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Direct Alkynyl Group Transfer from Silicon to Copper: New Preparation Method of Alkynylcopper (I) Reagents[1]

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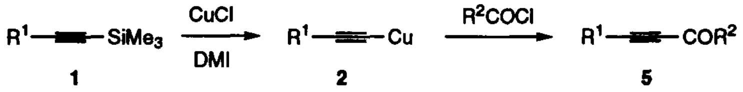
Abstract: A first observation of the direct alkynyl group transfer from silicon to copper is reported. The silicon group of alkynylsilanes was smoothly replaced by copper (I) chloride in DMI to give the corresponding copper (I) acetylides. This transformation was applied to the synthesis of alkynyl ketones catalyzed by CuCl. © 1997 Elsevier Science Ltd.

Organocopper reagents are widely used in organic synthesis. In the preparation of organocopper reagents, a combination of a copper (I) salt and reactive organometallics such as organolithiums and Grignard reagents was usually employed.[2] However, the isolation of organocopper reagents using organosilicon compounds as a mild reagent has not been known, though the carbon-carbon bond formation catalyzed by the copper salt took place between organosilanes and organic halides in a few cases.[3,4] We report herein not only the first isolation and a new direct preparation method of alkynylcopper (I) reagents using alkynylsilanes and CuCl, but also its application to the synthesis of alkynyl ketones catalyzed by CuCl. (eq. 1)



$$\underset{\mathbf{1}}{R^1{-}{\equiv}{-}SiMe_3} \xrightarrow[\text{DMI}]{\text{CuCl}} \underset{\mathbf{2}}{R^1{-}{\equiv}{-}Cu} \xrightarrow{R^2COCl} \underset{\mathbf{5}}{R^1{-}{\equiv}{-}COR^2} \qquad (1)$$

The trimethylsilyl group has been usually utilized to protect terminal acetylenes from organometallic reagents and transition metal catalysts during various synthetic transformations.[5] However, the Si-C bond of trimethylsilylacetylenes is selectively cleaved by the fluoride ion, Lewis acid and base, and is generally stable to neutral inorganic salts. Indeed, bis(trimethylsilyl)acetylene forms a π-complex with CuCl without the cleavage of the Si-C bond in Et_2O.[6] This shows that CuCl has π-acid behavior to bis(trimethylsilyl)acetylene. In sharp contrast, we found that this stability to CuCl was dramatically changed in 1,3-dimethyl-2-imidazolidinone (DMI). Thus on the addition of 1-phenyl-2-(trimethylsilyl)ethyne **1a** (872 mg, 5.0 mmol), a suspension of CuCl (495 mg, 5.0 mmol) in dry DMI (5.0 mL) became at first a clear solution at room temperature. After stirring for 10 min, slightly soluble phenylethynylcopper (I) **2a** was precipitated. After the mixture was allowed to react at 80 °C for 6 h, the precipitation was collected and washed with acetonitrile and ether to give a light-yellow solid, phenylethynylcopper (I) **2a** (667 mg, 81% yield).[7] This result is the first case of observation of the alkynyl group transfer from silicon to copper.[8] We tested various alkynylsilanes, solvents and copper (I) salts in order to investigate this transformation in detail. The results are shown in Table 1. The solvent plays an important role in this reaction. (entries 1-3) Only in DMI and DMF (dimethylformamide) the corresponding alkynylcopper (I) derivatives were obtained. Use of CuBr, CuI or

CuCN instead of CuCl decreased the yield of phenylethynylcopper (I) **2a**. (entries 4-6) 1-Trimethylsilyl-1-hexyne **1b** also gave the corresponding copper (I) acetylide **2b** in moderate yield. (eq. 2) However, for the bulky substrate **1c** the CuCl suspension did not change to a clear solution and gave no copper (I) acetylide **2c**. This indicates that the first step of this Cu-Si exchange reaction is the formation of a soluble π-complex **3** between an alkynylsilane and CuCl in DMI, and the bulky *t*-butyl substituent of **1c** would prevent the formation of π-complex **3**. (eq. 3)

