

Silyl Migration in Conjunction with Substitution on Silicon in Copper(I) *t*-Butoxide-promoted Coupling between *o*-Silylphenyl Ketones and Organic Halides

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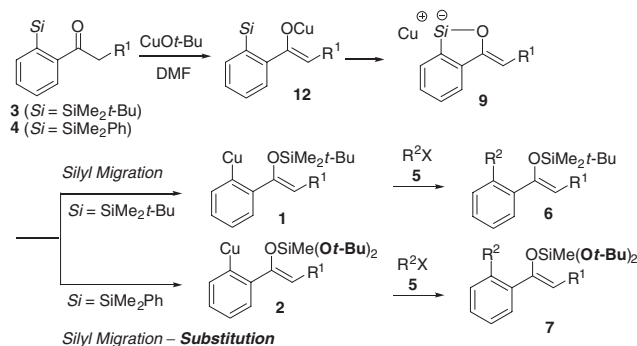
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(*Z*)-Di-*t*-butoxymethylsilyl enol ethers were stereoselectively produced by the copper(I) *t*-butoxide-promoted cross-coupling of *o*-(dimethylphenylsilyl)phenyl ketones with organic halides. The reaction proceeds via the formation of arylcopper species generated by silyl migration to enolate oxygen, accompanied by substitution of *t*-butoxy on silicon.

Organosilicon-based cross-coupling has emerged as an effective method for carbon–carbon bond formation.¹ With the aim of activating the unreactive Si–C bond, fluoro- or alkoxy-functionalized organosilanes as well as silacyclobutanes^{1d–1f} have successfully been employed for palladium-catalyzed cross-coupling. Recently the silyl group activation by intramolecular coordination of oxygen or nitrogen atom has been utilized for the cross-coupling.²

The cleavage of the Si–C bond in cyclic silicates formed by the intramolecular coordination of alkoxide is also essential for the formation of reactive organometallic species in the Brook rearrangements.³ The silyl migration from sp^2 carbon to oxygen has potential to generate functionalized alkenylmetal species; however, synthetic application has strictly been limited.⁴ In this context, we have studied copper(I) *t*-butoxide-promoted 1,4- and 1,3-silyl migrations from sp^2 carbon to alkoxide oxygen.^{4a,4c–4e,5} Such silyl migration has recently been extended to the migration to enolate oxygen, while the resulting alkenylcopper species possessing an enol silyl ether substructure react with various organic halides to afford cross-coupling products.⁶ Here we report the generation of arylcopper species **1** and **2** bearing an enol silyl ether substructure from *o*-silylphenyl ketones **3** and **4** by the copper(I) *t*-butoxide-promoted silyl migration from aromatic sp^2 carbon to carbonyl oxygen and their cross-coupling with organic halides **5** giving (*Z*)-enol silyl ethers **6** and **7** stereoselectively (Scheme 1). What is striking is that simultaneous intermolecular displacement of the phenyl and methyl groups on silicon with *t*-butoxy took place in these reactions, depending on the substituents of the silyl group. To our best knowledge, such substitution on silicon associated with the silyl migration has not been known.

1-[*o*-(*t*-Butyldimethylsilyl)phenyl]-1-butanone (**3a**) was treated with copper(I) *t*-butoxide (2 equiv), prepared prior to use by the reaction of copper(I) iodide with lithium *t*-butoxide,⁷ in DMF (25 °C, 4 h), and then with methyl chloride (**5a**) (2 equiv, 2 h) to produce the stereochemically pure (*Z*)-enol silyl ether **6a** in 54% yield (Table 1, Entry 1). The cross-coupling of **3a** proceeded not only with allylic halides, but also with alkyl halides such as ethyl iodide (**5b**) and chlorotributylstannane (**5c**) (Table 1, Entries 2 and 3). All reactions examined were stereoselective and (*Z*)-enol silyl ethers were obtained as single isomers.⁸



Scheme 1. Silyl group dependent formation of enol silyl ethers with and without *t*-butoxy substituent on silicon.

