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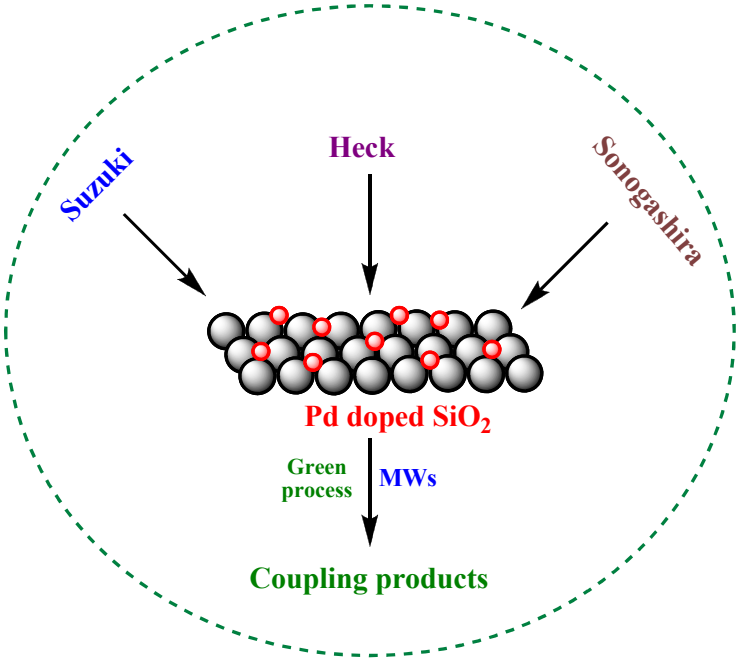
Graphical Abstract



Palladium doped silica (Pd/SiO_2) mesoporous material was synthesized via sol-gel route using the P123 triblock copolymer as structure directing agent. Pd/SiO_2 was efficiently used as catalyst for Suzuki, Heck and Sonogashira reactions under microwave irradiation. The catalyst exhibited high activity for all the coupling reactions and can be recycled nine times without a significant loss in its catalytic activity.

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ARTICLE TYPE

Pd-doped SiO_2 nanoparticles: An efficient recyclable catalyst for Suzuki, Heck and Sonogashira reactions

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Palladium doped silica (Pd/SiO_2) mesoporous material was synthesized via sol-gel route using the P123 triblock copolymer as structure directing agent. Pd/SiO_2 was efficiently used as catalyst for Suzuki, Heck and Sonogashira reactions under microwave irradiation. The catalyst exhibited high activity for all the coupling reactions and can be recycled nine times without a significant loss in its catalytic activity.

Introduction

Aromatic carbon-carbon cross coupling reactions are emerged as an important methodology for the preparation of complex organic molecules. Among all the coupling reactions, Heck, Suzuki and Sonogashira are the most important ones, as these reactions lead to key steps in the synthesis of natural products and a great variety of complex organic molecules used in many fields like drugs, pharmaceuticals and agrochemicals, etc.[1-5] Nowadays, the palladium-catalyzed cross-couplings are essential tool for carbon-carbon bond formation which demonstrates that carbon atoms in all hybridization state (mainly sp^2 carbon) undergoes C-C bond formation during the reactions.[1-6] It is very well reported that when these coupling reactions were performed using homogeneous palladium catalysts; high reaction rates, excellent activity and selectivity of coupling products were obtained. Practically all form of homogeneous palladium catalyst (either Pd salts or Pd catalyst in presence of phosphine ligands) can be used for activation of bulky and electronically unactivated substrates. Despite remarkable usefulness of these Pd catalysts, possibility of reuse in successive reaction is limited which leads to loss of expensive metal. As in many cases excess amount of Pd salts are used while in actual extremely small amounts of Pd (ppm or ppb level) are sufficient to give higher conversion. Another drawback is contamination of advanced chemical intermediates by palladium residues which is a serious issue for large-scale synthesis particularly for pharmaceutical industries. A heterogeneous palladium catalyst provides solution of these problems, where the palladium metal is immobilized on a solid support either in the metal complex form or as metal nanoparticles which makes it easy to remove by filtration leaving products virtually free of palladium residues.[1,2,7] The supports usually used for palladium heterogenization are organic polymers, carbon materials, silica, zeolites, various metal oxides, hybrid organic-inorganic supports like grafted silica and molecular complexes bound to a ligand anchored on a support.[1,2] Among these different supports, ordered mesoporous silica materials are very attractive for immobilizing/doping Pd catalysts because of their large pore size, high surface area and tuneable pore structure. Mesoporous silica nanoparticles, thus have received considerable attention for their use as catalyst, adsorption, polymer filter, optical devices, bio-imaging, drug delivery and biomedical applications due to as stated good morphology, particle size, uniformity and dispersity.[8] Since the discovery of mesoporous silica synthesized using cationic surfactant as templates, the templating method has been widely applied to prepare mesoporous silica with high surface areas, tuneable pore sizes, large pore volumes and rich morphology.[9,10] These properties make mesoporous silica as an excellent material for supported catalyst system. Palladium doped silica can be synthesized through various other routes which were reported earlier for hydrogenation, oxidation reactions, etc.[11-13] Apart from these applications, there are very few reports of Pd/SiO_2 or modified Pd/SiO_2 used as catalyst for coupling reactions like Suzuki, Heck, Sonogashira and Stille coupling.[14-18] Recently, Speziali et al. reported Pd and Au-Pd supported on large surface area containing commercial MCM-41 and silica both and used as catalyst for Suzuki cross coupling reactions.[19] Majority of the reports are based on the Pd supported metal oxide systems, mixed metal oxide systems or ligand based Pd catalyst either supported or complexed, for these reactions. To our knowledge till date no results have yet been reported for Suzuki, Heck and Sonogashira reaction over Palladium doped silica (Pd/SiO_2) synthesized through Evaporation Induced Self Assembly (EISA) method using P123 surfactant as a templating agent. In continuation of our efforts for to developing economical and eco-friendly synthetic pathways for organic transformations from the viewpoint of green chemistry,[20-23] here by we wish to report the synthesis of mesoporous Pd/SiO_2 nanoparticles using sol-gel process which is used as reusable catalyst for Suzuki, Heck and Sonogashira coupling reactions. The catalyst shows a high catalytic activity in the above mentioned classic carbon-carbon bond formation reactions under Microwave (MW) irradiation. In particular, short reaction time, easy catalyst recovery and excellent recycling efficiency of the catalyst make it an ideal system for the reaction under mild conditions.

