Markovnikov Alkyne Hydrosilylation Catalyzed by Ruthenium Complexes

Barry M. Trost* and Zachary T. Ball

Department of Chemistry, Stanford University
Stanford, California 94305-5080

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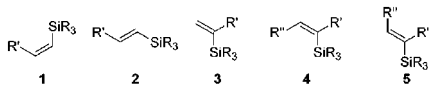
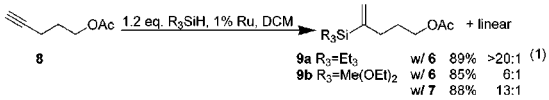
Vinyl−metal species are extremely important building blocks in organic synthesis.[1] Among these, vinylsilanes play a growing role due to their low cost, low toxicity, ease of handling, and simplicity of byproduct removal. Particularly significant is the potential of vinylsilanes as nucleophilic partners in Pd-catalyzed cross-coupling reactions.[2] Vinylsilanes are also useful as acceptors in conjugate addition reactions,[3] as masked ketones through Tamao−Fleming oxidation,[4] and as terminators for cation cyclizations.[5] Unlike vinyl boranes, vinylsilanes can be readily carried through many synthetic operations.

However, the utility of vinylsilanes has been inhibited by the inconvenience of accessing stereo- and regiodefined vinyl−metal compounds. Among the possible routes to these compounds, hydrosilylation of alkynes represents the most straightforward, atom-economical access.[6] Although there has been significant progress using a variety of metal-catalyzed approaches to provide stereodefined, 1,2-substituted vinylsilanes of the form **1** or **2**, there has been no reported general access to 1,1-disubstituted vinylsilanes[7] (**3**) and very little is known about selectivity in accessing trisubstituted (**4**, **5**) vinylsilanes.[8]



A large number of metal systems have been shown to be effective in the hydrosilylation of terminal alkynes to produce linear vinylsilanes. Some of these afford good control of olefin geometry.[9] The limited number of known hydrosilylations with ruthenium catalysts give the analogous linear products.[10,11] Free alcohols[10] and carbonyl groups[12] have been shown to direct hydrosilylation to provide internal silanes, presumably through coordination. However, to our knowledge, there are no published reports of nondirected terminal alkyne hydrosilylation to afford preferentially the internal vinylsilane.

Our recent success utilizing $CpRu(MeCN)_3^+$ PF_6^- (**6**) for catalytic reactions of alkynes, especially for halometalation leading to a variety of reaction cascades,[13] led us to examine the ability of $CpRu^+$ complexes to catalyze hydrometalation reactions. We were gratified to find that alkyne **8** was smoothly converted in 30 min at ambient temperature to the branched (1,1-disubstituted) vinylsilane **9a** in good yield with no detectable formation of linear (1,2-disubstituted) products with only 1 mol % catalyst (eq 1).[14]



Given the poor reactivity of alkylsilanes toward a variety of synthetically useful transformations, we sought to extend the methodology to more reactive yet still operationally convenient alkyoxysilanes. Thus, hydrosilylation with diethoxymethylsilane was performed under identical conditions and furnished clean conversion to the desired vinylsilane **9b**. However, in this case the desired branched product was produced along with the linear product (b:l 6:1[15]). A change in catalyst to the more sterically demanding $Cp^*Ru(MeCN)_3^+$ PF_6^- (**7**) under identical conditions for 20 min maintained reactivity and improved this selectivity to 13:1. Thus, complex **7** became our catalyst of choice.

A variety of terminal alkynes proved amenable to the reaction, including those with substantial steric bulk (Table 1). The reaction is tolerant to a wide range of functional groups, including sp^2 halides, alkenes, esters, free alcohols, protected amines, and even free carboxylic acids.[16] In addition, total selectivity for terminal alkynes in diyne substrates (entry g) is observed. Overall, good yields and good regioselectivity are maintained through a wide range of substrates.

