

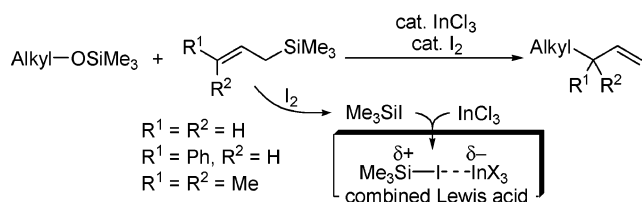
InCl₃/I₂-Catalyzed Cross-Coupling of Alkyl Trimethylsilyl Ethers and Allylsilanes via an in Situ Derived Combined Lewis Acid of InCl₃ and Me₃SiI

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Direct C_{sp3}–C_{sp3} coupling of various aliphatic trimethylsilyl ethers and allylsilanes is effectively catalyzed by InCl₃ and I₂. The transformation is thought to involve an in situ-derived combined Lewis acid of InCl₃ and Me₃SiI. The reaction can be used for the construction of quaternary–quaternary and quaternary–tertiary carbon–carbon bonds. This system enabled a highly chemoselective coupling to be conducted with a trimethylsilyl ether including an aryl halide moiety. Furthermore, couplings were possible using an alkynyltrimethylsilane and a trimethylsilyl ketene acetal.

Metal-catalyzed cross-coupling is one of the most important carbon–carbon bond-forming reactions in organic synthesis, and its application to the use of inexpensive and readily available substrates, such as alcohols¹ and their derivatives, is of current interest. However, this is a considerable challenge due to the strength of RC–OR' bond and the poor leaving ability of the OR' component. Recently, Gevorgyan et al.² demonstrated that a strong Lewis acid like B(C₆F₅)₃ promoted the substitution of the acetoxy group with carbon nucleophiles in high yield and the substitution of the hydroxyl group in low yield, but the siloxy group was not examined (Figure 1). Furthermore, Cho et al.³ reported that InBr₃ itself also promoted the substitution of the acetoxy group, but not the hydroxyl group. The leaving ability is generally arranged in the following order: OAc > OH ≫ OSiMe₃. However, direct substitution of siloxy groups, which are widely utilized as protecting groups, would be a very

	OR		
catalyst	OSiMe ₃	OH	OAc
B(C ₆ F ₅) ₃ (ref. 2)	0%	15–20%	96%
InBr ₃ (ref. 3)	–	0%	38% (95% at 40 °C)
In/Si Combined Lewis Acid This Study		77%	trace

FIGURE 1. Reverse of reactivity order.

important transformation protocol.⁴ Such a method would circumvent the need for deprotection of silyl-derivatized hydroxyls and their subsequent transformation into good leaving groups, such as halides and esters, in preparation for coupling. As noted in Figure 1, our combined system involving indium and silicon reversed the reactivity order of acetoxy and hydroxyl moieties.⁵ In view of this situation, our group focused on the direct substitution of siloxy moiety.

A few direct couplings between silyl ethers and allylic silanes which have been catalyzed by such the Lewis acids as Ph₃CCl/NaTFPB⁶ and Ti–fluoride complex have been reported.⁷ However, these elaborately prepared Lewis acid catalysts are limited to the coupling with benzylic silyl ethers or silyl acetals that form very stable carbocations. The coupling reaction promoted readily by ZnCl₂ has been reported, but is also limited to the allylic silyl ethers.⁸ Simple tertiary aliphatic silyl ethers have not been used in such couplings⁹ but would be of considerable value in the construction of quaternary carbon centers. Moreover, only a few reports of C_{sp3}–C_{sp3} coupling via simple tertiary aliphatic organic halides are known,¹⁰ given their tendency to undergo the β-elimination.¹¹ In this paper, we wish to report the cross-coupling reaction of simple tertiary aliphatic silyl ethers and allylsilanes catalyzed by InCl₃ and I₂ via a putative, in situ-derived combined Lewis acid of InCl₃ and Me₃SiI. Our system is very convenient and characteristically works just when the both components are combined, while each of them separately has no activity.

