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# Application of Pd-2A3HP-MCM-41 to the Suzuki, Heck and Stille coupling reactions and synthesis of 5-substituted 1*H*-tetrazoles

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An ecofriendly heterogeneous catalyst has been synthesized by anchoring palladium onto the surface of organically modified mesoporous silica. The prepared catalyst was characterized using X-ray diffraction, Fourier transform infrared and energydispersive X-ray spectroscopies, transmission and scanning electron microscopies, inductively coupled plasma and thermogravimetric techniques. The catalyst shows high activity in the Suzuki, Heck and Stille cross-coupling reactions and the synthesis of 5-substituted 1*H*-tetrazoles from sodium azide (NaN<sub>3</sub>). These methods have the advantages of high yields, green reaction conditions, simple methodology and easy separation and workup. Copyright © 2016 John Wiley & Sons, Ltd.

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Keywords: Suzuki; Heck; Stille; 5-substituted 1H-tetrazoles; cross-coupling reactions; mesoporous silica; palladium

# Introduction

The Heck,<sup>[1]</sup> Stille,<sup>[2]</sup> Kumada,<sup>[3]</sup> Negishi,<sup>[3]</sup> Hiyama<sup>[4]</sup> and Suzuki<sup>[5]</sup> reactions are efficient and well-established methods for the construction of new carbon-carbon bonds. Tetrazoles are heterocyclic compounds having a five-membered ring containing one carbon and four nitrogen atoms and are unnatural. Recently, tetrazoles have received considerable attention because they have a wide range of applications in pharmaceutical science.<sup>[6,7]</sup> Tetrazoles are used as plant growth regulators, herbicides and fungicides.<sup>[8]</sup> They possess anti-allergic, antihypertensive and antibiotic activities.<sup>[9,10]</sup> Amino-substituted tetrazoles have anti-inflammatory<sup>[11]</sup> receptor modulator and antiviral<sup>[12,13]</sup> activities. These reactions are usually promoted by a Pd-based catalyst, Pd being a precious metal. In this regard heterogeneous catalysis seems particularly well suited, since palladium catalysts immobilized on supports such as organic polymers,<sup>[14–19]</sup> silica,<sup>[20,21]</sup> MCM-41,<sup>[22]</sup> carbon nanotubes,<sup>[23–25]</sup> activated carbon,<sup>[26,27]</sup> clays<sup>[28,29]</sup> and molecular sieves<sup>[30]</sup> could be easily separated from products and recycled without any loss of metal residues. Among the supports mentioned above, mesoporous silica materials with nano-sized pores and controllable porous structure and pore volume, a huge specific surface area and excellent stability (chemical and thermal), and the fact that organic groups can be robustly anchored to the surface to provide catalytic centres,<sup>[31]</sup> are some of the most suitable catalyst supports, because they provide high dispersion of metal nanoparticles and facilitate the access of substrates to active sites.<sup>[32]</sup> The majority of novel heterogeneous catalysts are immobilized on silica supports.<sup>[33]</sup> In the last few years, several procedures including various catalysts have been reported for C&bond;C coupling reactions and synthesis of 5-substituted 1*H*-tetrazoles such as: Pd-SH-SBA-15,<sup>[34]</sup> Pd(II)–MCM-41,<sup>[35]</sup> Pd[N-MorphC(S)NP(O)(OiPr)<sub>2</sub>-O,S]<sub>2</sub>,<sup>[36]</sup> Pd(0)-MCM-41,<sup>[37]</sup> PEG-Q-PPh<sub>2</sub>,<sup>[38]</sup> Pd@MOF-5,<sup>[39]</sup> Pd@polymer,<sup>[40]</sup> Pd-dtz-Fe<sub>3</sub>O<sub>4</sub>,<sup>[41]</sup> Pd@UiO-66<sup>[42]</sup> and SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub>-Pd.<sup>[43]</sup> However, most of them have some drawbacks such as toxicity, instability, expensive,

require the use of microwaves, homogeneous or non-reusable and difficult synthetic procedure.

Therefore, in order to overcome some of these drawbacks, herein we report the use of modified MCM-41 as a catalyst vehicle to support palladium nanoparticles and the application of the system in Suzuki–Miyaura, Mizoroki–Heck and Stille coupling reactions and in the synthesis of 5-substituted 1*H*-tetrazoles from sodium azide (NaN<sub>3</sub>). This catalytic system can be well dispersed in the reaction medium, conveniently separated from the reaction mixture and reused several times without significant loss of its activity (Scheme 1).