Experimental Section

The block copolymer surfactant P123 [$(EO)_{20}$-$(PO)_{70}$-$(EO)_{20}$, MW-5750 g/mol], tetraethoxy silane (TEOS), $Pd(OAc)_2$, Tetrabutylammonium hexaflourophosphate ($TBAPF_6$) and the starting coupling substrates were purchased from Sigma-Aldrich, India. HCl and Ethanol used were of Analytical grade laboratory reagent. The Synthesized Pd doped nanoparticles were characterized for their structure and texture by XRD, BET, TEM, SEM, EDS and DLS. The XRD measurements were performed on a Rigaku D/max 2500 X-ray Diffractometer. Diffraction patterns were recorded with Cu Kα radiation (40kV, 30mA) over a 2θ range of 3-80°C at a scan rate of 2°/min. BET surface area, average pore volume, and average pore diameter were measured by physisorption of N_2. The adsorption isotherms were elaborated according to the BET (Brunauer, Emmett and Teller) method for surface area calculation, and pore size distribution curves derived from desorption branches for the porous materials with BJH (Barrett-Joyner-Halenda) methods on Micromeritics Gemini 2375 Surface area analyzer. The TEM measurements were conducted using a Philips Tecnai 20 (Holland) transmission electron microscope at an acceleration voltage of 200kV with a W emitter and LaB6 electron source. A single drop of the sample was deposited on a carbon-coated copper grid and dried at room temperature under atmospheric pressure. The SEM observations were carried out using JSM-7600F Field Emission Gun-Scanning Electron Microscopes (FEG-SEM) at an acceleration voltage of 0.1 to 30 kV. The DLS measurements were carried out on Malvern instrument, Zetasizer ZS-90 (for nanosizer) Particle size analyzer. The ICP analysis was carried out on Atomic Emission Spectrometer (Perkin Elmer Optima 3300 RL) with SCD detector; detection limit: up to ppb level.

All the coupling reactions were performed in oven-dried glassware. Reactions were monitored by thin layer chromatography using 0.25 mm E. Merck silica gel coated glass plates (60F-254) with UV light to visualize the course of reaction. The coupling products were analyzed by ^1H and ^{13}C NMR (400 MHz Bruker Scientific, Switzerland) and GC-MS (GC-Mass Spectrometer, Perkin Elmer, Auto system XL, GC+) spectroscopic techniques.

Preparation of Pd/SiO_2

Mesoporous doped silica was synthesized using a prehydrolyzed solution containing TEOS(42mmol), ethanol (5g) and HCl (37%) (0.055M) stirred for an hour. A second solution was prepared by dissolving the $Pd(OAc)_2$ in P123 surfactant-ethanol solution under acidic conditions, was then added to the former one. The resultant mixture was then kept for ageing for one day under humid atmosphere and then under atmospheric conditions for self evaporation of solvent which was then dried, grounded to form fine grey-black colored powder. The final doped silica was rinsed in ethanol for 2h at 80˚C to remove surfactant and then dried at 80˚C yielded into fine free flowing powder. The synthesized Pd/SiO_2 was then characterized.

General Procedure for the Suzuki Coupling Reactions

Aryl halides (1mmol), aryl boronic acid/ester (1.1mmol), KOH (2mmol), $TBAPF_6$ (0.2mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (40mg, 0.5 wt%) and water (5ml) were taken in MW flask. The mixture was irradiated at 245W MW power for desired time. After completion of reaction (confirmed by TLC analysis), the mixture was filtered through short pad of celite to remove catalyst. To the filtrate, ether and water were added and the layers were separated. The aqueous layer was extracted twice with ether and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo to get the desired product.

