Palladium-Catalyzed Direct Arylation of Cyclic Enamides with Aryl Silanes by sp² C–H Activation**

Hai Zhou, Yun-He Xu, Wan-Jun Chung, and Teck-Peng Loh*

The Hiyama coupling reaction, which involves the palladiumcatalyzed coupling between organohalides or other surrogates with organosilanes, is one of the most useful tools for C–C bond formation.^[1] Compared with similar coupling reactions using organostannane, Grignard, and organoboron reagents, Hiyama coupling has many advantages, such as environmental benignity, atomic efficiency, and safe handling. Recently, new C–C bond forming methods involving C–H activation have attracted much interest among chemists.^[2] Although many groups have reported direct arylation with organoboronic acids,^[3,2g] there is still very few studies on the direct coupling using organosilanes by C–H functionalization.^[2i] Herein, we present the first direct cross-coupling reaction between an enamide and organosilanes via vinylic C–H bond activation using a palladium catalyst.

Recently, our group has successfully developed a direct cross-coupling reaction between cyclic enamides and arylboronic acid^[4a] or acrylate^[4b] involving C–H bond activation. We envisioned the same substrate could also be used in the direct arylation with organosilane reagents. We began our investigation by studying the Hiyama-type coupling reaction of 4chromanone-derived enamide 1a with trimethoxyphenylsilane 2a in the presence of $Pd(OAc)_2$ as a catalyst under various reaction conditions (Table 1).^[5] In our initial screening of fluoride sources, it was gratifying to find that AgF could afford the desired product in high yield (Table 1, entry 4). We hypothesized that AgF not only plays a role as a simple fluoride to activate the organosilane, but also as an oxidant to reoxidize Pd⁰ to Pd^{II} and thus fulfill the catalytic cycle. Three equivalents each of both AgF and PhSi(OMe)₃ was found necessary for complete consumption of the substrates (Table 1, entries 4 versus 5). Other additional inorganic oxidants, such as Cu(OAc)2, were screened with this coupling reaction, but afforded the desired product in low yields. Among the different solvents screened, dioxane is the most suitable for this transformation (Table 1, entries 4, 6–9). Various palladium species were also examined, but the

[*]	H. Zhou, Y. H. Xu, W. J. Chung, Prof. T. P. Loh				
	Division of Chemistry and Biological Chemistry,				
	School of Physical and Mathematical Sciences,				
	Nanyang Technological University,				
	Singapore 637371 (Singapore)				
	Fax: (+65) 6515-8229				
	E-mail: teckpeng@ntu.edu.sg				

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,	NHAc + PhSi(OMe (3 equiv) 1a 2a	[Pd] (10 mo Fluoride (3 e Solvent, 80	quiv) $0^{\circ}C$ 3a	IHAc
Entry	[Pd]	Fluoride	Solvent	Yield [%] ^[b]
1	Pd(OAc) ₂	CuF ₂	dioxane	12
2	Pd(OAc) ₂	TBAF ^[d]	dioxane	0
3	Pd(OAc) ₂	CsF	dioxane	0
4	Pd(OAc) ₂	AgF	dioxane	73
5 ^[c]	Pd(OAc) ₂	AgF	dioxane	61
6	Pd(OAc) ₂	AgF	DCE	30
7	Pd(OAc) ₂	AgF	toluene	25
8	Pd(OAc) ₂	AgF	DMF	44
9	Pd(OAc) ₂	AgF	CH₃CN	37
10	$[Pd(PPh_3)_2Cl_2]$	AgF	dioxane	32
11	[Pd(OTFA) ₂] ^[d]	AgF	dioxane	47
12	[Pd(PhCN) ₂ Cl ₂]	AgF	dioxane	51
13	PdCL	ΔσF	diovane	18

Table 1: Screening conditions for the palladium(II)-catalyzed direct

arylation of **1a** with phenyltrimethoxysilane.^[a]

[a] Conditions: 10 mol% Pd(OAc)₂, 3 equiv of **2a**, 3 equiv of fluoride, 80 °C, 16 h. [b] Yields of isolated products. [c] Conditions: 10 mol% Pd(OAc)₂, 2 equiv of **2a**, 2 equiv of fluoride, 80 °C, 16 h. [d] OTFA = trifluoroacetate, TBAF = tetra-*n*-butylammonium fluoride.

transformation works well only in the presence of $Pd(OAc)_2$ as a catalyst (Table 1, entries 4, 10–13).

