Organic Letters
Letter
pubs.acs.org/OrgLett

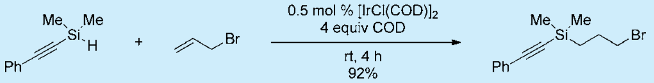
Sterically Directed Iridium-Catalyzed Hydrosilylation of Alkenes in the Presence of Alkynes

Jill A. Muchnij, Farai B. Kwaramba, and Ronald J. Rahaim*

107 Physical Sciences 1, Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078, United States

Supporting Information

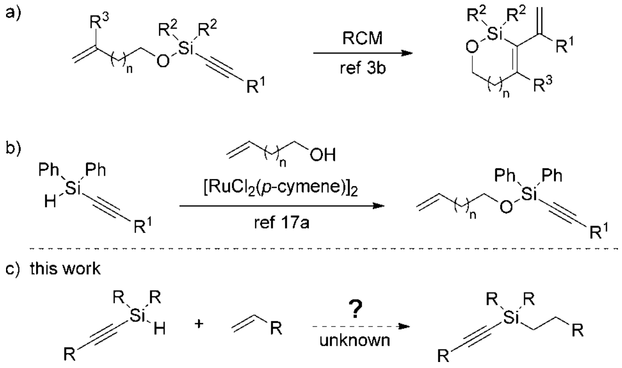
ABSTRACT: A selective iridium catalyzed hydrosilylation of alkenes in the presence of more reactive alkynes is described. By utilizing $[IrCl(COD)]_2$ in the presence of excess COD, hydrosilylation of alkenes and alkynes with ethynylsilanes is achieved with good chemo- and regioselectivity. This approach goes against the traditional reactivity trends of platinum and rhodium catalysts and allows access to highly substituted silicon alkyne tethers.



The application of temporary tethers[1] has been a versatile approach to facilitate rapid access to biologically active complex molecules and building blocks. A variety of temporary tethers[2] have been developed, ranging from silicon,[3] boron,[4] magnesium,[5] phosphorus,[6] and esters.[7] The advantages of tethered reactions are increased reaction rates between the coupling partners and high levels of regio- and stereoselectivity. Of the different approaches developed, temporary silicon tethers have been the most commonly utilized approach. Silicon tethers are versatile in that large assortments of silicon reagents are available and the tether can be prepared under standard conditions in high yields. They are tolerant to a range of reaction conditions, but can be efficiently cleaved via subjection to Tamao–Fleming oxidation[8] or Hiyama cross-couplings.[9] The most common temporary silicon tethers are based on disiloxane and siloxane structural motifs.

We have initiated a program in the development of dual[10]/synergistic[11] catalysis utilizing temporary tethers for applications in library development. As part of this endeavor we required a modular protocol to link a variety of terminal alkynes to an array of functionalized fragments. Silyl alkynes are ideal temporary tethers because they are easily and efficiently prepared from metal acetylides,[12] are stable under most standard reaction conditions, but can be easily cleaved under nucleophilic fluorine conditions.[13] Therefore, what is required is an approach to link the silyl alkyne to the second coupling partner through the silicon. This has previously been accomplished with alkenyl alcohols for subsequent applications in enyne-metathesis reactions (RCM) through formation of an alkynyl siloxane (Scheme 1a).[14] A drawback of the alkynyl siloxane tether is the instability of the siloxane, which makes isolation problematic. To complement this approach and satisfy our requirement for a temporary silicon linker that could be carried through multiple synthetic steps, we sought to develop a method for an alkynylsilane linker.

