CHAPTER 5

Section 5.1

Facile synthesis of Pd NPs with the aid of methanol decorated on biosilica: An excellent catalyst for ligand and copper free Sonogashira cross-coupling reaction at room temperature.

Section 5.2

Reducing agent free, simple and facile synthesis of Pd NPs decorated on biosilica and its implementation in ligand free Suzuki-Miyaura cross-coupling reaction at room temperature.

Section 5.1

Facile synthesis of Pd NPs with the aid of methanol decorated on biosilica: An excellent catalyst for ligand and copper free Sonogashira cross-coupling reaction at room temperature.

5.1.1. Introduction

Nano sized metal particles are nowadays considered to be most effective catalysts for chemical transformations because of their large surface area [1] compared to their bulk counterparts. Also their insolubility in reaction media renders them easily separable from the reaction mixture and thus they behave as heterogeneous catalysts, which in turn make the product isolation easier. Metal NPs for catalytic applications are generally prepared by the evaporation/condensation of the metal or by chemical/ electrochemical reduction of a metal salt. Recently, Pd NPs have gained great importance to their application both in heterogeneous and homogeneous catalysis, due to the high surface-to-volume ratio and also due to their high surface energy [2]. Normally, the synthetic methods used for producing Pd NPs involve chemical reduction of Pd(II) by using reducing agents like $NaBH_4$/ascorbic acid [3], N_2H_4 [4], PEG [5], $CNCH_2COOK$ [6], or sonochemical [7] and polyols reduction [8] processes. Though these types of synthetic processes are simple and provide high growth rate and high yield, however they are not environment friendly. Also, there are few reports available where plant extract or biomass was used for the production of Pd NPs, where the plant materials act both as a reducing agent and stabilizers [2,9].

The embedding of NPs into various porous supports offers potential for particle size control as well as protecting and stabilizing the NPs for use in different catalytic applications. In recent years, substantial affords have been given by researchers to immobilize and stabilize the Pd NPs in various heterogeneous supports such as organic matrix, organic–inorganic fluorinated hybrid materials, polymers, glass–polymer composites, and ionic liquids. Apart from these, Pd NPs are also synthesized in different inorganic supports such as carbon [10], carbon nanotubes [11], alumina [12], silica [13], zeolite [14], clays [15] and zinc ferrite [16]. Among this, biosilica or [diatomaceous earth (DE) or diatomite] a non-toxic, inorganic porous material draw special attention in the field of catalysis and can be used for the generation of supported Pd-NPs due to its high surface area. Biosilica [17] is a porous inorganic material with high surface area with hydroxyl groups on the surface. Its main constituents are 87-91% SiO_2 with small quantities of iron oxide and alumina [18]. Due to its porous structure, high silica content, low density, low conductivity coefficient etc., [19] it has widely been applied as filter aid [20], adsorbent [21], insulating material [22], catalyst support or carrier [23] and natural insecticide or grain protectant [24]. It also has excellent absorption power. The present

work deals with the development of an ecofriendly method for the generation Pd NPs using biosilica as support. The synthesis has been carried out at room temperature using methanol as solvent without using any reducing agent.

The palladium catalyzed Sonogashira coupling of terminal alkynes with aryl or vinyl halides is one of the most reliable methodologies for the construction of $C(sp^2)$-C(sp) bonds [25]. The synthesized alkyne have found extensive applications in the field of pharmaceuticals [26], dyes [27], sensors [28], electronics [29], polymers [30], guest-host constructs [31], natural products [32] and heterocyclic synthesis [33]. The reaction is generally accelerated by the addition of Cu-salt as co-catalyst and an amine base in the presence of suitable phosphine based ligands [34]. However, the use of copper salt as co catalysts can leads to the formation of undesirable Glaser-type homocoupling product of the alkynes and thereby decreasing the product efficiency which impose the researchers to develop a 'Cu free' protocol for Sonogashira reaction [35]. As a result, several alternative protocols have been developed where other co-catalysts such as Ag_2O [36], AuI [37], Zn [38], Sn [39] have been successfully employed as alternative to Cu co-catalyst. Nowadays, efforts have been given by researchers to carry out co-catalyst free Sonogashira reaction by employing Pd-complexes with *N*-heterocyclic carbene ligands [40], oximepalladacycle [41], salen [42], urea [43] etc. Although the reaction proceeds smoothly with these Pd-complexes, the major drawbacks are availability, stability and cost of the palladium complexes and related ligands. Also, the reactions are generally carried out at elevated temperature [44] in toxic organic solvents like DMF [45], THF [46], and dioxane [47] which can be considered as demerits of the above protocol.

In the work presented here, the author describes a method for the generation of biosilica supported Pd NPs catalyst at room temperature in methanol medium without using additional reducing agent. The prepared catalyst was characterized using various spectroscopic and microscopic tools. The Sonogashira coupling reaction between terminal alkynes with aryl or vinyl halides with different types of functional groups was assessed with the prepared catalyst, resulting good to high yield of the product.

5.1.2. Experimental

5.1.2.1. General Information

All the reactions were monitored employing TLC technique using aluminium coated TLC plates with silica gel $60F_{254}$ (Merck). Purifications of the products were done by Column chromatography technique using silica gel (60-120 mesh). ^{1}H and ^{13}C NMR spectra of the synthesized compounds were recorded in a 400 MHz NMR spectrophotometer (JEOL JNM-ECS) using tetramethylsilane (TMS) as the internal standard. Chemical shifts are expressed in ppm and the coupling constants are expressed in Hertz. Powder XRD pattern was recorded with Rigaku X-ray diffractometer over the range of 2θ=10-80° with a scanning rate of 2 °C min^{-1}.The surface morphology and EDX analyses of the prepared catalyst were done using JEOL SEM (JEOL, model JSM-6390 LV operating at an accelerating voltage of 15 kV). Size and distribution of NPs were determined by using TEM (JEOL, JEM-2010) equipped with a slow-scan CCD camera at an operating voltage of 200kV. Specific surface area, pore volume, average pore diameter were measured with the NOVA-1000, version: 3.70 (Quantachrome, USA). The specific surface area of the samples was determined by adsorption of nitrogen gas at 77 K and using the Brunauer–Emmett–Teller (BET) calculation. Before adsorption, the samples were degassed at 250 °C for 3 h. Pore size distributions were measured from desorption isotherms using the Barrett–Joyner–Halenda (BJH) method. Melting points were recorded in a Büchi B450 melting point apparatus.

5.1.2.2. Materials and chemical reagents

All the chemicals were purchased from different commercials firms. Biosilica was purchased from Rankem, India, Sulfuric acid (AR grade) from Qualigens, India, Palladium acetate from SRL India, potassium carbonate from Qualigens, India, MeOH from Merck, India, Isopropanol from Merck, India, different aryl halides substrates from SRL, India, also acetylene substrates from Merck, India as well as from SRL, India and silica gel for TLC and column chromatography from Merck, India. All these chemicals were of analytical grade and used without purification. Solvents such as ethyl acetate and hexane were distilled prior to use.

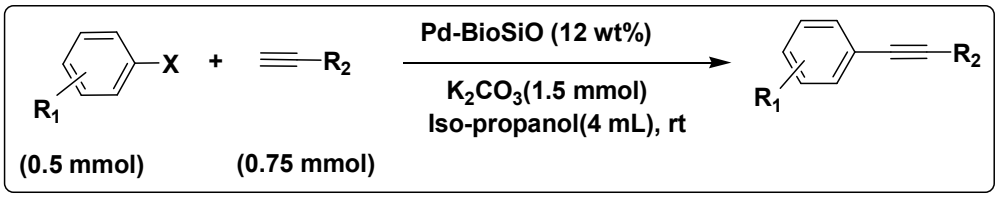
5.1.2.3. Preparation of the catalyst

At first 5 gm of biosilica was taken into a 250 mL round bottom flask and to it 100 mL of 4M H_2SO_4 was added. The dispersion was refluxed for 1 h. After cooling the supernatant liquid was discarded and the activated bio silica was repeatedly washed with deionized water and finely dried in an oven at 60 °C overnight to obtain the final solid product. This activated biosilica was used for the preparation of catalyst.

