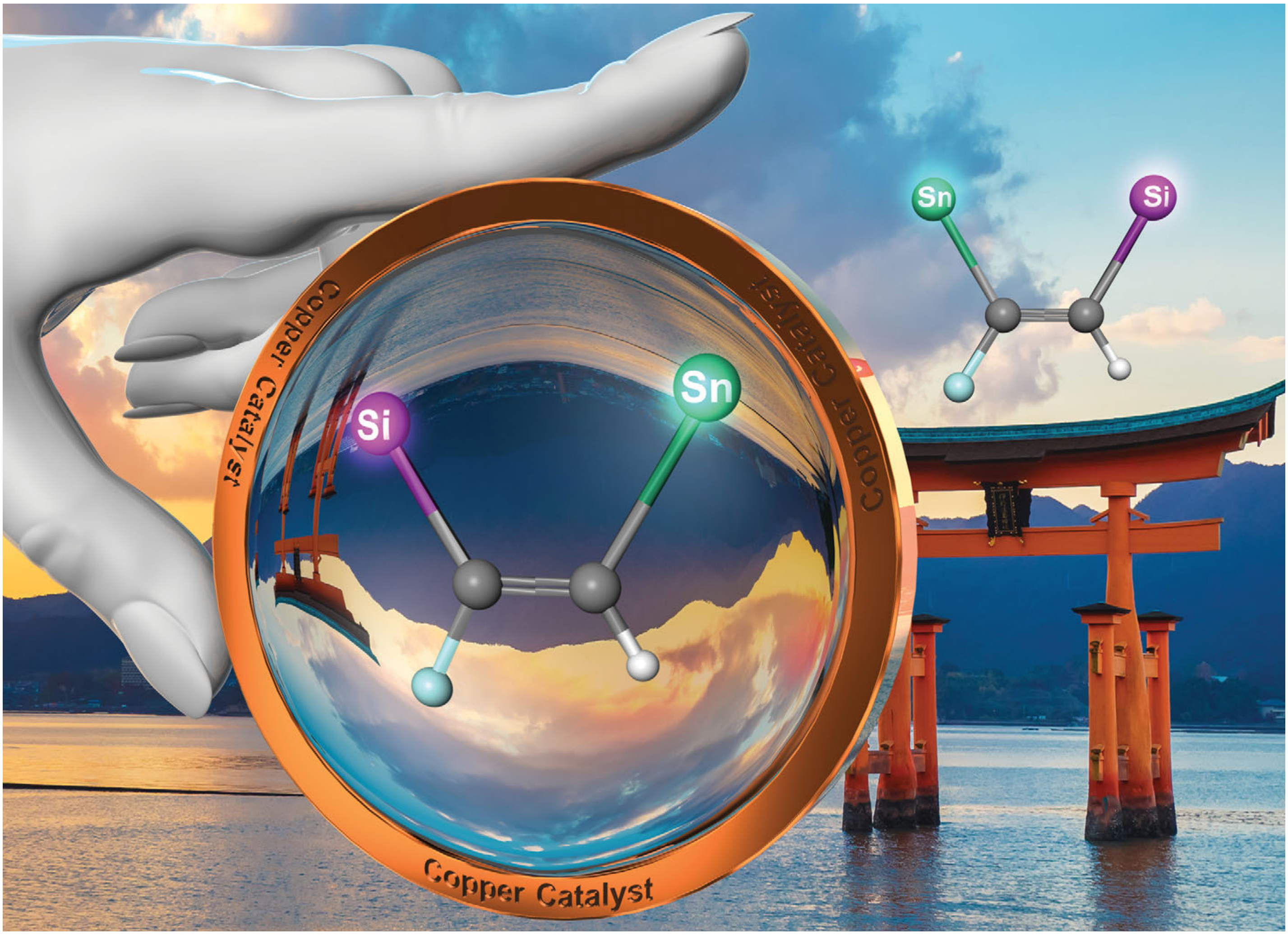


Showcasing research from Dr Hiroto Yoshida's Laboratory/ Department of Applied Chemistry, Hiroshima University, Japan

Inverse regioselectivity in the silylstannylation of alkynes and allenes: copper-catalyzed three-component coupling with a silylborane and a tin alkoxide

The regioselectivities of the silylstannylation of terminal alkynes and allenes can totally be reversed depending upon the copper-catalyzed three-component coupling using a silylborane and a tin alkoxide.

