

Preparation of Vinyl Silyl Ethers and Disiloxanes via the Silyl-Heck Reaction of Silyl Ditriflates

Sara E. S. Martin and Donald A. Watson*

Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716, United States

S Supporting Information

ABSTRACT: Vinyl silyl ethers and disiloxanes can now be prepared from aryl-substituted alkenes and related substrates using a silyl-Heck reaction. The reaction employs a commercially available catalyst system and mild conditions. This work represents a highly practical means of accessing diverse classes of vinyl silyl ether substrates in an efficient and direct manner with complete regioisomeric and geometric selectivity.

Vinylsilanes are ubiquitous reagents in organic synthesis,¹ in part because their high utility is complemented by low toxicity and high stability.² Among vinylsilanes, those bearing oxygen substitution at silicon are particularly useful, as these reagents consistently provide superior reactivity compared to their trialkylsilyl counterparts, especially when used in Hiyama–Denmark cross-coupling³ or in Tamao–Fleming oxidation.⁴

Though alkoxyvinylsilane reagents are highly useful, the traditional methods to access them all carry significant drawbacks, which can limit their utility. These reagents are most often prepared either by silylation of a vinyl organomagnesium or -lithium reagent with an electrophilic silane⁵ or through hydrosilylation of an alkyne.⁶ The first method requires the corresponding organometallic reagents, which have limited functional group compatibility, and as significantly, is often derived from relatively complex starting materials (i.e., vinyl bromides), which can take many steps to access. Similarly, while hydrosilylation is milder in nature, the reaction requires access to the corresponding alkynes, which also poses synthetic challenges and have limited commercial availability. Indeed, the limitations in accessing unsaturated silanes have been attributed to be one of the primary reasons for the slow adoption of Hiyama-type cross-coupling reactions compared to other cross-couplings.⁷

Alkenes are widely abundant, stable starting materials. However, to date, no direct methods exist to convert these highly attractive starting materials into vinyl silyl ethers and disiloxanes.^{8,9} A mild, functional group tolerant method to achieve this conversion would greatly increase the synthetic accessibility of oxygen-substituted vinylsilanes.

Herein we report the preparation of vinyl silyl ethers and disiloxanes using silyl ditriflates (Figure 1). We show that these reagents participate in the palladium-catalyzed silyl-Heck reaction with terminal aryl-substituted alkenes and, upon quenching with alcohol or water, provide *trans*-vinyl silyl ethers in high yield as single regioisomeric and geometric isomers. This

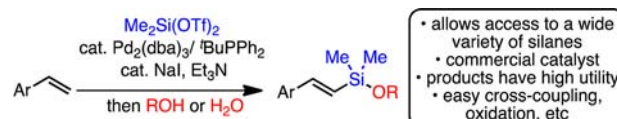


Figure 1. Preparation of vinyl silyl ethers from alkenes.

method uses a commercially available catalyst system and requires only catalytic amounts of iodide additives. When combined with Hiyama–Denmark cross-coupling, this chemistry provides superior yields and regioselectivities in the preparation of stilbene derivatives compared to direct Heck arylation. Furthermore, by varying the nature of the quenching reagent, this strategy allows the direct preparation of a wide variety of vinylsilanes with tunable reactivity.

We recently reported a palladium-catalyzed synthesis of vinyl and allyl trimethylsilanes from terminal alkenes and trimethylsilyl halides ($X = \text{Cl}, \text{I}$), which we believe proceeds through a Heck-type mechanism.¹⁰ Although this method displayed good functional group tolerance, it was limited to the preparation of trimethylsilanes. We recognized that an analogous reaction that allowed for the preparation of vinyl siloxyethers from simple alkenes would significantly increase the utility of this silyl-Heck reaction and allow facile access to this important class of reagents. A possible entry into silyl ethers would involve the use of dihalo or di(pseudo)halosilanes, however such substrates have not previously been examined in Heck-type reactions.¹¹