Scheme 1. Alkynyl-Silicon Linkers

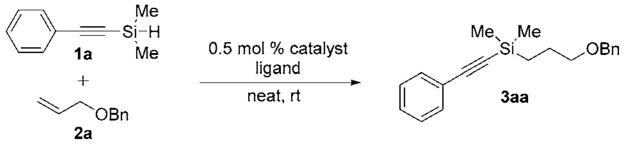


Hydrosilylation[15] of double and triple bonds has proven to be an important reaction/tool in organic synthesis.[16] The versatility of hydrosilylation reactions conducted with high levels of regio- and stereocontrol and functional group compatibility made this a desirable approach to connect an alkynylsilane linker to an olefin or alkyne (Scheme 1c). To the best of our knowledge, a method for the selective hydrosilylation of olefins in the presence of an alkyne has not been reported. This gap is most likely the result of the higher reactivity of the π-basic alkyne. However, there has been a spattering of reports demonstrating transition metal catalyzed silane alcoholysis in the presence of an alkyne (Scheme 1b).[17] Selective hydrosilylation of one alkene in the presence of another has been accomplished using either a directing group or steric bias. Based on these results, we speculated that it may be possible to override the inherent electronic bias for the more reactive alkyne through a steric directed approach. Prototypical transition metals that have been employed in hydrosilylation reactions are Pt,[18] Rh,[19] Pd,[20] Ru,[21] Ir,[22] and Fe.[23] As the starting point to this investigation we selected iridium as the metal of choice based on its selectivity in catalyzing hydrosilylation reactions of allyl substrates[24] in addition to iridium catalysts demonstrating chemo-[25] and regioselectivity[26] by favoring steric over electronic control.

Investigation into the feasibility of this approach began with optimization of the conditions for hydrosilylation of allyl benzyl ether (**2a**) with alkynylsilane (**1a**) (Table 1). The conditions

Received: January 7, 2014
Published: February 19, 2014

Table 1. Optimization of Hydrosilylation Reaction[a]



entry	catalyst	ligand (loading)	time (h)	% conv[b]	% yield[c]
1	$[IrCl(COD)]_2$	COD (0.5 equiv)	4	87	n.d.[d]
2	$[IrCl(COD)]_2$	COD (1 equiv)	4	86	n.d.
3	**$[IrCl(COD)]_2$**	**COD (4 equiv)**	**4**	**98**	**88**
4	$[IrCl(COD)]_2$	none	16	72	n.d.
5	$[IrCl(COD)]_2$	Limonene (4 equiv)	19	70	55
6	$[IrCl(COD)]_2$	1,10-phen (2 mol %)	4	90	47
7	$[IrCl(COD)]_2$	2,2′-Bipyr (1 mol %)	4	70	25
8[e]	$[IrCl(COD)]_2$	COD (0.5 equiv)	19	100	89
9[f]	$[IrCl(COD)]_2$	COD (0.5 equiv)	0.33	86	78
10[f,g]	$[IrCl(COD)]_2$	COD (0.5 equiv)	0.33	100	77
11	$[IrOMe(COD)]_2$	COD (4 equiv)	24	10	n.d.
12	$IrCl_3$	COD (4 equiv)	24	0	n.d.
13	H_2PtCl_6	none	2	100[h]	0
14	Karstedt[I]	none	2	100[h]	0
15	$[(Ph)_3P]_3RhCl$	none	16	100[h]	0

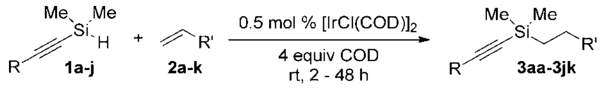
[a] Conditions: 1 mmol silane (**1a**), 1 mmol olefin (**2a**), 0.5 mol % catalyst, ligand, rt; all liquid reagents were degassed. [b] Monitored by GC and based on consumption of **2a**. [c] Isolated by flash chromatography. [d] n.d. = not determined. [e] 0.1 mol % $[Ir(COD)Cl]_2$, reaction 0.5 M in 1,2-dichloroethane. [f] MW, 60 °C. [g] 1 M in 1,2-dichloroethane. [h] Consumption of **1a** by GC. [I] $Pt_2[(Me_2SiCH{=}CH_2)_2O]_3$.

