# Palladium-Catalyzed N-Arylation of Bis(*ortho*-substituted aryl)amines: an Efficient Method for Preparing Sterically Congested Triarylamines

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**Abstract:** Bis(*ortho*-substituted aryl)amines were arylated on the nitrogen atom with various haloarenes in high yields using the palladium catalyst, which was generated from palladium(II) acetate and tri(*tert*-butyl)phosphine.

Key words: amination, arylation, cross-coupling, homogeneous catalysis, palladium

Triarylamine is an important structural motif, which is often seen in organic electronic devices, for example, hole transport or organic photovoltaic materials.<sup>1</sup> An access to the framework is the cross-coupling of diarylamines with halobenezenes using palladium<sup>2</sup> or copper catalyst.<sup>3</sup> In particular, the former catalyst is applicable to the aminations of a broad range of haloarenes, which include unreactive chloroarenes.<sup>4,5</sup> As for diarylamine substrates, the palladium-catalyzed cross-coupling is compatible with various functional groups on the para position in the aromatic ring.4,6 Only a few mono-ortho-substituted diarylamines are known to couple with haloarenes by palladium catalysis.<sup>7</sup> However, the carbon-nitrogen bond formation between aryl halides and bis(ortho-substituted aryl)amines has not been reported previously. The installation of methyl groups at the *ortho* positions in fluorescent triarylamines is known to cause blue shifts of the emission as well as enhancement of the fluorescent intensity.<sup>8</sup> Herein, we report that the N-arylation of bis(ortho-substituted aryl)amine proceeds in the presence of a (t-Bu)<sub>3</sub>P-ligated palladium catalyst. The catalytic carbonnitrogen bond formation affords a variety of sterically congested triarylamines in high yields.

We evaluated a series of ligands, which are known to be effective for the palladium-catalyzed amination of aryl halides, for the reaction between bromobenzene (**1a**) and bis(2-methylphenyl)amine (**2a**) with 5 mol% palladium loading in toluene at 80 °C for three hours (Table 1). No cross-coupling of **1a** with **2a** was observed in the reaction using a chelate bisphosphine ligand, such as DPPF<sup>9</sup> or BINAP<sup>10</sup> (entries 1 and 2). The desired cross-coupling was observed with a bulky and electron-rich proazaphosphatrane<sup>11</sup> or N-heterocyclic carbene<sup>12</sup> ligand, but **3a** was obtained in low yield (entries 3 and 4). Ligand

**L5** was the most effective among 2-(dialkylphosphino)biaryl ligands (entries 5–8).<sup>2b,13</sup> The *tert*-butyl group on the phosphorus is preferable to cyclohexyl for the arylation of **2a**. However, prolongation of the reaction time to 24 hours resulted in no change of the yield of **3a** in the reaction using the biarylphosphines **L5**.

The observation suggests that the **L5**-ligated palladium catalyst has a limited lifetime in the catalytic amination of haloarenes with **2a**. The ligands bearing a di(*tert*-bu-tyl)phosphino group, Q-Phos,<sup>5a</sup> cBRIDP,<sup>14</sup> cataCXium<sup>®</sup> A,<sup>15</sup> and (*t*-Bu)<sub>3</sub>P,<sup>4,16</sup> were found to enable sterically congested **2a** to couple with aryl bromide with high efficiency (entries 9–12). In particular, the (*t*-Bu)<sub>3</sub>P–palladium catalyst successfully produced **3a** in 86% yield at three hours.

Effects of other reaction parameters were investigated in the reaction using  $(t-Bu)_3P$  ligand. The cross-coupling of **1a** with **2a** was scarcely affected by the reaction solvent. Choice of base is crucial for the carbon–nitrogen bond formation. Little or no formation of **3a** was observed in the reaction using bases other than NaO(t-Bu) (entries 13– 16). As for palladium precursors, Pd(OAc)<sub>2</sub> was comparable to Pd(dba)<sub>2</sub> (entry 17). The loading of (t-Bu)<sub>3</sub>P–palladium catalyst was reduced to 1 mol% without a significant loss of catalyst efficiency (entry 18). Furthermore, the reaction produced the coupling product in 91% isolated yield when it was carried out at 120 °C (entry 19).<sup>17</sup>