We have previously reported the direct allylation of alcohols effectively catalyzed by the combined Lewis acid system of InCl₃/Me₃SiBr.⁵ We therefore tried to apply the system to the direct allylation of the simple tertiary aliphatic silyl ether **1a**

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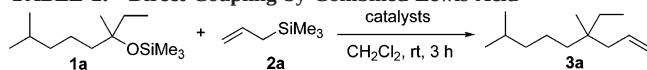
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TABLE 1. Direct Coupling by Combined Lewis Acid^a

entry	catalyst (mol %)	yield (%)
1	InCl ₃ (5) + Me ₃ SiCl (20)	32
2	InCl ₃ (5) + Me ₃ SiBr (20)	34
3	InCl ₃ (5) + Me ₃ SiI (20)	61
4	InCl ₃ (5) + I ₂ (20)	76
5	I ₂ (20) or Me ₃ SiI (20)	0
6	InCl ₃ (5)	0
7	AlCl ₃ (5) + I ₂ (20)	0
8	B(C ₆ F ₅) ₃ (5) + I ₂ (20)	0
9	ZnCl ₂ (5) + I ₂ (20)	27
10	Yb(OTf) ₃ (5) + I ₂ (20)	26

^a All reactions were carried out in dichloromethane (1 mL) with allylsilane **2a** (3.0 mmol) and silyl ether **1a** (1.0 mmol) at rt.

with allylsilane **2a**, and the desired product **3a** was obtained in only 34% yield (Table 1, entry 2). Using a combination of InCl₃/Me₃SiI, which represents stronger Lewis acidity,^{5a} increased the yield up to 61% at room temperature in dichloromethane (entry 3). The highest yield (76%) was obtained by means of the combination of InCl₃ and I₂, where Me₃SiI is presumably generated in situ from I₂ and allylsilane **2a** (entry 4).¹² The sole use of InCl₃ or Me₃SiI showed no activity (entries 5 and 6). Representative Lewis acids such as AlCl₃ and B(C₆F₅)₃ were ineffective, even in the presence of I₂ (entries 7 and 8). Interestingly, the milder acids, ZnCl₂ and Yb(OTf)₃,¹³ gave the desired product in low yields (entries 9 and 10).

Direct coupling of a variety of silyl ethers **1** with allylsilanes **2** was investigated under the optimized conditions (Table 2).

The cyclic tertiary silyl ether **1b** was allylated in good yield (entry 1). The transformation of adamantyl silyl ether **1c** into the desired product **3c** proceeded in 77% yield at 70 °C (entry 2). In the case of secondary ethers, norbornyl and benzylic systems were easily allylated, and the former gave the product **3d** as a single isomer (entries 3 and 4). Benzyl silyl ether **1f** was also allylated using the combined Lewis acid system, although simple normal silyl ether **1g** was unreactive (entries 5 and 6). These results strongly suggest that our system proceeds through the S_N1 mechanism including a carbocation. The tertiary aliphatic silyl ether **1h** was transformed to the corresponding coupling products **3h**, **4h**, and **5h** from allyl-, cynamyl-, and prenylsilane in 73, 66, and 81% yields, respectively (entries 7, 8, and 9). The reaction conditions are compatible with phthalimide moiety to give the allylated and prenylated products **3i** and **5i** in moderate yields (entries 10 and 11). The formation of carbon skeletons connecting two quaternary carbons was accomplished by means of the InCl₃/Me₃SiI system (entries 9 and 11). Our system also tolerates the phenolic OH to give the desired product **3j** in 83% yield (entry 12). The silyl ethers bearing chlorine and bromine moieties were transformed to the desired products **3k** and **3l** without affecting the halide moieties (entries 13 and 14).

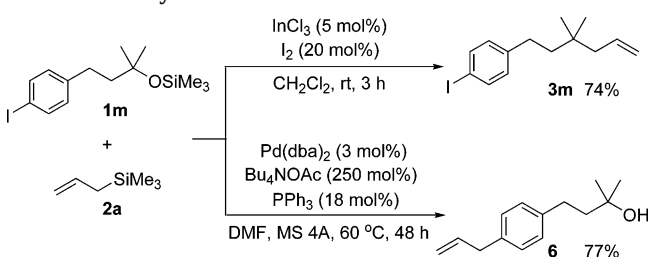
Even when the silyl ether **1m** including the iodine moiety was used, our system selectively provided the siloxy-coupling

