



Pd-catalyzed cross-coupling of alkynylsilanols with iodobenzenes

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Abstract—Alkynylsilanols were efficiently coupled with iodobenzene derivatives by a Pd catalyst in the presence of TBAF, and the corresponding substituted alkynes could be obtained in good to excellent yields. © 2001 Elsevier Science Ltd. All rights reserved.

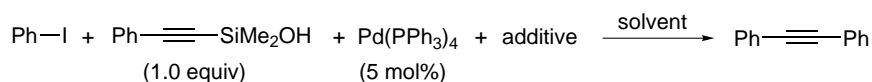
Alkynes are one of the most important structural building blocks in organic synthesis and material science¹ and numerous methods are now available for the preparation of alkyne derivatives; among those, the Pd-catalyzed acetylenic coupling reaction (Sonogashira protocol) is most notable.² Despite recent progress,³ new synthetic routes for the formation of substituted alkynes are still necessary to achieve milder reaction conditions and wider substrate scope. Since the pioneering works initiated by Hiyama⁴ and Denmark⁵ the Pd-catalyzed coupling reactions between alkynylsilanols or arylsilanols and aryl- or alkenylhalides (or their equivalents) have been emerging as a powerful new procedure for the formation of C–C bonds. These coupling reactions are especially notable because the silicon substrates are non-toxic and reaction conditions are usually mild.⁶ During the course of our recent studies on the practical synthesis of organosilanols,⁷ we

found for the first time that alkynylsilanols can serve as facile coupling partners to react with various iodobenzene derivatives, which will be described in this letter.⁸

With the use of iodobenzene and 1.0 equiv. of dimethyl(phenylethynyl)silanol as a standard set of coupling partners, various additives were examined for the coupling reaction (Table 1).

Among the various palladium catalysts tested, Pd(PPh₃)₄ was most effective for the coupling reaction in THF at 60°C. In accord with the previous reports,^{4,5} tetrabutylammonium fluoride (TBAF) and silver oxide turned out to be the best activators for the cross-coupling although silver oxide afforded a slightly lower conversion compared to TBAF (compare entries 4 and 5). Increasing the equivalents of TBAF did not exhibit

Table 1. Effects of various additives on the Pd-catalyzed coupling between dimethyl(phenylethynyl)silanol and iodobenzene^a



Entry	Additive (equiv.)	Solvent	T (°C)	Time (h)	Conversion (%) ^b
1	None	THF	60	12	<5
2	K ₂ CO ₃ (1.0)	THF	60	12	<5
3	CsF (1.0)	THF	60	12	<5
4	Ag ₂ O (1.0)	THF	60	2	78
5	TBAF (1.0)	THF	60	2	90
6	TBAF (2.0)	THF	60	2	90
7	TBAF (1.0)	Benzene	60	2	62
8	TBAF (1.0)	THF	40	2	45

^a All reactions were carried out in 0.1 M solutions.

^b Conversion was calculated by ¹H NMR integration.

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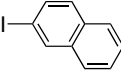
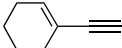
any enhanced effects on the reaction rates and conversion (entry 6). THF was the solvent of choice and other reaction media were less effective. Conversion of the coupling was significantly decreased at lower temperatures (entry 8). Other additives, such as K_2CO_3 or CsF , were much less effective for the coupling reaction compared to TBAF.

Good to excellent yields could be obtained from the Pd-catalyzed coupling reactions across a wide range of alkynylsilanols and iodobenzene derivatives using the established reaction conditions (Table 2).⁹

Dimethyl(phenylethynyl)silanol (**A**) reacted with various iodobenzenes to afford the corresponding coupled products in high yields. Electronic variation on the iodobenzenes exhibited little effect on the reaction rates and yields (entries 1–5). Reaction of **A** with 2-iodonaphthalene also proceeded with similar efficiency (entry 6). The coupling reaction of alkynylsilanols with bromobenzene was negligible under the employed con-

ditions and chemoselective coupling was possible with 3-bromiodobenzene (entry 5). A silanol bearing sterically bulky substituents on the silicon atom such as **B** was less reactive and reaction of the silanol with iodobenzene afforded the coupled product in moderate yield (entry 7). Derivatization of the substituents on alkyne¹⁰ had little effect on the reaction efficiency, and coupling reactions of the aliphatic alkynylsilanols proceeded with similar rates and yields when compared to aryl alkynylsilanols. For example, dimethyl(1-hexynyl)silanol (**C**) was readily coupled with several iodobenzene derivatives to generate alkynes bearing alkyl- or aryl-substituents in high yields (entries 8–10). In contrast, alkynylsilanols having a halogen group such as **D** were less effective in the coupling reactions and reaction using silanol **D** with iodobenzenes proceeded in moderate yields (entries 11 and 12). Conjugated enynylsilanol (**E**) was also competent for the coupling reaction to afford substituted alkynes in good yields (entries 13 and 14). Certain advantages of this new cross-coupling over the related reactions using

