New Access to Cross-Coupling Reaction between Arylsilanes or Heteroarylsilanes and Aryl Halides Mediated by a Copper(I) Salt[1]

Hajime Ito, Hiro-omi Sensui, Kikuo Arimoto, Katsukiyo Miura, and Akira Hosomi*
Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki 305

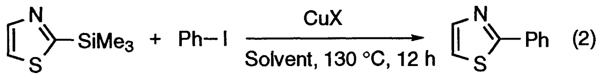
(Received March 27, 1997; CL-970224)

Copper(I) salt can be used as a promoter for the cross-coupling reactions between aryl- or heteroarylsilanes and aryl halides without a fluoride ion. Under these mild conditions, even a substrate containing a fluoride ion-sensitive silyloxyl group was employed directly.

Organosilanes have been extensively utilized in selective organic syntheses. Among them, palladium-catalyzed cross-coupling reactions between organosilanes and organic halides and triflates have been one of the most useful methods for the carbon-carbon bond formation under mild conditions.[2] However, in most cases except for organosilicates,[3] the addition of a fluoride ion as an activator of organosilanes is generally necessary for promoting these cross-coupling reactions. Unfortunately, a fluoride ion would cause desilylation of silyl ethers. We report here new fluoride ion-free cross-coupling reactions between aryl- or heteroarylsilanes and aryl halides mediated by a copper(I) salt (eq. 1).[4-6]

$$\underset{\mathbf{1}}{\mathrm{Ar^1\text{-}SiMe_n(OMe)_{3-n}}} + \underset{\mathbf{2}}{\mathrm{Ar^2\text{-}I}} \xrightarrow[\text{Solvent}]{\text{CuX}} \underset{\mathbf{3}}{\mathrm{Ar^1\text{-}Ar^2}} \qquad (1)$$

In order to optimize the general procedure of this reaction, we first examined the cross-coupling reaction of 2-trimethylsilylthiazole (**1a**)[7] with iodobenzene (**2a**) under various conditions (eq. 2). The results are summarized in Table 1.



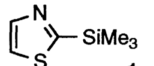
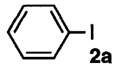
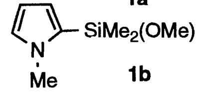
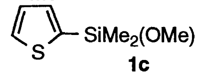
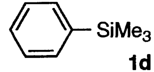
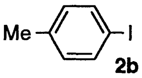
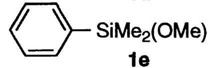
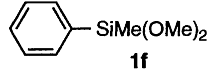
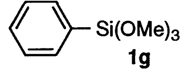
1a **2a** **3a**

Table **1**. CuX-mediated cross-couplings of trimethysilyllthiazole (**1a**) with iodobenzene (**2a**)[a]

Entry	Copper salt	Solvent	Yield of **3a** / %[b]
1	CuCl	Toluene	4
2	CuCl	Diglyme	48
3	CuCl	DMI	76
4[c]	CuCl	DMI	82
5[d]	$CuOC_6F_5$	DMI	93
6	CuBr	DMI	53
7	CuI	DMI	53
8	CuCN	DMI	12
9	$CuCl_2$	DMI	0

[a]A mixture of CuX (0.75 mmol), **1a** (118 mg, 0.75 mmol) and **2a** (102 mg, 0.5 mmol) was heated at 130 °C for 12 h under nitrogen. [b]Isolated yield. [c]2 equivalents of **1a** (157 mg, 1.0 mmol) and CuCl (99 mg, 1.0 mmol) were used. [d]$CuOC_6F_5$ was *in situ* prepared by the addition of $NaOC_6F_5$ to CuI. See ref. 8.

Table 2. Cu(I)-mediated cross-couplings of arylsilanes **1** with aryl halides **2**[a]

Entry	Arylsilanes **1**	Aryl halide **2**	**3**, Yield of / %[b]	
1	 **1a**	 **2a**	**3a**	93
2	 **1b**	**2a**	**3b**	93
3	 **1c**	**2a**	**3c**	75
4	 **1d**	 **2b**	**3d**	0
5	 **1e**	**2b**	**3d**	72
6	 **1f**	**2b**	**3d**	20
7	 **1g**	**2b**	**3d**	0

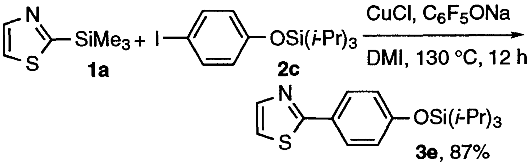
[a]A mixture of an aryl halide (1.0 mmol) and an arylsilane (0.5 mmol) in DMI (0.25 mL) was heated at 130 °C for 12 h in the presence of CuI (1.0 mmol) and sodium pentafluorophenoxide (4.0 M in DMI solution, 0.25 ml) under nitrogen. [b]Isolated yield.

