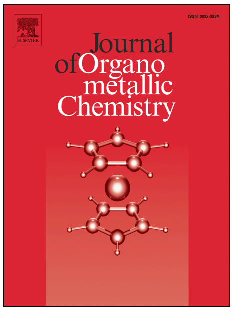

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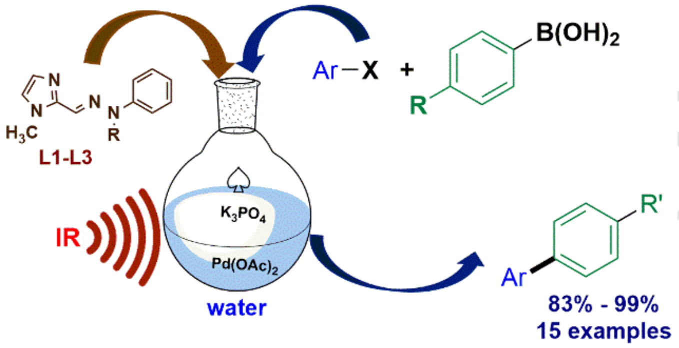
Graphical Abstract

An efficient and simple imidazole-hydrazone ligand for palladium-catalyzed Suzuki-Miyaura cross-coupling reactions in water under infrared irradiation

Martín Camacho-Espinoza, José Guillermo Penieres-Carrillo, Hulme Rios Guerra, Selene Lagunas-Rivera, Fernando Ortega-Jiménez.*



Efficient catalytic system [imidazole-hydrazone (**L1-L3**)/Pd(OAc)$_2$] has been developed for Suzuki–Miyaura reaction in water under IR-irradiation. A wide range of substrates could be coupled with phenylboronic acid to afford the desired products in good to excellent yields at low catalyst loadings and low time of reaction.

Imidazole-hydrazone efficient and simple ligand for palladium-catalyzed Suzuki-Miyaura cross-coupling reaction in water under IR-irradiation

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Abstract

A highly efficient catalytic system based on $Pd(OAc)_2$ and imidazole-hydrazone (**L1-L3**) has been developed for Suzuki–Miyaura cross-coupling reaction in water under aerobic conditions using IR irradiation. The system can tolerate a wide range of functionalized arylboronic acids and aryl halides. Furthermore, this protocol is also applicable and available for hetero-aryl bromides.

Keywords. Imidazole-hydrazone, Palladium-catalyzed, Cross-coupling reaction, water, IR-irradiation

1. Introduction

The palladium catalyzed Suzuki–Miyaura reaction between organoboron compounds and organic halides is one of the most powerful and convenient approaches for forming carbon–carbon bonds, particularly for the synthesis of biaryls.[1] Owing to the fact that the aryl–aryl structure motif is an important building block in organic chemistry, the Suzuki–Miyaura reaction is widely applied in academic research as well as in industrial synthesis of fine chemicals and highly complex pharmaceuticals.[2]

This application of the reaction results from the broad functional group tolerance, the commercial availability and low toxicity of the organoborons, the mild reaction conditions, ease of handling of products and by-products, and the possibility of using water as a solvent or co-solvent.[3,4]

The Suzuki–Miyaura cross-coupling reaction is usually catalyzed by a wide variety of Pd-based catalysts and the effectiveness of the catalytic system is dependent on the ligand environment around palladium. In the traditional Suzuki–Miyaura reactions, the electron-rich phosphine ligands were generally employed to improve the catalytic performance.[5] Since phosphine ligands are often water- and air-sensitive,[6] catalysis under phosphine-free conditions is still a challenge of high importance, different nitrogen based ligands such as *N*-heterocyclic carbenes,[7] palladacycle species,[8] N,O- or *N*,*N*-bidentate ligands,[9] aryloximes,[10] *O*-aryloxime ether,[11] arylimines,[12] *N*-acylamidines,[13] amines,[14] 2-aryl-2-oxazolines,[15] aylhydrazones,[16] among the others, have emerged as efficient ligands for Suzuki–Miyaura reaction with the potential to overcome most of the drawbacks of traditional phosphine ligands.

