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ARTICLE TYPE

Copper(I) 2-Hydroxyethoxide-Promoted Cross-coupling of Aryl- and Alkenyldimethylsilanes with Organic Halides

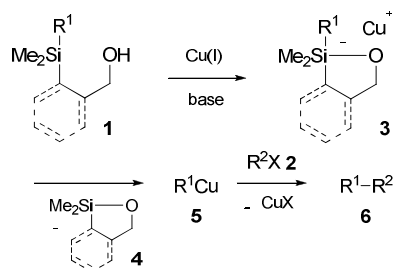
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Fluoride-free cross-coupling of aryl- and alkenyldimethylsilanes with organic halides proceeded in the presence of monocopper(I) alkoxide of ethylene glycol.

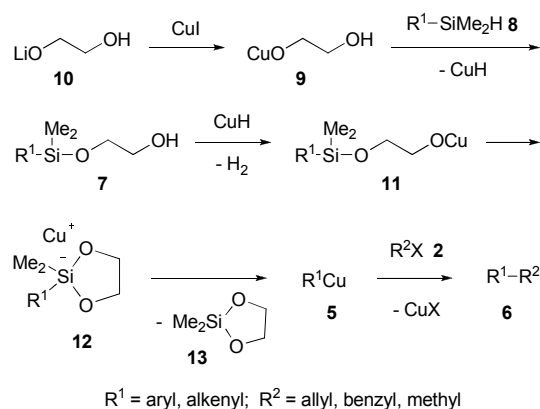
Organosilanes are useful synthetic intermediates due to their reactivity toward a variety of electrophiles. Recently palladium catalyzed cross-coupling of aryl- and alkenylsilanes with organic halides and related electrophiles, known as the Hiyama coupling, has attracted much attention as a useful tool for the carbon-carbon bond formation.¹ Aside from such the palladium-catalyzed reactions, we have explored copper(I)-promoted cross-couplings of aryl- and alkenylsilanes bearing a hydroxy or carbonyl group which proceed via the formation of organocopper(I) species.² Recently we reported an alternative copper(I)-promoted or catalyzed cross-coupling of aryl- and alkenylsilanes **1** having a 2-(hydroxymethyl)phenyl or 3-hydroxypropyl group on the silicon atom with organic halides **2** (Scheme 1).³



Scheme 1 Copper(I)-promoted cross-coupling of aryl- and alkenylsilanes bearing a γ -hydroxy group with organic halides

Although these reactions are useful as fluoride-free cross-couplings and employed for the preparation of functionalized unsaturated compounds, we were aware of a problem on unavailability of starting materials which restricts their synthetic application. Then we have further explored alternative fluoride-free copper(I)-promoted cross-coupling of aryl- and alkenylsilanes based on the assumption that the cross-coupling of **1** with organic halides **2** proceeds via the formation of five-membered cyclic silicates **3** and the following extrusion of oxasilacycles **4** to generate organocopper(I) species **5**, which afford the cross-coupling products **6** on treatment with organic halides **2**. It is well known that alcohols react with silanes via copper alkoxides to form alkoxy-silanes.⁴ Therefore we envisioned that the alkoxy-silanes **7** are produced by the reaction

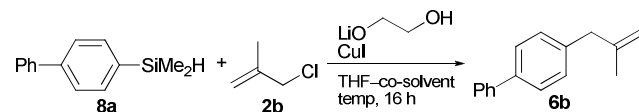
of aryl- and alkenyldimethylsilanes **8** with copper(I) 2-hydroxyethoxide **9**, generated by the treatment of lithium alkoxide **10** with copper (I) iodide, and their reaction with resulting copper(I) hydride affords the copper alkoxides **11**. The organocopper species **5** are formed through the formation of cyclic silicates **12** and subsequent elimination of dioxasilacycle **13**. Then **5** react with organic halides **2** to produce the cross-coupling products **6** (Scheme 2).