As featured in:


ChemComm

See H. Yoshida *et al.*,
Chem. Commun., 2015, **51**, 9440.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Registered charity number: 207890

ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2015, **51**, 9440

Received 4th March 2015,
Accepted 13th April 2015

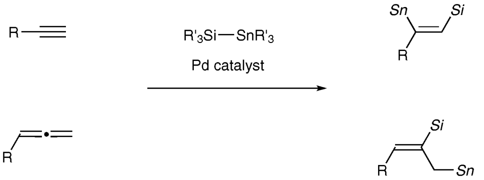
DOI: 10.1039/c5cc01856k

www.rsc.org/chemcomm

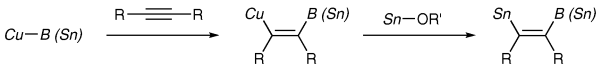
Inverse regioselectivity in the silylstannylation of alkynes and allenes: copper-catalyzed three-component coupling with a silylborane and a tin alkoxide†

H. Yoshida,*[ab] Y. Hayashi,[a] Y. Ito[a] and K. Takaki[a]

Silylstannylation of alkynes and allenes has been found to proceed by three-component coupling using a silylborane and a tin alkoxide in the presence of a Cu(I) catalyst. The regioselectivities are completely inverse to those of the conventional silylstannylation under palladium catalysis.



Scheme 1 Regioselectivity in Pd-catalyzed silylstannylation.



Scheme 2 Cu-catalyzed borylstannylation and distannylation.

Transition metal-catalyzed dual functionalization of a carbon–carbon multiple bond of unsaturated hydrocarbons such as alkynes and allenes with metallic elements (dimetallation)[1] has attracted considerable attention as a convenient and straightforward entry to synthetically potent *vic*-dimetallated compounds of defined structure, whose carbon–metal bonds are utilizable for construction of carbon frameworks[2] and introduction of functional groups. One of the most prevailing dimetallations is silylstannylation,[3] which has thus far been shown to proceed through direct addition of a silicon–tin bond of silylstannanes across unsaturated carbon linkages under palladium catalysis. The characteristic feature of the palladium-catalyzed silylstannylation is a high level of regioselectivity: the silyl addition commonly occurs at the terminal carbon of terminal alkynes[3a–f] and at the central carbon of allenes,[3g–j] irrespective of electronic and steric characters of ligands employed and substituents on the carbon–carbon multiple bonds (Scheme 1).[4]

Recently, we have devoted our attention to exploitation of potential copper catalysis toward the dimetallation of unsaturated hydrocarbons, and have already disclosed that diborylation,[5a] distannylation[5b] and three-component borylstannylation[5c–e] of carbon–carbon multiple bonds take place in an unique reaction mode,[6] where the oxidation state of a copper catalyst stays constant throughout the reaction, being in marked contrast to the conventional oxidative addition–insertion–reductive elimination sequence, which generally involves two-electron redox of a transition metal catalyst.[1,7] The key intermediates in these transformations are β-boryl (or stannyl)organocopper species arising from insertion of unsaturated hydrocarbons into boryl (or stannyl)copper species, and capturing them by a tin alkoxide finally affords the respective stannylated products as depicted in Scheme 2.[5b–e] Thus, we envisaged that silylstannylation of unsaturated hydrocarbons would also be feasible under copper catalysis by use of a suitable silylating reagent which allows facile generation of silylcopper[8] and β-silylorganocopper species.