Our prior study demonstrated that Si-OTf bonds can participate in silyl-Heck reactions in the presence of an iodide additive.¹⁰ Thus, we began our studies by examining reaction of dimethylsilyl ditriflate ($\text{Me}_2\text{Si}(\text{OTf})_2$ (**1**)),^{12,13} using model substrate *4-tert*-butylstyrene and EtOH (Table 1). Our initial reaction conditions mirrored those developed in the reactions of trimethylsilyl halides (catalytic $(\text{COD})\text{Pd}(\text{CH}_2\text{TMS})_2$ (**2**) and $^t\text{BuPPh}_2$ with stoichiometric LiI and Et_3N at 60 °C). When ethanol was added at the beginning of the reaction, modest yield of the desired ethoxyvinylsilane **3a** resulted (26%, Table 1, entry 1). This reaction presumably proceeds via *in situ* formation of $\text{Me}_2\text{Si}(\text{OEt})(\text{OTf})$. Although promising, attempts to optimize these reaction conditions were not successful. In contrast, simply waiting to add the alcohol until the end of the reaction resulted in a dramatically improved yield of the desired product (81%, entry 2). In this latter case, we assume that the initially formed product is the corresponding dimethylvinylsilyl triflate, which is then converted to the silyl ether upon addition

Received: July 30, 2013

Published: August 28, 2013

Table 1. Optimization of Silyl Ether Formation

entry	temp (°C)	Pd source (mol %)	amount of 1 (equiv)	M ⁺ I ⁻ (mol %)	yield by NMR (%)
1	60	2 (5)	1	LiI (100)	26 ^a
2	60	2 (5)	1	LiI (100)	81
3	60	Pd ₂ (dba) ₃ (2.5)	1	LiI (100)	81
4	40	Pd ₂ (dba) ₃ (2.5)	1	LiI (100)	78
5	rt	Pd ₂ (dba) ₃ (2.5)	1	LiI (100)	22
6	40	Pd ₂ (dba) ₃ (2.5)	1.5	LiI (100)	24
7	40	Pd ₂ (dba) ₃ (2.5)	1	LiI (0)	6
8	40	Pd ₂ (dba) ₃ (2.5)	1.1	LiI (5)	98
9	40	Pd ₂ (dba) ₃ (2.5)	1.1	NaI (5)	98
10	35	Pd ₂ (dba) ₃ (1.25)	1.1	NaI (5)	>99

^aEtOH added at start.

of the alcohol. Using this order of addition, commercially available Pd₂(dba)₃ can also be used as the precatalyst with equal success (entry 3). This result contrasts our earlier work wherein Pd₂(dba)₃ was ineffective. Modest decreases in the reaction temperature were tolerated without ill effect, but at room temperature the reaction was sluggish (entries 4 and 5). The reaction proved sensitive to the amount of 1 employed. A slight excess (1.1 equiv) of 1 proved optimal, but additional reagent rapidly eroded the yield (entry 6). As anticipated, iodide was a critical additive in the reaction (entry 7). However, only a catalytic amount was required and afforded superior yields (entry 8).¹⁴ Unlike our prior work, both LiI and NaI can be used with equal effect (entry 9). As NaI is both cheaper and more readily handled, we continued our studies with this additive. Finally, additional studies demonstrated that the reactions were best conducted at 35 °C and that only 2.5 mol % palladium was required to achieve quantitative yield (NMR).

