Organic LETTERS

Letter

pubs.acs.org/OrgLett

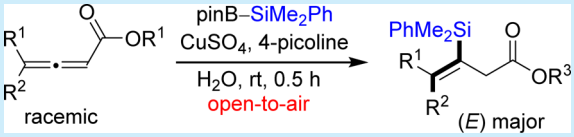
Regio- and Stereoselective Copper(II)-Catalyzed Hydrosilylation of Activated Allenes in Water: Access to Vinylsilanes

Srinath Pashikanti, Joseph A. Calderone, Matthew K. Nguyen, Christopher D. Sibley, and Webster L. Santos*

Department of Chemistry, Virginia Tech, Blacksburg, Virginia 24061, United States

Supporting Information

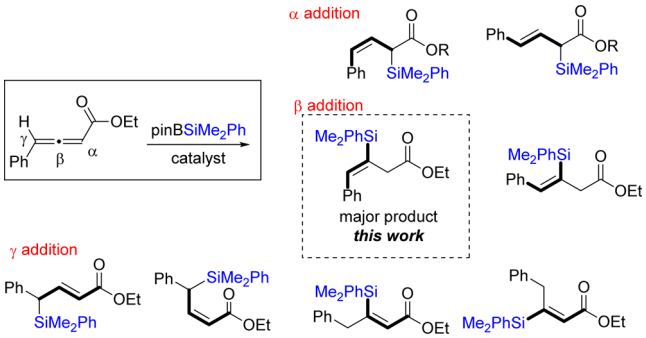
ABSTRACT: By using catalytic amounts of copper(II), 4-picoline, and dimethylphenylsilylpinacol borane, a series of allenoates were silylated on the β carbon in good to excellent yields and high (*E*)-selectivity. The mild and efficient silylation method is conducted in water under atmospheric conditions 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. Alkyne[3] 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 copper[12] 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 acid[14] and stoichiometric $Co_2(CO)_8$[15] 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 carbosilylations of substituted allenes have been reported.[17]

Given our interest in silylation reactions utilizing Suginome's silylboron reagent [dimethylphenylsilylpinacolborane (pinBSiMe$_2$Ph)][18] and development of sustainable reaction conditions,[19] we sought to develop a protocol for the silylation of substituted allenoates. 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



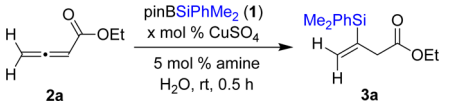
γ-[20] and β-additions[21] of various nucleophiles to allenoates is well precedented. Based on our experience with the regioselective transfer of Bpin to the β carbon of allenoates utilizing a preactivated sp^2-sp^3 hybridized diboron reagent (pinacolatodiisopropylaminato diboron) and Cu(I) catalyst,[22] we investigated the development of β-silylation of substituted allenoates. 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 allenoate, ethyl buta-2,3-dienoate (**2a**), with pinBSiMe$_2$Ph 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

Received: April 5, 2016

DOI: 10.1021/acs.orglett.6b00981
Org. Lett. XXXX, XXX, XXX−XXX

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]

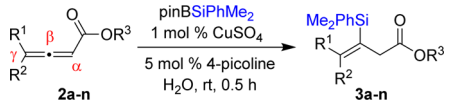
[a]General procedure: base (5 mol %), ethyl buta-2,3-dienoate **2a** (1 equiv), pinBSiPhMe$_2$ (1.1 equiv), and 1.3 mg/mL of $CuSO_4$ solution were mixed at rt for 30 min. [b]Determined by GC-MS of crude material. [c]1,8-Diazabicyclo[5.4.0]undec-7-ene. [d]NR = no reaction.