General Procedure for the Heck Reactions

Aryl halides (1.28mmol), alkenes (1.66mmol), triethylamine (2.56mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (60mg, 0.75 wt%) and DMF (5ml) were taken in MW flask. The mixture was irradiated at 280W MW power for desired time. After completion of reaction (confirmed by TLC analysis), the mixture was filtered through short pad of celite to remove catalyst. To the filtrate, ether and water were added and the layers were separated. The aqueous layer was extracted twice with ether and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo to get the desired product.

General Procedure for the Sonogashira Reactions

Aryl halides (1mmol), phenyl acetylene (1.1mmol), triethylamine (1.5mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (35mg, 0.47 wt%) and DMF (5ml) were taken in MW flask. The mixture was irradiated at 280W MW power for desired time. After completion of reaction (confirmed by TLC analysis), the mixture was filtered through short pad of celite to remove catalyst. To the filtrate, ether and water were added and the layers were separated. The aqueous layer was extracted twice with ether and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo to get the desired product.

All the coupling products have been previously reported and their identities were confirmed by comparison of their ^1H, ^{13}C NMR and GC-MS spectral data with the values of earlier reports.

Result and Discussion

Characterization of Pd/SiO_2

The ordered mesoporous Pd/SiO_2 nanoparticles were synthesized based on our earlier report using an EISA route[23] where $Pd(OAc)_2$ was introduced in initial sol for uniform distribution of Pd in silica matrix. As P123 block copolymer contains polyethylene oxide (PEO) units which has the capability to reduce metal salts to nanoparticles,[24,25] Pd^{2+} ions were reduced to Pd^0 (Pd black) *in-situ*. During the solvent evaporation, ~50% RH was maintained to obtain mesophase formation. In order to obtain mesoporous Pd/SiO_2 the obtained material was washed with hot ethanol for removal of polymeric surfactant giving very smooth free flowing powder which was subjected for structural and morphological characterization. Figure 1 portrays the powder X-ray diffraction pattern of Pd/SiO_2 at low angles, which shows the characteristic peaks of ordered structured of silica.[26] The figure for powder XRD at wide angles is depicted in Fig. S1 (supporting information) and confirm amorphous silica and no particular reflections of Pd NPs were found which might be due to low % Pd loading in the silica matrix.

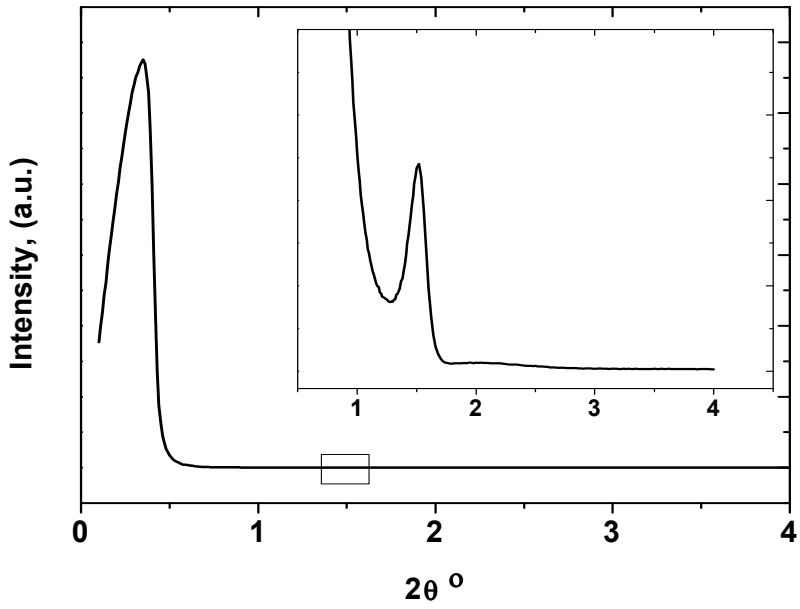


Fig. 1 Low angle XRD patterns of Pd/SiO_2 mesoporous materials. Inset Fig. represents the magnification of area marked with square on graph

Nitrogen adsorption-desorption isotherms and the pore diameter distribution of the Pd/SiO_2 was measured using Brunauer-Emmett-Teller (BET) and Barett-Joyner-Halenda (BJH) methods. The isotherm (Figure 2) of the Pd doped SiO_2 is classic type IV curves which indicates that the silica is mesoporous in nature (as such materials have pore sizes in the range of 2-50nm and are characterized by type IV isotherm which have a hysteresis).

