported the coupling of alcohols with various metallic nucleophiles such as allyl, alkynyl, aryl, allenyl and propargyl ones.[1,2] However, the catalytic coupling with alkenyl nucleophiles has been limited to the transition metal-catalyzed reaction of allylic alcohols based on a π-allylic species as a key intermediate.[3,4] Although Kabalka reported the coupling of non-allylic alcohols with vinylboron dihalides in terms of intramolecular rearrangement,[5] an equimolar amount of strong base (BuLi) was required. Here, we report the first practical example of direct catalytic coupling of alcohols including alkyl, benzylic and allylic ones with alkenylsilanes.

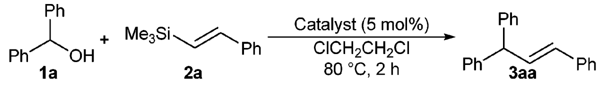
Coupling reaction of benzhydrol **1a** with (*E*)-2-phenyl-1-trimethylsilylethylene **2a** was carried out as a model reaction in the presence of 5 mol% of various Lewis acids (Table 1). No reaction took place when a catalyst was not loaded (Entry 1). We have recently developed the indium-catalyzed reactions of alcohols with various nucleophiles such as silyl compounds and 1,3-dicarbonyls,[1,6,7] and thus $InCl_3$ was examined to give the alkenyl product **3aa** in an excellent yield with complete *E*-selectivity (Entry 2). $InBr_3$ gave a lower yield of 85% (Entry 3). It was found that bismuth trihalide, which has been recently used as a Lewis acid,[8,9] also worked well (Entries 4 and 5) and that $BiBr_3$ showed a higher catalytic activity than $BiCl_3$. Other Lewis acids such as $BF_3{\cdot}OEt_2$, $AlCl_3$, $TiCl_4$, $Sc(OTf)_3$ and $Yb(OTf)_3$ afforded low yields (Entries 6–10).

In the presence of either $InCl_3$ or $BiBr_3$, various alcohols **1** were treated with (*E*)-2-phenyl-1-trimethylsilylethylene **2a**, and the results are summarized in Table 2. $InCl_3$ gave higher yields than $BiBr_3$ in most cases. 1-Phenylethanol **1b** and its *para*-substituted derivatives **1c–1e** effectively afforded the desired products (Entries 1–8). Reactions of benzhydrols bearing electron-donating substituents **1f** and **1g** proceeded in excellent yields, whereas *p*-chlorobenzhydrol **1h** gave a moderate yield (Entries 9–14). Although benzyl alcohol gave no product, the *p*-methoxy-substituted one **1i** successfully afforded the corresponding product **3ia** (Entries 15 and 16). In the case of propargyl alcohol **1j**, both $InCl_3$ and $BiBr_3$ gave satisfactory results (Entries 17 and 18). Allylic hydroxy groups were also substituted to give the products **3ka** and **3la** in high yields (Entries 19–22). A simple aliphatic alcohol was not applicable.[10] Adamantanol **1m**, however, produced the alkenyl adamantane **3ma** (Entries 23–24).

Next, Table 3 shows the scope and limitation of alkenylsilanes for this system. Electron-rich alkenylsilanes **2b** (Ar = 4-$MeOC_6H_4$) and **2c** (Ar = 4-MeC_6H_4) gave only moderate yields (Entries 1, 2, 4 and 5), perhaps because obtained styrene compounds were easily polymerized under the conditions. In contrast, the electron-deficient alkenylsilane **2d** (Ar = 4-ClC_6H_4) afforded satisfactory results (Entries 3 and 6). Unexpectedly, the coupling of *Z*-isomer of alkenylsilane **2e** did not proceed at all, and the starting material **2e** was recovered (Entries 7 and 8). Alkyl-substituted alkenylsilanes were also applicable although yields were somewhat low (Entries 9–14). 2,2-Dimethylalkenylsilane **2f** afforded the trisubstituted olefin in 32% yields along with 22% of isomerized olefin (Entry 9).[11] Interestingly, stereospecific reactions were observed in both of *E*- and *Z*-isomers of 1-trimethylsilyl-1-hexene (**2g** and **2h**), furnishing the corresponding *E*- and *Z*-geometries of coupling products (**3ag** and **3ah**), respectively (Entries 11–14).

