

RESEARCH PAPER

## Palladium nanoparticles immobilized on multifunctional hyperbranched polyglycerol-grafted magnetic nanoparticles as a sustainable and efficient catalyst for C-C coupling reactions

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### ABSTRACT

This study offers an exclusive class of magnetic nanoparticles supported hyperbranched polyglycerol (MNP/HPG) that was functionalized with citric acid (MNP/HPG-CA) as a host immobilization of palladium nanoparticles. The MNP/HPG-CA/Pd catalyst was fully characterized using some different techniques such as thermogravimetric analysis (TGA), x-ray diffraction (XRD), transmission electron microscopy (TEM), scanning electron microscopy (SEM), energy-dispersive x-ray spectroscopy (EDX), inductively coupled plasma (ICP) and x-ray photoelectron spectroscopy (XPS). The new catalytic system showed high activity for the Suzuki–Miyaura cross-coupling and Heck reaction under mild and green conditions. Besides, the MNP/HPG-CA/Pd was found to be a convenient catalyst for copper-free Sonogashira coupling reaction in water as a green solvent at room temperature. Moreover, the catalyst could be recovered easily and reused several times without significant loss of reactivity. Ease of preparation, oxygen insensitive, phosphine-free, air- and moisture-stable, and high reusability of this immobilized palladium catalyst are the noteworthy advantages of this catalytic system.

### How to cite this article

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### INTRODUCTION

Palladium catalysis has achieved an impressive place in numerous commercial chemical processes [1-3]. Palladium is actually expensive as gold, however, and this may limit its operation and employment in some cases. Moreover, because of the side effect of heavy metal impurities on molecular biological activity, palladium contamination of isolated desired product is a significant problem for pharmaceutical industry [4]. To address this issue, palladium has been immobilized on different natural and synthetic supports with the aim of reducing the amount of catalyst and palladium contamination of the isolated products by allowing the palladium

species to be separated, recovered, and reused [5-7]. This method would be exceedingly suitable and efficient for industrial purposes and applications as well as performing the reactions in multiple vessels for combinatorial chemical libraries.

Numerous research studies have been recently devoted to immobilizing palladium on various support materials such as activated carbon, silica gel, metal oxides, porous aluminosilicates, clays and other inorganic compounds [8-11]. In particular, encapsulation of palladium in nanomaterials containing covalently-bound polymers is an efficient and cost-effective approach to immobilize and retain palladium species [12-16].

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During the last years, hyperbranched polyglycerol grafted on solid supports has attracted much attention due to the unique properties such as three-dimensional structure, multiple internal and external functional groups and excellent solubility in water [17-21].

Up to now, hyperbranched polyglycerol polymers was grafted on diverse nanomaterials. Amongst, superparamagnetic oxide nanoparticles have been considered as suitable platform due to easy of surface modification, high surface area and facile recovery [22-26]. However, the use of different hyperbranched derivatives or polymers has rarely reported for immobilization and stabilization of palladium nanoparticles [24, 27, 28]. So, design and preparation of novel series of modified magnetic nanoparticles with hyperbranched polymers for palladium immobilization afford an opportunity to achieve new catalytic systems with practical high-performance engineering applications.

In the past decade, the application of encapsulated palladium nanoparticles as catalyst, especially in C-C bond-forming processes, have much lured researchers in modern organic synthesis [29-31]. Among palladium-catalyzed couplings, the Suzuki-Miyaura, Sonogashira, and Heck reactions are the most widely used for the preparation of molecules possessing interesting biological or physical properties [32-40]. Among the various catalytic systems used, phosphine based ligands show excellent activity in this transformation. However, the phosphine based ligands are usually toxic and sensitive to air and moisture restricting their wide spread application. On the other hand, some of the phosphine-free synthetic methods suffer from disadvantages such as high temperature, long reaction times, use of large amounts of palladium and organic solvents. Accordingly, the development of an efficient and eco-friendly method using a reusable and water-soluble catalyst for the synthesis of diverse molecules is still desirable. Besides, in comparison with Suzuki-Miyaura and Heck reactions, little attention has been paid to Sonogashira cross coupling catalyzed by palladium immobilized on polymer supports [41-46]. To the best of our knowledge, no report has been documented on the Sonogashira coupling reaction catalyzed by palladium entrapped on HPG-modified magnetic nanoparticles.