With these conditions in hand, we investigated the scope of the reaction (Table 2). On preparative scale (1–5 mmol), the model product 3a was isolated in 92% yield as the *trans*-vinyl silyl ether. A variety of other alcohols, including both secondary and tertiary alcohols, can also be used to quench the reaction, giving rise to a series of vinyl silyl ethers in similar isolated yields (3b, 3c). When water was used to quench the reaction, disiloxane 3d emerged in good isolated yield. In general, any of these quenching methods can be used to prepare vinylsilanes via this method, as demonstrated by the series of silanes 4–6

Table 2. Scope of Substrates for Silyl Ether and Disiloxane Formation

 3a , R = Et, 92% ^b 3b , R = <i>i</i> Pr, 91% 3c , R = <i>t</i> Bu, 90% 3d , R = SiMe ₂ R', 88%	 4a , R = Et, 87% ^b 4b , R = <i>i</i> Pr, 75% 4c , R = SiMe ₂ R', 90%	 5a , R = Et, 95% ^b 5b , R = <i>i</i> Pr, 83% 5c , R = SiMe ₂ R', 89%	 6a , R = Et, 95% ^b 6b , R = <i>i</i> Pr, 85% 6c , R = SiMe ₂ R', 92%	 7a , R = <i>i</i> Pr, 86% 7b , R = SiMe ₂ R', 85%
 8a , R = <i>i</i> Pr, 91% 8b , R = SiMe ₂ R', 79%	 9a , R = <i>i</i> Pr, 93% 9b , R = SiMe ₂ R', 95%	 10a , R = <i>i</i> Pr, 81% ^{c,d} 10b , R = SiMe ₂ R', 84% ^{c,d}	 11a , R = <i>i</i> Pr, 79% ^{c,d} 11b , R = SiMe ₂ R', 79% ^{c,e}	 12a , R = <i>i</i> Pr, 63% ^{c,e} 12b , R = SiMe ₂ R', 62% ^{c,e}
 13a , R = <i>i</i> Pr, 84% ^{c,d} 13b , R = SiMe ₂ R', 82% ^{c,d}	 14a , R = <i>i</i> Pr, 83% ^{c,d} 14b , R = SiMe ₂ R', 78% ^{c,e}	 15 , R = <i>i</i> Pr, 81% ^{c,d,f}	 16a , R = <i>i</i> Pr, 70% ^{d,e} 16b , R = SiMe ₂ R', 83% ^{d,e}	 17 , R = <i>i</i> Pr, 85% ^{c,d}
 18a , R = <i>i</i> Pr, 94% 18b , R = SiMe ₂ R', 93%	 19a , R = <i>i</i> Pr, 91% 19b , R = SiMe ₂ R', 89%	 20a , R = <i>i</i> Pr, 99% ^{c,e} 20b , R = SiMe ₂ R', 70% ^{c,e}	 21a , R = <i>i</i> Pr, 94% 21b , R = SiMe ₂ R', 91%	

^aIsolated yields (average of two runs), 1 mmol scale unless otherwise noted. ^b5 mmol scale. ^c2.5 mol % Pd₂(dba)₃, 11 mol % *t*BuPPh₂. ^d48 h. ^e50 °C. ^f60 °C.

(exceptions noted below). For simplicity, we elected to study quenching with isopropanol and water in the remaining examples. In all cases, only *trans*-1,2-disubstituted vinylsilanes were observed. No trace of the *cis*-vinyl isomer, nor the 1,1-disubstituted regioisomeric silane has been detected.

A wide variety of vinyl arenes also participate in the reaction. Both electron-donating and electron-withdrawing ethereal substrates generate products in high yields (5 and 6, Table 2). Dioxolane and silyl ether functionalities were well tolerated (7–9), as were fluorides, chlorides, esters, and tertiary amines (10–13). In general, substrates bearing electron-withdrawing substituents were slower to react than their electron-rich counterparts and required slightly elevated reaction temperature and time. In the extreme, substrates bearing highly electron-withdrawing groups, such as *p*-nitrostyrene (not shown) were unreactive. Steric hindrance on the arene did not adversely affect the reaction (14); however increased substitution on the alkene was not tolerated using the current catalyst (not shown).¹⁵

Alkenes bearing heterocycles are also substrates. Silyl ether 15 was formed from 2-vinylbenzofuran in good yield, and the reaction of *N*-tosyl-3-vinylindole led to vinylsilane 16 without incident. Finally, the reaction of *N*-vinylcarbazole provided silyl ether 17 in high yield. In the case of these heterocyclic substrates, alcohol quench proved to be superior to those using water. In the case of both 15 and 17, water quench led to complex mixtures of products.

