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Silicon-based C–N Cross-coupling Reaction

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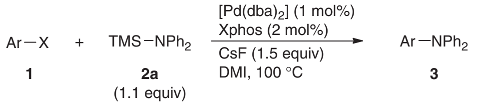
Palladium-catalyzed C–N bond-forming cross-coupling reaction of *N*-trimethylsilylamines with aryl bromides and chlorides is found to proceed in the presence of a fluoride activator in 1,3-dimethyl-2-imidazolidinone (DMI), giving triarylamines in excellent yields. When aryl bromide and bis(silyl)amine were used in this reaction, double C–N bond-forming products were obtained in high yields. The present reaction was successfully applied to C–N bond-forming polymerization.

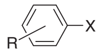
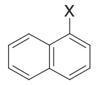
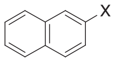
Arylamines are an important structural motif for various pharmaceuticals, natural products, dyes, agrochemicals, and functionalized polymers,[1] and can be prepared straightforwardly by the metal-catalyzed cross-coupling reaction of aryl halides or pseudohalides with nitrogen nucleophiles.[2,3] Particularly, the Pd-catalyzed reaction, so-called Buchwald–Hartwig amination,[2] is of great significance because of a straightforward approach and better functional group compatibility. The reaction usually requires strong bases for effective aromatic amination. Naturally, base-sensitive functional groups cannot tolerate the presence of such bases. In order to fulfill this drawback, milder reaction conditions were developed: use of active catalyst systems[4] and/or weak bases[5] and aqueous conditions.[6] However, improvement of nucleophilic nitrogen source has been largely absent since stannylamines were applied by Migita, Kosugi, et al.[7]

Our group has studied silicon-based C–C bond-forming cross-coupling reactions.[8] These reactions proceed under mild conditions since carbon nucleophiles are generated smoothly by the reaction of organosilicon compounds with a fluoride activator. The concept of organosilicon and fluoride activation to generate active nucleophiles has been applied to C–N coupling reaction with limited success. Barluenga and co-workers reported cross-coupling reaction of aryl halides with silylaldimines to give *N*-arylated aldimines.[9] Smith, Holmes, and co-workers developed the reaction of aryl halides with silylamines in supercritical carbon dioxide ($scCO_2$).[10] The latter is seminal. However, the use of $scCO_2$ limits its scope: substrates such as monosilyl primary amines cannot be applicable as they react with $scCO_2$. Moreover, the reaction needs special pressure bottles. Herein we report the Pd-catalyzed cross-coupling reaction of aryl halides with silylamines under mild conditions in 1,3-dimethyl-2-imidazolidinone (DMI).

On the basis of the silicon-based cross-coupling reaction, we examined the prototypical standard reaction conditions and soon found that 4-bromotoluene (**1a**) coupled with *N*-(trimethylsilyl)diphenylamine (**2a**) in the presence of $[Pd(dba)_2]$ (1 mol %), Xphos (2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl)[11] (2 mol %), and CsF (1.5 equiv) in DMI at 100 °C for 30 min gave diphenyl(*p*-tolyl)amine (**3aa**) in 97% yield with the generation of TMS–F detected by gas chromatography (Table 1, Entry 1). Other fluoride ion sources such as TBAF and KF decreased the yield of **3aa**.[12] The reaction conditions were applied to various aryl halides. Less reactive 4-chlorotoluene (**1′a**) also underwent the C–N coupling to form **3aa** in 77% yield (Entry 2). On the contrary, the reaction using 4-iodotoluene resulted in 35% yield. Phenyl and electron-rich aryl bromides having OMe, NMe_2, and NPh_2 groups on their *para*-positions did not hamper the reaction to give corresponding coupling products in excellent yields (Entries 3–6).

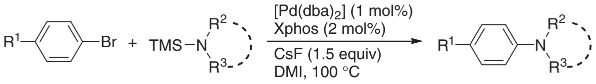
Table 1. Cross-coupling reaction of aryl halides with *N*-(trimethylsilyl)diphenylamine[a]



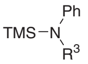
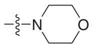
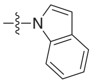
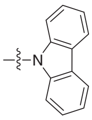
Entry	1	Ar	X	Time/h	3	Yield/%[b]
						