TABLE 2. Direct Allylation of Silyl Ethers by InCl₃/Me₃SiI^a

entry	silyl ether	allylsilane	conditions	product	yield (%)
1 ^b		2a	rt, 3 h		70
2 ^c		2a	70 °C, 1 h		77
3		2a	rt, 3 h		90
4		2a	rt, 30 min		88
5 ^d		2a	rt, 1 h		70
6 ^c		2a	70 °C, 1 h		0
7		2a	rt, 3 h		73
8 ^e		2b	rt, 3 h		66
9		2c	rt, 3 h		81
10 ^b		2a	rt, 3 h		58
11 ^b		2c	rt, 3 h		41
12 ^e		2a	rt, 3 h		83
13		2a	0 °C to rt, 3 h		82
14 ^c		2a	50 °C, 3 h		78

^a Reactions were carried out in dichloromethane (1 mL) with silyl ether **1** (1.0 mmol), silyl nucleophile **2** (3.0 mmol), I₂ (0.2 mmol), and InCl₃ (0.05 mmol) at rt unless otherwise stated. ^b Allylsilane (6 mmol). ^c 1,2-Dichloroethane (2 mL) was used as a solvent. ^d Allylsilane (4 mmol). ^e Allylsilane (5 mmol).

SCHEME 1. Chemoselective Allylation toward Iodo-Substituted Silyl Ether



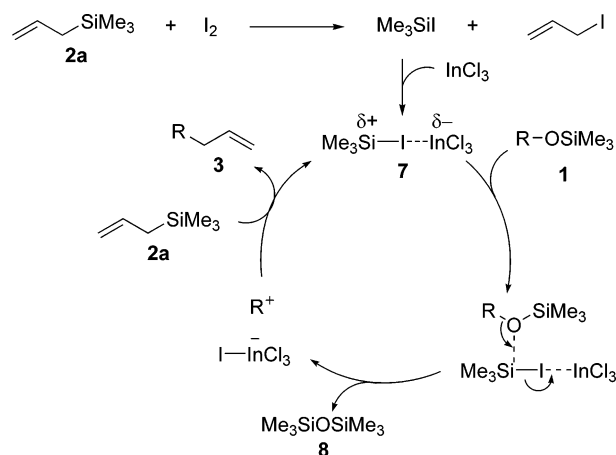
product **3m** in 74% yield (Scheme 1). This transformation was used to compliment allylation to the palladium-catalyzed Hiyama-coupling reaction with the aryl iodide to give **6**.¹⁴

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SCHEME 2. Plausible Mechanism



Scheme 2 proposes a plausible reaction route for the direct coupling between silyl ether **1** and allylsilane **2a** catalyzed by InCl_3/I_2 combined system (Scheme 2). At first, I_2 reacts with **2a** to give Me_3SiI ¹² which generates the combined Lewis acid **7**. The Lewis acidity of the silicon center is enhanced by coordination from iodine to indium trichloride. The C–O bond of **1** is activated by the coordination from the siloxy oxygen to the silicon center of the combined catalyst to form a carbocation and hexamethyldisiloxane (**8**). Then, nucleophilic attack of **2a** on the carbocation gives the coupling product **3** with regeneration of the combined catalyst ($\text{InCl}_3/\text{Me}_3\text{SiI}$). It is noted that the low oxophilicity of the indium species aids in completing the catalytic cycle.^{5,15} If stronger, the promoter species would be trapped by siloxane. The fact that **7** is the true catalyst is supported by the result of the reaction of **1a** with **2a** in the presence of InCl_3 , Me_3SiI and allyl iodide.¹⁶ In contrast to the reaction with alcohols, Me_3SiI is hardly decomposed because of the absence of active proton, and the facile formation of $\text{Me}_3\text{SiOSiMe}_3$ **8** may prevent the β -elimination, as seen for tertiary alcohols or halides.

The benzylic silyl ether **1e** coupled with the allylsilane **2a** in good yield under the mild combined Lewis acid of InCl_3 and Me_3SiBr (Scheme 3). This system can be applied to other types of nucleophiles. The alkynylsilane **2d** gave the product **9** in an α -addition manner. The coupling with trimethylsilyl ketene acetal **2e** smoothly proceeded to afford the desired ester **10** in high yield.¹⁷

In conclusion, we have demonstrated the direct formation of quaternary carbon centers by the direct coupling reaction between tertiary aliphatic silyl ethers and allylsilanes by the catalytic use of the indium-silicon combined system. The system has high chemoselectivity for the coupling with silyl ether moieties in contrast to Pd-catalyzed coupling.