When a less polar solvent such as toluene or diglyme was used in the presence of CuCl, the yield of the cross-coupling product **3a** was low (entries 1, 2). However, in 1,3-dimethyl-2-imidazolidinone (DMI) the product **3a** was obtained in good yield (entries 3, 4). Moreover, we found that $CuOC_6F_5$ was the best promoter for this reaction. The pentafluorophenoxide ion reveals strong affinity to the silicon atom of **1** to accelerate the transfer of the Ar[1] group on silicon to copper. On the contrary, a decrease in yield was observed by use of CuBr, CuI, or CuCN instead of CuCl or $CuOC_6F_5$ (entries 6-8).[8,9] A copper(II) salt such as $CuCl_2$ was not effective for this reaction (entry 9). For other less reactive organosilanes **1**, however, the product yield was improved by introduction of a methoxyl group on the silicon atom of the substrate (eq. 3). Representative results are summarized in Table 2.

$$\underset{\mathbf{1}}{\mathrm{Ar^1\text{-}SiMe_n(OMe)_{3-n}}} + \underset{\mathbf{2}}{\mathrm{Ar^2\text{-}I}} \xrightarrow[\text{DMI, 130 °C, 12 h}]{\mathrm{CuI,\ C_6F_5ONa}} \underset{\mathbf{3}}{\mathrm{Ar^1\text{-}Ar^2}} \qquad (3)$$

A general procedure for the coupling reaction of 2-trimethylsilylthiazole with iodobenzene is as follows. Iodobenzene (**2a**) (102 mg, 0.5 mmol) and **1a** (157 mg, 1.0 mmol) were added successively to a mixture of copper(I) iodide (190 mg, 1.0 mmol), sodium pentafluorophenoxide (4.0 M in DMI, 0.25 mL)[10] and DMI (0.25 mL) under nitrogen at room temperature. The mixture was stirred at 130 °C for 12 h. After cooling to room temperature, the reaction mixture was diluted with chloroform. Filtration through a short-column chromatography using Florisil® followed by purification by preparative TLC (SiO$_2$, ethyl acetate : hexane = 1 : 10) gave 75 mg (93% yield) of 2-phenylthiazole (**3a**). Under these conditions the cross-coupling reactions between various arylsilanes **1**[11,12] and aryl halides **2** proceeded in moderate to good yields. Monomethoxysilanes **1b**, **1c**, and **1e** were the most effective substrates (entries 2, 3, 5), though trimethylsilyl, dimethoxysilyl and trimethoxysilyl derivatives (**1d**, **1f**, and **1g**, respectively) gave poor yields (entries 4, 6, 7).

The synthetic utility of the present fluoride-free cross-coupling reaction can be demonstrated by the expedient reaction of a substrate containing a silyl ether moiety which is easily cleaved by a fluoride ion (eq. 4). For instance, 4-(triisopropylsiloxy)iodobenzene (**2c**) effectively reacted with **1a** in the presence of copper(I) iodide and sodium pentafluorophenoxide. The heterodiaryl product **3e** was obtained in good yield and no desilylation was observed.



(4)

In conclusion, we have developed a new fluoride- and palladium-free cross-coupling reaction between arylsilanes and aryl iodide mediated by a copper(I) salt. The present method provides a new synthetic route to C(sp^2)-C(sp^2) coupled compounds.

Financial support for this work is partly provided by Grants-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Japan and Pfizer Pharmaceuticals Inc. We thank Dow Corning Toray Silicone Co. Ltd., Chisso Co. Ltd., and Shin-Etsu Chemical Co. Ltd. for a gift of organosilicon compounds.

References and Notes

1 Studies on Organosilicon Chemistry. No. 135.

2 For recent reports, see: K. Goda, E. Ejiri, Y. Hatanaka, and T. Hiyama, *J. Org. Chem.*, **61**, 7232 (1996); T. Hiyama and Y. Hatanaka, *Pure Appl. Chem.*, **66**, 1471 (1994); K. Tamao, K. Kobayashi, and Y. Ito, *Tetrahedron Lett.*, **30**, 6051 (1989).

