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Regio- and Stereoselective Hydrosilylation of 1,3-Enynes Catalyzed by Palladium

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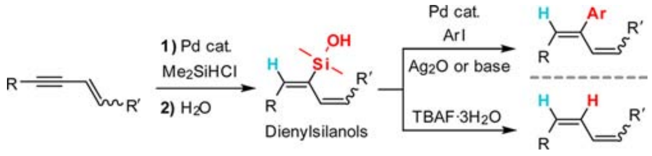
ABSTRACT



In the presence of Pd(0) and a phosphine, hydrosilylation of 1,3-enynes with Me_2SiHCl proceeds to yield dienylsilanes with the silicon function added to the internal alkyne carbon atom and with (*E*)-configuration of newly formed olefinic bond. The silanols isolated after hydrolysis of the primarily obtained products serve as precursors to conjugated dienes with different substitution patterns.

Hydrometalations transform alkynes to reactive vinylmetal or vinylmetalloid species, which are important building blocks in organic synthesis.[1] Hydrosilylations of alkynes are of particular interest since the product vinylsilanes have low toxicity, are easy to handle, and are tolerant to a wide range of reaction conditions. Vinylsilanes with a silicon–heteroatom bond are attractive reagents, which, for example, can participate as reactive nucleophilic partners in palladium-catalyzed cross-coupling reactions[2] and be subjected to Tamao–Fleming oxidations.[3] The stereo- and regiochemistry of the hydrosilane addition is a function of the substrate, the catalyst, which most commonly is a platinum, ruthenium, or cationic rhodium complex, and to some extent the reaction conditions.[4] Whereas terminal alkynes under appropriate conditions react with high stereo- and site selectivity, either in a syn or an anti fashion, reactions with internal alkynes often result in mixtures of products, unless a directing group[5] is present in the substrate.

Hydrometalated 1,3-enynes are valuable precursors for stereodefined 1,3-dienes. We are, however, aware of only a few examples of hydrosilylations of this type of compounds. Regio- and stereoselective platinum-catalyzed cis[6] and ruthenium-catalyzed trans[7] hydrosilylations have been used in natural product syntheses. Enynes with a terminal triple bond have been shown to yield dienes with the silicon function in terminal position,[8] whereas an internal dienyne gave a mixture of regioisomers.[9] 1,3-Enynes equipped with a propargylic alcohol function were shown to be subject to site-selective trans addition of triethylsilane in the presence of a ruthenium complex, but enynes lacking alcohol function were resistant to the reaction.[10] The most extensively

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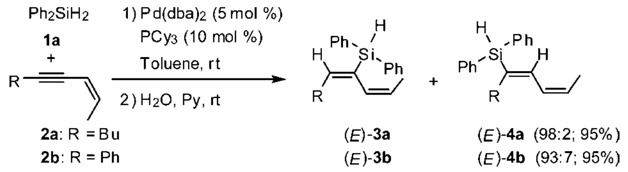
studied substrates are silicon-substituted butenynes;[11] other examples are rare.[12] The desired dienylsilanes have instead commonly been prepared by indirect methods, such as silylation of dienylmagnesium compounds,[13] ring-opening of silylated sulfolenes,[14] electrophilic addition to bissilylated 2-butynes,[15] Horner–Emmons reaction of the anion of silylated 2-propenylphosphonate,[16] and Suzuki coupling of an α-iodo vinylsilane.[17]

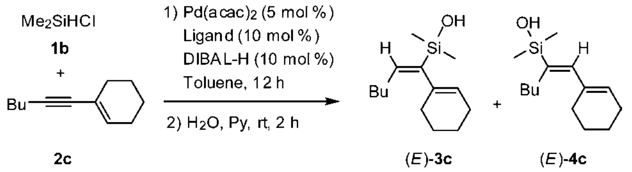
Intrigued by the lack of more general studies, we decided to investigate hydrosilylations of variously substituted 1,3-enynes, thereby getting access to less substituted 1,3-dienes than obtained via our previous silaborations of the same substrates.[18] Addition of diphenylsilane to (*Z*)-non-2-en-4-yne (**2a**) and (*Z*)-5-phenyl-2-en-4-yne (**2b**) in the presence of $Pd(dba)_2$ and PCy_3 was first attempted.[19] We were pleased to note that addition to the alkyne function occurred with high regioselectivity to yield the products of pure cis-addition (Scheme 1), as evidenced by NOE (see the Supporting Information). In the absence of phosphine ligand, low yields of products were obtained (7% from **2a**).

