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Palladium-Catalyzed Hiyama Cross-Coupling Reactions of Aryl Mesylates

Liang Zhang,[†] Jiang Qing,[†] Pengyuan Yang,*[,†] and Jie Wu*[,†,‡]

Department of Chemistry, Fudan University, 220 Handan Road,
Shanghai 200433, China, and State Key Laboratory of Organometallic Chemistry,
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road,
Shanghai 200032, China

jie_wu@fudan.edu.cn

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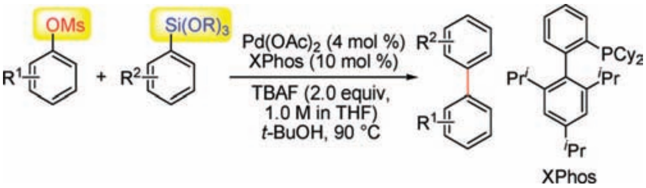
ABSTRACT



The combination of palladium acetate with XPhos shows high efficiency in the Hiyama cross-coupling reactions of aryl mesylates with arylsilanes. The reactions proceed smoothly to generate the corresponding biaryl compounds in good yields.

Recently, the use of aryl or vinyl arenesulfonates (such as tosylates and benzenesulfonates) as electrophiles in transition-metal-catalyzed C−C and C−X bond formations has attracted much attention.[1−4] There are advantages to employing aryl arenesulfonates in cross-coupling reactions over the corresponding aryl halides, since the phenol derivatives may be used as a directing group for the introduction of other functional groups on the aromatic ring, thus allowing access to a wider substrate scope. Moreover, they are less expensive, more stable, and easier to handle than the corresponding triflates. Both aryl arenesulfoantes and aryl mesylates[5,6] have been employed in transition-metal-catalyzed cross-coupling reactions and are easy to prepare from phenols. However, utilizing aryl mesylates as substrates in cross-coupling reactions has the advantage of a higher atom economy[7] than when the corresponding aryl tosylates are used, due to their significantly lower molecular weight. Thus, development of coupling reactions that use aryl mesylates as substrates should greatly contribute to the creation of environmentally benign processes. However, with respect to tosylates, mesylates are

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[†] Fudan University.

[‡] Shanghai Institute of Organic Chemistry.

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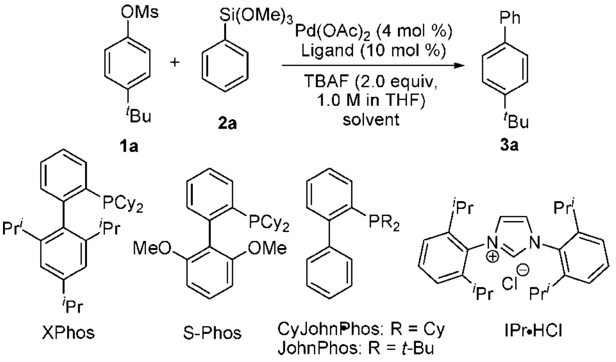
regarded as the least active sulfonate leaving group, which has limited their application in coupling reactions.[5,6] Therefore, it is of great importance to develop general and efficient methods for transition-metal-catalyzed couplings of unactivated aryl mesylate substrates.

Among the organometallic reagents employed in cross-coupling reactions, the palladium-catalyzed Hiyama coupling of organosilicon compounds with organic electrophiles is an attractive method for carbon−carbon bond formation,[8,9] due to their ease of handling, stability toward air/moisture, and/or low toxicity compared to some of the other organometallic reagents (Zn, Mg, Sn, etc.). Although couplings of aryl halides with organosilicon compounds have been well developed, to the best of our knowledge, aryl mesylates have never been involved in the Hiyama coupling reactions. Herein, we present the first example of palladium-catalyzed Hiyama couplings of aryl mesylates.

