



## Palladium-catalyzed cross-coupling reaction of aryl trimethoxysilanes with terminal alkynes

Zhishi Ye, Miaochang Liu, Baoda Lin, Huayue Wu, Jinchang Ding, Jiang Cheng\*

College of Chemistry and Materials Science, Wenzhou University, Wenzhou 325027, PR China

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### ABSTRACT

A palladium-catalyzed cross-coupling reaction of aryl trimethoxysilanes with terminal alkynes was described. Thus, di-substituted alkynes were prepared in moderate to good yields. The electron-deficient terminal alkynes also worked well in the procedure.

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Alkynes are a recurring functional group in a wide range of natural products and other bioactive compounds, as well as versatile intermediates in synthesis.<sup>1</sup> Since its introduction in 1975, the Sonogashira reaction is one of the most straightforward methods for the preparation of aforementioned compounds.<sup>2</sup> Although an impressive variety of modifications have been reported for this reaction,<sup>3</sup> some drawbacks still remained. For example, alkynes substituted with electron-withdrawing groups have indeed been generally poor nucleophiles in the Sonogashira alkylation. And excess alkynes were required due to the oxidative dimerization reaction of alkynes in Sonogashira reaction. In 2003, Zou et al. reported a new procedure for constructing arylalkynes through cross-coupling of terminal alkynes with arylboronic acids catalyzed by a palladium–silver system under mild conditions.<sup>4</sup> Very recently, Wu and co-workers described the cross-coupling reaction of arylboronic reagents with terminal alkynes catalyzed by cyclopalladated ferrocenylimine/silver(I) oxide at room temperature.<sup>5</sup> Compared with the organoborons, organosilane reagents especially aryl triethoxysilanes are of lower cost<sup>6</sup> and are easily purified by distillation or chromatography.<sup>7</sup> However, to the best of our knowledge, employing organosilanes in this transformation was scarcely reported or studied before.<sup>8</sup> Herein, we wish to report a mild palladium-catalyzed cross-coupling reaction of aryl trimethoxysilanes with terminal alkynes, providing the aryl alkynes in moderate to good yields.

Initial studies were conducted using phenyl trimethoxysilane (**1a**) and phenyl acetylene (**2a**) in CH<sub>2</sub>Cl<sub>2</sub> as a model reaction under air with the combination of 3.0 mol % of PdCl<sub>2</sub>(dppf), 3 equiv of various fluoride sources, and bases. The results suggested that the fluoride sources had dramatic effects on the yields of the cross-coupling reaction. Among the fluoride sources screened, only AgF and AgF<sub>2</sub> showed good catalytic activity (Table 1, entries 2 and 3). The bases were also crucial in this transformation. NaHCO<sub>3</sub> was

the most effective among the tested bases, and the yield of **3aa** was sharply increased to 87% (Table 1, entry 11). Other bases, such as KOAc and KHCO<sub>3</sub>, also accelerated the cross-coupling process but not as effectively as NaHCO<sub>3</sub> (Table 1, entries 9 and 10 vs entry 11). Remarkably, switching the solvent to CH<sub>3</sub>CN led to a superior yield (Table 1, entry 14). Several palladium sources were also examined, PdCl<sub>2</sub>(dppf) turned out to be better than other ones.

Under our optimized reaction conditions (3.0 mol % of PdCl<sub>2</sub>(dppf), 3 equiv of AgF and 3 equiv of NaHCO<sub>3</sub> in CH<sub>3</sub>CN), we examined the scope of this transformation. The results are summarized in Table 2. The aryl trimethoxysilane substrates

**Table 1**

Effects of Pd sources, solvents, bases, and F sources on the palladium-catalyzed cross-coupling reaction of phenyl trimethoxysilane with phenyl acetylene

