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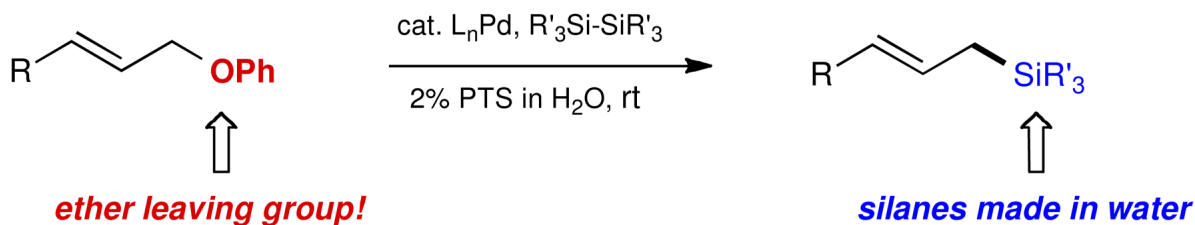
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Pd-Catalyzed Synthesis of Allylic Silanes from Allylic Ethers

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Abstract



Allylic phenyl ethers serve as electrophiles towards Pd(0) en route to a variety of allylic silanes. The reactions can be run at room temperature in water as the only medium using micellar catalysis.

Allylic silanes are among the most important and widely used reagents in organic synthesis.¹ Well known transformations, such as the Hosomi-Sakurai reaction,² or Hiyama couplings,³ underscore their value as building blocks, in particular for complex natural product syntheses.¹ Although a vast array of synthetic methods for the preparation of allylic silanes now exists,^{4,5} further development of selective entries to allylic silanes are still of considerable interest. Tsuji described a general silylation reaction of allylic esters with organodisilanes in the presence of a palladium catalyst at 100 °C.⁶ Terao and Kambe reported the synthesis of allylic silanes from chlorosilanes and allylic ethers using palladium or nickel catalysts and an excess of Grignard reagents.⁷ Takaki utilized allylic ethers en route to allylic silanes via allylic samarium reagents.⁸ Recently Woerpel reported metal-catalyzed insertions of highly reactive silylenes into allylic ethers to provide allylic silanes.⁹

Despite the advantages of less reactive allylic ethers, *e.g.* stability towards nucleophilic attack and resistance to strongly acidic and basic conditions, their use in allylation chemistry remains quite rare.^{10,11,12} Moreover, such silylation reactions reported to date all require strictly anhydrous conditions.

Herein we disclose an exceptionally mild entry to allylic silanes made possible by micellar catalysis¹³ in water at room temperature from the combination of allylic ethers and disilanes (Scheme 1).

An initial investigation focused on the reaction of cinnamyl phenyl ether (**1a**) with hexamethyldisilane (**2a**) in 2 wt % PTS/H₂O at room temperature (PTS = Polyoxyethanyl α -Tocopheryl Sebacate).¹⁴ Among several palladium catalysts screened, those bearing monodentate phosphine ligands or ligandless sources gave poor results; only PdCl₂(PPh₃)₂ led to a moderate level of conversion (Table 1, entry 1). However, reaction in the presence of

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Supporting Information Available: Experimental procedures and characterization of all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

bidentate ligands afforded generally better results (entries 2, 3), and in the case of pre-formed complex PdCl₂(DPEphos), full conversion with associated high isolated yield and excellent regioselectivity could be realized (entry 4). In previously reported silylations of more reactive allylic *acetates*, heating in organic solvents (e.g., DMF)⁶ was essential for activation of the disilane; under these new conditions, catalysis between cinnamyl phenyl ether (**1a**) and hexamethyldisilane (**2a**) proceeds at ambient temperature in the complete absence of organic solvent. Consistent results were best achieved in the presence of excess Et₃N (4 equiv; entries 5, 6), although the amounts of base could be reduced without significant loss in reactivity. Curiously, other amine bases led to little-to-no conversion (entry 7), whereas K₂CO₃ gave reasonable results (entry 8). Control experiments in the absence of PTS, or in Et₃N as solvent, confirmed the essential role of the surfactant.