# **Experimental**

### Materials

Tetraethylorthosilicate (TEOS; 98%), cationic surfactant cetyltrimethylammonium bromide (CTAB; 98%), solvents and other reagents were purchased from Merck, Aldrich or Fluka and were used as received without further purification.

#### Preparation of Pd-2A3HP-MCM-41

Silica MCM-41 was synthesized by adding 1 g of CTAB to a solution containing 3.5 ml of NaOH solution (2 M) and deionized water (480 ml) which was stirred at 80 °C. Then, 5 ml of TEOS was slowly added into the solution. The resulting mixture was refluxed for 2 h at the same temperature. The collected product was washed with deionized water and calcined at 823 K for 5 h at a rate of

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**Scheme 1.** Palladium-catalysed C&bond;C bond formation and synthesis of 5-substituted 1-*H*-tetrazole.

 $2 \,^{\circ}$ C min<sup>-1</sup> to remove the residual surfactant and afford MCM-41. Post-synthesis organic modification of mesoporous materials was performed by stirring 4.8 g of MCM-41 with 4.8 g of 3chloropropyltriethoxysilane and refluxing in n-hexane (96 ml) for 24 h. The resulting white solid (nPrCI-MCM-41) was filtered, washed with *n*-hexane and dried at 70 °C, and then this solid (0.5 g) was refluxed with trimethylamine (2 mmol, 0.202 g) and 2-amino-3hydroxypyridine (2A3HP; 1 mmol, 0.110 g) in toluene for 24 h. The resulting solid was washed with ethanol, and dried in vacuum. Finally Pd-2A3HP-MCM-41 was prepared by stirring 2A3HP-MCM-41 (0.25 g) with palladium acetate (0.57 mmol, 0.128 g) in ethanol (25 ml). The mixture was refluxed at 80 °C for 18 h. Afterward, the resulting mixture containing palladium(II) was reduced with NaBH<sub>4</sub> (0.057 mmol, 0.022 g) under the same conditions for another 2 h. The resulting black solid impregnated with the metal complex was filtered and washed with ethanol to afford the grey palladium(0) complex. The grimy solid was filtered, washed with ethanol and dried under vacuum (Scheme 2). The prepared catalyst (Pd-



Scheme 2. Synthesis of Pd-2A3HP-MCM-41 nanostructure.

2A3HP-MCM-41) was characterized using X-ray diffraction (XRD), Fourier transform infrared (FT-IR) spectroscopy, energy-dispersive X-ray spectroscopy (EDS), transmission electron microscopy (TEM), scanning electron microscopy (SEM), inductively coupled plasma (ICP) and thermogravimetric analysis (TGA) techniques. The obtained results indicate that Pd-2A3HP was successfully immobilized onto the modified MCM-41.

#### General procedure for synthesis of biphenyl derivatives

A mixture of arylhalide (1 mmol), PhB(OH)<sub>2</sub> (1 mmol) or Ph<sub>3</sub>SnCl (0.5 mmol), base (K<sub>2</sub>CO<sub>3</sub>, 3 mmol) and Pd-2A3HP-MCM-41 (4 mg, 0.89 mol%) as catalyst in PEG-400 solvent was stirred at 80 °C for an appropriate time. The progress of the reaction was monitored by TLC (eluent: *n*-hexane–acetone, 8:2). The catalyst was separated by filtration. After completion of the reaction, the products were extracted with diethyl ether and water. The solvent was evaporated and the products were obtained.

#### General procedure for synthesis of butyl cinnamate derivatives

A mixture of aryl halide (1.0 mmol), *n*-butyl acrylate (1.2 mmol), base ( $K_2CO_3$ , 3 mmol), Pd-2A3HP-MCM-41 (4 mg, 0.89 mol%) and 2 ml of dimethylformamide (DMF) as solvent was stirred at 120 °C for an appropriate time. The progress of the reaction was monitored by TLC (eluent: *n*-hexane–acetone, 8:2). After completion of the reaction, the catalyst was separated by filtration and the products were extracted with diethyl ether. The solvent was evaporated and the products were obtained in good to excellent yields.

