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Palladium-bisimidazol-2-ylidene complexes as catalysts for general and efficient Suzuki cross-coupling reactions of aryl chlorides with arylboronic acids

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Abstract

A series of bisimidazolium salts **1**–**6** were synthesized and evaluated as precursors to bisimidazol-2-ylidene ligands in palladium-catalyzed Suzuki cross-coupling reactions with aryl chlorides and arylboronic acids. The bisimidazolium salt **6** was found to be superior over imidazolium and other bisimidazolium salts affording high yields of biaryl products employing a wide variety of substrates. © 2000 Elsevier Science Ltd. All rights reserved.

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The palladium-catalyzed Suzuki cross-coupling reactions of aryl halides and triflates with arylboronic acids provide a general and efficient synthetic route to biaryl compounds and have found widespread use in many areas of organic synthesis.[1] Routinely these procedures employ phosphine-based catalyst systems and arylbromide, aryl iodide or aryl triflate substrates. The use of aryl chlorides as chemical feedstock in coupling chemistry has proven difficult but would economically benefit a number of industrial procedures.[2,3] Significant advances have been recently reported by Buchwald,[4] Fu[5] and Guram,[6] which used modified-phosphine palladium systems.

Nucleophilic *N*-heterocyclic carbenes, especially the imidazol-2-ylidenes have attracted considerable attention as possible alternatives for widely used phosphine ligands in homogeneous catalysis.[7] We recently reported on the Suzuki cross-coupling reactions of aryl chlorides and arylboronic acids employing a $Pd_2(dba)_3$/IMes·HCl catalyst system.[8] As part of an ongoing investigation aimed at the development of novel imidazol-2-ylidenes as ligands for transition metal catalysis, we wish to report the efficient Suzuki coupling reactions of aryl chlorides with aryl boronic acids using palladium-bisimidazol-2-ylidene (Pd–L) catalyst systems preformed from $Pd(OAc)_2$ and bisimidazolium salts (L·2HX).

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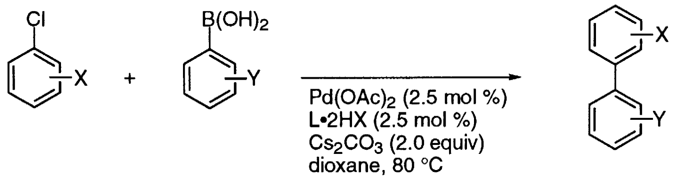


The bisimidazolium salts **1**–**6** (Fig. 1) were prepared by heating the corresponding dibromides or dichlorides and 2 equivalents of a 1-aryl-imidazole in xylene. As an example, a mixture of dibromomethane (1.0 mmol) and *N*-(3,5-dimethylphenyl)imidazole (2.0 mmol) was heated in xylene (5 mL) at 140°C for 2 days. This afforded the salt **2** in 70% yield. Alternatively, a mixture of 1,3-di(α-chloromethyl)-2,4,6-trimethylbenzene (1.0 mmol) and *N*-(2,4,6-trimethylphenyl)imidazole (2.0 mmol) was heated in xylene (5 mL) at 120°C for 48 h and furnished **6** in 85% yield.

