Silylcupration of styrenes followed by electrophilic trapping reaction

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Silylcupration reaction of styrene and its analogues with a silylcopper reagent PhMe$_2$SiCuCNLi followed by an electrophilic trapping has been reported for the first time.

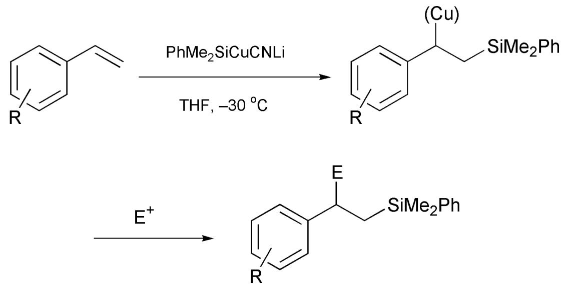
Silylcupration reaction of acetylenes and allenes has been studied by Fleming and co-workers.[1,2] Scarce literature data, however, is available on metallo-metallations of double bonds. Silylmanganation[3] and catalytic silicon–silicon bond addition to double bonds[4] and 1,3-dienes[5] involving silylpalladation have been reported. However, to the best of our knowledge, there are no reports in the literature on silylcupration of double bonds except for allenes.[2,6,7] Most of the silylcupration reactions have been done with the silylcuprate reagent (PhMe$_2$Si)$_2$CuLi·LiCN or more bulky silylcuprate reagents.[8] Recently, silylcopper reagent PhMe$_2$SiCuCNLi has been used by Pulido[6] and us[7] in allene silylcupration reactions. The advantage of the silylcopper reagent PhMe$_2$SiCuCNLi over the disilyl cuprate reagent is that it makes use of all the silyl on copper. With the latter reagent only one of the two groups is transferred and the remaining silylcopper reagent may lead to side products and hence separation problems.

Here we wish to report for the first time a silylcupration reaction of substituted and unsubstituted styrene. The copper intermediate obtained can be easily trapped by different electrophiles, including allylic phosphates, which are reactive and readily accessible allylic substrates for metal-catalysed reactions[7,9] (Scheme 1).

Reaction of styrene with silylcopper reagent PhMe$_2$SiCuCNLi proceeds smoothly at −30 °C to give an organocopper intermediate, which was trapped by allyl diphenyl phosphate to give compound **1** in 73% yield (Table 1, entry 1).† The corresponding silylcupration of substituted styrenes and subsequent quenching by different allylic phosphates afforded adducts **2**–**8** in yields varying between 44–63% (entries 2–8). When hexenyl phosphate **13** was employed a mixture of α- and γ-regioisomers was obtained in a ratio of 35 : 65 (entry 5). In one case the intermediate silylcupration adduct was trapped by acetyl chloride to give **9** (entry 9).

The silylcupration of styrene was much slower than that of acetylenes[1] and allenes.[2,7] Thus, while the silylcupration of the latter two classes of compounds proceeds within 1 h at −40 °C, the silylcupration of styrenes had to be run at −30 °C for 3 h (for one substrate for 16 h, Table 1, entry 4).

Silylcuprate reagent (PhMe$_2$Si)$_2$CuLi·LiCN[10] was also tried in the silylcupration reaction of styrene. Unfortunately, the desired product could not be isolated upon treatment with an electrophile since the cuprate reagent promoted polymerisation of the starting material, which resulted in a complex reaction mixture.



Scheme 1

Several styrenes substituted at the double bond such as α-methylstyrene, (*E*)-β-methylstyrene, indene, and (*E*)-stilbene were tried in this reaction but none of them was reactive enough to give any reaction product. In each case the starting material was recovered after the reaction. We believe that this is due to steric hindrance between the bulky phenyldimethylsilyl group and the substituent on the double bond.

In order to gain some insight into the reaction mechanism we studied the stereochemistry of the addition by the use of a specifically deuterated styrene. Reaction of (*E*)-β-deuteriostyrene[11] **10** with PhMe$_2$SiCuCNLi followed by allyl diphenyl phosphate gave a 1 : 1 mixture of the two diastereomers **11a** and **11b**, which shows that the addition is non-stereospecific (Scheme 2). (Characteristic NMR data for non-deuterated product **1** (for notations see entry 1, Table 1): $\delta\,H_A$ = 1.26, H_B = 1.16, H_C = 2.73; J_{AB} = 14.8 Hz, J_{AC} = 5.0 Hz, J_{BC} = 10.0 Hz). Trapping of the intermediate copper-species resulting from the silylcupration of deuterated styrene **10** with acetyl chloride as electrophile also resulted in a 1 : 1 mixture of diastereomeric products. This indicates that the addition step of PhMe$_2$SiCuCNLi to styrene is completely non-stereospecific.

A likely mechanism involves nucleophilic attack by the silylcopper at the terminal carbon of the styrene double bond in analogy with a conjugate addition. This may involve a copper(III)-intermediate[12] and leads to formation of a carbanion in the benzylic position. The latter carbanion would finally form a copper–carbon bond, which now can be formed with either configuration at carbon. A radical intermediate, which would also explain the 1 : 1 diastereomeric ratio of products from **10**, is less likely since in a control experiment in the presence of a radical inhibitor (1 mol% of 4-tBu-catechol) neither the rate nor the stereochemical outcome was changed.