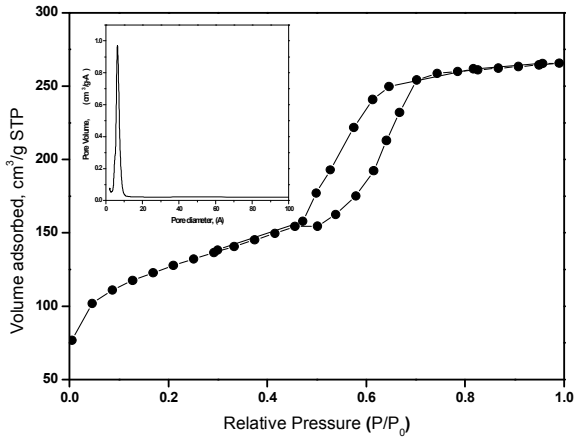


Fig. 2 N_2 adsorption–desorption isotherms of Pd/SiO_2 and the corresponding pore size distribution derived from adsorption isotherm (inset)

This type of isotherm indicates that capillary condensation is occurring during the adsorption process. Interestingly, on comparing BET results of Pd/SiO_2 and un-doped silica, it was found that the surface area of the Pd/SiO_2 is smaller than that of pure silica (undoped silica synthesized using this same process without Pd) without Pd nanoparticles. The average pore diameter and surface area of pure silica mesoporous material are 5.01nm and 58.63m^2/g respectively. Upon doping with palladium the values of pore diameter and surface area decreased to 3.6nm and 44.5m^2/g respectively. The pore size distribution of Pd/SiO_2 derived from the isotherm data using BJH model was quite broad with a maximum at 4.8nm.

The morphology of Pd/SiO_2 was studied using TEM, SEM, EDS and DLS measurements. The TEM image (Figure 3) clearly shows highly dispersed Pd particles on the SiO_2 surface. The palladium particles/clusters were found to be in spherical shape with average diameter 3-5nm with particles in the range of

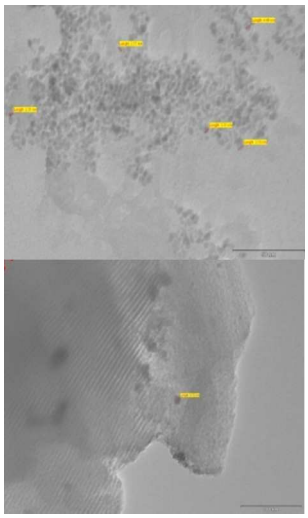


Fig. 3 TEM micrographs of Pd/SiO_2 mesoporous materials

15-20nm confined to the surface of SiO_2 particles. The SEM measurement (Figure 4) shows formation of mesoporous material with small and uniform particle size.

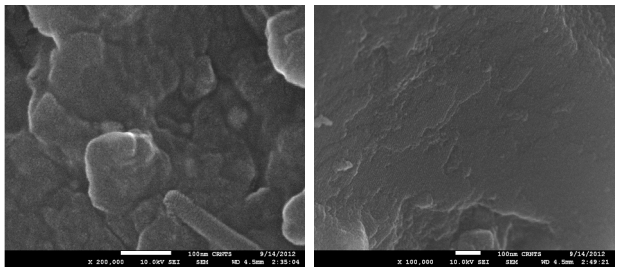


Fig. 4 SEM micrographs of Pd/SiO_2 mesoporous materials

The actual content of dopant was tested by Energy Dispersive Spectroscopy (EDS) analysis and a typical EDS spectrum is showed in Figure 5(a). Quantification of the EDS peaks gives the main elements Pd, Si, O and C in 3.1%, 19.4%, 39.0% and 49.7% by weight respectively. In order to correlate the morphology of nanoparticles, the material was characterized by Dynamic Light Scattering (DLS) measurements in aqueous media.

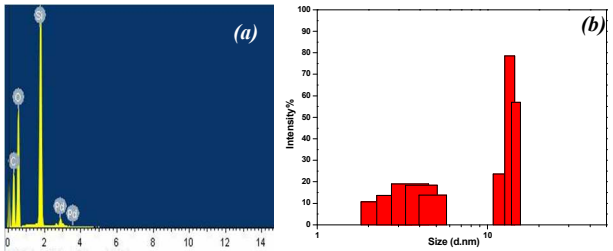


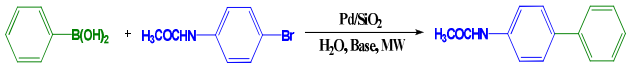
Fig. 5 (a) EDS and (b) DLS study or Particle size distribution of Pd/SiO_2 mesoporous materials

Figure 5(b) depicts the particle size distribution which shows the nanoparticles are polydispersed in shape with two different sizes, one in the range of 3-5nm for Pd nanoparticles (might be assign to non-incorporated Pd NPs in silica matrix) and the other between 13-15nm belongs to silica (with Pd NPs inside) and the DLS results are in correlation with the previously confirmed TEM and SEM data.

Catalytic activity of Pd/SiO_2

The Pd/SiO_2 heterogeneous system was tested as catalyst for Suzuki cross-coupling reactions. For the initial assessment of the reaction, we have chosen cross-coupling between *p*-bromoacetanilide with phenyl boronic acid as a model reaction to optimize the reaction conditions under MW irradiation. The test reaction was performed using different bases such as K_2CO_3, Na_2CO_3, Et_3N, NaOH and KOH in both solvent (water) and solvent less conditions at different power levels ranging from 140, 210, 245 to 280W.

