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A tandem allylsilane–vinylsilane difunctionalization by silylcupration of allene followed by reaction with α,β-unsaturated nitriles

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Silylcupration of allene using phenyldimethylsilylcopper 1 followed by BF_3-mediated reaction with α,β-unsaturated nitriles at −40 °C affords allylsilane–vinylsilane-containing ketones resulting from consecutive addition (1,2 and 1,4) of the intermediate allyl- and vinylcopper species formed in the silylcupration of allene.

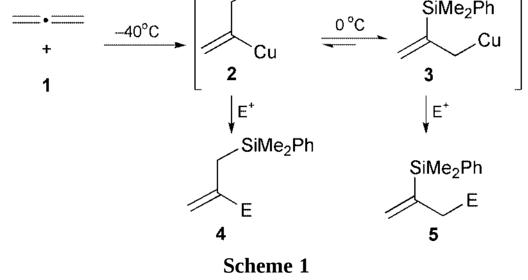
We recently reported[1–3] that addition of phenyldimethylsilylcopper ($PhMe_2SiCu{\cdot}LiCN$, **1**) to propa-1,2-diene leads to a silylated copper intermediate, which can be imprecisely formulated as a mixture of the allylsilane–vinylcopper species **2** and the vinylsilane–allylcopper species **3**. The reversibility of the reaction is one of its features. Quenching of the intermediate copper species with different electrophiles results in formation of compounds of type **4** or **5** (Scheme 1).

The reaction is temperature dependent and the presence of species **2** and **3** can be demonstrated by protonation of the reaction mixture at different temperatures. Thus, at −40 °C (or lower temperature) only formation of **4** (E = H) was observed, whereas **5** (E = H) was the major product obtained near to 0 °C.

In general, for most of the reported work[1] the reactive species at low temperature is **2**. Thus, at −40 °C, α,β-unsaturated ketones or aldehydes react with **2** giving exclusively 1,4-addition. However, at temperatures around −40 °C, simple ketones are unreactive toward species **2**, but they are readily attacked by **3** as the temperature increases to 0 °C, giving hydroxymethyls bearing the vinylsilane moiety.[1] In this case, conversion of species **2** into species **3** seems to occur rapidly as the temperature increases, which probably accounts for the observed result.

We now report an interesting and unusual tandem diaddition-hydrolysis process by successive addition (1,2 and 1,4) of species **3** and **2** to α,β-unsaturated nitriles. Protonation of the intermediate adduct, gives products that have both allylsilane and vinylsilane functionality.

Reaction of α,β-unsaturated nitriles with organocopper compounds has not been widely explored. Yamamoto[4] reported that the reaction of α,β-unsaturated nitriles with $RCu{\cdot}BF_3$ was not satisfactory; yields were low, and mixtures of monoalkylated and dialkylated products were obtained. Alexakis *et al.*[5] showed that introduction of an additive like TMSCl in the reaction of Me_2CuLi with some α,β-unsaturated nitriles gave the dialkylated ketone, whereas Lipshutz *et al.*[6] found that $Me_2CuCNLi_2$ slowly produced a poor yield of the methyl ketone resulting from 1,2 addition.



Scheme 1

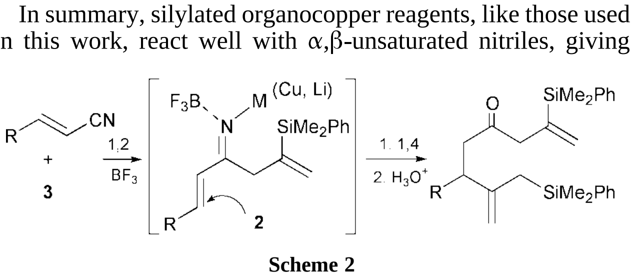
Silylcupration of allene (2 eq., following our usual protocol[1]) followed by addition of $BF_3{\cdot}Et_2O$ (2 equiv.) and subsequent slow addition of nitriles **6–9** (1 eq., THF, −40 to 0 °C) afforded, after hydrolysis at 0 °C, the ketones **10–13**, which seem to be produced by addition of the vinylsilane–allylcopper species **3** to the nitrile group and conjugate addition of the allylsilane–vinylcopper species **2** to the β position (Table 1).[7] The reaction (one pot) is clean and high yielding. Monoaddition products were not found. Remarkably, when this reaction is carried out with one equivalent each of allene and **1**, BF_3 and nitrile, the same diaddition products were formed, and almost half of the nitrile was wasted, which suggests that the second stage of the overall addition occurs quickly. It should be also noted that silylcupration of allene and further reaction with **8**, **9** (nitrile–organocopper; 1 : 2) at 0 °C, in the absence of BF_3, gives exclusively the 1,2-adducts **14** and **15** (Table 1).

