

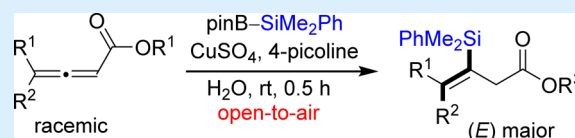
Regio- and Stereoselective Copper(II)-Catalyzed Hydrosilylation of Activated Allenes in Water: Access to Vinylsilanes

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S Supporting Information

ABSTRACT: By using catalytic amounts of copper(II), 4-picoline, and dimethylphenylsilylpinacol borane, a series of allenates were silylated on the β carbon in good to excellent yields and high (*E*)-selectivity. The mild and efficient silylation method is conducted in water under atmospheric conditions to afford vinylsilanes.

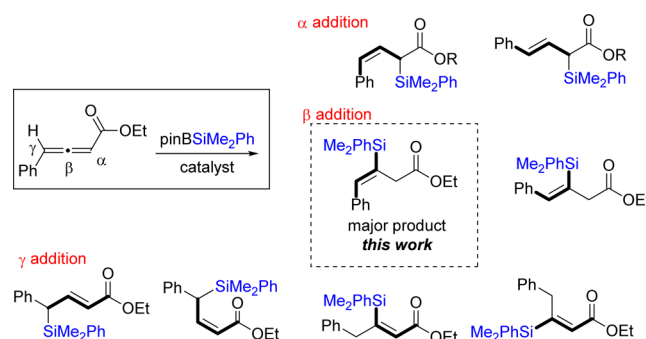


Vinylsilanes are an important class of synthetic building blocks in organic synthesis.¹ The carbon–silicon bond has unique properties that allow it to be stable under harsh reaction conditions and render it reactive under various conditions as in the case of Tamao–Fleming oxidation or Hiyama cross-coupling.² Consequently, interest in the development of new methods for their preparation is emerging. Alkyne³ hydrosilylation is an approach heavily exploited to synthesize vinylsilanes, and transition metal catalysts such as platinum,⁴ ruthenium,⁵ rhodium,⁶ palladium,⁷ iron,⁸ gold,⁹ cobalt,¹⁰ nickel,¹¹ and copper¹² play a prominent role in these transformations. An attractive alternative strategy that utilizes allenyl substrates can provide highly elaborated vinylsilane products. However, silylation reactions involving allenes are rare and underexplored. For example, Montgomery and co-workers demonstrated the regioselective allene hydrosilylation catalyzed by Ni and Pd N-heterocyclic carbene complexes.¹³ Lewis acid¹⁴ and stoichiometric Co₂(CO)₈¹⁵ mediated hydrosilylation has been reported for a limited number of phenyl- and sugar allenes, respectively. More occurs on the more substituted terminal allenes.¹⁶ However, this method is restricted to terminal allenes, as 1,3-disubstituted substrates were unreactive. The limited number of synthetic methods to access these important molecules highlights the urgent need for a general synthetic method for the silylation of allenes. Nonetheless, elegant copper-catalyzed carbosylations of substituted allenes have been reported.¹⁷

Given our interest in silylation reactions utilizing Sugimoto's silylboron reagent [dimethylphenylsilylpinacolborane (pinBSiMe₂Ph)]¹⁸ and development of sustainable reaction conditions,¹⁹ we sought to develop a protocol for the silylation of substituted allenates. Water is an excellent solvent choice because it is nontoxic, nonflammable, and environmentally benign. When combined with an inexpensive, abundant, and nontoxic transition metal such as copper used in a catalytic fashion, an environmentally and user-friendly protocol could be achieved. However, control of the regio- and stereoselectivity of the reaction can be challenging, as up to eight potential products are possible resulting from silyl addition to the α , β , or

γ carbon (Scheme 1). Whereas addition reactions on the α carbon are scarce, a Lewis base such as phosphine-promoted

Scheme 1. Possible Silylation Products



γ -²⁰ and β -additions²¹ of various nucleophiles to allenates is well precedented. Based on our experience with the regioselective transfer of Bpin to the β carbon of allenates utilizing a preactivated sp²–sp³ hybridized diboron reagent (pinacolatodisopropylaminato diboron) and Cu(I) catalyst,²² we investigated the development of β -silylation of substituted allenates. Herein, we describe our efforts toward transitioning this method in water and open to air using an air-stable, earth abundant Cu(II) source.