We next sought to extend the scope of our hydrosilylation to internal alkynes. Treatment of 4-octyne under the conditions described previously afforded extremely clean conversion to a single vinylsilane (Table 2, entry a). We were intrigued when nOe studies indicated that the product was the (*Z*) isomer resulting from *trans* addition. Although strong Lewis acids generally give *trans* products, exclusive *trans* hydrosilylation of internal alkynes with transition metal catalysts is quite rare,[17] and the complete selectivity exhibited under our reaction conditions is significant.[18] The *trans* addition product has been observed for other ruthenium catalysts only with terminal alkynes to afford 1,2-disubstituted vinylsilanes **1**.[10,11]

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(2) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845. Hiyama, T. Organosilicon Compounds in Cross-coupling Reactions. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P., Eds.; Wiley-VCH: Weinheim, 1998. For more results, see: Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137−2140; Denmark, S. E.; Neuville, L. *Org. Lett.* **2000**, *2*, 3221.

(3) Bunlaksananusorn, T.; Rodriguez, A. L.; Knochel, P. *Chem. Commun.* **2001**, 745.

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(5) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 7.

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(7) For an approach see Sharma, S.; Oehlschlager, A. C. *Tetrahedron Lett.* **1988**, *29*, 261.

(8) Molander, G. A.; Retsch, W. H. *Organometallics* **1995**, *14*, 0.

(9) For a recent example with extensive references to previous work,see: Dash, A. K.; Wang, J. Q.; Eisen, M. S. *Organometallics* **1999**, *18*, 4724. See also: Takeuchi, R.; Tanouchi, N. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2909; Mori, A.; Takahisa, E.; Kajiro, H.; Nishihara, Y.; Hiyama, T. *Polyhedron* **2000**, 567; Lewis, L. N.; Sy, K. G.; Bryant, G. L.; Donahue, P. E. *Organometallics* **1991**, *10*, 3750.

(10) Na, Y. G.; Chang, S. B. *Org. Lett.* **2000**, *2*, 1887.

(11) Esteruelas, M. A.; Herrero, J.; Oro, L. A. *Organometallics* **1993**, *12*, 2377.

(12) Murai, T.; Kimura, F.; Tsutsui, K.; Hasegawa, K.; Kato, S. *Organometallics* **1998**, *17*, 926.

(13) Trost, B. M.; Pinkerton, A. B. *J. Am. Chem. Soc.* **2000**, *122*, 8081; Trost, B. M.; Pinkerton, A. B. *J. Am. Chem. Soc.* **1999**, *121*, 1988; Trost, B. M.; Pinkerton, A. B. *Angew. Chem., Int. Ed.* **2000**, *39*, 360.

(14) Typical procedure: The alkyne **7** (50 μL, 0.38 mmol) under Ar was dissolved in DCM (0.75 mL, 0.5 M solution) and treated with triethylsilane (72 μL, 0.45 mmol). The flask was cooled to 0 °C, and solid **6** (1.6 mg, 0.0038 mmol) was added. The flask was immediately allowed to warm to ambient temperature and stirred for 30 min. The crude mixture was concentrated in vacuo and applied to a silica gel column (eluent with 20:1 pet. ether: ether) to afford 78 mg (86%) of the desired 1,1-disubstituted silane as a clear, colorless oil.

(15) Branched:linear ratios for terminal alkynes are given as a ratio of internal product to total terminal silane, both isomers of which are sometimes observed

(16) We have not examined ketone substrates, but the reaction proceeds in acetone solvent, indicating compatibility with ketone functionality. The yields of free alcohol products are uniformly lower, although crude NMR analysis indicates a clean reaction. We suspect decomposition during purification as the source of these somewhat decreased yields. Purification on Florisil instead of silica ameliorates this problem somewhat.

