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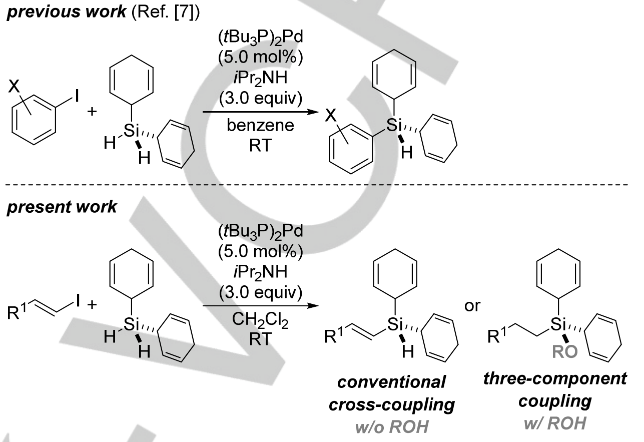
Palladium-Catalyzed Three-Component Reaction of Dihydrosilanes and Vinyl Iodides in the Presence of Alcohols: Rapid Assembly of Silyl Ethers of Tertiary Silanes

Weiming Yuan, Patrizio Orecchia, and Martin Oestreich*[a]

Abstract: A one-pot reaction that directly converts dihydrosilanes into silyl ethers of tertiary silanes is reported. Under palladium catalysis, one Si–H bond of the dihydrosilane formally engages in C(sp^3)–Si bond formation with a vinyl iodide while the other Si–H bond is transformed into a silyl iodide that undergoes facile alcoholysis with an alcohol. The C–C double bond is reduced in that process. This three-component reaction provides in a single synthetic operation an access to silyl ethers of functionalized and hindered alcohols. Several of those would otherwise be difficult to make but the intermediacy of a highly silyl iodide even allows for *tert*-butanol to react at room temperature.

The transition metal-catalyzed cross-coupling of hydrosilanes and C(sp^2)–X bonds with X being mainly iodide is a useful method for the formation C(sp^2)–Si bonds.[1] Unlike the well-established silylation of aryl halides,[2–4] related couplings of vinyl halides have been far less investigated.[3d,5–6] A palladium-catalyzed silylation of vinyl iodides was published by Masuda and co-workers almost two decades ago,[5] followed by a rhodium-catalyzed variant from Yamanoi and Nishihara.[3d] The scope is relatively narrow and currently limited to monohydrosilanes.

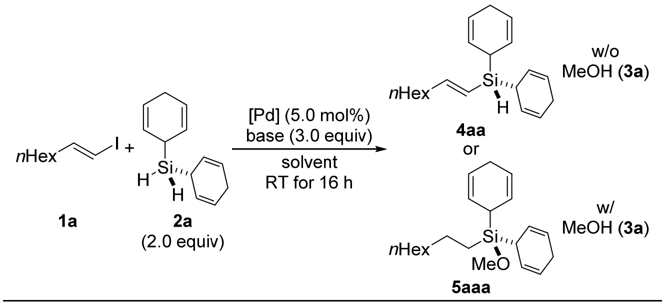
We recently reported a monoselective Yamanoi-type cross-coupling of a monosilane surrogate decorated with two cyclohexa-2,5-dien-1-yl substituents and a broad range of aryl iodides (Scheme 1, top).[7] By this, we have been able to access aryl-substituted di(cyclohexa-2,5-dien-1-yl)silanes as central building blocks for our custom synthesis of hydrosilanes. One of the obvious next steps was the development of a related vinylation to further expand the scope of that hydrosilane synthesis (Scheme 1, bottom). However, while that cross-coupling did indeed work, the reaction could be steered toward a totally different outcome in the presence of alcohols or water. The net result of this three-component reaction of a dihydrosilane, a vinyl iodide, and an alcohol is a silyl ether of a tertiary silane. We demonstrate the broad utility of this new method in this Communication.



Scheme 1. Palladium-catalyzed cross-coupling of aryl and vinyl Iodides with a dihydrosilane.