A study on the scope of the cross-coupling revealed that the above silyl migration was accompanied by nucleophilic substitution at the silicon atom with *t*-butoxy when *o*-(dimethylphenylsilyl)phenyl ketones **4** were employed. Thus, the successive treatment of 1-[*o*-(dimethylphenylsilyl)phenyl]-1-butanone (**4a**) with CuOt-Bu (2 equiv) in DMF and **5a** (2 equiv) gave (*Z*)-Di-*t*-butoxymethylsilyl enol ether **7a** in 44% yield. The yield was improved to 55% when 3 equiv of CuOt-Bu was used (Table 1, Entry 4). The enol silyl ether **7a** was also obtained by the reaction of diphenylmethylsilyl-substituted phenyl ketone **8** (Entry 10). The ²⁹SiNMR spectrum of **7a** showed a signal at –58.2 ppm, typical of the chemical shifts of trialkoxyalkylsilanes,⁹ and **7a** was hydrolyzed to the corresponding ketone with TBAF. Under similar conditions, the concomitant cross-coupling and the substitution on silicon underwent to afford *t*-butoxy-substituted (*Z*)-enol silyl ethers **7^b** predominantly when various silyl ketones **4** were treated with organic halides **5**. Successive treatment of **4a** with CuOt-Bu and H₂O produced the protonated enol silyl ether **7d** (Entry 7). This cross-coupling was successfully extended to palladium(0)-catalyzed arylation (Entry 11). The products of these reactions, alkoxy-substituted silyl enol ethers, have recently attracted much attention due to their unique reactivities.¹⁰

A plausible mechanism for the concomitant substitution is shown in Scheme 2. The Si–Ph bond cleavage in preference to the silyl migration proceeds in the cyclic silicate **9** to produce the cyclic silyl ether **10**.^{2b–2d,4a,11} Displacement of the methyl group of **10** with CuOt-Bu and subsequent formation of the silicate **11** by nucleophilic attack of another CuOt-Bu promote the silyl migration to give **2**.¹²

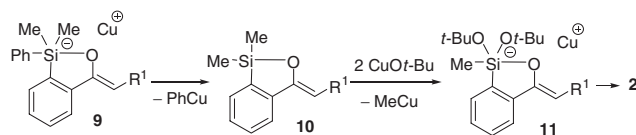
Stereoselective formation of (*Z*)-enol silyl ethers **6** and **7** can be explained by formation of the thermodynamically more stable (*Z*)-enolates **12** in preference to (*E*)-enolates which experience steric repulsion between the *o*-silylphenyl group and R¹ (Scheme 1).

Table 1. Formation of enol silyl ethers **6** and **7** by the coupling of **3** and **4** with organic halides **5**^a

Entry	<i>o</i> -Silylphenyl ketone	Halide	Product (Isolated yield/%)
1 ^b			
2 ^b	3a	EtI 5b	
3 ^b	3a	<i>n</i> -Bu ₃ SnCl 5c	
4		5a	
5	4a		
6	4a	5b	
7	4a	— ^c	
8 ^d		5a	
9 ^e		5a	
10		5a	
11 ^f	4a	PhI 5e	

^aThe *o*-silylphenyl ketones were treated with CuOt-Bu (3 equiv) in DMF (25 °C, 4 h) and then with **5** (2 equiv) unless otherwise noted. ^b2 equiv of CuOt-Bu were used. ^cQuenched without treatment with the organic halide. ^d**4b** was reacted with **5a** for 16 h. ^eA mixture of **4c** and **5a** (3.5 equiv) was treated with CuOt-Bu (3.2 equiv) in DMF (25 °C, 1 h). ^fCarried out in the presence of Pd(PPh₃)₄ (3 mol %).

In summary, we have demonstrated an unprecedented silyl migration to enolate oxygen “with substitution on silicon” in copper(I) *t*-butoxide-promoted cross-coupling of silylphenyl ketones with organic halides.¹³ The enol silyl ethers thus obtained are useful intermediates in organic synthesis.