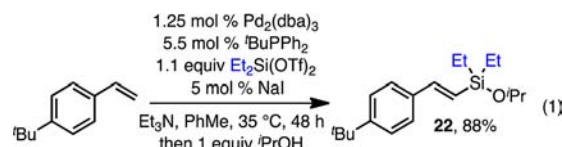
This silyl-Heck protocol is also compatible with a range of more complex vinylic substrates. For example, vinylferrocene can be silylated in near quantitative yield to give redox-active vinylsilanes 18a and 18b. We anticipate that these products will be highly useful in the preparation of topologically defined redox probes.¹⁶ Similarly, 4-vinylbenzocyclobutene is also an excellent substrate. Isopropyl silyl ether 19a was isolated in 91% yield. Water quench led to the formation of divinylsiloxane bis-benzocyclobutene (19b) in similar yield. This latter product is the key monomer of Cyclotene photoresist resins.¹⁷

Bis-functionalized silyl boronic esters 20a and 20b were readily prepared from (4-vinylphenyl)pinacolboronic ester. In this reaction, no C–B bond activation was observed. These products provide a lynch-pin substrate for orthogonal Suzuki and Hiyama–Denmark coupling reactions.¹⁸

As a final example of a complex substrate, we examined the preparation of estradiol-derived vinylsilanes 21a and 21b. As in the previous examples, these complex materials can be prepared without incident in high yield with either isopropanol or water quench. Not only do these results demonstrate that highly complex substrates are compatible with the silyl-Heck reaction conditions, but the products for this and similar transformations will be highly useful in preparing bimolecular conjugates.

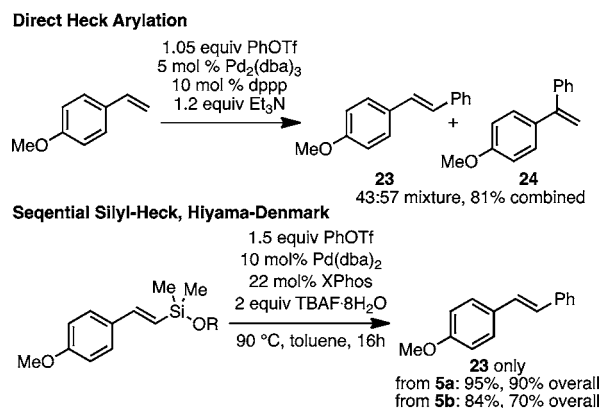
We also have begun to explore the scope of the groups on the silyl ditriflate. We were pleased to find that diethylsilyl ditriflate is also an excellent silylating agent. Under the optimized reaction conditions, similar yields were observed for diethylvinylsilanes with this reagent. For example, 4-*tert*-butylstyrene can be silylated in 88% yield, after isopropanol quench (eq 1).¹⁹ This strategy will allow for tuning of the reactivity of the vinylsilane products.

The formation of vinyl silyl ethers presented herein has numerous advantages. First, the fact that only a single regioisomeric and geometric isomer is obtained provides a significant advantage over competing technologies. For



example, it is well known that direct Heck arylation of electron-rich styrenes leads to a mixture of regioisomeric products.²⁰ Selectivity is particularly poor for triflate electrophiles. For example, arylation of *p*-methoxystyrene with phenyl triflate gives a 57:43 mixture of α and β products, which in our hands were obtained in 81% yield (Scheme 1, top).²¹ In