The direct arylation of 4-chromanone-derived enamide 1a with various trialkoxy aryl silanes was surveyed with 10 mol% Pd(OAc)₂ and 3 equiv AgF in dioxane (Table 2). Triethoxyphenylsilane was a little less reactive than trimethoxyphenylsilane (Table 2, entries 1 versus 2). The arylated products were obtained in moderate to high yields by the coupling with different triethoxy aryl silanes having electrondonating or electron-withdrawing groups on the phenyl ring. The position of these substituents has a great influence on this transformation. Meta and para substituents introduced on the phenyl ring of phenylsilane could afford the coupling products in good yields. However, ortho-substituted phenylsilanes give very little of the desired products, which perhaps arises from steric effects. It is noteworthy that a chloro substituent on the trialkoxy phenylsilane shows tolerance toward this coupling reaction, which could serve as a handle for further transformation (Table 2, entry 5).

To examine the scope of this direct arylation, various cyclic enamides were subjected to the reaction conditions (Table 3). Both electron-donating and electron-withdrawing groups on the phenyl ring of 4-chromanone-derived enamides 1 afforded the coupling products in moderate to excellent yields (Table 3, entries 1–4). Of note, a chloro group on the phenyl ring of enamide, which tolerated the reaction con-







Table 2: Palladium-catalyzed direct arylation of 1 a with silyl reagents 2.^[a]

 Table 3:
 Palladium-catalyzed direct arylation of various cyclic enamides 1
with phenyltrimethoxysilane 2a.^[a]



[a] Conditions: 10 mol% Pd(OAc)₂, 3 equiv of **2a**, 3 equiv of fluoride, 80°C, 16 h. [b] Yields of isolated products. [c] 55% of the starting material was recovered. [d] Some aromatized byproduct of the starting material was observed in the reaction.

cycle 4 to give palladium species 5, which, upon reductive elimination, produced the cross-coupling product and palla-



[a] Conditions: 10 mol% Pd(OAc)₂, 3 equiv of **2**, 3 equiv of fluoride,

80°C, 16 h. [b] Yields of isolated products.

Although there is the possibility of a Heck-type reaction pathway for this coupling reaction, we believe that the reaction may go through palladation of cyclic enamides, which is similar to the mechanism of direct arylation of enaminones^[2m] and to that of aromatic C-H activation reported by the groups of Inuoe^[6] and Shi^[2i] (Scheme 1). Assisted by the acetamino group, six-membered palladacycle **4** is first formed. Next, with activation by fluoride, the aryl group from trialkoxy silane 2 is transmetalated with pallada-



Scheme 1. Proposed mechanism of the direct arylation of cyclic enamides.

dium(0). The elemental palladium is then reoxidized to Pd^{II} by Ag^{I} to fulfill the catalytic cycle.

In conclusion, we have developed a palladium-catalyzed direct cross-coupling method for arylation of cyclic enamides with trialkoxy aryl silanes by a C–H activation to produce a wide variety of enamide derivatives.^[7] Future studies will focus on its potential application and on understanding of the mechanism of this transformation.

Experimental Section

General procedure for cross-coupling of cyclic enamides with trialkoxy aryl silanes: Cyclic enamide 1 (0.27 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol, 10 mol%), trialkoxy aryl silane 2 (0.81 mmol), 3 equiv) and anhydrous 1,4-dioxane (4 mL) were added to a 8 mL vial. AgF (102 mg, 0.81 mmol, 3 equiv) was slowly added to the mixture, and the vial was then capped tightly and stirred for 10 min at room temperature. The reaction was heated for 16 h at 80°C in an oil bath and the progress of the reaction monitored by thin-layer chromatography. After removal of the solvent, the residue was purified by flash chromatography to give pure products **3**.

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