#### General procedure for synthesis of 5-substituted 1 h-tetrazoles

Pd-2A3HP-MCM-41 (30 mg, 6.69 mol %) was added to benzonitrile (1 mmol), sodium azide (0.08 g, 1.2 mmol) and PEG-400 (2 ml). The mixture was stirred at 120 °C for 3 h. After completion of the reaction as indicated by TLC (eluent: *n*-hexane–acetone, 8:2), the catalyst was separated by filtration and the filtrate was treated with ethyl acetate and 0.1 N HCl (5 ml). The resultant organic layer was separated and the aqueous layer was extracted with ethyl acetate (20 ml).

## **Results and discussion**

Figure 1 illustrates the low-angle powder XRD patterns of MCM-41 and Pd-2A3HP-MCM-41 samples. The XRD pattern of MCM-41 shows the presence of three reflection peaks corresponding to  $d_{100}$ ,  $d_{110}$  and  $d_{200}$  planes at  $2\theta = 2.41^{\circ}$ ,  $3.87^{\circ}$  and  $4.33^{\circ}$ , respectively,



Figure 1. XRD patterns of MCM-41 and Pd-2A3HP-MCM-41.

typically confirming the presence of ordered hexagonal mesoporous structure of MCM-41. However, upon post-synthetic grafting, the d<sub>110</sub> and d<sub>200</sub> reflections are no longer observed and an overall decrease in intensity of d<sub>100</sub> is observed. This is probably due to the difference in scattering contrast of the pores and the walls, and to the irregular immobilization of Pd(0) complex on nano-channels. The pattern at higher diffraction angles of Pd-2A3HP-MCM-41 is shown in Fig. 2. In this wide-angle powder XRD pattern of the catalyst there are reflection peaks at  $2\theta = 39.84^\circ$ , 46.17° and 67.75° corresponding to d<sub>111</sub>, d<sub>200</sub> and d<sub>220</sub> planes, respectively, that relate to Pd nanoparticles (Fig. 2). These observations and the absence of impurity peaks indicate the high purity and good dispersion of the Pd (0) complex on the inner pore channels of MCM-41.<sup>[44]</sup>



Figure 2. XRD pattern of Pd-2A3HP-MCM-41 for high diffraction angles.



Figure 3. FT-IR spectra: (a) pure MCM-41; (b) nPrCI-MCM-41; (c) 2A3HP-MCM-41; (d) Pd-2A3HP-MCM-41.

The Pd-2A3HP-MCM-41 catalyst was characterized using FTIR spectroscopy and the corresponding spectra are depicted in Fig. 3. The FTIR spectrum of the MCM-41 sample displays characteristic absorption peaks at 1059, 963 and 451 cm<sup>-1</sup> corresponding to Si&bond;O&bond;Si asymmetric stretching, Si&bond;O&bond;Si symmetric stretching and Si&bond;O&bond;Si bending vibrations, respectively (Fig. 3(a)). The FTIR spectrum of the chlorofunctionalized MCM-41 indicates the stretching band around 2900  $\text{cm}^{-1}$  related to the aliphatic C&bond;H group, which shows that 3-chloropropyltriethoxysilane (nPrCl) is successfully anchored on MCM-41 (Fig. 3(b)). Bands at 1479  $\text{cm}^{-1}$  (C&dbond;C bond) and 1627 cm<sup>-1</sup> (C&dbond;N bond) confirm the presence of 2-amino-3hydroxypyridine (2A3HP) ring (Fig. 3(c)). The free ligand exhibits a stretching band at 1528 cm<sup>-1</sup> while in the Pd-2A3HP-MCM-41 spectrum this band is shifted to higher frequency and appears at 1540  $\text{cm}^{-1}$  indicating the formation of Pd–ligand bond (Fig. 3(d)).

Figure 4 shows SEM micrographs of MCM-41 and Pd-2A3HP-MCM-41, which confirms the presence of uniform nanometric particles with spherical shape for the catalyst. Moreover, the Pd content in the complex anchored on MCM-41 was determined using EDS in combination with TEM. The EDS data (Fig. 5) indicate the presence of Pd as well as nitrogen and carbon in the complex. Also, to extend the scope of catalyst characterization, we determined the loading of Pd on MCM-41 using the ICP atomic emission spectroscopy technique. The amount of Pd of the catalyst immobilized on MCM-41 is found to be  $2.10 \times 10^{-3}$  mol g<sup>-1</sup>.