Additionally, the classic Suzuki–Miyaura reaction was often carried out in organic media, such as DMF,[17] THF,[18] dioxane,[19] toluene,[20] CH_3CN,[21] and methanol,[22]. Recently, this coupling reaction has strongly benefited from aqueous media,[23] most of substrates used are insoluble in water but numerous efforts have been made, such as synthesizing water-soluble ligands,[24] adding surfactants and/or phase-transfer agents,[25] or using microwave[26] or ultrasound[27]. Yet, most aqueous protocols for cross coupling reactions have some drawbacks such as high catalyst loading,[24b, 25d, 28] long reaction times[29] or require the addition of organic co-solvents, [30] including protocols ligand-free[25d, 28, 30b]. From these standpoints, the development of efficient, stable, economical, and environmentally friendly catalytic system remains a challenging task.

On the other hand, new alternative heating methodologies such as microwave,[31] ultrasound,[32] and infrared (IR) irradiation[33] have been applied in organic synthesis and catalysis with reduced reaction times, cleaner reaction mixtures and good yields. As a research program focused on the use of IR irradiation in C-C coupling reactions, recently we explore the use of IR to assist the Mizoroki-Heck [34,35] and Suzuki-Miyaura [36,37] cross-coupling reactions; in addition, we demonstrated an air stable phosphine-free hydrazone containing a heterocycle moiety as an effective ligand for palladium catalyzed Mizoroki-Heck[35,37] and Suzuki-Miyaura[37] cross-coupling under IR irradiation.

However, does not exist any papers about using arylhydrazones containing a heterocycle moiety as ligands for the Suzuki–Miyaura reaction in water using IR irradiation as the energy source. Herein, we report the synthesis of arylhydrazone derivatives containing the imidazole moiety as the effective ligand for palladium-catalyzed Suzuki-Miyaura cross-coupling reactions in water using IR irradiation, as an efficient, convenient, and environmentally friendly protocol for this cross-coupling reaction.

2. Experimental

2.1. Apparatus, materials, and measurements

All operations were carried out in open atmosphere. Column chromatography was performed using 70–230 mesh silica gel. All reagents and solvents were obtained from commercial suppliers and used without further purification. All compounds were characterized by IR spectra, recorded with a Perkin-Elmer 283B or 1420 spectrophotometer, by means of film and KBr techniques, and all data are expressed in wavenumbers (cm^{-1}). Melting points were obtained on a Melt- Temp II apparatus and are uncorrected. NMR spectra were measured with a Varian Eclipse +300 using $CDCl_3$ as solvents. Chemical shifts are in ppm (δ), relative to TMS. The MS-EI spectra were obtained on a JEOL SX 102a, the MS-DART spectra were obtained with a AccuTOF JMS-T100LC, the values of the signals are expressed in mass/charge units (m/z), followed by the relative intensity with reference to a 100% base peak.

The equipment used for irradiation with IR energy was created by employing an empty cylindrical metal vessel in which an Osram lamp (bulb model Thera-Therm, 250 W, 125 V) was inserted.[34]

2.2. General synthetic procedure for de compounds L1-L3.

A solution of the corresponding phenylhydrazine (1.8 mmol) in methanol (5 mL) was added dropwise to a magnetically stirred solution of 1-methyl-2-imidazolcarbaldehyde (1.8 mmol) in methanol (5 mL). The reaction mixture was refluxed using IR irradiation for 1.5 h, to give a yellow solid, which was recovered by filtration and recrystallized from methanol.

