11196 *J. Am. Chem. Soc.* **1998,** *120,* 11196−11197

New Method for Introduction of a Silyl Group into α,*β*-Enones Using a Disilane Catalyzed by a Copper(I) Salt[1]

Hajime Ito, Tomoko Ishizuka, Jun-ichi Tateiwa,
Motohiro Sonoda, and Akira Hosomi*

Department of Chemistry, Graduate School of Chemistry
University of Tsukuba, Tsukuba
Ibaraki 305-8571, Japan

Received June 29, 1998

Introduction of silyl functionalities into organic compounds along with the formation of the Si−C bond is of great interest in organic synthesis.[2] Conjugate silylation of α,*β*-unsaturated carbonyl compounds is an important tool, and this reaction is usually achieved by the use of silyl nucleophiles.[3] In the hitherto known methods, stoichiometric preparation of a silyl anionic species, relatively inaccessible, has been indispensable for the generation of silyl nucleophilic reagents. Although the Pd-catalyzed reactions of a disilane and α,*β*-unsaturated carbonyl compounds are comparable with the method using silyl nucleophiles, there are some limitations to both the silyl groups and substrates available for these reactions.[4] We wish to report herein, as a partial solution to these problems, an unprecedented cleavage reaction of the silicon−silicon bond in a disilane with a Cu(I) salt to generate a silyl nucleophile and its new 1,4-addition reaction toward α,*β*-enones in the presence of a catalytic amount of a Cu(I) salt. (Scheme 1).

Scheme 1. Conjugate Silylation of an α,*β*-Unsaturated Carbonyl Compound and a Disilane catalyzed by a Copper(I) Salt

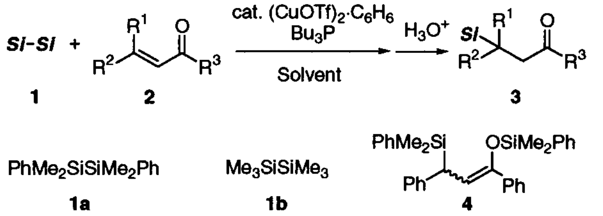
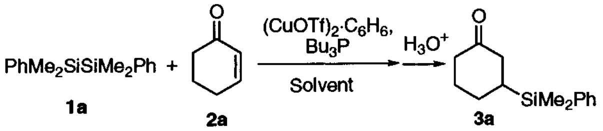


Table 1. Reaction of 1,2-Diphenyltetramethyldilsilane (**1a**) and 2-Cyclohexen-1-one (**2a**) in the presence of a Cu(I) Catalyst under Various Conditions



entry[a]	disilane **1a**/equiv	Cu(I)/ equiv	Bu_3P/ equiv	solvent	temp/ °C	time/ h	yield of **3a**/%[b]
1	1.0	1.0		DMI	r.t.	24	20
2	1.0	0.1		DMI	100	24	33
3	1.2	0.1	0.11	DMI	100	21	88
4	1.2	0.1	0.11	DMF	100	4	91
5	1.2	0.1	0.11	Diglyme	100	21	77

[a] A mixture of a disilane (1.0−1.2 mmol), an α,*β*-unsaturated compound (1.0 mmol), $(CuOTf)_2{\cdot}C_6H_6$ (0.05−1.0 mmol) and tributylphosphine (0−0.11 mmol) was stirred in a solvent (1.0 ml). [b] Isolated yield.

We have recently reported exchange reactions of a silyl group of alkynyl-, aryl- and hydrosilanes with a Cu(I) salt in an aprotic polar solvent such as 1,3-dimethyl-2-imidazolidinone (DMI) and various synthetic procedures using organocopper(I) reagents based on this exchange reaction.[5] Although there are many reports of the cleavage reaction of a Si−Si bond in disilanes to generate a silyl nucleophile with alkali metal,[6] alkyllithium,[3b] metal alcoholate,[7] metal hydride,[8] fluoride ion,[9] and transition metal complex,[10,11] to our knowledge, the cleavage reaction of disilanes with a Cu(I) salt is unknown. We started our investigation of the reaction between a disilane and a copper(I) salt in DMI analogous to the reaction between hydrosilanes and CuCl, previously reported.[5a]

