

# Cross-Coupling of Aryl Iodides with Malononitrile Catalyzed by Palladium *N*-Heterocyclic Carbene Complex System

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Eight *N*-heterocyclic carbenes (NHC), generated *in situ* from their imidazolium salts, as ligands of palladium complexes were used for the catalytic coupling of iodobenzene with malononitrile anion. It was found that 1,3-bis(2,4,6-trimethylphenyl)-imidazolium chloride (IMesHCl)-Pd<sub>2</sub>(dba)<sub>3</sub> catalytic system has the highest activity to obtain phenyl malonitrile among the imidazolium salts. The substituted iodoarenes reacted with malononitrile anions by using the catalytic system to give cross-coupling products in yields from 50% to 96%.

**Keywords** palladium complex, *N*-heterocyclic carbene, imidazolium salt, cross-coupling, arylmalononitrile

Nucleophilic *N*-heterocyclic carbenes (NHC) or so-called "phosphine mimics", are a novel class of ligands and have attracted considerable attention as promising alternatives to the widely used phosphine ligands in homogeneous catalysis.<sup>1-9</sup> Particularly, the carbon-carbon bond coupling catalyzed by transition metal/*N*-heterocyclic carbene system is an attractive scope in Heck,<sup>4,5,10</sup> Suzuki,<sup>3,10-12</sup> Stille<sup>3</sup> and Kumada<sup>13,14</sup> reactions. It has opened new opportunities in homogeneous catalytic synthesis.<sup>15,16</sup> Additional advantages of these ligands over classic phosphine ligands include ease of preparation, easy derivatization with low cost, higher stability and simple operation.

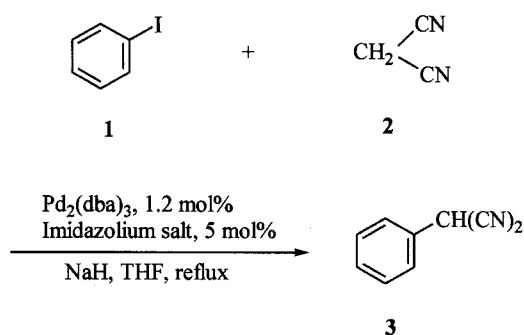
It is known that malononitrile derivatives are key intermediates<sup>17-19</sup> in the syntheses of heterocyclic compounds and organic electric-conductors. But aryl halides are not reactive enough to directly undergo intermolecular substitution reaction with malononitrile anion under normal condition. Uno *et al.* reported that palladium phosphine complexes could catalyze the cross-coupling of aryl iodides with malononitrile anions and gave satisfactory arylation

products.<sup>20-22</sup> Obviously, the effective synthetic routes are still homogeneous palladium-catalyzed syntheses using ubiquitous phosphine ligands (PR<sub>3</sub>)<sup>23,24</sup> in the homogeneous catalysis.

Herein we synthesized a series of 1,3-diaryl and dialkyl substituted imidazolium salts as the precursors of *N*-heterocyclic carbene ligands and investigated their ancillary catalytic properties in the cross-coupling of aryl iodides with malononitrile anions employing the catalytic system of Pd<sub>2</sub>(dba)<sub>3</sub> and 1,3-disubstituted imidazol-2-ylidene (NHC) generated *in situ* from the imidazolium salts (Scheme 1).

In the coupling model of iodobenzene and malononitrile anion, two kinds of 1,3-disubstituted imidazolium salts (Scheme 2, LHCl) were synthesized and tested in the catalytic coupling. The arylmalononitrile preparation demonstrated the catalytic system of Pd<sub>2</sub>(dba)<sub>3</sub>/imidazolium salts could promote the reaction yields. In the absence

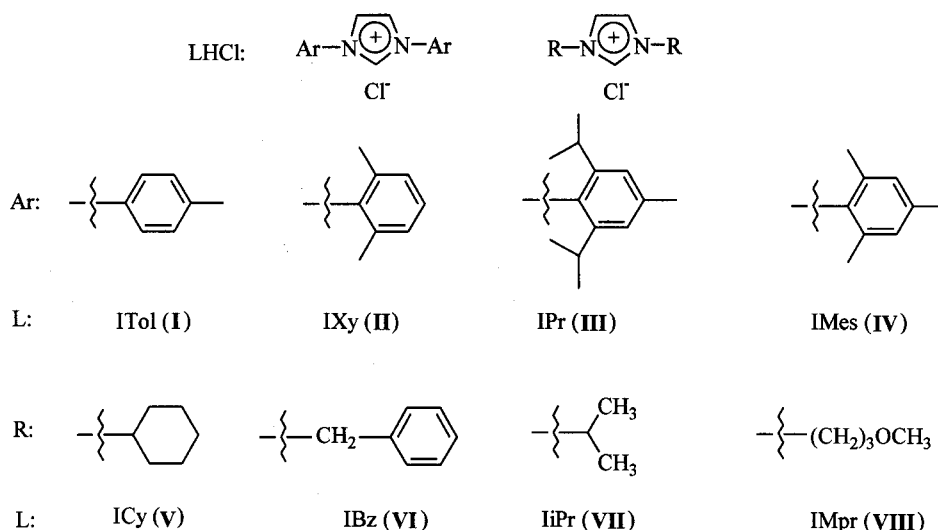
Scheme 1



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Scheme 2 Imidazolium salts (LHCl)



of imidazolium salts the lower yield of phenylmalononitrile was obtained (Table 1, Entry 1, 12% yield).

