

## Palladium-Catalyzed Cross-Coupling Reaction of Aryltriethoxysilanes with Aryl Bromides under Basic Aqueous Conditions

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**Abstract:** Aryltriethoxysilanes were cross-coupled with aryl bromides in high yield in the presence of a palladium catalyst and aqueous sodium hydroxide.

**Keyword:** Siloxane derivatives, Cross-coupling, Palladium catalyst, Aryl bromides, Biaryls

Palladium-catalyzed cross-coupling reactions of organometallic reagents, such as organoboron (Suzuki-Miyaura reaction)<sup>1</sup> and -tin compounds (Stille-Kosugi-Migita reaction),<sup>2</sup> have been shown to be versatile methods for carbon-carbon bond formation. Particularly, the Suzuki-Miyaura reaction is performed without special precautions and has achieved prominence, because it is unaffected by the presence of water and yields non-toxic by-products. From the economic and environmental points of view, however, silicon reagents should be more convenient coupling reagents. Although Hiyama and Hatanaka have developed fluoride ion-promoted cross-coupling reactions of moisture-sensitive organofluorosilanes,<sup>3</sup> considerable attention has been paid to organoalkoxysilanes due to their stability and reactivity.<sup>4</sup> The coupling reaction of aryltrimethoxysilanes in the presence of fluoride ion has recently been investigated independently by Shibata<sup>4b</sup> and DeShong,<sup>4c</sup> but the electronic characteristics of aryl halides have a significant impact on the reactions.

In this paper, we describe a practical example of the cross-coupling reaction of aryltriethoxysilanes **1** with aryl bromides **2** (eq 1) in the presence of an aqueous base. We have recently developed the atom-economical and chemoselective silylation of organic halides utilizing triethoxysilane as silylating reagents in the presence of

palladium complexes to afford the corresponding **1**.<sup>5, 6</sup> Considering the availability of ethyl siloxane derivatives **1**, the present coupling should have several advantages to allow for a wide range of biaryls **3**.

<<eq. 1, Table 1>>

A series of reactions of phenyltriethoxysilane **1a** (0.6 mmol) with **2a** (0.5 mmol) were performed under several conditions for optimization studies. This coupling work was achieved with the aid of an aqueous base analogous to the Suzuki–Miyaura reaction.<sup>1</sup> In the presence of PdCl<sub>2</sub>(MeCN)<sub>2</sub> (0.015 mmol) and an aqueous solution of hydroxide ion (1.5 mmol) as an accelerating additive, the reaction in dioxane (2 ml) gave the desired biaryl **3** in 78-94% yields along with a small quantity of homo-coupled product **4** (Table 1, entries 1 and 2). Recently, Hiyama and co-workers reported that NaOH powder was an effective promoter for the coupling reaction of organochlorosilanes in the absence of water,<sup>7</sup> but the aqueous base was essential for the present work (entry 3). Fluoride ion, one of the more well-known activators of organosilanes, was less effective (entries 4 and 5). Several solvents including DME and toluene were tested, and it was observed that the reaction in ether solvents afforded the cross-coupled product **3** (entries 6 and 7).

The presence of a phosphine ligand slowed down the reaction rate and significantly increased the by-product yield (entry 10). Thus, the present reaction was efficiently catalyzed by the phosphine-free palladium catalyst (entries 1, 8, and 9). Nevertheless, palladium black as a precipitate was observed during the reaction. As well, in the case of aryl halides **2d** having electron-donating groups, the decomposition of catalyst resulted in low conversion (entry 11). We then examined a treatment which involved an additional 10 mol% of P(O<sup>*i*</sup>Pr)<sub>3</sub>, which coordinated palladium complexes to stabilize the catalyst, and the reaction of **2d** proceeded efficiently (entry 12).<sup>8</sup>

<<Table 2>>

The results obtained with representative **2**, which gave product **3** in a manner similar to the above, are listed in Table 2. Although the addition of P(O<sup>*i*</sup>Pr)<sub>3</sub> and a longer reaction time were required in cases where aryl bromides **2** contained electron-donating

substituent or steric hindrance (entries 1, 3, and 7), the differences in the yields and on the selectivity among electronic characteristics of the substituent on **1** or **2** were not particularly large. A heteroaromatic halide was also coupled without any difficulty (entry 5). Furthermore, the present reaction was tolerated by functional groups such as carbonyls (entries 2, 4, and 6).