We initiated our studies using conditions previously determined by silylation of α,β -unsaturated carbonyl substrates.¹⁹ Treatment of commercially available allenate, ethyl buta-2,3-dienoate (2a), with pinBSiMe₂Ph in the presence of a catalytic amount of Cu(II) and 4-picoline using water as the solvent at room temperature and open to the atmosphere resulted in >99% conversion to vinylsilane 3a as determined by GC-MS analysis of the crude reaction mixture (Table 1, entry 1). The reaction was facile and reached completion within 30 min. Substitution of 4-picoline with pyridine afforded a similar

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Table 1. Optimization of Reaction Conditions^a

entry	base	mol % Cu	prod:SM ^b 3a:2a
1	4-picoline	1.0	>99:1
2	pyridine	1.0	>99:1
3	triethylamine	1.0	8:1
4	DBU ^c	1.0	11:1
5	benzylamine	1.0	45:1
6	diethylamine	1.0	2.4:1
7	none	1.0	NR ^d
8	4-picoline	0	NR ^d

^aGeneral procedure: base (5 mol %), ethyl buta-2,3-dienoate **2a** (1 equiv), pinBSiPhMe₂ (1.1 equiv), and 1.3 mg/mL of CuSO₄ solution were mixed at rt for 30 min. ^bDetermined by GC-MS of crude material. ^c1,8-Diazabicyclo[5.4.0]undec-7-ene. ^dNR = no reaction.

conversion (entry 2); however, a screen of other bases such as triethylamine, DBU, benzylamine, and diethylamine resulted in a significant decrease in product conversion (entries 3–6). As expected, removal of 4-picoline or the copper catalyst afforded no reaction, suggesting the key role of these reagents in the reaction (entries 7–8).

With the optimized conditions in hand (5 mol % 4-picoline, 1 mol % CuSO₄, 1.1 equiv pinBSiPhMe₂), we investigated the substrate scope of the developed reaction (Table 2). The reaction of model substrate **2a** resulted in 76% isolated yield of product **3a** with exclusive addition of the silicon group on the β position (entry 1). Changing the ester functional group to either a benzyl or phenyl afforded the desired products **3b** and **3c** in excellent yields (entries 2–3). However, allylallenoate **2d** diminished the yield; when propargylallenoate **2e** was used instead of **2d**, only trace amounts of product were observed (entries 4–5). The homologation of the propargyl group in **2f** similarly afforded the product in trace amounts. The inefficient conversion of terminal alkynes may result from the insertion of copper into the C–H bond, severely inhibiting the silylation reaction. To test this hypothesis, we synthesized an alkyne without an acidic hydrogen such as 2-butyne ester **2g**. The reaction of **2g** under the same reaction conditions produced the silylated **3g** in 60% yield. Further, this result demonstrates the chemoselectivity of the reaction as silicon was added to the β carbon in the presence of alkyne substituent. To explore the substrate scope further, we investigated the effect of substitutions on the α carbon of allenes (**2h–i**). A small alkyl group such as a methyl (**3h**) or a more functionally diverse moiety such as an ester (**3i**) resulted in very good yields (entries 8–9). Finally, we investigated the reactivity of 1,3-disubstituted allenoates, substrates bearing additional groups on the γ carbon. Methyl substituted allenes bearing a benzyl (**2j**) or *ortho*-nitrobenzyl (**2k**) ester yielded the corresponding products in 95% and 51% yields, respectively. The lower yield in **3k** may arise from the instability of the photoreactive *ortho*-nitrobenzyl group. In both cases, the (*E*)-olefin geometry was preferred (~9:1). When a much larger phenyl ring was placed on the γ carbon, high (*E*)-selectivity and yields were observed regardless of the ester functional group (entries 12–14).

