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Palladium-catalyzed Direct C–H Bond Arylation of Simple Arenes with Aryltrimethylsilanes

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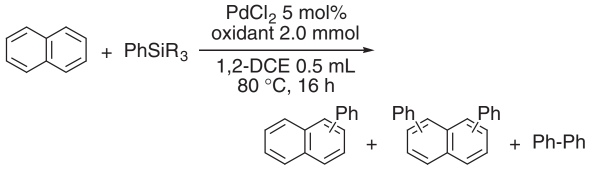
Direct C–H bond arylation of arenes with aryltrimethylsilanes catalyzed by $PdCl_2$ in the presence of $CuCl_2$ as an oxidant has been developed. In addition to the role as the oxidant, $CuCl_2$ is found to be necessary for the selective cross-coupling reaction.

Biaryl structures are very important units in fine chemicals, such as organic electronic materials, pharmaceuticals, and agrochemicals. The cross-coupling reactions of various arylmetal reagents with aryl halides catalyzed by nickel or palladium have been widely utilized for the biaryl synthesis.[1,2] In recent years, transition-metal-catalyzed direct C–H bond arylation has attracted significant attention as an efficient and useful method for biaryl synthesis.[3] There have been many studies of direct arylation of highly electron-rich heteroaromatic compounds[4] and arenes involving nitrogen- or oxygen-based directing groups.[5] In contrast, the direct arylation of simple aromatic hydrocarbons, such as naphthalene and phenanthrene, has been less studied.[6]

In the previous work, we reported the direct C–H bond arylation of simple arenes with aryltin trichlorides in the presence of a catalytic amount of Pd(II) salt and stoichiometric amount of $CuCl_2$.[6b] The reaction mechanism is proposed to involve a highly electrophilic arylpalladium intermediate which would easily react with arenes via electrophilic substitution. Since aryltin trichlorides are difficult to handle and highly toxic, we set out to develop more practical direct C–H bond arylation using arylsilicon compounds, which are easy to handle, show low toxicity, and are easily available, as alternative arylmetal reagents. Herein, we report that aryltrimethylsilanes successfully reacted with simple arenes to give the corresponding cross-coupling products in the presence of palladium catalyst and $CuCl_2$ as the oxidant and activator of the catalyst. To the best of our knowledge, there has been no example of the direct C–H bond arylation using aryltrialkylsilanes.[7]

At first, the reactions of naphthalene (0.5 mmol) with phenylsilicon reagents (1.0 mmol) were examined using $PdCl_2$ (5 mol %, 0.025 mmol) and oxidants (2.0 mmol) in 1,2-dichloroethane (1,2-DCE, 0.5 mL) at 80 °C for 16 h (Table 1). After the screening, desired products **2a** and **3a** were obtained in moderate yields by the use of $PhSiMe_3$ (**1a**) and $CuCl_2$ (Entry 1). When the amount of **1a** was increased to 2.0 mmol, the total yield of the cross-coupling products was increased to 59% (Entry 2). In the case of phenylsilanes with bulky alkyl groups on the silicon, the yields of the coupling products were decreased considerably (Entries 3 and 4). The use of phenylalkoxysilanes, which are known to be good reagents for coupling reactions,[8] decreased the yields of **2a** and **3a** (Entries 5–7). The reaction of $PhSiCl_3$ did not proceed in the present catalytic system (Entry 8). Among the several oxidants examined, $CuCl_2$ showed the best result (Entries 9–12). In addition, the reaction without the oxidant did not proceed at all (Entry 13). The use of other palladium catalysts, such as $Pd(OAc)_2$, $[PdCl_2(MeCN)_2]$, $[PdCl_2(PhCN)_2]$, $[PdCl_2(cod)]$, and $[Pd_2(dba)_3]$, decreased the yield of the cross-coupling product (4–26% yield) and increased the yield of biphenyl (**4**) (30–81% yield). Palladium complexes with electron-donating ligands, such as $[PdCl_2(PPh_3)_2]$ and $[PdCl_2(bpy)]$, did not give any coupling products. As a control experiment, the reaction without palladium catalyst did not proceed (Entry 14). The predominant formation of the α-coupling product strongly suggests that the reaction pathway involves an electrophilic substitution on the naphthalene ring.