In a 50 mL round bottom flask, 0.54 gm of activated biosilica and 0.054 gm (10 wt %) of $Pd(OAc)_2$ were taken followed by addition of 15 mL of methanol. The mixture was mechanically stirred at room temperature for 4 days, until the color of the solution turns black and uniform. After completion, the solvent was evaporated using rotary evaporator and finally dried in a desiccator for 12 h.

5.1.2.4. General experimental procedure for Pd-BioSiO catalyzed Sonogashira cross-coupling reaction

A 50 mL round-bottom flask was charged with a mixture of phenylacetylene (0.75 mmol), aryl halide (0.5 mmol) and 4 mL of *iso*-propanol. To this mixture, 12 wt% of the catalyst was added followed by the addition of 1.5 mmol of K_2CO_3. The whole reaction mixture was stirred for the required time. The monitoring of the reaction was done by TLC technique. After completion, the reaction mixture was first diluted with distilled water and then distilled ethyl acetate was used to extract the product from the reaction mixture (3 times). Thereafter it was washed with brine (3 times) and then anhydrous Na_2SO_4 was used for removal of traces quantities of water left. Finally, column chromatography technique (60-120 mesh silica gel and ethyl acetate-hexane solvent mixture) was used to purify the product and confirmed by ^1H and ^{13}C NMR spectroscopy.



Scheme 1: Model reaction for Sonogashira cross-coupling reaction.

5.1.3. Results and discussion

5.1.3.1. Characterization of the catalyst, Pd-BioSiO

5.1.3.1.1. BET surface area analysis

In Fig. 1, below, the N_2 adsorption–desorption isotherm and pore size distribution (Fig. 2) of biosilica and the prepared catalyst under study were shown. From Fig. 1, we can predict that the compounds are mesoporous material with highly uniform pore size distribution (Type IV isotherm).

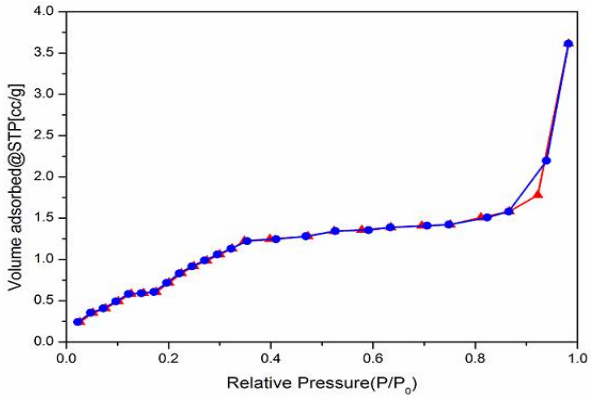


Fig. 1: N_2 adsorption-desorption isotherm.

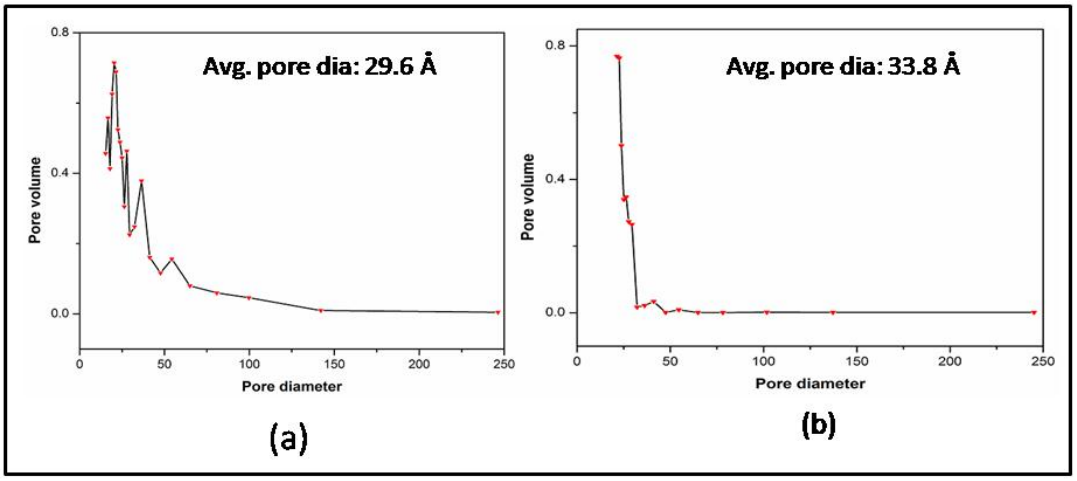


Fig. 2: Pore size distribution curve of Biosilica (a) and Pd-BioSiO (b).

Table 1: Surface properties of biosilica and biosilica supported catalyst.

Sample	Surface properties of surface/catalyst	
	Specific surface area(m^2g^{-1})	Average Pore diameter(Å)
Biosilica	14	29.6
Pd-BioSiO	4	33.8

The appreciable decrease in the specific surface area after supporting Pd NPs (Table 1) indicates the incorporation of the metal into biosilica support. This might be due to clogging of some pores by Pd NPs. However, the increase in pore diameter may be due to rupture of some smaller pores to generate bigger ones during the formation of Pd NPs into the pores.

5.1.3.1.2. EDX analysis

The EDX analysis (Fig. 3) of the catalyst (Pd- BioSiO) clearly shows the presence of Pd in the catalyst (8.11 wt%).

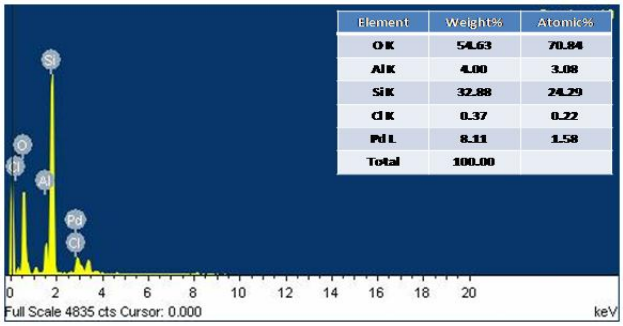


Fig. 3: EDX analysis of Pd-BioSiO.

5.1.3.1.3. Powder XRD analysis

Powder XRD technique was used to determine the crystal domain size and the structure of the NPs formed. Powder XRD pattern of biosilica and the catalyst Pd-BioSiO were taken and assembled in Fig. 4. The X-ray diffraction pattern of biosilica revealed the planes at (100), (101), (110), (200), (201), (112) (211) and (203) which correspond to their relative intensities at 2θ = 20.95°, 26.75°, 34.75°, 42.50°, 45.75°, 50.15°, 60.05° and 68.35° respectively. Biosilica is a hexagonal system having primitive lattice sites (JCPDS ≠ 89-8949). The XRD pattern of Pd-BioSiO showed some significant changes. In

addition to the above peaks, the XRD pattern of Pd-BioSiO shows three peaks at 2θ= 39.95°, 46.45° and 67.95° corresponding to the reflection of (111), (200) and (220) planes respectively that could be indexed to fcc phase of Pd NPs (JCPDS ≠ 88-2335). The broadening of the peak indicated that the palladium particles were of nano-size. The intensities of the planes (111), (200) and (220) of Pd NPs diminished when they were entrapped into the pores of biosilica that indicates strong interaction between them. The intensities of the planes corresponding to diatomaceous earth also decrease to some extent during this course of strong interaction. Thus, we can say that biosilica acts as a support for holding Pd NPs tightly into its pores.

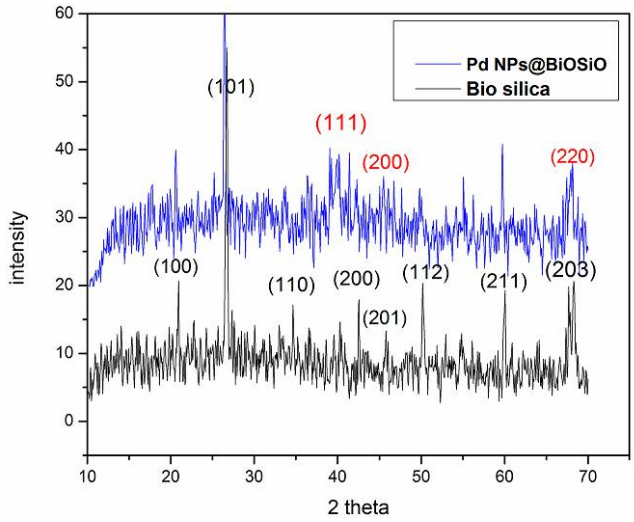


Fig. 4: PXRD pattern of the biosilica and Pd-BioSiO.

