

Boc-protected 2-pyrrolyldimethylsilanol: a potent nucleophile in Pd-catalyzed cross-coupling

### Alkyne Hydrosilylation

- $[\text{Cp}^*\text{Ru}(\text{MeCN})_3]\text{PF}_6$  and Other Catalysts

### Organosilanes for Cross-coupling

- Dimethylsilanols
- Triethoxysilanes
- Polyvinylsiloxanes

### Multicomponent Couplings

- 2-Silyl-1,3-dithianes

## Introduction

Silicon has long held a privileged status in organic synthesis. Indeed, the use of silicon protecting groups in the majority of lengthy multi-step natural product syntheses illustrates the necessity of organosilicon compounds. Other silicon reagents, such as allyl and crotyl silanes, have also become omnipresent within the field as powerful methods for the construction of new C–C bonds. Organosilicon chemistry has matured substantially over the course of the past decade and new methods have been developed for both the introduction of silicon groups, as well as new methods for chemical manipulation of those groups. Of particular importance are the use of catalytic methods such as hydrosilylation of alkynes and cross-coupling of organosilanes.

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### About Our Cover

The cover graphic depicts the structure of a dimethylsilanol reagent, (*N*-Boc-2-pyrrolyl)-dimethylsilanol, which has been successfully employed in Pd-catalyzed cross-coupling reactions. Dimethylsilanols have recently emerged as attractive reagents for facile construction of new C–C bonds.

## ChemFiles

Vol. 6 No. 5

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## Alkyne Hydrosilylation

### [Cp\*Ru(MeCN)<sub>3</sub>]PF<sub>6</sub> and Other Catalysts

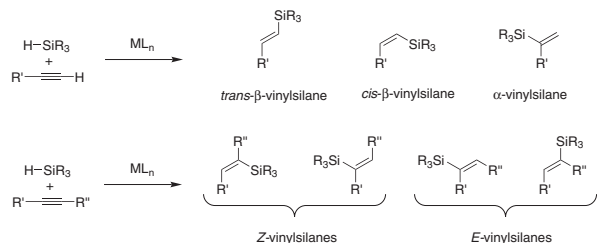
Vinyl-metal reagents play a pivotal role in organic synthesis. Among the vinyl-metal reagents available, silicon-based reagents are of increasing importance. This is largely due to their low cost, minimal toxicity, ease of handling, and the simplicity of byproduct removal. Particularly attractive is the ability to carry the silyl moiety through a series of synthetic manipulations. Much of the impetus for the growing relevance of vinylsilanes arises from the successful cross-coupling strategies developed for these useful organometallic species. Vinylsilanes are also useful as Michael acceptors in conjugate addition reactions and as masked ketones in Tamao–Fleming oxidations.

Of the available methods for preparation of vinylsilanes, the hydrosilylation of alkynes is the most direct and atom-economical approach (**Scheme 1**). A number of transition metal catalysts have been devised to execute these reactions in a regio- and stereocontrolled fashion (**Figure 1**). Methods for hydrosilylation of terminal alkynes were developed some time ago, particularly for the preparation of *cis*- and *trans*- $\beta$ -vinylsilanes. Classical Pt-catalysis (Speier's<sup>1</sup> and Karstedt's<sup>2</sup> catalysts), as well as Rh-based catalysis ([Rh(cod)<sub>2</sub>]BF<sub>4</sub> and [RhCl(nbd)]<sub>2</sub>), remain powerful methods for synthesis of *trans*- $\beta$ -vinylsilanes. Wilkinson's catalyst was also demonstrated to yield the *trans* product in polar solvents, with the *cis* isomer predominating in non-polar media.<sup>5</sup> Ru-based catalysts (e.g. [Ru(benzene)Cl<sub>2</sub>]<sub>2</sub> or [Ru(*p*-cymene)Cl<sub>2</sub>]<sub>2</sub>) allow for access to *cis*- $\beta$ -vinylsilanes.<sup>6</sup> Under certain conditions, Grubbs' 1st generation catalyst also gives *cis* products, although the stereo- and regioselectivity of the hydrosilylation is highly dependent on the alkyne, silane, and solvent.<sup>7</sup> While there exists a wealth of methods for preparation of linear  $\beta$ -vinylsilanes, until recently there were no *general* methods for the preparation of 1,1-disubstituted  $\alpha$ -vinylsilanes.<sup>8</sup> Moreover, although selective intramolecular hydrosilylation of internal alkynes can be achieved,<sup>9</sup> a selective intermolecular variant was virtually unknown.<sup>10</sup> The Trost group at Stanford University developed a remarkably robust protocol for hydrosilylation of terminal acetylenes to give  $\alpha$ -vinylsilanes, relying on the ruthenium(II) catalyst, [Cp\*Ru(MeCN)<sub>3</sub>]PF<sub>6</sub>.<sup>11,12</sup> This catalyst also provides a competent method for regioselective intra- and intermolecular hydrosilylation of internal alkynes, giving exclusively Z-trisubstituted alkenes.

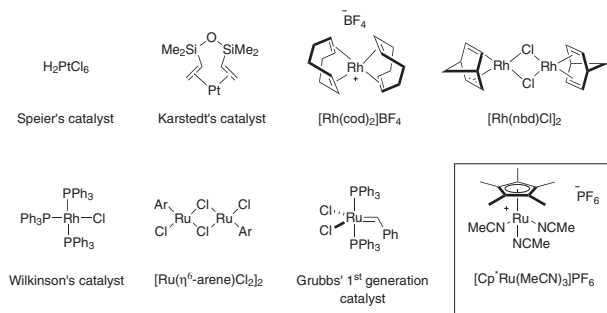
#### Terminal Alkynes

A diverse set of terminal alkynes underwent rapid and mild hydrosilylation in the presence of [Cp\*Ru(MeCN)<sub>3</sub>]PF<sub>6</sub> to give 1,1-disubstituted  $\alpha$ -vinylsilanes in good to excellent yield, often with low catalyst loadings (**Scheme 2**, **Table 1**). The reaction is tolerant to a wide range of functional groups including halogens, free alcohols, alkenes, internal alkynes, esters, and amines. Moreover, a breadth of silanes can be used in the reaction with excellent predictability.

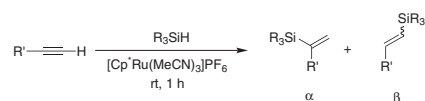
The  $\alpha$ -vinylsilanes are useful intermediates that can participate in a host of synthetically valuable transformations. The simplest manipulation, protodesilylation, is achieved by treatment of the vinylsilane with TBAF in the presence of catalytic CuI (**Scheme 3**).<sup>13</sup>



**Scheme 1**



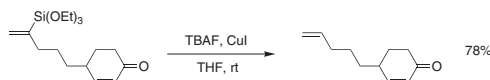
**Figure 1**



**Scheme 2**

Entry	Alkyne	R <sub>3</sub> SiH	Loading (%)	Ratio (α:β)	Yield (%)
1		(EtO) <sub>2</sub> MeSiH	1	9:1	86 (α)
2		(EtO) <sub>3</sub> SiH	1	13:1	92 (α+β)
3		(EtO) <sub>3</sub> SiH	4	n.d.	61 (α)
4		(EtO) <sub>3</sub> SiH	10	20:1	87 (α+β)
5		(EtO) <sub>3</sub> SiH	1	13:1	77 (α)
6		BnMe <sub>2</sub> SiH (BDMS-H)	1	>20:1	99 (α+β)
7		BDMS-H	1	14:1	91 (α+β)
8		(EtO) <sub>3</sub> SiH	1	9:1	71 (α+β)

**Table 1**



**Scheme 3**

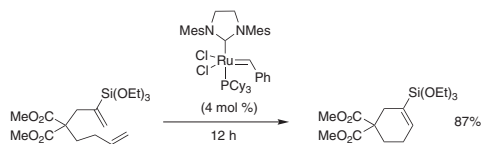
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Internal vinylsilanes are also active towards ring-closing metathesis with Grubbs' 2nd generation catalyst, yielding silicon-functionalized carbocycles that are amenable to further elaboration (Scheme 4).<sup>11</sup> For example, both triethoxysilanes<sup>11</sup> and benzyldimethylsilanes<sup>14</sup> are active participants in fluoride-promoted, Pd-catalyzed cross-coupling (Schemes 5 and 6).