1-methylimidazole-2-carbaldehyde *N,N*-diphenylhydrazone **L1**. (98 %) yellow crystals, mp 122-125 °C, IR: ν (cm^{-1}): 3138, 3024, 2957, 2925 y 2858, (H-Csp^2 y H-Csp^3), 1585 (C=N) y 1490 (C=C_{arom}). MS-EI (70 eV) *m/z* (%): 276 $M^{+\bullet}$ (100), 167 $[C_{12}H_9N]^+$ (50). ^{1}H-NMR: (300 MHz, $CDCl_3$) δ (ppm) 4.10 (s, 1H, NCH_3), 6.89 (s, 1H, $H5_{imidazole}$), 7.00 (s, 1H, $H4_{imidazole}$), 7.11 (d, J = 7.5 Hz, 4H, H_{arom} *o*), 7.19 (t, J = 7.5 Hz, 2H, H_{arom} *p*), 7.31 (s, 1H, *H*C=NNPh$_2$), 7.41 (t, J = 7.5 Hz, 4H, H_{arom} *m*). ^{13}C-NMR: (75 MHz, $CDCl_3$) δ (ppm) 35.9 (N*C*H$_3$), 122.2 (C_{arom} *o*), 123.3 ($C5_{imidazole}$), 124.7 (C_{arom} *p*), 128.4 ($C4_{imidazole}$), 129.0 (H*C*=NNPh$_2$), 129.9 (C_{arom} *m*), 142.7 (C_{ipso} N), 143.4 ($C2_{imidazole}$).

1-methylimidazole-2-carbaldehyde *N*-phenyl-*N*-methylhydrazone **L2** (92 %) brown crystals mp. 84-88°C. IR: ν (cm^{-1}): 3124, 3028, 2958, 2925 y 2848, (H-Csp^2 y H-Csp^3), 1590 (C=N) y 1496 (C=C aromático). EM-DART: *m/z* (%), 214 $M^{+\bullet}$, 163 $[C_9H_{13}N_3]^+$.^{1}H-NMR: (300 MHz, $CDCl_3$) δ (ppm) 3.30 (s, 1H, NCH_3), 3.91 (s, 1H, $NCH_{3imidazole}$), 6.78 (s, 1H, $H5_{imidazole}$), 6.86 (t, J = 7.5 Hz, 2H, H_{arom} *p*), 6.97 (s, 1H, H4$_{imidazole}$), 7.14-7.23 (m, 4H, H$_{arom}$ *o,p*), 7.50 (s, 1H, *H*C=NNPh$_2$). ^{13}C RMN: (75 MHz, CDCl$_3$) δ (ppm) 32.9 (NCH$_3$), 36.0 (NCH$_{3\ imidazole}$), 115.2 (C$_{arom}$ *o*), 121.1 (C$_{arom}$ *p*), 123.0 (C5$_{imidazole}$), 124.7 (C4$_{imidazole}$), 127.3 (H*C*=NNPh$_2$), 129.1 (C$_{arom}$ *m*), 143.7 (C$_{ipso}$ N), 147.3 (C2$_{imidazole}$).

1-methylimidazole-2-carbaldehyde *N*-phenylhydrazone **L3**. (90%) yellow crystals, mp. 68-72 °C. IR: *ν* (cm^{-1}): 3191, 3126, 3103, 3017, 2944, 2856 (H-Csp^2 y H-Csp^3), 1588 (C=N), 1490, 1461 (C=C$_{arom}$). MS-EI: *m/z* (%), 200 M$^{+\cdot}$(100), 95 [C$_5$H$_7$N$_2$]$^+$ (30), 77 [C$_6$H$_5$]$^+$ (15). ^{1}H RMN: (300 MHz, CDCl$_3$) δ (ppm) 3.86 (s, 1H, NCH$_3$), 6.74-6.79 (m, 2H, H5$_{imizole}$, H$_{arom}$ *p*), 6.90-6.95 (m, 3H, H4$_{imizole}$, H$_{arom}$ *o*), 7.16 (t, 2H, *J* = 7.5 Hz, 2H, H$_{arom}$ *m*), 7.73 (s, 1H, *H*C=NNPh$_2$), 8.73 (s, 1H, N-H). RMN ^{13}C: (75 MHz, CDCl$_3$) δ (ppm) 35.6 (NCH$_3$), 112.3 (C$_{arom}$ *o*), 119.8 (C$_{arom}$ *p*), 123.5 (C5$_{imidazole}$), 128.5 (C4$_{imidazole}$), 129.1 (C$_{arom}$ *m*), 129.4 (H*C*=NNPh$_2$), 142.8 (C$_{ipso}$ N), 144.4 (C2$_{imidazole}$).