Table 1. Reactions of 1-phenyl-2-(trimethylsilyl)ethyne **1a** and copper (I) chloride[a]

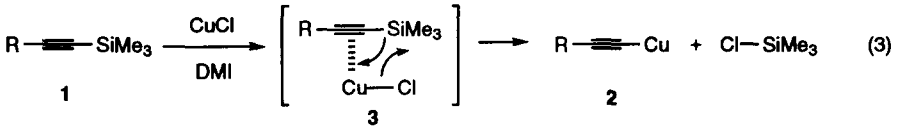
Entry	Copper salt	Solvent	Yield of **2** / %[b]	Entry	Copper salt	Solvent	Yield of **2** / %[b]
1[c]	CuCl	DMI	81	4	CuBr	DMI	32
2	CuCl	DMF	64	5	CuI	DMI	0
3	CuCl	CH_3CN	0	6	CuCN	DMI	18

[a] A mixture of copper (I) salt (1.0 mmol) and an alkynylsilane (1.0 mmol) was heated at 80 °C for 6 h in solvent (1.0 mL). [b] Yield after filteration. [c] CuCl (5.0 mmol) and an alkynylsilane (5.0 mmol) were used in DMI (5.0mL).

$$R{-}{\equiv}{-}SiMe_3 + CuCl \xrightarrow[\text{DMI, 80 °C, 6 h}]{} R{-}{\equiv}{-}Cu \qquad (2)$$

1a: R = Ph
1b: R = Hex
1c: R = *t*-Bu

2a: R = Ph; 81%
2b: R = Hex; 58%
2c: R = *t*-Bu; 0%



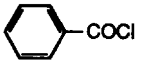
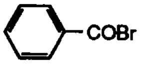
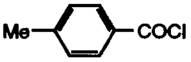
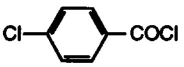
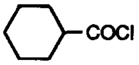
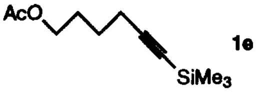
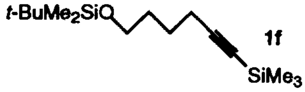
Copper (I) acetylides, thus obtained, react with acid halides to afford alkynyl ketones smoothly[9] and we found that this transformation could be applied to a new route for the synthesis of alkynyl ketones by the CuCl-catalyzed reaction of alkynylsilanes **1** with acid halides **4**. (eq. 4) Representative results are listed in Table 2. Coupling reactions between alkynylsilanes and acyl halides proceeded smoothly in the presence of a catalytic and stoichiometric amount of CuCl. A general procedure is given as follows. To a mixture of 1-phenyl-2-(trimethylsilyl)ethyne **1a** (174 mg, 1.0 mmol) and CuCl (20 mg, 0.2 mmol) in DMI (0.5 mL) was added benzoyl chloride **4a** (155 mg, 1.1 mmol) at room temperature. After stirring for 5 h at 80°C, the reaction mixture was diluted with chloroform. Filtration through a short-column chromatography using Frolisil® followed by purification with column chromatography (SiO_2, ethyl acetate : hexane = 1: 20) gave 1,3-diphenylpropyn-1-one (177 mg, 85% yield). No precipitation of copper (I) acetylides was observed during the reaction.

$$\underset{\mathbf{1}}{R^1{-}{\equiv}{-}SiMe_3} + \underset{\mathbf{4}}{R^2COX} \xrightarrow[\text{DMI, 80°C}]{\text{CuCl}} \underset{\mathbf{5}}{R^1{-}{\equiv}{-}COR^2} \qquad (4)$$

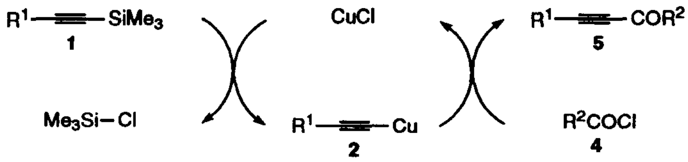
In the first step of the catalytic cycle, the trimethylsilyl group of alkynylsilane **1** is replaced by copper

(I) atom to give copper (I) acetylides. (Scheme 1) Successive nucleophilic reaction of copper (I) acetylides **2** with acyl chloride **4** gives the corresponding alkenyl ketone **5** and regenerates CuCl. Thus, a catalytic amount of CuCl is sufficient for this reaction. When benzoyl bromide was used as an electrophile, a less reactive CuBr was regenerated and, therefore, the yield was decreased. (entry 2) This clearly shows that the regeneration of CuCl plays an important role in this reaction.

