

Suzuki–Miyaura Cross-Coupling in Aqueous Medium Using Recyclable Palladium/Amide-Silica Catalyst

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Abstract Silica-immobilized benzamide palladium complex was prepared and characterized. The complex exhibits excellent catalytic activity and stability for Suzuki–Miyaura cross-coupling reaction under mild aqueous reaction condition. Various aryl bromides were coupled with arylboronic acids in *i*-PrOH/H₂O, under open air at room temperature, in the presence of 0.22 mol% of the catalyst to afford corresponding cross-coupled products in high yields. Furthermore, the novel heterogeneous catalyst can be conveniently recovered by simple filtration and reused several times without significant loss in activity.

Graphical Abstract

Keywords Silica-immobilized · Heterogeneous catalyst · Suzuki–Miyaura cross-coupling · Biaryls · Aqueous solvent · Room temperature

1 Introduction

The palladium-catalyzed Suzuki–Miyaura cross-coupling reaction is one of the important, powerful and frequently employed protocols in organic synthesis for the construction of carbon– carbon bond [1–7]. This reaction has been widely used to synthesize molecules possessing significant biological or physical properties [8–12], and can be extended to large scale synthesis.



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In the last three decades numerous homogeneous palladium catalysts ligated with phosphines [13–15], NHC [16–19], imidazole [20], imine [21], oxime [22], oxazoline [23], triazole [24], amino acid [25], amine [26, 27], Schiff-base [28–30], oxime-ether [31], hydrazone [32], etc. have been employed in this cross-coupling method, due to their high reactivity and high turnover numbers. Moreover, many unique ligandfree protocols were also developed in recent years for this transformation [33–40]. However, the use of homogeneous catalysis has some inherent disadvantage, as the expensive metal catalysts are not easily reusable, hard to separate from reaction mixture (a frequent industrial concern) and often contaminates the final products, especially the pharmaceuticals, and poses a serious issue for large-scale synthesis. To overcome these issues, heterogeneous catalysis seems promising and advantageous over homogenous catalysts, owing to easy recovery of the highly stable solid catalyst from the reaction mixture with minimum contamination of products, and many of the heterogeneous systems are recyclable and retain their reactivity even after several catalytic cycles.

Palladium can be immobilized on several solid supports such as organic polymers, clays, oxides, activated carbon, zeolites etc. [41-49]. However, the most common heterogeneous supports are based on silica, because of their easy availability, high stability and porosity, which allows easy binding of organic groups on the surface [41–49]. The presence of highly active silanol-sites in the silica-surface promotes effective anchoring of organic ligands, followed by the immobilization of the metal on the support. Numerous efficient silica-supported palladium catalyst have been synthesized and used in Suzuki-Miyaura reaction [50–52]. But they still suffer from the problem concerning the use of volatile organic solvent system, elevated reaction temperature, high metal loading and poor recyclability [50–52]. Hence, there is a strong need to develop recyclable heterogeneous catalyst which can perform efficiently under mild aqueous condition with diverse range of substrates.

In continuation of our studies in developing novel supported heterogeneous catalysts, herein we report an efficient, easily accessible and widely applicable silica immobilized benzamide palladium complex and its application in Suzuki–Miyaura cross-coupling reaction.

2 Results and Discussion

2.1 Synthesis and Characterization of the Catalyst

The palladium complex was synthesized in three steps, following a previously reported procedure, summarized in Scheme 1 [53, 54]. The first step involves the modification of silica surface by the reaction of solid silica gel (60–120 mesh) and APTES in dry toluene under N₂ atmosphere at refluxing temperature. In the second step, the condensation of APTES@SiO₂ and benzoyl chloride in diethyl-ether at reflux condition produces the corresponding benzamide complex, benzamide@SiO₂, which was light yellow colored solid after purification. Finally, the benzamide@SiO₂ precursor was used for the synthesis of Pd–benzamide@SiO₂ complex by treatment with Pd(OAc)₂ in acetone at room temperature for 24 h.

Due to insolubility of the Pd–benzamide@SiO₂ complex in most of the organic solvents, its structural investigations were limited to its physicochemical properties, such as FT-IR, BET surface area measurements, SEM, SEM–EDX, EDS-mapping and ICP-AES analysis.