Scheme 1. Palladium-Catalyzed Addition of Diphenylsilane to 1,3-Enynes



After these preliminary attempts, we turned our attention to heterosubstituted silanes, which are crucial as nucleophilic partners in palladium-catalyzed cross-coupling reactions.[20] The conditions which proved to be successful for additions described in Scheme 1 unfortunately resulted in no or unsatisfactory yields of products when diphenylsilane was exchanged for chlorodimethylsilane, even at elevated temperature (80 °C, see the Supporting Information, Table S1). However, improved results were observed in the presence of Pd(0) catalysts obtained by in situ reduction of Pd(II). Thus, $Pd(acac)_2$ was reduced with DIBAL-H in the presence of a phosphine prior to the addition of enyne and silane. After completed reaction, water and pyridine were added, which resulted in hydrolysis to the desired silanol. In order to find the most suitable reaction conditions, various ligands were screened in the reaction with enyne **2c** (Table 1, entries 1–5) . Use of triphenylphosphine and diphenylcyclohexylphosphine resulted in poor yields, most likely due to inefficient oxidative addition of the silane to Pd(0) (Table 1, entries 1 and 2). Highest site selectivity, in combination with a high yield, was observed with electron-rich PEt_3 (Table 1, entry 4). A temperature of 80 °C was required, as lower temperature resulted in lower yields (Table 1, entries 6–8).

Table 1. Screening of Reaction Conditions for Hydrosilylation of **2c**



entry	temp (°C)	ligand	yield[a] (%)	**3c**:**4c**[b]
1	80	PPh_3	10	87:13
2	80	PPh_2Cy	15	84:16
3	80	PCy_3	92	84:16
4	80	PEt_3	90	93:7
5	80	SPhos	61	75:25
6	20	PEt_3	14	93:7
7	40	PEt_3	50	93:7
8	60	PEt_3	72	93:7

[a] Isolated yield. [b] Determined by ^1H NMR analysis of crude reaction mixture.

The high preference for formation of the product with the silicon function at the internal position is probably a result of electronic factors and can be explained by the preference for addition of palladium to the allylic position, assuming that the reaction proceeds via the Chalk–Harrod mechanism, which involves oxidative addition[21] of the silane to the zerovalent metal center followed by insertion of the olefin into the M–H bond.[22] Equally high site selectivity was observed in platinum-catalyzed hydrosilylations of conjugated ynones.[23]

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(11) (a) Kusumoto, T.; Hiyama, T. *Chem. Lett.* **1985**, 1405–1408. (b) Kusumoto, T.; Ando, K.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1280–1290. (c) Maruyama, Y.; Yoshiuchi, K.; Ozawa, F.; Wakatsuki, Y. *Chem. Lett.* **1997**, 623–624. (d) Maruyama, Y.; Yoshiuchi, K.; Ozawa, F. *J. Organomet. Chem.* **2000**, *609*, 130–136.

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(17) Frank, S. A.; Chen, H.; Kunz, R. K.; Schnaderbeck, M. J.; Roush, W. R. *Org. Lett.* **2000**, *2*, 2691–2694.

(18) Zhou, H.; Moberg, C. *J. Am. Chem. Soc.* **2012**, *134*, 15992–15999.

(19) $Pd_2(dba)_3 \cdot CHCl_3/PCy_3$ has previously been used for the hydrosilylation af alkynes; see: Motoda, D.; Shinokubo, H.; Oshima, K. *Synlett* **2002**, 1529–1531.

(20) (a) Hirabayashi, K.; Kawashima, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Org. Lett.* **1999**, *1*, 299–301. (b) Denmark, S. E.; Wehrli, D. *Org. Lett.* **1999**, *1*, 565–568.

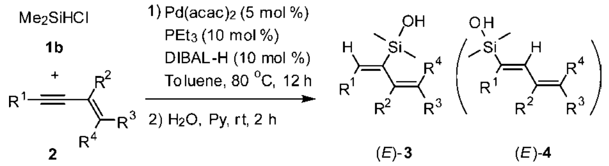
(21) The formation of a palladium hydride by oxidative addition of silanes has been demonstrated; see: Boyle, R. C.; Mague, J. T.; Fink, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 3228–3229.