We used (*E*)-1-iodooct-1-ene (**1a**) and dihydrosilane **2a** for the initial optimization of the reaction conditions (Table 1). Applying the optimal setup previously found for the arylation of **2a**,[7] we did observe the coupling product **4aa** in 71% yield (entry 1). Subsequent screening of other reaction parameters (entries 2–6) showed that the result was best with Cy_2NH as base in CH_2Cl_2 (entry 4); the amine base was crucial, and K_3PO_4 completely suppressed the reaction (entry 6). Control experiments verified that both catalyst and base are required for this transformation (not shown). We were then surprised to find that the addition of 3.0 equiv of MeOH (**3a**) had a dramatic effect on the reaction outcome (entry 7); instead of vinyl-substituted **4aa**, a new product characterized as **5aaa** was formed exclusively. The double bond had disappeared and the alcohol was incorporated in form of a silyl ether. The same result was obtained with other palladium (pre)catalysts (entries 8–10), and the yield was highest with $(Ph_3P)_2PdCl_2$ (entry 10). A lower alcohol loading of 2.0 equiv had little effect (entry 11) but the yield decreased with equimolar amounts (entry 12); excess alcohol was not detrimental (entry 13).

Table 1. Optimization of both the conventional vinylation and the three-component reaction.[a]



Entry	Palladium	Base	MeOH	Solvent	Yield [%][b]

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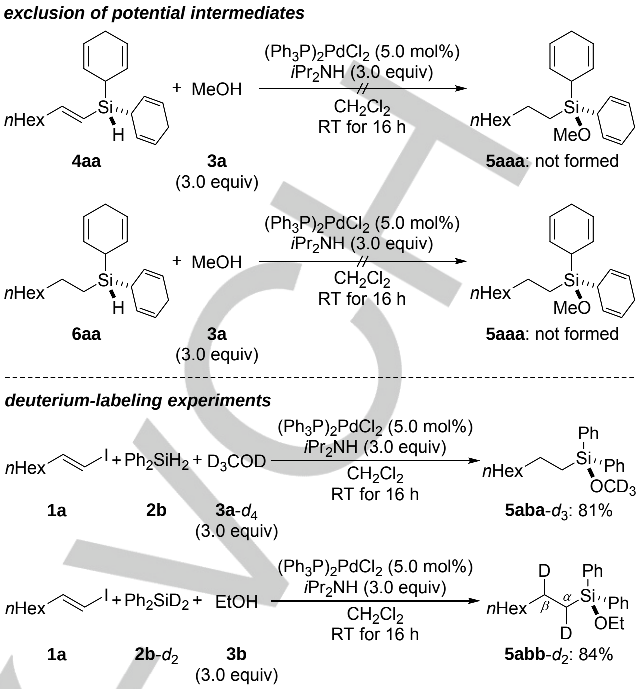
	source		(equiv)		
1	$(tBu_3P)_2Pd$	iPr_2NH	—	benzene	71 (**4aa**)
2	$(tBu_3P)_2Pd$	iPr_2NH	—	CH_2Cl_2	73 (**4aa**)
3	$(tBu_3P)_2Pd$	iPr_2NH	—	1,2-$Cl_2C_6H_4$	62 (**4aa**)
4	$(tBu_3P)_2Pd$	Cy_2NH	—	CH_2Cl_2	80 (**4aa**)
5	$(tBu_3P)_2Pd$	Et_3N	—	CH_2Cl_2	64 (**4aa**)
6	$(tBu_3P)_2Pd$	K_3PO_4	—	CH_2Cl_2	0 (**4aa**)
7	$(tBu_3P)_2Pd$	iPr_2NH	3	CH_2Cl_2	65 (**5aaa**)
8	$(Ph_3P)_4Pd$	iPr_2NH	3	CH_2Cl_2	85 (**5aaa**)
9	$Pd(OAc)_2$	iPr_2NH	3	CH_2Cl_2	25 (**5aaa**)
10	$(Ph_3P)_2PdCl_2$	iPr_2NH	3	CH_2Cl_2	93 (**5aaa**)
11	$(Ph_3P)_2PdCl_2$	iPr_2NH	2	CH_2Cl_2	89 (**5aaa**)
12	$(Ph_3P)_2PdCl_2$	iPr_2NH	1	CH_2Cl_2	60 (**5aaa**)
13	$(Ph_3P)_2PdCl_2$	iPr_2NH	5	CH_2Cl_2	94 (**5aaa**)