A plausible mechanism is shown in Scheme 1. The oxygen atom of the alcohol **1** coordinates to MtX_3 and the R–O bond

Table 1 Effect of catalysts in the coupling reaction of benzhydrol **1a** with (*E*)-2-phenyl-1-trimethylsilylethylene **2a**[a]



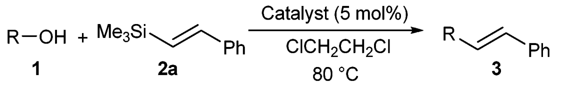
Entry	Catalyst	Yield (%)
1	None	0
2	$InCl_3$	91
3	$InBr_3$	85
4	$BiCl_3$	56
5	$BiBr_3$	82
6	$BF_3{\cdot}OEt_2$	7
7	$AlCl_3$	5
8	$TiCl_4$	20
9	$Sc(OTf)_3$	33
10	$Yb(OTf)_3$	8

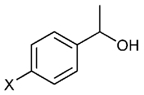
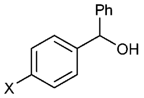
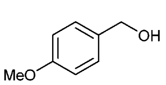
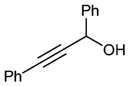
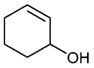
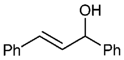
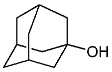
[a] Alcohol: 1 mmol, alkenylsilane: 2 mmol, catalyst: 5 mol%: $ClCH_2CH_2Cl$: 1 mL.

Department of Applied Chemistry, Center for Atomic and Molecular Technologies (CAMT), Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan. E-mail: baba@chem.eng.osaka-u.ac.jp; Fax: +81-6-6879-7387; Tel: +81-6-6879-7386

† Electronic supplementary information (ESI) available: Experimental section. See DOI: 10.1039/b816072d

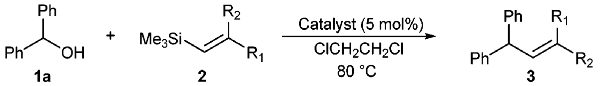
Table 2 Coupling reactions of various alcohols with (*E*)-2-phenyl-1-trimethylsilylethylene **2a**[a]

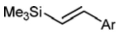
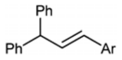
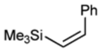
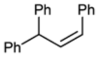
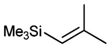
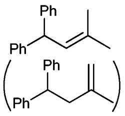
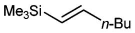
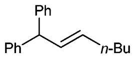
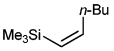
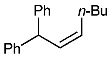


Entry	R–OH	X		Cat.	*t*/h	Product	Yield (%)
1		H	**1b**	$InCl_3$	2	**3ba**	51
2		OMe	**1c**	$InCl_3$	2	**3ca**	68
3		Me	**1d**	$InCl_3$	2	**3da**	79
4		Cl	**1e**	$InCl_3$	2	**3ea**	52
5		H	**1b**	$BiBr_3$	2	**3ba**	43
6		OMe	**1c**	$BiBr_3$	2	**3ca**	63
7		Me	**1d**	$BiBr_3$	2	**3da**	69
8		Cl	**1e**	$BiBr_3$	2	**3ea**	49
9[d]		OMe	**1f**	$InCl_3$	1	**3fa**	87
10[d]		Me	**1g**	$InCl_3$	2	**3ga**	97
11[d]		Cl	**1h**	$InCl_3$	2	**3ha**	57
12[d]		OMe	**1f**	$BiBr_3$	1	**3fa**	78
13[d]		Me	**1g**	$BiBr_3$	2	**3ga**	87
14[b,d]		Cl	**1h**	$BiBr_3$	2.5	**3ha**	59
15			**1i**	$InCl_3$	2	**3ia**	66
16[c]				$BiBr_3$	4		53
17			**1j**	$InCl_3$	2	**3ja**	63
18				$BiBr_3$	2		79
19			**1k**	$InCl_3$	2	**3ka**	46
20				$BiBr_3$	2		42
21[d]			**1l**	$InCl_3$	2	**3la**	57
22[d]				$BiBr_3$	2		60
23[b,d]			**1m**	$InCl_3$	2	**3ma**	57
24[b,d]				$BiBr_3$	6		71

[a] Alcohol: 1 mmol, alkenylsilane: 3 mmol, catalyst: 5 mol%: $ClCH_2CH_2Cl$: 1 mL. [b] PhCl instead of $ClCH_2CH_2Cl$: 1 mL, 130 °C. [c] CH_3CN instead of $ClCH_2CH_2Cl$: 1 mL, 80 °C. [d] Alkenylsilane: 2 mmol.