Very recently, the MNP/HPG-CA nanocarrier has been reported by our research group and used as a unique platform for biocatalytic systems [47].

In continuation of our efforts on the development of efficient catalytic systems [48-54] and encouraged by the exclusive properties of palladium immobilized on silica encapsulated magnetic nanoparticles grafted hyperbranched polyglycerol, we wish to demonstrate at this time, the preparation and characterization of a new oxygen insensitive, phosphine-free, air- and moisture-stable, and reusable immobilized palladium nanoparticles on citric acid functionalized MNP/HPG (MNP/HPG-CA/Pd) catalyst and its application in C-C coupling reactions *via* the Suzuki-Miyaura cross-coupling, Heck and Sonogashira reactions under green conditions.

## EXPERIMENTAL

### General Remarks

The chemicals used in this work were obtained from Merck, Acros and Aldrich chemical companies. FT-IR spectra were recorded on a JASCO 6300 spectrophotometer. <sup>1</sup>H NMR (400 MHz) spectra were recorded on a Bruker Avance 400 MHz spectrometer using CDCl<sub>3</sub> as solvent. The Pd content of the catalysts was determined by a Jarrell-Ash 1100 ICP analysis. Field Emission Scanning electron microscopy (FE-SEM) was performed on a Hitachi S-4160 field emission-scanning electron microscope. The transmission electron microscopy (TEM) was carried out on a Philips CM30 Transmission Electron Microscope operating at 100 kV. X-ray powder diffraction (XRD) spectra were taken on a Bruker D8-Advance X-ray diffractometer with Cu K $\alpha$  radiation. The X-ray photoelectron spectroscopy (XPS) measurements were performed using a Gamma data-scienta ESCA200 hemispherical analyzer equipped with an Al (K $\alpha$  = 1486.6 eV) X-ray source. Thermogravimetric analysis (TGA) was carried out on a Mettler TG50 instrument under air flow at a uniform heating rate of 5 °C/min in the range of 30-600 °C. Substances were identified and quantified by gas chromatography (GC) on an Agilent GC 6890 equipped with a 19096C006 80/100 WHP packed column and a flame ionization detector (FID).

### Preparation of MNP/HPG-CA/Pd

A mixture of PdCl<sub>2</sub> (240 mg, 1.36 mmol) and NaCl (88 mg, 1.52 mmol) in methanol (8 mL) was stirred at room temperature for 24 h and then filtered. The filtrates were diluted with methanol (40 mL) and MNP/HPG-CA (1 g) was added to

this solution. The resulting mixture was stirred at 60 °C for 24 h. At the end of the reaction, the mixture was cooled to room temperature; sodium acetate (0.76 g, 9.28 mmol) was added and stirred at room temperature for 1 h. The product was collected by a magnet, washed with deionized water several times and finally with methanol, and dried under vacuum.

#### General procedure for Suzuki-Miyaura cross-coupling reactions catalyzed by MNP/HPG-CA/Pd

A mixture of aryl halide (1 mmol), arylboronic acid (1 mmol),  $K_2CO_3$  (1 mmol) and MNP/HPG-CA/Pd (0.05 mol% Pd) in 2 mL of DMF/ $H_2O$  (3:1) was stirred at 50 °C. The reaction progress was monitored by GC. After completion of the reaction, the reaction mixture was cooled to room temperature, and the catalyst was separated by a magnet and washed with diethyl ether (2×10 mL), deionized water (2×10 mL), and then dried under vacuum for the next run. The coupling products were obtained after addition of water (10 ml) to the filtrates and extraction with diethyl ether (2×10 mL) (Table 2).