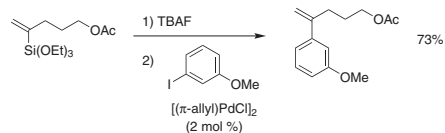
### Internal Alkynes

As illustrated in Scheme 1, non-selective hydrosilylation of internal alkynes would potentially give four isomeric addition products. The Trost group has demonstrated that hydrosilylation of internal alkynes with  $[\text{Cp}^*\text{Ru}(\text{MeCN})_3]\text{PF}_6$  gives trisubstituted Z-vinylsilanes exclusively, as a result of *trans* addition of the silane to the alkyne (Scheme 7, Table 2).<sup>11</sup> Importantly, the hydrosilylation reaction is regioselective as well. The regioselectivity can be summarized as follows: (i) hydrosilylation of 2-alkynes results in the formation of Z-alkenes with the silyl group occupying the less sterically-demanding position (entries 1 and 2); (ii) for substrates where the alkyne is not in the 2-position, the silyl substituent will occupy the more sterically-demanding position in the Z-alkene (entry 4); (iii) for propargylic, homopropargylic, and bishomopropargylic alcohol substrates, hydrosilylation occurs such that the silyl group resides distal to the hydroxyl functionality of the Z-alkene (entries 5–9); (iv) in the case of  $\alpha,\beta$ -alkynylcarbonyls, the silyl group again selectively occupies the distal position of the Z-alkene (entries 10–13).<sup>11,15</sup> For free propargylic, homopropargylic, and bishomopropargylic alcohols, hydrosilylation with a silane bearing a leaving group (e.g., an ethoxy substituent) results in the formation of a cyclic siloxane (entries 5 and 8). Significantly, the hydrosilylation using  $[\text{Cp}^*\text{Ru}(\text{MeCN})_3]\text{PF}_6$  can be performed while maintaining the stereochemical integrity of asymmetric centers residing in the alkyne substrate (entry 9).

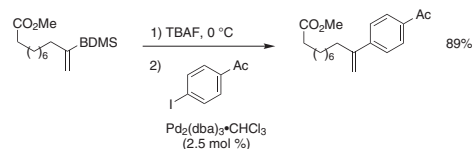
Like  $\alpha$ -vinylsilanes, hydrosilylation products resulting from internal addition are active in numerous reaction processes including: protodesilylation, cycloaddition, Tamao–Fleming oxidation, and Pd-catalyzed cross-coupling.<sup>14</sup> For example, though non-sterically differentiated alkynes may undergo stereo- but non-regioselective hydrosilylation (entry 3), protodesilylation of the product mixture provides a single *trans* diastereomer.<sup>13</sup> Therefore, the hydrosilylation-protodesilylation protocol provides a useful method for alkyne reduction to a *trans* alkene and is a complement to the *cis*-selectivity observed in the Lindlar reduction. As shown in Scheme 8, even highly reactive silanes can participate in hydrosilylation reaction, with excellent predictability.<sup>11b</sup> The resultant alkenylchlorosilane was trapped with a hexadienol to give a siloxane linkage. Heating the triene resulted in an intramolecular Diels-Alder (IMDA) reaction, yielding a siloxane with four contiguous stereocenters. The adduct could then be treated to protodesilylation or Tamao–Fleming conditions to furnish the primary alcohol or the diol respectively.



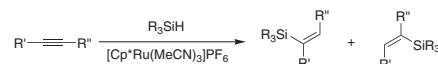
Scheme 4



Scheme 5



Scheme 6

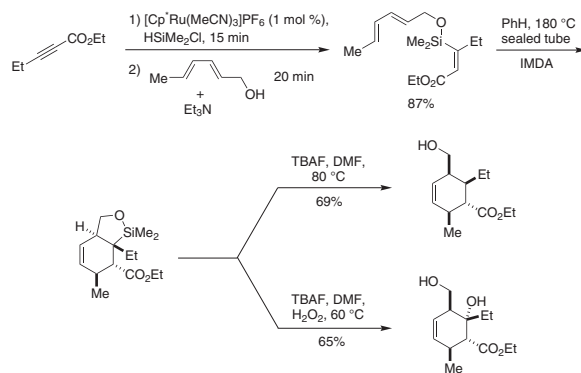


Scheme 7

Entry	Alkyne	R <sub>3</sub> SiH	Loading (%)	Major Product	Ratio	Yield (%)
1		(EtO) <sub>3</sub> SiH	1		5:1	86
2		Et <sub>3</sub> SiH (TES-H)	1		>20:1	70 (major)
3		(EtO) <sub>3</sub> SiH	1		1:1	96*
4		(EtO) <sub>3</sub> SiH	1		6:1	92
5		(EtO) <sub>3</sub> SiH	1		5:1	71 (major)
6		TES-H	1		13:1	99
7		BnMe <sub>2</sub> SiH (BDMS-H)	2		14:1	91 (major)
8		Me <sub>2</sub> (EtO)SiH	2		5:1	73 (major)
9		BDMS-H	3		6:1	98
10		BDMS-H	0.5		>20:1	98
11		BDMS-H	1		>20:1	94
12		(EtO) <sub>3</sub> SiH	1		5:1	99
13		BDMS-H	1		7:1	88

\*Yield of *trans* alkene after protodesilylation with TBAF/CuI.

Table 2



Scheme 8

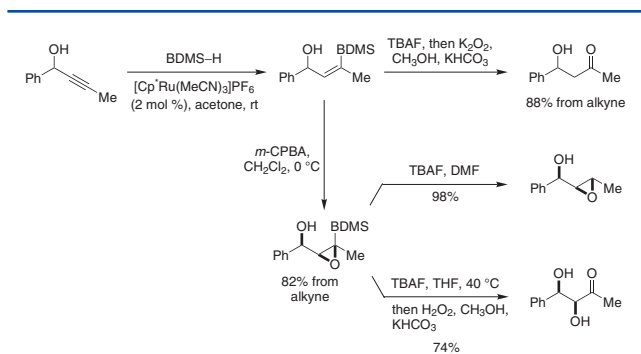
Manipulation of the alkene prior to protodesilylation or oxidation is also feasible. For example, vinylsilanes are readily epoxidized by *m*-CPBA in a diastereoselective fashion (**Scheme 9**). Subsequent protodesilylation furnishes the corresponding *syn*-epoxy alcohol, while Tamao–Fleming oxidation provides a *syn*-diol. Therefore, this process can be used as a surrogate to the aldol condensation.

### Intramolecular Hydrosilylation

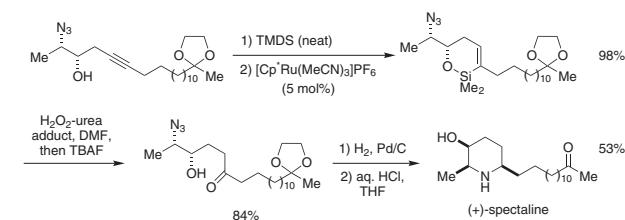
Finally, intramolecular hydrosilylation is possible using hydroxyalkynes, as illustrated in the concise synthesis of the 3-hydropiperidine alkaloid (+)-spectaline (**Scheme 10**).<sup>16b</sup> Treatment of the homopropargyl alcohol with tetramethyldisilazane (TMDS), followed by regio- (distal) and stereoselective (*Z*) intramolecular hydrosilylation, gave a cyclic azidosiloxane. Tamao–Fleming oxidation followed by reduction with concomitant cyclization gave (+)-spectaline in respectable yield.