The order in which the two steps (1,2 and 1,4) of addition take place and the mechanistic pathway are not certain. Weiberth and Hall[8] have proposed the intervention of Cu(III) intermediates in the copper-activated reaction of benzonitriles with Grignard reagents. Although we defer any definitive statement about the mechanism, it seems feasible—in view of the absence of 1,4-monoaddition products—that the reaction proceeds by initial addition of species **3** to the nitrile group followed by BF_3-catalyzed conjugate addition of species **2** to the intermediate α,β-unsaturated ketimine (Scheme 2). The chemoselectivity observed and the preference for the attack of **3** to the nitrile and of **2** to the conjugate position can be related to the different hardness of the nucleophilic species.

A completely different pattern of reaction is observed when the bulky *tert*-butyldiphenysilyl group is used instead of $PhMe_2Si$. Silylcupration of propa-1,2-diene with *tert*-$BuPh_2Si$-$Cu{\cdot}LiCN$[9] followed by addition of BF_3 and reaction with **6** and **8**—under the same conditions used before—affords selectively the 1,4-adducts **16** and **17** as the only products (Table 1). We have noted before[1] that species of type **2**, but carrying the bulky *tert*-butyldiphenysilyl group, are regiochemically stable at any temperature between −40 °C and 0 °C.

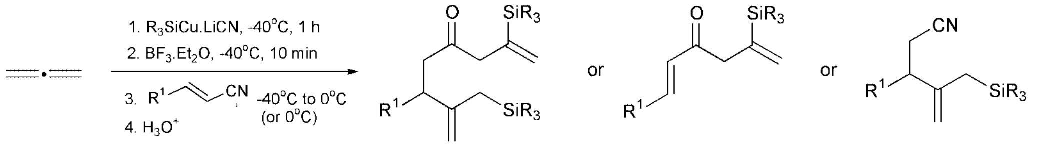
The one-pot tandem diaddition-hydrolysis process reported here could be of importance in synthetic work since the allylsilane and vinylsilane moieties are versatile synthons for organic synthesis. Thus, the diadducts undergo selective intramolecular allylsilane terminated cyclization,[1] while the vinylsilane unit remains unchanged, as shown in Scheme 3 with the conversion of **10–12** into **18–20**.

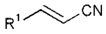
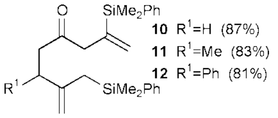
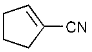
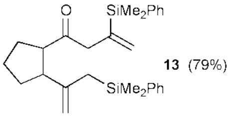
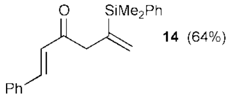
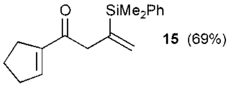
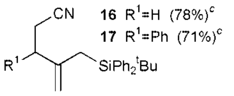
In summary, silylated organocopper reagents, like those used in this work, react well with α,β-unsaturated nitriles, giving



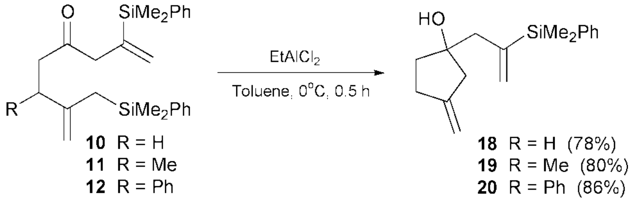
Scheme 2

Table 1 Reaction of α,β-unsaturated nitriles with silicon containing allyl- and vinylcopper reagents



Nitrile	Ratio nitrile : organocopper	R$_3$Si	Temp.	Product (yield)[a]
 **6** R^1=H **7** R^1=Me **8** R^1=Ph	1 : 2	PhMe$_2$Si	−40 to 0 °C	 **10** R^1=H (87%) **11** R^1=Me (83%) **12** R^1=Ph (81%)
 **9**	1 : 2	PhMe$_2$Si	−40 to 0 °C	 **13** (79%)
8	1 : 1	PhMe$_2$Si	0 °C[b]	 **14** (64%)
9	1 : 1	PhMe$_2$Si	0 °C[b]	 **15** (69%)
6 R^1=H **8** R^1=Ph	1 : 2	^{t}BuPh$_2$Si	−40 to 0 °C	 **16** R^1=H (78%)[c] **17** R^1=Ph (71%)[c]

[a] Yields refer to isolated pure compounds. [b] Reaction was carried out in the absence of BF$_3$. [c] Yield refers to the starting nitrile.