Experimental Section

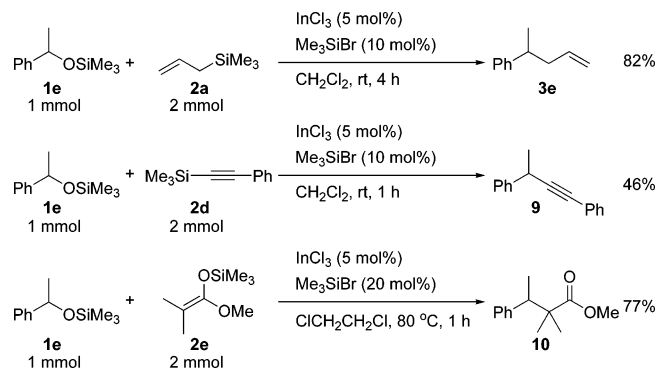
Typical Procedure for Allylation of **1a** (Table 1, Entry 3).

To a suspended solution of InCl_3 (0.05 mmol) and allyltrimethylsilane **2a** (3 mmol) in CH_2Cl_2 (1 mL) was added I_2 (0.2 mmol). To

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(16) The reaction of **1a** (1 mmol) with **2a** (3 mmol) in the presence of InCl_3 (0.05 mmol), Me_3SiI (0.2 mmol), and allyl iodide (0.2 mmol) at room temperature afforded **3a** in 59% yield.

(17) In cases of the alkynylsilane and the silyl enolate, $\text{InCl}_3/\text{Me}_3\text{SiBr}$ system was superior to $\text{InCl}_3/\text{Me}_3\text{SiI}$ system.

SCHEME 3. Direct Coupling by Combined Lewis Acid of $\text{InCl}_3/\text{Me}_3\text{SiBr}$ 

the mixture was added 3,7-dimethyl-3-trimethylsiloxyoctane **1a** (1.0 mmol) at room temperature. The mixture was stirred for 3 h at room temperature and then quenched by saturated NaHCO_3 aq (30 mL). The mixture was extracted with diethyl ether (10×3 mL). The collected organic layer was dried (MgSO_4). The evaporation of the ether solution gave the crude product which was analyzed by NMR. The details of further purification performed for the new compounds are described in the Supporting Information.

Hiyama Cross-Coupling Reaction of **2a** with **1m** (Scheme 1).

A suspended solution of Bu_4NOAc (7.5 mmol) and 4A MS in DMF (6 mmol) was stirred for 1 h. To the stirred solution were added $\text{Pd}(\text{dba})_2$ (0.12 mmol), PPh_3 (0.54 mmol), 4-(4-iodophenyl)-2-methyl-2-trimethylsiloxybutane **1m** (3 mmol), and allyltrimethylsilane **2a** (15 mmol). The reaction mixture was stirred at 60°C for 40 h. After the mixture was cooled to room temperature, diethyl ether (10 mL) was added and the resulting mixture filtered over Celite. The filtrate was washed with water (10 mL) and dried over MgSO_4 . The evaporation of the ether solution gave the crude product which was analyzed by NMR. The details of further purification performed for the new compounds are described in the Supporting Information.

Allylation of **1e** Using Combined Lewis Acid of $\text{InCl}_3/\text{Me}_3\text{SiBr}$ (Scheme 3).

To a mixture of InCl_3 (0.05 mmol) and 1-phenylethanol **1e** (1.0 mmol) in CH_2Cl_2 (1 mL) was added allyltrimethylsilane **2a** (2.0 mmol) and Me_3SiBr (0.1 mmol) under nitrogen. The mixture was stirred for 4 h at room temperature and then quenched with saturated NaHCO_3 aq (30 mL). The mixture was extracted with diethyl ether (10×3 mL). The collected organic layer was dried (MgSO_4). The evaporation of the ether solution gave the crude product which was analyzed by NMR. The details of further purification performed for the new compounds are described in the Supporting Information.

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Supporting Information Available: Reaction procedures and spectroscopic details of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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