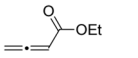
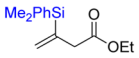
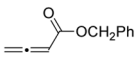
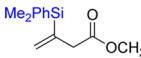
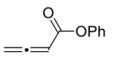
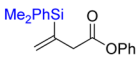
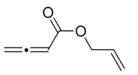
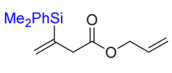
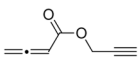
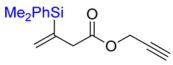
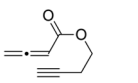
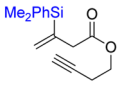
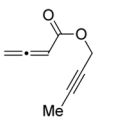
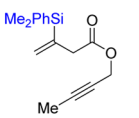
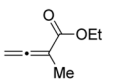
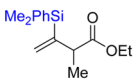
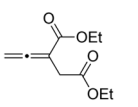
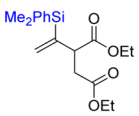
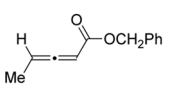
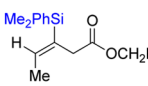
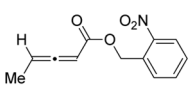
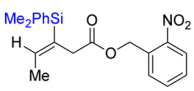
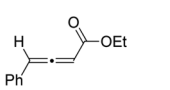
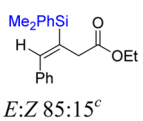
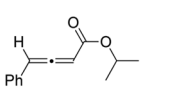
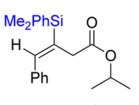
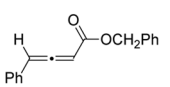
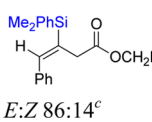
conversion (entry 2); however, a screen of other bases such as triethylamine, DBU, benzylamine, and diethylamine resulted in a significant decrease in product conversion (entries 3−6). As expected, removal of 4-picoline or the copper catalyst afforded no reaction, suggesting the key role of these reagents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

With the optimized conditions in hand (5 mol % 4-picoline, 1 mol % $CuSO_4$, 1.1 equiv pinBSiPhMe$_2$), 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-butynyl ester **2g**. The reaction of **2g** under the same reaction conditions produced the silylated **3g** in 60% yield. Further, this result demonstrate 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]



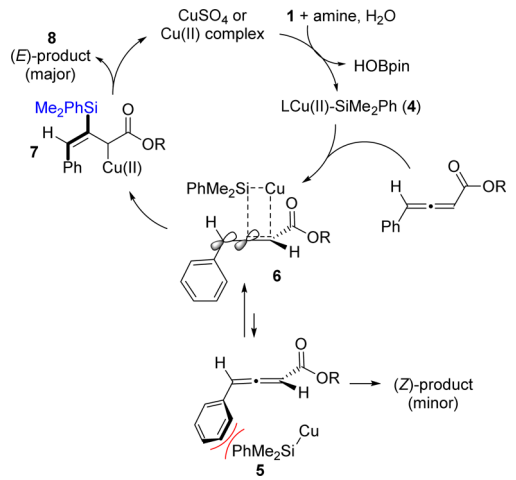
entry	substrate	product		yield[b]
1			**3a**	76
2			**3b**	96
3			**3c**	83
4			**3d**	30
5			**3e**	trace
6			**3f**	trace
7			**3g**	60
8			**3h**	76
9			**3i**	81
10		 *E*:*Z* 87:13[c]	**3j**	95
11		 *E*:*Z* 88:12[c]	**3k**	51
12		 *E*:*Z* 85:15[c]	**3l**	61
13		 *E*:*Z* 85:15[c]	**3m**	73
14		 *E*:*Z* 86:14[c]	**3n**	75

[a]Reaction conditions identical to Table 1, entry 1. [b]Isolated yield. Isolated yields averaged from two or more experiments. [c]Stereoselectivity was determined by ^{1}H 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

DOI: 10.1021/acs.orglett.6b00981
Org. Lett. XXXX, XXX, XXX−XXX

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)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: santosw@vt.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge financial support by the National Science Foundation (CHE-1414458).

■ 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.

DOI: 10.1021/acs.orglett.6b00981
Org. Lett. XXXX, XXX, XXX−XXX

(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 pinBSiMe$_2$Ph; 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) Plotzitzka, 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.

DOI: 10.1021/acs.orglett.6b00981
Org. Lett. XXXX, XXX, XXX−XXX