To explore the scope of this Pd-catalyzed silylation, various allylic phenyl ethers were examined (Table 2). While (*E*)-cinnamyl phenyl ether (**1a**) gave mainly the *E*-olefinic product **3a** (entry 1; also Table 1, entry 4), the (*Z*)-educt **1b** afforded the corresponding cinnamyl silane **3a** in high yield with decreased stereoselectivity, favoring the (*E*)-isomer (entry 2). Cinnamyl derivatives **1c** and **1d**, e.g., those bearing an electron-donating methoxy substituent in either the *meta* or *ortho* position readily underwent the silylation reaction, the latter substitution pattern showing a strong preference for the *E*-product **3c** (entries 3, 4). Surprisingly, alkyl substituted allylic phenyl ether **1e** did not undergo full conversion under the optimized conditions. Ultimately, use of a mixed catalyst system consisting of PdCl₂(PPh₃)₂ and PdCl₂(DPEphos)¹⁵ gave the long chain allylic silane **3d** in high yield, again favoring the *E*-isomer (entry 5). Each of these Pd-catalyzed allylic silylation reactions occurred with excellent regioselectivity favoring the corresponding linear products.

The alternative allylic dimethylphenylsilanes **3e–k** (Table 3) could also be prepared in an analogous fashion, using commercially available 1,2-diphenyltetramethyl-disilane (**2b**). In general, these cross-couplings are both efficient and more selective than those forming the corresponding TMS derivatives. For example, (*E*)-cinnamyl phenyl ether (**1a**) gave product **3e** in high yield with an *E:Z* ratio of > 25:1 (entry 1), although the (*Z*)-isomer **1b** gave the same 3:1 preference favoring the (*E*)-derivative (entry 2; compare with Table 2, entry 2). Substitution on the aryl ring in cinnamyl phenyl ethers, whether electron-donating (entries 4–6) or -withdrawing (entry 7), and seemingly independent of location on the ring, gave the corresponding allylic silanes in high yields and with excellent regio- and stereoselectivity. Dibenzylamine-substituted methallyl substrate **1i** also smoothly undergoes silylation (entry 8).

When the silylation reaction of alkyl substituted allylic phenyl ether **1e** was carried out in pure MeOH, essentially no conversion was observed (Scheme 2). In PTS/H₂O, however, the desired product allylic dimethylphenylsilane **3l** was isolated in high yield (cat Pd = 3 mol % PdCl₂(DPEphos); 4:1 *E:Z*). Thus, while nanomicelles are clearly involved when water is the medium,¹⁴ it is not known how PTS behaves in alcoholic solvent.

The relative reactivity of an allylic acetate compared to an allylic phenyl ether is as expected: reaction first occurs at the former site. Under optimized conditions, the combination of catalytic [allylPdCl]₂ ligated by Xantphos gave chemoselective amination of allylic acetate **4** (Scheme 3). Without isolation, introduction of PdCl₂(DPEphos) and disilane **2b** resulted in silylation at the allylic ether fragment. This 1-pot amination/silylation sequence, done in its entirety in water at room temperature, could be applied to generation of dibenzylaminated methallylsilane **3k**, and amino acid-substituted allylic silane **3m** in good overall yields.

Scheme 4 illustrates one pathway accounting for the observed silylations, although details on the mechanism await further investigation. Initial oxidative addition of Pd(0) to allylic ether **1**, aided by presumably high concentrations within micellar nanoreactors,¹⁶ produces allyl

palladium intermediates **5**, **5'** and **5''**, each containing the bidentate ligand. Slow transmetallation of a π -allyl palladium complex **5''**¹⁷ suggests that σ -allyl palladium species **5** and/or **5'** more likely undergoes transmetallation with disilane to give allyl silyl palladium **6** and/or **6'**, leading to the corresponding branched and/or linear products, respectively, strongly favoring the latter.

In conclusion, new technology has been developed for Pd-catalyzed formation of allylic silanes from allylic ethers. These cross-couplings are very efficient, and occur under "green" conditions: without heat, without organic solvent, and within a micellar environment where water is the only external medium. Readily available disilanes serve as the stoichiometric source of silicon. Both the regio- as well as stereoselectivity associated with the catalysis are well-controlled. Further applications of micellar catalysis to transition metal chemistry are currently underway and will be reported in due course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

