

Copper-catalyzed Twofold Silylmetalation of Alkynes

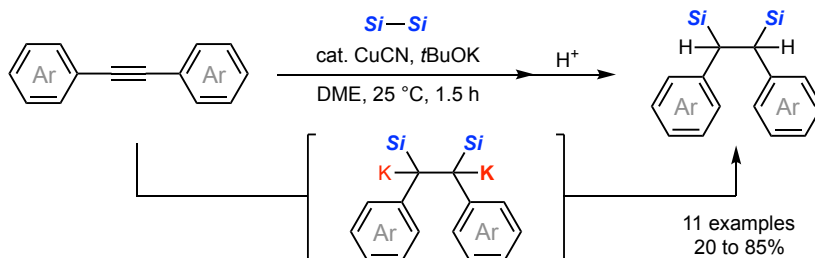
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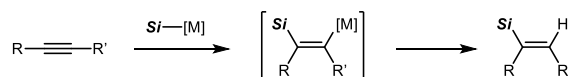
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Abstract The first twofold silylmetalation across a C-C triple bond is achieved. In the presence of a catalytic amount of copper cyanide, diarylacetylenes were converted to 1,2-dimetalated 1,2-disilyl-1,2-diarylethanes on treatment with silylpotassium species generated in situ from disilane and *t*BuOK. The dimetalated species were protonated to yield a series of 1,2-disilyl-1,2-diarylethanes.

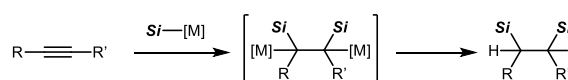
Key words silylmetalation, disilane, copper, ate complex, dianion

Organosilicon compounds have attracted much attention both as synthetic intermediates¹ and functional materials.² Development of methods for the formation of C–Si bonds is thus considered as an important research topic in organic chemistry. Among such methods, transition-metal-catalyzed silylations of C–C multiple bonds represent a straightforward method. Particularly, silylmetalation of alkynes is useful for the synthesis of highly functionalized alkenylsilanes and has hence been investigated well (Scheme 1a)³ with a combination of copper species and silyl alkali metal species. All the reported silylmetalation reactions of alkynes occur only once to yield the corresponding silylmetalated alkenes. Thus, there are no reports about twofold addition of silylmethyls across alkynes to yield doubly silylmethylated alkanes. Here we report the first twofold silylmetalation of alkynes with the aid of a copper catalyst and disilanes as a precursor of silylpotassium species (Scheme 1b). The doubly silylmethylated species thus obtained could be protonated to provide accesses to 1,2-disilylethanes.

(a) Typical silylmetalation of alkyne

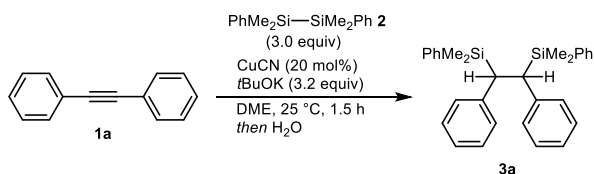


(b) Twofold silylmetalation of alkyne (This work)



Scheme 1 Mono-silylmetalation and Twofold Silylmetalation of Alkyne

For devising the standard reaction conditions, an extensive screening of silicon sources, copper species, bases, and solvents were conducted. This optimization eventually revealed that treatment of diphenylacetylene (**1a**) with copper cyanide (20 mol%), 1,1,2,2-tetramethyl-1,2-diphenyldisilane (**2**, 3.0 equiv) and *t*BuOK (3.2 equiv) in 1,2-dimethoxyethane (DME) as the solvent at 25 °C for 1.5 h, followed by aqueous workup provided 1,2-disilyl-1,2-diphenylethane (**3a**) in 88% (66% isolated⁴) yield as a 1:1.2 diastereomeric mixture (Table 1, entry 1).⁵ In the absence of a copper catalyst, the reaction was more complicated and **3a** was obtained in much lower yield (35%) (entry 2). Other copper species gave slightly reduced yields (entries 3, 4). The reaction did not proceed without any bases (entry 5). Lithium or sodium *t*-butoxide did not mediate the reaction due to the inefficiency of cleaving the Si–Si bond (entries 6, 7). These results underscore the importance of potassium alkoxide for in situ generation of silylpotassium species.⁶ This species would then mediate the formation of silylcopper species. This direct formation of silylcopper species from disilanes differentiates the current methodology from the past ones.³ KHMDS was not effective, which indicates the importance of nucleophilic alkoxide for this reaction (entry 8). The reaction was relatively sluggish in THF, and no desired product was observed in 1,4-dioxane and toluene (entries 9–11).