**Table 1** Palladium-catalyzed coupling of iodobenzene with malononitrile using different 1,3-disubstituted imidazolium salts<sup>a</sup>

Entry	Ligand (LHX)	Time (h)	Yield <sup>b</sup> (%)
1	None	12	12
2	ITolHCl	12	20
3	IXyHCl	12	23
4	IPrHCl	12	74
5	IMesHCl	10	92
6 <sup>c</sup>	ICyHCl	14	41
7 <sup>c</sup>	IBzHCl	14	24
8 <sup>c</sup>	IiPrHCl	14	Trace
9	IMprHCl	14	Trace

<sup>a</sup>The reactions were carried out according to the conditions indicated by Scheme 1. For typical procedure: iodobenzene: malononitrile: base: catalyst: ligand = 1:1.5:2.5:0.012:0.05 (mmol) at reflux using 10–12 mL of THF as solvent under argon. <sup>b</sup> Isolated yields were based on PhI and the average of two runs after chromatography. <sup>c</sup> The imidazolium chlorides were quantitatively added with 0.1 mol/L of imidazolium chloride in the DMF solution.

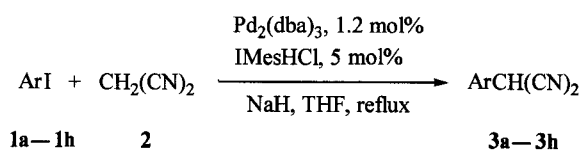
The tendency of the catalytic efficiencies of 1,3-diaryl substituted imidazolium salts (Scheme 2, LHCl, L = I–IV) being superior to that of 1,3-dialkyl substituted imidazolium salts (L = V–VIII) was observed clearly. As a result of our study, the catalytic activity of the 1,3-diaryl substituted carbene ligands is in the order: IMes >

IPr > IXy ≈ ITol, and ICy > IBz > IiPr ≈ IMpr for 1,3-dialkyl substituted ligands. As shown in Table 1, the highest catalytic activity of the coupling was given (Entry 5) by the IMes [IV, 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] with a yield of 92% of phenylmalononitrile, which is better in comparison with IPr [III, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] (Entry 4). However, other imidazolium salts showed only moderate catalytic activity with yields lower than 41%.

The results of the cross-coupling of a number of aryl iodides (Scheme 3, 1a–1h) with malononitrile using the Pd<sub>2</sub>(dba)<sub>3</sub>/IMesHCl catalytic system are shown in Table 2. On the basis of above results, the application scope of the palladium/imidazol-2-ylidene system was extended to the synthesis of substituted arylmalononitriles. For most of aryl iodides, the iodine atom on the aromatic ring could be smoothly replaced by a dicyanomethyl group and the corresponding arylmalononitriles were produced in 50%–96% yields (Table 2). Unsubstituted iodobenzene and 1-iodonaphthalene demonstrated excellent reactivity with satisfactory yield (3a, 92%; 3h, 96%).

The steric and electronic effects of the substituents on the aromatic ring were also observed. The electron-donating groups (in 1f and 1g) would affect the activation of the coupling reaction and led to a considerable decrease in product yield (for 3f, 53% and 3g, 50%). Furthermore, the presence of the *ortho*- or *para*-chloro-functional group on the benzene ring seemed to have no influence on the formation of the products, as there was only a small extent decrease of the yields in 3d and 3e.

## Scheme 3



**Table 2** Coupling of aryl iodide with malononitrile anion catalyzed by Pd<sub>2</sub>(dba)<sub>3</sub>/IMesHCl<sup>a</sup>

Compd	Ar	Time (h)	Product <sup>b</sup>	Yield <sup>c</sup> (%)
1a	C <sub>6</sub> H <sub>5</sub>	10	3a	92
1b	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	10	3b	86
1c	<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	11	3c	64
1d	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	12	3d	84
1e	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	12	3e	85
1f	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	13	3f	53
1g	<i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	13	3g	50
1h	1-Naphthyl	8	3h	96

<sup>a</sup>The reactions were carried out according to the conditions indicated by Scheme 3 except for special indication. For a typical procedure: aryl iodide:malononitrile:NaH:cat.:IMesHCl = 1:1.5:2.5:0.012:0.05 (mmol) at reflux using 10–12 mL of THF as solvent under argons. <sup>b</sup>The products were identified by means of <sup>1</sup>H NMR and m. p., which are in agreement with literature data.<sup>26,27</sup> <sup>c</sup>The isolated yields were based on ArI and the average of two runs after chromatography.

In conclusion, a general and efficient method is presented for the preparation of arylmalononitriles through Kumada cross-coupling of aryl iodides with nucleophilic carbon anions by simply employing the catalytic system comprising Pd(0) and 1,3-disubstituted imidazol-2-ylidene generated *in situ* from the imidazolium salts ligand. In our investigation of cross-coupling of aryl iodides with malononitrile anion using the Pd<sub>2</sub>(dba)<sub>3</sub>/IMesHCl as catalytic system, the 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride showed obvious catalytic activation. Other 1,3-disubstituted imidazolium salts only exhibited moderate catalytic efficiency under the similar condition.

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