For the purpose of trapping a reactive intermediate of this reaction generated in situ, the reaction using 1,1,2,2-tetramethyl-1,2-diphenyldisilane **1a** and $(CuOTf)_2{\cdot}C_6H_6$[12] in DMI was examined in detail in the presence of 2-cyclohexen-1-one as an electrophile, after trials using several combinations between a Cu(I) salt and a solvent (Table 1). In entry 1, a mixture of 1,1,2,2-tetramethyl-1,2-diphenyldisilane (1.0 mmol), $(CuOTf)_2{\cdot}C_6H_6$ (1.0 mmol) and 2-cyclohexen-1-one **2a** (1.0 mmol) in DMI (1.0 mL) was stirred for 24 h at room temperature.[13] After acidic workup, a conjugate silylation product **3a** was obtained in 20% yield. To confirm the synthetic feasibility of this reaction, we explored reaction conditions for a catalytic use of the Cu(I) salt. However, the use of 10 mol % of the copper(I) salt as a catalyst for the conjugate silylation of α,*β*-enones resulted in low yield at 100 °C together with unidentified side products (entry 2). Under these conditions, the precipitation of Cu(0) was observed. Then, we found that the addition of a catalytic amount of tributylphosphine dramatically improved this reaction (entry 3). The silylation product **3a** was obtained in good yield even with 5 mol % (10 mol % for Cu(I)) of $(CuOTf)_2{\cdot}C_6H_6$ in the presence of tributylphosphine (11 mol %) (entries 3−5). DMI and DMF are both good solvents for this reaction. The rate of the silylation reaction

---

(1) Studies on Organosilicon Chemistry. No. 145.

(2) (a) Fleming, I. *Organocopper Reagents: A Practical Approach;* Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 257−292. (b) Colvin, E. W. *Silicon Reagents in Organic Synthesis;* Academic Press: London, 1988; pp 51−55.

(3) (a) Lipshutz, B. H.; Sclafani, J. A.; Takanami, T. *J. Am. Chem. Soc.* **1998**, *120*, 4021−4022. (b) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063−3064. (c) Ager, D. J.; Fleming, I.; Patel, S. K. *J. Chem. Soc., Perkin. Trans. 1* **1981**, 2520−2526. (d) Lipshutz, B. H.; Reuter, D. C.; Ellsworth, E. L. *J. Org. Chem.* **1989**, *54*, 4975−4977. (e) Crump, R. A. N. C.; Fleming, I.; Urch, C. J. *J. Chem. Soc., Perkin. Trans. 1* **1994**, 701−706. (f) Smith, J. G.; Quinn, N. R.; Viswanathan, M. *Synth. Commun.* **1983**, *13*, 1−5. (g) Kawachi, A.; Tamao, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 945−955.

(4) For the Pd-catalyzed 1,4-bis-silylation of α,*β*-unsaturated ketones, see: (a) Tamao, K.; Okazaki, S.; Kumada, M. *J. Organomet. Chem.* **1978**, *146*, 87−93. (b) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc*. **1988**, *110*, 5579−5581.

(5) (a) Ito, H.; Ishizuka, T.; Arimoto, K.; Miura, K.; Hosomi, A. *Tetrahedron Lett.* **1997**, *38*, 8887−8890. (b) Ito, H.; Arimoto, K.; Sensui, H.; Hosomi, A. *Tetrahedron Lett.* **1997**, *38*, 3977−3980. (c) Ito, H.; Sensui, H.; Arimoto, K.; Miura, K.; Hosomi, A. *Chem. Lett.* **1997**, 639−640. (d) See also: Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1998**, *39*, 4075−4078.

(6) Gilman, H.; Lichtenwalter, G. D. *J. Am. Chem. Soc.* **1958**, *80*, 608−611.

(7) (a) Sakurai, H.; Okada, A.; Kira, M.; Yonezawa, K. *Tetrahedron Lett.* **1971**, *12*, 1511−1514. (b) Dervan, P. B.; Shippey, M. A. *J. Am. Chem. Soc.* **1976**, *98*, 1265−1267.

(8) Corriu, R. J. P.; Guerin, C. *J. Chem. Soc., Chem. Commun.* **1980**, 168−169.

(9) Hiyama, T.; Obayashi, M.; Mori, I.; Nozaki, H. *J. Org. Chem.* **1983**, *48*, 912−914.

(10) For recent reviews with respect to transition metal-mediated reactions using a Si−Si bond, see: (a) Sharma, H. K.; Pannell, K. H. *Chem. Rev.* **1995**, *95*, 1351−1374. (b) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1317−1350.