The sequence of intramolecular hydrosilylation and subsequent cross-coupling provides an excellent method for introducing a new carbon bond at an alkyne carbon that is in a remote position from a free hydroxyl group (**Scheme 11**).<sup>17</sup>

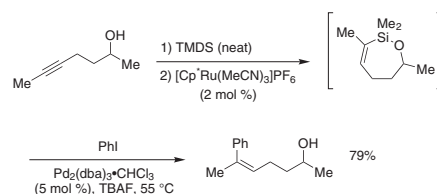
We are pleased to offer [Cp\*<sup>+</sup>Ru(MeCN)<sub>3</sub>]PF<sub>6</sub><sup>-</sup>, as well as a number of other catalysts and silanes for hydrosilylation.



Scheme 9



Scheme 10



Scheme 11

### Pentamethylcyclopentadienyltris(acetonitrile)-ruthenium(II) hexafluorophosphate

C<sub>16</sub>H<sub>24</sub>F<sub>6</sub>N<sub>3</sub>PRu  
FW: 504.42  
[99604-67-8]



667412-250MG

250 mg

### Chloroplatinic acid hydrate, 99.9%

Speier's Catalyst  
H<sub>2</sub>PtCl<sub>6</sub> · H<sub>2</sub>O  
FW: 409.81  
[26023-84-7]



398322-1G

1 g

398322-5G

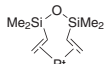
5 g

398322-25G

25 g

### Platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex solution, 0.10 M in xylene

Karstedt's Catalyst  
C<sub>8</sub>H<sub>18</sub>OSi<sub>2</sub>Pt  
FW: 381.48  
[68478-92-2]



479519-5G

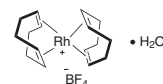
5 g

479519-25G

25 g

### Bis(1,5-cyclooctadiene)rhodium(I) tetrafluoroborate hydrate, 97%

C<sub>16</sub>H<sub>24</sub>BF<sub>4</sub>Rh · H<sub>2</sub>O  
FW: 406.07  
[207124-65-0]



334987-100MG

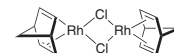
100 mg

334987-500MG

500 mg

### (Bicyclo[2.2.1]hepta-2,5-diene)rhodium(I) chloride dimer

C<sub>14</sub>H<sub>16</sub>Cl<sub>2</sub>Rh<sub>2</sub>  
FW: 460.99  
[12257-42-0]



249939-100MG

100 mg

249939-500MG

500 mg

### Tris(triphenylphosphine)rhodium(I) chloride

Wilkinson's Catalyst  
C<sub>54</sub>H<sub>45</sub>ClP<sub>3</sub>Rh  
FW: 925.22  
[14694-95-2]



199982-250MG

250 mg

199982-1G

1 g

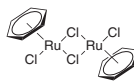
199982-5G

5 g

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**Benzenedichlororuthenium(II) dimer**

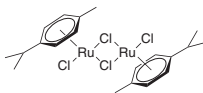
$C_{12}H_{12}Cl_4Ru_2$   
FW: 500.18  
[37366-09-9]



341568-1G	1 g
341568-5G	5 g

**Dichloro(p-cymene)ruthenium(II) dimer**

$C_{20}H_{28}Cl_4Ru_2$   
FW: 612.39  
[52462-29-0]



343706-1G	1 g
343706-5G	5 g

**Benzylidene-bis(tricyclohexylphosphine)dichlororuthenium(II)**

Grubbs' 1st Generation Catalyst

$C_{43}H_{72}Cl_2P_2Ru$   
FW: 822.96  
[172222-30-9]



579726-1G	1 g
579726-5G	5 g

**Triethylsilane, 99%**

TES-H  
 $C_6H_{16}Si$   
FW: 116.28  
[617-86-7]



230197-5G	5 g
230197-25G	25 g
230197-100G	100 g

**Benzyltrimethylsilane, 99%**

BDMS-H  
 $C_9H_{14}Si$   
FW: 150.29  
[1631-70-5]



483141-10ML	10 mL
-------------	-------

**Trimethoxysilane, 95%**

$C_3H_{10}O_3Si$   
FW: 122.20  
[2487-90-3]



282626-25G	25 g
282626-100G	100 g

**Triethoxysilane, 95%**

$C_6H_{16}O_3Si$   
FW: 164.27  
[998-30-1]



390143-10ML	10 mL
390143-50ML	50 mL

**Chlorodimethylsilane, 98%**

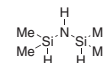
$C_2H_7ClSi$   
FW: 94.62  
[1066-35-9]



144207-50G	50 g
------------	------

**1,1,3,3-Tetramethyldisilazane, 97%**

TMDS  
 $C_4H_{15}NSi_2$   
FW: 133.34  
[15933-59-2]



139246-1G	1 g
139246-10G	10 g

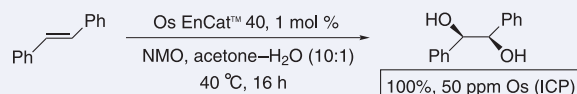
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Osmium tetroxide, microencapsulated**

$OsO_4$   
FW: 254.23  
[20816-12-0]

658685-500MG	500 mg
658685-1G	1 g
658685-5G	5 g

**4-Methylmorpholine N-oxide, 97%**

$C_5H_{11}NO_2$   
FW: 117.15  
[7529-22-8]

224286-5G	5 g
224286-25G	25 g
224286-100G	100 g

## Organosilanes for Cross-coupling

### Dimethylsilanols

Over the past several years, Pd-catalyzed cross-coupling of silicon compounds has rapidly gained acceptance as a suitable alternative to more commonly known methods such as: Stille (Sn), Kumada (Mg), Suzuki (B), and Negishi (Zn) cross-couplings.<sup>18</sup> Organosilicon compounds are easily prepared from inexpensive starting materials, have low toxicity, and are active nucleophiles in coupling reactions with organohalides and pseudohalides. Among the many available organosilicon compounds, the cross-coupling of dimethylsilanols is the most mature.

Dimethylsilanols are readily prepared by directed metallation of heterocycles (**Scheme 12**)<sup>19,20</sup> or by metal-halogen exchange of aryl or alkenyl bromides (**Scheme 13**),<sup>1,21</sup> followed by quenching with a silicon-based electrophile. Hexamethylcyclotrisiloxane and dichlorodimethylsilane are particularly attractive silylating reagents, due to their affordability.

Alternatively, aryl dimethylsilanols can be synthesized by a sequence of transition metal-catalyzed silylation of aryl bromides with a diethoxydisilane reagent, followed by acid hydrolysis of the silyl ether (**Scheme 14**, **Table 3**). The use of Hünig's base and BPTBP as a ligand additive gave the most optimal results in the silylation reaction.

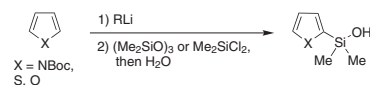
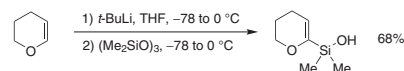
In the presence of a fluoride activation source, alkenyldimethylsilanols readily react with both aryl and alkenyl halides to give the coupled adducts in very good yield (**Scheme 15**).<sup>19</sup> Alternatively, the Pd-catalyzed cross-coupling can also be performed under basic activation using TMSOK for in situ generation of a nucleophilic silanolate.<sup>23</sup> The utility of performing the cross-coupling under basic activation lies in the ability to perform the reaction in the presence of fluoride-sensitive silyl protecting groups (**Scheme 16**).<sup>24</sup> Alkynylsilanols have also been found to be active coupling partners under similar conditions.<sup>25</sup>

Both strategies, fluoride and basic activation, were demonstrated in the total synthesis of the antifungal polyene macrolide RK-397 (**Figure 2**).<sup>26</sup> Specifically, the polyene segment of the natural product was prepared by sequential cross-coupling of a differentiable 1,4-bissilylbutadiene unit (**Scheme 17**).<sup>27</sup> The dimethylsilanol moiety readily couples under basic activation, while the other silyl substituent remains inert. Subsequent fluoride-promoted coupling of the benzyldimethylsilyl group provided the necessary tetraenoate linkage for completion of the target molecule.