3 A. Hosomi, *Heteroatom Chemistry*, **7**, 214 (1992); M. Hojo, C. Murakami, H. Aihara, E. Komori, S. Kohra, Y. Tominaga, and A. Hosomi, *Bull. Soc. Chim. Fr.*, **132**, 499 (1995).

4 The fluoride ion-free cross-coupling reaction between alkenylfluorosilanes and allylic carbonates catalyzed by a Pd complex was reported, see: H. Matsuhashi, Y. Hatanaka, M. Kuroboshi, and T. Hiyama, *Tetrahedron Lett.*, **36**, 1539 (1995).

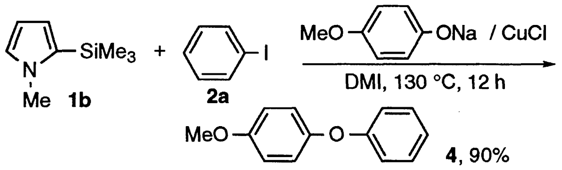
5 Trifluoromethylation of organic halides using trifluoromethyltriethylsilane, KF and Cu(I) was reported, see: H. Urata and T. Fuchikami, *Tetrahedron Lett.*, **32**, 91 (1991). In this reaction the fluoride ion was essential for the promotion of the reaction.

6 The solid-state homo-coupling reaction of alkenylpentafluorosilicates promoted by CuCl was reported, see: J. Yoshida, K. Tamao, T. Kakui, and M. Kumada, *Tetrahedron Lett.*, **1979**, 1141.

7 A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, and P. Pedrini, *J. Org. Chem.*, **53**, 1748 (1988).

8 This trend can be reasonably explained by the formation energies of Si-X bonds produced by this group transfer reaction from silicon to copper.

9 Other copper(I) alkoxides and aryloxides such as methoxide, *t*-butoxide, and phenoxide show stronger affinity to the organic halides than the organosilicon compounds. In particular, an addition of sodium phenoxide or 4-methoxyphenoxide selectively produced diphenyl ether derivatives (*e.g.*, eq. 5).



(5)

10 Sodium pentafluorophenoxide was prepared from sodium hydride (2.26 g, 94 mmol) and pentafluorophenol (11.3 g, 61.4 mmol) in dry THF (50 mL). After filtration and evaporation *in vacuo*, the residue (12.6 g, 61.2 mmol) was dissolved in dry DMI (15.3 mL).

11 A procedure of the preparation of 1-methyl-2-[(methoxy)dimethylsilyl]pyrrole (**1b**) is as follows: A solution of 2-lithio-1-methylpyrrole (100 mmol) in diethyl ether was added to a solution of dichlorodimethylsilane (19.4 g, 150 mmol) in dry diethyl ether (150 mL) at 0 °C. After stirring at an ambient temperature for 1 h and successively the addition of triethylamine (20.3 g, 200 mmol) and methanol (6.41 g, 200 mmol) at 0° C, the mixture was stirred for 1 h. After usual workup, the mixture was extracted. The organic extracts were washed with aqueous NaHCO$_3$ and brine, dried over Na$_2$SO$_4$, and concentrated. Distillation gave pure **1b** (8.15 g, 48%), bp 70 °C / 5 mmHg. ^{1}H NMR (270 MHz, CDCl$_3$) δ 0.44 (s, 6H), 3.45 (s, 3H), 3.82 (s, 3H), 6.19 - 6.22 (m, 1H), 6.49 - 6.52 (m, 1H), 6.86 (s, 1H); ^{13}C NMR (67.5 MHz, CDCl$_3$) δ -1.7, 36.5, 50.3, 107.9, 120.6, 127.3, 130.0. See, S. Gronowitz and R. Kada, *J. Heterocyclic Chem.*, **21**, 1041 (1984).

12 2-[(Methoxy)dimethylsilyl]thiophene (**1c**) was prepared by a similar procedure described above (63%). bp 99 °C / 80 mmHg. ^{1}H NMR (270 MHz, CDCl$_3$) δ 0.44 (s, 6H), 3.45 (s, 3H), 7.21-7.26 (m, 1H), 7.36-7.38 (m, 1H), 7.64-7.66 (m, 1H); ^{13}C NMR (67.5 MHz, CDCl$_3$) δ 1.29, 50.7, 128.2, 131.2, 135.1, 136.7.