Scheme 3

1,2-adducts, 1,4-adducts or diaddition adducts, depending on the reaction conditions and on the nature of the silyl group.† We are not totally clear why we succeeded where others did not, but most probably it is connected with the nature of the equilibrium mixture of species and with the fact that a Lewis acid (BF$_3$)-activated organocopper is used. The effects of Lewis acid on cuprates have been examined recently, and they show that a strong chemoselectivity enhancement is frequently observed when Lewis acid-modified organocopper reagents are used.[10]

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Notes and references

† Satisfactory analytical data were obtained for the new compounds. The purity and structure of all new compounds were confirmed by ^{1}H and ^{13}C NMR, IR and GC-MS.

1 A. Barbero, C. García and F. J. Pulido, *Tetrahedron*, 2000, **56**, 2739, and references therein.

2 A. Barbero, C. García and F. J. Pulido, *Tetrahedron Lett.*, 1999, **40**, 6649.

3 F. J. Blanco, P. Cuadrado, A. M. González, F. J. Pulido and I. Fleming, *Tetrahedron Lett.*, 1994, **35**, 8881.

4 Y. Yamamoto, S. Yamanoto, H. Yatagai, Y. Ishibara and K. Maruyama, *J. Org. Chem.*, 1982, **47**, 119.

5 A. Alexakis, J. Berlan and Y. Besace, *Tetrahedron Lett.*, 1986, **27**, 1047.

6 B. H. Lipshutz, R. S. Wilhelm and J. A. Kozlowski, *J. Org. Chem.*, 1984, **49**, 3938.

7 *Typical procedure*: a solution of 6 mmol of PhMe$_2$SiCu·LiCN (see ref. 1) in THF (16 ml) was cooled to −40 °C and a slight excess of propa-1,2-diene was added from a balloon. The mixture was stirred for 1 h at this temperature, then BF$_3$·Et$_2$O (6 mmol) was added at −40 °C and the solution stirred for an additional period of 10 min. The nitrile (3 mmol) in THF (3 ml) was slowly dropped in at −49 °C, and the resulting mixture stirred at this temperature for 1 h. The reaction mixture was left to warm to 0 °C and was quenched with saturated ammonium chloride solution. Purification by flash-chromatography gave the ketones **10**–**13** (Table 1).

6-Phenyl-2-[dimethyl(phenyl)silyl]-7-{[dimethyl(phenyl)silyl]-methyl}octa-1,7-dien-4-one (**12**): ^{1}H NMR (300 MHz, CDCl$_3$): 7.53–7.02 (m, 15H), 5.58 (d, J = 2.5, 1H), 5.52 (d, J = 2.5, 1H), 4.64 (d, J = 0.7, 1H), 4.62 (d, J = 0.7, 1H), 3.52 (dd, J = 6.7 and 7.9, 1H), 2.98 (d, J = 14.7, 1H), 2.93 (d, J = 14.7, 1H), 2.69 (dd, J = 16.5 and 6.7, 1H), 2.54 (dd, J = 16.5 and 7.9, 1H), 1.66 (d, J = 13.8, 1H), 1.44 (d, J = 13.8, 1H), 0.41 (s, 6H), 0.34 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$): 206.6, 148.2, 143.2, 142.6, 138.9, 137.3, 133.9, 133.6, 130.6, 129.1, 128.9, 128.3, 128.1, 127.7, 127.6, 126.4, 107.6, 50.4, 47.8, 47.2, 25.7, −2.9, −3.2; CIMS: m/z 483 (M + 1).

8 F. J. Weiberth and S. S. Hall, *J. Org. Chem.*, 1987, **52**, 3901.

9 P. Cuadrado, A. M. González, B. González and F. J. Pulido, *Synth. Commun.*, 1989, **19**, 275. See also ref. 1.

10 *Comprehensive Organic Synthesis*, eds. B. Trost and I. Fleming, Pergamon Press, Oxford, 1991, Vol. 4, pp. 148 and 179.