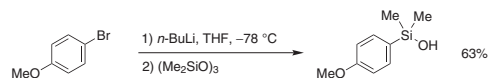
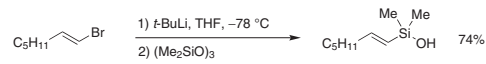
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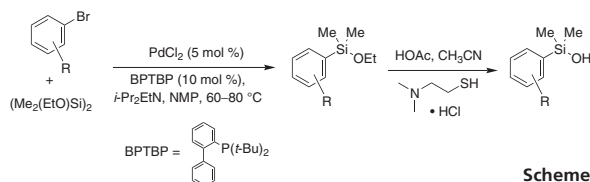
[sigma-aldrich.com/chemnews](http://sigma-aldrich.com/chemnews)



**Scheme 12**



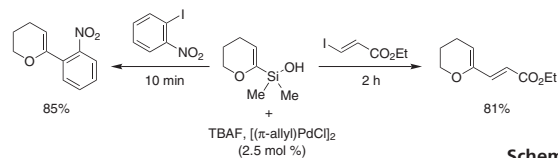
**Scheme 13**



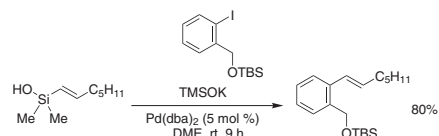
**Scheme 14**

Entry	R	Time (h)	Yield (%)
1	4-OMe	18	76
2	4-Ac	4	70
3	4-NO <sub>2</sub>	4	72
4	4-CO <sub>2</sub> Et	4	81
5	4-CN	4	80
6	4-Me	12	71
7	2-CN	12	82
8	2-CO <sub>2</sub> Et	24	56

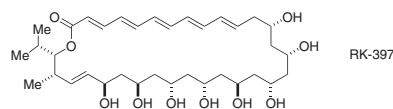
**Table 3**



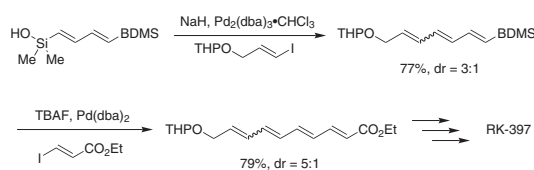
**Scheme 15**



**Scheme 16**



**Figure 2**



**Scheme 17**

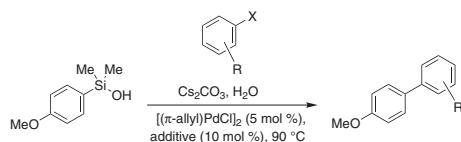
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Robust experimental protocols have been developed for biaryl coupling of a variety of aryl iodides and bromides. Good to excellent yields were obtained in the coupling of (4-methoxyphenyl)dimethylsilanol with a diverse set of aryl halides using  $\text{Cs}_2\text{CO}_3$  to generate the silanolate in situ (**Scheme 18, Table 4**). Bromides could be coupled using dppb as a ligand additive in toluene, while coupling of iodides was most effective using  $\text{Ph}_3\text{As}$  in dioxane.

Until recently, mild and general methods for cross-coupling of 2-heteroaryl nucleophiles were lacking. Boc-protected indoles were particularly challenging, owing to the decreased nucleophilicity at C-2. Typical procedures called for harsh reaction conditions (Stille coupling<sup>29</sup>) or failed to deliver the coupled product in acceptable yield (Suzuki coupling<sup>30</sup>). Denmark and co-workers have developed a set of general protocols for efficient coupling of these difficult substrates (**Scheme 19, Table 5**). Both protocols call for generation of a sodium silanolate (basic activation). Silanolates generated in situ from NaOt-Bu undergo Pd-catalyzed cross-coupling with aryl iodides in the presence of CuI.<sup>31</sup> Alternatively, silanolates generated in situ from NaH can be coupled without an additive.<sup>20</sup> Finally, sodium dimethylsilanolates are also isolable and storable materials whose reactivity parallels that of in situ-formed silanolates.

This methodology is applicable to cross-coupling of other heteroaryldimethylsilanolates with aryl iodides in the presence of  $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ .<sup>20,32</sup> Thiophene, furan, and pyrrole nucleophiles easily couple with both electron-rich and electron-deficient aryl iodides (**Scheme 20, Table 6**).

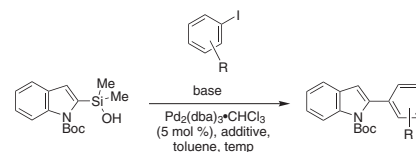
Less expensive aryl bromides can be used in the reaction by changing to a highly-active Pd(I) catalyst developed by Weissman and Moore (**Scheme 21, Table 7**).<sup>33</sup> The reactions times are generally shorter than with aryl iodides, and no discernible decreases in yields are observed. The Pd(I) catalyst displays very high activity that is superior to many commonly used cross-coupling catalysts for organosilicon nucleophiles. It is readily prepared from (2-methylallyl)palladium(II) chloride dimer and  $\text{P}(t\text{-Bu})_3$  in the presence of base.



Scheme 18

Entry	R	X	Time (h)	Additive	Solvent	Yield (%)
1	4-CO <sub>2</sub> Et	Br	24	dppb	toluene	90
2	4-Me	Br	18	dppb	toluene	90
3	4-H	Br	12	dppb	toluene	85
4	4-OMe	Br	18	dppb	toluene	92
5	4-Cy	Br	18	dppb	toluene	79
6	2-Me	I	24	$\text{Ph}_3\text{As}$	dioxane	85
7	2-CF <sub>3</sub>	I	24	$\text{Ph}_3\text{As}$	dioxane	82
8	2-NO <sub>2</sub>	I	24	$\text{Ph}_3\text{As}$	dioxane	83
9	4-Ac	I	3	$\text{Ph}_3\text{As}$	toluene	91

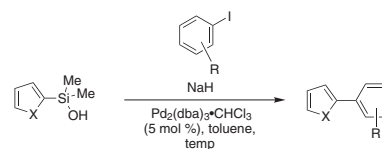
Table 4



Scheme 19

Entry	R	Base	Additive	Temp (°C)	Time (h)	Yield (%)
1	4-NO <sub>2</sub>	NaOt-Bu	CuI	rt	6	84
2	4-CF <sub>3</sub>	NaOt-Bu	CuI	rt	22	82
3	2-OMe	NaOt-Bu	CuI	50	24	75
4	4-OMe	NaOt-Bu	CuI	50	24	72
5	4-CN	NaH	—	rt	3	81
6	4-CO <sub>2</sub> Et	NaH	—	rt	3	82
7	4-OMe	NaH	—	80	3	68

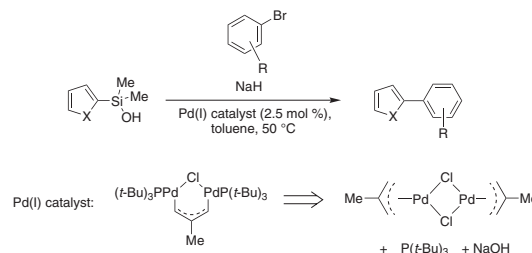
Table 5



Scheme 20

Entry	X	R	Temp (°C)	Time (h)	Yield (%)
1	NBoc	4-OMe	50	36	72
2	NBoc	4-CO <sub>2</sub> Et	rt	3	76
3	S	4-OMe	80	24	72
4	S	4-CO <sub>2</sub> Et	rt	3	78
5	O	4-CO <sub>2</sub> Et	rt	1	82
6	O	2-Me	rt	3	61