5.1.3.1.4. TEM and particle size distribution analysis

The particle size and surface morphology of the synthesized catalyst was studied by Transmission Electron Microscopy (TEM) and high resolution Transmission Electron Microscopy (HR-TEM) as shown in Fig. 5.

From the TEM image we can say that Pd NPs are uniformly dispersed on the surface of biosilica and most of the particles are spherical in nature. The interplaner distance of 0.20 nm as calculated from the HRTEM image Fig. 5(e) corresponds to (200) plane. The average size of the NPs as calculated from the particle size distribution plot was found to be about 9.4 nm [Fig. 5(f)]. The diffraction dots observed in the SAED images, as shown in Fig. 5(a), proves the crystalline nature of the synthesized NPs formed.

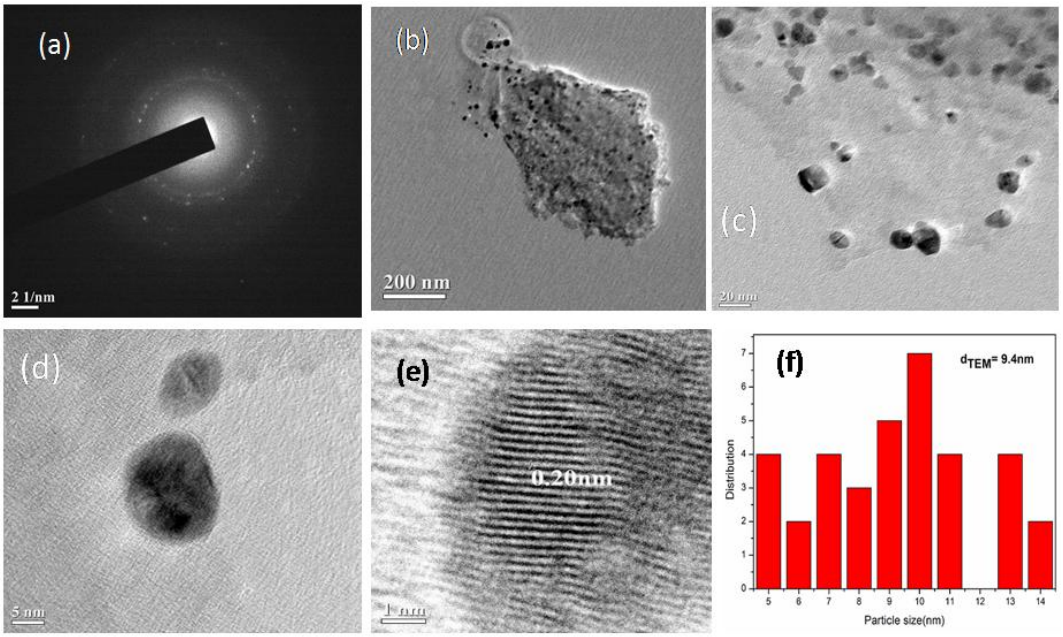


Fig. 5: TEM images of Pd-BioSiO: (a) SAED pattern, (b-d) TEM images, (e) HR-TEM image along with particle size distribution (f).

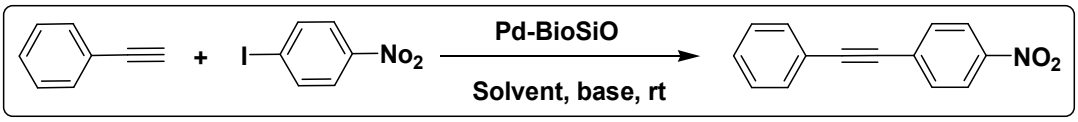
The Pd content in the catalyst, Pd-BioSiO, as analyzed by ICP-AES, reveals that the amount of Pd loaded in the catalyst is 0.0539 g (9.98 wt%).

5.1.3.2. Optimization of the reaction condition for solvent and base and catalyst

To explore the new catalytic system for Sonogashira cross-coupling reaction, a model reaction using phenyl acetylene and aryl halide was investigated in detail by varying different parameters such as amount of catalyst, base and solvent in order to find out a suitable reaction condition for the coupling protocol. Initially, to ascertain the efficacy of Pd-BioSiO as catalyst we started our work with 0.75 mmol of phenylacetylene and 0.5 mmol of 4-iodonitrobenzene as model substrates. The reaction was carried out at room temperature. The results are summarized in table 2. An initial screening of the effect of solvents using K_2CO_3 as base showed that isopropanol was the most effective one affording excellent yield (entry 5, Table 2) with 5 wt% of the catalyst and 1.5 mmol of base K_2CO_3. The catalytic activity decreased significantly when H_2O was used as solvent (entry 2, Table 2), which may be due to insolubility of the substrates in H_2O. Next, we optimized the reaction condition for the amount of catalyst in isopropanol as solvent and

found that 12 wt% of the catalyst was the optimum amount (entry 8, Table 2). Increasing the catalytic amount to 15 wt% did not significantly increase the yield (entry 9, Table 2). Base plays a significant role in Sonogashira reaction. The reaction was also screened using different inorganic bases (entries 10 and 11, Table 2). Among the bases used, considering the cost, efficiency and reliability factors, K_2CO_3 was found to be most effective. However, a comparably similar result was also found for Cs_2CO_3 (entry 11, Table 2). For optimizing the amount of base, we carried out the same reaction with 1 mmol amount of the base K_2CO_3 (entry 12, Table 2) and we found that the yield decreased to 86%. Thus, from the above discussion we found that the best reaction condition was with 12 wt% of the catalyst in isopropanol solvent and in the presence of base K_2CO_3 (1.5 mmol) at room temperature (entry 8, Table 2).

Table 2 : Optimization of reaction condition for catalyst, solvent and base:[a]



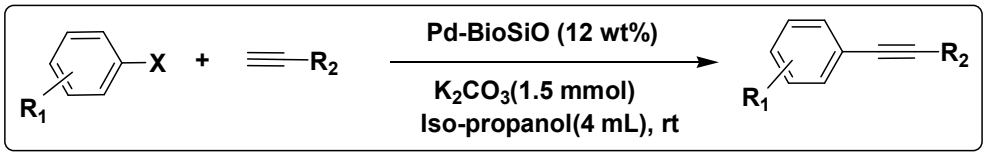
Entry	Catalyst (wt%)	Solvent (4 mL)	Base (1.5 mmol)	Time (h)	Yield (%)[b]
1	5	H_2O	No base	24	Trace
2	5	H_2O	K_2CO_3	24	38
3	5	Ethanol	K_2CO_3	12	76
4	5	Methanol	K_2CO_3	10	80
5	5	Isopropanol	K_2CO_3	3	85
5	5	Isopropanol:H_2O	K_2CO_3	12	72
7	10	Isopropanol	K_2CO_3	3	89
8	**12**	**Isopropanol**	**K_2CO_3**	**3**	**94**
9	15	Isopropanol	K_2CO_3	8	95
10	12	Isopropanol	Na_2CO_3	5	90
11	12	Isopropanol	Cs_2CO_3	3	93
12[C]	12	Isopropanol	K_2CO_3	5	86

[a]Reaction condition: phenylacetylene (0.75 mmol), 4-iodonitrobenzene (0.5 mmol), rt. [b]Isolated yield, [c]1 mmol of K_2CO_3 used.

5.1.3.3. Substrate study

To study the scope and limitation of the reaction procedure, wide varieties of electronically diverse halides and substituted terminal acetylenes were investigated with the optimized reaction conditions. The results are summarized in Table 3.