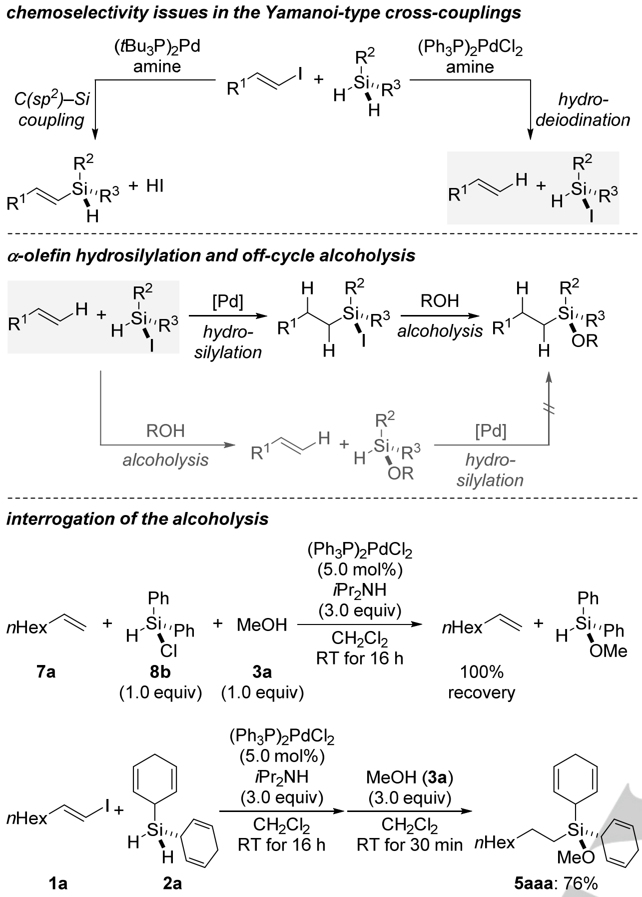
[a] All reactions were performed on a 0.1 mmol scale. [b] NMR yield with CH_2Br_2 as internal standard.

We found the unexpected reaction outcome more interesting than the initially planned hydrosilane vinylation. To gain insight into the mechanism of the formation of silyl ether **5aaa**, we performed a number of control experiments (Scheme 2). The conventional cross-coupling product **4aa** did not convert into **5aaa** under the optimized setup with the alcohol (Scheme 2, top). Moreover, independently prepared, hypothetical intermediate **6aa** did not undergo dehydrogenative Si–O coupling with MeOH (**3a**) with this catalytic system (top). By this, vinylsilane **4aa** and alkylsilane **6aa** were excluded as potential intermediates. To further substantiate these results, both reactions were repeated in the presence of 1.0 equiv of (*E*)-1-iodooct-1-ene (**1a**) but silyl ether **5aaa** was still not obtained (not shown). Additional deuterium-labeling experiments using dihydrosilane **2b** provided useful evidence for the origin of **5aba** and **5abb**, respectively (Scheme 2, bottom). When using CD_3OD (**3a**-d_4), no deuterium incorporation into the alkyl chain of **5aba**-d_3 was seen. In turn, selective deuteration *α* and *β* to the silicon atom, i.e., the position of the former alkene unit, was found in **5abb**-d_2 with Ph_2SiD_2 (**2b**-d_2).



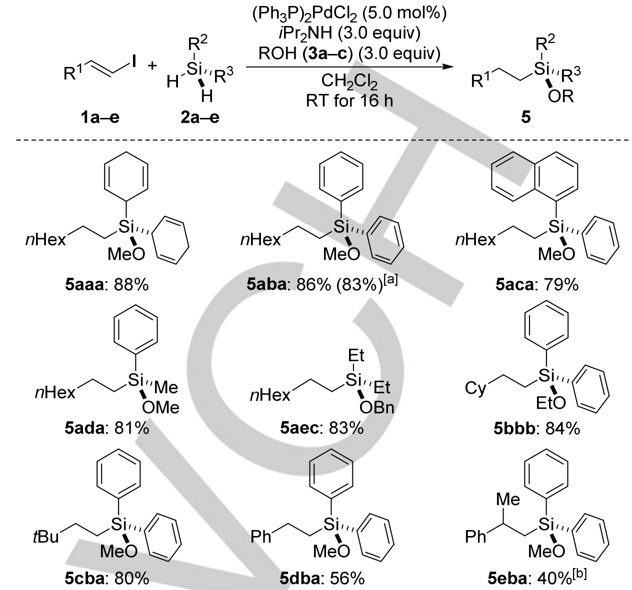
Scheme 2. Control experiments for understanding the mechanism.