Table 3 Coupling reactions of benzhydrol **1a** with various alkenylsilanes[a]



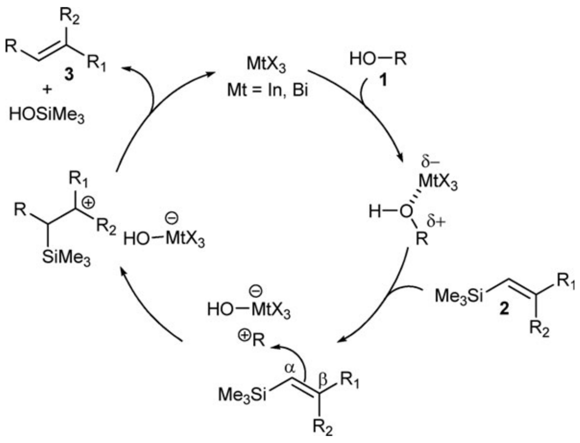
Entry	Alkenylsilane		Cat.	*t*/h	Product		Yield (%)
1		**2b**	$InCl_3$	4		**3ab**	39[b]
2		**2c**	$InCl_3$	2		**3ac**	58
3		**2d**	$InCl_3$	2		**3ad**	85
4		**2b**	$BiBr_3$	2		**3ab**	36[b]
5		**2c**	$BiBr_3$	2		**3ac**	59
6		**2d**	$BiBr_3$	2		**3ad**	82
7		**2e**	$InCl_3$	2		**3ae**	0
8			$BiBr_3$	2			0
9		**2f**	$InCl_3$	1		**3af**	35 (27)[c,d]
10			$BiBr_3$	1.5			29 (11)[c]
11	 (*E*:*Z* = 96:4)	**2g**	$InCl_3$	2		**3ag**	35[e]
12			$BiBr_3$	2			17[e]
13	 (*Z* = >99)	**2h**	$InCl_3$	2		**3ah**	26
14			$BiBr_3$	2			4

[a] Alcohol: 1 mmol, alkenylsilane: 2 mmol, catalyst: 5 mol%: $ClCH_2CH_2Cl$: 1 mL. [b] CH_2Cl_2: 1 mL, rt. [c] The value in the parenthesis indicates the yield of the isomerization product. [d] At 50 °C. [e] Alkenylsilane: 3 mmol.

is activated to increase the positive charge on the R group. Then, the carbocation R^+ is produced,[12] and the α-carbon of alkenylsilane **2** attacks R^+ to generate a cation on the β-carbon, which is stabilized by the silyl group.[13,14] The substituents that can stabilize the cation also effect the formation of **3**, as shown in Table 3. The leaving of the silyl group affords the product **3** along with the regeneration of MtX_3. The characteristic features of $InCl_3$ and $BiBr_3$, such as the stability toward active protons, moderate Lewis acidity and low oxophilicity, synergistically complete the catalytic cycles.

Fig. 1 explains the stereospecificity in the coupling of *E*- and *Z*-isomers of alkenylsilanes. Simultaneously with the addition of carbocation R^+ to the double bond, rotation occurs about the developing carbon–carbon single bond in the direction to permit the silyl group to continuously stabilize the incipient β-cation by hyperconjugation of the Si–C bond. Immediately, the silyl group leaves and the olefin is stereoselectively given.[15] A large steric interaction in the rotation disturbs the coupling, and the reaction of benzhydrol **1a** with (*Z*)-2-phenyl-1-trimethylsilylethylene **2e** gives no product (Table 3, Entries 7 and 8).

Intramolecular cyclization reactions are important for the synthesis of ring skeletons that constitute a part of biological compounds.[16] We demonstrated that our reaction system is



Scheme 1 Plausible mechanism.

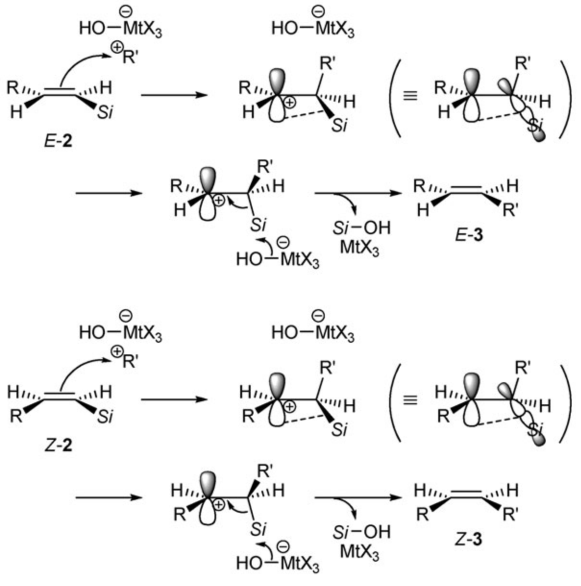
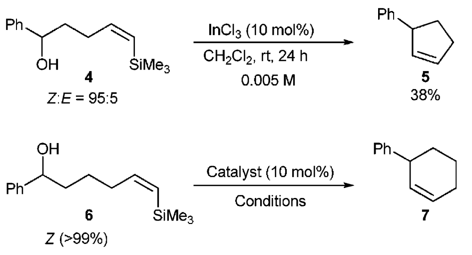


Fig. 1 Stereoselectivity and stereospecificity.