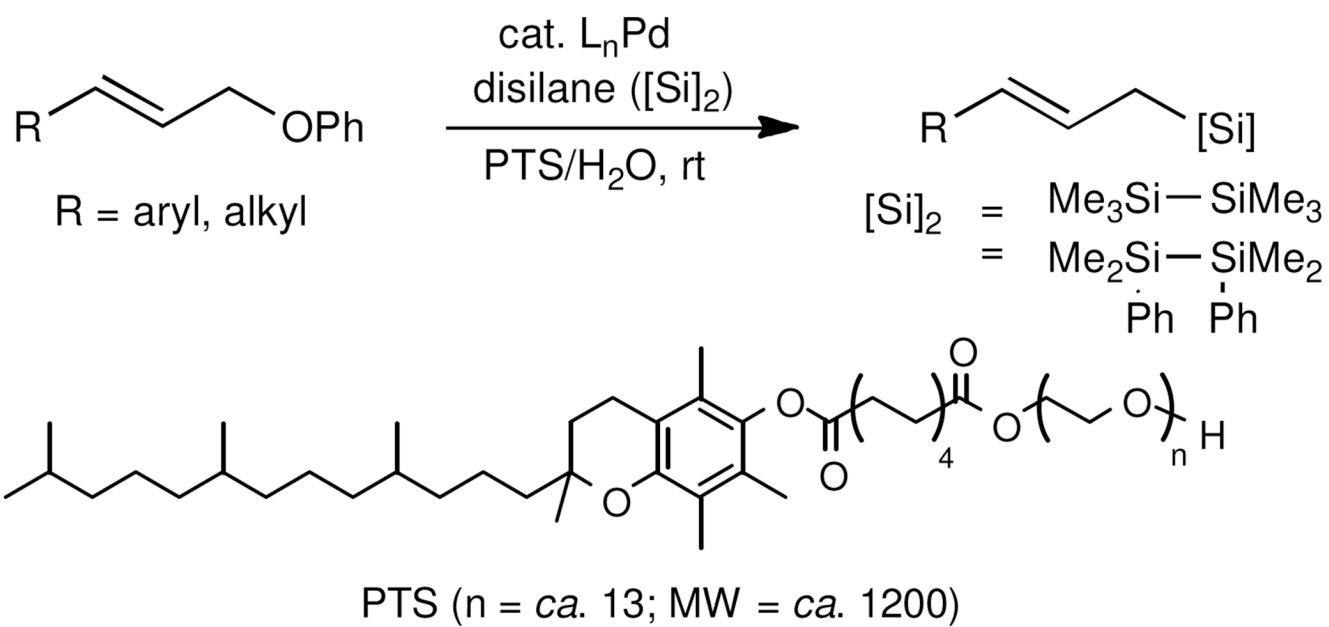
Acknowledgments

We thank the NIH (GM 86485) for support, and Johnson Matthey for supplying Pd catalysts.