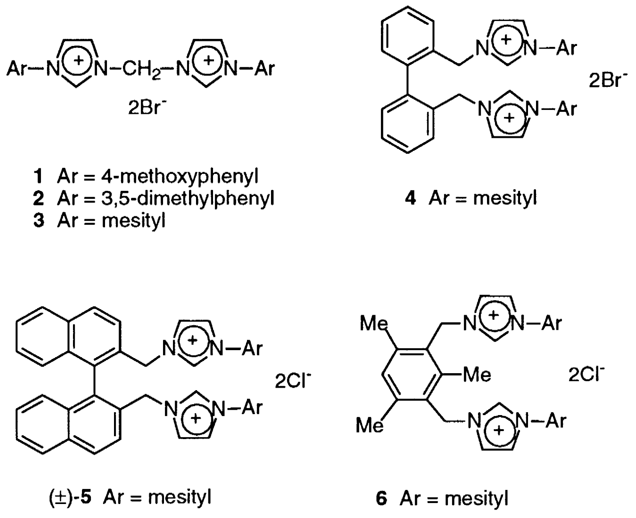


Fig. 1. Bisimidazolium salts

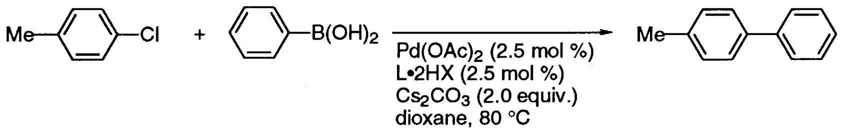
The Pd(OAc)$_2$/L·2HX catalyzed reaction of 4-chlorotoluene and phenylboronic acid was selected as a model reaction for investigating the efficiencies of these bisimidazolylidene (L) ligand precursors. As shown in Table 1, the bisimidazolium salts (±)-**5** and **6** were found to be effective substrates and afforded the desired biaryl product in high yields. The salt **4** provided a moderate yield of the biaryl compound while the salts **1**, **2**, and **3**, which possessed considerably less steric hindrance, were found to be less efficient and exhibited very low conversion.

The utility of the Pd(OAc)$_2$/bisimidazolium salt **6** catalyst system for general Suzuki cross-coupling reactions of aryl chlorides was further investigated to determine the scope and limitations of reaction (Table 2). The Pd(OAc)$_2$/**6** catalyst system was found to be generally efficient in catalyzing the cross-coupling reactions of a variety of aryl chlorides and arylboronic acids. Electron-donating and electron-withdrawing substituents were both well tolerated by the catalytic system and provided the corresponding biaryl products in excellent yields. Moreover, the ancillary bisimidazol-2-ylidene ligand generated from **6** was found to exhibit higher efficiency than that of imidazol-2-ylidene ligand generated from IMes·HCl (comparison of entry 1 and entry 2 in Table 2).

In summary, the novel bisimidazolium salts were prepared as bisimidazol-2-ylidene ligand precursors for Pd-catalyzed Suzuki coupling reactions of aryl chlorides with arylboronic acids. The Pd(OAc)$_2$/**6** catalyst system has been shown to be generally very efficient for high yielding cross-coupling reactions of aryl chlorides and arylboronic acids. The catalytic system involving air stable components Pd(OAc)$_2$

Table 1

Ligand effects in $Pd(OAc)_2$/L·2HX-catalyzed Suzuki reaction of 4-chlorotoluene and phenylboronic acid[9]



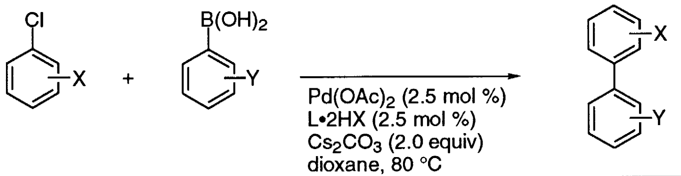
Entry	L•2HX	Time(h)[a]	Yield(%)[b]
1	**1**	24	trace[c]
2	**2**	24	<5[c]
3	**3**	6	32[c]
4	**4**	4	65[c]
5	**5**	4	87
6	**6**	1.5	99

[a] Reaction time after 30 min catalyst activation period. [b] Isolated yields.

[c] 4-Chlorotoluene was not completely consumed and precipitation of Pd black was observed.

Table 2

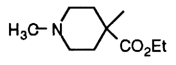
$Pd(OAc)_2$/**6**-catalyzed Suzuki cross-coupling reactions of aryl chlordes with arylboronic acids[9]



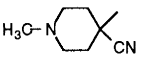
Entry	X	Y	L•2HX	Time(h)[a]	Yield(%)[b]
1	4-Me	2-Me	IMes·HCl[c]	4	60
2	4-Me	2-Me	**6**	4	99
3	4-Me	H	**6**	1.5	99
4	4-Me	4-Me	**6**	4	99
5	2,5-dimethyl	H	**6**	4	84
6	4-CO_2Me	H	**6**	2	99
7	4-R_1[d]	H	**6**	4	96
8	4-R_2[e]	H	**6**	4	91

[a] Reaction time after 30 min catalyst activation period. [b] Isolated Yields. [c] See reference 10.

[d] R_1 =



[e] R_2 =



and bisimidazolium salt **6**, should be amenable for large scale synthesis. Further investigations of this catalytic system and other transition metal-catalyzed organic transformations are ongoing.[10]

Acknowledgements

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