R¹ = aryl, alkenyl; R² = allyl, benzyl, methyl

Scheme 2 Copper(I) 2-hydroxyethoxide (**9**)-promoted cross-coupling of aryl- and alkenyldimethylsilanes **8** with organic halides **2**

In line with this idea, we first examined the reaction of (4-biphenyl)dimethylsilane (**8a**) and methyl chloride (**2b**) using copper(I) 2-hydroxyethoxide (**9**). The copper alkoxide **9** was prepared by the reaction of copper(I) iodide with the lithium alkoxide **10** generated in situ from ethylene glycol and butyllithium in THF. The treatment of a DMF solution of **8a** and **2b** with a THF solution of the copper(I) alkoxide **9** at 50 °C for 16 h produced the coupling product, 4-(2-methylprop-2-en-1-yl)biphenyl (**6b**), in 50% yield as we expected (Table 1, entry 1). The yield of **6b** was increased by using 2 equiv of the lithium alkoxide **10** (entry 2). Although DMSO and HMPA were also found to be good solvents for the cross-coupling (entries 3 and 4), the reaction carried out in acetonitrile gave virtually no coupling product (entry 5). The yield was also increased by the use of 2 equiv of **2b** (entry 6). The use of lower (entry 7) or higher (entry 8) reaction temperature resulted in the formation of **6b** in much lower yields.

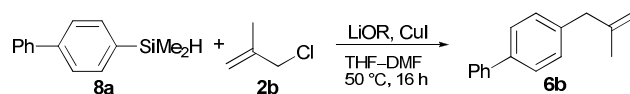
Table 1 Copper(I) 2-hydroxyethoxide (**9**)-promoted cross-coupling of (4-biphenyl)dimethylsilane (**8a**) with methallyl chloride (**2b**)^a

entry	10 (equiv)	2b (equiv)	co-solvent	temp (°C)	yield (%) ^b
1	1.0	1.5	DMF	50	50
2	2.0	1.5	DMF	50	72
3	2.0	1.5	DMSO	50	69
4	2.0	1.5	HMPA	50	66
5	2.0	1.5	CH ₃ CN	50	trace
6	2.0	2.0	DMF	50	83
7	2.0	2.0	DMF	25	51
8	2.0	2.0	DMF	90	48

^aAll reactions were performed using **8a** (0.3 mmol), **2b** (0.45 or 0.6 mmol), ethylene glycol (0.3 or 0.6 mmol), a hexane solution of BuLi (1.6 M, 0.33 or 0.66 mmol), copper(I) iodide (0.3 mmol), THF (0.5 mL) and co-solvent (1.5 mL) at 25-90 °C for 16 h. ^bIsolated yield based on **8a** used.

Next the cross-coupling between **8a** and **2b** using various lithium alkoxides was examined (Table 2). The fact that lithium methoxide did not act as a promoter supports our assumption that the formation of cyclic silicates **12** is indispensable for the cross-coupling (entry 1). The lithium alkoxides of secondary diols partly mediated the coupling (entries 3 and 4) and the reaction carried out in the presence of lithium alkoxide of sterically demanding pinacol (entry 5) produced the coupling product **6b** only in 18% yield. These results indicate that the facile formation of cyclic silicate is crucial to obtain the cross-coupling products in satisfactory yields. The coupling product **6b** was produced in the same yield by the reaction using pre-prepared powdered lithium 2-hydroxyethoxide (**10**), which made it possible to simplify the experimental procedure (entry 2).

Table 3 summarizes the results of reactions of various aryl- and alkenylsilanes **8** with organic halides **2** under the optimized conditions. As shown in the reactions of **8a** with 3-chloro-1-butene (**2c**) and its isomer, 1-chloro-2-butene (**2d**), the regioselectivity of allylic coupling seems to be controlled by steric factors (entries 3 and 4). The reaction of **8a** with the benzylic chloride **2e** also proceeded to give the coupling product **6e** (entry 5). Although the reaction of **8a** with methyl iodide (**2f**) produced 4-methylbiphenyl (**6f**) in a moderate yield (entry 6), no formation of the cross-coupling product was observed when ethyl iodide was employed. Halogen, amino, and ester functional groups were compatible to the present reaction (entries 7-9). The allylation of alkenyldimethylsilanes was performed under the same conditions, and the 1,4-dienes **6m-q** were obtained in good yields with complete retention of the configuration of double bond (entries 13-17).

Table 2 Cross-coupling of **8a** with **2b** using various lithium alkoxides^a

entry	lithium alkoxide	yield (%) ^b
1	LiOMe	-
2	LiOCH ₂ CH ₂ OH	83 (83) ^c
3	LiOCH ₂ CH(OH)CH ₂ CH ₃	74
4	LiO-C ₆ H ₁₁ -OH	50
5	LiO-C ₆ H ₁₁ -OH (pinacol)	18

^aAll reactions were performed using **8a** (0.3 mmol), **2b** (0.6 mmol), alcohol (0.6 mmol), a hexane solution of BuLi (1.6 M, 0.66 mmol), copper(I) iodide (0.3 mmol), THF (0.5 mL) and co-solvent (1.5 mL) at 50 °C for 16 h. ^bIsolated yield based on **8a** used. ^cCarried out using pre-prepared powdered **10** (0.6 mmol) in DMF (1.5 mL).