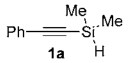
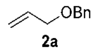
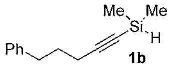
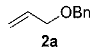
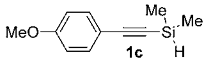
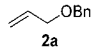
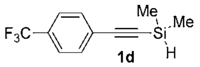
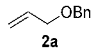
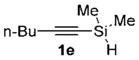
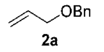
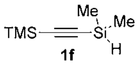
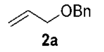
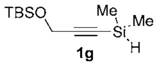
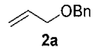
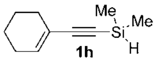
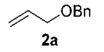
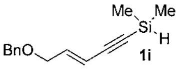
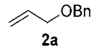
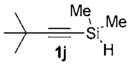
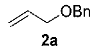
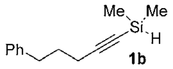
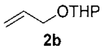
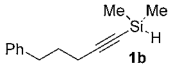
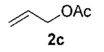
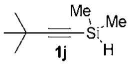
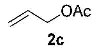
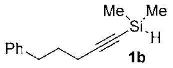
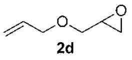
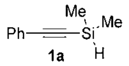
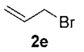
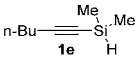
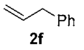
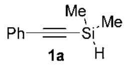
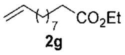
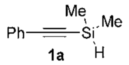
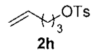
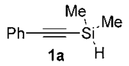
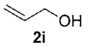
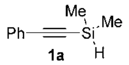
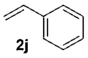
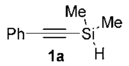
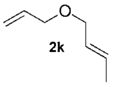
developed for iridium catalyzed hydrosilyation of allyl halides with chlorodimethylsilane were used as the starting point.[27] The desired silylation product (**3a**) was formed under neat conditions with 0.5 mol % $[IrCl(COD)]_2$, but full conversion could only be accomplished when a large excess of coadditive ligand 1,8-cyclooctadiene (COD) was used (Table 1, entries 1−4). To obtain reproducible results and high yields of **3a**, it was determined that all liquid reagents needed to be degassed prior to use. Screening alternative diene, olefin, and amine ligands (entries 5−7) resulted in decreased conversion of starting materials to product or promoted undesired side reactions.[28] A solvent screening established that the amount of COD additive could be decreased, from 4.07 to 0.5 equiv when a nonpolar solvent (e.g., $ClCH_2CH_2Cl$, CH_2Cl_2, or toluene) was used, but at the cost of prolonged reaction times (entry 8) and inconsistent conversion to products in substrate screenings. Attempts to shorten reactions times further under thermal microwave irradiation resulted in high conversion in less than 20 min (entries 9−10). Unfortunately, under the thermal conditions undesirable reaction pathways became more favorable, diminishing the yield of the desired product. To establish the original hypothesis that the feasibility of this reaction was reliant upon the use of an iridium catalyst, Speier's (H_2PtCl_6), Karstedt's ($Pt_2[(Me_2SiCH{=}CH_2)_2O]_3$), and Wilkinson's ($[(Ph)_3P]_3RhCl$) catalysts were screened (entries 13−15). As expected, these classical platinum and rhodium catalysts promoted the silyl alkyne to react with itself, affording none of the desired hydrosilylation product.