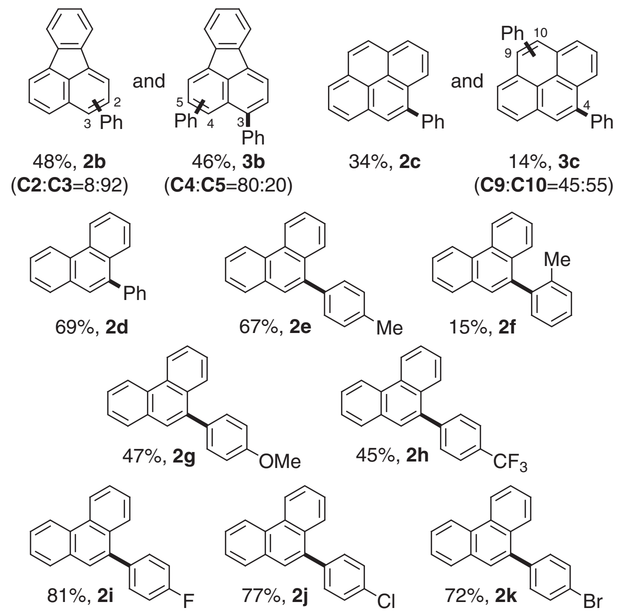
Table 1. Direct C–H bond arylation of naphthalene with phenylsilicon reagents[a]



2a **3a** **4**

Entry	$PhSiR_3$	Oxidant	Yield/%[b]			
			2a[c]	(α:β)	**3a**[c]	**4**[d]
1	$PhSiMe_3$ (**1a**)	$CuCl_2$	38	(87:13)	7	0
2[e]	**1a**	$CuCl_2$	35	(89:11)	24	12
3	$PhSiEt_3$	$CuCl_2$	30	(83:17)	0	3
4	$PhSi\textit{i}\text{-}Pr_3$	$CuCl_2$	0		0	0
5	$PhSiMe_2(OEt)$	$CuCl_2$	23	(83:17)	0	31
6	$PhSiMe(OMe)_2$	$CuCl_2$	16	(81:19)	0	1
7	$PhSi(OMe)_3$	$CuCl_2$	4	(100:0)	0	0
8	$PhSiCl_3$	$CuCl_2$	0		0	0
9	**1a**	$Cu(OAc)_2$	2	(79:21)	0	1
10	**1a**	$CuSO_4$	6	(94:6)	0	0
11	**1a**	CuF_2	4	(88:12)	0	0
12	**1a**	$CuBr_2$	0		0	1
13	**1a**	none	0		0	0
14[f]	**1a**	$CuCl_2$	0		0	0

[a]Reaction conditions: Naphthalene (0.5 mmol), phenylsilicon reagent (1.0 mmol), $PdCl_2$ (0.025 mmol), and oxidant (2.0 mmol) in 1,2-DCE (0.5 mL) at 80 °C for 16 h. [b]Determined by GC. [c]Based on naphthalene. [d]Based on phenylsilicon reagent. [e]2.0 mmol of $PhSiMe_3$ was used. [f]Reaction without $PdCl_2$.

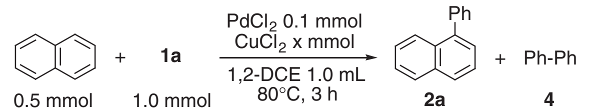


Scheme 1. Direct C–H bond arylation of several arenes with aryltrimethylsilanes.

Scheme 1 shows the results of the direct arylation of several arenes with various aryltrimethylsilanes under the optimized reaction conditions (Table 1, Entry 2). The reaction of fluoranthene with **1a** afforded mono- and diphenylated products in 48% (**2b**, **C2**:**C3** = 8:92) and 46% yield (**3b**, **C4**:**C5** = 80:20), respectively. Phenylation of pyrene gave 4-phenylpyrene (**2c**) in 34% yield and diphenylated pyrene **3c** in 14% yield (**C9**:**C10** = 45:55). The reactions of phenanthrene with various aryltrimethylsilanes having both electron-donating and -withdrawing groups at their 4-positions gave the corresponding 9-arylphenanthrenes **2d**, **2e**, and **2g**–**2k** in 45 to 81% yields. A clear correlation between the electronic properties of the aryltrimethylsilanes and the product yields was not observed. It is noted that 4-halogenated phenyltrimethylsilanes gave halogen-substituted products **2i**–**2k**, which can be used for further coupling reactions at the halogen substituents. The reaction using sterically hindered *o*-tolyltrimethylsilane gave the product **2f** in a low yield of 15%.[13]