(17) For complete *trans* addition with a transition metal catalyst, see: Fuchikami, T.; Ubukata, Y.; Tanaka, Y. *Tetrahedron Lett.* **1199**, 1199. For Lewis acid catalysis: Asao, N.; Sudo, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 7654; Sudo, T.; Asao, N.; Gevorgyan, V.; Yamamoto, Y. *J. Org. Chem.* **1999**, 2494.

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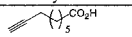
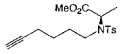
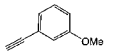
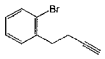
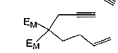
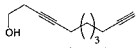
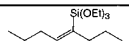
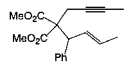
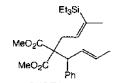
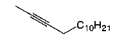
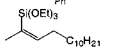
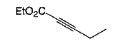
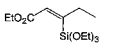
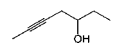
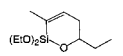
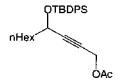
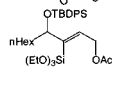
Table 1. Hydrosilylation of Terminal Alkynes to Afford Markovnikov Addition Products **3**[1]

Entry	Alkyne	Silane	Cat (%)	Ratio[2](b:l)	% Yield[3]
a		Et_3SiH	**6** (1)	20:1	89[5]
d		Et_3SiH	**6** (1)	20:1	88
c		$(EtO)_2MeSiH$	**7** (1)	9:1	86[4]
d		$(EtO)_3SiH$	**7** (1)	13:1	58[4,5]
e		$(EtO)_3SiH$	**7** (1)	13:1	92
f		$(EtO)_3SiH$	**7** (5)	N.D.[6]	61[4]
g		$(EtO)_3SiH$	**7** (1)	9:1	71[7]
h		$(EtO)_3SiH$	**7** (5)	20:1	87

[1] All reactions performed 0.5 M in DCM on 0.2−0.5 mmol scale. Reactions were generally complete within 1 h. [2] Ratio of branched (b) to linear (l) regioisomers determined by crude NMR and GC, where applicable. [3] Isolated yield for the mixture of branched and linear isomers unless otherwise indicated. [4] Yield refers to isolated pure branched product. [5] 100% conv. See ref 14. [6] The complicated olefinic region of the ^{1}H NMR made a reliable determination of the product ratios difficult, though significant linear material was not isolated. [7] 1.05 equiv of silane. No reaction at the internal alkyne was observed.

Table 2. Hydrosilylation of Internal Alkynes[1]

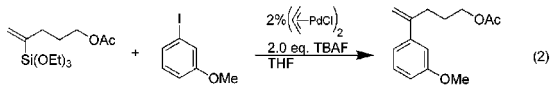
Entry	Alkyne	Major Product	Ratio[2] (major: minor)	Yield[3]
a			n.a.	99
b[4,6]			>20:1	70[5]
c			2.4:1	100
d			5:1	99
e			5:1	71[5]
f[6]			6:1	92

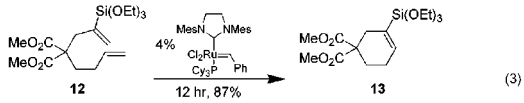
[1] All reactions performed 0.5 M in DCM on 0.2−0.5 mmol scale. 1.2 equiv of $(EtO)_3SiH$ and 1 mol % catalyst loading is employed unless otherwise indicated. Reactions were generally complete within 1 h. [2] Ratio of regioisomers determined by NMR and GC analysis of the crude reaction mixture. [3] Isolated yield is for the mixture of regioisomers unless otherwise indicated. [4] Triethylsilane was used as the silane. [5] Yield refers to isolated pure major product. [6] 5% catalyst loading.