With the optimized conditions in hand, 0.5 mol % $[IrCl(COD)]_2$ and 4.07 equiv of COD at room temperature with all substrates/reagents degassed, substrate screening was initiated (Table 2). In all of the terminal alkenes tested, only anti-Markovnikov selectivity was detected. Hydrosilylation of allyl benzyl ether (**2a**) with various alkynylsilanes (Table 2, entries 1−10) occurred in moderate to high yields regardless of whether the substituent on the alkyne was aliphatic or aromatic. There was no effect on yield or reaction times when electron-donating or -withdrawing functional groups were incorporated into the aryl alkynylsilanes (entries 3−4). However, the presence of a conjugated olefin resulted in prolonged reactions of 44−48 h (entries 8−9). Standard alcohol protecting groups were well tolerated (entries 7 and 9), and the steric hindrance of a *tert*-butyl group (entry 10) did not inhibit the reaction. Variation of the alkene demonstrated that the system tolerates an acid labile tetrahydropyran allyl ether (entry 11), an epoxide (entry 14), the reactive allyl bromide (entry 15), an ester (entry 17), and a primary tosylate (entry 18). While allyl bromide formed the product (**3ae**) in near-quantitative yield, allyl acetate (entries 12−13) only afforded moderate yields of the hydrosilylation product with the remaining mass balance being unreacted allyl acetate. The diminished yields for the allyl acetate may be due to coordination of the carbonyl to the electrophilic iridium.[29] Subjection of allyl alcohol (entry 19) to the reaction conditions afforded a complex mixture,[30] whereas styrene was completely unreactive (entry 20).[31−33] Hydrosilylation of (*E*)-1-(allyloxy)-but-2-ene was chemoselective for the terminal olefin over the internal disubstituted alkene (entry 21) with chelation to the catalyst contributing to the poor conversion.

Terminal alkynes[34] were examined next (Table 3). Phenylacetylene was efficiently hydrosilylated with both an aromatic and aliphatic alkynylsilane (entries 1−2). Electron-donating and -withdrawing groups on the phenylacetylene (entries 3−4) had no effect on the yield, but the electron-donating methoxy group afforded a mixture of regioisomers.[35] Subjection of a diyne to the reaction conditions afforded a mixture of mono- and dihydrosilylation products with *E*-selectivity. Increasing the concentration of the silane to 2 equiv increased the overall yield but did not affect the ratio of mono- to dihydrosilylation (entries 5−6). Hydrosilylation of a sterically congested *tert*-butyl acetylene (entry 7) occurred without incedent. The system was chemoselective for the terminal alkyne of an enyne (entry 8) and in the presence of a nitrile (entry 9), although the nitrile did inhibit full

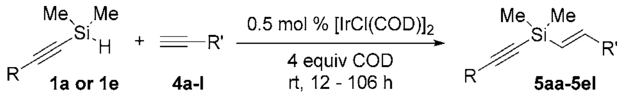
Table 2. Substrate Screening between Alkynylsilanes and Alkenes[a]

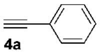
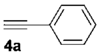
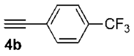
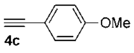
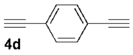
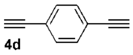
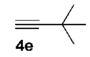
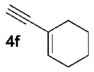
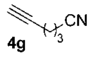
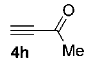
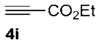
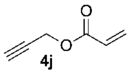
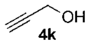
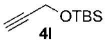


entry	silane	alkene	%conv[b]	%yield[c]
1	 1a	 2a	98	88
2	 1b	 2a	91	78
3	 1c	 2a	96	88
4	 1d	 2a	97	88
5	 1e	 2a	99	86
6	 1f	 2a	93	94
7	 1g	 2a	89	80
8	 1h	 2a	84	82
9	 1i	 2a	100	64
10	 1j	 2a	80	75
11	 1b	 2b	97	81
12	 1b	 2c	90	60
13	 1j	 2c	94	37
14	 1b	 2d	94	83
15	 1a	 2e	100	92
16	 1e	 2f	96	81
17	 1a	 2g	84	82
18	 1a	 2h	100	81
19	 1a	 2i	100	C.M.[d]
20[e]	 1a	 2j	0	0
21	 1a	 2k	28	26

[a]Conditions: 1 equiv of **1a–j** (1 mmol), 1 equiv of **2a–k** (1 mmol), 0.5 mol % [IrCl(COD)]$_2$, 4.07 equiv of COD (0.5 mL), rt, all reagents degassed. [b]Determined by GC. [c]Average isolated yield of two runs. [d]A complex mixture was obtained. [e]**1a** and **2j** were isolated again in near-quantitative yield.