Figure 4. SEM images: (a) MCM-41; (b) Pd-2A3HP-MCM-41.



Figure 5. EDS spectrum of Pd-2A3HP-MCM-41.

The TEM image of Pd-2A3HP-MCM-41 shows clearly highly ordered hexagonal mesostructure (Fig. 6). It is clear that MCM-41 still retains its mesostructure after grafting of the 3-chloro-propyltriethoxysilane and the organic moiety (2A3HP). The size of particles is around 50 nm.<sup>[45]</sup>

TGA was used to determine the presence of chemisorbed organic functional groups on mesoporous MCM-41. The TGA measurements were conducted in nitrogen and oxygen. The TGA data fir MCM-41 and Pd-2A3HP-MCM-41 catalyst are shown in Fig. 7. The TGA trace of the synthesized MCM-41 shows a one-step weight loss of approximately 4% below 100 °C, which is due to desorption of physically absorbed water and organic solvent.<sup>[46]</sup> The TGA trace of 2A3HP-MCM-4 indicates three weight losses. The first weight loss (2%) below 200 °C is the result of loss of physically adsorbed water and other solvents, the second (12%) at 200–400 °C is related to the decomposition of organic moieties and the third (2%) at 650 to *ca* 670 °C is likely attributed to decomposition of silanol groups.

# Application of Pd-2A3HP-MCM-41 complex in organic reactions

In our study of the application of the Pd-2A3HP-MCM-41 catalyst in organic synthesis, we investigated the applicability of the catalyst for the synthesis of biaryl derivatives using aryl halide (1 mmol), PhB (OH)<sub>2</sub> (1 mmol) and base (3 mmol) in the presence of Pd-2A3HP-MCM-41 with short reaction times in good to excellent yields.



Figure 6. TEM micrograph of Pd-2A3HP-MCM-41.



Figure 7. TGA thermograms of (red curve) MCM-41 and (green curve) Pd-2A3HP-MCM-41.

The catalytic activity of Pd-2A3HP-MCM-41 was first tested in the Suzuki cross-coupling reaction between iodobenzene as model substrate and phenylboronic acid. Solvent and base have a marked influence on the activity of the catalyst in the Suzuki cross-coupling reaction. Reaction time was 30 min. The coupling reaction does not occur in the absence of the catalyst (Table 1, entry 16). Keeping K<sub>2</sub>CO<sub>3</sub> as the base, it is found that notable activity of the catalyst can be achieved when PEG-400 is used as solvent. However, the yield of product is zero when the reaction is carried out in 1,4dioxane. Other bases do not give satisfactory results (Table 1, entries 6-9). In the case of KOH, negligible amount of product is obtained (Table 1, entry 7). Optimization of temperature shows that 80 °C is the best temperature. Furthermore the amount of catalyst was evaluated. An amount of 4 mg (0.89 mol%) of catalyst is found to be the optimal amount. When the amount of catalyst is decreased, lower yield is achieved (Table 1, entry 15). The results are summarized in Table 1.

A series of biphenyl derivatives were prepared successfully with excellent yields. The results are summarized in Table 2.

The activity of the prepared catalyst was investigated in the Heck coupling reaction. In order to determine the optimum reaction conditions, the influence of n-butyl acrylate and styrene was investigated. The results show that the stereoselectivity and conversion for styrene are lower than for *n*-butyl acrylate (Table 3, entries 1-4). Therefore, 1.2 mmol of *n*-butyl acrylate, 1 mmol of iodobenzene and 3 mmol of base in the presence of Pd-2A3HP-MCM-41 were selected for model reaction, which was studied with various solvents, temperatures, catalyst concentrations and bases. The reactions are sensitive to temperature and therefore we investigated the effect of temperature on the outcome of reaction. It is obvious that higher temperatures (more than 100 °C) strongly improve the selectivity and conversion and shorten the reaction time (Table 3, entries 8, 10, 11). Further studies reveal stereoselectivity for the Heck reaction at 120 °C (Table 3, entry 8). We employed PEG-400 as solvent, but only low conversion of the aryl halides is achieved. The use of more polar solvents such as DMF produces a clear in-