Herein we report that the silylstannylation of alkynes and allenes facilely occurs by the copper-catalyzed three-component coupling with a silylborane,[9] and that the regioselectivities become totally inverse to those of the conventional silylstannylation[3] in both cases.

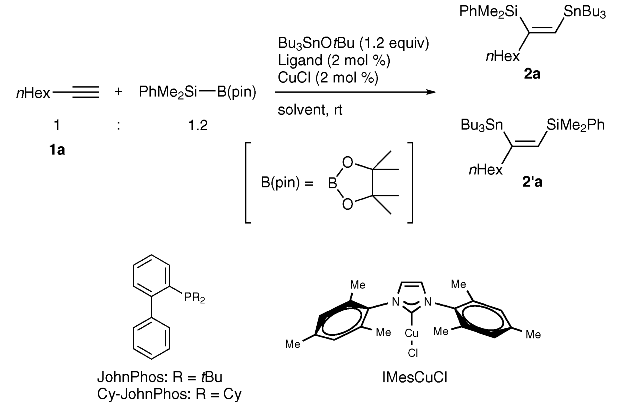
The three-component silylstannylation was found to readily occur to afford **2a** and **2′a** in 86% yield with regioselectivity inverse to those of the previous Pd-catalyzed silylstannylation (**2a** : **2′a** = 93 : 7), when the reaction of 1-octyne (**1a**), a silylborane (PhMe$_2$Si–B(pin), pin: pinacolato) and tributyltin *tert*-butoxide[10] was carried out in acetonitrile at room temperature in the presence of a CuCl–P(*t*Bu)$_3$ catalyst (Table 1, entry 1). Although the silylstannylation products were also formed with other monodentate phosphines (PPh$_3$, JohnPhos and Cy-JohnPhos) and N-heterocyclic carbene (IMes), the yields and the regioselectivities were unsatisfactory (entries 2–5). Acetonitrile has been proven

---

[a] *Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University, Higashi-Hiroshima 739-8527, Japan. E-mail: yhiroto@hiroshima-u.ac.jp; Fax: +81-82-424-5494; Tel: +81-82-424-7724*
[b] *ACT-C, Japan Science and Technology Agency, Higashi-Hiroshima 739-8527, Japan*

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data. See DOI: 10.1039/c5cc01856k

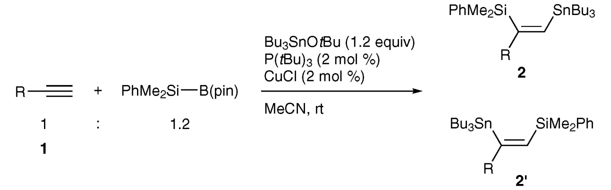
Table 1 Ligand and solvent effect on Cu-catalyzed silylstannylation of 1-octyne[a]



Entry	Ligand	Solvent	Time (h)	Yield[b] (%)	$2a:2'a$
1	P(*t*Bu)$_3$	MeCN	6	86	93 : 7
2	PPh$_3$	MeCN	3	88[c]	80 : 20
3	JohnPhos	MeCN	23	58[c]	86 : 14
4	Cy-JohnPhos	MeCN	27	54[c]	85 : 15
5	IMes[d]	MeCN	3	84[c]	75 : 25
6[e]	P(*t*Bu)$_3$	Toluene	4	69	99 : 1
7[f]	P(*t*Bu)$_3$	THF	3	63	99 : 1
8	P(*t*Bu)$_3$	DMF	1.5	79	90 : 10

[a] General procedure: **1a** (0.30 mmol), PhMe$_2$Si–B(pin) (0.36 mmol), Bu$_3$SnO*t*Bu (0.36 mmol), CuCl (6.0 μmol), ligand (6.0 μmol), solvent (1 mL). [b] Isolated yield. [c] NMR yield. [d] IMesCuCl (2 mol%) was used. [e] A hydrosilylation product, *n*Hex(PhMe$_2$Si)C=CH$_2$, was formed in 6% NMR yield. [f] A hydrosilylation product, *n*Hex(PhMe$_2$Si)C=CH$_2$, was formed in 10% NMR yield.