Table 3. Substrate Screening between Alkynylsilanes and Alkynes[a]



entry	silane	alkyne	%conv[b]	%yield[c]
1	**1a**	 4a	99	81
2	**1e**	 4a	88	72
3	**1e**	 4b	89	80
4	**1e**	 4c	88	73 74:19:7 E:Z:Int[d]
5	**1a**	 4d	77	51 62:38 Di:Mono[d]
6[e]	**1a**	 4d	78	80 63:37 Di:Mono[d]
7	**1a**	 4e	92	77
8	**1a**	 4f	100	87
9	**1a**	 4g	68	51
10	**1a**	 4h	100	14
11	**1a**	 4i	61	11 43:56 E:Int[d]
12	**1a**	 4j	85	74 63:37 E:Int[d]
13	**1a**	 4k	100	C.M.
14	**1a**	 4l	100	89 78:22 E:Int[d]

[a]Conditions: 1 equiv of **1a** or **1e** (1 mmol), 1 equiv of **4a–l** (1 mmol), 0.5 mol % [IrCl(COD)]$_2$, 4.07 equiv of COD (0.5 mL), rt, all reagents degassed. [b]Determined by GC. [c]Average isolated yield of two runs. [d]Ratio determined by ^{1}H NMR of the crude reaction. [e]Used 2 equiv of **1a**.

conversion. Examination of conjugated carbonyls revealed that deactivated alkynes require extended reaction times and were low yielding (entries 10–11), whereas the alkyne of propargyl acrylate (entry 12) underwent hydrosilylation in high yield but afforded a mixture of *E* and internal regioisomers.[36] As with allyl alcohol (Table 2, entry 19), propargyl alcohol (Table 3, entry 13) also afforded a complex mixture,[37] but simple protection of the alcohol with a TBS group (entry 14) afforded the desired hydrosilylation product in high yield, favoring the *E* isomer.

In summary, by employing a sterically controlled approach we were able to hydrosilylate alkenes with alkynylsilanes under iridium catalysis. The system demonstrated good chemo- and regioselectivity, allowing efficient and easy access to highly functionalized alkynylsilane tethers. Application of these tethers in dual/synergistic catalysis will be reported in due course.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, product characterization data, and further discussion. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: Rahaim@okstate.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Oklahoma State University for the generous support. We thank the reviewers for helpful critiques. Mass spectrometry analyses were performed in the DNA/Protein Resource Facility at Oklahoma State University, using resources supported by the NSF MRI and EPSCoR programs (DBI/0722494).

■ REFERENCES

(1) Gautheir, D. R., Jr.; Zandi, K. S.; Shea, K. J. *Tetrahedron* **1998**, *54*, 2289−2338.

(2) (a) Deng, J.; Hsung, R. P.; Ko, C. *Org. Lett.* **2012**, *14*, 5562−5565. (b) Taillefumier, C.; Chapleur, Y.; Bayeul, D.; Aubry, A. *J. Chem. Soc., Chem. Commun.* **1995**, 937−938. (c) Ishikawa, T.; Senzaki, M.; Kadoya, R.; Morimoto, T.; Miyake, N.; Izawa, M.; Saito, S.; Kobayashi, H. *J. Am. Chem. Soc.* **2001**, *123*, 4607−4608.

(3) (a) Bracegirdle, S.; Anderson, E. A. *Chem. Soc. Rev.* **2010**, *39*, 4114−4129. (b) Cusak, A. *Chem. Eur. J.* **2012**, *18*, 5800−5824. (c) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253−1277.

(4) (a) Yamamoto, Y.; Ishii, J.-I.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2004**, *126*, 3712−3713. (b) Micalizio, G. C.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 3272−3276. (c) Batey, R. A.; Thadani, A. N.; Lough, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 450−451.

(5) (a) Fang, Y.-Q.; Bio, M. M.; Hansen, K. B.; Potter, M. S.; Clausen, A. *J. Am. Chem. Soc.* **2010**, *132*, 15525−15527. (b) Stork, G.; Chan, T. Y. *J. Am. Chem. Soc.* **1995**, *117*, 6595−6596.