Table 6



Scheme 21

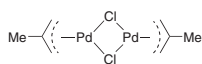
Entry	X	R	Time (h)	Yield (%)
1	S	4-OMe	3	71
2	S	4-CN	3	78
3	S	4-CF <sub>3</sub>	3	86
4	S	2-Me	3	77
5	O	4-OMe	6	66
6	O	4-CN	3	73
7	O	4-CF <sub>3</sub>	3	71
8	O	2-Me	3	71

Table 7

**(2-Methylallyl)palladium(II) chloride dimer**

NEW

$C_8H_{14}Cl_2Pd_2$   
FW: 393.94  
[12081-18-4]



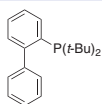
673064-250MG  
673064-1G

250 mg  
1 g

**(2-Biphenyl)di-tert-butylphosphine, 97%**

NEW

BPTBP  
 $C_{20}H_{27}P$   
FW: 298.40  
[224311-51-7]

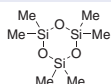


638439-1G  
638439-5G  
638439-25G

1 g  
5 g  
25 g

**Hexamethylcyclotrisiloxane, 98%**

$C_6H_{18}O_3Si_3$   
FW: 222.46  
[541-05-9]



235687-25G  
235687-100G

25 g  
100 g

**Dichlorodimethylsilane, 99%**

$C_2H_6Cl_2Si$   
FW: 129.06  
[75-78-5]



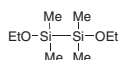
440272-100ML  
440272-1ML

100 mL  
1 L

**1,2-Diethoxy-1,1,2,2-tetramethyldisilane, 97%**

NEW

$C_8H_{22}O_2Si_2$   
FW: 206.43  
[18419-84-6]



667897-1G  
667897-5G

1 g  
5 g

**Dimethylphenylsilanol, 97%**

NEW

$C_8H_{12}OSi$   
FW: 152.27  
[5272-18-4]



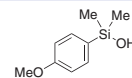
667110-1G  
667110-5G

1 g  
5 g

**(4-Methoxyphenyl)dimethylsilanol, 96%**

NEW

$C_9H_{14}O_2Si$   
FW: 182.29  
[22868-26-4]

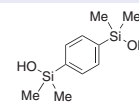


667951-1G  
667951-5G

1 g  
5 g

**1,4-Bis(hydroxydimethylsilyl)benzene, 95%**

$C_{10}H_{18}O_2Si_2$   
FW: 226.42  
[2754-32-7]



497193-5G

5 g

**(N-Boc-2-pyrrolyl)dimethylsilanol**

NEW

$C_{11}H_{19}NO_3Si$   
FW: 241.36



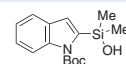
669164-1G

1 g

**(N-Boc-2-indolyl)dimethylsilanol**

NEW

$C_{15}H_{21}NO_3Si$   
FW: 291.42



667900-1G  
667900-5G

1 g  
5 g

**Dimethyl(2-thienyl)silanol, 97%**

NEW

$C_6H_{10}OSSi$   
FW: 158.29  
[197009-90-8]



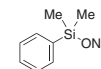
667099-1G  
667099-5G

1 g  
5 g

**Sodium dimethylphenylsilanolate**

NEW

$C_8H_{11}NaOSi$   
FW: 174.25



673269-1G  
673269-5G

1 g  
5 g

**Sodium 2-furyldimethylsilanolate**

NEW

$C_6H_9NaO_2Si$   
FW: 164.21



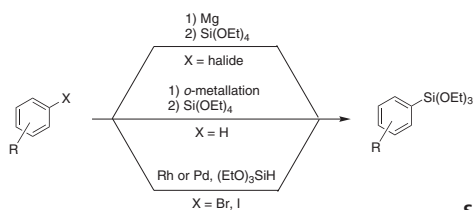
673250-1G  
673250-5G

1 g  
5 g

## Triethoxysilanes

The DeShong group at the University of Maryland has demonstrated triethoxysilanes to be active substrates in a variety of synthetically useful C–C bond forming reactions. Aryl triethoxysilanes are readily prepared by Grignard,<sup>34</sup> *o*-metallation,<sup>35</sup> or transition metal-catalyzed silylation reactions (**Scheme 22**).<sup>36</sup>

In the presence of a fluoride activator, siloxanes participate in Pd-catalyzed cross-coupling with aryl,<sup>35,37</sup> alkenyl,<sup>38</sup> and alkyl halides.<sup>39</sup> For example, coupling of 5-bromotropolone with an arylsiloxane gave similar or better results than the analogous Suzuki or Stille reagent (**Scheme 23**).<sup>38</sup> Triethoxysilanes also act as nucleophiles towards both Michael acceptors<sup>40</sup> and Pd-allyl complexes (**Scheme 24**).<sup>41</sup>



Scheme 22

### Tetraethyl orthosilicate, 98%

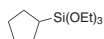
C<sub>8</sub>H<sub>20</sub>O<sub>4</sub>Si  
FW: 208.33  
[78-10-4]



131903-25ML	25 mL
131903-500ML	500 mL
131903-1L	1 L
131903-4L	4 L

### Cyclopentyltriethoxysilane, 98%

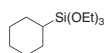
C<sub>11</sub>H<sub>24</sub>O<sub>3</sub>Si  
FW: 232.39  
[154733-91-2]



596043-5G	5 g
-----------	-----

### Cyclohexyltriethoxysilane, 98%

C<sub>12</sub>H<sub>26</sub>O<sub>3</sub>Si  
FW: 246.42  
[18151-84-3]



592420-1G	1 g
592420-5G	5 g

### Triethoxyvinylsilane, 97%

C<sub>8</sub>H<sub>18</sub>O<sub>3</sub>Si  
FW: 190.31  
[78-08-0]



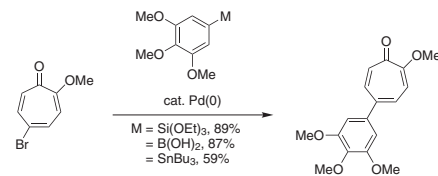
175560-100ML	100 mL
175560-500ML	500 mL

### 1-(Triethoxysilyl)-2-pentene, predominantly *cis*

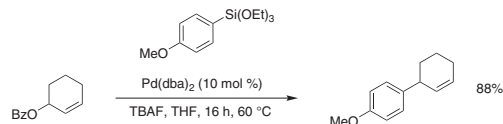
C<sub>11</sub>H<sub>24</sub>O<sub>3</sub>Si  
FW: 232.39  
[698999-32-5]



592641-1G	1 g
592641-5G	5 g



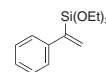
Scheme 23



Scheme 24

### Triethoxy(1-phenylethenyl)silane, 98%

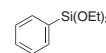
C<sub>14</sub>H<sub>22</sub>O<sub>3</sub>Si  
FW: 266.41  
[90260-87-0]



596353-1G	1 g
596353-10G	10 g

### Triethoxyphenylsilane, 98%

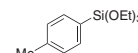
C<sub>12</sub>H<sub>20</sub>O<sub>3</sub>Si  
FW: 240.37  
[780-69-8]



175609-5G	1 g
175609-250G	250 g
175609-1KG	1 kg

### Triethoxy-*p*-tolylsilane, 97%

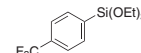
C<sub>13</sub>H<sub>22</sub>O<sub>3</sub>Si  
FW: 254.40  
[18412-57-2]



591572-1G	1 g
591572-5G	5 g

### Triethoxy[4-(trifluoromethyl)phenyl]silane, 97%

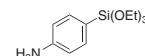
C<sub>13</sub>H<sub>19</sub>F<sub>3</sub>O<sub>3</sub>Si  
FW: 308.37  
[188748-63-2]