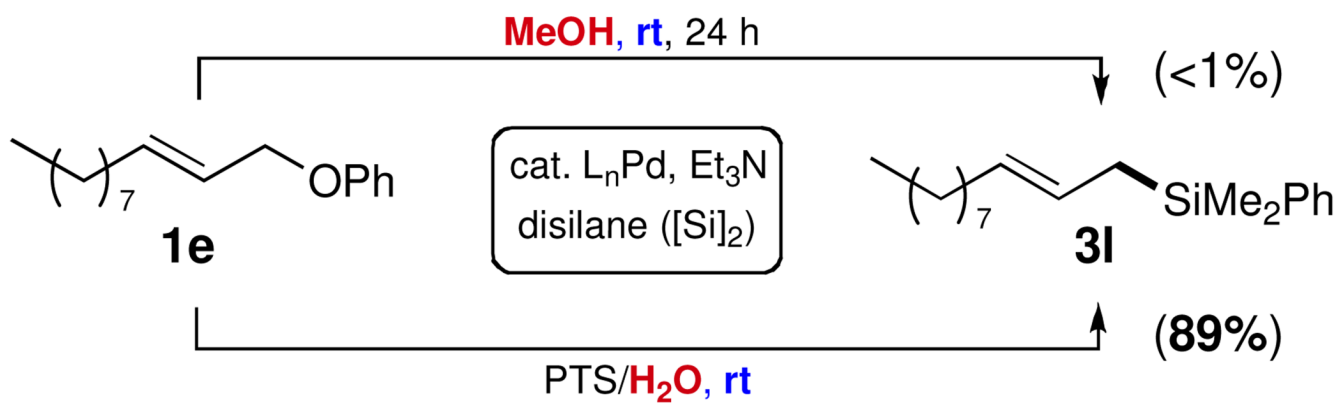
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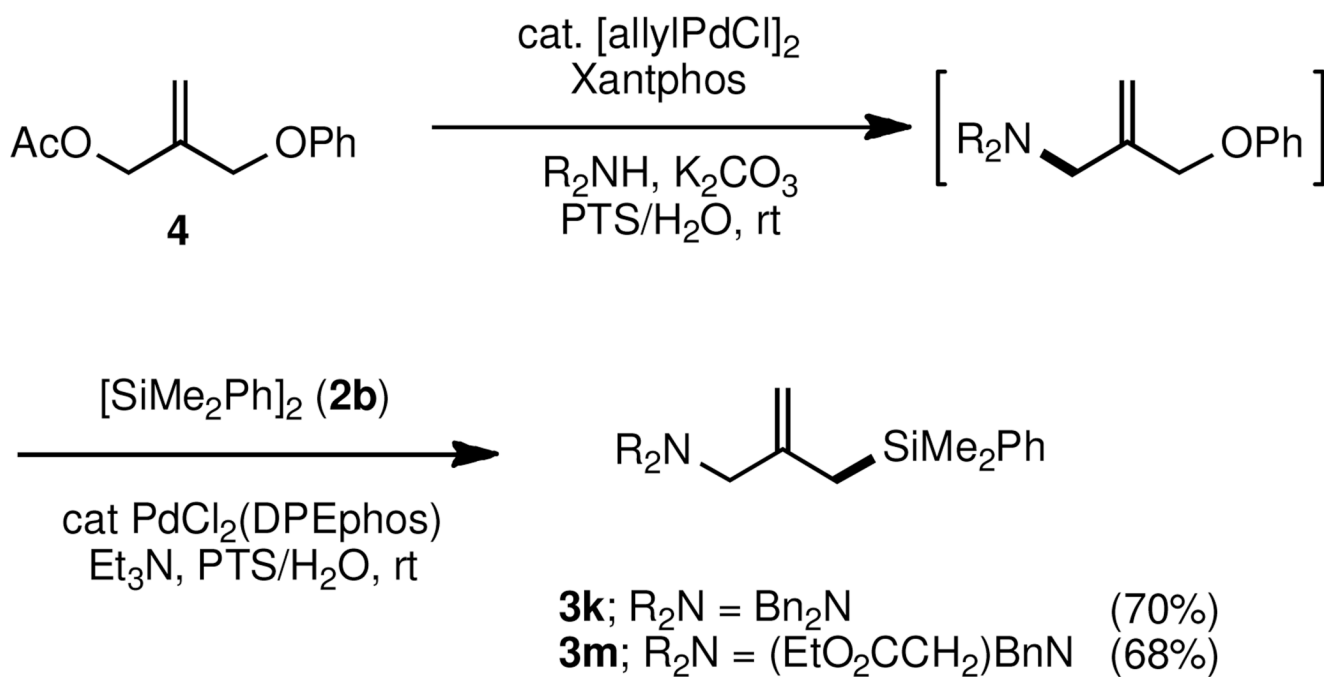
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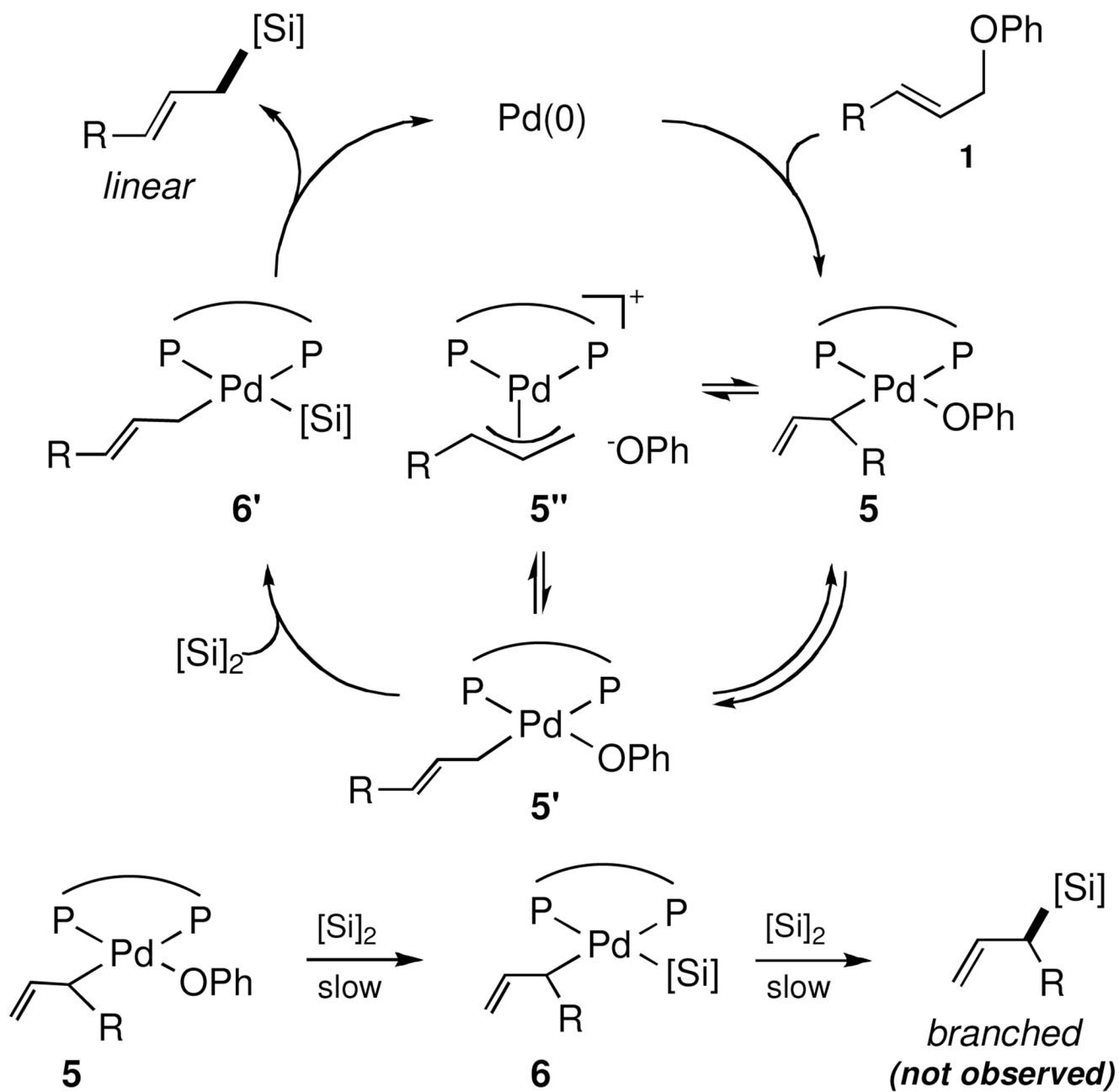
Scheme 1.