**Table 1.** Optimization of solvent, base, temperature and concentration of catalyst for the synthesis of biphenyl in 30 min

Entry	Temperature (°C)	Solvent	Base (eq.)	Catalyst (mg, mol%)	Time (min)	Yield (%) <sup>a</sup>
1	80	DMSO	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	45
2	80	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	75
3	80	EtOH	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	30
4	80	1,4-Dioxane	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	b
5	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	96
6	80	PEG-400	Et₃N	4, 0.89	30	93
7	80	PEG-400	KOH	4, 0.89	30	Trace
8	80	PEG-400	$Na_2CO_3$	4, 0.89	30	93
9	80	PEG-400	NaHCO <sub>3</sub>	4, 0.89	30	90
10	25	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	30	Trace
11	50	PEG-400	$K_2CO_3$	4, 0.89	30	45
12	60	PEG-400	$K_2CO_3$	4, 0.89	30	75
13	70	PEG-400	$K_2CO_3$	4, 0.89	30	84
14	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	5, 1.11	30	96
15	80	PEG-400	$K_2CO_3$	3, 0.22	30	83
16	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	0	24 h	b
<sup>a</sup> lsolat <sup>b</sup> No re	ed yield.					

 Table 2.
 Suzuki coupling of aryl halides with phenylboronic acid in the presence of Pd-2A3HP-MCM-41 (4 mg, 0.89 mol%) as catalyst<sup>a</sup>

Entry	Х	R	Time (min)	Yield (%) <sup>b</sup>	Melting point (°C)	TOF (h <sup>-1</sup> )
1	Ι	Н	30	96	64-66 <sup>[47]</sup>	215.25
2	I	p-CH <sub>3</sub>	20	96	45-46 <sup>[47]</sup>	322.87
3	I.	2-CO <sub>2</sub> H	45	93	106–108 <sup>[48]</sup>	139.01
4	I.	p-OCH <sub>3</sub>	40	91	83-86 <sup>[47]</sup>	153.03
5	Br	Н	40	97	62–65 <sup>[47]</sup>	163.12
6	Br	<i>p</i> -CN	55	86	82 <sup>[48]</sup>	105.18
7	Br	p-CHO	45	90	56-57 <sup>[41]</sup>	134.53
8	Br	<i>p</i> -OH	80	93	160–164 <sup>[47]</sup>	78.19
9	Br	p-NO <sub>2</sub>	25	92	112–114 <sup>[49]</sup>	247.53
10	Br	$p-NH_2$	50	98	50–53 <sup>[50]</sup>	131.84
11	Br	<i>p</i> -CO₂H	20	93	126–127 <sup>[50]</sup>	312.78
12	Br	2-CH <sub>2</sub> OH	50	90	60-62 <sup>[51]</sup>	121.08
13	Br	3-CHO	35	91	Oil <sup>[52]</sup>	174.89
14	Br	p-CH₃	25	93	43-46 <sup>[47]</sup>	250.22
15	Br	p-Cl	45	94	70–73 <sup>[47]</sup>	140.51

<sup>a</sup>Reaction conditions: aryl halide (1 mmol), PhB (OH)<sub>2</sub> (1 mmol),  $K_2CO_3$ (3 mmol), Pd-2A3HP-MCM-41 (4 mg, 0.89 mol%), PEG-400 (2 ml). <sup>b</sup>Isolated yield.

crease in conversion and selectivity. To investigate the effect of the base, systematic studies were carried out in the presence of different bases (Table 3, entries 8–10). The best yield is found in the presence of  $K_2CO_3$  as base. Finally, the amount of catalyst was evaluated

(Table 3, entries 13 and 14). Hence, the optimized amount of catalyst is 0.89 mol% (4 mg). The results are summarized in Table 3.

Under the optimized reaction conditions, various aryl halides are rapidly converted to corresponding products in excellent yields. The results are given in Table 4. The results clearly demonstrate that the Pd-2A3HP-MCM-41 catalyst is effective for the Heck reaction.

The reaction between 4-iodotoluene (1 mmol) and Ph<sub>3</sub>SnCl (0.5 mmol) was selected as a model Stille reaction and the influence of various reaction parameters such as base, solvent, temperature and catalyst loading was studied (Table 5). Several solvent systems



<sup>a</sup>Reaction mixture consisted of aryl halide (1.0 mmol), *n*-butyl acrylate (1.2 mmol), base (3 mmol), catalyst (4 mg, 0.89 mol%), and 2 ml of DMF at 120 °C.