2.3. General procedure for Suzuki-Miyaura coupling reactions

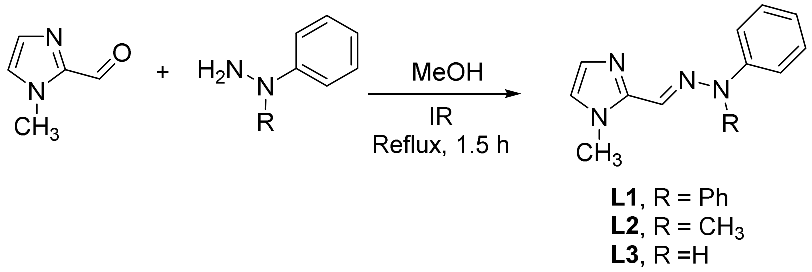
Inside a 50-mL round-bottom flask, a mixture of aryl halide (0.5mmol), phenylboronic acid (0.6 mmol), and base (1 mmol) was placed in 3 mL of solvent; then Pd source and corresponding arylhydrazone **1** were added. The reaction was irradiated with IR energy[34-37] for the time reported in Tables 1 and 2. Thereafter, the reaction was cooled at room temperature; the mixture was diluted with 10 mL of water and extracted with hexane or AcOEt (3 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate. The crude product was finally purified by column chromatography on silica-gel to give the isolated products.

The purified product was identified by means of mp determination and by ^{1}H and ^{13}C-NMR; the data obtained are consistent with literature.[38]

3. Results and discussion

3.1. Synthesis and characterization of hydrazones L1-L3.

The arylhydrazone ligands **L1–L3** were prepared employing the condensation reaction of the corresponding arylhydrazine and 1-metyl-2-imidazolcarbaldehyde in 1:1 mole ratio in methanol under IR irradiation for 1.5 h (Scheme 1). After of crystallization of methanol the ligand **L1-L3** was obtained as a solid in a 98, 92 and 90 % yields respectively and were fully characterized by conventional spectroscopic methods, ^{1}H NMR, ^{13}C NMR, IR and MS.



Scheme 1. Synthesis of imidazole-hydrazone **L1-L3**.

The infrared spectra of **L1**-**L**3 show an absorption band in in a range between 1585-1588 cm^{-1}, which is assigned to the vibration of the νC=N bond, that indicated the arylhydrazone formation. The NMR and mass spectra of compounds **L1-L3** are found to be in agreement with their molecular structures. The singlet signals of the ^{1}H NMR spectra at 7.31 ppm, 7.50 ppm and 7.73 ppm for **L1**-**L3** respectively; respect are characteristic of hydrogen of imine fragment. The corresponding signals of the ^{13}C NMR spectra are presented at 129.0 ppm for **L1**, 127.3 ppm for **L2** and 129.4 ppm for **L3**. Additionally, the structures are supported by mass spectra, the DART mass spectra show the base peak at $[M + H]^+$ for molecular cation in *m/z* = 276 and *m/z* = 214 for **L1** and **L2** respectively, finally the mass spectra MS-EI of **L3** show molecular ions *m/z* = 200 for molecular ion.

3.2. Suzuki.Miyaura cross-coupling reaction.

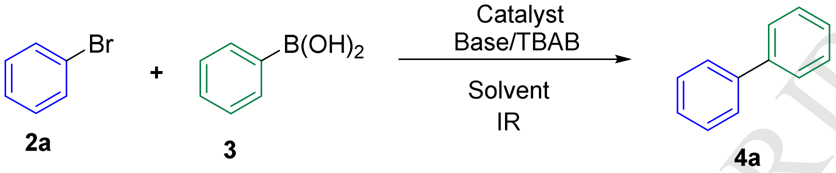
Initially with expected ligand **L1-L3** in hand, tested the reaction of phenylboronic acid with bromobencene in 3 mL aqueous media ($V_{water}/V_{methanol}$, 1/1) as a model reaction under 75 °C using K_3PO_4 as base, **L1** as ligand in the presence of $Pd(OAc)_2$ and TBAB as additive, under IR irradiation. We evaluate the concentration of catalytic system [$Pd(OAc)_2$/**L1**], when using 1 % mol and 0.5 % mol the reaction proceeded in excellent yields in a short time (entre 1 and 2, table 1).