1	**1a**	R = 4-Me	Br	0.5	**3aa**	97
2	**1′a**	R = 4-Me	Cl	4	**3aa**	77
3	**1b**	R = H	Br	1	**3ba**	97
4	**1c**	R = 4-MeO	Br	1	**3ca**	94
5	**1d**	R = 4-NMe_2	Br	1	**3da**	89
6	**1e**	R = 4-NPh_2	Br	3	**3ea**	99
7	**1f**	R = 4-CO_2Me	Br	0.5	**3fa**	99
8	**1g**	R = 4-PhCO	Br	0.5	**3ga**	99
9	**1h**	R = 4-CF_3	Br	0.5	**3ha**	98
10	**1i**	R = 4-NO_2	Br	0.5	**3ia**	97
11	**1j**	R = 2-Me	Br	12	**3ja**	99
12	**1k**	R = 3,5-Me_2	Br	1	**3ka**	98
13	**1l**		Br	3	**3la**	94
14	**1m**		Br	1	**3ma**	99

[a]Unless otherwise noted, a mixture of **1** (0.50 mmol), **2a** (0.55 mmol), $[Pd(dba)_2]$ (5.0 µmol), Xphos (10 µmol), CsF (0.75 mmol), and DMI (0.50 mL) were heated at 100 °C. [b]Isolated yields.

Table 2. Cross-coupling reaction aryl bromides with *N*-silylamines[a]



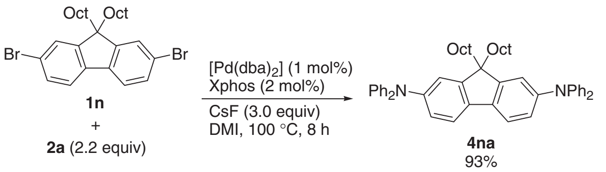
1 **2** (1.1 equiv) **3**

Entry	1	2	R^2, R^3	Time/h	3	Yield/%[b]
						
1	**1a**	**2b**	$R^3 =$ *m*-tolyl	0.5	**3ab**	90
2	**1a**	**2c**	$R^3 =$ 1-naphthyl	0.5	**3ac**	99
3	**1a**	**2d**	$R^3 =$ Me	1	**3ad**	75
4	**1a**	**2e**	$R^3 =$ H	5.5	**3ae**	96
5	**1a**	**2f**		12	**3af**	70
6	**1h**	**2g**		13	**3hg**	76
7[c]	**1h**	**2h**		24	**3hh**	99

[a]Unless otherwise noted, a mixture of **1** (0.50 mmol), **2** (0.55 mmol), [Pd(dba)$_2$] (5.0 µmol), Xphos (10 µmol), CsF (0.75 mmol), and DMI (0.50 mL) were heated at 100 °C. [b]Isolated yields. [c][Pd(dba)$_2$] (10 µmol), Xphos (20 µmol), and KF (2.50 mmol) were used.

Substrates with base-sensitive carbonyl groups (**1f** and **1g**)[4b] smoothly reacted to give **3fa** and **3ga** quantitatively (Entries 7 and 8). Electron-withdrawing groups such as CF_3 and NO_2 did not interfere with the reaction (Entries 9 and 10). Sterically hindered 2-bromotoluene (**1j**) reacted without any problem, and coupling product **3ja** was obtained in 99% yield (Entry 11). *meta*-Dimethylphenyl bromide (**1k**) gave **3ka** in 98% yield (Entry 12). 1- and 2-Bromonaphthalenes (**1l** and **1m**) gave corresponding C–N coupling products **3la** and **3ma** in 94% and 99% yields, respectively (Entries 13 and 14).

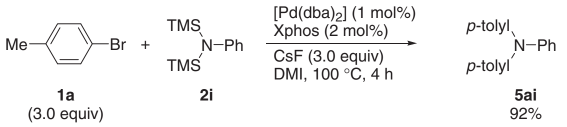
With arylene dibromides, double C–N bond-forming reaction readily took place as was seen with 2,7-dibromo-9,9-dioctylfluorene (**1n**), which underwent sequential double amination smoothly to give bis(diphenylamino) derivative **4na** in 93% yield without formation of a mono-amination or reduction product (eq 1).[13]



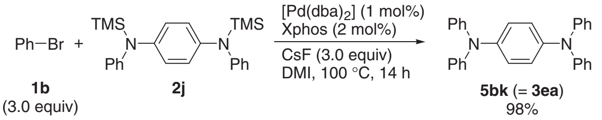
(1)