<sup>b</sup>Isolated yield.

Table 3.	Catalytic results for the He	ck reaction <sup>a</sup>					
Entry	Temperature (°C)	Solvent	Base (eq.)	Alkene	Catalyst (mg, mol%)	Time (min)	Yield (%) <sup>b</sup>
	120	EtOH	K <sub>2</sub> CO <sub>3</sub>	Styrene	4, 0.89	20	c
2	120	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	Styrene	4, 0.89	20	c
3	120	PEG-400	K <sub>2</sub> CO <sub>3</sub>	Styrene	4, 0.89	20	52
4	120	DMF	K <sub>2</sub> CO <sub>3</sub>	Styrene	4, 0.89	20	67
5	120	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	c
6	120	EtOH	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	c
7	120	PEG-400	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	75
8	120	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	94
9	120	DMF	Et₃N	n-Butyl acrylate	4, 0.89	20	92
10	120	DMF	NaHCO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	75
11	110	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	87
12	100	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	4, 0.89	20	62
13	120	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	5, 1.11	20	94
14	120	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	3, 0.22	20	88
15	120	DMF	K <sub>2</sub> CO <sub>3</sub>	n-Butyl acrylate	0	1440	c
30				(1.2 ))   (2			

<sup>a</sup>Reaction mixture consisted of aryl halide (1.0 mmol), *n*-butyl acrylate or styrene (1.2 mmol), base (3 mmol), catalyst and 2 ml of solvent. Reaction time was 20 min.

<sup>b</sup>Isolated yield.

<sup>c</sup>No reaction.

Table 5.	Catalytic	results for the	Stille react	ion <sup>a</sup>		
Entry Te	mperature (°C)	Solvent	Base (eq.)	Catalyst (mg, mol%)	Time (min)	Yield (%) <sup>b</sup>
1	80	DMSO	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	30
2	80	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	70
3	80	EtOH	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	Trace
4	80	1,4-Dioxane	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	c
5	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	90
6	80	PEG-400	Et₃N	4, 0.89	130	90
7	80	PEG-400	KOH	4, 0.89	130	Trace
8	80	PEG-400	Na <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	93
9	80	PEG-400	NaHCO₃	4, 0.89	130	90
10	25	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	c
11	50	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	30
12	60	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	54
13	70	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	78
14	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	4, 0.89	130	94
15	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	5, 1.11	130	94
16	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	3, 0.22	130	80
17	80	PEG-400	K <sub>2</sub> CO <sub>3</sub>	0	24 h	c

<sup>a</sup>Reaction mixture consisted of aryl halide (1.0 mmol), Ph<sub>3</sub>SnCl (0.5 mmol), base (3 mmol), catalyst and 2 ml of solvent. Reaction time was 130 min.

<sup>b</sup>Isolated yield.

<sup>c</sup>No reaction.

were tested (Table 5, entries 1–5). In addition K<sub>2</sub>CO<sub>3</sub>, KOH, Na<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub> and Et<sub>3</sub>N were employed as bases (Table 5, entries 5–9). Based on the above observation, K<sub>2</sub>CO<sub>3</sub> as base and PEG-400 as solvent is the best combination in terms of yield and reaction time for the Stille reaction. The effect of temperature on the reaction was examined at 25-80 °C (Table 5, entries 10-14). With increasing temperature the yield of product also increases and it is found that the optimal reaction temperature is 80 °C. To investigate the role of the Pd-2A3HP-MCM-41 catalyst in the Stille reaction, various amounts

Table 6. Stille reaction of aryl halides with Ph<sub>3</sub>SnCl using heteroge-



Table 7. Catalytic results for the synthesis of 5-substituted 1Htetrazoles

Entry	Temperature (°C)	Solvent	Catalyst (mg, mol%)	Time (h)	Yield (%) <sup>b</sup>
1	110	PEG-400	5, 1.11	3	Trace
2	110	PEG-400	10, 2.23	3	58
3	110	PEG-400	15, 3.34	3	78
4	110	PEG-400	20, 4.46	3	96
5	110	PEG-400	25, 5.57	3	96
6	100	PEG-400	20, 4.46	3	87
7	120	PEG-400	20, 4.46	3	96
8	110	DMF	20, 4.46	3	93
9	110	DMSO	20, 4.46	3	90
10	110	EtOH	20, 4.46	3	_c
11	110	Water	20, 4.46	3	30

<sup>a</sup>Reaction mixture consisted of nitrile (1.0 mmol), sodium azide (1.2 mmol), catalyst and 2 ml of solvent. Reaction time was 3 h.