Table 1 Optimization of Conditions^a

Entry	Deviations from the standard conditions	Yield (%) ^a
1	None	88 (66 ^b)
2	No CuCN	35
3	Cu(IPr)Cl instead of CuCN	79
4	CuI instead of CuCN	76
5	No <i>t</i> BuOK	0
6	<i>t</i> BuOLi instead of <i>t</i> BuOK	0
7	<i>t</i> BuONa instead of <i>t</i> BuOK	0
8	KHMDS instead of <i>t</i> BuOK	0
9	THF instead of DME	74
10	1,4-dioxane instead of DME	0
11	toluene instead of DME	0

^aDetermined by ¹H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard. ^bIsolated yield. dr = 1:1.2.

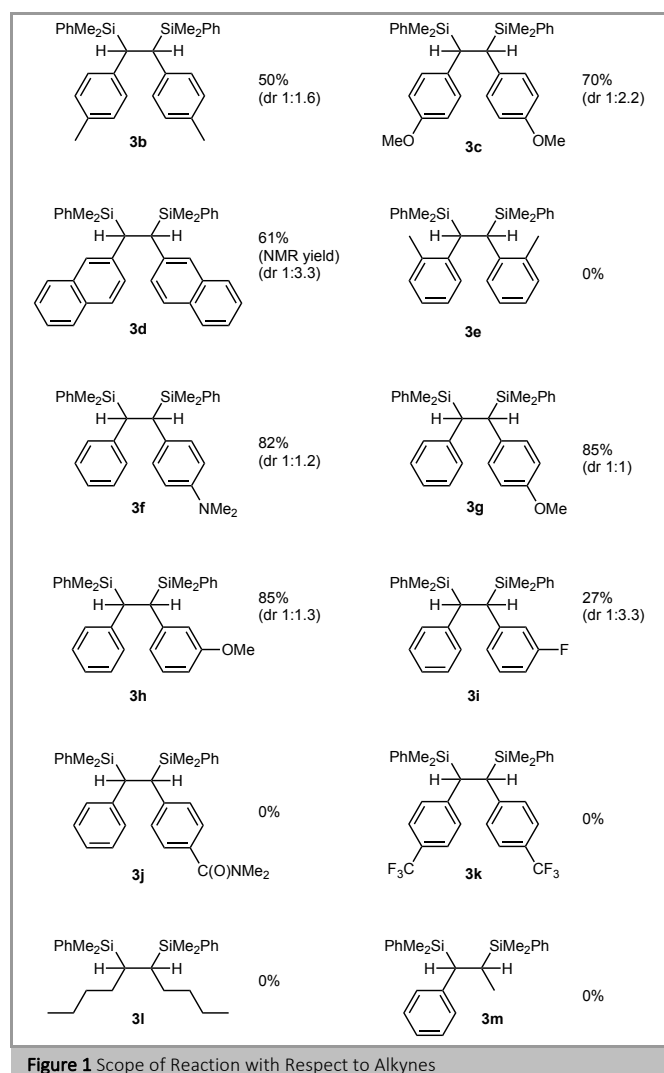


Figure 1 Scope of Reaction with Respect to Alkynes

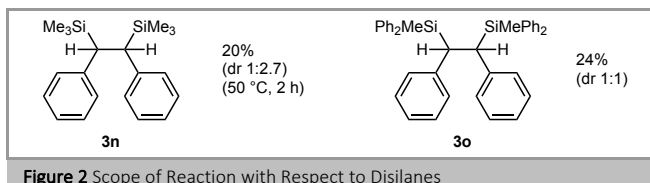
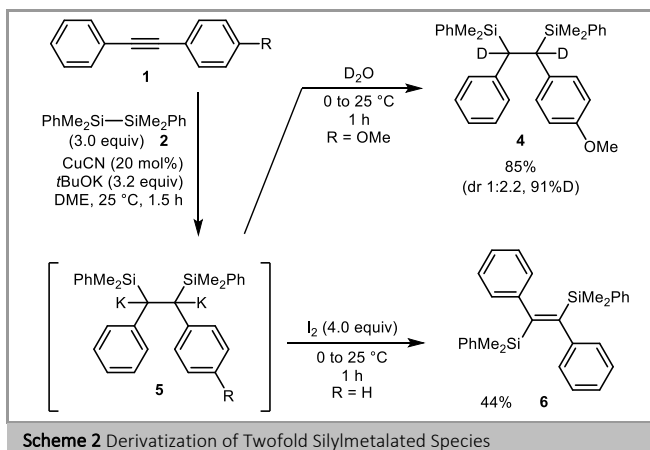


Figure 2 Scope of Reaction with Respect to Disilanes

With the optimized conditions in hand, we surveyed the scope of this double-silylmatalation with respect to alkynes (Figure 1). Di-*p*-tolyl (**3b**), di-*p*-methoxyphenyl (**3c**), di-2-naphtyl (**3d**) adducts were obtained in good yields. Di-*o*-tolyl adducts **3e** was not obtained, probably due to the steric effect of the *o*-methyl groups. Less symmetrical *p*-dimethylaminophenyl (**3f**), *p*-methoxyphenyl (**3g**), *m*-methoxyphenyl (**3h**) substituted products were obtained in high yields. While an electron-withdrawing *m*-fluorophenyl substituent was barely tolerated to give a 27% yield of the product **3i**, no products **3j**, **3k** were formed when the para position was substituted with electron withdrawing groups. Alkyl acetylenes were not good substrates for this transformation and no desired products **3l** and **3m** were obtained. The reaction is not applicable to terminal alkynes to rapidly generate an unidentified precipitate probably through the formation of an acetylide.