A plausible mechanism and rationale for the stereoselectivity of the reaction is shown in Scheme 2. The boron–silicon bond in **1** is activated by a base-mediated nucleophilic water molecule

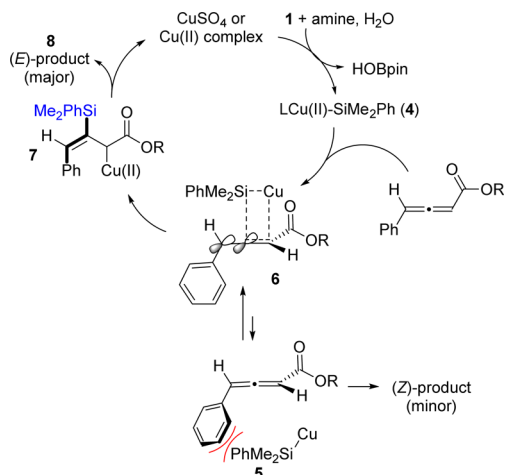
Table 2. Silyl Addition to Substituted Allenoates^a

entry	substrate	product	yield ^b
1			76
2			96
3			83
4			30
5			trace
6			trace
7			60
8			76
9			81
10		 <i>E:Z</i> 87:13 ^c	95
11		 <i>E:Z</i> 88:12 ^c	51
12		 <i>E:Z</i> 85:15 ^c	61
13		 <i>E:Z</i> 85:15 ^c	73
14		 <i>E:Z</i> 86:14 ^c	75

^aReaction conditions identical to Table 1, entry 1. ^bIsolated yield. Isolated yields averaged from two or more experiments. ^cStereoselectivity was determined by ¹H NMR of the crude material and confirmed by NOE of the isolated product.

binding to boron.^{19a} In the presence of a copper(II) source,²³ transmetalation proceeds to generate a nucleophilic silyl-copper intermediate (**4**). 3,4-Addition of **4** to the allenoate

Scheme 2. Proposed Mechanism



regioselectively adds silicon on the β carbon to generate copper enolate **7**, which is supported by density functional theory investigation of the analogous boryl addition to α,β -unsaturated esters.²⁴ Since the double bonds in allenes are orthogonal, the more electron-deficient olefin participates in the hydrosilylation reaction.²⁵ The selective formation of the (*E*) stereoisomer results from a steric interaction between the phenyl γ substituent in **5**,²⁶ which forces the complex to form a more favorable arrangement in **6**, and affording intermediate **7**. Hydrolysis of the carbon–copper bond in water provides vinylsilane **8** and the copper catalyst to complete the cycle.

In conclusion, we developed a facile, copper(II)-catalyzed, regioselective silylation reaction of substituted allenoates. Silicon adds to the β carbon and stereoselectively affords (*E*)-olefin geometry. These vinylsilane products can be utilized in complex molecule synthesis.²⁷ A significant advantage of the operationally simple synthetic protocol is the employment of catalytic amounts of air stable copper(II) in water, which is conducted at room temperature and in open air. Current efforts to expand the utility of the method are underway.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00981.

Detailed experimental procedures and full characterization of products (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) Barbero, A.; Pulido, F. J. *Acc. Chem. Res.* **2004**, *37*, 817. (b) Fleming, I. *Organocopper Reagent*; Oxford University Press: New

York, 1994. (c) Denmark, S. E.; Liu, J. H. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2978.

(2) (a) Tamao, K.; Kumada, M.; Maeda, K. *Tetrahedron Lett.* **1984**, *25*, 321. (b) Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, *40*, 4893.

(3) Díez-González, S.; Nolan, S. P. *Acc. Chem. Res.* **2008**, *41*, 349.

(4) (a) Rooke, D. A.; Ferreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3225. (b) Rooke, D. A.; Ferreira, E. M. *J. Am. Chem. Soc.* **2010**, *132*, 11926.

(5) (a) Trost, B. M.; Ball, Z. T.; Jöge, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 3415. (b) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17644. (c) Ding, S.; Song, L.-J.; Chung, L. W.; Zhang, X.; Sun, J.; Wu, Y.-D. *J. Am. Chem. Soc.* **2013**, *135*, 13835. (d) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2001**, *123*, 12726. (e) Sumida, Y.; Kato, T.; Yoshida, S.; Hosoya, T. *Org. Lett.* **2012**, *14*, 1552. (f) Na, Y.; Chang, S. *Org. Lett.* **2000**, *2*, 1887. (g) Arico, C. S.; Cox, L. R. *Org. Biomol. Chem.* **2004**, *2*, 2558. (h) Berthon-Gelloz, G.; Schumers, J.-M.; De Bo, G.; Markó, I. E. *J. Org. Chem.* **2008**, *73*, 4190.