<sup>b</sup>Isolated yield.

<sup>c</sup>No reaction.

 
 Table 8.
 Synthesis of 5-substituted 1H-tetrazoles with sodium azide in
 the presence of Pd-2A3HP-MCM-41 catalyst (20 mg, 4.46 mol%)



<sup>a</sup>lsolated yield.



Figure 8. Reusability of Pd-2A3HP-MCM-41 in the reaction of phenyl iodide with phenylboronic acid in Suzuki reaction.

Entry	Substrate	Catalyst	Time (min)	Conditions	Yield (%) <sup>a</sup>
1	I-C <sub>6</sub> H₅	Pd(II)-MCM-41	120	H <sub>2</sub> O/EtOH, 60 °C	<b>99</b> <sup>[35]</sup>
2	I-C <sub>6</sub> H₅	Pd(0)-MCM-41	20	H <sub>2</sub> O/EtOH, 80 °C	93 <sup>[61]</sup>
3	I-C <sub>6</sub> H₅	MCM-41-2 N-Pd(II)	240	Xylene, 90 °C	<b>93</b> <sup>[62]</sup>
4	I-C <sub>6</sub> H₅	SDPP/Pd(0)	180	EtOH, 80 °C	99 <sup>[63]</sup>
5	I-C <sub>6</sub> H₅	NHC-Pd(II)	180	DMA, 120 °C	85 <sup>[64]</sup>
6	I-C <sub>6</sub> H₅	Pd-2A3HP-MCM-41	30	PEG-400, 80 °C	96 (this work)
7	I-C <sub>6</sub> H₅	3Pd-(MCM-41)	1440	Ethylene glycol/toluene, 140 °C	55 <sup>[31]</sup>
8	I-C <sub>6</sub> H₅	3Pd-(MCM-41) (Si/AI_15)	1440	Ethylene glycol/toluene, 140 °C	40 <sup>[31]</sup>
9	I-C <sub>6</sub> H₅	4Pd-(MCM-41)	1440	Ethylene glycol/toluene, 140 °C	58 <sup>[31]</sup>
10	I-C <sub>6</sub> H₅	5Pd-(MCM-41)	1440	Ethylene glycol/toluene, 140 °C	64 <sup>[31]</sup>
11	I-C <sub>6</sub> H₅	Pd(0)/SDPP	60	Solvent- free, 130 °C	99 <sup>[63]</sup>
12	I-C <sub>6</sub> H₅	Pd(OAc)2/[HQ-PEG-4001000-DIL] [BF4]	120	100 °C	93 <sup>[65]</sup>
13	I-C <sub>6</sub> H₅	NHC-Pd(II)	360	160 °C, DMA	99 <sup>[64]</sup>
14	I-C <sub>6</sub> H <sub>5</sub>	Pd-2A3HP-MCM-41	30	120 °C, DMF	94 (this work)

of catalyst were examined (Table 5, entries 15 and 16). As evident from Table 5, increasing the amount of Pd-2A3HP-MCM-41 catalyst to 1.11 mol% (5 mg) does not improve the result to an appreciable extent. Hence 0.89 mol% (4 mg) of catalyst was chosen. The results are summarized in Table 5.

The optimized reactions of various aryl halides with  $Ph_3SnCl$ , using  $K_2CO_3$  as base and PEG-400 as solvent in the presence of 0.89 mol% (4 mg) of Pd-2A3PH-MCM-41, were carried out. The results show that coupling of aryl halides with  $Ph_3SnCl$  proceeded smoothly to afford good to excellent yields of the corresponding coupled products (Table 6).

In continuation of this work on the applications of Pd-2A3HP-MCM-41, we report the preparation of 5-substituted 1*H*-tetrazoles from a wide variety of nitriles. Initially, we examined the reaction of benzonitrile (1 mmol) and sodium azide (1.2 mmol) as a model reaction to synthesize the corresponding tetrazoles.