Table 1 Test experiments for optimization of Suzuki Coupling reactions of *p*-bromoacetanilide with phenyl boronic acids[a]

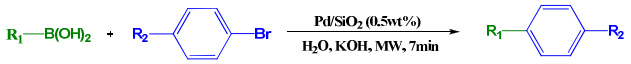


Entry	Base	Catalyst	Time (min)	Microwave Power (W)	Yield[$] (%)
1	KOH	Pd/SiO_2	20	140	52
2	KOH	Pd/SiO_2	20	210	78
3	KOH	Pd/SiO_2	7	245	97
4	KOH	Pd/SiO_2	7	280	94
5	K_2CO_3	Pd/SiO_2	7	245	92
6	Na_2CO_3	Pd/SiO_2	7	245	86
7	Et_3N	Pd/SiO_2	7	245	89
8	NaOH	Pd/SiO_2	7	245	90
9	KOH	-	7	245	>5
10	KOH	Pd/SiO_2	7	245	83[b]
11	KOH	Pd/SiO_2	12	245	69[c]
12	K_2CO_3	Pd/SiO_2	12	245	71[c]
13	KOH	$Pd(OAc)_2$	7	245	54
14	KOH	$Pd(OAc)_2/SiO_2$	7	245	85
15	KOH	SiO_2	7	245	>5
16	KOH	Pd/SiO_2	120	-	87[d]

[a] Reaction conditions - aryl halides (1mmol), aryl boronic acid (1.1mmol), KOH (2mmol), $TBAPF_6$ (0.2mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (0.5 wt%) and water (5ml) under MW irradiation, [b]Reaction carried out using Pd/SiO_2 (0.3 wt%), [c] Solvent less conditions, [d]Reaction carried out under conventional conditions at 60°C. [$] Uncertainty = ± 2%

Among the different base used, KOH gave better coupling yield of 97% than other bases as shown in Table 1, Entry 3. For the reaction to precede well, choice of solvent is a key parameter and for that the model reaction was carried out in water, which proved to be an excellent solvent giving superior results compared to reaction which carried out in solvent less condition. Water has clear advantages as a solvent for use in MW mediated synthesis, as is non-toxic, readily available, non-flammable and above all, MW active due to its polar nature. The use of water as a solvent significantly improves the catalyst activity probably because the bromine atoms of substituted aryl bromides could efficiently contact the palladium metal on the hydrophilic support, SiO_2, in aqueous media due to their increased relative lipophilicity/hydrophobicity.[27] The Pd/SiO_2 (0.5wt%) catalysed Suzuki cross coupling reaction was strongly suppressed at lower MW powers as the temperature required to occurred the reaction was not achieved. However, the reaction was remarkably enhanced at higher MW power (Table 1, Entry1-4) with maximum reaction temperature reached around 85˚C. Thus 245W MW power proved to be the best choice for the reaction to progress under MW irradiation. The active role of Pd in Pd/SiO_2 as catalyst was established by control experiments. In an initial experiment, the reaction was carried out without catalyst in presence of water and KOH at 245W MW power where no product formation was observed (Table 1, Entry 9). Next we examined the catalytic effect of $Pd(OAc)_2$ salt (Table 1, Entry 13) and SiO_2 (Table 1, Entry 14) individually as a catalyst for the coupling reaction under same reaction conditions and it was found that $Pd(OAc)_2$ has less prominent effect compared to Pd/SiO_2 which could be due to the combined role of Pd and support for the reaction. The use of Pd/SiO_2 as catalyst showed excellent results for the coupling reaction proving to have better catalytic sites compared to others. Reaction time of 7-10 minutes was required for completion of reaction under MW conditions. It was worthy to note that the reactions could also be completed in 2h at 60°C under conventional heating conditions. We have also screened the amount of Pd/SiO_2 required for the efficient conversion of reactants and as shown in Table 1, (Entry 3 and 10) 0.5 wt% of Pd/SiO_2 was found to be optimal for reaction to proceed.

Table 2 The Suzuki Coupling reactions of aryl bromides with aryl boronic acids[a]



Entry	R_1	R_2	Yield (%)[$]
1	Phenyl	$-NHCOCH_3$	97
2	Phenyl	$-COCH_3$	96
3	Phenyl	$-COC_6H_5$	96
4	Phenyl	-OH	89
5	Phenyl	-CHO	95
6	Phenyl	-COOH	92
7	Phenyl	$-OCH_3$	97
8	Phenyl	-CN	95
9	Naphthyl	$-OCH_3$	93
10	Naphthyl	$-COCH_3$	91
11	Naphthyl	-CN	93
12	Naphthyl	$-NHCOCH_3$	90
13	Phenyl boronic acid 1,3-propanediol ester	$-OCH_3$	98
14	Phenyl boronic acid 1,3-propanediol ester	$-COCH_3$	97
15	Phenyl boronic acid 1,3-propanediol ester	-CN	95