As known, the base shows an important role in this reaction, various bases on the Suzuki–Miyaura reaction were investigated (entries 2, 4-6, table 1). Among the bases employed, K_3PO_4 and K_2CO_3 were found to be the best in the present protocol (entries 2 and 4, table 1). However, with K_3PO_4 the coupling reaction proceeded in a reduced time in comparison with K_2CO_3.

If we kept the catalyst, base, and ligand **L1** constant and used different solvents such as MeOH/H_2O, MeOH, EtOH, EtHO/H_2O, the desired product was obtained in 70–99% yields (entries 7–10, table 1). As was evidenced in Table 1 entry 8, the reaction afforded the biphenyl in an excellent yield after 5 min. shown the water was the best media for this catalyst system. After, we evaluated the reaction in the absence of TBAB (entrie 11, table 1), and we observed excellent yields in 10 min.

We have also studied the influence of ligands **L2** and **L3** on catalytic activity and tested the ligand **L2** and **L3** under the same reaction conditions as **L1**. The results are summarized in table 1 (entries 12 and 13, table 1). As can be observed, ligand **L1** compared to **L3** shows similar catalytic activity (entries 11 and 13, table 1), but when using **L1** the time of reaction is minor.

Table 1. Optimization of conditions for the Suzuki-Miyaura cross-coupling reaction using the ligands **L1-L3**.



Entry	Ligand (% mol)	Source of Pd (% mol)	Base	Solvent	Additive	Time (min)[a]	Yield (%)[b]	TON[j]	TOF (h^{-1})[k]
1	L1 (1)	$Pd(OAc)_2$ (1)	K_3PO_4	MeOH/ H_2O[c]	TBAB	25	95	95	231
2	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	MeOH/ H_2O[c]	TBAB	10	99	198	1237
3	L1 (0.1)	$Pd(OAc)_2$ (0.1)	K_3PO_4	MeOH/ H_2O[c]	TBAB	20	70	700	2333
4	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_2CO_3	MeOH/ H_2O[c]	TBAB	25	99	198	1414
5	L1 (0.5)	$Pd(OAc)_2$ (0.5)	KOAc	MeOH/ H_2O[c]	TBAB	30	85	170	340
6	L1 (0.5)	$Pd(OAc)_2$ (0.5)	KOH	MeOH/ H_2O[c]	TBAB	15	95	190	760
7	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	MeOH[d]	TBAB	10	70	140	875
8	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	H_2O[e]	TBAB	5	99	198	2385
9	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	EtOH[f]	TBAB	10	75	150	937
10	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	EtOH/H_2O[g]	TBAB	15	80	160	640
11	L1 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	H_2O[e]	-	10	95	190	1187
12	L2 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	H_2O[e]	-	10	80	160	1000
13	L3 (0.5)	$Pd(OAc)_2$ (0.5)	K_3PO_4	H_2O[e]	-	20	95	190	575
14	L1 (0.5)	$Pd(CNPh)_2Cl_2$ (0.5)	K_3PO_4	H_2O[e]	-	10	85	170	1062
15	L1 (0.5)	$Pd(PPh_3)_2Cl_2$ (0.5)	K_3PO_4	H_2O[e]	-	10	80	160	1000
16	**L1 (0.25)**	**$Pd(OAc)_2$ (0.25)**	**K_3PO_4**	**H_2O[e]**	**-**	**15**	**95**	**380**	**1520**
17	L1 (0.1)	$Pd(OAc)_2$ (0.1)	K_3PO_4	H_2O[e]	-	15	75	750	3000
18[h]	L1 (0.25)	$Pd(OAc)_2$ (0.25)	K_3PO_4	H_2O[e]	-	120	90	360	90
19[i]	L1 (0.25)	$Pd(OAc)_2$ (0.25)	K_3PO_4	H_2O[e]	-	720	76	304	25
20	-	$Pd(OAc)_2$ (0.25)	K_3PO_4	H_2O[e]	-	60	20	80	80
21[l]	L1 (0.25)	$Pd(OAc)_2$ (0.25)	K_3PO_4	H_2O[e]	-	15	95	380	1520

