

## Homocoupling of Aryl Iodides Catalyzed by Cyclopalladated Complexes of Tertiary Arylamines

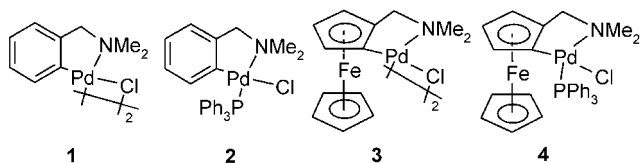
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Homocoupling of aryl iodides catalyzed by cyclopalladated complexes of tertiary arylamines gives symmetric biaryls with good yields in DMA or ionic liquid [Bmim]BF<sub>4</sub>. This catalytic alternative of the Ullmann reaction has proved to be sensitive to both electronic and steric factors of substrates.

**Keywords**    cyclopalladated complex, tertiary arylamine, homocoupling, aryl iodide, ionic liquid

The preparation of biaryl compounds is an important synthetic field. There are many methods to prepare symmetrical biaryls, the main way being the Ullmann reaction that requires stoichiometric amounts of copper.<sup>1</sup> The main drawbacks of the Ullmann reaction include the requirement of at least equimolar amounts of copper and heterogeneous reaction conditions. Homocoupling of aryl halides catalyzed by palladium has been developed with high loading of 5%—20% palladium.<sup>2</sup> Palladacycles have been by far the most developed and studied palladium catalysts for the homocoupling of aryl halides because of their structural versatility and easy synthetic accessibility and high catalytic activity in the above C—C bond-forming reactions.<sup>3</sup> The previous study by our group demonstrated that thermally and air stable cyclopalladated complexes of tertiary arylamines (**1**—**4**) could promote the Heck couplings with impressive turnover numbers of up to  $9.6 \times 10^6$ .<sup>4</sup> As a part of our systematic exploration of the chemistry of these cyclopalladated complexes,<sup>5</sup> the application of complexes **1**—**4** as catalysts for the synthesis of symmetric biaryls via reductive couplings of aromatic iodides was reported.



**Figure 1** Cyclopalladated complexes of tertiary arylamines.

The dimeric complexes **1** and **3** could be conveniently prepared by treatment of Li<sub>2</sub>[PdCl<sub>4</sub>] or Na<sub>2</sub>[PdCl<sub>4</sub>] with the corresponding amines.<sup>6</sup> Treatment of the respective dimers with PPh<sub>3</sub> in benzene gave the mono-

meric complexes **2** and **4** quantitatively. When iodobenzene was initially subjected to catalytic amount of complex **1** in the presence of triethylamine in DMA, biphenyl was produced in good yield with only 0.2 mol% of Pd loading. Reaction parameters were optimized with 0.2 mol% of Pd catalyst using iodobenzene as the model substrate and the results were compiled in Table 1.

**Table 1** Palladium-catalyzed homocoupling of aryl iodides<sup>a</sup>

Entry	Cat.	Sol.	Base	Time/h	Temp. <sup>c</sup> /°C	Yield <sup>d</sup> /%
1	<b>1</b>	DMA	Et <sub>3</sub> N	5	120	39
2	<b>1</b>	DMA	Et <sub>3</sub> N	5	132	100
3	<b>2</b>	DMA	Et <sub>3</sub> N	5	132	91
4	<b>3</b>	DMA	Et <sub>3</sub> N	5	132	98
5	<b>4</b>	DMA	Et <sub>3</sub> N	5	132	85
6	PdCl <sub>2</sub>	DMA	Et <sub>3</sub> N	5	132	45
7	Pd(OAc) <sub>2</sub>	DMA	Et <sub>3</sub> N	5	132	83
8	<b>1</b>	DMA	NaOAc	5	132	<5
9	<b>1</b>	DMA	Pyridine	5	132	Trace
10	<b>1</b>	DMA	K <sub>2</sub> CO <sub>3</sub>	5	132	<5
11	<b>1</b>	DMA	K <sub>2</sub> CO <sub>3</sub> <sup>b</sup>	5	132	66
12	<b>1</b>	DMA	Et <sub>3</sub> N	4	132	94
13	<b>1</b>	dioxane	Et <sub>3</sub> N	4	132	<5
14	<b>1</b>	toluene	Et <sub>3</sub> N	4	132	<5
15	<b>1</b>	DMF	Et <sub>3</sub> N	4	132	88