2.2 FT-IR, XRD, SEM–EDX, ICP-AES and EDS Mapping Analysis

The FT-IR spectra of SiO₂, APTES@SiO₂, benzamide@SiO₂ and Pd-benzamide@SiO₂ are presented in Fig. 1. The FT-IR spectra of the silica samples shows absorption bands at 1642 cm⁻¹ for v_{O-H} bending vibrations of the adsorbed water. The absorption peaks at 1080–1140 cm⁻¹ are due to the stretching vibrations of the Si–O–Si groups. Except in Fig. 1(i), the peak for v_{N-H} in the region 1500–1600 cm⁻¹ appears in all samples (Fig. 1). This indicates the attachments of APTES onto the silica



Scheme 1 Preparation of the silica-supported Pd-benzamide@SiO2

matrix. The bands observed at 1680 cm⁻¹ in (iii) shifts to 1670 cm⁻¹ in (iv), which could be attributed to the $v_{C=O}$ stretching frequency, and 540 cm⁻¹ in (iv) indicates the v_{Pd-N} stretching frequency [55]. The presence of a less intense band at 1440 cm⁻¹ may be assigned to v_s (CH₃CO₂-) group of palladium acetate [56].

The silica immobilized Pd catalyst was examined by powder X-ray diffraction (XRD) study (Fig. 2). It is observed that the distinct Pd nano-particles peaks are not observed in the XRD diffractogram, probably due to the very low concentration of palladium particles within the complex or due to amorphous nature of the silica matrix. The major peak at 20 values ~ 20° to 25° indicates the presence of silica in a high concentration. The presence of PdNPs could be inferred from the 20 values observed at 39°, 46° and 66° which corresponds to (111), (200) and (220) plane (JCPDS card No. 001-1310 and 001-12010). Similarly, the 20 values observed of 33°, 44° and 61° corresponds to (101), (102) and (113) planes of PdO (JCPDS card No. 043-1024 and 002-1432).

The SEM–EDX analyses of the silica gel before and after palladium immobilization are shown in Fig. 3a and b. The results shows the palladium content along with the silica and oxygen proportions, which indicate the formation



Fig. 1 FT-IR spectra of *i* SiO₂, *ii* APTES@SiO₂, *iii* benzamide@SiO₂ and *iv* Pd–benzamide@SiO₂



Fig. 2 XRD pattern of the Silica supported Pd catalyst

of palladium complex with the anchored benzamide ligand at various sites. The palladium content of the supported catalyst was determined by ICP-AES, which suggests 2.2 wt% or 0.022 mol% palladium loading in the immobilized complex.

The change in surface morphology of free silica and the supported Pd-catalyst are clearly visible from the SEM images (Fig. 4a, b).

To further confirm the components of the Pd–benzamide@SiO₂ we record the elemental mapping by energy dispersive X-ray absorption spectroscopy (EDS). Figure 5 shows a uniform distribution of active palladium sites throughout the matrix.

2.3 N₂ Adsorption–Desorption Isotherm

The N₂ adsorption–desorption isotherms analysis, measured at 77 K, of the silica based samples are shown in Fig. 6, and the respective textural parameters, such as the specific surface area (A_{BET}), pore volume (Vp) and pore radius are presented in Table 1. The isotherms of all the samples exhibited typical type IV patterns according to the IUPAC definition of porosity [57], featuring mesoporous material with uniform pore size distribution.