Table 3. Pd-BioSiO catalyzed Sonogashira reaction:[a]



Entry	R_1	R_2	X	Time (h)	Yield (%)[b]
1	4-NO_2	C_6H_5	I	3	94
2	4-Me	C_6H_5	I	4	96
3	3-Me	C_6H_5	I	3	92
4	4-OMe	C_6H_5	I	5	86
5	3-NO_2	C_6H_5	I	4	90
6	H	C_6H_5	I	3	96
7	4-Me	4-MeC_6H_4	I	3	95
8	4-OMe	4-MeC_6H_4	I	4	93
9	4-NO_2	4-MeC_6H_4	I	3	94
10	H	C_6H_{11}	I	5	90
11	4-NO_2	C_6H_5	Br	8	50
12	4-OMe	C_6H_5	Br	8	55

[a]Reaction conditions: aryl halide (0.5 mmol), acetylene (0.75 mmol)

[b]Isolated yield.

From the above results we can conclude that the reaction was equally effective for both electron donating and electron withdrawing groups at *para* position in aryl iodides and afforded good to excellent yield of the products (entries 1, 2 and 4, Table 3). In case of electron donating and electron withdrawing groups present in *meta* position of aryl iodides, excellent yields of the products were also obtained (entries 3 and 5, Table 3). The reaction also proceeds smoothly with substituted phenylacetylenes and affords good yield of the isolated cross-coupled product (entries 7-9, Table 3). To check the feasibility of the Sonogashira reaction with

aliphatic alkynes, we tried the reaction with cyclohexyl substituent and obtained appreciably good yield of the cross-coupled product (entry 10, Table 3). Finally, to extend the scope and limitation of the above protocol, aryl bromides were investigated, but the results that we found were not satisfactory and which was only 50% and 55% (entries 11 and 12, Table 3).

5.1.3.4. Reusability study

From the green chemistry point of view, the reusability/recyclibility of the catalyst is a very important and vital parameter to be considered. Here, we also investigated the reusability of our prepared catalyst. For that, we chose the initial reaction (Scheme 1) as the model reaction. Initially, we took 1.5 mmol of phenylacetylene and 1 mmol of 4-bromonitrobenzene in 8-10 mL of *iso*-propanol. To this reaction mixture 24 wt% of the catalyst and 3 mmol of the base K_2CO_3 were added. Considering the recovery issue, the scale of the model reaction was increased two folds.

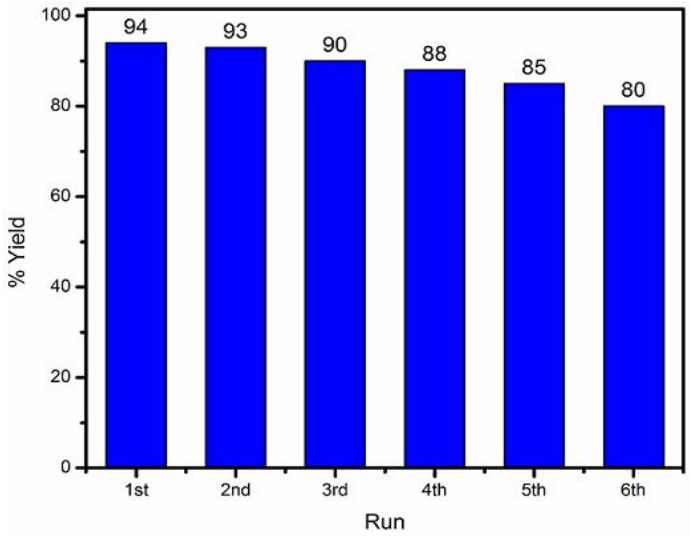


Fig. 6: Reusability of the catalyst.

From Fig. 6 it is obvious that the catalyst was reusable up to 3rd run without any significant loss of its catalytic activity.

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5.1.3.5. Hot filtration technique

To check the heterogeneity of the catalyst, and also for testing the leaching of Pd from the catalyst, a hot filtration experiment was done. For this the model reaction was again performed under the optimized reaction condition. The reaction was stopped after 1.5 h and approximately 60 % isolated yield of the product was recorded. After removal of the catalyst through filtration, the filtrate was allowed to proceed for another 10 h but no significant increase in the yield of the cross-coupled product was observed which proves the heterogeneous nature of the catalyst and also proves that Pd doesn't leached out from the support (Fig. 7).

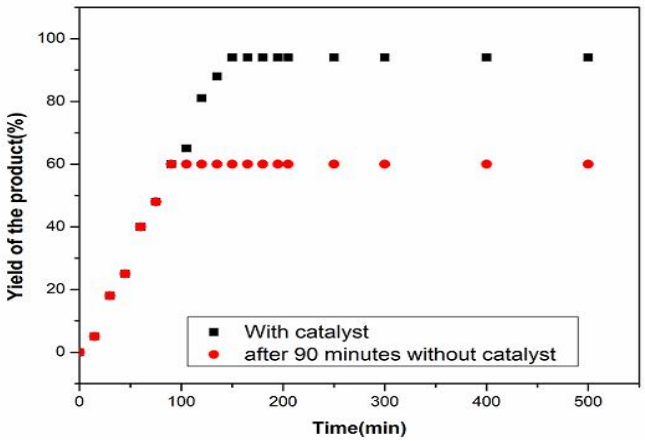
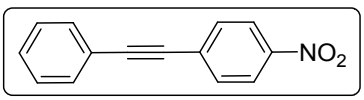


Fig. 7: Hot filtration test of the catalyst.

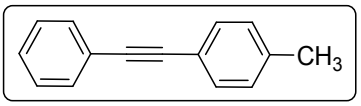
5.1.4. Conclusions

In conclusion, a simple and highly efficient heterogeneous catalyst Pd-BioSiO has been developed which exhibit excellent catalytic activity for amine and copper free Sonogashira cross-coupling reaction at room temperature. The compatibility of the reaction to a wide range of electronically diverse aryl iodides has been tested and found good result. Also the catalytic system has potential to couple with aromatic and aliphatic alkynes. The reusability of the catalyst was assessed and found that it was reusable up to 3rd runs without any significant loss of catalytic activity.

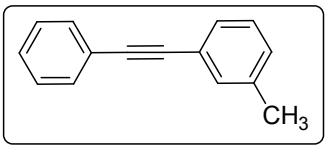
Characterization data of the products



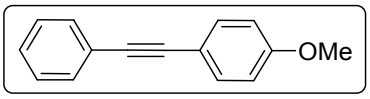
1-nitro-4-(2-phenylethynyl)benzene (entry 1, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 2H, *J*=8.7Hz), 7.65 (d, 2H, *J*=8.7Hz), 7.56-7.53 (m, 2H), 7.39-7.36 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 132.2, 131.8, 130.2, 129.2, 128.5, 123.6, 122.0, 94.7, 87.5.



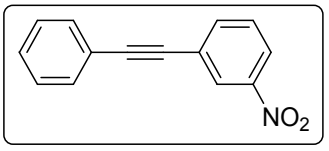
1-methyl-4-(2-phenylethynyl)benzene (entry 2, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.50 (m, 2H), 7.42 (d, 2H, *J*=7.7Hz), 7.34-7.31 (m, 3H), 7.14 (d, 2H, *J*=7.7Hz), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 132.5, 131.6, 131.5, 129.1, 128.5, 128.3, 128.1 123, 89.6, 88.7, 21.5.



1-methyl-3-(2-phenylethynyl) benzene (entry 3, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52-7.50 (m, 2H), 7.42 (d, 2H, *J*=7.7Hz), 7.35-7.31 (m, 3H), 7.14 (d, 2Hz, *J*=7.7), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 132.5, 131.6, 129.2, 128.5, 128.4, 128.3, 128.1, 123.5, 120.2, 89.6, 88.7, 21.6.

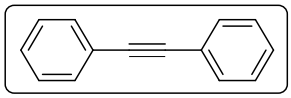


1-(2-(4-methoxyphenyl)ethynyl)benzene (entry 4, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ7.53-7.51 (m, 2H), 7.48 (d, *J*=8.2Hz 2H), 7.36-7.30 (m, 3H), 6.88 (d, 2H, *J*=8.2Hz), 3.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 133.1, 131.5, 128.4, 128.0, 123.6, 115.4, 114.1, 89.4, 88.1, 55.3.