Scheme 2.

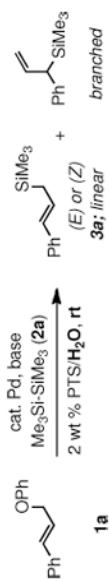


Scheme 3.



Scheme 4.

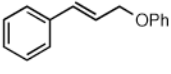
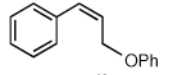
Table 1

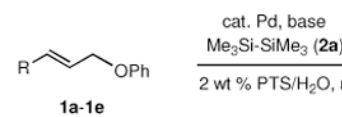
Optimization of Pd-catalyzed silylation reactions.^a

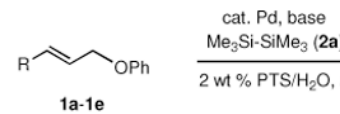
entry	catalyst	base (equiv)	convn (%) ^b	<i>i</i> : <i>b</i> ^b	<i>E</i> : <i>Z</i> ^b
1	PdCl ₂ (PPh ₃) ₂	Et ₃ N (6)	44	25:1	19:1
2	PdCl ₂ (D/BPF)	Et ₃ N (6)	40	7:1	25:1
3	PdCl ₂ (D/PPF)	Et ₃ N (6)	60	24:1	25:1
4	PdCl ₂ (DPEphos)	Et ₃ N (6)	100 (<i>91</i>) ^c	25:1	10:1
5	PdCl ₂ (DPEphos)	Et ₃ N (4)	95	25:1	10:1
6	PdCl ₂ (DPEphos)	Et ₃ N (2)	95	25:1	10:1
7	PdCl ₂ (DPEphos)	amines ^d	0		
8	PdCl ₂ (DPEphos)	K ₂ CO ₃ (3)	73	25:1	13:1

^aReaction conditions: **1a** (1.0 equiv, 0.25 mmol), **2a** (1.5 equiv), catalyst (3 mol %), base, 2 wt % PTS/H₂O (1.5 mL), rt, 20 h.^bDetermined by GCMS and ¹H NMR.^cIsolated yield.^d*n*Bu₃N and Et^tPr₂N were used.