Investigation on the effect of organosilicon source is shown in Figure 2. Hexamethyldisilane and 1,2-dimethyl-1,1,2,2-tetraphenyldisilane showed lower reactivity to yield **3n** and **3o** in 20% and 24% respective yields. The lower yield of **3n** may be ascribed to the elevated temperature that is required for generating trimethylsilylcopper by cleaving the less reactive Si-Si bond. The formation of **3o** may be hampered by the steric hindrance of Ph₂MeSi group.



Scheme 2 Derivatization of Twofold Silylmatalated Species

To probe the reaction mechanism, the reaction mixture was treated with D₂O to afford the corresponding doubly deuterated 1,2-disilylated diphenylethane **4** in 85% yield with 91% deuterium incorporation (Scheme 2).⁷ We thus confirmed the formation of a dianionic intermediate **5** generated in situ. This dianionic intermediate **5** could also be oxidized in situ with iodine⁸ to selectively afford (*E*)-1,2-bis(dimethylphenylsilyl)-1,2-diphenylethane (**6**) in 44% yield. Notably, the overall transformation represents a rare intermolecular *anti*-disilylation of alkynes.⁹ The reaction with other electrophiles such as *n*BuCl and chloromethyl methyl ether did not provide the doubly

alkylated product probably due to the bulkiness of the metalated species **5**.

A plausible reaction mechanism is accordingly proposed as shown in Figure 3. Copper cyanide would react with two equivalents of silylpotassium species that is generated in situ from disilane and *t*BuOK.^{6,10} Copper-ate complex **7** thus formed would be susceptible to the silylcupration with diarylacetylene to form adduct **8**.¹¹ The remaining silyl group on the copper atom would migrate to the adjacent carbon to lead to carbanion **9**. With the aid of two equivalents of silylpotassium species, the copper atom in **9** would be replaced with potassium to afford 1,2-dimetalated species **5**. The copper-ate species **7** would be concomitantly regenerated to close the catalytic cycle. The efficient double silylmethylation may be ascribed to smooth 1,2-silyl migration from **8** with the aid of potassium as the counteranion.¹²