On the basis of the above experiments and according to the literature precedence,[8] we suggest the following order of bond-forming events (Scheme 3). Particularly for the related arylation of hydrosilanes, it is documented that it competes with hydrodehalogenation.[9] Yamanoi had introduced bulky $(tBu_3P)_2Pd$ as a catalyst that would usually disfavor the undesired defunctionalization pathway.[8a,8b] This experimental finding was indeed explained by an in-depth quantum-chemical investigation but three different catalytic cycles are needed to rationalize the subtle effects of the phosphine ligand and the amine base.[10] Our vinylation of dihydrosilanes is in agreement with this (Scheme 3, top): C(sp^2)–Si bond formation is seen with $(tBu_3P)_2Pd$ and hydrodeiodination is found with $(Ph_3P)_2PdCl_2$; the fact that the alcohol additive steers the reaction toward defunctionalization even with $(tBu_3P)_2Pd$ shows how sensitive these cross-couplings are toward modifications (cf. entry 7 in Table 1). The *α*-olefin emerging from the hydrodeiodination was detected by ^1H NMR spectroscopy. This then undergoes a palladium-catalyzed hydrosilylation[11–13] directly with the in-situ-generated silyl iodide $R_2Si(H)I$ or with $R_2Si(H)OMe$ after preceding alcoholysis[14] (Scheme 3, middle). Either way, this is how deuterium is incorporated into the *β* position (cf. Scheme 2, bottom). When the alcoholysis[14] is downstream, the silyl ether arises from the newly formed alkyl-substituted silyl iodide. A control experiment where the *α*-olefin **7a** was brought to reaction with $Ph_2Si(H)Cl$ (**8b**) and MeOH (**3a**) under the standard setup essentially ruled out the alcoholysis–hydrosilylation pathway (gray); the alkene was fully recovered and the silyl chloride had undergone partial alcoholysis (Scheme 3, bottom). Also, when the alcohol was added at the end of the reaction, silyl ether formation was seen within minutes, lending further support to the hydrosilylation– alcoholysis pathway (Scheme 3, bottom).[15]



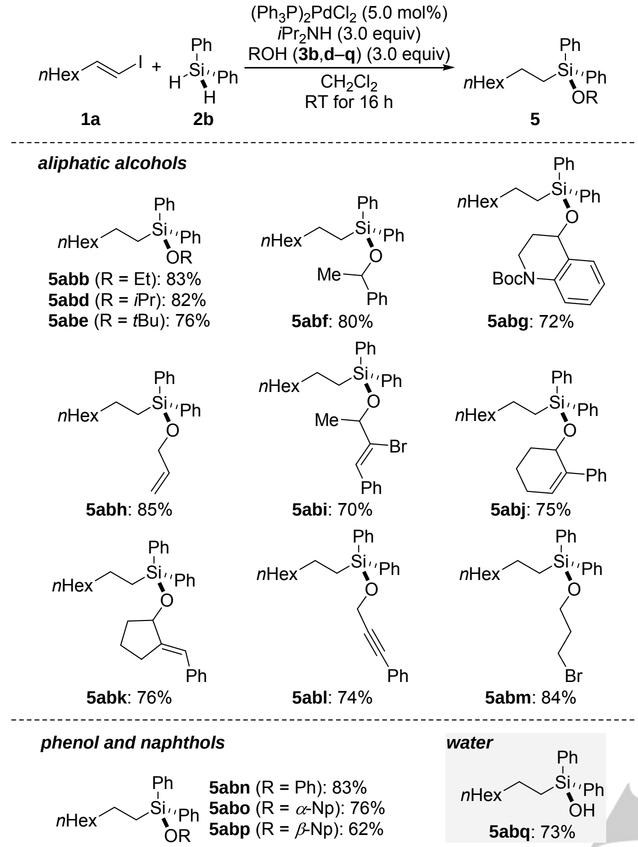
Scheme 3. Investigation of the order of bond-forming events.