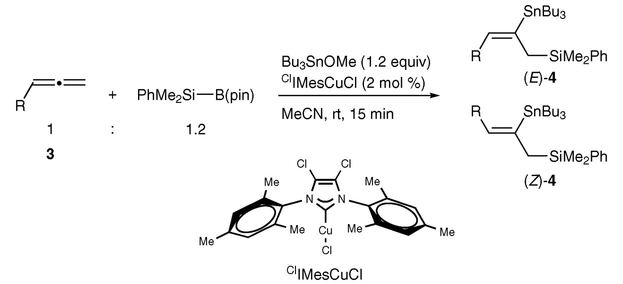
Table 2 Cu-catalyzed silylstannylation of terminal alkynes[a]

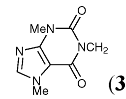
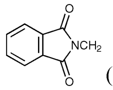


Entry	R	Time (h)	Yield[b] (%)	$2:2'$
1	*n*Bu (**1b**)	3	76	95 : 5
2	*n*Oct (**1c**)	1.5	68	94 : 6
3	Cyp[c] (**1d**)	7	65	93 : 7
4	iBu (**1e**)	4	64	97 : 3
5	iAmyl (**1f**)	19	61	90 : 10
6	NC(CH$_2$)$_3$ (**1g**)	3.5	56	94 : 6
7	Br(CH$_2$)$_2$ (**1h**)	16	47	91 : 9
8	HO(CH$_2$)$_2$ (**1i**)	4	43	97 : 3
9	Et$_2$NCH$_2$ (**1j**)	25.5	39	90 : 10
10	THPOCH$_2$ (**1k**)	6.5	75	10 : 90
11	MeOCH$_2$ (**1l**)	12.5	59	1 : 99
12	1-Cyclohexenyl (**1m**)	27	61	61 : 39
13	Ph (**1n**)	7	64	14 : 86

[a] General procedure: **1** (0.30 mmol), PhMe$_2$Si–B(pin) (0.36 mmol), Bu$_3$SnO*t*Bu (0.36 mmol), CuCl (6.0 μmol), P(*t*Bu)$_3$ (6.0 μmol), MeCN (1 mL). [b] Isolated yield. [c] Cyp = cyclopentyl.

Table 3 Cu-catalyzed silylstannylation of terminal allenes[a]



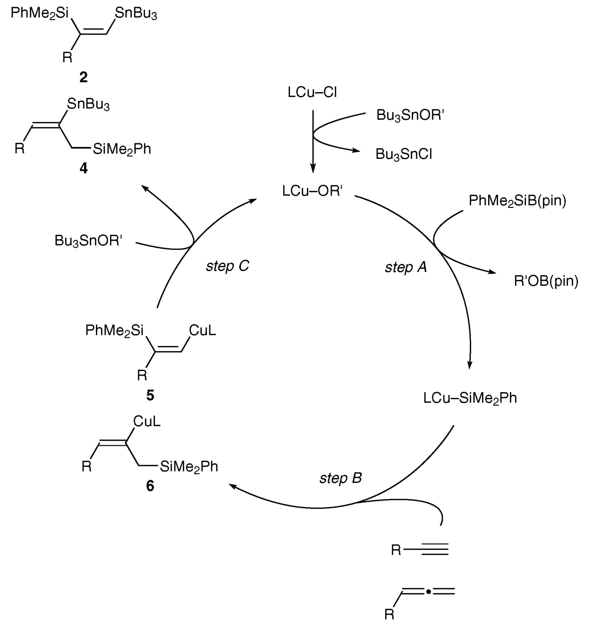
Entry	R	Yield[b] (%)	$E:Z$
1	Dodecyl (**3a**)	87	78 : 22
2	Ph(CH$_2$)$_2$ (**3b**)	86	77 : 23
3	Cy (**3c**)	77	87 : 13
4	*n*Oct (**3d**)	71	91 : 9
5	TBSO(CH$_2$)$_2$ (**3e**)	93	75 : 25
6	 (**3f**)	76	83 : 17
7	 (**3g**)	63	79 : 21
8	THPOCH$_2$ (**3h**)	56	75 : 25