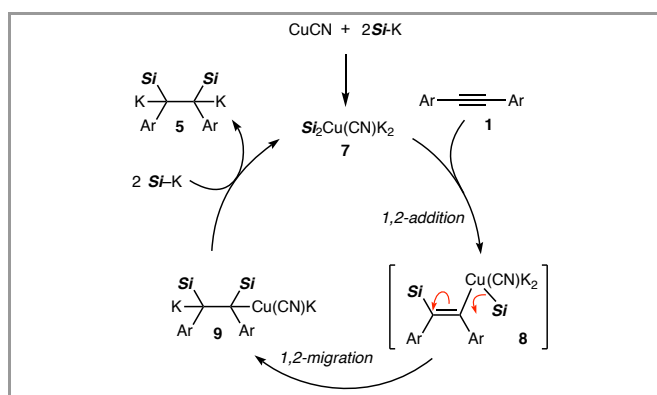


Figure 3 Proposed Reaction Mechanism

In conclusion, we have developed the first twofold silylmethylation across a C-C triple bond. The reaction is conducted in the presence of copper cyanide catalyst and silylpotassium species generated from disilane and *t*BuOK. Protonation of the 1,2-dimetalated species provided a series of 1,2-disilyl-1,2-diarylethanes. Further applications of cuprate species and detailed mechanistic study will be reported in due course.