#### General procedure for Heck coupling reactions of styrene with aryl halides catalyzed by MNP/HPG-CA/Pd

A mixture of aryl halides (1 mmol), styrene (1 mmol),  $K_2CO_3$  (1 mmol) and the catalytic amount of catalyst (0.08 mol% Pd) in DMF (2 mL) was stirred at 80 °C. The progress of the reaction was monitored by GC. At the end of the reaction, the mixture was cooled to room temperature. The catalyst recovery and isolation of the products were done as described above (Table 4).

#### General procedure for Sonogashira reactions of phenylacetylene with aryl halides catalyzed by MNP/HPG-CA/Pd

A mixture of aryl halide (1.0 mmol), aryl or alkyl acetylene (1.1 mmol),  $K_2CO_3$  (1 mmol) and MNP/HPG-CA/Pd (0.05 mol% Pd) in 2 mL of  $H_2O$  was stirred at room temperature. The reaction progress was monitored by GC. After the reaction was completed, ethyl acetate (15 mL) was added, and the catalyst was separated by a magnet. The organic phase was washed with  $H_2O$  (2 × 10 mL), and dried with anhydrous  $MgSO_4$ , and the solvents were evaporated. The residue was recrystallized from ether and ethyl acetate (3:1) to give the pure product (Table 6).

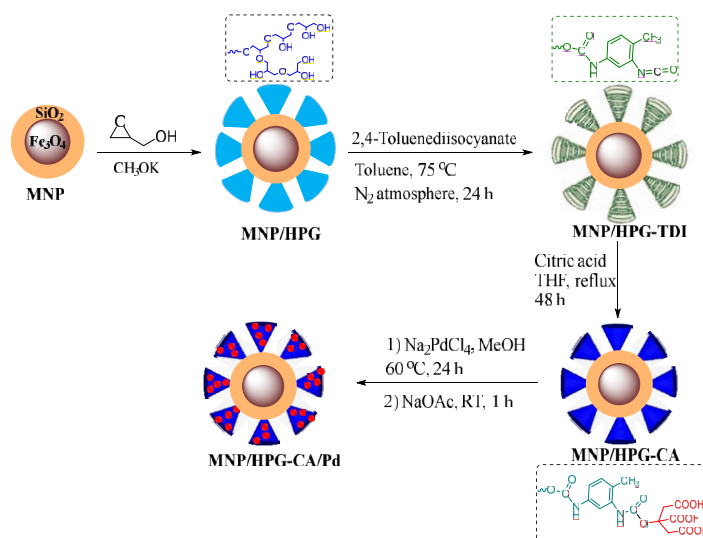
#### Catalyst recovery and reuse

In the recyclability experiment, a mixture of iodobenzene (1.0 mmol), phenylacetylene (1.1 mmol),  $K_2CO_3$  (1 mmol) and MNP/HPG-CA/Pd (0.05 mol% Pd) in 2 mL of  $H_2O$  was stirred at room temperature for 5 hours. At the end of each reaction, the catalyst was separated by a magnet and washed with diethyl ether (2×10 mL), deionized water (2×10 mL), and then dried under vacuum before using in the next run. The recovered catalyst was used with fresh starting materials.

## RESULTS AND DISCUSSION

### Synthesis and characterization

The preparation strategy for the MNP/HPG-CA/Pd catalyst is shown in Scheme 1. First, iron oxide magnetic nanoparticles ( $Fe_3O_4$ ) were prepared by co-precipitation method using a