The specific surface area (A_{BET}) obtained by the BET method for free SiO₂ was 422.7 m² g⁻¹ which upon functionalization with APTES and subsequent benzoyl chloride treatment decreased to 333.2 and 314.5 m²g⁻¹ respectively. A further decrease in A_{BET} for Pd–benza-mide@SiO₂ (247.1 m² g⁻¹) compared to benza-mide@SiO₂ confirms the successful immobilization of palladium onto silica surface. In a similar manner, a gradual decrease in pore volume (*Vp*) from SiO₂ (0.448 cm³ g⁻¹) to Pd–benzamide@SiO₂ (0.279 cm³ g⁻¹) was observed, to further ascertain the immobilization of palladium onto silica. N₂-isotherm indicates an increase in



Fig. 3 SEM-EDX spectra of a SiO₂ (Figure copyright the Royal Society of Chemistry and reproduced with permission) and b Pd-benzamide@SiO₂



Fig. 4 SEM image of a SiO₂ (Figure copyright the Royal Society of Chemistry and reproduced with permission) and b Pd-benzamide@SiO₂

pore radius in the case of Pd–benzamide@SiO₂ (3.05 nm) than the parent SiO₂ (2.05 nm). Thus, the BET surface area, pore volume and pore radius suggest the successful anchoring of the palladium-organic moieties on the surface of SiO₂.

2.4 Pd-Benzamide@SiO₂ Catalyzed Suzuki-Miyaura Reaction

2.4.1 Catalyst Screening and Base-Solvent Optimization

To investigate the catalytic efficiency of the silica-APTES immobilized benzamide based palladium catalyst, in the Suzuki–Miyaura reaction, the coupling between 4-bromonitrobenzene and phenylboronic acid was chosen as the prototype reaction. Initially, single solvent such as EtOH, *i*-PrOH, PEG₄₀₀, THF, CH₃CN, DMF, toluene and H₂O were studied. It may be noted that, the use of single solvent gave moderate to excellent yields at the room temperature (Table 2, entries 1–8). However, when

aqueous/organic co-solvent was used, high yields of 87-99 % were obtained within lower reaction time (Table 2, entries 9–11). The advantage of the aqueous co-solvent may be attributed to the good solubility of the inorganic base and boronic acid substrates. Finally, we found that the *i*-PrOH/H₂O (1:1) combination is the best solvent system for the present benzamide-Pd-based Suzuki–Miyaura coupling.

Further investigations were carried out to test the influence of different bases on Suzuki reaction in *i*-PrOH/ H_2O (1:1) at room temperature. The inorganic bases like K_2CO_3 , Na_2CO_3 , Cs_2CO_3 , $Na_3PO_4.12H_2O$, NaOH and KOH were investigated (Table 3, entries 1–6).

As shown in Table 3, K_2CO_3 was the best base for the reaction with very short reaction time (3.5 h) (Table 3, entry 1). The use of Na₃PO₄·12H₂O provides good yield although within extended reaction time (Table 3, entry 4). We studied the effect of alkali metal hydroxides under present reaction conditions. Both NaOH and KOH have provided comparably identical amount (78 and 81 %) of

Fig. 5 a SEM image; EDS mapping of elements: **b** Pd, **c** Si, **d** oxygen and **e** Pd + Si + O





Fig. 6 N₂-adsorption-desorption isotherm of the prepared samples

isolated product (Table 3, entries 5 and 6). However, with organic base (NEt₃) negligible conversion was noticed (Table 3, entry 7). Different catalyst loadings were also

tested for the cross-coupling reaction. As illustrated in Table 3, 10 mg of catalyst showed very high efficiency (Table 3, entry 1), whereas, with lower amount of catalyst poor yield was obtained (Table 3, entry 10). Thus, we selected K_2CO_3 as the base, *i*-PrOH/H₂O in ratio of 1:1, and 10 mg (0.22 mol% Pd) of catalyst as the optimal conditions for the reaction.

2.4.2 Substrate Screening

Encouraged by the excellent efficiency of the reaction system, we applied the optimized condition for the Suzuki–Miyaura cross-coupling of structurally diverse aryl and hetero-aryl bromide with arylboronic acids. As shown in Table 4, the reaction tolerates a wide range of functional groups in both coupling partners. The coupling between aromatic bromides and arylboronic acids, bearing both electron-donating and electron-withdrawing groups, proceeded readily to afford the corresponding products in 92–100 % yields. We next tried to examine the activity of chloride containing substrates

Entry	Materials	Surface area a (A_{BET}) (m ² g ⁻¹)	Pore volume (Vp) (cm ³ g ⁻¹)	Pore radius ^b (nm)
1	SiO ₂	422.7	0.448	2.05
2	APTES@SiO ₂	332.2	0.413	2.21
3	Benzamide@SiO ₂	314.5	0.394	2.33
4	Pd-benzamide@SiO ₂	247.1	0.279	3.05