<sup>a</sup> PhI (5 mmol), base (7.5 mmol) and Pd catalyst (0.2 mol%) in 10 mL of solvent. <sup>b</sup> In the presence of isopropanol. <sup>c</sup> Bath temperature. <sup>d</sup> GC yields.

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From Table 1, it can be seen that temperature has a dramatic effect on the reaction (Table 1, Entries 1 and 2). The reaction was very slow below 130 °C (bath temperature). Thus satisfactory results were achieved when the homocoupling reaction was conducted in DMA or DMF (Table 1, Entries 2 and 15) while over 90% iodobenzene was recovered in refluxing toluene or dioxane (Table 1, Entries 13 and 14). Triethylamine was more efficient than potassium carbonate, sodium acetate and pyridine as base for the homocoupling reaction (Table 1, Entries 2, 8—10).

Lemaire *et al.*<sup>2a</sup> reported that a reductive reagent such as isopropanol could promote the homocoupling of aryl halides using inorganic bases such as K<sub>2</sub>CO<sub>3</sub>. In our system, addition of isopropanol to the reaction mixture using potassium carbonate as base could really increase the yield of the desired biphenyl, but it was still less efficient than Et<sub>3</sub>N (Table 1, Entries 2, 10 and 11).

Among the palladium sources tested, phosphine-free cyclopalladated complexes **1** and **3** showed higher catalytic activity than **2** and **4** with one molecule triphenylphosphine coordinated (Table 1, Entries 2—5). Inorganic palladium catalysts such as Pd(OAc)<sub>2</sub> or PdCl<sub>2</sub> could also catalyze the coupling, but they were obviously less efficient than the cyclopalladated complexes of tertiary arylamines **1**—**4** under otherwise identical conditions (Table 1, Entries 6 and 7). Compared to the palladacycle-based system for the homocoupling of aryl iodides reported in literature,<sup>3</sup> our system is among the most active ones.

The reactivity of various aryl halides in the homocoupling reaction was investigated under the optimized reaction conditions (Table 2). Both electronic and steric effects were observed for the homocoupling, which is similar to that obtained from a cyclopalladated complex of sulfide.<sup>3d</sup> Electron-donating substitution on the aryl halides, such as 4-iodoanisole, displayed a similar reactivity to iodobenzene (Table 2, Entry 2). However, 4-iodophenol showed lower reactivity while 4-*N,N*-dimethylaminophenyl iodide was converted smoothly although with dehalogenation (Table 2, Entries 7 and 8). Electron-withdrawing substitution, for example methyl

4-iodobenzoate, gave desired product in very low yield (Table 2, Entry 5). Steric factor also affected the reaction significantly. 4-Methyl iodobenzene gave 99% yield while 2-methyl iodobenzene remained almost untouched under a similar condition (Table 2, Entries 3 and 4). Aryl bromides looked like to be inert since only trace amount of bromobenzene was converted under the optimized condition that worked well for aryl iodides.