(6) (a) Chegondi, R.; Maitra, S.; Markley, J. L.; Hanson, P. R. *Chem. Eur. J.* **2013**, *19*, 8088−8093. (b) Thomas, C. D.; McParland, J. P.; Hanson, P. R. *Eur. J. Org. Chem.* **2009**, 5487−5500. (c) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. *Chem. Rev.* **2004**, *104*, 2239−2258.

(7) (a) Saito, A.; Ono, T.; Hanzawa, Y. *J. Org. Chem.* **2006**, *71*, 6437−6443. (b) Saito, A.; Ito, H.; Taguchi, T. *Org. Lett.* **2002**, *4*, 4619−4621.

(8) (a) Tamao, K.; Kakui, T.; Akita, M.; Iwahara, T.; Kanatani, R.; Yoshida, J.; Kumada, M. *Tetrahedron* **1983**, *39*, 983−990. (b) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229−4232. (c) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599−7662. (d) Tamao, K. *Adv. Silicon Chem.* **1996**, *3*, 1−62.

(9) Chang, W.-T. T.; Smith, R. C.; Regens, C. S.; Bailey, A. D.; Werner, N. S.; Denmark, S. E. *Cross-Couplings with Organosilicon Compounds. Organic Reactions*; Wiley: New York, 2011; Vol. 75, pp 213−746.

(10) (a) Shao, Z.; Zhang, H. *Chem. Soc. Rev.* **2009**, *38*, 2745−2755. (b) Zhong, C.; Shi, X. *Eur. J. Org. Chem.* **2010**, 2999−3025.

(11) Allen, A. E.; MacMillan, D. W. C. *Chem. Sci.* **2012**, *3*, 633−658.

(12) (a) Davidsohn, W. E.; Henry, M. C. *Chem. Rev.* **1967**, *67*, 73−106. (b) Taniguchi, Y.; Inanaga, J.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3229−3230. (c) Rahaim, R. J., Jr.; Shaw, J. T. *J. Org. Chem.* **2008**, *73*, 2912−2915.

(13) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, 1999; pp 654−659.

(14) See ref 3b and references cited therein.

(15) Larson, G. L.; Fry, J. L. *Ionic and Organometallic-Catalyzed Organosilane Reductions. Organic Reactions*; Wiley: New York, 2008; Vol. 71, pp 1−737.

(16) (a) Ojima, I.; Li, Z.; Zhu, J. Recent Advances in Hydrosilylation and Related Reactions. In *The Chemistry of Organic Silicon Compounds*; Rappoport, Z., Apeloig, Y., Eds.; Wiley: Chichester, U.K., 1998; Vol. 2, pp 1687−1792. (b) Marciniec, B.; Maciejewski, H.; Pietraszuk, C.; Pawluc, P. In *Hydrosilylation: A Comprehensive Review on Recent Advances*; Matisons, J., Marciniec, B., Eds.; *Advances in Silicon Science*, Vol. *1*; Springer: 2009; pp 1−408. (c) Mayes, P. A.; Perlmutter, P. Alkene Reduction: Hydrosilylation. In *Modern Reduction Methods*; Andersson, P. G., Munslow, I. J., Eds.; Wiley-VCH: Weinheim, 2008; pp 87−105.

(17) (a) Miller, R. L.; Maifeld, S. V.; Lee, D. *Org. Lett.* **2004**, *6*, 2773−2776. (b) Scott, C. N.; Wilcox, C. S. *J. Org. Chem.* **2010**, *75*, 253−256.

(18) (a) Marko, I. E.; Sterin, S.; Buisine, O.; Mignani, G.; Branlard, P.; Tinant, B.; Declercq, J. P. *Science* **2002**, *298*, 204−207. (b) Lewis, L. N.; Sy, K. G.; Bryant, G. L. *Organometallics* **1991**, *10*, 3750−3759.