The optimized catalyst in hand was applied to the amination of a range of bromoarenes with diarylamine 2a (Table 2). As with **1a**, *p*-bromotoluene (**1b**) was coupled with 2a in high yield (entry 1). The catalytic N-arylation of 2a was not hampered by the substituent at the meta position of the electrophilic substrate (entries 2 and 3). The o-methyl group of **1e** or **1f** significantly obstructed the carbon-nitrogen bond formation, but the sterically congested triarylamines, 3e and 3f could be obtained in pure form from the palladium-catalyzed reactions (entries 4 and 5). Electron-donating or -withdrawing substituents on bromoarenes 3g-i scarcely affected the formation of triarylamine (entries 6-8). However, alkoxycarbonyl group caused no formation of the desired coupling product. Bis(o-methylaryl)amines 2b and 2c were also arylated with **1a** by  $(t-Bu)_3P-Pd(OAc)_2$  catalyst (entries 9 and 10). It is noteworthy that electron-rich 2c was coupled with ortho-substituted 1e or 1f to form tris(ortho-substituted aryl)amine **3l** or **3m** in good yield (entries 11 and 12). The methoxy group of 2c might accelerate the amination of (aryl)(bromo)palladium(II) intermediate.

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### Table 1 Optimization of Reaction Conditions<sup>a</sup>



<sup>a</sup> Reactions were conducted in toluene (0.5 mL) at 80 °C. The ratio of **1a/2a** (0.20 mmol)/NaO(*t*-Bu)/[Pd]/ligand was 110:100:150:5:10 unless otherwise noted.

<sup>b</sup> Catalyst loading is in parentheses.

<sup>c</sup> GC yield (average of two runs).

<sup>d</sup> The ratio of [Pd]/ligand is 1:1.

<sup>e</sup> The reaction was conducted in the presence of  $C_{14}H_{29}NMe_3Br$  (3.0 mol% to 2a).

		Mi R1 Br + 1 Mi	$\begin{array}{c} 0 \text{ mol}\%), \\ 0 \text{ mol}\%), \\ 10 \text{ mol}\%) \\ R1 \\ R1 \\ R20 \text{ °C} \\ Me \\ R^2 \\ R^2 \end{array}$	$R^2$ $R^1$ N Me $R^2$		
Entry	<b>1</b> R <sup>1</sup> =	<b>2</b> R <sup>2</sup> =	Time (h)	Product <b>3</b>	Yield (%) <sup>b</sup>	
1	<b>1b</b> 4-Me	<b>2a</b> H	2		92	
2	<b>1c</b> 3-Me	<b>2a</b> H	2	3b Me Me Ne	91	
3	<b>1d</b> 3,5-Me <sub>2</sub>	2a H	2	3c Me $Me$ $Ne$ $Ne$ $Ne$ $Ne$ $Ne$ $Ne$ $Ne$ $N$	89	
4	<b>1e</b> 2-Me	<b>2a</b> H	2	3d Me Me Me	35	
5	<b>1f</b> 2,6-Me <sub>2</sub>	<b>2a</b> H	24	3e Me Me Me Me Me Me Me	17	
6	1g 4-MeO	<b>2a</b> H	2		80	
7	<b>1h</b> 3-MeO	<b>2a</b> H	2	MeO Me Ne Ne Me	97	

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Tab	le 2	Amination of Bromoarenes	l with D	Diarylamines 2	$2^{a}$ (continued	1)
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<sup>a</sup> Reactions were conducted in toluene (2.0 mL) at 120 °C. The ratio of 1/2 (1.0 mmol)/NaO(*t*-Bu)/Pd(OAc)<sub>2</sub>/(*t*-Bu)<sub>3</sub>P was 110:100:150:1:2 unless otherwise noted.

<sup>b</sup> Isolated yield.

<sup>c</sup> The ratio of **1/2** was 1.5:1.

<sup>d</sup> The ratio of 1/2 was 1.2:1.