Table 1 Surface area and pore size distribution of the silica based samples

^a BET method used in N₂ sorption, ^b Adsorption average pore radius (by BET method)

Table 2 Optimization of the Pd-benzamide@SiO2 catalyzed Suzuki-Miyaura reaction

$$O_2 N \longrightarrow Br + (HO)_2 B \longrightarrow Pd-benzamide@SiO_2 (10 mg) \longrightarrow O_2 N \longrightarrow$$

Entry	Solvent (4 mL)	Time (h)	Yield (%) ^a
1	Ethanol	5.5	97
2	<i>i</i> -PrOH	5	99
3	PEG_{400}	8	63
4	THF	6	93
5	MeCN	7	91
6	DMF	8	51
7	Toluene	8	62
8	H ₂ O	8	55
9	Ethanol/ H_2O (1:1)	4.5	95
10	PEG ₄₀₀ /H ₂ O (1:1)	6.5	87
11	<i>i</i> -PrOH/H ₂ O (1:1)	3.5	99

Reaction conditions: 4-bromonitrobenzene (0.5 mmol), phenylboronic acid (0.55 mmol), Pd–benzamide@SiO₂ (10 mg, 0.22 mol% Pd), solvent (4 mL), K₂CO₃ (1 mmol), ca. 28 °C, in air, ^a Isolated yield

towards this Suzuki reaction. However, lower conversion was obtained with chloroarenes after prolonged reaction time at $80 \text{ }^{\circ}\text{C}$ (Table 4, entries 16–17).

2.4.3 Scale-Up Synthesis

The Suzuki coupling reactions have wide applications in many chemical industries due to the easy accessibility and broad functionality of organoboron derivatives. Thus, we have explored the scale-up scope to prepare in grams scale instead in milligrams of biaryl derivatives.

With the optimized reaction conditions we next investigated the performance of the reaction upon gram scale. The reaction with excess 4-bromonitrobenzene (5 mmol), phenylboronic acid (5.5 mmol), K₂CO₃ (10 mmol), Pd– benzamide@SiO₂ (100 mg, 2.2 mol% Pd) and *i*-PrOH/ H₂O (25 mL) was performed at room temperature for 4 h. Finally, we were able to isolate 0.9895 grams (99.4 %) of 4-nitrobiphenyl.

2.4.4 Role of Pd–Benzamide@SiO₂ in the Suzuki–Miyaura Reaction

Most of the solid supported catalysts are known to follow heterogeneous pathway, however, in certain condition they were found to serve as precatalyst which liberates highly active soluble palladium species or nanoparticles into the reaction [58, 59]. Thus, to evaluate the actual role of the silica catalyst, we have performed various control experiments that are often used to distinguish homogenous and heterogeneous catalysis [55, 60, 61].

In the filtration test, we pretreated 10 mg (0.22 mol% Pd) of Pd–benzamide@SiO₂ with K_2CO_3 in *i*-PrOH/H₂O (1:1) for 2 h and then passed the reaction mixture through a filter paper. The filtrate was subjected to a fresh run of cross-coupling by charging with required amount of 4-bromonitrobenzene and phenylboronic acid at room temperature. However, no significant progress (3 % by GC–MS analysis) in the reaction was observed upon

Table 3 Screening of bases for the synthesis of biphenyl



Entry	Base	Time (h)	Yield (%) ^a
1	K ₂ CO ₃	3.5	99
2	Na ₂ CO ₃	4	91
3	Cs ₂ CO ₃	5.5	95
4	Na ₃ PO ₄ .12 H ₂ O	5	96
5	NaOH	8	78
6	КОН	8	81
7	Et ₃ N	24	trace
8	_	24	no reaction
9	K ₂ CO ₃	3.5	99 ^b
10	K ₂ CO ₃	6	72 ^c