In the presence of aqueous NaOH, aryltriethoxysilanes **1** were more efficient and synthetically useful transmetalation substances than other silicon compounds employed in the previous studies. Under similar conditions, changing the coupling reagent from **1a** to phenyltrimethoxysilane PhSi(OMe)<sub>3</sub><sup>4</sup> gave a lower yield of the cross-coupled product **3** (49% from **2a**) accompanied by a considerable amount of the homo-coupled **4** (18%). Similarly, replacing the coupling agent with dichloromethylphenylsilane PhSiMeCl<sub>2</sub><sup>7</sup> resulted only in a low yield of **3** (25%).

Additional detailed studies in this area are currently underway.

## Experimental Section

All the experiments were carried out under an argon atmosphere. Dioxane was distilled from sodium benzophenone ketyl before use.

**Aryltriethoxysilanes.** Aryltriethoxysilanes were prepared according to a method reported previously,<sup>5</sup> or shown in the following.

Tetraethyl orthosilicate (1.3 ml, 5.8 mmol) and 4-bromotoluene (447 mg, 2.6 mmol) were added successively to magnesium (80 mg, 3.3 mmol) in ether (5 ml). The reaction mixture was refluxed for 6 h, and then filtered to remove the salt. The filtrate was purified by Kugelrohr distillation to give 398 mg (72% yield) of 4-tolyltriethoxysilane.

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ= 1.24 (t, *J* = 7.0 Hz, 9 H), 2.36 (s, 3 H), 3.86 (q, *J* = 7.0 Hz, 6 H), 7.19 (d, *J* = 7.9 Hz, 2 H), 7.57 (d, *J* = 7.9 Hz, 2 H).

<sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>): δ= 18.16, 21.50, 58.59, 127.41, 128.59, 134.82, 140.20.

HRMS (EI): *m/z* calcd for C<sub>13</sub>H<sub>22</sub>O<sub>3</sub>Si (M<sup>+</sup>) 254.1363, found: 254.1338.

**Synthesis of Biaryls. Typical Procedure.** The general procedure for the synthesis of biaryls is illustrated by the synthesis of 4'-chlorobiphenyl-4-carbaldehyde. To a solution of PdCl<sub>2</sub>(MeCN)<sub>2</sub> (5 mg, 0.02 mmol) and 4-bromobenzaldehyde (187 mg, 1.01

mmol) in dioxane (4 ml), aqueous NaOH solution (2 M, 1.5 ml) and 4-chlorophenyltriethoxysilane (329 mg, 1.2 mmol) were added. After being stirred for 4 h at 80 °C, the mixture was extracted with ether. The extract was washed with water, dried over MgSO<sub>4</sub>, and concentrated. The residue was purified by column chromatography on a silica gel (hexane/ether = 4/1) to give 175 mg (80% yield) of the corresponding biaryl.

IR (KBr):  $\nu$  = 2823, 2722, 1701, 1091 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.43 (d, *J* = 8.7 Hz, 2 H), 7.55 (d, *J* = 8.7 Hz, 2 H), 7.70 (d, *J* = 8.3 Hz, 2 H), 7.94 (d, *J* = 8.3 Hz, 2 H), 10.04 (s, 1H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 127.45, 128.52, 129.13, 130.26, 134.63, 135.28, 138.03, 145.75, 191.64.

MS (EI): *m/z* = 216 (90, M<sup>+</sup>), 152 (100).

HRMS (EI): *m/z* calcd for C<sub>13</sub>H<sub>9</sub>O<sup>35</sup>Cl (M<sup>+</sup>) 216.0342, found: 216.0330.