630438-1G	1 g
630438-5G	5 g

### 4-(Triethoxysilyl)aniline, 97%

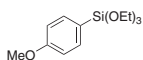
C<sub>12</sub>H<sub>21</sub>NO<sub>3</sub>Si  
FW: 255.39  
[7003-80-7]



596477-1G	1 g
596477-10G	10 g

**Triethoxy(4-methoxyphenyl)silane, 97%**

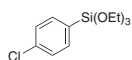
C<sub>13</sub>H<sub>22</sub>O<sub>4</sub>Si  
FW: 270.40  
[21130-91-6]



597015-5G	5 g
597015-20G	20 g

**(4-Chlorophenyl)triethoxysilane, 97%**

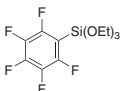
C<sub>12</sub>H<sub>19</sub>ClO<sub>3</sub>Si  
FW: 274.82  
[21700-74-3]



597910-1G	1 g
597910-10G	10 g

**(Pentafluorophenyl)triethoxysilane, 97%**

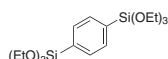
C<sub>12</sub>H<sub>15</sub>F<sub>5</sub>O<sub>3</sub>Si  
FW: 330.32  
[20083-34-5]



592757-5G	5 g
592757-10G	10 g

**1,4-Bis(triethoxysilyl)benzene, 96%**

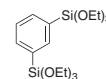
C<sub>18</sub>H<sub>34</sub>O<sub>6</sub>Si<sub>2</sub>  
FW: 402.63  
[2615-18-1]



598038-5G	5 g
598038-20G	20 g

**1,3-Bis(triethoxysilyl)benzene, 96%**

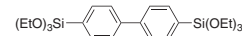
C<sub>18</sub>H<sub>34</sub>O<sub>6</sub>Si<sub>2</sub>  
FW: 402.63  
[16067-99-5]



598135-1G	1 g
598135-10G	10 g

**4,4'-Bis(triethoxysilyl)-1,1'-biphenyl, 95%**

C<sub>24</sub>H<sub>38</sub>O<sub>6</sub>Si<sub>2</sub>  
FW: 478.73  
[123640-93-7]



638102-1G	1 g
638102-10G	10 g

**3-(Triethoxysilyl)furan, 96%**

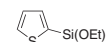
C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>Si  
FW: 230.33  
[75905-12-3]



592315-5G	5 g
-----------	-----

**2-(Triethoxysilyl)thiophene, 97%**

C<sub>10</sub>H<sub>18</sub>O<sub>3</sub>Si  
FW: 246.40  
[17984-89-3]



597007-1G	1 g
597007-10G	10 g

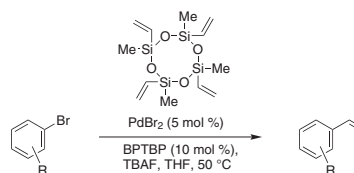
**Polyvinylsiloxanes**

2,4,6,8-Tetramethyl-2,4,6,8-tetravinylcyclotetrasiloxane has emerged as an inexpensive but powerful reagent for preparation of styrenes from the corresponding aryl iodides<sup>42</sup> or bromides (**Scheme 25, Table 8**).<sup>43</sup> Both electron-withdrawing and electron-donating groups are well tolerated in the vinylation reaction.

**2,4,6,8-Tetramethyl-2,4,6,8-tetravinylcyclotetrasiloxane**

C<sub>12</sub>H<sub>24</sub>O<sub>4</sub>Si<sub>4</sub>  
FW: 344.66  
[2554-06-5]

396281-10ML	10 mL
396281-50ML	50 mL



Scheme 25

Entry	R	Time (h)	Yield (%)
1	4-Ac	3	91
2	4-CO <sub>2</sub> Et	5	83
3	4-OMe	10	86
4	4-CH <sub>2</sub> OH	14	54
5	2-CO <sub>2</sub> Et	5	86
6	2-Et	17	75
7	2-OMe	20	80

Table 8

## Multicomponent Couplings

### 2-Silyl-1,3-dithianes

Dithianes are valuable tools in organic synthesis, particularly in their use as acyl anion equivalents in C–C bond construction (**Scheme 26**). Since their introduction over forty years ago in the pioneering work of Corey and Seebach,<sup>44</sup> dithiane chemistry has matured substantially. Contemporary reactions have evolved to the extent that multicomponent couplings are possible, yielding advanced, optically active and heteroatom-rich intermediates. Much of the progress in this field can be attributed to the recent work of Amos B. Smith III (University of Pennsylvania) in the field of 2-silyl-1,3-dithiane multicomponent linchpin couplings for use in complex molecule synthesis.

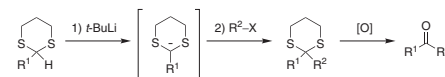
For example, one-pot, three-component couplings have been performed using the combination of 2-TBS-1,3-dithiane and tandem alkylation by two unique epoxide electrophiles to give extraordinarily advanced synthetic intermediates (**Scheme 27**).<sup>45</sup> Treatment of the metallated 2-silyl-1,3-dithianes with an epoxide generates an intermediate alkoxide anion. Addition of HMPA to the reaction results in a solvent-controlled Brook rearrangement, with simultaneous migration of the nucleophilic site back to the dithiane carbon. This species is then positioned to react with a second epoxide electrophile. Importantly, the final location of the silyl protecting group can be orchestrated simply by altering the order of epoxide additions. This methodology has been used in the syntheses of several complex natural product intermediates.<sup>46</sup>

The use of optically-active epichlorohydrin as the second electrophile results in the formation of a terminal epoxide by nucleophilic attack at the epoxide carbon followed by S<sub>N</sub>2 displacement of chloride (**Scheme 28**). Vinyl epoxides have also been reported to be active electrophiles, with nucleophilic addition occurring at the vinyl terminus.<sup>47</sup>

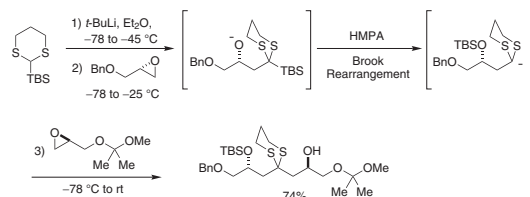
Smith and co-workers used a modified methodology to prepare a C<sub>2</sub>-symmetric masked polyol fragment that could be converted to the Schreiber's trisacetone subtarget<sup>48</sup> in the syntheses of mycoticins (**Scheme 29**).<sup>49</sup> In this instance, a five-component linchpin coupling tactic was used that relied on the use of a bisepoxide for the second electrophile.

The total syntheses of the neotropical frog-derived alkaloids, (–)-indolizidine 223AB and alkaloid (–)-205B relied on the controlled addition of silylated dithiane nucleophiles to aziridines (**Scheme 30**).<sup>50</sup>

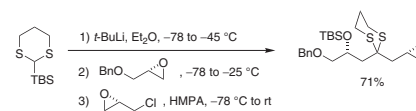
Finally, the Smith group has broadened the multicomponent linchpin coupling protocol to involve the concept of anion relay chemistry (ARC), in which a nucleophilic site is relayed between two distinct dithiane units (**Scheme 31**). A variety of masked 1,3,5-oxygenated systems were prepared in good yield using this methodology.<sup>51</sup>