Reaction condition: Bromobencene **2a** (0.5 mmol), phenylboronic acid (**3**) (0.6 mmol), solvent (3 mL), Base (1 mmol), TBAB 0.5 mol. [a] Based on total consumption of bromobencene determined by TLC. [b] Isolated yields. [c] T = 75 °C. [d] T = 65 °C, [e] T = 96 °C, [f] T = 78 °C [g] T = 82 °C. [h] Under conventional heating T = 96 °C. [i] Under room temperature. [j] TON = ratio of moles of product formed to moles of catalyst used. [k] TOF = TON/t (h). [l] Preparing separately the [$Pd(AcO)_2$/**L1**] catalyst system.

Once the best ligand (**L1**) and appropriate solvent and base were identified, different palladium sources such as $Pd(CNPh)_2Cl_2$ and $Pd(PPh_3)_2Cl_2$ (entries 14 and 15, table 1) were tested and **4a** was achieved in good yields; however, these yields did not exceed the efficiency of $Pd(OAc)_2$ (entry 11, table 1).

Finally, in order to use small amounts of catalyst, we carried out the reaction using 0.25 % mol and 0.1 % mol of system catalytic [$Pd(OAc)_2$/**L1**] (entries 16 and 17, table 1) and the best yield was obtained when 0.25 % mol were used. Thus, optimized conditions for this cross-coupling reaction involves the use of 0.25 % mol of system catalytic [$Pd(OAc)_2$/**L1**], H_2O as a solvent, K_3PO_4 as base, in the absence of TBAB under IR irradiation.

Furthermore, when the reaction is carried out under reflux conditions using conventional heating (entry 18, table 1), obtaining a excellent yield of the coupling product **4a** in a longer time. The same reaction was performed at room temperature and achieved **4a** in 76 % yield, during 12 h (entry 19, table 1). In absence of ligand, we obtained 20% of yield (entry 20, table 1) which indicated the essential role of hidrazone ligand.

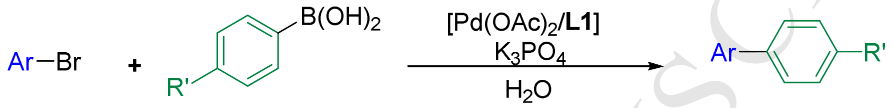
In an effort to understand the role of the molecular structure in the complex between the hydrazone **L1** and $Pd(OAc)_2$, we carried out different reaction conditions, observed in all cases total spend of ligand, however, it was not possible to isolate the reaction product in neither case. In our experience, believe that hydrazone behaves as [N,N] ligand, as in other structurally similar hydrazone ligands we have detected[34].

Additionally, we tried to formed the complex between hydrazone **L1** and $Pd(OAc)_2$ (entry 21, table 1) before added the substrates and base, then the reaction mixture was refluxed under IR irradiation and obtained 95 % yield. Similar yield when the reaction was made in one pot (entry 16, table 1).

With a reliable set of conditions in hand (entry 16, table 1) the scope and generality of the developed protocol with respect to various aryl bromides and phenylboronic acids were investigated using our catalytic system [$Pd(OAc)_2$/**L1**]. When phenylboronic acid was coupled with several aryl bromides containing both electron-donating and electron-withdrawing groups, the corresponding products were obtained in excellent yields (entries 1-8, table 2). Due to the steric hindrance of 4-bromotoluene, 2-bromotoluene and 2-bromo-1,3-dimethylbencene, the desired products were obtained in god yield (entries 3-5, table 2). Similarly, when the bromobencene was coupled with several phenyl boronic acids containing both electron-donating and electron-withdrawing groups, the reaction proceeds in excellent yields and similar reaction time (entries 9-11, table 2) in comparison with the aryl bromides.