[a] General procedure: **3** (0.30 mmol), PhMe$_2$Si–B(pin) (0.36 mmol), Bu$_3$SnOMe (0.36 mmol), ^{Cl}IMesCuCl (6.0 μmol), MeCN (1 mL). [b] Isolated yield.

to be the solvent of choice: the reaction in less polar solvents (toluene and THF) produced a hydrosilylation product, *n*Hex(PhMe$_2$Si)C=CH$_2$, as a by-product (entries 6 and 7), and the regioselectivity became lower with DMF (entry 8).

Under the optimized reaction conditions, 1-hexyne (**1b**), 1-decyne (**1c**) and branched aliphatic terminal alkynes (**1d–1f**) could undergo the regioselective silylstannylation, where the stannyl moieties were predominantly attached to the terminal carbon of the alkynes (Table 2, entries 1–5). This unique regioselectivity was also achievable with functionalized alkynes bearing a cyano (**1g**), bromo (**1h**), hydroxy (**1i**) or amino (**1j**) group (entries 6–9), and the results that these reactive moieties remained intact demonstrate the high functional group compatibility of the silylstannylation. In contrast, the stannyl moiety was selectively introduced into the internal carbon of THP-protected propargyl alcohol (**1k**) and propargyl ether (**1l**) to provide **2′k** and **2′l** as the major products (entries 10 and 11), and the reaction of enyne (**1m**) or phenylacetylene (**1n**) resulted in low regioselectivity (entries 12 and 13).

The three-component silylstannylation of allenes was found to also proceed smoothly with regioselectivity inverse to those of the previous silylstannylation under palladium catalysis. Thus, treatment of pentadeca-1,2-diene (**3a**) with a silylborane and tributyltin methoxide[11] in the presence of the ^{Cl}IMesCuCl catalyst[12] afforded an 87% yield of (*E*)- and (*Z*)-**4a** (ratio = 78 : 22), whose stannyl moiety was exclusively installed into the central carbon of the allene (Table 3, entry 1). The regioselective formation of silylstannylated products (**4b–4d**) bearing allylsilane and alkenylstannane units was observed with 5-phenyl-penta-1,2-diene (**3b**), cyclohexylallene (**3c**) and undeca-1,2-diene (**3d**) (entries 2–4), and furthermore functionalized allenes possessing a silyl ether (**3e**), a theobromine (**3f**), a phthalimide (**3g**) or an acetal (**3h**) moiety underwent the silylstannylation with a similar regioselectivity to provide the respective products (**4e–4h**) without damaging these functional groups (entries 5–8).



Scheme 3 A plausible catalytic cycle for silylstannylation.

Generation of a silylcopper species, Cu–SiMe$_2$Ph, *via* σ-bond metathesis between a copper alkoxide and a silylborane would trigger the silylstannylation (Scheme 3, step A).[13] Then an alkyne or an allene was inserted into the Cu–Si bond to give a β-silylalkenylcopper species (**5** or **6**) (step B),[14] which was subsequently trapped by a tin alkoxide to furnish a silylstannylation product with regeneration of a copper alkoxide (step C).[15–17] The regiochemical outcome of the reaction with an alkyne or an allene should be ascribable to the regioselective formation of **5**[18] or **6**, the latter of which has been demonstrated to be kinetically favored in the stoichiometric reaction using a silylcopper species.[8a] On the other hand, electronic directing effect of a propargylic functional group (**1k** and **1l**) or a phenyl group (**1n**), which induces the addition of the copper moiety to the internal carbon of the alkynes in step B,[19] should become dominant to provide **2′** as the major product.