**Scheme 2.** A plausible mechanism for the substitution on silicon.

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References and Notes

- For review of the Hiyama coupling, see: a) T. Hiyama, E. Shirakawa, *Top. Curr. Chem.* **2002**, 219, 61. b) S. E. Denmark, R. F. Sweis, in *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed., ed. by A. de Meijere, F. Diederich, Wiley-VCH, Weinheim, **2004**, 163. c) J. Tsuji, in *Palladium Reagents and Catalysis*, ed. by J. Tsuji, John Wiley & Sons, Chichester, **2004**, p. 338. For cross-coupling of silacyclobutanes, see: d) S. E. Denmark, J. Y. Choi, *J. Am. Chem. Soc.* **1999**, 121, 5821. e) S. E. Denmark, Z. Wu, *Org. Lett.* **1999**, 1, 1495. f) S. E. Denmark, Z. Wang, *Synthesis* **2000**, 999.
- a) T. Takeda, T. Uruga, K. Gohroku, T. Fujiwara, *Chem. Lett.* **1999**, 821. b) M. Shindo, K. Matsumoto, K. Shishido, *Angew. Chem., Int. Ed.* **2004**, 43, 104. c) Y. Nakao, H. Imanaka, A. K. Sahoo, A. Yada, T. Hiyama, *J. Am. Chem. Soc.* **2005**, 127, 6952. d) Y. Nakao, H. Imanaka, J. Chen, A. Yada, T. Hiyama, *J. Organomet. Chem.* **2007**, 692, 585.
- a) A. G. Brook, *Pure Appl. Chem.* **1966**, 13, 215. b) A. G. Brook, *Acc. Chem. Res.* **1974**, 7, 77. c) W. H. Moser, *Tetrahedron* **2001**, 57, 2065. d) M. Kira, T. Iwamoto, in *The Chemistry of Organosilicon Compounds*, ed. by Z. Rappoport, Y. Apeloig, Wiley, Chichester, **2001**, Vol. 3, p. 853.
- a) H. Taguchi, K. Ghoroku, M. Tadaki, A. Tsubouchi, T. Takeda, *J. Org. Chem.* **2002**, 67, 8450. b) W. H. Moser, J. Zhang, C. S. Lecher, T. L. Frazier, M. Pink, *Org. Lett.* **2002**, 4, 1981. c) H. Taguchi, A. Tsubouchi, T. Takeda, *Tetrahedron Lett.* **2003**, 44, 5205. d) H. Taguchi, K. Takami, A. Tsubouchi, T. Takeda, *Tetrahedron Lett.* **2004**, 45, 429. e) A. Tsubouchi, M. Itoh, K. Onishi, T. Takeda, *Synthesis* **2004**, 1504. f) S. Akai, T. Ikawa, S. Takayanagi, Y. Morikawa, S. Mohri, M. Tsubakiyama, M. Egi, Y. Wada, Y. Kita, *Angew. Chem., Int. Ed.* **2008**, 47, 7673.
- For synthetic application of the catalytic CuOt-Bu–Xantphos system, see: H. Ito, Y. Sasaki, M. Sawamura, *J. Am. Chem. Soc.* **2008**, 130, 15774, and references cited therein.
- a) H. Taguchi, H. Miyashita, A. Tsubouchi, T. Takeda, *Chem. Commun.* **2002**, 2218. b) A. Tsubouchi, K. Onishi, T. Takeda, *J. Am. Chem. Soc.* **2006**, 128, 14268.
- T. Tsuda, T. Hashimoto, T. Saegusa, *J. Am. Chem. Soc.* **1972**, 94, 658.
- Stereochemistry of the enol silyl ethers **6b**, **6c**, **7a**, and **7c–7f** was determined as Z configuration by NOE and/or NOESY experiment. The other enol silyl ethers were estimated as Z by analogy with the above results.
- P. Sormunen, E. Iiskola, E. Vähäsarja, T. T. Pakkanen, T. A. Pakkanen, *J. Organomet. Chem.* **1987**, 319, 327.
- a) A. Yanagisawa, Y. Nakatsuka, K. Asakawa, M. Wadamoto, H. Kageyama, H. Yamamoto, *Bull. Chem. Soc. Jpn.* **2001**, 74, 1477. b) X. Wang, Q. Meng, N. R. Perl, Y. Xu, J. L. Leighton, *J. Am. Chem. Soc.* **2005**, 127, 12806. c) Y. Orito, S. Hashimoto, T. Ishizuka, M. Nakajima, *Tetrahedron* **2006**, 62, 390.
- H. Horie, Y. Kajita, S. Matsubara, *Chem. Lett.* **2009**, 38, 116, and references cited therein.
- When **8** was treated with CuOt-Bu (3.3 equiv) and benzyl bromide (3.6 equiv) at 70 °C, diphenylmethane (64%), formed by the reaction of PhCu with the halide, was isolated together with the corresponding *t*-butoxy-substituted enol silyl ether (54%).
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