Aryl chlorides **4** were also coupled with the bis(*ortho*-substituted aryl)amines by the  $(t-Bu)_3P$ -palladium catalyst (Table 3). The aminations of non-, *para*-, or *meta*-substitued chlorobenzenes **4a**-**c** with **2a** produced the corresponding triarylamines **3a**-**c** in 87–89% yields (entries 1– 3). However, the reactions of the chloroarenes required a longer reaction time for the complete conversion of **2a** than those of the corresponding bromoarenes. Tris(*o*-methylphenyl)amine **3e** could be obtained from the arylation of **2a** with 2-chlorotoluene (**4d**). The reaction of **4d** was comparable in the yield of **3e** to that of bromoarene **1e**.

The present N-arylation of bis(*o*-methylaryl)amines **2** proceeds through a typical mechanism of palladium-catalyzed cross-coupling of haloarenes with amines (Scheme 1). The catalytic cycle starts from the oxidative addition of haloarenes to  $(t-Bu)_3P$ -palladium(0) species

**A**.<sup>18</sup> The resulting (aryl)(halo)palladium(II) **B** undergoes ligand exchange with tert-butoxide to form palladium alkoxide C.<sup>19</sup> The alkoxo ligand in C abstracts the proton from 2 and is replaced by diarylamido ligand. The reductive elimination from (amido)(aryl)palladium(II) D produces the triarylamine **3** and regenerates the palladium(0) A.<sup>20</sup> The oxidative addition is believed to be the ratecontrolling step in the typical palladium-catalyzed amination of haloarene.<sup>21</sup> However, electron-rich bromoarene 1g exhibited reactivity comparable to electron-deficient 1i in the catalytic amination with 2a.<sup>22</sup> This observation suggests that the substitution of alkoxo with amido ligand controls the rate of the cross-coupling of 1 with 2. The two o-methyl groups may hinder the interaction between palladium and amine substrate. As for the amination of obromotoluene, the electron-rich diarylamine 2c was transformed to the desired triarylamine in higher yield than 2a (entries 4 vs. 11 in Table 2).<sup>23</sup> The formation of (amido)palladium **D** might be facilitated by the methoxy groups of 2c, which enhance the nucleophilicity of the nitrogen atom.24

 Table 3
 Amination of Chloroarenes 4 with Diarylamine 2a<sup>a</sup>



<sup>a</sup> Reactions were conducted in toluene (2.0 mL) at 120 °C for 24 h. The ratio of 4/2a (1.0 mmol)/NaO(*t*-Bu)/Pd(OAc)<sub>2</sub>/(*t*-Bu)<sub>3</sub>P was 110:100:150:1:2 unless otherwise noted.

<sup>b</sup> Isolated yield.



Scheme 1 A possible mechanism of arylation of 2 with halobenzenes

In summary, bis(*ortho*-substituted aryl)amines were arylated on their nitrogen atoms with bromo- or chloroarenes in high yields by using the  $(t-Bu)_3P-Pd(OAc)_2$  catalyst. The catalytic carbon–nitrogen bond formation produced a variety of sterically congested triarylamines in high yields. The arylation of bis(*ortho*-substituted aryl)amines is applicable to the preparation of sterically congested tris(*ortho*-substituted aryl)amines.

**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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- (17) **Typical Procedure for the N-Arylation of Bis**(*ortho***substituted aryl)amines 2** Under a nitrogen atmosphere, a haloarene 1 or 4 (1.5 mmol) was added to a mixture of  $(t-Bu)_3P$  (4.1 mg, 20 µmol), Pd(OAc)<sub>2</sub> (2.2 mg, 10 µmol), NaOt-Bu (144 mg, 1.5 mmol), and a diarylamine 2 (1.0 mmol) in toluene (2.0 mL). The reaction mixture was stirred at 120 °C for 2–24 h, cooled to r.t., diluted with H<sub>2</sub>O, and then extracted with EtOAc. The combined organic layer was washed with brine, dried over

 $Na_2SO_4$ , and then evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc–hexane) to give the desired triarylamine **3**.

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- (22) The competitive experiment using an equimolar mixture of 1g and 1i afforded 3g and 3i by a ratio of 48:52. See details in the Supporting Information.
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