According to the proposed reaction mechanism (Scheme 2), it is reasonable to assume that the cross-coupling proceeds with only a catalytic amount of copper(I) iodide. Indeed, the reaction of **8** with allylic chlorides **2** using 15 mol% of copper(I) iodide produced the coupling products **6** in comparable yields (entries 1-3, 10, 11). The catalytic allylation also proceeded when the *E*- and *Z*-alkenylsilanes **8g** and **8h** were employed, albeit with lower yields (entries 14 and 16). It was confirmed that no formation of coupling product was observed when **8a** was treated with **2b** in the absence of copper(I) iodide. The result might deny the possible pathways for cross-coupling via the cyclic lithium silicates similar to **12** or organolithium species which were suggested by Hudrlik and co-workers for the reaction of allyl- or benzyl group substituted (3-hydroxypropyl)dimethylsilanes with electrophiles.⁵

In conclusion, we have developed a new fluoride free cross-coupling of aryl- and alkenylsilanes with organic halides. The starting materials are readily available and easy to handle in air. The coupling consists of multiple steps, but the operation is extremely straightforward; just mixing the four reagents, two of which are stable powders, affords the coupling products. Further extension of the present cross-coupling and exploration of detailed reaction mechanism are currently under way.

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Table 3 Copper(I) 2-hydroxyethoxide (9)-promoted cross-coupling^a

entry	8	2	6	yield (%) ^b
1	8a	2a		85 (82) ^c
2	8a	2b		83 (84) ^c
3	8a	2c ^d		80 (71) ^c
			6c:6d = 8:92 (E:Z = 86:14)	
4	8a	2d ^e		75
			6c: 6d = 51:49 (E:Z = 70:30)	
5	8a	2e		41
6	8a	2f		38 ^f
7 ^g	8b	2b		60
8 ^h	8c	2b		63
9 ^h	8d	2b		83
10	8e	2a		84 (61) ^c
11	8e	2b		60 (59) ^c

R¹ = 4-biphenyl (**8a**), 4-ClC₆H₄ (**8b**), 4-Me₂NC₆H₄ (**8c**), 4-^tBuO₂CC₆H₄ (**8d**), 1-Naph (**8e**), (*E*)-2-NaphCH=CH (**8f**), (*E*)-Ph(CH₂)₂CH=CH (**8g**), (*Z*)-Ph(CH₂)₂CH=CH (**8h**)
 R²X = H₂C=CHCH₂Cl (**2a**), H₂C=CMeCH₂Cl (**2b**), H₂C=CHCMeHCl (**2c**), MeHC=CHCH₂Cl (**2d**), 4-MeOBnCl (**2e**), MeI (**2f**)

Table 3 (continued)

12	8e	2e		61	42
13	8f	2b		6m	63
14	8g	2a		6n	61
15	8g	2b		6o	70 (42) ^c
16	8h	2a		6p	60
17	8h	2b		6q	60 (30) ^c

^aAll reactions were performed using **8** (0.3 mmol), **2** (0.6 mmol), pre-prepared powdered **10** (0.6 mmol), copper(I) iodide (0.3 mmol) and DMF (1.5 mL) at 50 °C for 16 h, unless otherwise noted. ^bIsolated yield based on **8** used. ^cCarried out using a catalytic amount of copper(I) iodide (15 mol%) and **10** (0.6 mmol) in DMF (1.5 mL). ^dA mixture of **2c**, *E*-**2d** and *Z*-**2d** (**2c**:*E*-**2d**:*Z*-**2d** = 71:28:1). ^eA mixture of *E*-**2d**, *Z*-**2d** and **2c** (*E*-**2d**:*Z*-**2d**:**2c** = 86:13:1). ^fContaminated with biphenyl. The yield was determined by ¹H NMR spectroscopy. ^gCarried out at 70 °C for 6 h. ^hCarried out at 60 °C for 16 h.

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† Electronic Supplementary Information (ESI) available: [typical experimental procedure and characterization data for all products]. See DOI: 10.1039/b000000x/

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