The anionic mechanism is also supported by the fact that styrenes with electron-attracting groups react faster than those with electron-donating groups. This can be seen by the change of colour of the reaction mixture to deep violet, which in the case of 4-fluorostyrene appears almost immediately after the addition of 4-fluorostyrene but for styrene itself it takes longer to form the characteristic colour. Note that for 4-Me-styrene the reaction time had to be extended to 16 h in order to get the desired reaction product (Table 1, entry 4).

In conclusion, the silylcupration of styrenes followed by electrophilic trapping is reported for the first time. The reaction provides an extension to the widely studied silylcupration reaction of other unsaturated compounds. Mechanistic studies suggest that the reaction proceeds through anionic intermediates.

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Notes and references

† *A typical procedure is as follows (Table 1, entry 6)*: 0.7 mmol of phenyldimethylsilyllithium[10] (~1 M solution in THF) was added to a

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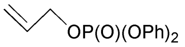
Table 1 Tandem silylcupration–electrophilic trapping reaction

12 =


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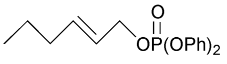

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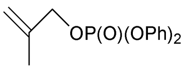

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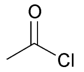
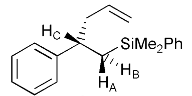
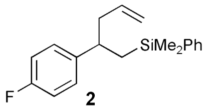
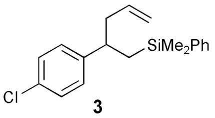
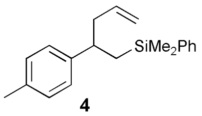
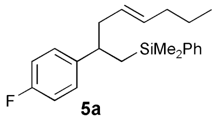
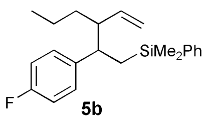
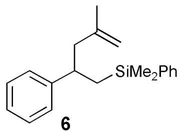
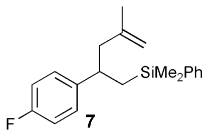
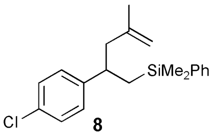
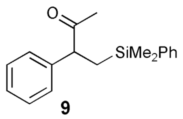
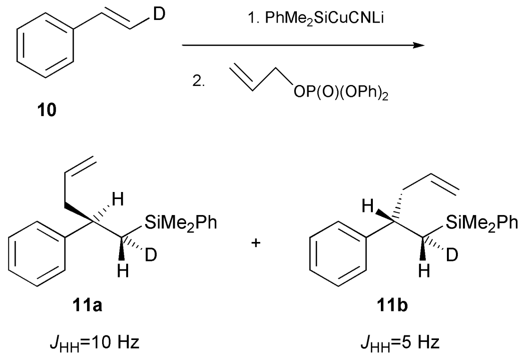


Entry	R on Styrene	Electrophile	Product	Yield, %[a]
1	—	**12**	 **1**	73%[b]
2	4-F-	**12**	 **2**	51%
3	4-Cl-	**12**	 **3**	54%
4	4-Me-	**12**	 **4**	44%[c]
5	4-F-	**13**	 **5a** +  **5b**	63% α+γ (35:65)
6	—	**14**	 **6**	55%
7	4-F-	**14**	 **7**	59%
8	4-Cl-	**14**	 **8**	46%
9	—	**15**	 **9**	49%

[a] Isolated yields. [b] 3 equiv. of styrene were used. [c] 16 h reaction time.



Scheme 2

stirred suspension of CuCN (1 equiv.) in dry THF (0.5 ml) at 0 °C and stirred at this temperature for 30 min. The mixture was cooled down to -30 °C (cryostat), styrene (2 equiv.) was added dropwise, and the resulting reaction mixture was stirred for 3 h at this temperature. Then allylic phosphate **14** (1.3 equiv.) in 0.7 ml THF was added slowly over 15 min. After the reaction mixture had been stirred for 1 h at -30 °C and for 30 min. at 0 °C, 4 ml of saturated aqueous NH_4Cl was added and the aqueous phase was extracted with hexane (5 $\times$ 3 ml). Column chromatography on silica with pentane as eluent afforded compound **6** as a colourless oil in 55% yield. R_f = 0.29 (hexane). ^{1}H NMR ($CDCl_3$ 300 MHz): δ 7.50–7.14 (m, 10H), 4.72 (m, 1H), 4.61 (m, 1H), 2.89 (dtd, J = 10.3, 7.5, 4.6 Hz, 1H), 2.34 (d, J = 7.5 Hz, 2H), 1.62 (t, J = 1.1 Hz, 3H), 1.31 (dd, J = 14.8, 4.6 Hz, 1H), 1.15 (dd, J = 14.8, 10.3 Hz, 1H), 0.12 (s, 3H), 0.04 (s, 3H). ^{13}C NMR ($CDCl_3$ 75.4 MHz): δ 146.9, 143.9, 139.5, 133.6, 128.8, 128.2, 127.7, 127.6, 126.1, 112.4, 49.7, 40.3, 23.4, 22.4, -1.8, -2.8.