The effect of various parameters such as catalyst concentration, temperature and solvent was studied for the model reaction. Initially, the catalyst concentration was investigated and the results show that the amount of catalyst plays a very important role in the reaction. It is evident that a small loading of catalyst (1.11 mol %) leads to very poor yield of final compound and a higher ratio of catalyst (4.46 and 5.57 mol%) improves the yield of tetrazoles (Table 7, entries 1–5). Next, in order to get the optimal temperature we carried out the model reaction at various temperatures (Table 7, entries 6 and 7). It is observed that the reaction is successfully completed at 110 °C in 3 h with a yield of 96% (Table 7, entry 4). With an increase in temperature above 110 °C, no change in the yield of product is observed (Table 7, entry 7). So, 110 °C was fixed as the most suitable temperature. For this work we also examined the reactions in several solvents (Table 7, entries 8-11). PEG-400 is found to be the most suitable solvent giving a maximum yield of 96%. Although other solvents such as DMF and dimethylsulfoxide (DMSO) give suitable yield, PEG-400 was selected because it is a more desirable solvent from an environmental viewpoint. The results are summarized in Table 7.

To determine the scope of this synthesis, we studied the effect of substituents on the aromatic nitriles under the optimized conditions. The results are presented in Table 8. Aromatic nitriles having both electron-donating and electron-withdrawing groups at any position result in the corresponding tetrazoles in good to excellent yields.

#### Reuse property of heterogeneous catalyst

The recovery of the catalyst supported on mesoporous silica was performed using the Suzuki reaction. After completion of each run, the catalyst was separated by centrifugation and was subjected into another batch of the reaction. As shown in Fig. 8, the Pd-2A3HP-MCM-41 catalyst can be reused seven times without significant loss of activity.

In order to determine whether the catalyst was behaving in a truly heterogeneous manner or from leaching of palladium released from the solid catalyst during the reaction, a hot filtration test was performed. In this experiment, Pd-2A3HP-MCM-41 (4 mg, 0.89 mol%), phenyl iodide (1 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol) and PEG-400 (2 ml(were added to a round-bottom flask and stirred at 80 °C. The catalyst was rapidly separated by centrifugation after 15 min reaction time (the conversion reached 48%) and the hot liquid mixture allowed to react for a further 15 min under the same conditions. There is no detectable increase in the product concentration, which might be evidence for a heterogeneous mechanism during the recycling. Also, the amount of Pd species dissolved into solution caused by leaching of the catalyst was determined using ICP after recovery of the catalyst  $(1.90 \times 10^{-3} \text{ mol g}^{-1})$ . The ICP results show that 2% of the total amount of the original palladium species is lost into solution during the course of the reaction. These results illustrate that minimal leaching of palladium takes place during the reaction and the catalyst is heterogeneous in nature.

The activity of Pd-2A3HP-MCM-41 in comparison with that of other reported catalysts was evaluated (Table 9). The obtained results indicate the superiority of the present catalyst in terms of yield or reaction time compared with the other catalysts reported in the literature. On the other hand, some of the reported catalysts have not covered the conversion of a wide range of aryl halides.<sup>[60]</sup>

#### Conclusions

Palladium with chloropropyltriethoxysilane and 2-amino-3hydroxypyridine immobilized on MCM-41 was found to be an active and selective catalyst for the Suzuki coupling of aryl halides with phenylboronic acid and Heck coupling of aryl halides with *n*-butyl acrylate as well as Stille coupling of aryl halides with Ph<sub>3</sub>SnCl and the synthesis of 5-substituted 1*H*-tetrazoles from sodium azide (NaN<sub>3</sub>). The coupling reactions occurred in a short time, under mild conditions to give the corresponding biphenyl derivatives in moderate to high yields for aryl halides with electron-donating as well as electron-withdrawing groups. In the synthesis of 5-substituted 1*H*-tetrazoles, among the various nitrites tested, aromatic nitrile compounds with electron-withdrawing substituents in comparison with electron-donating substituents were shown to give excellent yields in lower reaction times. This heterogeneous catalyst was easily separable from the reaction mixture by filtration. The recovered catalyst was able to be used in more than seven reaction cycles without losing activity.

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