In conclusion, we have demonstrated that the regioselectivities of the silylstannylation of terminal alkynes and allenes can totally be reversed depending upon the copper-catalyzed three-component coupling using a silylborane and a tin alkoxide, which leads to convenient and direct access to diverse 2-silyl-1-stannyl-1-alkenes (from alkynes) and 1-silyl-2-stannyl-2-alkenes (from allenes) of high synthetic utility. Further studies on copper-catalyzed silylation reactions of unsaturated carbon–carbon bonds as well as synthetic application of the silylstannylation are in progress.

Notes and references

1 For reviews, see: (*a*) I. Beletskaya and C. Moberg, *Chem. Rev.*, 1999, **99**, 3435; (*b*) M. Suginome and Y. Ito, *Chem. Rev.*, 2000, **100**, 3221; (*c*) I. Beletskaya and C. Moberg, *Chem. Rev.*, 2006, **106**, 2320.
2 *Metal-Catalyzed Cross-Coupling Reactions*, ed. A. de Meijere and F. Diederich, Wiley-VHC, Weinheim, 2004.
3 For representative silylstannylation of alkynes, see: (*a*) B. L. Chenard, E. D. Laganis, F. Davidson and T. V. RajanBabu, *J. Org. Chem.*, 1985, **50**, 3666; (*b*) T. N. Mitchell, H. Killing, R. Dicke and R. Wickenkamp, *J. Chem. Soc., Chem. Commun.*, 1985, 354; (*c*) T. N. Mitchell, R. Wickenkamp, A. Amamria, R. Dicke and U. Schneider, *J. Org. Chem.*, 1987, **52**, 4868; (*d*) I. Hemeon and R. D. Singer, *Chem. Commun.*, 2002, 1884; (*e*) M. Murakami, T. Matsuda, K. Itami, S. Ashida and M. Terayama, *Synthesis*, 2004, 1522; (*f*) T. E. Nielsen, S. Le Quement and D. Tanner, *Synthesis*, 2004, 1381; For representative silylstannylation of allenes, see: (*g*) T. N. Mitchell and U. Schneider, *J. Organomet. Chem.*, 1991, **407**, 319; (*h*) A. G. M. Barrett and P. W. H. Wan, *J. Org. Chem.*, 1996, **61**, 8667; (*i*) S. Shin and T. V. RajanBabu, *J. Am. Chem. Soc.*, 2001, **123**, 8416; (*j*) M. Jeganmohan, M. Shanmugasundaram, K.-J. Chang and C.-H. Cheng, *Chem. Commun.*, 2002, 2552.
4 An alkoxyalkyne exceptionally accepts the silyl addition at the internal carbon. See: M. Murakami, H. Amii, N. Takizawa and Y. Ito, *Organometallics*, 1993, **12**, 4223.
5 (*a*) H. Yoshida, S. Kawashima, Y. Takemoto, K. Okada, J. Ohshita and K. Takaki, *Angew. Chem., Int. Ed.*, 2012, **51**, 235; (*b*) H. Yoshida, A. Shinke and K. Takaki, *Chem. Commun.*, 2013, **49**, 11671; (*c*) Y. Takemoto, H. Yoshida and K. Takaki, *Chem. – Eur. J.*, 2012, **18**, 14841; (*d*) Y. Takemoto, H. Yoshida and K. Takaki, *Synthesis*, 2014, 3024; (*e*) H. Yoshida, Y. Takemoto and K. Takaki, *Chem. Commun.*, 2015, **51**, 6297.
6 We have also reported other borylation reactions of unsaturated hydrocarbons under copper or silver catalysis. See: (*a*) H. Yoshida, I. Kageyuki and K. Takaki, *Org. Lett.*, 2013, **15**, 952; (*b*) H. Yoshida, Y. Takemoto and K. Takaki, *Chem. Commun.*, 2014, **50**, 8299; (*c*) I. Kageyuki, H. Yoshida and K. Takaki, *Synthesis*, 2014, 1924; (*d*) H. Yoshida, Y. Takemoto and K. Takaki, *Asian J. Org. Chem.*, 2014, **3**, 1204; (*e*) H. Yoshida, I. Kageyuki and K. Takaki, *Org. Lett.*, 2014, **16**, 3512.