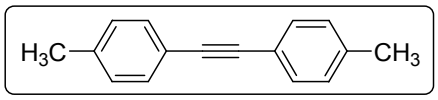


1-nitro-3-(2-phenylethynyl)benzene (entry 5, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 8.18-8.15 (m, 1H), 7.81 (d, 1H, *J*=7.7Hz), 7.56-7.52 (m, 3H), 7.38-7.36 (m,

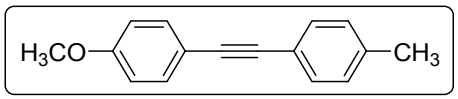
3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 137.2, 131.8, 129.4, 129.1, 128.6, 126.4, 125.2, 122.9, 122.2, 92.0, 86.9.



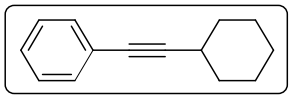
1,2-diphenylethyne (entry 6, Table 3): ^{1}H NMR(400 MHz, $CDCl_3$): δ 7.58-7.55 (m, 4H), 7.37-7.34 (m, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.6, 128.2, 127.4, 124.1, 94.5.



1,2-di-*p*-tolylethyne (entry 7, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J*=8Hz, 4H), 7.14 (d, *J*=8Hz, 4H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2, 131.5, 129.2, 120.4, 88.9, 21.6 ppm.

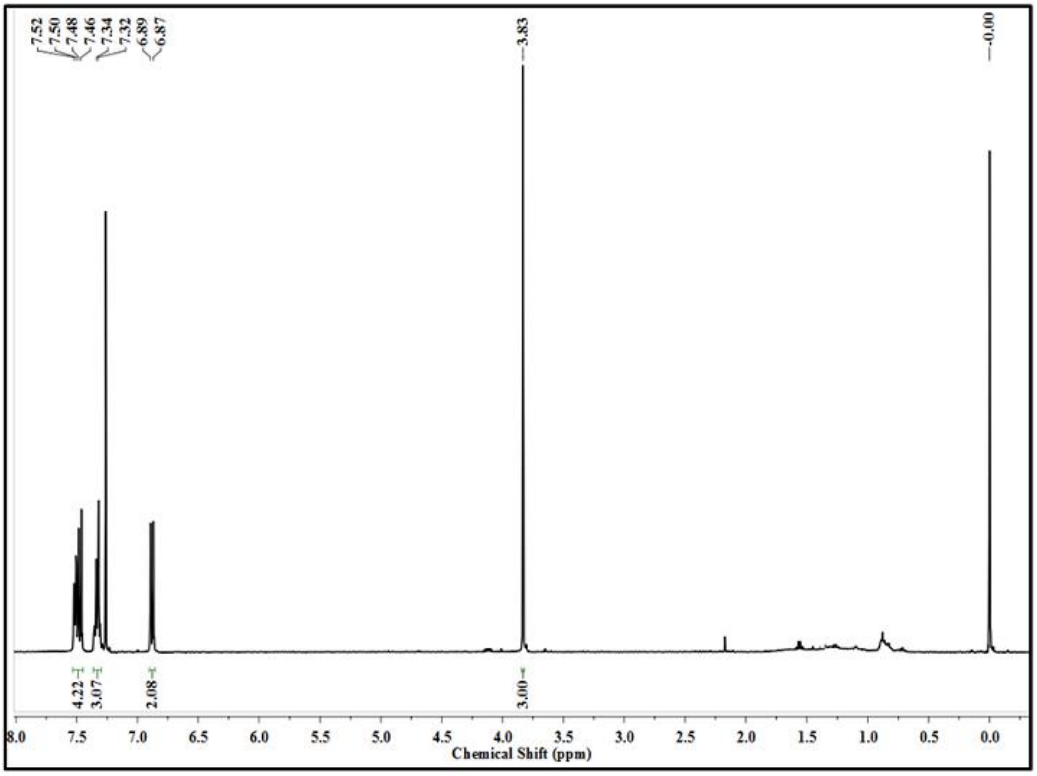


1-methoxy-4-(2-*p*-tolylethynyl)benzene (entry 8, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ7.45 (d, *J*=8Hz, 2H), 7.39 (d, *J*=8Hz, 2H), 7.13 (d, *J*=8Hz, 2H), 6.86 (d, *J*=8Hz, 2H), 3.82 (s, 3H), 2.35 (s, 3H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$): δ 133.0, 131.4, 129.1, 114.0, 55.3, 21.5 ppm.

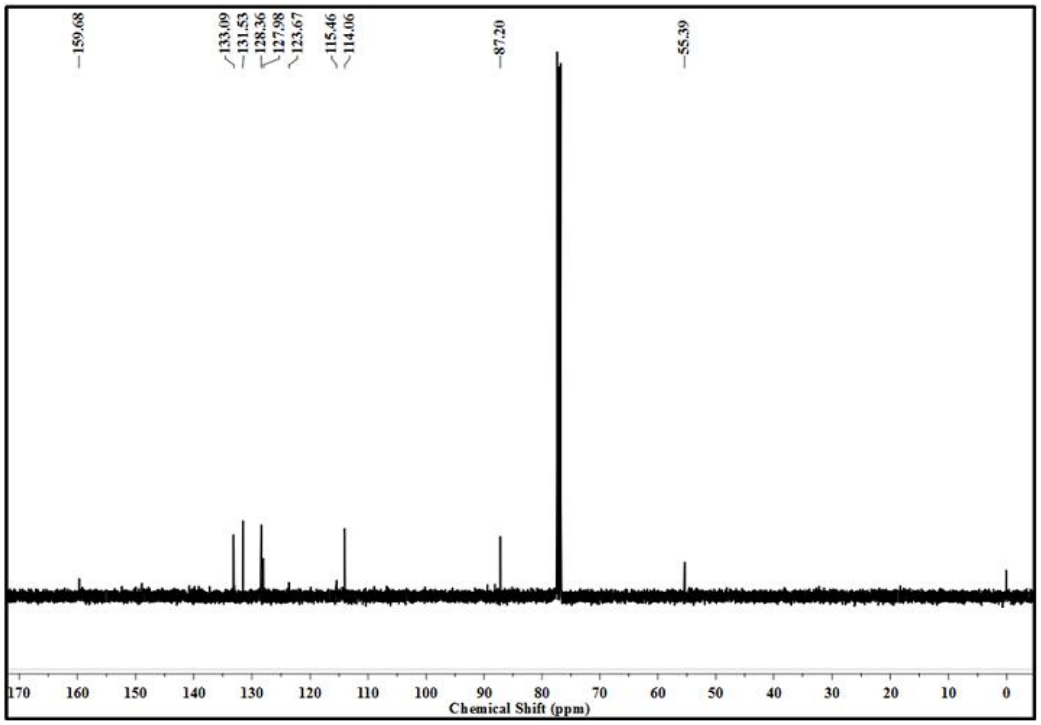


1-(2-cyclohexylethynyl)benzene (entry 10, Table 3): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.38 (m, 2H), 7.25-7.24 (m, 3H), 2.60-2.54 (m, 1H), 1.62-1.51 (m, 7H), 0.94-0.92 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ131.6, 128.2, 127.4, 124.1, 90.5, 32.8, 29.7, 26.0, 24.9.

^{1}H NMR spectrum of 1-(2-(4-methoxyphenyl)ethynyl)benzene



^{13}C NMR spectrum of1-(2-(4-methoxyphenyl)ethynyl)benzene



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Section 5.2

Reducing agent free, simple and facile synthesis of Pd NPs decorated on biosilica and its implementation in ligand free Suzuki-Miyaura cross-coupling reaction at room temperature.

5.2.1. Introduction

As discussed earlier in the introduction part of Chapters 1 and 2, the Pd catalyzed Suzuki-Miyaura cross-coupling reaction is considered to be one of the most powerful and widely used method for the constructing C-C bond, as it found utmost applications in numerous fields like pharmaceuticals, natural products etc which is due to its associated mild reaction conditions and large substrate scope [1, 2]. So far as the catalyst, reaction condition and substrate scopes are concerned the reaction had undergone tremendous development. Traditionally, the catalytic system for Suzuki coupling reaction comprises of either Pd(0) or Pd(II) species, and also suitable phosphine or nitrogen based ligands are added [3]. Also, the reaction is performed under inert atmosphere and due to sensitivity of the catalytic system to oxygen and moisture the reaction was generally performed in hazardous organic solvents. As such the use of environmently favourable solvents such as water [4], ionic liquids [5], or supercritical carbondioxide [6] are considered to be more favourable alternatives which also fullfils dream of the green chemistry perspectives.