(6) (a) Ohmiya, H.; Ito, H.; Sawamura, M. *Org. Lett.* **2009**, *11*, 5618. (b) Iglesias, M.; Aliaga-Lavrijsen, M.; Miguel, P. J. S.; Fernández-Alvarez, F. J.; Pérez-Torrente, J. J.; Oro, L. A. *Adv. Synth. Catal.* **2015**, *357*, 350.

(7) (a) Planellas, M.; Guo, W.; Alonso, F.; Yus, M.; Shafir, A.; Pleixats, R.; Parella, T. *Adv. Synth. Catal.* **2014**, *356*, 179. (b) Zhou, H.; Moberg, C. *Org. Lett.* **2013**, *15*, 1444.

(8) Belger, C.; Plietker, B. *Chem. Commun.* **2012**, *48*, 5419.

(9) Shore, G.; Organ, M. G. *Chem. - Eur. J.* **2008**, *14*, 9641.

(10) Yong, L.; Kirleis, K.; Butenschön, H. *Adv. Synth. Catal.* **2006**, *348*, 833.

(11) Berding, J.; van Paridon, J. A.; van Rixel, V. H. S.; Bouwman, E. *Eur. J. Inorg. Chem.* **2011**, *2011*, 2450.

(12) (a) Zhou, H.; Wang, Y.-B. *ChemCatChem* **2014**, *6*, 2512. (b) Wang, P.; Yeo, X.-L.; Loh, T.-P. *J. Am. Chem. Soc.* **2011**, *133*, 1254.

(c) Wang, M.; Liu, Z.-L.; Zhang, X.; Tian, P.-P.; Xu, Y.-H.; Loh, T.-P. *J. Am. Chem. Soc.* **2015**, *137*, 14830. (d) Vyas, D. J.; Hazra, C. K.; Oestreich, M. *Org. Lett.* **2011**, *13*, 4462. (e) Hendrix, A. J. M.; Jennings, M. P. *Org. Lett.* **2010**, *12*, 2750. (f) Xuan, Q.-Q.; Ren, C.-L.; Liu, L.; Wang, D.; Li, C.-J. *Org. Biomol. Chem.* **2015**, *13*, 5871. (g) Hazra, C. K.; Fopp, C.; Oestreich, M. *Chem. - Asian J.* **2014**, *9*, 3005. (h) Linstadt, R. T. H.; Peterson, C. A.; Lippincott, D. J.; Jette, C. I.; Lipshutz, B. H. *Angew. Chem., Int. Ed.* **2014**, *53*, 4159. (i) Meng, F.; Jang, H.; Hoveyda, A. H. *Chem. - Eur. J.* **2013**, *19*, 3204. (j) García-Rubia, A.; Romero-Revilla, J. A.; Mauleón, P.; Gómez Arrayás, R.; Carretero, J. C. *J. Am. Chem. Soc.* **2015**, *137*, 6857.

(13) (a) Miller, Z. D.; Li, W.; Belderrain, T. R.; Montgomery, J. J. *Am. Chem. Soc.* **2013**, *135*, 15282. (b) Miller, Z. D.; Montgomery, J. *Org. Lett.* **2014**, *16*, 5486. (c) Miller, Z. D.; Dorel, R.; Montgomery, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 9088.

(14) Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2494.

(15) Huang, G.; Isobe, M. *Tetrahedron* **2001**, *57*, 10241.

(16) Kidonakis, M.; Stratakis, M. *Org. Lett.* **2015**, *17*, 4538.

(17) (a) He, Z.-T.; Tang, X.-Q.; Xie, L.-B.; Cheng, M.; Tian, P.; Lin, G.-Q. *Angew. Chem.* **2015**, *127*, 15028. (b) Rae, J.; Hu, Y. C.; Procter, D. J. *Chem. - Eur. J.* **2014**, *20*, 13143. (c) Tani, Y.; Yamaguchi, T.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. Lett.* **2015**, *44*, 271. (d) Tani, Y.; Fujihara, T.; Terao, J.; Tsuji, Y. *J. Am. Chem. Soc.* **2014**, *136*, 17706.