Reaction conditions: 4-bromonitrobenzene (0.5 mmol), phenylboronic acid (0.55 mmol), Pd–benzamide@SiO₂ (10 mg, 0.22 mol% Pd), *i*-PrOH/ H₂O (4 mL), base (1 mmol), ca. 28 °C, in air, ^a Isolated yield, ^b Pd–benzamide@SiO₂ (20 mg), ^c Pd–benzamide@SiO₂ (5 mg)

Table 4 Suzuki-Miyaura reaction of aryl halides with a variety of arylboronic acids

$$R^{1} \xrightarrow{X} R^{2} \xrightarrow{\text{II}} B(OH)_{2} \xrightarrow{\text{Pd-benzamide}@SiO_{2} (10 \text{ mg})} R^{1} \xrightarrow{R^{2}} R^{2}$$

Entry	Х	\mathbb{R}^1	R^2	Time (h)	Yield (%) ^a
1	Br	NO_2	Н	3.5	99
2	Br	NO_2	4-Cl	4	96
3	Br	NO_2	4-OCH ₃	6	94
4	Br	OCH ₃	Н	2.5	98
5	Br	OCH ₃	4-Cl	3.5	94
6	Br	OCH ₃	4-OCH ₃	4.5	92
7	Br	Н	Н	1	100
8	Br	Н	4-OCH ₃	2.5	97
9	Br	СНО	4-OCH ₃	3.5	95
10	Br	СНО	Н	4.5	96
11	Br	COCH ₃	Cl	4	96
12	Br	N= N−−Br	4-OCH ₃	6.5	97
13	Br	N= N−−−Br	(HO) ₂ B-OCH ₃	5	95
14	Br	OCH ₃	3-CN	5	96
15	Br	OCH ₃	2-CH ₃	3	94
16	Cl	CH ₃	Н	12	43 ^b
17	Cl	OCH ₃	Н	12	41 ^b

Reaction conditions: aryl bromide (0.5 mmol), arylboronic acid (0.55 mmol), Pd-benzamide@SiO₂ (10 mg, 0.22 mol% Pd), *i*-PrOH/H₂O (4 mL), K₂CO₃ (1 mmol), ca. 28 °C in air unless otherwise noted, ^a Isolated yield, ^b at 80 °C



Fig. 7 Recycling of the catalyst for the Suzuki-Miyaura reaction

stirring the reaction mixture for 6 h. The leached palladium in the filtrate was analyzed by inductively coupled plasma atomic emission spectrometry (ICP-AES), and determined to be 0.16 ppm.

To confirm the catalytic nature of the Pd-benzamide@SiO₂, we have performed the metal poisoning test using mercury (Hg(0)). The ability of Hg(0) to poison Pd, Rh and Ni-based heterogeneous catalysts, by amalgamating with the metal or adsorbing on the metal surface, has been known for more than 90 years [62, 63] and is a commonly used test [64-71]. The Hg(0)-poisoning experiment is performed by adding excess Hg(0) to the reaction solution during the course of the reaction. The suppression of catalysis by Hg(0) is an evidence for the presence of Pd(0)in heterogeneous catalyst, however, if the catalyst retains its activity, the presence of palladium in high oxidation state can be assumed. For the mercury poisoning test, we have performed a coupling reaction using 4-bromonitrobenzene and phenylboronic acid. After 1 h of reaction (37 % conversions vide GC-MS) excess Hg(0) (molar ratio to [Pd] ~ 600) was added to the reaction solution and the mixture was stirred at room temperature. After stirring for another 2.5 h no further increase in the yield was observed (indicated by GC-MS). This suggests the presence of palladium in zero oxidation state during the reaction. However, these data do not exclude the process of "release and re-depositing" back of the soluble palladium particles on the insoluble support during the reaction [72-74].