We also investigated the reaction of heteroaryl bromides and aryl chlorides. The reaction the Suzuki–Miyaura cross-coupling reaction of heteroaryl halides such as 2-bromopyridine, 3-bromopyridine, 2-bromothiophene and 3-bromothiophene with phenylboronic acid gave the corresponding coupled products in a good yield, (entries 12-15, table 2) but we observed the coupling reaction required extended reaction time. Unfortunately, the coupling of 4-nitrochlorobenzene with phenylboronic acid did not perform as well as aryl bromides, even we when raised the Pd loading up to 0.1 mol % and prolonged the reaction time to 10 h (scheme 2) with 15 % yield.

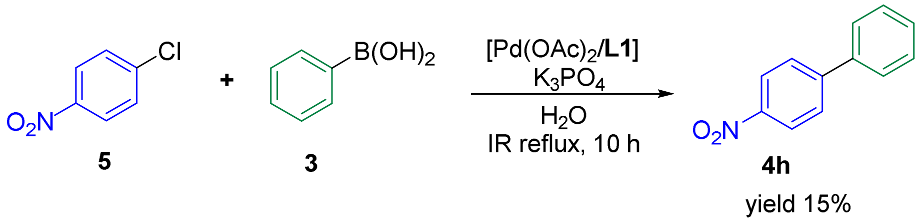
Table 2. Scope of Suzuki-Miyaura cross-coupling of aryl bromides and phenyl boronic acids under IR irradiation.



2 **3** **4a-m**

Entry	**Ar**	**R'**	**Compound**	**Time (min)[a]**	**Yield (%)[b]**	**TON[c]**	**TOF (h^{-1})[d]**
1	Ph	H	4a	15	95	380	1520
2	4-CH_3Ph	H	4b	10	99	396	2475
3	3-CH_3Ph	H	4c	20	70	280	848
4	2-CH_3Ph	H	4d	30	90	360	720
5	1,3-dimethylPh	H	4e	50	70	280	337
6	4-OCH_3Ph	H	4f	15	99	396	1584
7	4-ClPh	H	4g	10	95	380	2375
8	4-NO_2Ph	H	4h	15	99	396	1584
9	Ph	OCH_3	4f	15	95	380	1520
10	Ph	Cl	4g	15	85	340	1360
11	Ph	CF_3	4i	15	99	396	1584
12	2-Pyridyl	H	4j	40	70	280	424
13	3-Pyridyl	H	4k	40	72	288	436
14	2-thienyl	H	4l	60	75	300	300
15	3-thienyl	H	4m	60	65	260	260

Reaction condition: Aryl halide **2** (0.5 mmol), phenylboronic acid (**3**) (0.6 mmol), H_2O (3 mL), K_3PO_4 (1 mmol), [Pd(OAc)$_2$/**L1**] = 0.25 % mol, T = 96 °C. [a] Based on total consumption of aryl halide determined by TLC. [b] Isolated yields after extraction with hexane and SiO_2 column chromatography. [c] TON = ratio of moles of product formed to moles of catalyst used. [d] TOF = TON/t (h).

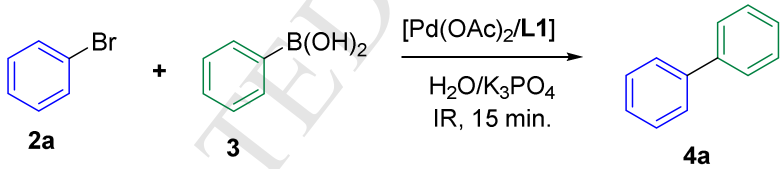


5 **3** **4h**

Scheme 2. Suzuki-Miyaura reaction using 4-nitrochlorobenzene.