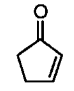
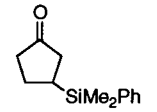
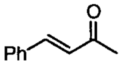
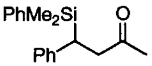
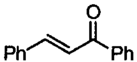
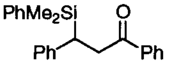
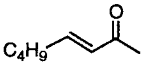
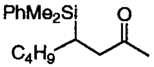
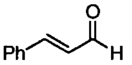
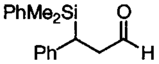
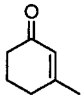
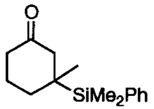
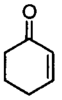
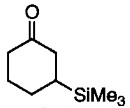
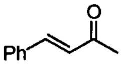
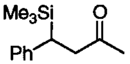
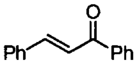
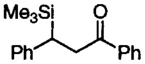
(11) Palladium-catalyzed reaction of hexamethyldisilane, see: (a) Ito, Y.; Suginome, M.; Murakami, M. *J. Org. Chem.* **1991**, *56*, 1948−1951. (b) Yamashita, H.; Reddy, N. P.; Tanaka, M. *Chem. Lett.* **1993**, 315−318. (c) Yamashita, H.; Reddy, N. P.; Tanaka, M. *Macromolecules* **1993**, *26*, 2143-2144. (d) Obora, Y.; Tsuji, Y.; Kawamura, T.; *J. Am. Chem. Soc.* **1995**, *117*, 9814−9821.

(12) $(CuOTf)_2{\cdot}C_6H_6$ is highly sensitive for both moisture and air. It should be weighed in a glovebox under nitrogen (see Supporting Information). Cohen, T.; Ruffner, R. J.; Shull, D. W.; Fogel, E. R.; Flack, J. R. *Org. Synth.* **1980**, *59*, 202−210.

(13) In the absence of **2a**, a mixture of recovered **1a** (38%) and $PhMe_2$-$SiOSiMe_2Ph$ (55%) was obtained.

10.1021/ja9822557 CCC: $15.00

Table 2. Reactions of α,β-Unsaturated Carbonyl Compound **2** and Disilane **1** in the Presence of a Copper(I) Catalyst

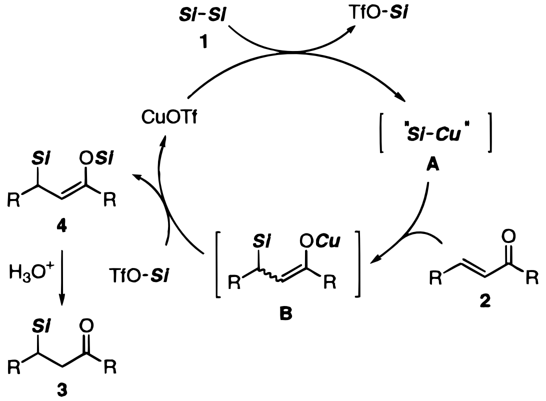
entry[a]	disilane 1	substrate 2	conditions	product 3, yield / %[b]
1	**1a**	 **2b**	11 mol % Bu$_3$P, 80 °C, DMF, 24 h	 **3b**, 91%
2	**1a**	 **2c**	11 mol % Bu$_3$P, 80 °C, DMF, 11 h	 **3c**, 95%
3	**1a**	 **2d**	11 mol % Bu$_3$P, 80 °C, DMF, 10 h	 **3d**, 92%
4[c]	**1a**			**3d**, 50%, **4**, 43%
5	**1a**	 **2e**	11 mol% Bu$_3$P, 80 °C, DMF, 24 h	 **3e**, 84%
6	**1a**	 **2f**	11 mol% Bu$_3$P, 80 °C, DMF, 19 h	 **3f**, 79%
7	**1a**	 **2g**	11 mol% Bu$_3$P, 60 °C, DMF, 66 h	 **3g**, 35%
8[d]	**1b**	 **2a**	11 mol% Bu$_3$P, 100 °C, 48 h DMI, diglyme(1:1)	 **3h**, 76%
9[d,e]	**1b**	 **2c**	100 °C, DMI, 43 h	 **3l**, 95%
10[d,e]	**1b**	 **2d**	100 °C, DMI, 19 h	 **3j**, quant.
11[e,f]	**1b**	**2d**	100 °C, DMI, 24 h	**3j**, 96%

[a] A mixture of a disilane (1.2 mmol), an α,β-unsaturated compound (1.0 mmol), (CuOTf)$_2$ · C$_6$H$_6$ (0.05 mmol) and tributylphosphine (0.11 mmol) was stirred in a solvent (1.0 ml). [b] Isolated yield unless otherwise noted. [c] Without addition of an acid at workup. [d] Three equivalents of a disilane were used. [e] Tributylphosphine was not used. [f] Reaction was carried out with 1.2 equivalent of a disilane under a sealed tube.