Table 2Pd-catalyzed silylation reactions with hexamethyldisilane. ^a

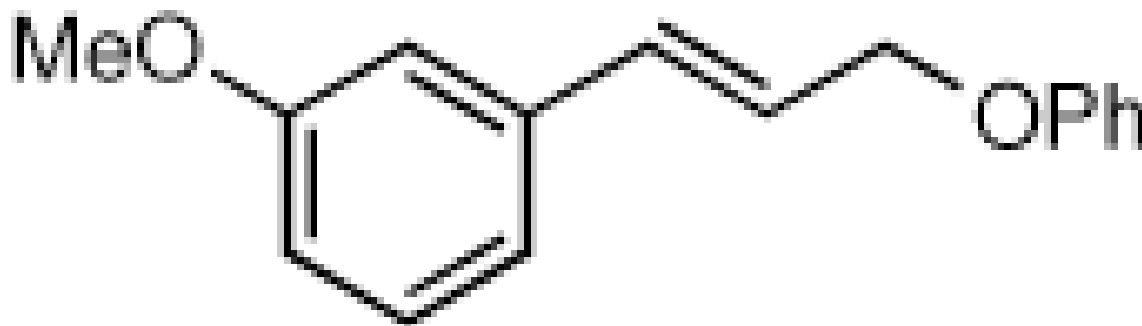
entry	substrate
1	 1a
2 ^d	 1b

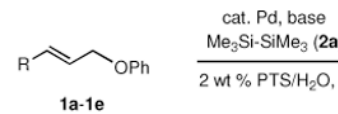




entry

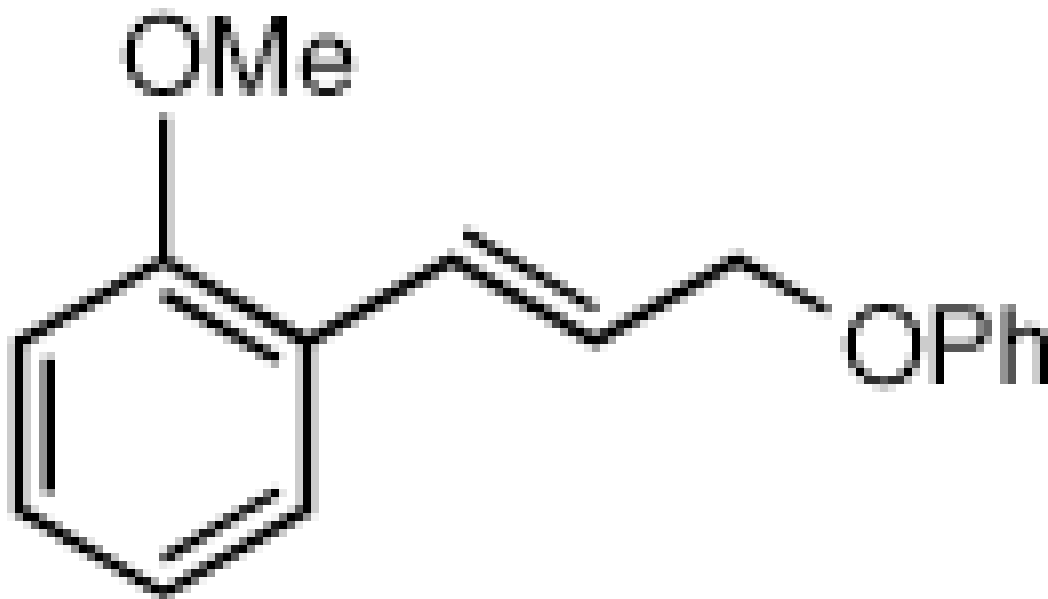
substrate

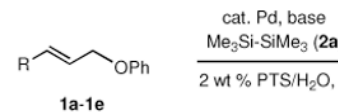
^{3d}**1c**



entry

substrate

4^d**1d**



entry

substrate

5^e**1e**

^a All reactions were carried out on 0.25 mmol scale.

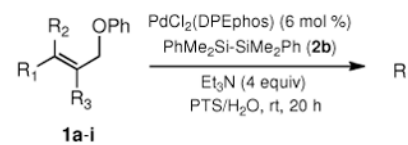
^b *l:b* and *E:Z* ratio determined by GCMS and ¹H NMR methods.