Scheme 1. Silyl-Heck/Hiyama–Denmark vs Direct Heck Reactions

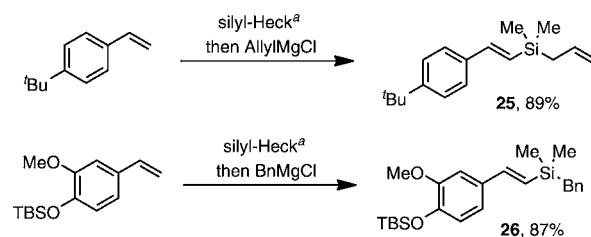


contrast, Hiyama–Denmark coupling of vinyl silyl ethers 5a and 5b proceeded in 95% and 84% yield, respectively, to give exclusively stilbene product 23 (Scheme 1, bottom).²² As 5a and 5b are obtained in high yields as single isomers from *p*-methoxystyrene in the silyl-Heck reaction, this two-step protocol is vastly superior in overall yield and avoids the difficult separation of regioisomeric products.

In addition, because of the intermediacy of the vinylsilyl triflate, this strategy provides a divergent approach to differentially substituted vinylsilanes. For example, quenching with allyl- or benzylmagnesium chloride leads to the corresponding dimethylvinylsilanes 25 and 26 in high yields (Scheme 2). Allyl- and benzylsilanes have proven highly useful in a variety of applications,^{3c,4,23} and this method provides a convenient method for accessing these materials via the silyl-Heck reaction.

In summary, we have developed a novel method to generate reactive and versatile vinyl silyl ethers and disiloxanes from aryl-substituted alkenes and related starting materials. This method

Scheme 2. Preparation of Diverse Vinylsilanes



^a1.25 mol % Pd₂(dba)₃, 5.5 mol % ^tBuPPh₂, 1.1 equiv Me₂Si(OTf)₂, 5 mol % NaI, Et₃N, PhMe, 35 °C.

exhibits broad functional group tolerance, and products are generated in good to excellent isolated yields and as single regioisomeric and geometric isomers. The reaction proceeds with readily accessible reagents and an inexpensive, commercially available catalyst. Not only does this reaction dramatically expand the utility of the silyl-Heck reaction by allowing access to a wide variety of highly useful vinyl silyl ethers and related reagents, for the first time, it demonstrates that silane (bis)electrophiles can be used in a Heck-type process. Future studies will be directed toward expanding this transformation to other classes of alkenes and related molecules.

■ ASSOCIATED CONTENT

● Supporting Information

Experimental procedures and spectral data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

dawatson@udel.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Mr. Scott Shuler is thanked for assistance. The University of Delaware (UD), the NSF (CAREER CHE1254360), and the Research Corporation (Cottrell Scholars Program) are gratefully acknowledged. S.E.S.M. acknowledges graduate fellowship support from NIH 5T32 GM 08550-16. Data were acquired at UD on instruments obtained with the assistance of NSF and NIH funding (NSF CHE0421224, CHE1229234, and CHE0840401; NIH P20 GM103541 and S10 RR02692). Dedicated to Professor Larry E. Overman on the occasion of his 70th birthday.