Initial studies were performed by using 4-*tert*-butylphenyl mesylate **1a** and trimethoxy(phenyl)silane **2a** as model substrates, in the presence of palladium acetate as catalyst (Table 1). Due to the relatively inert leaving group activity of aryl mesylate, bulky electron-rich phosphines[10,11] were screened in this palladium-catalyzed Hiyama reaction. Gratifyingly, in the presence of XPhos (10 mol %) and TBAF (2.0 equiv), this reaction proceeded smoothly in THF to afford the corresponding product **3a** in 45% yield (Table 1, entry 1). Further investigation revealed that the solvent combination of THF/*t*-BuOH was the best choice for solvent screening, and the desired biaryl product **3a** was generated in 92% yield (Table 1, entry 8). Under these conditions, the catalyst and substrates were soluble.[1b] Inferior results were displayed when other ligands were employed in the reaction (Table 1, entries 9−14).

Table 1. Initial Studies for Pd-Catalyzed Hiyama Coupling of 4-*tert*-Butylphenyl Mesylate **1a** with Trimethoxy(phenyl)silane **2a**



entry	ligand	solvent	*T* (°C)	yield[a] (%)
1	XPhos	none	80	45
2	XPhos	DMF	110	trace
3	XPhos	dioxane	110	12
4	XPhos	DMSO	110	nr
5	XPhos	toluene	110	18
6	XPhos	CH_3CN	110	10
7	XPhos	DCE	90	nr
8	XPhos	*t*-BuOH	90	92
9	S-Phos	*t*-BuOH	90	38
10	JohnPhos	*t*-BuOH	90	trace
11	CyJohnPhos	*t*-BuOH	90	11
12	PCy_3	*t*-BuOH	90	trace
13	DPPP	*t*-BuOH	90	15
14	IPr•HCl	*t*-BuOH	90	trace

[a] Isolated yield based on 4-*tert*-butylphenyl mesylate **1a**.

With this preliminary result in hand, the scope of these Pd-catalyzed Hiyama coupling reactions of aryl mesylates was investigated under the optimized conditions [Pd(OAc)$_2$

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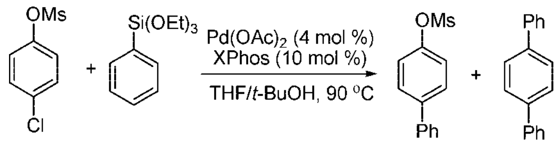
(4 mol %), Xphos (10 mol %), TBAF (2.0 equiv), THF/*t*-BuOH, 90 °C], and the results are shown in Table 2. From Table 2, it was found that, for most cases, this Pd-catalyzed Hiyama cross-coupling reactions of aryl mesylates **1** and arylsilane **2** furnished the corresponding biaryl compounds **3** in good to excellent yields. For example, reaction of mesylate **1a** with triethoxy(phenyl)silane **2b** gave rise to product **3a** in 96% yield (Table 2, entry 2). A better result was observed when an arylsilane with an electron-donating group on the aromatic ring was employed in the reaction of mesylate **1a** (Table 2, entries 3−6). For instance, 71% yield of the corresponding product **3c** was obtained when trimethoxy(4-methylphenyl)silane **2d** was utilized in the reaction (Table 2, entry 4). However, only a moderate yield was observed when trimethoxy(4-trifluoromethylphenyl) silane **2e** was used in the reaction (55% yield, Table 2, entry 5). The silane bearing *ortho*-substitution was also employed in the reaction of 4-*tert*-butylphenyl mesylate **1a** under the same conditions, and the desired product **3e** was generated in 77% yield (Table 2, entry 6). α- and *β*-Naphthyl mesylates **1b** and **1c** were also suitable partners in this process. For example, *β*-naphthyl mesylate **1c** reacted with silane **2c**, leading to the formation of compound **3h** in almost quantitative yield (Table 2, entry 11). An 85% yield of product **3j** was obtained when trimethoxy(2-methylphenyl)silane **2f** was employed in the reaction (Table 2, entry 13). A similar result was obtained when other mesylates **1d** or **1e** were used as replacements (Table 2, entries 14−18). Reaction of ester-substituted mesylate **1f** with the arylsilane also proceeded smoothly, which gave rise to the desired product in moderate to good yield (Table 2, entries 19−21). Under the conditions, the ester group was tolerated. The reactivity of *N*-heteroaryl mesylate was also tested. For instance, 3-pyridinyl mesylate **1g** reacted with trimethoxy(4-methylphenyl)silane **2d** leading to the formation of product **3p** in 40% yield (Table 2, entry 22). However, only a trace amount of product was detetced when 2-methylphenyl mesylate **1h** was used as substrate in the reaction of triethoxy(phenyl)silane **2b** (Table 2, entry 23).