Catalyst	Conditions	**7**
$InCl_3$	CH_2Cl_2 (0.01 M), rt, 6 h	85%
$BiBr_3$	CH_2Cl_2 (0.05 M), rt, 24 h	43%

Scheme 2 Intramolecular cyclization reactions.

effective for the intramolecular coupling shown in Scheme 2. Under dilution conditions, $InCl_3$-catalyzed intramolecular cyclization of alkenylsilanes **4** and **6** gave the five- and six-membered ring compounds **5** and **7** in 38 and 85% yields, respectively. Unfortunately, $BiBr_3$ did not work under the dilution conditions, and only a 43% yield of **7** was achieved. These results indicate that $InCl_3$ has catalytic activity that is higher than that of $BiBr_3$.

In summary, we have accomplished stereospecific direct coupling of alcohols with alkenylsilanes catalyzed by either $InCl_3$ or $BiBr_3$. Various alcohols and alkenylsilanes including aromatic- and alkyl-substituted ones were successfully employed in this reaction system, and its application to intramolecular coupling gave five- or six-membered ring compounds. The details of the mechanism for this reaction are under further investigation.

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6 M. Yasuda, T. Somyo and A. Baba, *Angew. Chem., Int. Ed.*, 2006, **45**, 793.

7 For the selected review, see: G.-L. Chua and T.-P. Loh, in *Acid Catalysis in Modern Organic Synthesis*, eds. H. Yamamoto and K Ishihara, Wiley-VCH, Weinheim, 2008, vol. 1, ch. 8, pp. 377–468.

8 For selected reviews, see: (*a*) H. Gaspard-Ilangovan, in *Acid Catalysis in Modern Organic Synthesis*, eds. H. Yamamoto and K. Ishihara, Wiley-VCH, Weinheim, 2008, vol. 2, ch. 11, pp. 551–588; (*b*) N. Komatsu, in *Organobismuth Chemistry*, eds. H. Suzuki and Y. Matano, Elsevier, Amsterdam, 2001, ch. 5, pp. 371–440; Recently C–C bond formation reaction using bismuth catalyst as a Lewis acid: (*c*) S. Tanaka, N. Tagashira, K. Chiba, M. Yasuda and A. Baba, *Angew. Chem., Int. Ed.*, 2008, **47**, 6620; (*d*) S. K. De and R. A. Gibbs, *Tetrahedron Lett.*, 2005, **46**, 8345; (*e*) S. Kobayashi, T. Ogino, H. Shimizu, S. Ishikawa, T. Hamada and K. Manabe, *Org. Lett.*, 2005, **7**, 4729; (*f*) P. A. Evans, J. Cui, S. J. Gharpure and R. J. Hinkle, *J. Am. Chem. Soc.*, 2003, **125**, 11456.

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10 *tert*-Butyl alcohol gave no desired product.

11 D. A. Evans and Y. Aye, *J. Am. Chem. Soc.*, 2006, **128**, 11034.

12 The coupling reaction of (*R*)-(+)-phenylethanol (*R*)-**1b** (Tokyo Chemical Industry Co., Ltd.) with (*E*)-2-phenyl-1-trimethylsilylethylene **2a** in the presence of either $InCl_3$ or $BiBr_3$ gave the racemic product **3ba** in $<1\%$ ee. See ESI† for experimental details.

13 The result of the reaction using **2e** (Table 3, Entries 7 and 8) was additionally explained that the intermediate cation was unstable because the sp^2 plane of the cation and the benzene ring are noncoplanar and the cation dose not conjugate the phenyl group due to the steric hindrance between the silyl and the phenyl group.

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16 (*a*) K. Miura and A. Hosomi, *Synlett*, 2003, 143; (*b*) E. Langkopf and D. Schinzer, *Chem. Rev.*, 1995, **95**, 1375; (*c*) T. A. Blumenkopf and L. E. Overman, *Chem. Rev.*, 1986, **86**, 857.