Table 2. Synthesis of alkynyl ketones **5** from alkynylsilanes **1** and acyl halides **4** mediated by CuCl[a]

Entry	Alkynylsilane 1	Acyl halide 4	CuCl / equiv.	Time / h	Yield of 5 / %[b]
1	 **1a**	 **4a**	0.2	5	86
2	**1a**	 **4b**	0.2	5	10
3	**1a**	 **4c**	0.2	4	84
4	**1a**	 **4d**	0.2	6	77
5	**1a**	*t*-BuCOCl **4e**	0.2	5	98
6	**1a**	 **4f**	1.0[c]	4	83
7	*n*-Hex—≡—SiMe$_3$ **1b**	**4a**	0.2	8	85
8	**1b**	**4e**	0.2	5	85
9	EtOCO—≡—SiMe$_3$ **1d**	**4a**	0.2	1.5	69
10	 **1e**	**4a**	1.0[c]	4	91
11[d]	 **1f**	**4a**	1.0[c]	5	73

[a] A mixture of an alkynylsilane (1.0 mmol), an acyl halide (1.1 mmol) and CuCl (0.2 mmol) was heated at 80 °C in DMI (0.5 mL), unless otherwise noted. [b] Yield after isolation. [c] In the case of the use of a catalytic amount of CuCl, both the reaction rate and the yield decreased, resulting in the formation of unidentified by-products. [d] The reaction was carried out at 60 °C and diisopropylamine (0.5 mmol) was used as an additive in order to prevent desilylation.



Scheme 1. A catalytic cycle for the reaction of alkynylsilane with acyl halide

Although it has been known that a Lewis acid such as $AlCl_3$ promotes the reaction of alkynylsilanes with acyl halides, acid-sensitive substrates could not be employed in this reaction.[10] However, we found that an acid- and fluoride ion-sensitive substrate **1f** was also converted into the corresponding alkynyl ketone in good yield (entries 11), although an attempt to obtain the same product with an $AlCl_3$-catalyst was unsuccessful.[11]

In conclusion, the direct silicon-copper exchange reaction occurred easily in DMI in the absence of the fluoride ion. These results provide not only valuable insight into organosilicon chemistry but also an effective catalytic synthetic route to alkynyl ketones from alkynylsilanes by avoiding deprotection of silylated terminal alkynes under mild conditions.

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7. The spectroscopic data are identical with those of the authentic sample prepared by the literature method. Sazonova, V. A.; Kronrod, N. Ya. *Zh. Obshch. Khim.* **1956**, *26*, 1876.
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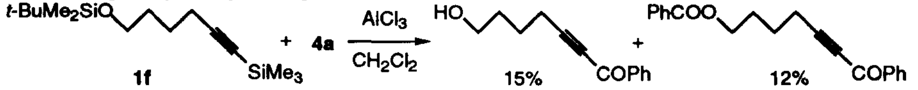
10. For the acylations using copper (I) acetylides prepared from terminal alkynes, see: Posner, G. H. *Org. React.* **1975**, *22*, 380.
11. To a mixture of **1f** (285 mg, 1.0 mmol) and benzoyl chloride (168.7 mg, 1.1 mmol) in dry dichloromethane was added $AlCl_3$ (400 mg, 3.0 mmol) at room temperature under nitrogen. After stirring for 4 h, **1f** completely disappeared. After the separation of products by preparative TLC followed by usual workup, only desilylation products were obtained. (eq. 5)



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