PhSi(OMe) <sub>3</sub> + Ph—C≡C—H		Pd, F source		Ph—C≡C—Ph	
<b>1a</b>		<b>2a</b>		<b>3aa</b>	
Entry	Pd source	Solvent	F source	Base	Yield <sup>a</sup> (%)
1	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	KF	K <sub>2</sub> CO <sub>3</sub>	<5
2	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	K <sub>2</sub> CO <sub>3</sub>	62
3	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	59
4	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	CuF <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	<5
5	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	TBAF·3H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	<5
6	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	Na <sub>2</sub> CO <sub>3</sub>	<5
7	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	AcOK	31
8	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	<sup>t</sup> BuOK	<5
9	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	K <sub>3</sub> PO <sub>4</sub> ·3H <sub>2</sub> O	35
10	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	KHCO <sub>3</sub>	85
11	PdCl <sub>2</sub> (dppf)	CH <sub>2</sub> Cl <sub>2</sub>	AgF	NaHCO <sub>3</sub>	87
12	PdCl <sub>2</sub> (dppf)	Toluene	AgF	NaHCO <sub>3</sub>	20
13	PdCl <sub>2</sub> (dppf)	THF	AgF	NaHCO <sub>3</sub>	42
14	PdCl <sub>2</sub> (dppf)	CH <sub>3</sub> CN	AgF	NaHCO <sub>3</sub>	93
15	PdCl <sub>2</sub> (dppf)	DMF	AgF	NaHCO <sub>3</sub>	34
16	PdCl <sub>2</sub>	CH <sub>3</sub> CN	AgF	NaHCO <sub>3</sub>	84
17	Pd(OAc) <sub>2</sub>	CH <sub>3</sub> CN	AgF	NaHCO <sub>3</sub>	84

<sup>a</sup> PhSi(OMe)<sub>3</sub> (59 mg, 0.3 mmol), phenyl acetylene (20 mg, 0.2 mmol), palladium source (3 mol %), indicated base (0.6 mmol), and fluoride source (0.6 mmol) in dry solvent (3 mL), rt, 3 h. Isolated yield.

\* Corresponding author. Tel./fax: +86 577 88156826.  
E-mail address: jiangcheng@wzu.edu.cn (J. Cheng).

**Table 2**  
Cross-coupling reaction of aryl trimethoxysilane with phenyl acetylene

$\text{ArSi(OMe)}_3 + \text{Ph-C}\equiv\text{C-H} \xrightarrow[\text{NaHCO}_3, \text{CH}_3\text{CN}]{\text{Pd, AgF}} \text{Ph-C}\equiv\text{C-Ar}$			
1	2a	3	
Entry	Ar	Product	Yield <sup>a</sup> (%)
1	Ph <b>1a</b>	Ph-C≡C-Ph <b>3aa</b>	93
2	4-Tolyl <b>1b</b>	Ph-C≡C-4-tolyl <b>3ba</b>	90
3	2-Tolyl <b>1c</b>	Ph-C≡C-2-tolyl <b>3ca</b>	93
4	2-Anisoyl <b>1d</b>	Ph-C≡C-2-anisoyl <b>3da</b>	93
5	4-Anisoyl <b>1e</b>	Ph-C≡C-4-anisoyl <b>3ea</b>	99
6	3,5-Xylenyl <b>1f</b>	Ph-C≡C-3,5-xylenyl <b>3fa</b>	94
7	Naphthenyl <b>1g</b>	Ph-C≡C-naphthenyl <b>3ga</b>	88
8	2-Naphthenyl <b>1h</b>	Ph-C≡C-2-naphthenyl <b>3ha</b>	64

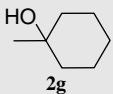
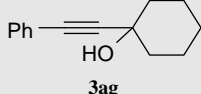
<sup>a</sup> ArSi(OMe)<sub>3</sub> (0.3 mmol), phenyl acetylene (20 mg, 0.2 mmol), PdCl<sub>2</sub>(dppf) (4.4 mg, 3 mol %), NaHCO<sub>3</sub> (50 mg, 0.6 mmol), and AgF (76 mg, 0.6 mmol) in dry CH<sub>3</sub>CN (3 mL), rt, 3 h. Isolated yield.

worked well under the reaction conditions. Electron-donating as well as electron-neutral aryl trimethoxysilanes coupled efficiently with phenylacetylene, and good yields were obtained (Table 2, entries 1–6). The dimerization of terminal alkynes, which is a serious side-reaction in the Sonogashira reaction, was inhibited in the procedure. And nearly quantitative yield of **3ea** was produced based on the phenyl acetylene used. The method is also tolerant of *ortho*-substitution in aryl trimethoxysilanes, and the hindrance had little effect on the reaction (Table 2, entries 3 and 4). When naphthalen-1-yl trimethoxysilane (**1f**) and naphthalen-2-yl trimethoxysilane (**1h**) were employed as the substrates, **3ga** and **3ha** were obtained in 88% and 64% yields, respectively (Table 2, entries 7 and 8).