Nano-catalysis is nowadays regarded as an emerging area in the field of synthetic organic chemistry. The peculiar size dependent properties of the NPs [7] compared to their bulky counterparts are the main factors responsible for their exceptional catalytic activity. Pd NPs of different various shapes and sizes are synthesized using different physical and chemical methods. In order to control the size and morphology of the NPs formed in wet chemical methods the reduction of Pd(II) species is generally done in presence of different types of stabilizing agents, capping agents or solid supports [8, 9]. Although these types of methods synthesized Pd NPs which shows good catalytic activity butthey are associated with drawbacks like requirement of high temperature, ultrasonication etc and also contamination from precursor chemicals, use of toxic solvents and formation of by-products are additional demerits along with these methods. Consequently, there is a growing demand for the development of eco-friendly methods for the synthesis of NPs which minimises the losses of chemicalsand also to carry out in environmentally friendly solvents.

Again as the synthesized NPs are thermodynamically not stable and leads to agglomeration, so different types of stabilizers such as surfactants, organic ligands

(viz. Sulphur, phosphine and nitrogen based ligands), polymers and dendrimers are used to stabilise the NPs from agglomerization [10].

As we already discussed in the previous section of this chapter significant affords has been given by the researchers to immobilize and stabilize the Pd NPs in various heterogeneous supports such as organic matrix, organic–inorganic fluorinated hybrid materials, polymers, glass–polymer composites, and ionic liquids. Bio-silica (diatomaceous earth (DE)) a non-toxic, inorganic porous material draw special attention in the field of catalysis and can be used for the generation of supported Pd-NPs due to its high surface area with hydroxyl groups on its surface. Its main constituents are 87-91% SiO_2 with small quantities of iron oxide and alumina [11]. It is non-toxic and has excellent absorption power. In this section of this chapter, the Suzuki cross coupling reaction between different electronically substituted subtracts were examined with the same catalyst and found good to excellent yield of the product. The syntheses of the catalyst as well as its characterizations are already discussed in section 5.1, so these portions are not included here and only the catalysis part has been presented here.

5.2.2. Experimental

5.2.2.1. General Information

All the reactions are monitored using TLC technique using aluminium coated TLC plates with silica gel 60 F_{254} (Merck). Purifications of the products are done by Column chromatography technique using silica gel (60-120 mesh). ^{1}H and ^{13}C NMR spectra of the synthesized compounds were recorded in a 400 MHz NMR spectrophotometer (JEOL JNM-ECS) using tetramethylsilane (TMS) as the internal standard. Chemical shifts are expressed in ppm and the coupling constants are expressed in Hertz. Powder XRD pattern was recorded with Rigaku X-ray diffractometer over the range of 2θ=10-80° with a scanning rate of 2 °C min^{-1}. The surface morphology and EDX analysis of the prepared catalyst were done using JEOL SEM (JEOL, model JSM-6390 LV operating at an accelerating voltage of 15 kV). Size and distribution of NPs were determined by using TEM (JEOL, JEM-2010) equipped with a slow-scan CCD camera at an operating voltage of 200kV. Specific surface area, pore volume, average pore diameter were measured with the NOVA-1000, version: 3.70 (Quantachrome, USA). The specific surface area of the samples was determined by adsorption of nitrogen gas at 77 K and

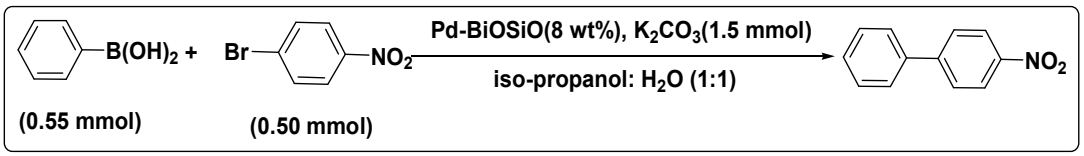
using the Brunauer–Emmett–Teller (BET) calculation. Before adsorption, the samples were degassed at 250 °C for 3 h. Pore size distributions were measured from desorption isotherms using the Barrett–Joyner–Halenda (BJH) method. Melting points was recorded in Büchi B450 melting point apparatus.

5.2.2.2. Materials and chemical reagents

All the chemicals were purchases from different commercials firms. Biosilica was purchased from Rankem, India, Sulfuric acid (AR grade) from Qualigens, India, Palladium acetate from SRL India, potassium carbonate from Qualigens, India, MeOH from Merck, India, bromobenzene from G.S. Chemical Testing Labs, Bombay, India other chemicals were purchased from Sisco-Research-Laboratories Pvt. Ltd. India and silica gel for TLC and column chromatography from Merck, India. All these chemicals were of analytical grade and used without purification. Solvents such as ethyl acetate and hexane were distilled prior to use.

5.2.2.3. General experimental procedure for Pd-BioSiO catalyzed Suzuki-Miyaura cross-coupling reaction

The efficiency of the catalyst for Suzuki-Miyaura reaction was evaluated using phenylboronicacid and *p*-bromonitrobenzene as model substrates. To a 50 mL round-bottom flask a mixture of *p*-bromonitrobenzene (0.5 mmol), phenylboronicacid (0.55 mmol), K_2CO_3 (1.5 mmol), and 8 wt% of the nanocatalyst with respect to boronicacid were added and stirred at room temperature in *iso*-propanol:water (1:1) solvent system for the required time. The monitoring of the reaction was done by TLC technique. After completion, the reaction mixture was first diluted with distilled water and then distilled ethyl acetate was used to extract the product from the reaction mixture (3 times). Thereafter it was washed with brine (3 times) and then anhydrous Na_2SO_4 was used for removal of traces of water left. Finally, column chromatography technique (60-120 mesh silica gel and ethyl acetate-hexane solvent mixture) was used to purify the product and confirmed by ^{1}H and ^{13}C NMR spectroscopy.



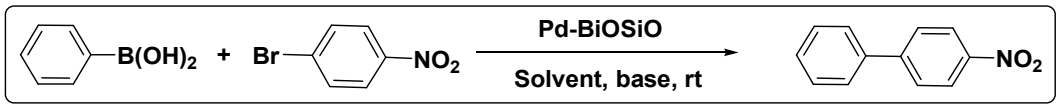
Scheme 1: Model reaction for Suzuki-Miyaura cross-coupling reaction.

5.2.3. Results and discussion

5.2.3.1. Optimization of the reaction condition for solvent and base and catalyst

After characterization of the catalyst, our next endeavor was to find out a suitable reaction condition for the Suzuki-Miyaura coupling reaction. 4-Bromonitrobenzene and phenylboronic acids were chosen as the model substrates for the optimization purpose. The system shows significantly good catalytic activity in *iso*-propanol: water (1:1) as solvent at room temperature. The results are summarized in table 1. It was obvious from entry 1 of table 1 that in the absence of base the reaction did not proceed which suggests that presence of base was a very essential parameter for the reaction to occur. The effect of solvent on the reaction was screened using K_2CO_3 (1.5 mmol) as base. The result shows that *iso*-propanol:H_2O (1:1) was the most effective one, affording highest yield (entry 6, Table 1). Other inorganic bases like Na_2CO_3, KOH etc. also have similar effect on the reaction and proceeds with comparable yield (entries 7 & 8, Table 1). Again optimizing the amount of the catalyst, we obtained that 8 wt% of the nanocatalyst with respect to phenyl boronic acid substrate was the optimized amount for best conversion (entry 6, Table 1). Again if we decreased the amount of base, K_2CO_3 to 1 mmol (entry 12, Table 1) the yield was also found to decreased to 80%. Thus, from above discussion we come to the conclusion that 8 wt% of the catalyst in *iso*-propanol:water (1:1) solvent and in the presence of base, K_2CO_3 (1.5 mmol) at room temperature was the most favoured reaction condition for the formation of biaryl (entry 6, Table 1).