(18) (a) Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **2000**, *19*, 4647. (b) Xu, Y.-H.; Wu, L.-H.; Wang, J.; Loh, T.-P. *Chem. Commun.* **2014**, *50*, 7195. For an authoritative review, see: (c) Oestreich, M.; Hartmann, E.; Mewald, M. *Chem. Rev.* **2013**, *113*, 402.

(19) (a) Calderone, J. A.; Santos, W. L. *Org. Lett.* **2012**, *14*, 2090. (b) Calderone, J. A.; Santos, W. L. *Angew. Chem., Int. Ed.* **2014**, *53*, 4154.

(20) For select examples, see: (a) Trost, B. M.; Li, C.-J. *J. Am. Chem. Soc.* **1994**, *116*, 3167. (b) Kalek, M.; Fu, G. C. *J. Am. Chem. Soc.* **2015**, *137*, 9438. (c) Wang, T.; Yu, Z.; Hoon, D. L.; Phee, C. Y.; Lan, Y.; Lu, Y. *J. Am. Chem. Soc.* **2016**, *138*, 265. (d) Fang, Y.-Q.; Tadross, P. M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2014**, *136*, 17966.

- (21) (a) Chai, G.; Lu, Z.; Fu, C.; Ma, S. *Adv. Synth. Catal.* **2009**, 351, 1946. (b) Chen, B.; Ma, S. *Org. Lett.* **2013**, 15, 3884.
- (22) Thorpe, S. B.; Guo, X.; Santos, W. L. *Chem. Commun.* **2011**, 47, 424.
- (23) There are a limited number of Cu(II)-catalyzed formal hydrosilylation using pinBSiMe₂Ph; see: (a) Kitanosono, T.; Zhu, L.; Liu, C.; Xu, P.; Kobayashi, S. *J. Am. Chem. Soc.* **2015**, 137, 15422. (b) Zhu, L.; Kitanosono, T.; Xu, P.; Kobayashi, S. *Chem. Commun.* **2015**, 51, 11685. (c) Xuan, Q.-Q.; Zhong, N.-J.; Ren, C.-L.; Liu, L.; Wang, D.; Chen, Y.-J.; Li, C.-J. *J. Org. Chem.* **2013**, 78, 11076.
- (24) Dang, L.; Lin, Z.; Marder, T. B. *Organometallics* **2008**, 27, 4443.
- (25) For conjugate silylation, see: (a) Lee, K. S.; Wu, H.; Haeffner, F.; Hoveyda, A. H. *Organometallics* **2012**, 31, 7823. (b) O'Brien, J. M.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, 133, 7712. (c) Lee, K. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, 132, 2898. (d) Pace, V.; Rae, J. P.; Harb, H. Y.; Procter, D. J. *Chem. Commun.* **2013**, 49, 5150. (e) Pace, V.; Rae, J. P.; Procter, D. J. *Org. Lett.* **2014**, 16, 476. (f) Plotzicka, J.; Kleeberg, C. *Organometallics* **2014**, 33, 6915.
- (26) Conjugate addition to substituted allenes to afford (*E*)-products has been reported; see: Elsner, P.; Bernardi, L.; Salla, G. D.; Overgaard, J.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2008**, 130, 4897.
- (27) (a) Denmark, S. E.; Liu, J. H. C.; Muhuhi, J. M. *J. Am. Chem. Soc.* **2009**, 131, 14188. (b) Denmark, S. E.; Liu, J. H. C.; Muhuhi, J. M. *J. Org. Chem.* **2011**, 76, 201. (c) Nagano, T.; Pospíšil, J.; Chollet, G.; Schulthoff, S.; Hickmann, V.; Moulin, E.; Herrmann, J.; Müller, R.; Fürstner, A. *Chem. - Eur. J.* **2009**, 15, 9697. (d) Fürstner, A.; Nagano, T. *J. Am. Chem. Soc.* **2007**, 129, 1906.