Funding Information

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Supporting Information

Supporting information for this article is available online

References and Notes

- (1) (a) *Handbook of Reagents for Organic Synthesis*: Reagents for Silicon-Mediated Organic Synthesis; Fuchs, P. L., Ed.; John Wiley & Sons: Chichester, U.K., **2011**; (b) *Chemistry of Organosilicon Compounds*, Vol 3; Rappoport, Z.; Apeloig, Y., Eds.; Wiley-VCH: New York, **2001**; (c) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: London, **1988**.
- (2) (a) *Silicon Polymers*; Muzafarov, A. M., Ed.; Springer: Heidelberg, **2011**. (b) *Silicon-Containing Polymers*; Jones, R. G.; Ando, W.; Chojnowski, J., Eds.; Kluwer Academic: Dordrecht, **2000**.
- (3) (a) Fleming, I.; Roessler, F. J. *Chem. Soc., Chem. Commun.* **1980**, 276. (b) Fleming, I.; Newton, T. W.; Roessler, F. J. *Chem. Soc., Perkin Trans. 1* **1981**, 2527. (c) Hayami, H.; Sato, M.; Kanemoto, S.; Morizawa, Y.; Oshima, K.; Nozaki, H. *J. Am. Chem. Soc.* **1983**, 105, 4491. (d) Okuda, Y.; Morizawa, Y.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, 25, 2483. (e) Okuda, Y.; Wakamatsu, K.; Tückmantel, W.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, 26, 4629. (f) Wakamatsu, K.; Nonaka, T.; Okuda, Y.; Tückmantel, W.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1986**, 42, 4427. (g) Cuadrado, P.; González-Nogal, A. M.; Sánchez, A. J. *Org. Chem.* **2001**, 66, 1961. (h) Liepins, V.; Karlström, A. S.; Bäckvall, J.-E. *J. Org. Chem.* **2002**, 67, 2136. (i) Barbero, A.; Pulido, F. J. *Acc. Chem. Res.* **2004**, 37, 817. (j) Auer, G.; Oestreich, M. *Chem. Commun.* **2006**, 37, 311. (k) Wang, P.; Yeo, X.-L.; Loh, T.-P. *J. Am. Chem. Soc.* **2011**, 133, 1254. (l) Fujihara, T.; Tani, Y.; Semba, K.; Terao, J.; Tsuji, Y. *Angew. Chem. Int. Ed.* **2012**, 51, 11487. (m) Hazra, C. K.; Fopp, C.; Oestreich, M. *Chem. Asian J.* **2014**, 9, 3005. (n) Garcia-Rubia, A.; Romero-Revilla, J. A.; Mauleon, P.; Gomez Arrayas, R.; Carretero, J. C. *J. Am. Chem. Soc.* **2015**, 137, 6857. (o) Shintani, R.; Kurata, H.; Nozaki, K. *J. Org. Chem.* **2016**, 81, 3065.
- (4) The reduced isolated yield is due to difficulty in chromatographically separating the product from *t*BuOSiMe₂Ph that is generated during the formation of silyl potassium species.
- (5) **Twofold Silylmethylation of Alkynes**. An oven-dried Schlenk tube was charged with diphenylacetylene (**1a**, 53.5 mg, 0.300 mmol), CuCN (5.4 mg, 0.060 mmol) and potassium *tert*-butoxide (108 mg, 0.960 mmol). DME (2.0 mL) and 1,2-diphenyl-1,1,2,2-tetramethyldisilane (**2**, 244 mg, 0.900 mmol) were sequentially added to the mixture. The resulting mixture was stirred at 25 °C. After 1.5 h, H₂O (30 mL) was added at 0 °C, and the resulting biphasic solution was extracted with Et₂O (15 mL × 3). The combined organic layer was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The resulting residue was purified by column chromatography with hexane as an eluent and then GPC with CHCl₃ as an eluent to give **3a** (89.2 mg, 0.198 mmol, 66%) (minor/major = 1/1.2 as an inseparable mixture) as a white solid. Data for 1,2-bis(dimethylphenylsilyl)-1,2-diphenylethane (**3a**): ¹H NMR (CDCl₃): δ 7.38–7.36 (m, 2H×0.55), 7.34–7.30 (m, 8H×0.55), 7.22 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 2H×0.45), 7.14–7.11 (m, 6H×0.55 + 4H×0.45), 7.07–7.01 (m, 6H×0.45), 6.98 (dd, *J* = 7.2, 1.2 Hz, 4H×0.45), 6.92 (d, *J* = 7.2 Hz, 4H×0.45), 6.84–6.83 (m, 4H×0.55), 2.88 (s, 2H×0.45), 2.75 (s, 2H×0.55), 0.10 (s, 6H×0.55), –0.17 (s, 6H), –0.22 (s, 6H×0.45); ¹³C NMR (CDCl₃): δ 142.5, 141.6, 138.5, 138.4, 134.1, 134.0, 131.5, 129.5, 128.8, 128.2, 127.7, 127.6, 127.3, 127.0, 125.1, 125.1, 38.5, 36.8, –2.36, –2.42, –3.36, –4.04; HRMS calcd for C₃₀H₃₄Si₂ [M⁺]: 450.2194, found: 450.2197.
- (6) (a) Sakurai, H.; Okada, A.; Kira, M.; Yonezawa, K. *Tetrahedron Lett.* **1971**, 12, 1511. (b) Sakurai, H.; Kondo, F. *J. Organomet. Chem.* **1975**, 92, C46. (c) Watanabe, H.; Higuchi, K.; Kobayashi, M.; Hara, M.; Koike, Y.; Kitahara, T.; Nagai, Y. *J. Chem. Soc., Chem. Commun.* **1977**, 534. (d) Buncel, E.; Venkatachalam, T. K.; Edlund, U. *J. Organomet. Chem.* **1992**, 437, 85.
- (7) A different isomeric ratio was observed when intermediate **5** was quenched with D₂O. So far, the reason for this phenomenon is unclear.

- (8) Yamaguchi, S.; Xu, C.; Tamao, K. *J. Am. Chem. Soc.* **2003**, *125*, 13662.
- (9) The oxidation of dianionic species **5** with iodine probably proceeds through the formation of a radical intermediate that would lose the stereochemical information. Thus, the less stereochemically congested **6** was selectively obtained. Garst, J. F.; Roberts, R. D.; Pacifici, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 3528.
- (10) Even though a free silylpotassium species seems to function in the reaction, the formation of the silicate species generated from disilane and *tert*-butoxide could not be excluded.
- (11) In ref. 3b, an example of mono-silylcupration of $(R_3Si)_2Cu(CN)Li_2$ to a C–C triple bond was reported. However, no report of any type of addition of $(R_3Si)_2Cu(CN)K_2$ is known.
- (12) In the presence of smaller amounts of disilane (1.0 equiv) and *t*BuOK (1.2 equiv), we observed recovered alkyne **1a** (32%) and disilylated product **3a** (19%) as well as the monosilylated alkene (25%) after protic workup. This result suggests the formation of monosilylated copper species just before consuming up the silylpotassium species. The monosilylated copper species may also add to the alkyne to eventually provide the monosilylated alkene.