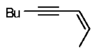
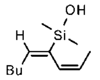
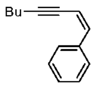
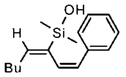
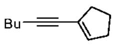
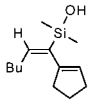
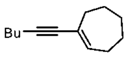
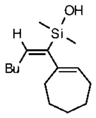
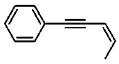
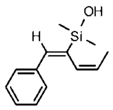
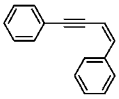
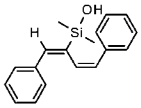
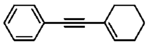
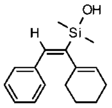
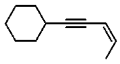
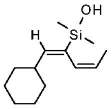
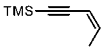
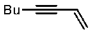
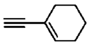
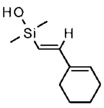
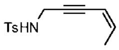
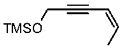
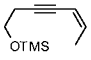
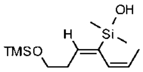
(22) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16–21.

(23) (a) Rooke, D. A.; Ferreira, E. M. *J. Am. Chem. Soc.* **2010**, *132*, 11926–11928. (b) Rooke, D. A.; Ferreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3225–3230. (c) Sumida, Y.; Kato, T.; Yoshida, S.; Hosoya, T. *Org. Lett.* **2012**, *14*, 1552–1555.

(24) A decrease in catalyst loading from 5 to 1 mol % resulted in a decreased yield (70% instead of 90% for the reaction in entry 1) under otherwise identical conditions.

Table 2. Palladium-Catalyzed Hydrosilylation of Various 1,3-Enynes to Silanols with Dimethylchlorosilane



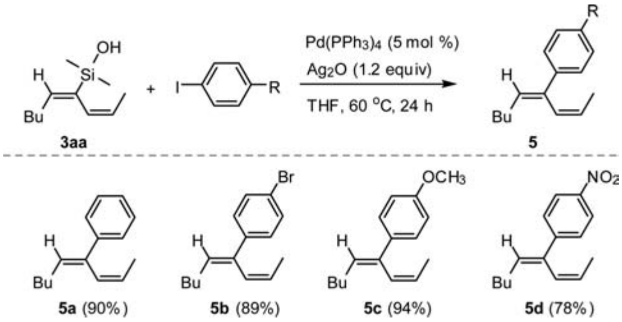
entry	enynes, **2**		product, **3**		yield (%)[a] (**3**:**4**)[b]
1		**2a**		**3aa**	90 (97:3)[c,d]
2		**2d**		**3d**	94 (99:1)
3		**2e**		**3e**	90 (80:20)
4		**2f**		**3f**	92 (93:7)
5		**2b**		**3ba**	96 (95:5)
6		**2g**		**3g**	92 (96:4)
7		**2h**		**3h**	96 (91:9)
8		**2i**		**3i**	90 (95:5)
9		**2j**	complex mixture	-	-
10		**2k**	-	-	NR[e]
11		**2l**		**4l**	50 (8:92)
12		**2m**	complex mixture	-	-
13		**2n**	complex mixture	-	-
14		**2o**		**3o**	95 (99:1)

[a] Isolated yield. [b] Determined by ^{1}H NMR analysis of crude reaction mixture. [c] Replacement of Pd(acac)$_2$ by Pd(OAc)$_2$ gave identical results. [d] 0.15 mmol enyne was used. From a reaction using 1.5 mmol of enyne, 94% product was isolated. [e] No reaction.

The optimized conditions were applied to hydrosilylations of a variety of enynes (Table 2).[24] From most reactions, high yields of cis-addition products with the silyl function at the internal position, and with retained configuration of the original olefinic bond, were obtained (Table 2, entries 1–8). A substrate with a terminal olefin was unreactive (Table 2, entry 10), and enynes with a silicon substituent or a heteroatom in propargylic position resulted in complex mixtures (Table 2, entries 9, 12–13). However, enyne **2o**, with a heteroatom in a position more remote from the alkyne function, was smoothly transformed to the desired product (Table 2, entry 14). Reaction of an enyne with terminal alkyne function resulted in a moderate yield of an adduct with opposite site selectivity (Table 2, entry 11); this mode of addition is that commonly observed with terminal alkynes. No allene derivatives were observed in any of the reaction mixtures.

The vinylsilanols obtained proved to serve as versatile nucleophiles in palladium-catalyzed cross-couplings.[2b] As expected, reaction with iodoarenes in the presence of Pd(PPh$_3$)$_4$ mediated by Ag$_2$O[25] gave high yields of coupling products (Scheme 2).