In the next stage, we explored the reaction of a variety of alkynes with PhSi(OMe)<sub>3</sub>, as shown in Table 3. It is notable that the electron-deficient ethyl propiolate (**2b**) also gave good yields (Table 3, entry 1), whereas the traditional Sonogashira reaction does not work well for electron-deficient alkynes. As such, this represents a simple and practical complementary method for the Sonogashira reaction. However, for hydroxy containing alkynes (**2d** and **2g**) and aliphatic alkyne (**2c**), lower yields were obtained (Table 3, entries 3, 5, and 2).

Based upon the experimental results and the mechanism of previous reports,<sup>5</sup> a plausible mechanism is outlined (Scheme 1). The catalytic cycle may contain four steps: (1) transmetalation of palladium(II) with [ArSiF(OMe)<sub>3</sub>]<sup>−</sup> gives the palladium(II) species **5**; (2) palladium(II) intermediate **5** then encounters the second transmetalation with alkynylsilver(I) to afford palladium(II) species **6**; (3) intermediate **6** reductively eliminates to form the desired product **3** and produces palladium(0); (4) the palladium(0) species is oxidized by the silver(I) species, and palladium(II) is regenerated.

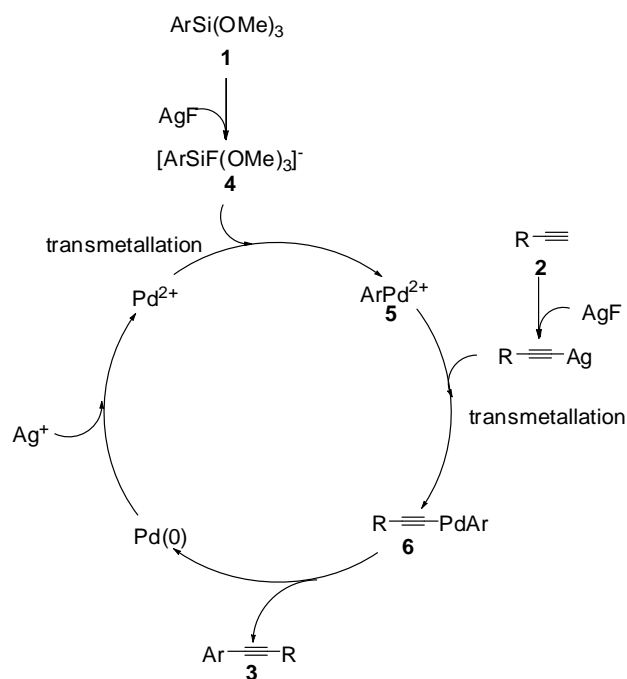
**Table 3**  
Cross-coupling reaction of phenyl trimethoxysilane with alkynes

$\text{PhSi(OMe)}_3 + \text{R-C}\equiv\text{C-H} \xrightarrow[\text{NaHCO}_3, \text{CH}_3\text{CN}]{\text{Pd, AgF}} \text{Ph-C}\equiv\text{C-R}$			
1a	2	3	
Entry	R	Product	Yield <sup>a</sup> (%)
1	COOEt <b>2b</b>	Ph-C≡C-COOEt <b>3ab</b>	76 <sup>b</sup>
2	Bn <b>2c</b>	Ph-C≡C-Bn <b>3ac</b>	51 <sup>b</sup>
3	CH <sub>2</sub> OH <b>2d</b>	Ph-C≡C-CH <sub>2</sub> OH <b>3ad</b>	45
4	CH <sub>2</sub> N(Et) <sub>2</sub> <b>2e</b>	Ph-C≡C-CH <sub>2</sub> N(Et) <sub>2</sub> <b>3ae</b>	59
5	CH(OEt) <sub>2</sub> <b>2f</b>	Ph-C≡C-CH(OEt) <sub>2</sub> <b>3af</b>	38
6	 <b>2g</b>	 <b>3ag</b>	50

<sup>a</sup> PhSi(OMe)<sub>3</sub> (59 mg, 0.3 mmol), aryl acetylene (0.2 mmol), PdCl<sub>2</sub>(dppf) (4.4 mg, 3 mol %), NaHCO<sub>3</sub> (50 mg, 0.6 mmol), and AgF (76 mg, 0.6 mmol) in dry CH<sub>3</sub>CN (3 mL), rt, 3 h. Isolated yield.

<sup>b</sup> Dry CH<sub>2</sub>Cl<sub>2</sub> (3 mL). Isolated yield.

In conclusion, we have successfully developed a new method of palladium-catalyzed cross-coupling reaction of aryl trimethoxysilanes with terminal alkynes. The procedure possessed a broad scope, including electron-poor alkynes, for which the traditional



## Acknowledgments

Scheme 1. Plausible mechanism.