Table 1: Optimization of reaction condition for catalyst, solvent and base:[a]



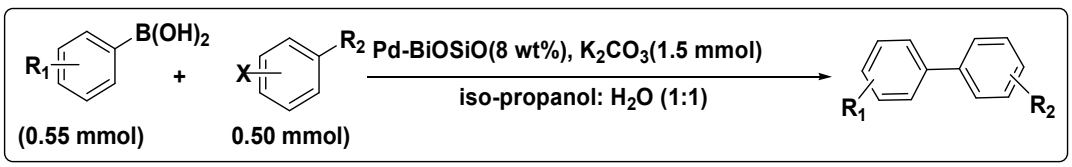
Entry	Catalyst (wt %)	Solvent	Base (1.5 mmol)	Time (h)	Yield[b] (%)
1	8	H_2O	No base	24	0
2	8	No solvent	K_2CO_3	10	12
3	8	H_2O	K_2CO_3	24	65
4	8	DMF	K_2CO_3	24	70
5	8	MeOH:H_2O	K_2CO_3	24	75
6	**8**	**Isopropanol:H_2O**	**K_2CO_3**	**1.5**	**92**
7	8	Isopropanol:H_2O	Na_2CO_3	1.5	90
8	8	Isopropanol:H_2O	KOH	3	80
9	5	Isopropanol:H_2O	K_2CO_3	5	82
10	12	Isopropanol:H_2O	K_2CO_3	1.5	92
11	15	Isopropanol:H_2O	K_2CO_3	1.5	93
12[c]	8	Isopropanol:H_2O	K_2CO_3	0.5	80

[a]Reaction condition: Phenylboronic acid (0.55 mmol), 4-bromonitrobenzene (0.50 mmol), rt. [b]Isolated yield. [c]1 mmol of base was used.

5.2.3.2. Substrate study

The scope and limitation of the optimized reaction procedure, has been tested with wide varieties of electronically diverse arylhalides with arylboronic acids. The results are summarized below (Table 2):

Table 2: Suzuki-Miyaura cross-coupling reactions of various aryl halides and arylboronic acids catalyzed by Pd-BioSiO.[a]



Entry	R_1	R_2	X	Time (h)	Yield[b] (%)
1	H	H	I	1.5	94

2	H	H	Br	1.5	92
3	-4-Cl	-NO_2	4-Br	2	92
4	-4-F	-OCH_3	4-Br	3	88
5	H	NO_2	4-Br	1.5	92
6	-4-OCH_3	H	4-Br	2	88
7	-4-OCH_3	-OCH_3	4-I	1.5	92
8	-4-Me	-OCH_3	4-Br	2	89
9	-4-CHO	-OCH_3	4-Br	2.5	80
10	-4-CHO	H	4-Br	2.5	88
11	-4-$COCH_3$	H	4-Br	3	82
12	-4-$COCH_3$	-OCH_3	4-I	2.5	85
13	H	-OCH_3	4-I	1.5	90

[a]Reaction Conditions: arylbromide or iodide (0.5 mmol), aryl boronic acid (0.55 mmol), Pd-BioSiO (8 wt%), K_2CO_3 (1.5 mmol), rt, in air. [b]Isolated yield.

It was clear from the substrate study, that the reaction proceed smoothly with aryl halides and arylboronic acids bearing different electron-withdrawing and electron-donating groups by the synthesized nanocatalyst. However, from table 2 we can say that if the aryl boronic acid contains electron donating groups (entries 6-8, Table 2), the reaction proceeded smoothly requiring less reaction time as compared to aryl boronic acid containing electron withdrawing groups (entries 10-12, Table 2).

5.2.4. Reusability study:

From the green chemistry point of view, the reusability or recyclability of the catalyst is a very important parameter that needs to be addressed. Accordingly we also examine the reusability of our prepared catalyst for Suzuki-Miyaura cross-coupling reaction. The initial reaction (Scheme 1) was choosen as the model reaction here. The reaction was started by taking 1.1 mmol of phenylboronic acid and 1 mmol of 4-bromonitrobenzene in 8 mL of solvent. To this 16 wt% of the catalyst and 3 mmol of base K_2CO_3 was added and stirred for the required time. The scale of the model reaction was increased by two folds, considering the recovery issue.

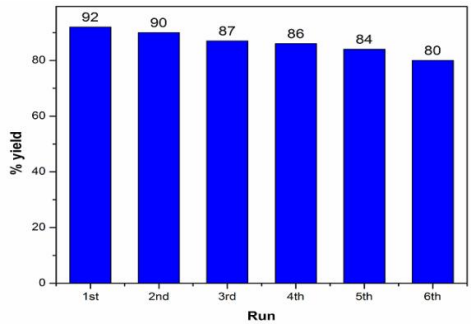


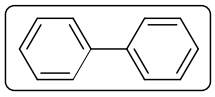
Fig. 1: Reusability of the catalyst.

From Fig. 1 it is obvious that the catalyst was reusable up to 5th run with slight loss of its catalytic activity which may be due to deactivation of the catalyst during the course of the reaction and recovery process.

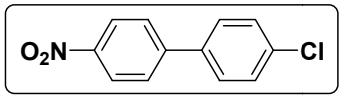
5.2.5. Conclusions

In conclusion a simple and highly efficient heterogeneous catalyst Pd-BioSiO has been developed which exhibit excellent catalytic activity for ligand free Suzuki-Miyaura reaction at room temperature. The compatibility of the reaction to a wide range of electronically diverse arylhalides with arylboronic acids has been tested and found good result.

Characterization data of the products

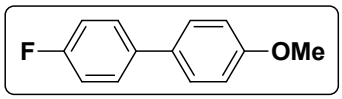


Biphenyl (entries 1 & 2, Table 2): White crystal, m.p. 69.2 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.61-7.59 (m, 4H), 7.46-7.42 (m, 4H), 7.37-7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 140.9, 128.9, 127.3.

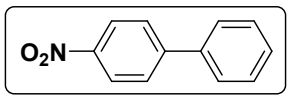


4-Chloro-4′-nitrobiphenyl (entry 3, Table 2): White crystal, m.p. 140 °C, ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.29 (d, *J*=8Hz, 2H), 7.69 (d, *J*=8Hz, 2H), 7.55 (d, *J*=8Hz, 2H),

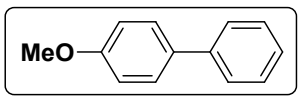
7.46 (d, *J*=8Hz, 2H); ^{13}C NMR (100 MHz, CDCl3), δ (ppm): 146.4, 137.2, 135.3, 129.4, 128.6, 127.7, 124.3.



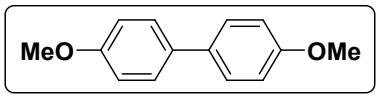
4-Fluro-4′-methoxybiphenyl (entry 4, Table 2): White crystal, m.p. 110 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.50-7.45 (m, 4H), 7.11-7.06 (m, 2H), 6.97-6.95 (m, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 163.3, 159.1, 137.0, 132.9, 128.2, 128, 115.6, 115.4, 114.3, 55.4.



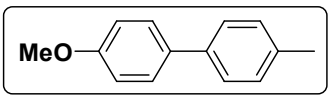
4-Nitrobiphenyl (entry 5, Table 2): Yellow solid, m.p. 113 °C,^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.33-8.30 (m, 2H), 7.76-7.73 (m, 2H), 7.64-7.62 (m, 2H), 7.52-7.45 (m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm):147.6, 138.8, 129.2, 128.9, 127.8, 127.4, 124.1.



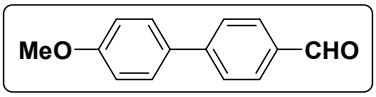
4-Methoxybiphenyl (entries 6, & 13, Table 2): White crystal, m.p. 90 °C,^{1}H NMR (400MHz, $CDCl_3$) δ(ppm): 7.56-7.52 (m, 4H), 7.42 (t, *J*=8Hz, 2H), 7.30 (t, *J*=8Hz, 1H), 6.98 (d, *J*=8Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ(ppm): 159.2, 140.9, 133.8, 128.8, 126.8, 126.7, 114.2, 55.1.