Table 2. Pd-catalyzed coupling of alkynylsilanols with iodobenzene derivatives^a

$\text{Ar-I} + \text{R}_1\text{-}\equiv\text{-Si(R}_2)_2\text{OH} + \text{Pd(PPh}_3)_4 + \text{TBAF} \xrightarrow[60\text{ }^\circ\text{C}]{\text{THF}} \text{Ar}\text{-}\equiv\text{-R}_1$				
$\begin{matrix} & (1.5 \text{ equiv}) & (5 \text{ mol}\%) & (1.0 \text{ equiv}) & \\ & & & & \end{matrix}$				
entry	silanol	iodobenzene	time (h)	yield (%) ^b
1	Ph- \equiv -SiMe ₂ OH (A)	I-Ph	2.5	97
2	(A)	I-C ₆ H ₄ (<i>p</i> -Me)	3	99
3	(A)	I-C ₆ H ₄ (<i>m</i> -Me)	2.5	95
4	(A)	I-C ₆ H ₄ (<i>p</i> -COMe)	2	78
5	(A)	I-C ₆ H ₄ (<i>m</i> -Br)	2	73
6	(A)		3	71
7	Ph- \equiv -Si(<i>i</i> -Pr) ₂ OH (B)	I-C ₆ H ₄ (<i>p</i> -COMe)	3	52
8	CH ₃ (CH ₂) ₂ - \equiv -SiMe ₂ OH (C)	I-Ph	2	95
9	(C)	I-C ₆ H ₄ (<i>p</i> -Me)	3	90
10	(C)	I-C ₆ H ₄ (<i>p</i> -COMe)	2	72
11	Cl(CH ₂) ₃ - \equiv -SiMe ₂ OH (D)	I-Ph	2	66
12	(D)	I-C ₆ H ₄ (<i>p</i> -Me)	2	62
13	 - \equiv -SiMe ₂ OH (E)	I-Ph	2	70
14	(E)	I-C ₆ H ₄ (<i>p</i> -Me)	1	77

^a All reactions were carried out in 0.1 M solutions.

^b Isolated yields after silica-gel column chromatography.

trimethylsilyl (TMS) acetylenes (Sila–Sonogashira coupling) can be clearly found. For example, this method does not require expensive tris(diethylamino)sulfonium trimethyldifluorosilicate (TASF)^{8a,b} or CuCl^{8c} as an additive. In addition, the presented procedure provides coupled alkyne products with higher yields in shorter reaction times when compared to those obtained for the TMS variant, in general.

In conclusion, we have demonstrated that various types of alkynylsilanols could be efficiently coupled with iodobenzenes with the use of a Pd/TBAF system to afford the corresponding substituted alkyne derivatives in good to excellent yields. High efficiency of the coupling reaction combined with practical preparation of the alkynylsilanols would make this procedure an appealing alternative to the existing methods for the generation of substituted alkynes.¹¹

Acknowledgements

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9. **Representative experimental procedure:** To a stirred solution of iodobenzene (40.8 mg, 0.20 mmol) in THF (2.0 mL) was added dimethyl(phenylethynyl)silanol (55.4 mg, 0.3 mmol) followed by Pd(PPh₃)₄ (12.0 mg, 5 mol%) and tetrabutylammonium fluoride (1.0 M in THF, 0.20 mL). The reaction mixture was stirred at 60°C for 2.5 h. After removal of the solvent under the reduced pressure, the residue was purified by flash column chromatography on silica gel (hexane) to afford diphenylacetylene in 94% yield.
10. All alkynylsilanols used in this study were prepared in almost quantitative yields according to the procedure reported from this laboratory (Ref. 7).
11. Although a recent report by the Mori group (Ref. 3) showed that the coupling could be carried out without Cu-cocatalyst or amines, the reaction times were generally longer and the product yields were lower than those of the present procedure.