2.4.5 Recycling of Pd–Benzamide@SiO₂ in Suzuki– Miyaura Reaction

We have demonstrated the generality and scope of the present catalytic system by investigating the Suzuki–Miyaura reactions. All these reactions proceeded smoothly to produce the desired products with excellent yields. For practical and industrial applications, the lifetime of the heterogeneous catalyst and its level of reusability are important features. Therefore, we explored the reusability of the Pd– benzamide@SiO₂ catalyst again with the reaction of 4-bromonitrobenzene with phenylboronic acid as the model reaction. After the first run, the catalyst was centrifuged and recovered from the reaction mixture by centrifugation and filtration, washed thoroughly with *i*-PrOH/H₂O followed by EtOAc, dried and reused for another runs. It was observed that the catalyst could be reused consistently up to six consecutive cycles without any significant decrease in activity (Fig. 7; 1st cycle: 99 % vs 6th cycle: 95 %). Determination of palladium content by ICP-AES analysis shows a very negligible decrease (<6 %) in the Pd content on the solid catalyst after sixth cycle. Although, no significant leaching of palladium occurs during the catalysis, the slight decrease in the yield of the reaction may be due to the deactivation of the catalyst after successive cycles. The results of catalyst leaching and reusability test strongly suggest that the Pdbenzamide@SiO2 catalyzed Suzuki-Miyaura reaction proceeds via heterogeneous mechanism.

3 Conclusions

In summary, we have successfully prepared a silica immobilized benzamide palladium complex which was used as heterogeneous catalyst for the room temperature Suzuki–Miyaura cross-coupling reaction in aqueous solvent. The supported catalyst has showed excellent catalytic activities for the reaction affording a wide range of biphenyls in high yields. Moreover, the solid catalyst could be recovered easily by simple filtration and reused up to six times without significant loss in activity. The excellent catalytic activity as well as the recyclability made this catalyst an effective alternative to the existing systems.

4 Experimental Sections

4.1 Instrumentation and Chemicals

All chemicals were reagent grade and used as received without further purification. Silica gel (60–120 mesh) was purchased from Merck, India. 3-Aminopropyltriethoxysilane (APTES) was purchased from Sigma Aldrich. Pd(OAc)₂ was purchased from Spectrochem Pvt. Ltd. Infrared spectra (4000–250 cm⁻¹) were recorded in KBr on a *Shimadzu Prestige*-21 FT-IR spectrophotometer. The surface area of the silica samples were determined by BET surface area analysis using liquid nitrogen at -78 °C on BET, Quantachrome Instrument, BOYNTON BEACH, FL 33426. The specific surface area of the silica samples were calculated according to the BET equation. ¹H spectra were recorded in CDCl₃ operating at 400 on a *JEOL*, JNM ECS NMR spectrometer, and chemical shifts were calculated

relative to TMS. All reaction products were known compounds and were identified by ¹H and confirmed by comparing with those reported in the literature. The following abbreviations are used for the description of signals: s (singlet), d (doublet), t (triplet), m (multiplet). Coupling constants (J) were measured in Hz. GC-MS was performed on an Agilent Technologies GC system 7820A coupled with a mass detector 5975 and SHRXI-5MS column (15 m length, 0.25 mm inner diameter, 0.25 micron film thickness). SEM analyses were carried out using JEOL, JSM Model 6390 LV scanning electron microscope, operating at an accelerating voltage of 15 kV. Elemental mapping and EDX spectra were performed in the same instrument attached to the scanning electron microscope. Palladium content of the catalyst and its possible leaching during catalysis was determined using inductively coupled plasma-atomic emission spectrometry (ICP-AES) on a Thermo Electron IRIS Intrepid II XSP DUO. Progress of the reactions was monitored by TLC using aluminumcoated Merck silica gel 60 F254 plates under UV light.

5 Preparation of Catalyst

5.1 Synthesis of APTES Functionalized Silica Gel: APTES@SiO₂

The silica gel (60–120 mesh) was dehydrated by heating at 100 °C for 2 h prior to use. 2.5 g of silica gel was added to dry toluene (30 mL) and refluxed with 1 mmol (221.35 mg) of APTES for 6 h under nitrogen atmosphere. After reaction, the solids were filtered and washed repeatedly through Soxhlet extraction with dry toluene. The residue was dried overnight in oven at 100 °C and the resulting material is denoted as APTES@SiO₂.