(19) Hua, Y.; Nguyen, H. H.; Scaggs, W. R.; Jeon, J. *Org. Lett.* **2013**, *15*, 3412−3415.

(20) (a) Junge, K.; Wendt, B.; Enthaler, S.; Beller, M. *ChemCatChem* **2010**, *2*, 453−458. (b) Widenhoefer, R. A. *Acc. Chem. Res.* **2002**, *35*, 905−913.

(21) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17644−17655.

(22) Calimano, E.; Tilley, T. D. *J. Am. Chem. Soc.* **2009**, *131*, 11161−11173.

(23) (a) Peng, D.; Zhang, Y.; Du, X.; Zhang, L.; Leng, X.; Walter, M. D.; Huang, Z. *J. Am. Chem. Soc.* **2013**, *135*, 19154−19166. (b) Tondreau, A. M.; Atienza, C. C. H.; Weller, K. J.; Nye, S. A.; Lewis, K. M.; Delis, J. G. P.; Chirik, P. J. *Science* **2012**, *335*, 567−570.

(24) Troegel, D.; Stohrer, J. *Coord. Chem. Rev.* **2011**, *255*, 1440−1459.

(25) For an example of iridium catalyzed hydrosilylation of a terminal alkyne in the presence of an internal alkyne, see: Tanke, R. S.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 7984−7989.

(26) (a) Cho, J. Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R. *Science* **2002**, *295*, 305−308. (b) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864−873.

(27) Aoki, K.; Shimada, T.; Hayashi, T. *Tetrahedron: Asymmetry* **2004**, *15*, 1771−1777.

(28) A detailed listing of ligands and solvents screened can be found in the Supporting Information.

(29) Formation of an iridium π-allyl was not detected. For an example of the formation of an iridium π-allyl, see: Garcia-Yebra, C.; Janssen, J. P.; Rominger, F.; Helmchen, G. *Organometallics* **2004**, *23*, 5459−5470.

(30) For an example of an iridium π-allyl formed from an allyl alcohol, see: Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2013**, *135*, 994−997.

(31) For examples of formation of vinyl arene metal complexes, see: Osswald, T.; Mikhel, I. S.; Ruegger, H.; Butti, P.; Mezzetti, A. *Inorg. Chim. Acta* **2010**, *363*, 474−480.

(32) For examples of iridium catalyzed hydrosilylation of styrenes, see: (a) Cipot, J.; Freguson, M. J.; Stradiotto, M. *Inorg. Chim. Acta* **2006**, *359*, 2780−2785. For examples of iridium catalyzed hydroboration of styrenes, see: (b) Crudden, C. M.; Hleba, Y. B.; Chen, A. C. *J. Am. Chem. Soc.* **2004**, *126*, 9200−9201.

(33) 1,3-Dienes, isoprene and myrcene, were unreactive, presumably due to chelation to the catalyst.

(34) (a) Miyake, Y.; Isomura, E.; Iyoda, M. *Chem. Lett.* **2006**, *35*, 836−837. (b) Sridevi, V. S.; Fan, W. Y.; Leong, W. K. *Organometallics* **2007**, *26*, 1157−1160.

(35) The *Z*-isomer may result from *E*−*Z* isomerization during the prolonged reaction time: Seyferth, D.; Vaughn, L. G.; Suzuki, R. *J. Organomet. Chem.* **1964**, *1*, 437−448.

(36) For examples of regioselective hydrosilylation of electron-deficient alkynes, see: (a) Sumida, Y.; Kato, T.; Yoshida, S.; Hosoya, T. *Org. Lett.* **2012**, *14*, 1552−1555. (b) Rooke, D. A.; Ferreira, E. M. *J. Am. Chem. Soc.* **2010**, *132*, 11926−11928.

(37) Examination of the crude reaction mixture by ^{1}H NMR showed that hydrosilylation of the alkyne and silane alcoholysis did occur.