With a high-yielding protocol for the three-component reaction in hands, we tested different dihydrosilanes **2a**–**e** and representative vinyl iodides **1a**–**e** (Scheme 4). Aside from di(cyclohexa-2,5-dien-1-yl)-substituted **2a**, other dihydrosilanes such as Ph_2SiH_2 (**2b**), *α*-Np(Ph)SiH_2 (**2c**), Me(Ph)SiH_2 (**2d**), and Et_2SiH_2 (**2e**) were compatible, and the corresponding silyl ethers **5** were isolated in good yields throughout. Other vinyl iodides were prepared and subjected to the reaction. Besides the primary alkyl substituent (as in **1a**), a secondary (as in **1b**) and a tertiary (as in **1c**) were tolerated equally well. Isolated yields for **5** were consistently high. (*E*)-*β*-iodostyrene (**1d**) did also work yet with somewhat diminished yield of **5dba**. Even (*E*)-*β*-iodo-*α*-methylstyrene (**1e**) participated but the intermediate *α*-methylstyrene did not fully convert in the hydrosilylation; silyl ether **5eba** was nevertheless isolated in 40% yield. This could not be improved by increasing the reaction temperature to 45 °C and 80 °C, respectively (sealed tube). A 1,2-disubstituted vinyl iodide such as (*E*)-1-trimethylsilyl-2-iodoprop-1-ene afforded hydrodeiodination exclusively; (*E*)-1-trimethylsilylprop-1-ene was detected in 63% NMR yield (not shown). At a 1.0 mmol scale, **5aba** was isolated with similarly high yield (86% vs 83%).



Scheme 4. Scope I: Variation of the dihydrosilane and the vinyl iodide. [a] Reaction performed on a 1.0 mmol scale. [b] The reaction mainly stops at the hydrodeiodination stage, and *α*-methylstyrene is formed in major quantities.

A variety of alcohols was also examined (Scheme 5). Alcohols **3b**,**d**–**m** irrespective of steric hindrance led to good isolated yields for **5**. Functional groups such as alkyl or vinyl bromides, terminal and internal alkenes (even allylic alcohol), alkynes, and a Boc-protected secondary amine were fully compatible with this palladium catalysis. Phenol (**3n**) and naphthols **3o** and **3p** furnished **5abn**–**abp**. Remarkably, H_2O (**3q**) could be employed, yielding silanol **5abq** in 73% isolated yield (gray box).



Scheme 5. Scope II: Variation of the alcohol and experiment with H_2O.

In summary, we reported here a new one-pot synthesis of silyl ethers[16] from vinyl iodides, dihydrosilanes, and alcohols. The alcohol component governs the reaction outcome. The three-component reaction occurs in the presence of the alcohol independent of the palladium (pre)catalyst used. Without the alcohol additive and with $(t\mathrm{Bu}_3\mathrm{P})_2\mathrm{Pd}$ as catalyst, the conventional C(sp^2)–Si cross-coupling is observed. The new method directly transforms a wide range of dihydrosilanes into silyl ethers of tertiary silanes by C(sp^3)–Si and Si–O bond formation in a single synthetic operation. Even hindered alcohols, *tert*-butanol as an extreme example, participate at room temperature as a result of the intermediacy of a highly reactive silyl iodide. This distinguishes the present reaction from the more conventional yet rare[16] two-step approach, that is transition-metal-catalyzed hydrosilylation of *α*-olefins with $R_2Si(H)Cl$ followed by Lewis-base-catalyzed silyl ether formation of the far less reactive tertiary silyl chlorides.[16,17]

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Keywords: cross-coupling • hydrosilylation • multi-component reactions • palladium • silicon

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[15] We did consider the formation of silylene intermediates but NMR spectroscopic analysis of stoichiometric experiments with no alcohol addition showed no indication of this.

[16] Alcoholysis of silyl chlorides is very sensitive toward the steric hindrance of both the silyl chloride and the alcohol. Tertiary silyl chlorides with more than one phenyl group are often even stable against moisture. Known examples are largely limited to RMe_2SiCl with R = alkyl.

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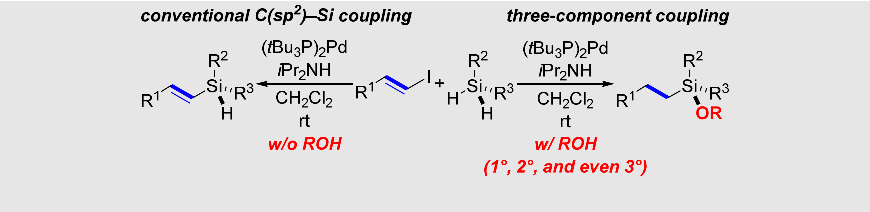
Suggestion for the Entry for the Table of Contents

COMMUNICATION



Consuming alcohol. A conventional Yamanoi-type C(sp^2)–Si cross-coupling turns into a C(sp^3)–Si bond formation accompanied by formal alkene hydrogenation in the presence of alcohols or water. By this, dihydrosilanes are directly converted into silyl ethers of tertiary silanes. Even bulky alcohols participate in this reaction because of the intermediacy of a highly reactive silyl iodide.

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