5.2 Synthesis of Benzamide Functionalized Silica Gel

In a suspension of 1.25 g of APTES@SiO₂ in 30 mL diethyl ether 2 mmol (281.2 mg) of benzoyl chloride was added and the resulting mixture was refluxed for 6 h. The resulting yellow colored solid was separated by filtration and washed repeatedly through Soxhlet extraction with ethanol and acetone. The final benzamide grafted silica was dried in oven at 100 °C for overnight and denoted as benzamide@SiO₂.

5.3 Immobilization of Pd(OAc)₂ onto Benzamide@SiO₂

1.0 g of benzamide@SiO₂ was added to the solution containing 50 mg of $Pd(OAc)_2$ in acetone (20 mL) and the

mixture was stirred at room temperature for 24 h. The gradual change in the color of the supported material from light yellow to brown indicates the palladium uptake by benzamide@SiO₂. The resulting solid was filtered off and washed with acetone in Soxhlet and then dried in oven. The catalyst was denoted as Pd–benzamide@SiO₂.

5.4 General Information About Catalytic Experiments

Cross-coupling reactions were carried out under aerobic conditions at room temperature (ca. 28 °C). Progress of the reactions was monitored by thin layer chromatography. The reaction products were purified by column chromatographic using silica gel (60–120 mesh). The isolated products were confirmed by comparing the ¹H spectral data with literature data.

5.5 Standard Procedure for Suzuki–Miyaura Reaction

A 50 ml round-bottom flask was charged with a mixture of aryl halide (0.5 mmol), arylboronic acid (0.55 mmol), K_2CO_3 (1 mmol), catalyst (10 mg, 0.22 mol% Pd) and *i*-PrOH/H₂O (4 mL). The mixture was stirred at room temperature for the indicated time. After completion, the reaction mixture was subjected to centrifugation followed by filtration and the residual solid was washed with the same solvent (3 × 5 mL). The resultant filtrate was diluted with brine (10 mL) and extracted with diethyl ether (3 × mL), dried over anhydrous Na₂SO₄, and evaporated under reduced pressure. The crude residue was subjected to silica gel column chromatography (ethyl acetate–hexane, 0.5: 9.5) to obtain the desired products.

For recycling experiments, the residue catalyst was recovered from the reaction mixture by centrifugation and filtration and washed thoroughly with *i*-PrOH/H₂O followed by EtOAc. After drying for overnight at 100 °C overnight in an oven, the residual catalyst was subjected to subsequent run of the cross-coupling by charging with the required amount of substrates (aryl halide, arylboronic acid), K_2CO_3 and solvent, without further addition of catalyst.

5.6 Analytical Data of the Prepared Biaryl Derivatives

4-Nitrobiphenyl (Table 4, entry 1) [75]. Yellow solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ: 8.31–8.28 (m, 2H), 7.75–7.73 (m, 2H), 7.62–7.61 (m, 2H), 7.50–7.48 (m, 3H); GC–MS *m/z*: 199.1 (M⁺, 100).

4-Chloro-4'-nitro-biphenyl (Table 4, entry 2) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 8.30–8.29 (m, 2H), 7.71–7.70 (m, 2H), 7.57–7.56 (m, 2H), 7.48–7.46 (m, 2H); GC–MS *m*/*z*: 233.10 (M⁺, 100).

4-Methoxy-4'-nitro biphenyl (Table 4, entry 3) [75]. Yellow solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 8.28–8.27 (m, 2H), 7.67–7.65 (m, 2H), 7.58–7.55 (m, 2H), 7.02–7.01 (m, 2H), 3.87 (s, 3H); GC–MS *m*/*z*: 229.3 (M⁺, 100).

4-Methoxybiphenyl (Table 4, entry 4 & 8) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.53–7.51 (m, 4H), 7.42–7.39 (m, 2H), 7.32–7.22 (m, 1H), 6.98–6.95 (m, 2H), 3.81 (s, 3H); GC–MS *m*/*z*: 184.1 (M⁺, 100).

4-Chloro-4'-methoxybiphenyl (Table 4, entry 5) [75] White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.48–7.46 (m, 4H), 7.11–7.09 (m, 2H), 6.96–6.95 (m, 2H), 3.85 (s, 3H); GC–MS *m*/*z*: 218.4 (M⁺, 100).