1 (*a*) I. Fleming and F. Roessler, *J. Chem. Soc., Chem. Commun.*, 1980, 276; (*b*) I. Fleming, T. W. Newton and F. Roessler, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2527; (*c*) I. Fleming and E. Martinez de Marigorta, *J. Chem. Soc., Perkin Trans. 1*, 1999, 889.

2 (*a*) I. Fleming and F. J. Pulido, *J. Chem. Soc., Chem. Commun.*, 1986, 1010; (*b*) P. Cuadrado, A. M. Gonzalez, F. J. Pulido and I. Fleming, *Tetrahedron Lett.*, 1988, **29**, 1825; (*c*) P. Cuadrado, A. M. Gonzalez, F. J. Pulido, I. Fleming and M. Rowley, *Tetrahedron*, 1989, **45**, 413; (*d*) A. Barbero, P. Cuadrado, A. M. Gonzalez, F. Pulido and I. Fleming, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2811; (*e*) I. Fleming, Y. Landais and P. R. Raithby, *J. Chem. Soc. Perkin Trans. 1*, 1991, 715.

3 (*a*) K. Fugami, S. Nakatsukasa, K. Oshima, K. Utimoto and H. Nozaki, *Chem. Lett.*, 1986, **6**, 869; (*b*) K. Fugami, K. Oshima, K. Utimoto and H. Nozaki, *Tetrahedron Lett.*, 1986, **27**, 2161; (*c*) K. Fugami, J. Hibino, S. Nakatsukasa, S. Matsubara, K. Oshima, K. Utimoto and H. Nozaki, *Tetrahedron*, 1988, **44**, 4277.

4 T. Hayashi, T. Kobayashi, A. M. Kawamoto, H. Yamashita and M. Tanaka, *Organometallics*, 1990, **9**, 280.

5 (*a*) K. Tamao, S. Okazaki and M. Kumada, *J. Organomet. Chem.*, 1978, **146**, 87; (*b*) H. Matsumoto, K. Shono, A. Wada, I. Matsubara, H. Watanabe and Y. Nagai, *J. Organomet. Chem.*, 1980, **199**, 185; (*c*) H. Sakurai, Y. Eriyama, Y. Kamiyama and Y. Nakadaira, *J. Organomet. Chem.*, 1984, **264**, 229; (*d*) C. W. Carlson and R. West, *Organometallics*, 1983, **2**, 1801.

6 (*a*) F. J. Blanco, P. Cuadrado, A. M. Gonzalez, F. J. Pulido and I. Fleming, *Tetrahedron Lett.*, 1994, **35**, 8881; (*b*) A. Barbero, C. Garcia and F. J. Pulido, *Tetrahedron Lett.*, 1999, **40**, 6649; (*c*) A. Barbero, C. Garcia and F. J. Pulido, *Tetrahedron*, 2000, **56**, 2739.

7 V. Liepins, A. S. E. Karlström and J. E. Bäckvall, *Org. Lett.*, 2000, **2**, 1237.

8 A. Barbero, P. Cuadrado, A. M. Gonzalez, F. J. Pulido and I. Fleming, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2811.

9 Allylic phosphates have previously been used as electrophiles in a copper-catalysed cross coupling reaction with Grignard reagents: (*a*) A. Yanagisawa, Y. Noritake, N. Nomura and H. Yamamoto, *Synlett*, 1991, 251; (*b*) A. Yanagisawa, N. Nomura and H. Yamamoto, *Synlett*, 1993, 689; (*c*) A. Yanagisawa, N. Nomura and H. Yamamoto, *Tetrahedron*, 1994, **50**, 6017.

10 (*a*) I. Fleming, in *Organocopper reagents. A practical approach*, ed. R. J. K. Taylor, Oxford University Press, New York, 1994, 12, 257; (*b*) I. Fleming, R. S. Roberts and S. C. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1209.

11 (*a*) J. C. Colberg, A. Rane, J. Vaquer and J. A. Soderquist, *J. Am. Chem. Soc.*, 1993, **115**, 6065; (*b*) J. E. Bäckvall, *Tetrahedron Lett.*, 1978, **2**, 163.

12 (*a*) S. Woodward, *Chem. Soc. Rev.*, 2000, **29**, 393; (*b*) C. L. Kingsbury and R. A. J. Smith, *J. Org. Chem.*, 1997, **62**, 4629; (*c*) M. Uerdingen and N. Krause, *Tetrahedron*, 2000, **56**, 2799; (*d*) A. E. Dorigo, J. Wanner and P. von R. Schleyer, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 476; (*e*) E. Nakamura and M. Yamanaka, *J. Am. Chem. Soc.*, 1999, **121**, 8941; (*f*) E. Nakamura and S. Mori, *J. Am. Chem. Soc.*, 1998, **120**, 8273; (*g*) E. Nakamura, M. Yamanaka and S. Mori, *J. Am. Chem. Soc.*, 2000, **122**, 1826.