Scheme 1. Preparation route for MNP/HPG-CA/Pd

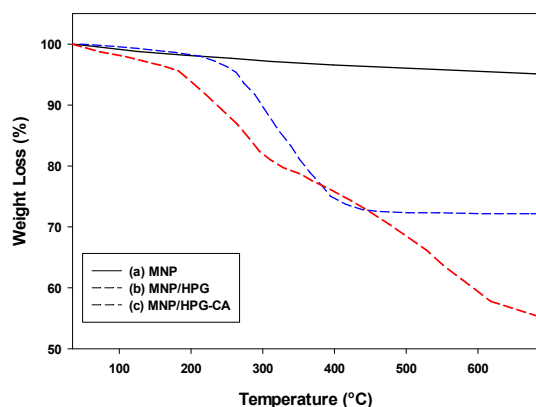


Fig. 1. The TGA spectra of: a) MNP; b) MNP/HPG; c) MNP/HPG-CA

procedure in the literature [55, 56]. This protocol is one of the convenient and simple methods for the large-scale synthesis of  $\text{Fe}_3\text{O}_4$ . Next, the prepared nanoparticles were coated by silica using Stöber method to obtain core-shell magnetic nanoparticles [57]. According to the process by hydrolysis and then condensation of tetraethyl orthosilicate (TEOS) the silica layer is formed on  $\text{Fe}_3\text{O}_4$ . Subsequently, hyperbranched polyglycerol grafted on MNP (MNP/HPG) was prepared according to the literature [8]. Then, the multifunctionalized hyperbranched polymer grafted on magnetic nanoparticles was prepared as described previously [47] by modification of MNP/HPG with 2,4-toluenediisocyanate (TDI) and citric acid (CA), respectively.

The thermal gravimetric analysis (TGA) technique was used to measure organic content of the modified nanoparticles (Fig. 1). The TGA showed a slight weight loss below 200 °C in all cases, which was attributed to the loss of physisorbed water from the samples. The weight loss from the samples in the range 200–700 °C on the thermogravimetric traces was attributed mainly to the loss of organic groups. In this temperature range, only 4 wt% weight loss was observed for MNP. While after the polymerization and post-functionalization, the weight losses from MNP/HPG and MNP/HPG-CA were 25.2 and 41.4 wt%, respectively. These observations confirmed the successful synthesis of MNP/HPG-CA.

As shown in Scheme 1, the palladium nanoparticles immobilized on citric acid functionalized MNP/HPG (MNP/HPG-CA/Pd) were prepared by reduction of  $\text{Na}_2\text{Pd}_2\text{Cl}_4$  [58] (prepared *in situ* from  $\text{PdCl}_2$  and  $\text{NaCl}$ ) in methanol at 60 °C in the

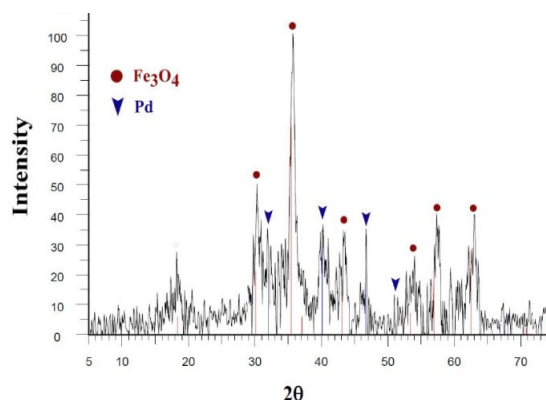


Fig. 2. XRD patterns of MNP/HPG-CA/Pd

presence of MNP/HPG-CA.

The loading amount of Pd, determined by ICP analysis, was found to be about  $0.254 \text{ mmol g}^{-1}$  of MNP/HPG-CA/Pd. The XRD patterns of the catalyst were shown in Fig. 2.

As can be seen, the characteristic diffraction peaks at  $2\theta = 30.09, 35.44, 43.07, 53.43, 56.96$  and  $62.55$  are in agreement with face centered cubic (fcc) of  $\text{Fe}_3\text{O}_4$ . Furthermore, the presence of the characteristic diffraction peaks ( $2\theta = 32.01, 40.11, 47.53$  and  $51.23$ ) corresponding to palladium, confirmed the presence of palladium on catalyst.

Since the XRD patterns of magnetite and maghemite are highly similar, X-ray photoelectron spectroscopy (XPS) measurement has to be checked to clearly assign the crystal phase, because XPS is very sensitive to  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$  species [59].