**Table 2** Reductive coupling of aryl halides catalyzed by palladacycle **1** in DMA<sup>a</sup>

Entry	R	X	Product	Yield <sup>b</sup> /%
1	H	I	Biphenyl	94
2	4-OCH <sub>3</sub>	I	4,4'-Dimethoxybiphenyl	93
3	4-CH <sub>3</sub>	I	4,4'-Dimethylbiphenyl	99
4	2-CH <sub>3</sub>	I	2,2'-Dimethylbiphenyl	<1
5	4-COOCH <sub>3</sub>	I	Dimethyl 4,4'-biphenyl-dicarboxylate	11
6	2-COOCH <sub>3</sub>	I	Dimethyl 2,2'-biphenyl-dicarboxylate	7
7	4-OH	I	4,4'-Biphenol	30 <sup>c</sup>
8	4-NMe <sub>2</sub>	I	4,4'-Bis( <i>N,N</i> -dimethyldiamino)-biphenyl	58 <sup>d</sup>
9	H	Br	Biphenyl	<5

<sup>a</sup> **Reaction conditions:** aryl halide (5 mmol), NEt<sub>3</sub> (7.5 mmol) and Pd catalyst (0.2 mol%) in 10 mL of DMA, bath temperature 132 °C, reaction time 4 h. <sup>b</sup> GC yields. <sup>c</sup> Isolated yield. <sup>d</sup> 37% *N,N*-dimethylaniline detected.

Considering that the cyclopalladated complex catalyzed homocoupling of aryl iodides required high temperature and polar solvents, such as DMA, which would unavoidably lead to tedious work-up procedures, we further investigated the reaction in ionic liquids, which has emerged as a green reaction medium especially for transition metal-catalyzed organic procedures,<sup>7</sup> and the results were compiled in Table 3.

**Table 3** Homocoupling of aryl iodides catalyzed by **1** in ionic liquids<sup>a</sup>

Entry	Substrate	Ionic liquid	Product	Yield <sup>b</sup> /%
1	C <sub>6</sub> H <sub>5</sub> I	[Bmim]Br	Biphenyl	trace
2	C <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	Biphenyl	99
3	C <sub>6</sub> H <sub>5</sub> I	[Omim]BF <sub>4</sub>	Biphenyl	33
4	2-CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	2,2'-Dimethylbiphenyl	trace
5	3-CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	3,3'-Dimethylbiphenyl	93 <sup>c</sup>
6	4-CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	4,4'-Dimethylbiphenyl	90
7	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	4,4'-Dimethoxybiphenyl	74 <sup>d</sup>
8	4-BrC <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	4,4'-Dibromobiphenyl	36
9	4-CH <sub>3</sub> OCC <sub>6</sub> H <sub>5</sub> I	[Bmim]BF <sub>4</sub>	Dimethyl 4,4'-biphenyldicarboxylate	trace

<sup>a</sup> **Reaction conditions:** arylhalides (1.0 mmol), Et<sub>3</sub>N (1.5 mmol) and **1** (0.2 mol%) in 1.0 mL of ionic liquids were heated at 160 °C for 5

h. <sup>b</sup> GC yields. <sup>c</sup> 7% toluene was detected. <sup>d</sup> 12% anisole was detected.

When the homocoupling of iodobenzene catalyzed by **1** was conducted in ionic liquids consisting of bromide, such as [Bmim]Br no desired product was detected even at higher temperature. However, modest to high conversion could be achieved when the reaction was switched to bromide-free ionic liquids, such as [Bmim]BF<sub>4</sub> (Table 3, Entries 1—3). Although the catalytic activity of the cyclopalladated complexes decreased in ionic liquids, the product-separation procedure was greatly simplified. Extraction with ether or direct sublimation gave products, and the ionic liquid could be reused. A similar trend for the effects of electronic and steric factors of substrates on the coupling in ionic liquid was observed as in DMA (Table 3, Entries 4—9). Electron-deficient substrates displayed much lower reactivity compared with the electron-rich ones.

In summary, the readily available cyclopalladated complexes of tertiary arylamines **1—4** have proved to be very efficient catalysts for the reductive couplings of aryl iodides. The ready availability and stability of these cyclopalladated complexes of tertiary arylamines against air, moisture and temperature make them very practical catalysts for the synthesis of symmetric bi-phenyls. The successful conduction of the above reaction in ionic liquids further has made the reaction practical by simplifying the work-up procedure.

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