The scope of silylamine reagents was next examined and the results are summarized in Table 2. *N*-(Trimethylsilyl)diarylamine derivatives **2b** ($R^2 =$ Ph, $R^3 =$ *m*-tolyl) and **2c** ($R^2 =$ Ph, $R^3 =$ 1-naphthyl) gave triarylamines **3ab** and **3ac** in 90% and 99% yields, respectively (Entries 1 and 2). *N*-(trimethylsilyl)-phenylmethylamine (**2d**) proceeded to form coupling product **3ad** in 75% yield (Entry 3). The reaction of *N*-(trimethylsilyl)aniline (**2e**) proceeded to afford mono-arylated product **3ae** in 96% yield without generation of triarylamine via N–H bond cleavage (Entry 4). When 2.0 equiv of **1a** was used in the reaction with **2e**, **3ae** was formed in high yield while triarylamine was hardly observed. These result clearly demonstrate that an N–$SiMe_3$ bond dominantly undergoes the coupling in preference to an N–H bond. *N*-(Trimethylsilyl)morpholine (**2f**) was successfully converted to **3af** in 70% yield (Entry 5). *N*-(Trimethylsilyl)azole derivatives are also applicable to this reaction. For example, the reaction of 1-(trimethylsilyl)indole (**2g**) with **1h** gave *N*-arylated products **3hg** in 76% yield (Entry 6); *N*-trimethylsilylcarbazole **2h** coupled in the presence of twice the amount of palladium catalysts to afford *N*-(4-trifluoromethylphenyl)carbazole (**3hh**) in 99% yield (Entry 7). In the case of *N*-trimethylsilylcarbazole, less basic KF gave better results than CsF. *N*-Arylcarbazoles have received much attention as electronic materials[14] and are now readily accessible by the present C–N coupling reaction of *N*-(trimethylsilyl)carbazole.[3,15]

The reaction of 3.0 equiv of **1a** with *N*,*N*-bis(trimethylsilyl)aniline (**2i**) took place in freshly distilled DMI using rigorously dried CsF to give triarylamine **5ai** in 92% via double C–N bond formation (eq 2). In this case, direct use of commercially available "dry" DMI and CsF resulted in low yields because **2i** is moisture sensitive. Similarly, *N*,*N*′-bis(trimethylsilyl)-*p*-phenylenediamine (**2j**) gave *N*,*N*,*N*′,*N*′-tetraphenyl-*p*-phenylenediamine (**5bk**) in 98% yield (eq 3).

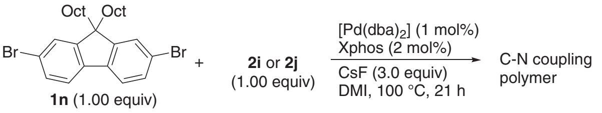


(2)

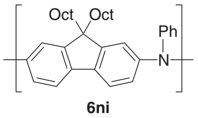


(3)

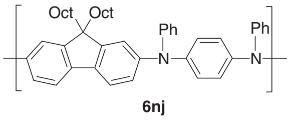
Finally, the present reaction was applied to the cross-coupling polymerization to synthesize poly(triarylamine)s[16] which are considered to be unique organic materials (eq 4).[17] The reaction of 2,7-dibromo-9,9-dioctylfluorene (**1n**) with *N*,*N*-bis(trimethylsilyl)aniline (**2i**) gave copolymer **6ni** with $M_n = 4400$, $M_w = 9900$, and $M_w/M_n = 2.2$ in 85% yield. *p*-Phenylenediamine-based bis(silyl)amine **2j** also reacted with **1n** to give copolymer **6nj** with $M_n = 6000$, $M_w = 12000$, and $M_w/M_n = 2.0$ in 90%.



(4)



6ni
85%, $M_n = 4400$, $M_w = 9900$
$M_w/M_n = 2.2$



6nj
90%, $M_n = 6000$, $M_w = 12000$
$M_w/M_n = 2.0$

In conclusion, we have disclosed that the Pd(0)-catalyzed C–N bond-forming cross-coupling of aryl halides with *N*-trimethylsilylamines proceeds smoothly in the presence of a Pd catalyst and cesium fluoride in DMI. The feature of the present

C–N coupling is attributed to high reactivity of nitrogen nucleophiles generated by the fluoride-mediated desilylation of *N*-TMS amines. In addition, the present reaction allows us to use variously functionalized substrates and thus demonstrates wide applicability which might lead to invention of novel functionalized organic materials by double and multiple C–N bond-forming couplings. Currently, our interest is focused on extension of the scope of the reaction.

References and Notes

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