Scheme 1. Reaction of 4-Chlorophenyl Mesylate **1i** with Arylsilane **2b**

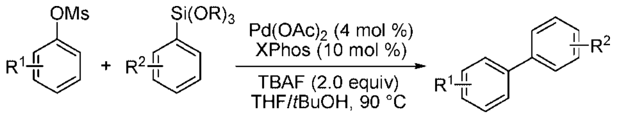


1i **2b** **1j** **3r**

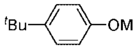
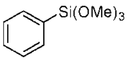
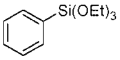
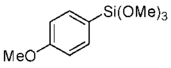
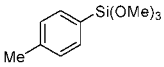
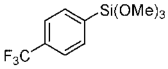
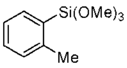
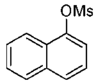
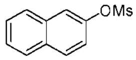
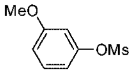
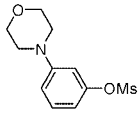
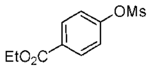
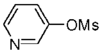
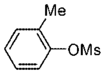
2b	additive	1j	3r
1.5 equiv	TBAF (1.5 equiv)	70%	22%
3.0 equiv	TBAF (3.0 equiv)	18%	68%

Pd-Catalyzed cross-coupling reaction of 4-chlorophenyl mesylate **1i** with triethoxy(phenyl)silane **2b** was investigated under the standard conditions shown in Table 2 (Scheme 1). As described previously, mesylates are regarded as the least active sulfonate leaving group. Thus, as expected, the mesyloxy group in compound **1i** was retained during the transformation. From this reaction, it was found that an aryl chloride is more active than an aryl mesylate under these conditions.

Table 2. Pd-Catalyzed Hiyama Couplings of Aryl Mesylates **1**



1 **2** **3**

entry	mesylate **1**	silane **2**	product	yield (%)[a]
1	 **1a**	 **2a**	**3a**	92
2	**1a**	 **2b**	**3a**	96
3	**1a**	 **2c**	**3b**	67
4	**1a**	 **2d**	**3c**	71
5	**1a**	 **2e**	**3d**	55
6	**1a**	 **2f**	**3e**	77
7	 **1b**	**2a**	**3f**	81
8	**1b**	**2b**	**3f**	71
9	 **1c**	**2a**	**3g**	83
10	**1c**	**2b**	**3g**	84
11	**1c**	**2c**	**3h**	96
12	**1c**	**2e**	**3i**	90
13	**1c**	**2f**	**3j**	85
14	 **1d**	**2a**	**3k**	94
15	**1d**	**2b**	**3k**	97
16	**1d**	**2d**	**3l**	96
17	 **1e**	**2a**	**3m**	87
18	**1e**	**2b**	**3m**	92
19	 **1f**	**2a**	**3n**	65
20	**1f**	**2b**	**3n**	78
21	**1f**	**2c**	**3o**	50
22	 **1g**	**2d**	**3p**	40
23	 **1h**	**2b**	**3q**	<5

[a] Isolated yield based on aryl mesylate **1**.

In conclusion, we have described an efficient and general method for Hiyama cross-coupling reactions of aryl mesylates with arylsilanes catalyzed by the combination of palladium acetate and XPhos in the presence of TBAF as additive. Method development using aryl mesylates as substrates in other coupling reactions is under investigation and will be reported in due course.

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Supporting Information Available: Experimental procedures, characterization data, and copies of ^{1}H and ^{13}C NMR of compound **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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