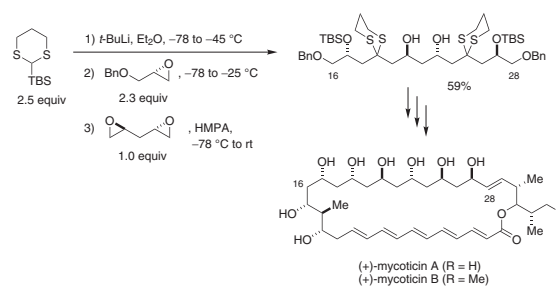
Scheme 26



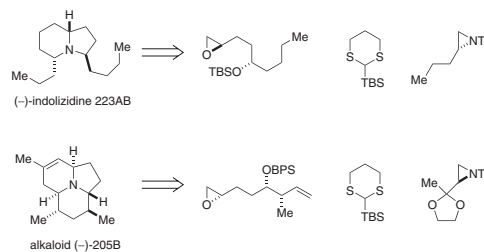
Scheme 27



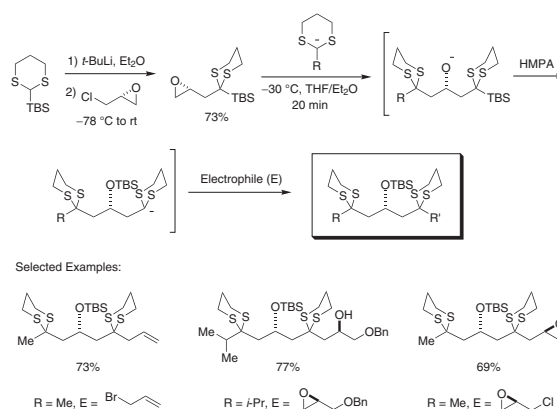
Scheme 28



Scheme 29



Scheme 30



Scheme 31

**2-(tert-Butyldimethylsilyl)-1,3-dithiane, 97%**

C<sub>10</sub>H<sub>22</sub>S<sub>2</sub>Si  
FW: 234.50  
[95452-06-5]



514241-1G	1 g
-----------	-----

**2-(Triisopropylsilyl)-1,3-dithiane, 97%**

C<sub>13</sub>H<sub>28</sub>S<sub>2</sub>Si  
FW: 276.58  
[145251-89-4]



409413-1G	1 g
-----------	-----

**2-Trimethylsilyl-1,3-dithiane, ≥99%**

C<sub>7</sub>H<sub>16</sub>S<sub>2</sub>Si  
FW: 192.42  
[13411-42-2]



220817-1G	1 g
220817-5G	5 g
220817-25G	25 g

**1,3-Dithiane, 97%**

C<sub>4</sub>H<sub>8</sub>S<sub>2</sub>  
FW: 120.24  
[505-23-7]



157872-1G	1 g
157872-5G	5 g
157872-25G	25 g
157872-100G	100 g

**2-Methyl-1,3-dithiane, 99%**

C<sub>5</sub>H<sub>10</sub>S<sub>2</sub>  
FW: 134.26  
[6007-26-7]



359130-1ML	1 mL
359130-5ML	5 mL

**2-Phenyl-1,3-dithiane, 97%**

C<sub>10</sub>H<sub>12</sub>S<sub>2</sub>  
FW: 196.33  
[5425-44-5]

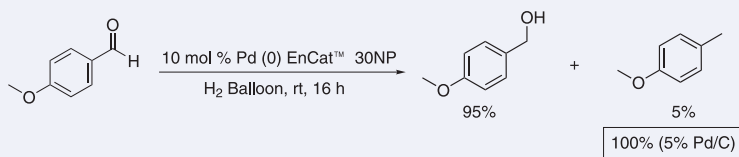
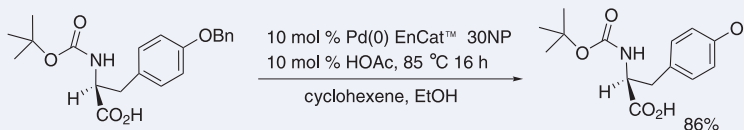


279617-5G	5 g
279617-25G	25 g

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Pd  
FW: 106.42

653667-1G	1 g
653667-10G	10 g
653667-100G	100 g

(1) Bremeyer, N.; Ley, S. V.; Ramarao, C.; Shirley, I. M.; Smith, S. C. *Synlett* **2002**, 1843. (2)(a) Yu, J.-Q.; Wu, H.-C.; Ramarao, C.; Spencer, J. B.; Ley, S. V. *Chem. Commun.* **2003**, 678. (b) Ley, S. V.; Mitchell, C.; Pears, D.; Ramarao, C.; Yu, J.-Q.; Zhou, W. *Org. Lett.* **2003**, 5, 4665.