In order to observe the recycling capacity of the catalytic system [Pd(OAc)$_2$/**L1**], we conduct the coupling between bromobenzene and phenylboronic acid under the optimal reaction conditions (Table 3). A flask was charged with bromobenzene, phenylboronic acid, catalytic system [Pd(OAc)$_2$/**L1**], K_3PO_4, and water. The mixture in open air was irradiated under IR for the 15 min.. After the mixture was cooled, the aqueous layer was extracted with *n*-Hexane (3 x 5 mL), and the flask was charged again with bromobenzene and phenylboronic acid and K_3PO_4. Every time after cooling and extraction with *n*-Hexane, the reagents and base were added and the reaction was repeated. The recovered catalyst was successfully reused in the subsequent three cycles, the coupled product was obtained in good yields (entries 1-3 table 3). Nevertheless, the coupled product was significantly dropped in fourth and fifth cycles (entries 4 and 5). Finally, a drastic decrease was observed in the six run (entries 6, table 3) probably due to decomposition of catalyst system [Pd(OAc)$_2$/**L1**].

Table 3. Recycling of catalyst.



2a **3** **4a**

Cycle	Yiels (%)^a	TON^b	TOF (h-1)^c
1	95	380	1520
2	90	360	1440
3	80	320	1280
4	60	240	960
5	45	180	720
6	15	68	240

Reaction condition: Aryl halide **2** (0.5 mmol), phenylboronic acid (**3**) (0.6 mmol), H_2O (3 mL), K_3PO_4 (1 mmol), [Pd(OAc)$_2$/**L1**] = 0.25 % mol, T = 96 °C. t = 15 min. ^{a} Isolated yields. ^{b} TON = ratio of moles of product formed to moles of catalyst used. ^{c} TOF = TON/t (h).

Finally, we made a comparison of the activity of various Pd catalysts in water [Pd(OAc)$_2$/LI] catalytic system in the Suzuki-Miyaura coupling reaction and found that this catalyst system is advantageous in terms of lower reaction times (entries 1-6, table 4), low catalyst loading (entries 1,3,4 and 6, table 4) and the absence of additives (entries 2-4, table 4).

Table 4. Catalytic performance of different catalysts in the Suzuki-Miyaura cros-coupling reaction.

Entry	Catalyst (% mol)	Conditions	Time	Yield	Ref
1	B-cyclodextrin-Pd(II) complex (3%)	K_2CO_3, H_2O, rt.	50 min	75	[24b]
2	[NHC-Pd(II) complex] (0.2)	K_3PO_4 $3H_2O$, H_2O, TBAB, 40 °C	6 h	90	[25e]
3	Ligand free-Pd(OAc)$_2$ (5%)	Stilbazo (5 mol%), K_2CO_3, H_2O, rt	4 h	92	[25d]
4	Ligand free-$PdCl_2$ (2 %)	Na_2SO_4 (8 mol%), K_2CO_3, i-PrOH or H_2O, rt	7h	98	[28]
5	N-Heterocyclic Carbene–Pd (II) (0.1)	Cs_2CO_3, H_2O, 80 °C.	24 h	99	[29b]
6	L-arginine/$PdCl_2$ (100/1)	H_2O/EtOH, r.t.	1 h	96	[30a]
7	[Imidazole-hydrazone/ Pd(OAc)$_2$] (0.25)	H_2O, K_3PO_4, 96 °C	15 min	99	This work

4. Conclusions

In conclusion, we have developed a series of efficient ligands imidazole-hydrazone **L1-L3**, which was easy to prepare from inexpensive and commercially available starting materials. The catalytic system derived from these ligands and Pd(OAc)$_2$ is an efficient catalytic system for Suzuki-Miyaura cross coupling reaction, which can be employed in mild conditions for the coupling reaction of aryl and heteroaryl halides. A wide range of substrates could be coupled with phenylboronic acid to afford the desired products in good to excellent yields at low catalyst loadings and low time of reaction. Overall, the present protocol offers a mild, efficient and attractive alternative to the existing methods because of the use of non-toxic solvent, inorganic base and broad substrate scope.

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An efficient and simple imidazole-hydrazone ligand for palladium-catalyzed Suzuki-Miyaura cross-coupling reactions in water under infrared irradiation

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Highlights

Efficient catalytic system [imidazole-hydrazone (**L1-L3**)/Pd(OAc)$_2$] has been developed

The system catalyzed Suzuki-Miyaura reaction in water under IR irradiation

The system tolerates a wide range of arylboronic acids and aryl halides

The products were obtained in good yields at low catalyst loadings and low time.