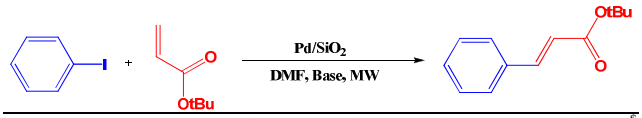
[a] Reaction conditions - Aryl halides (1mmol), Aryl boronic acid (1.1mmol), KOH (2mmol), $TBAPF_6$ (0.2mmol), Dodecane (40mg, as internal standard), Pd/SiO_2 (0.5 wt%) and Water (5ml) under MW irradiation. [$] Uncertainty = ± 2%

With the optimised reaction conditions (0.5 wt% Pd/SiO_2, KOH, H_2O, 245W power, 7min), the catalytic system was further extended to the coupling reaction of different aryl bromides with varying aryl boronic acids (Table 2). A wide variety of aryl bromides bearing electron withdrawing and electron donating groups were coupled efficiently with phenyl and naphthyl boronic acids generating the corresponding products in excellent yields under MW irradiations. Of the different aryl bromides used, both

electron withdrawing and releasing groups were found to react efficiently by giving highest yields. The reaction under MW irradiation reached a temperature of 85°C within 3 minutes of initiation. The yields of coupling products were determined by GC-MS. The result exhibited biphenyl products in good to excellent yields along with a little by product formed from phenyl boronic acid. To obtain maximum higher yields, we replaced aryl boronic acid with boronates which are useful substitutes of aryl boronic acids owing to their high stability to heat and solubility in a variety of organic solvents. We carry out the Suzuki coupling reaction using Phenyl boronic acid 1,3-propanediol ester (Table 2, Entry 13-15) in presence of KOH, $TBAPF_6$, 0.5 wt% Pd/SiO_2 and water. All the three substrates, 4-bromoanisole, 4-bromoacetopheneone and 4-bromobenzonitrile were smoothly cross-coupled with the phenyl boronic acid propyl ester in water to afford corresponding biphenyl derivatives in excellent yields. The GC-MS result shows excellent coupling yield without any by product formation. We also tested the catalytic yields using conventional heating system in a preheated oil bath at 110°C for 30, 60, 90 and 120 minutes of reaction time. Nearly the same yields were observed when the Suzuki coupling reaction was carried out in a preheated oil bath at 110°C for 120min under conventional process.

Further, the alternative way by which the reaction is taking place in this heterogeneous system for Suzuki coupling reaction was studied. The Pd/SiO_2 system in water can be viewed as three-phase system: A solid catalyst Pd/SiO_2 which is hydrophilic in nature, a lipophilic phase which comprising organic substrates and an aqueous phase of water. The hydrophilic Pd/SiO_2 catalyst would more likely to be confined in aqueous phase with minimum possible contact with the organic substrates. The presence of $TBAPF_6$, a phase transfer agent together with MWs brings in the activity by increasing the contacts of the catalyst and organic substrates, resulting in an ultimate increase in the activity of catalyst suggesting that the reaction takes place at the phase boundary near the catalyst surface in truly heterogeneous fashion.

Table 3 Test experiments for optimization of the Heck Coupling reactions of iodobenzene and *t*-butylacrylate[a]

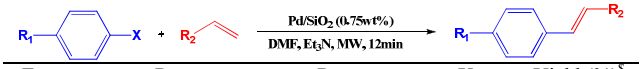


Entry	Base	Catalyst	Time (min)	Microwave Power (W)	Yield (%)[$]
1	Et_3N	Pd/SiO_2	20	280	40[b]
2	Et_3N	Pd/SiO_2	17	210	74
3	Et_3N	Pd/SiO_2	12	245	87
4	Et_3N	Pd/SiO_2	12	280	96
5	Et_3N	Pd/SiO_2	12	350	94
6	K_2CO_3	Pd/SiO_2	12	280	91
7	NaOAc	Pd/SiO_2	12	280	85
8	Et_3N	Pd/SiO_2	5	280	79
9	Et_3N	Pd/SiO_2	10	280	92
10	Et_3N	Pd/SiO_2	150	-	94[c]
11	Et_3N	$Pd(OAc)_2$	12	280	63
12	Et_3N	SiO_2	12	280	10

[a] Reaction conditions - Aryl halides (1.28mmol), alkenes (1.66mmol), triethylamine (2.56mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (0.75 wt%) and DMF (5ml) under MW irradiation, [b]Reaction carried out in water, [c]Reaction carried out under conventional conditions at 80°C, giving Trans-isomer as the major product. [$] Uncertainty = ± 2%