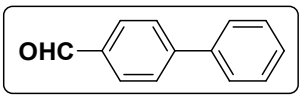
4,4′-dimethoxybiphenyl (entry 7, Table 2): White Crystalline solid, m.p. 175.5 °C, ^{1}H NMR (400MHz, $CDCl_3$) δ(ppm): 7.48(d, *J*=8Hz, 4H), 6.96(d, *J*=8Hz, 4H), 3.84(s, 6H); ^{13}C NMR (100MHz, $CDCl_3$) δ(ppm): 159.0, 133.1, 127.7, 114.1, 55.5.



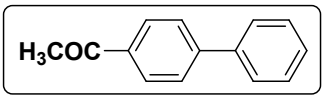
4-Methyl-4′-methoxybiphenyl (entry 8, Table 2): White crystal, m.p. 105 °C, ^{1}H NMR (400MHz, $CDCl_3$) δ (ppm): 7.52(d, *J*=8Hz, 2H), 7.45(d, *J*=8Hz, 2H), 7.23(d, *J*=8Hz, 2H), 6.97(d, *J*=8Hz, 2H), 3.84(s, 3H), 2.39(s, 3H) ;^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 158.6, 138.0, 135.5, 133.9, 129.4, 127.7, 126.5, 113.7, 54.7, 20.9.



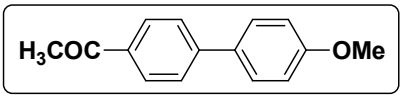
4-Formyl-4′-methoxybiphenyl (entry 9, Table 2): White crystal, m.p. 98 °C,^{1}H NMR (400MHz, $CDCl_3$) δ(ppm): 10.04(s, 1H), 7.93(d, *J*=8Hz, 2H), 7.72(d, *J*=8Hz, 2H), 7.60(d, *J*=8Hz, 2H), 7.01(d, *J*=8Hz, 2H), 3.85(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ(ppm): 191.6, 160.2, 146.6, 131.3, 129.7, 128.1, 126.8, 114.4, 55.7.



4-Formylbiphenyl (entry 10, Table 2): Light yellow crystal, m.p. 58 °C,^{1}H NMR (400MHz,$CDCl_3$) δ(ppm): 10.07 (s, 1H), 7.96(d, *J*=8Hz 2H), 7.78-7.75(d, *J*=8Hz, 2H), 7.66-7.64(m, 2H), 7.51-7.41(m, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ(ppm): 192.0, 147.2, 139.7, 135.2, 130.3, 129.1, 127.7, 127.3.

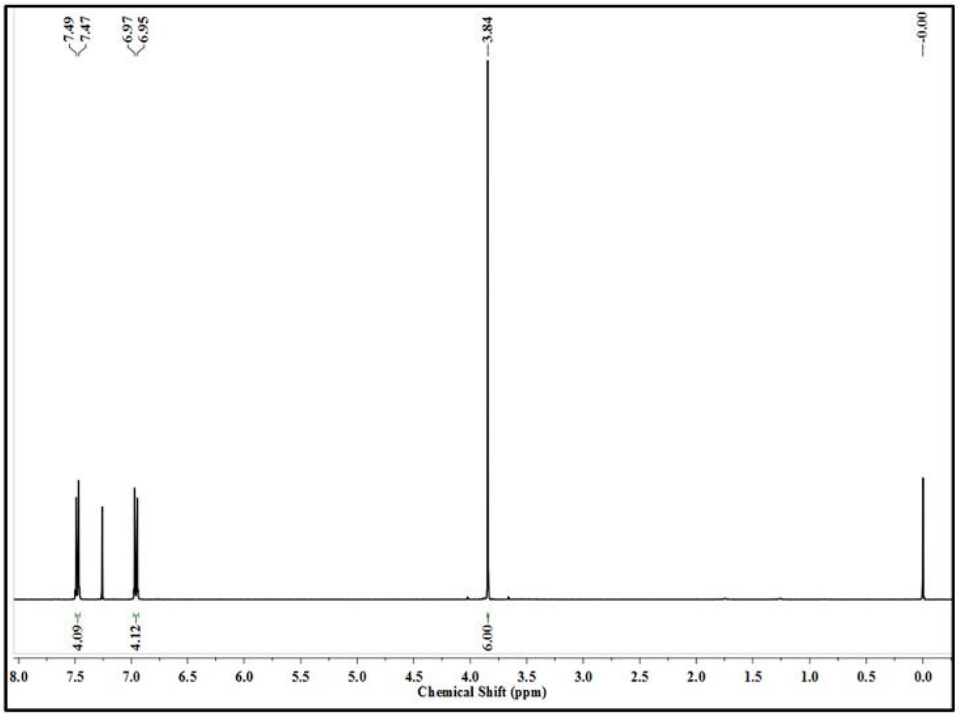


4-Acetylbiphenyl (entry 11, Table 2): White crystal, m.p. 118 °C,^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.04(d, *J*=12Hz, 2H), 7.70(d, *J*=8Hz, 2H), 7.64(d, *J*=8Hz, 2H), 7.50-7.46(t, *J*=8Hz, 2H), 7.43-7.39(d, *J*=8Hz, 1H), 2.65(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 197.8, 145.8, 139.9, 135.9, 129.6, 128.8, 128.2,127.2, 26.7.

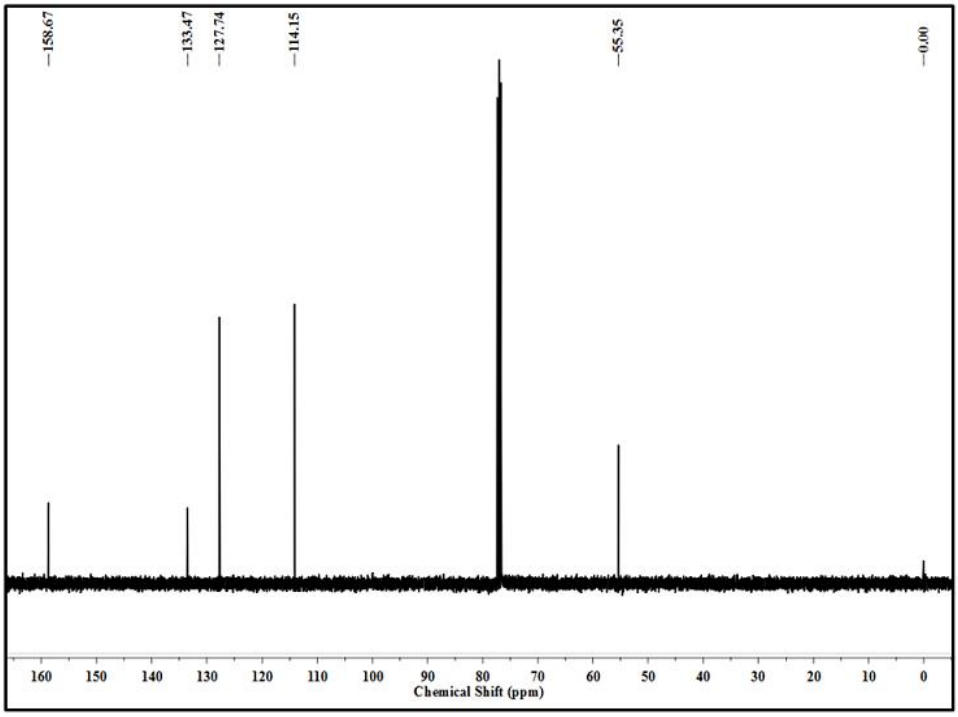


4-Acetyl-4′-methoxybiphenyl (entry 12, Table 2): White crystal, m.p. 153 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 8.01(d, *J*=8Hz, 2H), 7.65(d, *J*=8Hz, 2H), 7.60-7.57(d, *J*=8Hz, 2H), 7.02-6.99(d, *J*=8Hz, 2H), 3.87(s, 3H), 2.63(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 187.4, 145.3, 132.3, 129.0, 128.4, 126.7, 114.4, 98.4, 87.2, 55.4, 26.7.

^{1}H NMR spectrum of 4,4′-dimethoxybiphenyl



^{13}C NMR spectrum of 4,4′-dimethoxybiphenyl



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