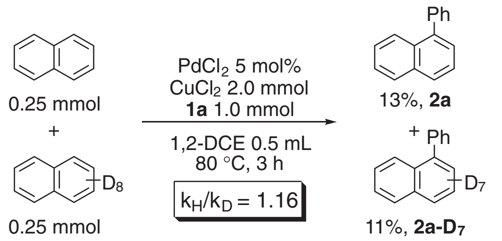
To clarify the role of $CuCl_2$, effect of the amount of $CuCl_2$ was then examined in the reaction of naphthalene (0.5 mmol) with **1a** (1.0 mmol) using $PdCl_2$ (0.10 mmol) in 1,2-DCE (1.0 mL) at 80 °C (Table 2). The reactions were carried out for 3 h to form only monophenylated product **2a**. The reaction without $CuCl_2$ did not give any coupling products, because of insolubility of $PdCl_2$ (Entry 1). Thus, the use of soluble $[PdCl_2(MeCN)_2]$ without $CuCl_2$ gave only biphenyl (**4**) as the homocoupling product of **1a** (Entry 2). The reaction using $PdCl_2$ with 1.0 mmol of $CuCl_2$ afforded the cross-coupling product **2a** together with almost the same amount of **4** (Entry 3). On the other hand, the use of $[PdCl_2(MeCN)_2]$ with 1.0 mmol of $CuCl_2$ gave **4** predominantly (Entry 4). Addition of larger amounts of $CuCl_2$ to $PdCl_2$ catalyst then resulted in the preferential formation of **2a** (Entries 5 and 6). These results show that the amount of $CuCl_2$ affects the reaction selectivity between cross-coupling and homocoupling reactions. It is reasonable to suppose that this reaction selectivity is caused by the formation of polymetallic Pd–Cu clusters.[9,10] It is also possible that $CuCl_2$ oxidizes a Pd(II) intermediate to a Pd(III) or Pd(IV) species.[11] Acetonitrile ligands on the palladium catalyst would prevent such interactions between palladium and copper.

Table 2. Investigation of the effect of $CuCl_2$

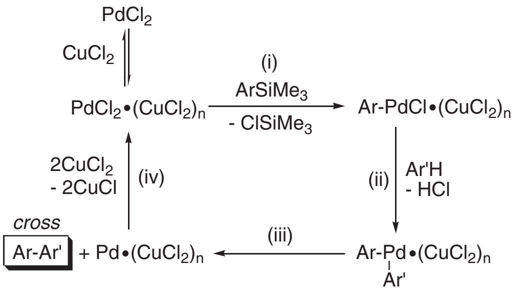


Entry	$CuCl_2$, x/mmol	mmol by GC		**2a**:**4**
		2a	**4**	
1	0	0	0	—
2[a]	0	0	0.071	0:1
3	1.0	0.044	0.040	1.1:1
4[a]	1.0	0.015	0.40	1:27
5	2.0	0.049	0.005	10:1
6	3.0	0.074	0.003	25:1

[a] $[PdCl_2(MeCN)_2]$ (0.1 mmol) was used instead of $PdCl_2$.



Scheme 2. Kinetic isotope effect on the reaction of naphthalene with **1a**.



Scheme 3. A presumed reaction pathway.

Kinetic isotope effect was also investigated by the competitive reaction between naphthalene and naphthalene-D_8 with **1a** (Scheme 2). The k_H/k_D ratio was determined to be 1.16. This suggests that the C–H bond cleavage of naphthalene by a palladium intermediate proceeds via the electrophilic substitution mechanism.

A presumed reaction pathway is shown in Scheme 3. Electrophilic transmetalation of $PdCl_2$ with $ArSiMe_3$ at the *ipso*-Si position[12] generates an arylpalladium intermediate in the presence of $CuCl_2$ (i). Aromatic electrophilic substitution of Ar′–H with the arylpalladium intermediate occurs to form a diarylpalladium intermediate (ii). The exact structure of the arylpalladium intermediate has not yet been clear, the interaction with $CuCl_2$ would be crucial in this step. Reductive elimination from the diarylpalladium species gives the cross-coupling products (iii). Finally, oxidation of palladium species by $CuCl_2$ regenerates $PdCl_2$ (iv).

In summary, palladium-catalyzed direct C–H bond arylation of simple arenes with aryltrimethylsilanes is described. In this reaction, $CuCl_2$ is essential to obtain the desired cross-coupling products in high selectivity. Further studies to expand the substrate scope and their applications, as well as the investigations for the reaction mechanism are now in progress.

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