Sonogashira reaction did not work well. Efforts to apply the catalytic system in other cross-coupling transformations are underway in our laboratory.<sup>9</sup>

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tetlet.2008.11.049](https://doi.org/10.1016/j.tetlet.2008.11.049).

### References and notes

- (a) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387; (b) Maier, M. E. *Synlett* **1995**, 13; (c) Grissom, J. W.; Gunawardena, G. U.; Kingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453; (d) Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605; (e) Tour, J. M. *Acc. Chem. Res.* **2000**, *33*, 791; (f) Siems, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632; (g) Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1350.
- (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467; (b) Cassar, L. J. *Organomet. Chem.* **1975**, *93*, 253; (c) Dieck, H. A.; Heck, F. R. J. *Organomet. Chem.* **1975**, *93*, 259.
- For recent reviews, see: (a) Negishi, E.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979; (b) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874. For recent examples, see: (c) Liang, B.; Dai, M.; Chen, J.; Yang, Z. *J. Org. Chem.* **2005**, *70*, 391; (d) Li, J.-H.; Hu, X.-C.; Xie, Y.-X. *Tetrahedron* **2006**, *62*, 31; (e) Li, J.-H.; Zhang, X.-D.; Xie, Y.-X. *J. Org. Chem.* **2005**, *70*, 4256; (f) Cheng, J.; Sun, Y.; Wang, F.; Guo, M.; Xu, J.-H.; Pan, Y.; Zhang, Z. *J. Org. Chem.* **2004**, *69*, 5428; (g) Zhang, W.; Wu, H.; Liu, Z.; Zhong, P.; Zhang, L.; Huang, X.; Cheng, J. *Chem. Commun.* **2006**, 4826; (h) Doucet, H.; Hierso, J. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 834; (i) Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5993; (j) Mori, A.; Kawashima, J.; Shimada, T.; Suguro, M.; Hirabayashi, K.; Nishihara, Y. *Org. Lett.* **2000**, *2*, 2935; (k) Urganonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 5752; (l) Elangovan, A.; Wang, Y. H.; Ho, T. I. *Org. Lett.* **2003**, *5*, 1841; (m) Mino, T.; Shirae, Y.; Saito, T.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 9499; (n) Ma, D.; Liu, F. *Chem. Commun.* **2004**, 1934; (o) Carril, M.; Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 4862.
- Zou, G.; Zhu, J.; Tang, J. *Tetrahedron Lett.* **2003**, *44*, 8709.
- Yang, F.; Wu, Y.-J. *Eur. J. Org. Chem.* **2007**, 3476.
- Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1; pp 125–162.
- Manoso, A. S.; Ahn, C.; Soheil, A.; Handy, C. J.; Correia, R.; Seganiash, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 8305.
- Selected examples in the cross-coupling employing ArSi(OMe)<sub>3</sub>: (a) Shi, S.; Zhang, Y. *J. Org. Chem.* **2007**, *72*, 5927; (b) Li, J.-H.; Deng, C.-L.; Xie, Y.-X. *Synthesis* **2006**, 969; (c) Seganiash, W. M.; DeShong, P. *Org. Lett.* **2006**, *8*, 3951; (d) Li, J.-H.; Deng, C.-L.; Liu, W.-J.; Xie, Y.-X. *Synthesis* **2005**, 3039; (e) Wolf, C.; Lerebours, R. *Org. Lett.* **2004**, *6*, 1147; (f) Ranu, B. C.; Dey, R.; Chattopadhyay, K. *Tetrahedron Lett.* **2008**, *49*, 3430; (g) Ju, J.; Nam, H.; Jung, H. M.; Lee, S. *Tetrahedron Lett.* **2006**, *47*, 8673; (h) Lee, H. M.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 2053; (i) Pan, C.; Liu, M.; Zhao, L.; Wu, H.; Ding, J.; Cheng, J. *Catal. Commun.* **2008**, *9*, 1685.
- General procedure*: Under air, a reaction tube was charged with terminal alkynes (0.2 mmol), aryl trimethoxysilane (0.3 mmol), PdCl<sub>2</sub>(dppf) (4.4 mg, 3 mol %), NaHCO<sub>3</sub> (50 mg, 0.6 mmol), AgF (76 mg, 0.6 mmol), and dry CH<sub>2</sub>CN or dry CH<sub>2</sub>Cl<sub>2</sub> (3 mL). The mixture was stirred at room temperature. The mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on a silica gel to give the desired product.