4, 4'-Dimethoxybiphenyl (Table 4, entry 6) [75]. Colourless solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.48–7.46 (m, 4H), 6.96–6.94 (m, 4H), 3.84 (s, 6H); GC– MS *m*/*z*: 214.10 (M⁺, 100).

1,1'-Biphenyl (Table 4, entry 7) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.63–7.59 (m, 4H), 7.47–7.41 (m, 4H), 7.35–7.32 (m, 2H); GC–MS *m*/*z*: 154.10 (M⁺, 100).

4'-Methoxy-[1,1'-biphenyl]-4-carbaldehyde (Table 4, entry 9) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 10.03 (s, 1 H), 7.92 (d, J = 8.24 Hz, 2H), 7.71 (d, J = 8.24 Hz, 2H), 7.59 (d, J = 8.72 Hz, 2H), 7.01 (d, J = 8.72 Hz, 2H), 3.87 (s, 3H); GC–MS *m*/*z*: 212.1 (M⁺, 100).

[1,1'-Biphenyl]-4-carbaldehyde (Table 4, entry 10) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 10.05 (s, 1H), 7.95 (d, J = 8.28 Hz, 2H), 7.75 (d, J = 8.28 Hz, 2H), 7.63 (d, J = 7.36 Hz, 2H) 7.47 (d, J = 7.36 Hz, 2H), 7.42–7.40 (m, 1H); GC–MS m/z: 182.1 (M⁺, 100).

1-(4'-Chloro-[1,1'-biphenyl]-4-yl)ethanone (Table 4, entry 11) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 8.03 (d, J = 8.68 Hz, 2H), 7.65 (d, J = 8.68 Hz, 2H), 7.56 (d, J = 8.72, 2H), 7.44 (d, J = 8.72 Hz, 2H), 2.64 (s, 3H); GC–MS *m/z*: 230.10 (M⁺, 100).

5-(4-Methoxyphenyl)pyrimidine (Table 4, entry 12) [75]. Yellow solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 9.16 (s, 1H), 8.92 (s, 2H), 7.53 (d, J = 8.72 Hz, 2H), 7.05 (d, J = 8.72, 2H), 3.87 (s, 3H); GC–MS *m*/*z*: 186.1 (M⁺, 100).

5-(6-Methoxypyridin-3-yl)pyrimidine (Table 4, entry 13) [75]. Yellow solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 9.21 (s, 1H), 8.92 (s, 2H), 8.40 (d, J = 2.32 Hz, 1H), 7.80–7.78 (m, 1H), 6.91–6.89 (m, 1H), 4.01 (s, 3H); GC–MS *m*/*z*: 187.1 (M⁺, 100).

4'-Methoxy-[1,1'-biphenyl]-3-carbonitrile (Table 4, entry 14) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.81 (m, 1H), 7.75 (m, 1H), 7.56 (m, 1H),

7.52–7.50 (m, 3H), 7.03–6.97 (m, 2H), 3.86 (s, 3H); GC– MS *m*/*z*: 209.1 (M⁺, 100).

4'-Methoxy-2-methyl-1,1'-biphenyl (Table 4, entry 15) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.25–7.22 (m, 6H), 7.0–6.95 (s, 2H), 3.85 (s, 3H), 2.28 (s, 3H); GC–MS *m*/*z*: 198.3 (M⁺, 100).

4-Methylbiphenyl (Table 4, entry 16) [75]: White solid, Yield: 98 %, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.73 (d, J = 8.0 Hz, 2H), 7.59–7.56 (m, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.44–7.39 (m, 1H), 7.34–7.31 (m, 2H), 2.39 (s, 3H); GC–MS *m*/*z*: 168.10 (M⁺, 100).

4-Methoxybiphenyl (Table 4, entry 17) [75]. White solid, ¹H NMR (CDCl₃, 400 MHz, ppm) δ : 7.52–7.51 (m, 4H), 7.44–7.41 (m, 2H), 7.31–7.24 (m, 1H), 6.99–6.95 (m, 2H), 3.85 (s, 3H); GC–MS *m*/*z*: 184.2 (M⁺, 100).

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