## References

1. (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 49. (c) Miyaura, N. *Adv. Organomet. Chem.*, **1998**, *6*, 187.
2. (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1. (c) Mitchell, T. N. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 167.
3. (a) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845. (b) Hiyama, T. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; pp 421.
4. (a) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051. (b) Shibata, K.; Miyazawa, K.; Goto, Y. *Chem. Commun.* **1997**, 1309. (c) Mowery, M. E.; DeShong, P. J. *Org. Chem.* **1999**, *64*, 1684. (d) Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2140. (e) Lee, H. M.; Nolan, S. P. *Org. Lett.* **2000**, *2*, 2053.
5. (a) Murata, M.; Suzuki, K.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, *62*,

8569. (b) Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **1999**, *40*, 9255.
6. Generally, aryltrimethoxysilanes could be prepared from the corresponding arylchlorosilanes. The major product using tetramethyl orthosilicate was diaryl(dimethoxy)silane. See also ref 4b. Unlike methyl derivatives, ethyl siloxane derivatives are directly prepared by reacting aryl Grignard reagents with tetraethyl orthosilicate in acceptable yields. See Experimental Section.
7. Hagiwara, E.; Gouda, K.; Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1997**, *38*, 439.
8. For the cross-coupling reaction using a phosphite ligand, see: Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.

[ Single Column Table ]

**Table 1.** Reaction of Triethoxyphenylsilane **1a** with **2** under Various Conditions<sup>a</sup>

entry	<b>2</b>	catalyst	base	solvent	yield (%) <sup>b</sup>	
					<b>3</b>	<b>4</b>
1	<b>2a</b>	PdCl <sub>2</sub> (MeCN) <sub>2</sub>	NaOH aq.	dioxane	94	2
2		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	KOH aq.	dioxane	78	6
3		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	NaOH <sup>c</sup>	dioxane	2	0
4		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	KF aq.	dioxane	0	0
5		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	TBAF <sup>d</sup>	dioxane	46	2
6		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	NaOH aq.	DME	40	7
7		PdCl <sub>2</sub> (MeCN) <sub>2</sub>	NaOH aq.	toluene	0	0
8		Pd(OAc) <sub>2</sub>	NaOH aq.	dioxane	79	2
9		Pd(dba) <sub>2</sub>	NaOH aq.	dioxane	43	5
10		PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	NaOH aq.	dioxane	27	14
11	<b>2d</b>	PdCl <sub>2</sub> (MeCN) <sub>2</sub>	NaOH aq.	dioxane	10	7
12		PdCl <sub>2</sub> (MeCN) <sub>2</sub> <sup>e</sup>	NaOH aq.	dioxane	93	4

<sup>a</sup> Reactions of **1a** (0.6 mmol) with **2** (0.50 mmol) were carried out for 4 h at 80 °C in 2 mL of solvent by using catalyst (0.01 mmol) and base (2 M, 1.5 mmol). <sup>b</sup> GLC yields based on **2**. <sup>c</sup> Pellets were crushed prior to use. <sup>d</sup> 1 M solution in THF. <sup>e</sup> In the presence of P(O<sup>i</sup>Pr)<sub>3</sub> (0.05 mmol).

**Table 2.** Cross-Coupling Reaction of **1** with **2**

entry	<b>1</b>	<b>2</b>	time (h)	yield (%) <sup>a</sup>
1 <sup>b, c</sup>	<b>1a</b>	<b>2e</b>	12	89 <sup>d</sup>
2	<b>1b</b>	<b>2b</b>	4	81
3 <sup>b</sup>	<b>1b</b>	<b>2f</b>	8	84
4	<b>1c</b>	<b>2c</b>	4	80
5	<b>1d</b>	<b>2g</b>	4	91
6	<b>1e</b>	<b>2b</b>	4	94
7 <sup>b</sup>	<b>1e</b>	<b>2f</b>	8	90

<sup>a</sup> Isolated yields based on **2**. <sup>b</sup> The reaction was performed in the presence of P(O<sup>i</sup>Pr)<sub>3</sub> (0.1 equiv). <sup>c</sup> 2 equiv of **1a** was used. <sup>d</sup> GLC yields.



[ Graphic Abstract ]