7 (*a*) M. Hada, Y. Tanaka, M. Ito, M. Murakami, H. Amii, Y. Ito and H. Nakatsuji, *J. Am. Chem. Soc.*, 1994, **116**, 8754; (*b*) F. Ozawa, Y. Sakamoto, T. Sagawa, R. Tanaka and H. Katayama, *Chem. Lett.*, 1999, 1307; (*c*) T. Sagawa, Y. Sakamoto, R. Tanaka, H. Katayama and F. Ozawa, *Organometallics*, 2003, **22**, 4433.
8 For reviews, see: (*a*) A. Barbero and F. J. Pulido, *Acc. Chem. Res.*, 2004, **37**, 817; (*b*) F. J. Pulido and A. Barbero, Silyl and Stannyl Derivatives of Organocopper Compounds, in *The Chemistry of Organocopper Compounds Part 2*, ed. Z. Rappoport and I. Marek, Wiley, Chichester, 2009, pp. 775–856.
9 For representative examples of copper-catalyzed silylation of unsaturated hydrocarbons with a silylborane, see: (*a*) P. Wang, X.-L. Yeo and T.-P. Loh, *J. Am. Chem. Soc.*, 2011, **133**, 1254; (*b*) T. Fujihara, Y. Tani, K. Semba, J. Terao and Y. Tsuji, *Angew. Chem., Int. Ed.*, 2012, **51**, 11487; (*c*) F. Meng, H. Jang and A. H. Hoveyda, *Chem. – Eur. J.*, 2013, **19**, 3204; (*d*) Y. Tani, T. Fujihara, J. Terao and Y. Tsuji, *J. Am. Chem. Soc.*, 2014, **136**, 17706; (*e*) Y.-H. Xu, L.-H. Wu, J. Wang and T.-P. Loh, *Chem. Commun.*, 2014, **50**, 7195; (*f*) J. Rae, Y. C. Hu and D. J. Procter, *Chem. – Eur. J.*, 2014, **20**, 13143.
10 The reaction with tributyltin methoxide resulted in lower regioselectivity (**2a** : **2′a** = 89 : 11).
11 The use of tributyltin *tert*-butoxide resulted in lower yield. See the ESI† for details.
12 For the ligand effect on the silylstannylation of an allene, see the ESI†.
13 C. Kleeberg, M. S. Cheung, Z. Lin and T. B. Marder, *J. Am. Chem. Soc.*, 2011, **133**, 19060.
14 For stoichiometric reactions of a silylcopper species with an alkyne or an allene that produce a β-silylalkenylcopper species, see ref. 8*a*.
15 Generation of a silylcopper species (step A) and insertion of an alkyne or an allene into the Cu–Si bond (step B) have been widely accepted as fundamental elementary steps in the copper-catalyzed silylation reactions of alkynes or allenes with a silylborane. See ref. 9.
16 We have already demonstrated that an alkenylcopper species is readily captured with a tin alkoxide to give an alkenylstannane. See ref. 5*c*.
17 Intermediacy of a silylstannane (PhMe$_2$Si–SnBu$_3$) in the present silylstannylation could be ruled out, because the copper-catalyzed reaction of **3d** with PhMe$_2$Si–SnBu$_3$ did not produce **4d** at all.
18 Regioselective formation of this alkenylcopper species was also observed in the copper-catalyzed formal hydrosilylation of terminal alkynes. See ref. 9*a*.
19 A similar regioselectivity was obtained in borylcupration of alkynes. See: (*a*) H. R. Kim and J. Yun, *Chem. Commun.*, 2011, **47**, 2943; (*b*) A. L. Moure, R. G. Arrayás, D. J. Cárdenas, I. Alonso and J. C. Carretero, *J. Am. Chem. Soc.*, 2012, **134**, 7219.