Regioselectivity in the hydrosilylation of internal alkynes has not been well studied.[8] In an attempt to achieve regioselectivity for unsymmetrical substrates, a series of disubstituted alkynes was examined. Although 2-tetradecyne (entry c) gave modest regioselectivity, switching to an α-branched substrate gave significantly enhanced selectivity (entry f). In addition, an ynoate gave clean reaction to afford the *β*-silyl compound with the expected (*Z*) geometry (entry d). Although 1,6- and 1,7- diynes and enynes are generally more sluggish reaction partners, an enyne gave exclusively the 2-silyl product (entry b), presumably the result of olefin coordination to the metal during an initial silylruthenation step. Appropriately positioned homo-propargylic alcohols also impart significant selectivity to a substrate (entry e). In this case, the major product is isolated after cyclization under the reaction conditions. The reasons for this direction are at present unclear. However, the exclusive chemoselectivity exhibited by diynes (Table 1, entry g) indicates that silyl transfer followed by *intra*molecular hydrosilylation may not be operable in this case.

It has been postulated that *trans* hydrosilylation reactions proceed through initial *syn* silylmetalation, with subsequent isomerization of the olefin prior to reductive elimination.[19] However, the high selectivity for *trans* addition in this case with internal alkynes raises questions whether any equilibration rationale is viable.

The mild, isomerically distinct hydrosilylation protocol outlined here has many potential applications in the synthesis of complex molecules. Vinylsilane **9c** (prepared in 86% total yield and b:l = 10:1 according to the general procedure) readily couples with 3-iodoanisole (**10**) employing $[(allyl)PdCl]_2$[20] to afford **11** (eq 2). Preliminary results with unsubstituted trialkoxyvinylsilanes[21] in cross-metathesis reactions encouraged us to explore such vinylsilanes in ring-closing metathesis. Indeed regiodefined cyclohexenylsilane **13** could be efficiently generated by ring-closing metathesis (eq 3) upon treatment with Grubbs' carbene metathesis catalyst.[22]





In summary, the first general nondirected terminal alkyne hydrometalation to afford 1,1-disubstituted vinylsilanes with high regioselectivity is presented. The catalyst system extends to internal alkynes to give a single olefin geometry from an unusual *trans* addition. The mild conditions and functional group tolerance—and the inclusion of alkoxysilanes—open a host of potential subsequent transformations toward the construction of complex target molecules. Regiodistinct hydrosilylation also opens the door to unusual or cross-linked silicones. Additional investigations into the mechanism and subsequent synthetic utility of this transformation are currently underway in these laboratories.

Acknowledgment. We thank Dr. Olivier Dirat for helpful discussions. We also acknowledge the National Science Foundation and the National Institutes of Health for their generous support of our programs. Mass spectra were provided by the Mass Spectrometry Facility, University of San Francisco, supported by the NIH Division of Research Resources.

Supporting Information Available: Characterization data for all vinylsilane products, as well as experimental procedures and data for compounds **11** and **13** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) We have performed nOe experiments demonstrating *trans* addition for entries a, b, and d (Table 2). The olefin geometries of other entries are assumed by analogy. We have not detected any *cis* addition in any of our studies with internal alkynes. Initial isotope-labeling studies indicate that *trans* addition is the major pathway for terminal alkynes as well. However, possible isotope scrambling leads to uncertainty about a quantitative analysis.

(19) For an Ir catalyst: Jun, C. H.; Crabtree, R. H. *J. Organomet. Chem.* **1993**, *447*, 177; for a Rh catalyst: Ojima, I.; Clos, N.; Donovan, R. J.; Ingallina, P. *Organometallics* **1990**, *9*, 3127.

(20) Compare: Denmark, S. E.; Pan, W. T. *Org. Lett.* **2001**, *3*, 61.

(21) Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783; Pietraszuk, C.; Fischer, H.; Kujawa, M.; Marciniec, B. *Tetrahedron Lett.* **2001**, *42*, 1175. Pietraszuk, C.; Marciniec, B.; Fischer, H. *Organometallics* **2000**, 913. Mo catalysts have also been used: Denmark, S. E.; Yang, S. M. *Org. Lett.* **2001**, *3*, 1749.

(22) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953.