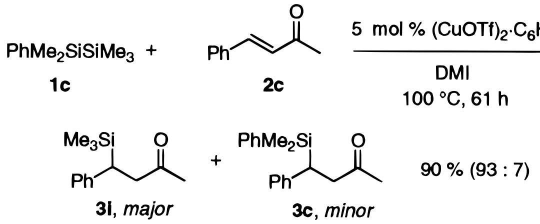
of **3a** was increased in DMF. Diglyme can also be used as a solvent (entry 5).

This catalytic reaction was applied to 3-silylation of various α,β-unsaturated carbonyl compounds (Scheme 1). Representative results are listed in Table 2. Optimized reaction time and solvent depend on the substrates. The conjugate silylation product of a dimethylphenylsilyl group was obtained in good yield for various α,β-unsaturated ketones (entries 1−5). Without acidic workup, the corresponding silyl enol ether **4** was isolated (entry 4). An α,β-unsaturated aldehyde **2f** can be also used as a good acceptor (entry 6). However, 3-methyl substitution of the substrate **2** retarded this reaction, presumably due to the steric effect (entry 7). The products were obtained in good yield even with hexamethyldisilane **1b**, which is relatively unreactive for the Si−Si cleavage reaction (entries 8−11).[7,11] For increasing the solubility of hexamethyldisilane, a mixed solvent of DMF and diglyme (1:1) was employed (entry 8). This method is useful for the introduction of a trimethylsilyl group to α,β-enones, since the preparation of trimethylsilylcopper is not easily accessible.[14]

Scheme 2. Proposed Mechanism for the Conjugate Silylation of an a,b-Unsaturated Carbonyl Compound and a Disilane in the Presence of a Copper(I) Catalyst



Interestingly, the trimethylsilyl group was mainly introduced into the substrate when using unsymmetrical disilane **1c** (eq 1).



(1)

This result provides a clear contrast with the case of palladium-catalyzed 1,4-disilylation of α,β-unsaturated ketones with 1,1-dichrolo-1-phenyl-2,2,2-trimethyldisilane.[15]

A plausible catalytic cycle is shown in Scheme 2. Reaction between a disilane and a copper(I) salt forms reactive intermediate **A**, and conjugate addition to α,β-enones takes place. The copper(I) salt is regenerated by the reaction between the resultant copper(I) enolate and silyl triflate, which is formed at the first stage of this cycle. Tributylphosphine coordinates to copper(I) and presumably plays an important role in the stabilization of the intermediate **A** and copper(I) enolate **B**. After the reaction was completed, acidic workup gave **3**.

In conclusion, we have found an unprecedented and exclusive cleavage reaction of disilanes followed by the conjugate silylation to α,β-enones with a catalytic amount of a Cu(I) salt.[16] The present procedure provides a convenient and synthetically useful route for introduction of a silyl group into α,β-enones without prior stoichiometric preparation of silylmetals. Further work on the precise mechanism for these reactions and on the structure of the active species is actively underway.

Acknowledgment. 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.

Supporting Information Available: Experimental details for the general procedure of the catalytic reactions, ^{1}H, ^{13}C NMR spectra of all products (7 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA9822557

---

(14) In the hitherto known methods for the preparation of trimethylsilylmetal species, HMPA (hexamethylphosphoramide), known as a strong carcinogen, is needed as the solvent.

(15) (a) Hayashi, T.; Matsumoto, Y.; Ito, Y. *Tetrahedron Lett.* **1988**, *29*, 4147−4150. (b) Matsumoto, Y.; Hayashi, T.; Ito, Y. *Tetrahedron* **1994**, *50*, 335−346.

(16) Although α,β-unsaturated esters instead of α,β-enones gave a silylated product in poor yield (at most, ca. 20%) under the same conditions, efforts to explore better conditions are now under way.