■ REFERENCES

- (1) (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063–2192. (b) Brook, M. A., *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: Chichester, 2000. (c) Fleming, I.; Dunoguès, J.; Smithers, R. The Electrophilic Substitution of Allylsilanes and Vinylsilanes. In *Organic Reactions*; John Wiley & Sons, Inc.: New York, 2004; pp 57–575.
- (2) Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, *40*, 4893–4901.
- (3) (a) Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, *41*, 1486–1499. (b) Denmark, S. E.; Liu, J. H. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2978–2986. (c) Sore, H. F.; Galloway, W. R. J. D.; Spring, D. R. *Chem. Soc. Rev.* **2012**, *41*, 1845–1866.
- (4) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.
- (5) (a) Oshima, K. Vinylsilanes. In *Science of Synthesis*; Fleming, I., Ed.; Thieme: Stuttgart, 2001; Vol. 4, pp 713–754. (b) Denmark, S. E.; Neuville, L.; Christy, M. E. L.; Tymonko, S. A. *J. Org. Chem.* **2006**, *71*, 8500–8509.
- (6) (a) Denmark, S. E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073–1076. (b) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17644–17655.
- (7) Corbet, J.-P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651–2710.
- (8) Intramolecular alkene metathesis has been used to effectively prepare cyclic vinylsiloxy ethers; however, the intermolecular version of the reaction remains much less studied and is highly dependent on the nature of the starting alkenes: (a) Pietraszuk, C.; Fischer, H.; Rogalski, S.; Marciniak, B. *J. Organomet. Chem.* **2005**, *690*, 5912–5921. (b) Denmark, S. E.; Yang, S.-M. *Org. Lett.* **2001**, *3*, 1749–1752. For a related reaction see: (c) Wakatsuki, Y.; Yamazaki, H.; Nakano, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 703–704. Also see ref 3b.
- (9) As this manuscript was in preparation, a report appeared demonstrating the preparation of predominately *cis*-vinyl silyl ethers from terminal alkenes using iridium-catalyzed hydrosilylation and a sacrificial oxidant: Cheng, C.; Simmons, E. M.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2013**, *52*, 8984–8989.
- (10) McAtee, J. R.; Martin, S. E. S.; Ahneman, D. T.; Johnson, K. A.; Watson, D. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 3663–3667.
- (11) Tanaka has demonstrated the oxidative addition of Pt(0) complexes to dichlorosilanes in stoichiometric reactions: Yamashita, H.; Tanaka, M.; Goto, M. *Organometallics* **1997**, *16*, 4696–4704.
- (12) Matyjaszewski, K.; Chen, Y. L. *J. Organomet. Chem.* **1988**, *340*, 7–12.
- (13) This reagent is easily prepared from the reaction of neat Ph₂SiMe₂ and TfOH. It can be stored under nitrogen indefinitely after removal of the resulting PhH under vacuum, or used directly without diminished yield in the silyl-Heck reaction. See Supporting Information.
- (14) We believe iodide additives result in *in situ* generation of Si-I species, which enable oxidative addition: Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247–1251.
- (15) Terminal alkenes bearing allylic hydrogen atoms are also reactive but give poor allyl vs vinyl selectivity. See Supporting Information for an example.
- (16) Gietter, A. A. S.; Pupillo, R. C.; Yap, G. P. A.; Beebe, T. P.; Rosenthal, J.; Watson, D. A. *Chem. Sci.* **2013**, *4*, 437–443.
- (17) (a) Gros, W. A. Benzocyclobutene-based Die Attach Adhesive Compositions. U.S. Patent 4759874, 1988. (b) Kirchhoff, R. A.; Bruza, K. J. *Prog. Polym. Sci.* **1993**, *18*, 85–185.
- (18) Lim, D. S. W.; Anderson, E. A. *Org. Lett.* **2011**, *13*, 4806–4809.
- (19) Some reactivity was also observed with diisopropylsilyl ditriflate. However, the yields remain low with the present catalyst system.
- (20) (a) Fristrup, P.; Le Quement, S.; Tanner, D.; Norrby, P.-O. *Organometallics* **2004**, *23*, 6160–6165. (b) Oestreich, M., *The Mizoroki–Heck Reaction*; John Wiley & Sons: Chichester, UK, 2008.
- (21) With the use of phenyl iodide, selectivity is only marginally better in this reaction (90:10 β:α).
- (22) (a) Denmark, S. E.; Sweis, R. F. *Org. Lett.* **2002**, *4*, 3771–3774. (b) Denmark, S. E.; Regens, C. S. *Tetrahedron Lett.* **2011**, *52*, 2165–2168.
- (23) Bennetau, B., Benzylsilanes. In *Science of Synthesis*; Fleming, I., Ed.; Thieme: Stuttgart, 2002; Vol. 4, pp 825–836.