^c Isolated yield after column chromatography.

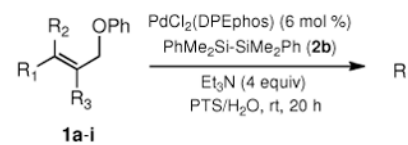
^d 6 mol % catalyst and 4 equiv NEt₃ were used.

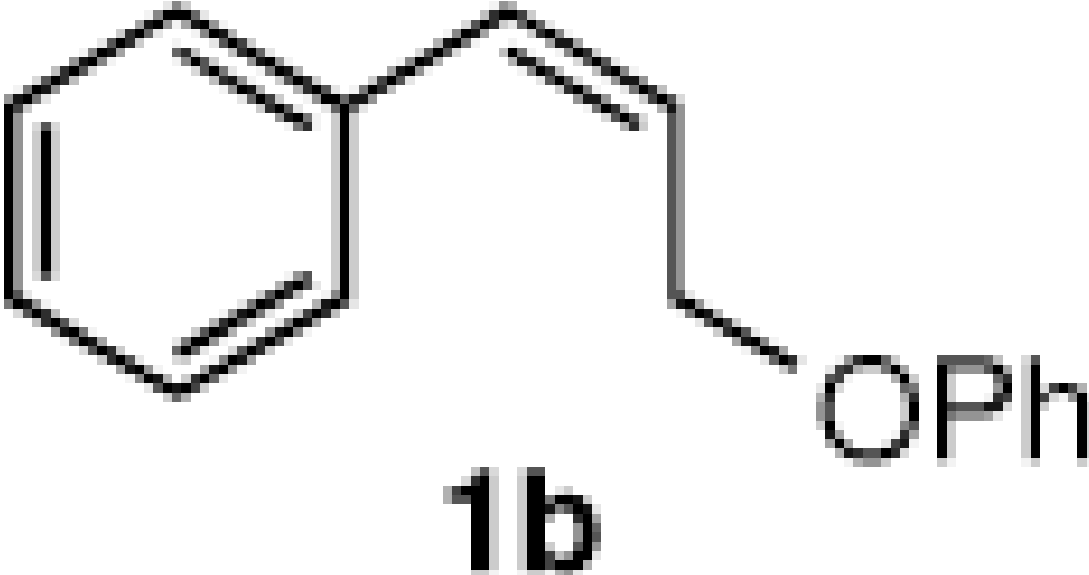
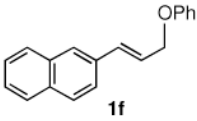
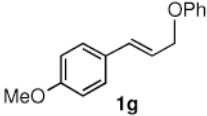
^e 1.5 mol % PdCl₂(PPh₃)₂ and 1.5 mol % PdCl₂(DPEphos) were used.

Table 3

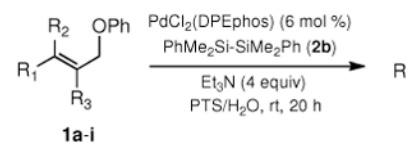
Pd-catalyzed silylations with 1,2-diphenyltetramethyldisilane **2b**.^a