Furthermore, the Heck reaction between *p*-iodobenzene and *t*-butylacrylate to give *t*-butyl cinnamate ester using Pd/SiO_2 as catalyst was performed. In order to adjust the effect of various parameters on the reaction time and yield, the reaction was carried out using different bases under MW irradiations as shown in Table 3. When iodobenzene was stirred in water with *t*-butylacrylate , Pd/SiO_2 (0.75wt%), Et_3N as base at 280W MW power for 20 min the reaction was incomplete producing the desired *t*-butyl cinnamate in only 40% yield (Table 3, Entry 1). The use of polar aprotic solvent such as DMF (Dimethyl formamide) significantly improved the progress of reaction and the same is completing within 12min (Table 3, Entry 4). Presence of base plays a very vital role in Heck reaction, thus test reactions were performed for screening Et_3N, K_2CO_3 and NaOAc as base (Table 4, Entry 4, 6, 7) in DMF for the iodobenzene and *t*-butylacrylate reaction. However, the use of K_2CO_3 and NaOAc slightly decreased the reaction efficiency, while the use of Et_3N leads to better reaction progress with excellent coupling yields. Although the reaction in Et_3N and DMF at lower MW power (Table 3, Entry 2) tends to produce lesser yields of cinnamate products, while the reaction efficiency significantly increased as the MW power were raised to 280W (Table 3, Entry 4). However, no improvement in efficiency was observed at 350W MW power (Table 3, Entry 5), thus opting 280W as the optimal MW power range for the reaction where maximum temperature achieved is 105°C. For the optimization purpose the coupling reaction was also individually catalysed by $Pd(OAc)_2$ salt and SiO_2 (Table 3, Entry 11, 12), but their catalytic sites are inferior to that of Pd/SiO_2. Therefore, the following Heck reactions were performed in DMF and Et_3N with Pd/SiO_2 at 280W MW power.

Table 4 The Heck Coupling reactions of aryl halides with alkenes[a]



Entry	R_1	R_2	X	Yield (%)[$]
1	-H	$-CO_2C_4H_9$-*t*	I	97
2	$-CH_3$	$-CO_2C_4H_9$-*t*	I	92
3	-COOH	$-CO_2C_4H_9$-*t*	I	96
4	$-COCH_3$	$-CO_2C_4H_9$-*t*	Br	96
5	-CN	$-CO_2C_4H_9$-*t*	Br	94
6	$-OCH_3$	$-CO_2C_4H_9$-*t*	Br	97
7	$-NHCOCH_3$	$-CO_2C_4H_9$-*t*	Br	91
8	-CHO	$-CO_2C_4H_9$-*t*	Br	89
9	-H	$-C_6H_5$	I	90
10	$-CH_3$	$-C_6H_5$	I	90
11	-COOH	$-C_6H_5$	I	93
12	$-OCH_3$	$-C_6H_5$	Br	95

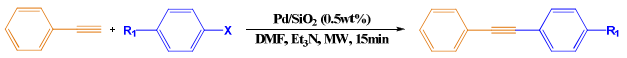
[a] Reaction conditions - Aryl halides (1.28mmol), Alkenes (1.66mmol), Triethylamine (2.56mmol), Dodecane (40mg, as internal standard), Pd/SiO_2 (0.75 wt%) and DMF (5ml) under MW irradiation, giving Trans-isomer as major product. [$] Uncertainty = ± 2%

A variety of aryl halides reacts with various alkenes such as acrylates and styrene, to give the required products in good to excellent yields (Table 4). Interestingly, the ability of Pd/SiO_2 to promote coupling reactions of different alkenes with a variety of activated and non-activated aryl bromides is satisfactory. Aryl bromides possessing either an electron withdrawing (-COOH, $-COCH_3$, -CN, -CHO) or electron releasing ($-OCH_3$, $-CH_3$, $-NHCOCH_3$) substituent on the benzene ring efficiently cross-coupled with acrylates, regardless of the substituent position to afford the products in good to excellent yields. The Pd/SiO_2

catalyzed cross-coupling reactions were next investigated for styrene (Table 4, Entry 9-12) which proves to be a suitable substrate that worked effectively as acrylates showing Pd/SiO_2 to be excellent catalyst for Heck reaction also.

Encouraged by the above satisfactory results for Suzuki and Heck reactions, the synthetic potential of Pd/SiO_2 was then evaluated for Sonogashira reaction (cross-coupling of aryl or vinyl halides with terminal alkynes). The major drawbacks associated with this reaction is the use of homogeneous catalysts (which are difficult to remove from the reaction mixture), the use of copper salts to promote the reaction,[28] and the use of expensive and specific phosphine ligands.[29-32] The use of Pd/SiO_2 as heterogeneous catalyst for the Sonogashira reaction in absence of copper salt and phosphine ligand might prove useful in our present studies. Interestingly, the Sonogashira reaction of aryl iodides and activated aryl bromides under the optimized reaction conditions (0.5wt% Pd/SiO_2, DMF, Et_3N, MW 280W, 15-20 minutes) in absence of copper salts were performed.