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## References

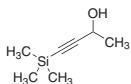
- (1) For a recent example, see: Denmark, S. E.; Wehrli, D. *Org. Lett.* **2000**, *2*, 565.
- (2) For recent examples, see:
  - (a) Itami, K. et al. *J. Org. Chem.* **2002**, *67*, 2645.
  - (b) Denmark, S. E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073.
  - (c) Denmark, S. E.; Wang, Z. *Org. Synth.* **2005**, *81*, 54.
- (3) Takeuchi, R. et al. *J. Org. Chem.* **1995**, *60*, 3045.
- (4) Sato, A. et al. *Org. Lett.* **2004**, *6*, 2217.
- (5) Takeuchi, R.; Tanouchi, N. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2909.
- (6) Na, Y.; Chang, S. *Org. Lett.* **2000**, *2*, 1887.
- (7) (a) Maifeld, S. V. et al. *Tetrahedron Lett.* **2005**, *46*, 105.  
 (b) Menozzi, C. et al. *J. Org. Chem.* **2005**, *70*, 10717.  
 (c) Aricó, C. S.; Cox, L. R. *Org. Biomol. Chem.* **2004**, *2*, 2558.
- (8) While references 7a and 7b illustrate access to  $\alpha$ -vinylsilanes using  $\text{Ph}_3\text{SiH}$ , the method does not appear to be general. Isomeric mixtures are often formed with other silanes.
- (9) For recent examples, see:
  - (a) Denmark, S. E.; Pan, W. *Org. Lett.* **2003**, *5*, 1119.
  - (b) Denmark, S. E.; Pan, W. *Org. Lett.* **2002**, *4*, 4163.
  - (c) Denmark, S. E.; Pan, W. *Org. Lett.* **2001**, *3*, 61.
- (10) For a recent example, see: Hamze, A. et al. *Org. Lett.* **2005**, *7*, 5625.
- (11) (a) Trost, B. M. et al. *J. Am. Chem. Soc.* **2001**, *123*, 12726.  
 (b) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17644.
- (12) For a mechanistic rationale of this Ru-catalyzed hydrosilylation, see: Chung, L. W. et al. *J. Am. Chem. Soc.* **2003**, *125*, 11578.
- (13) Trost, B. M. et al. *J. Am. Chem. Soc.* **2002**, *124*, 7922.
- (14) Trost, B. M. et al. *Org. Lett.* **2003**, *5*, 1895.
- (15) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2004**, *126*, 13942.
- (16) (a) Trost, B. M. et al. *Angew. Chem. Int. Ed.* **2003**, *42*, 3415.  
 (b) Trost, B. M. et al. *J. Am. Chem. Soc.* **2005**, *127*, 10028.  
 (c) Trost, B. M. et al. *Org. Lett.* **2005**, *7*, 4911.
- (17) Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2003**, *125*, 30.
- (18) For recent reviews, see:
  - (a) Denmark, S. E.; Sweis, R. F. *Acc. Chem. Res.* **2002**, *35*, 835.
  - (b) Denmark, S. E.; Sweis, R. F. *Chem. Pharm. Bull.* **2002**, *50*, 1531.  
 (c) Denmark, S. E.; Ober, M. H. *Aldrichimica Acta* **2003**, *36*, 75.
- (19) Denmark, S. E.; Neuville, L. *Org. Lett.* **2000**, *2*, 3221.
- (20) Denmark, S. E.; Baird, J. D. *Org. Lett.* **2006**, *8*, 793.
- (21) Hirabayashi, K. et al. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1409.
- (22) Denmark, S. E.; Kallemeyn, J. M. *Org. Lett.* **2003**, *5*, 3483.
- (23) For mechanistic implications of fluoride vs. basic activation of dimethylsilanols in Pd-catalyzed cross-coupling, see:
  - (a) Denmark, S. E. et al. *J. Am. Chem. Soc.* **2004**, *126*, 4865.
  - (b) Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2004**, *126*, 4876.
  - (c) Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 6439.
  - (d) Denmark, S. E.; Tymonko, S. A. *J. Org. Chem.* **2003**, *68*, 9151.
  - (e) Denmark, S. E.; Fujimori, S. *J. Am. Chem. Soc.* **2005**, *127*, 8971.
  - (f) Denmark, S. E.; Tymonko, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 8004.
  - (g) Denmark, S. E.; Ober, M. H. *Org. Lett.* **2003**, *5*, 1357.  
 (h) Denmark, S. E.; Ober, M. H. *Adv. Synth. Catal.* **2004**, *346*, 1703.
  - (i) Labadie, S. S.; Teng, E. *J. Org. Chem.* **1994**, *59*, 4250.
  - (j) (a) Tyrell, E.; Brookes, P. *Synthesis* **2003**, 469.  
 (b) Johnson, C. N. et al. *Synlett* **1998**, 1025.
  - (k) Denmark, S. E.; Baird, J. D. *Org. Lett.* **2004**, *6*, 3649.
  - (l) For examples of cross-coupling of dimethyl(4-isoxazolyl)silanols, see: Denmark, S. E.; Kallemeyn, J. M. *J. Org. Chem.* **2005**, *70*, 2839.
  - (m) (a) Weissman, H. et al. *Organometallics* **2004**, *23*, 3931.  
 (b) Werner, H.; Kühn, A. *J. Organomet. Chem.* **1979**, *179*, 439.
  - (n) Manoso, A. S. et al. *J. Org. Chem.* **2004**, *69*, 8305.
  - (o) Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 6790.
  - (p) (a) Manoso, A. S.; DeShong, P. *J. Org. Chem.* **2001**, *66*, 7449.  
 (b) Murata, M. et al. *Org. Lett.* **2002**, *4*, 1843.  
 (c) Murata, M. et al. *J. Org. Chem.* **1997**, *62*, 8569.
  - (q) (a) Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 1684.  
 (b) McElroy, W. T.; DeShong, P. *Org. Lett.* **2003**, *5*, 4779.  
 (c) Tamao, K. et al. *Tetrahedron Lett.* **1989**, *30*, 6051.
  - (r) Seganish, W. M. et al. *J. Org. Chem.* **2005**, *70*, 8948.
  - (s) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616.
  - (t) Oi, S. et al. *Org. Lett.* **2002**, *4*, 667.
  - (u) DeShong, P.; Correia, R. *J. Org. Chem.* **2001**, *66*, 7159.
  - (v) (a) Denmark, S. E.; Wang, Z. *Synthesis* **2000**, 999.  
 (b) Denmark, S. E.; Wang, Z. *J. Organomet. Chem.* **2001**, *621*, 372.
  - (w) Denmark, S. E.; Butler, C. R. *Org. Lett.* **2006**, *8*, 63.
  - (x) Corey, E. J.; Seebach, D. *Angew. Chem. Int. Ed.* **1965**, *4*, 1075.
  - (y) (a) Smith, A. B., III; Boldi, A. M. *J. Am. Chem. Soc.* **1997**, *119*, 6925.  
 (b) Smith, A. B., III et al. *J. Am. Chem. Soc.* **2003**, *125*, 14435.
  - (z) For an example, see: Smith, A. B., III et al. *Org. Lett.* **2002**, *4*, 783.
  - (aa) Smith, A. B., III et al. *Org. Lett.* **2003**, *5*, 2751.
  - (ab) Poss, C. S. et al. *J. Am. Chem. Soc.* **1993**, *115*, 3360.
  - (ac) Smith, A. B., III; Pitram, S. M. *Org. Lett.* **1999**, *1*, 2001.
  - (ad) (a) Smith, A. B., III; Kim, D.-S. *Org. Lett.* **2005**, *7*, 3247.  
 (b) Smith, A. B., III; Kim, D.-S. *J. Org. Chem.* **2006**, *71*, 2547.
  - (ae) Smith, A. B., III; Xian, M. *J. Am. Chem. Soc.* **2006**, *128*, 66.

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## 4-(Trimethylsilyl)-3-butyn-2-ol, 97% NEW

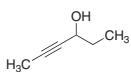
C<sub>7</sub>H<sub>14</sub>OSi  
FW: 142.27  
[6999-19-5]



666955-5G	5 g
666955-25G	25 g

## 4-Hexyn-3-ol, 97% NEW

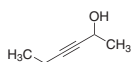
C<sub>6</sub>H<sub>10</sub>O  
FW: 98.14  
[20739-59-7]



669318-1G	1 g
669318-10G	10 g

## 3-Hexyn-2-ol, 97% NEW

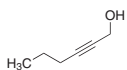
C<sub>6</sub>H<sub>10</sub>O  
FW: 98.14  
[109-50-2]



669296-5G	5 g
669296-25G	25 g

## 2-Hexyn-1-ol, 97%

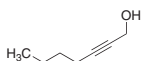
C<sub>6</sub>H<sub>10</sub>O  
FW: 98.14  
[764-60-3]



630829-5G	5 g
630829-25G	25 g

## 2-Heptyn-1-ol, 97%

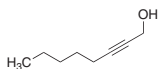
C<sub>7</sub>H<sub>12</sub>O  
FW: 112.17  
[1002-36-4]



630810-5G	5 g
630810-25G	25 g

## 2-Octyn-1-ol, 97%

C<sub>8</sub>H<sub>14</sub>O  
FW: 126.20  
[20739-58-6]



630837-5G	5 g
630837-25G	25 g

## 1-Pentyn-3-ol, 98%

C<sub>5</sub>H<sub>8</sub>O  
FW: 84.12  
[4187-86-4]



E28404-1G	1 g
E28404-10G	10 g

## 2-(2-Fluorophenyl)-3-butyn-2-ol

C<sub>10</sub>H<sub>9</sub>FO  
FW: 164.18



648949-1G	1 g
-----------	-----

## 1-Ethynyl-1-cyclohexanol, 99%

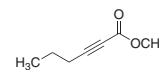
C<sub>8</sub>H<sub>12</sub>O  
FW: 124.18  
[78-27-3]



E51406-5ML	5 mL
E51406-100ML	100 mL

## Methyl 2-hexynoate, 98%

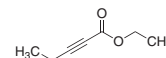
C<sub>7</sub>H<sub>10</sub>O<sub>2</sub>  
FW: 126.15  
[18937-79-6]



649090-5G	5 g
649090-25G	25 g

## Ethyl 2-pentynoate, 97%

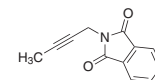
C<sub>7</sub>H<sub>10</sub>O<sub>2</sub>  
FW: 126.15  
[55314-57-3]



632112-5G	5 g
632112-25G	25 g

## N-(2-Butynyl)phthalimide, 97%

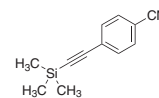
C<sub>12</sub>H<sub>9</sub>NO<sub>2</sub>  
FW: 199.21  
[113439-83-1]



663034-5G	5 g
663034-25G	25 g

## 4-Trimethylsilylethynylbenzonitrile, 97%

C<sub>12</sub>H<sub>13</sub>NSi  
FW: 199.32  
[75867-40-2]



658391-1G	1 g
658391-10G	10 g

## 3-Cyclopentyl-1-propyne, 97%

C<sub>8</sub>H<sub>12</sub>  
FW: 108.18  
[116279-08-4]



632074-1G	1 g
632074-5G	5 g

## 3-Cyclohexyl-1-propyne, 97%

C<sub>9</sub>H<sub>14</sub>  
FW: 122.21  
[17715-00-3]



632066-1G	1 g
632066-5G	5 g

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