entry	substrate
1	<p>1a</p>



entry	substrate
2	
3	
4	

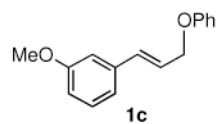
Me



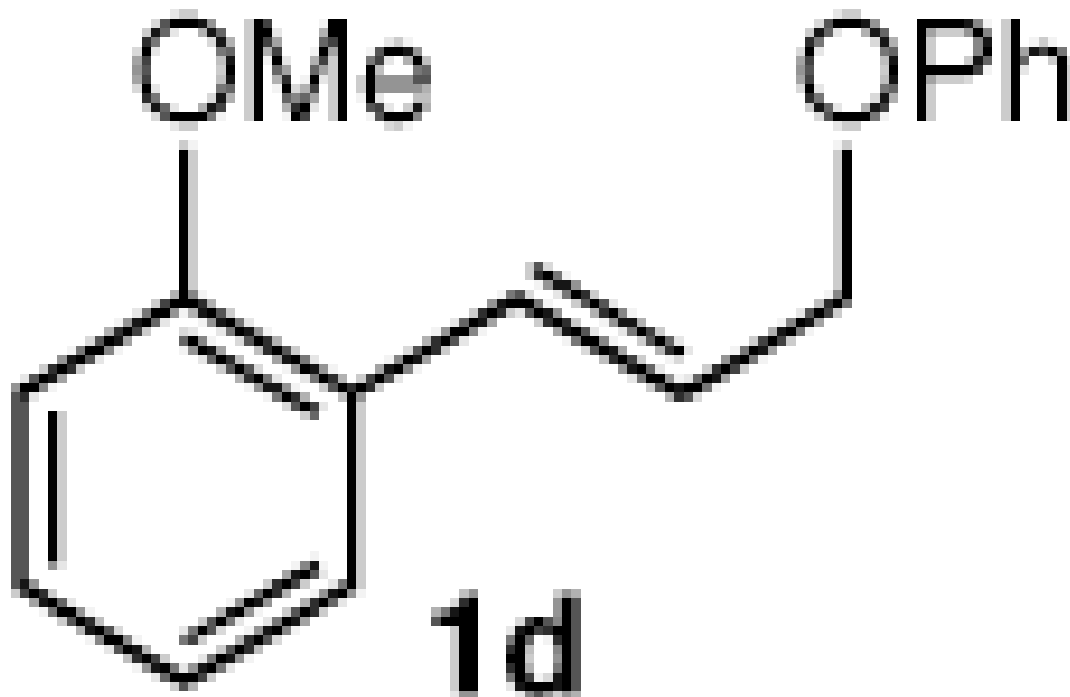
entry

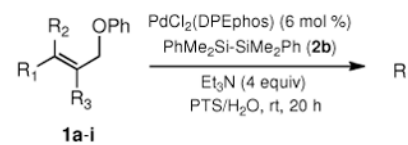
substrate

5



6

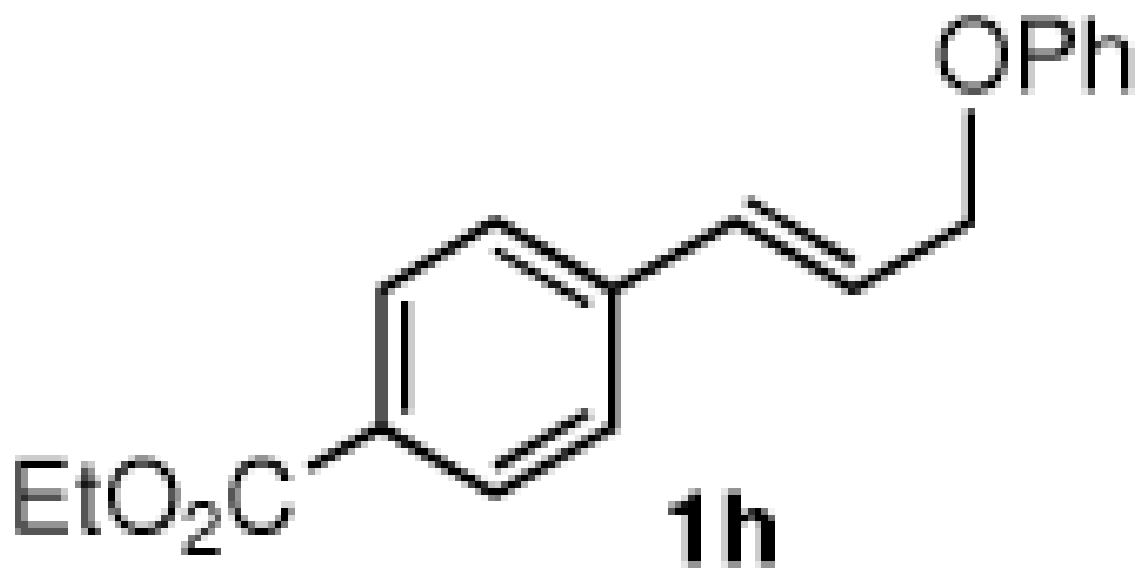


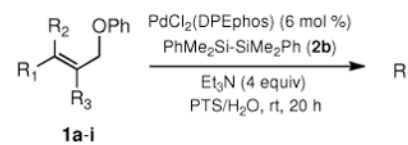


entry

substrate

7





entry	substrate
<i>8^d</i>	<p style="text-align: center;">1i</p>

^a All reactions were carried out on 0.25 mmol scale.

^b *l:b* and *E:Z* ratio determined by GCMS and ¹H NMR methods.

^c Isolated yield after column chromatography.

^d 10 mol % $\text{PdCl}_2(\text{DPEphos})$ used.