Table 5 The Sonogashira Coupling reaction of aryl halides with phenyl acetylenes[a]



Entry	R_1	X	Yield (%)[$]
1	$-COCH_3$	Br	94
2	$-OCH_3$	Br	96
3	$-NHCOCH_3$	Br	91
4	-CHO	Br	88
5	$-COC_6H_5$	Br	93
6	-CN	Br	92
7	-H	Br	81
8	-H	I	83
9	$-CH_3$	I	89
10	-COOH	I	93
11	$-COCH_3$	Br	85[b]

[a] Reaction conditions - Aryl halides (1mmol), phenyl acetylene (1.1mmol), triethylamine (1.5mmol), dodecane (40mg, as internal standard), Pd/SiO_2 (0.5 wt%) and DMF (5ml) under MW irradiation, [b] reaction carried out under conventional heating at 80 °C for 120 min [$] Uncertainty = ± 2%

Most of the coupling reactions proceeded completely and generated the corresponding products in very good yields. The reaction goes smoothly with the halobenzenes possessing both electron withdrawing and electron releasing group as substrates in presence of Pd/SiO_2. While the Sonogashira cross-coupling of a neutral arylbromide or iodide with terminal alkyne, for example, the coupling of iodobenzene with phenyl acetylene generated the corresponding products in good to moderate yields (Table 5, Entry 7, 8). This might be due to the possible homocoupling of the alkynes which in turn decreases the reaction rate of the cross-coupling using the less reactive neutral aryl halides.[33]

Hot filtration test and Reusability test for the Suzuki-Miyaura cross-coupling reaction

A strong test for assessing the heterogeneity of the catalyst is the hot filtration test, also known as split test in which solid pre-catalysts are filtered out of the reaction and the filtrate is monitored for continued activity.[34] In order to determine whether the reaction proceeded in a homogeneous or heterogeneous fashion, hot filtration test was performed for Suzuki coupling reaction of *p*-bromoacetophenone and phenylboronic acid. Rapid separation of Pd/SiO_2 catalyst from the reaction mass after a reaction time of 3 min under MW conditions was carried out and the hot reaction mass was allowed to react further under similar conditions. It was found that no further reaction occurred , thus no coupling product formation was observed (GC-MS). The ICP test confirmed the presence of about 6 ppm of Pd in the reaction media. Thus both these analysis confirm that presence of very few amount of Pd is not affecting the coupling reactions, which provides evidence of SiO_2 acting as a good scaffold for Pd catalyst precursors.

For heterogeneous catalyst, the most crucial thing is the reusability of the catalyst. The major advantage of the heterogeneous catalyst is its easy recovery by filtration or centrifugation. The recycling of Pd/SiO_2 was investigated for the Suzuki coupling of *p*-bromoacetophenone with phenyl boronic acid using the optimized conditions under MW irradiations. After the reaction was over, the catalyst was simply filtered and washed successively with water, diethyl ether and acetone until TLC confirmation of the filtrate showed no detectable amount of reactant and products. The catalyst was then dried under vacuum for overnight before doing reusability test and was found to be recycled at least nine times without significant loss in its activity (Figure S1, ESI).

It is not easy to compare the catalytic results with the literature data due to wide range of different reaction conditions and catalysts. But a tentative comparison is proposed here for Suzuki coupling reaction using homogeneous and heterogeneous catalyst. Nonnenmacher et. al. investigated $et(impy)_2PdBr_2$ complex as a catalyst precursor in Suzuki reaction using Cs_2O_3 as base where maximum coupling yield obtained was 80%.[35] In similar manner Srinivas et. al. used Thiopseudourea liganted Pd complexes for coupling reactions and maximum Suzuki coupling yield obtained was 99% in 3h of reaction time using H_2O/DMF solvent system at 80°C.[36] Li and co-workers synthesized magnetic nanaoparticles-supported palladium (SiO_2@Fe_3O_4-Pd) for coupling reactions where the coupling yield obtained was 99% in presence of K_3PO_4 as base and methanol as solvent at 60°C.[37] Our findings are in consonance with LI and co-workers where a maximum of 98% coupling yield was obtained with Pd/SiO_2 catalyst using water as solvent within 7min under microwave irradiations. It can be summarized from above discussions that in both the earlier cases, homogeneous Pd catalyst was used where, though the yield obtained was very good but lack of catalyst recyclability effected the cost and greenness of the reaction, while it was not the case with heterogeneous Pd catalysts. Among all, our reaction conditions show far more superiority in terms of reaction time, yield, solvent and also greenness of the reaction.

Conclusions

In summary, Palladium metal doped Silica (Pd/SiO_2) catalyst has been successfully prepared in a stable form through sol-gel route. The synthesized Pd/SiO_2 was characterized by XRD, BET, TEM, SEM, EDS and DLS techniques. The size of Pd/SiO_2 mesoporous nanomaterials ranges from 3-20nm. The formation of metal nanoparticles of Pd on SiO_2 is supported by EDS which shows 3.09 wt% of Pd. The Pd doped SiO_2 as catalyst exhibited high activity for Suzuki, Heck and Sonogashira reactions in presence

of water and DMF respectively under MW irradiation. The synthetic reaction conditions maintained here are environmentally benign giving very high yields for the respective coupling products, while the catalyst can be recycled more than nine times. The combination of advantages displayed by the Pd/SiO_2 catalyst such as ease of preparation, high catalytic activity, stability, reusability, versatility (organic or aqueous solvent catalysis) and no measurable Pd leaching, proves that the catalyst should be considered as a viable alternative in cross-coupling reactions on efficiency, environmental and economical grounds.

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