Scheme 2. Ag$_2$O-Mediated Cross-Coupling



In our previous studies, we showed that the type of product obtained from palladium-catalyzed cross-coupling of 1,1-disubstituted 2-dienylsilanols was dependent on the activator used.[16] Whereas Ag$_2$O-mediated coupling afforded 1,3-dienes, like in the above examples, coupling performed in the presence of base gave 1,2-dienes. We were therefore surprised to note that, under the same conditions, the present substrates resulted in clean conversion to 1,3-dienes (Table 3). The use of bases with sodium as counterion resulted in no or low yields (Table 3, entries 1, 3–5), even under microwave conditions (Table 3, entry 2), while those with potassium as counterion gave higher yields (Table 3, entries 6–9).[26]

Finally, treatment of vinylsilane **3** with tetrabutylammonium fluoride resulted in desilylation (Scheme 3). The

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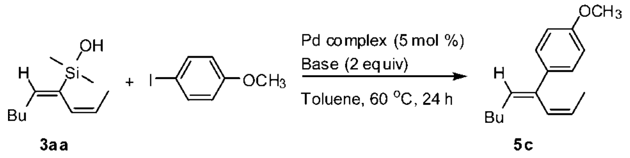
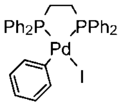
(25) Weibel, J.-M.; Blanc, A.; Pale, P. *Chem. Rev.* **2008**, *108*, 3149–3173.

(26) A similar difference in reactivity was previously observed for coupling with aryl chlorides; see: Denmark, S. E.; Kallemeyn, J. M. *J. Am. Chem. Soc.* **2006**, *128*, 15958–15959.

(27) (a) Lu, G.-P.; Voigtritter, K. R.; Cai, C.; Lipshutz, B. H. *J. Org. Chem.* **2012**, *77*, 3700–3703. (b) Semba, K.; Fujihara, T.; Xu, T.; Terao, J.; Tsuji, Y. *Adv. Synth. Catal.* **2012**, *354*, 1542–1550.

Table 3. Base-Mediated Cross-Coupling

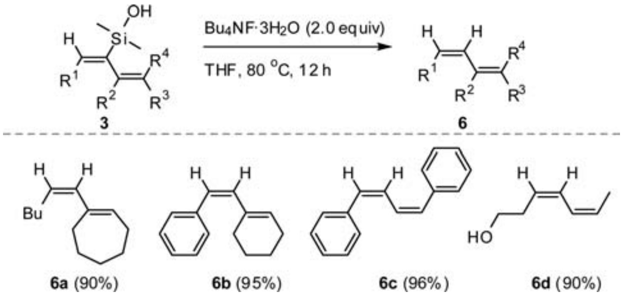


entry	Pd complex	base	yield (%)[a]
1	Pd(dba)$_2$	NaH	NR[b]
2[c]	Pd(dba)$_2$	NaH	NR
3	Pd(dba)$_2$	NaO*t*-Bu	NR
4	Pd(dba)$_2$/PCy$_3$	NaH	NR
5	Pd(dba)$_2$/P(*t*-Bu)$_3$	NaH	20
6	Pd(dba)$_2$	KO*t*-Bu	88
7	Pd(dba)$_2$	KOSiMe$_3$	85
8	PEPPSI	KO*t*-Bu	90
9		KO*t*-Bu	90

[a] Isolated yield. [b] No reaction. [c] Reaction conditions: microwave, 100 °C, 2 h.

(*Z*)-configuration of the newly formed olefinic bond in **6b** was confirmed by comparison of its ^{1}H NMR spectrum with those previously published for the same compound[27] and the configuration of the remaining compounds by their ^{1}H coupling constants. The overall process constitutes a convenient method for the semihydrogenation of 1,3-enynes, occurring without *E*–*Z* isomerization and over-reduction, which are commonly encountered problems in this type of reductions.[28]

Scheme 3. Fluoride-Mediated Protiodesilylation



In summary, we have demonstrated that dimethylchlorosilane undergoes palladium-catalyzed cis-addition to 1,4-disubstituted and 1,2,4-trisubstituted 1,3-enynes, conveniently accessible via Sonogashira coupling of terminal alkynes and vinyl halides,[29] to yield dienylsilanols with the silicon function at the internal position. Palladium-catalyzed coupling of the products with iodoarenes, using Ag$_2$O as well as base, resulted in stereo- and regiochemically defined 1,3-dienes, whereas desilylation with tetrabutylammonium fluoride resulted in overall cis-hydrogenation of the triple bond.

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Supporting Information Available. Experimental procedures, compound characterization data, and spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(28) For a recently reported selective process, see ref 23b.
(29) Negishi, E.-i.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979–2017.

The authors declare no competing financial interest.