The characteristic XPS spectra of nanoparticles indicates (Fig. 3a) that the levels of Fe ( $2p_{3/2}$ ) and Fe ( $2p_{1/2}$ ) are 710.9 and 724.5 eV. It is corresponding to the literature that the peaks shift to high binding energy and broaden for  $\text{Fe}_3\text{O}_4$  owing to the appearance of  $\text{Fe}^{2+}(2p_{3/2})$  and  $\text{Fe}^{2+}(2p_{1/2})$ . This result clearly indicates the formation of a mixed oxide of Fe(II) and Fe(III), namely  $\text{Fe}_3\text{O}_4$ .

Additionally, in the XPS of MNP/HPG-CA/Pd, the  $3d_{5/2}$  and  $3d_{3/2}$  peaks of  $\text{Pd}^0$  appear at 335.58 and 339.85 eV, respectively (Fig. 3b). It is important to note that no evident peak of  $\text{Pd}^{2+}$  is observed, indicating that palladium is in the reduced form. The peaks corresponding to iron, oxygen, carbon, nitrogen, and palladium are also clearly observed in XPS elemental investigation of the catalyst (Fig. 3c).

The morphology of the surface of catalyst was directly visualized by field emission scanning electron microscopy (FE-SEM) (Fig. 4). As can be seen, particles are spherical and have diameters in

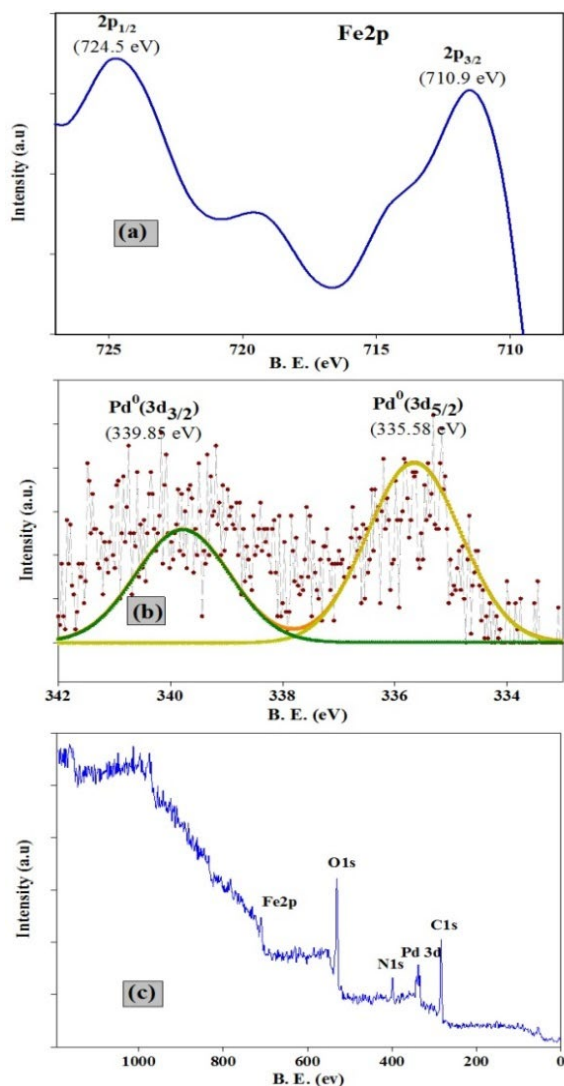


Fig. 3. (a) Fe 2p core-level XPS spectrum of MNP/HPG-CA/Pd, (b) Pd  $3d_{3/2}$  and  $3d_{5/2}$  binding energies of MNP/HPG-CA/Pd and (c) the elemental survey scan of MNP/HPG-CA/Pd

the range of nanometre. Furthermore, the energy dispersive X-ray spectroscopy (EDS) results, obtained from SEM analysis for MNP/HPG-CA and MNP/HPG-CA/Pd are shown in Figs. 3c and d, which clearly show the presence of Pd nanoparticles in the MNP/HPG-CA/Pd catalyst.

Further characterization of the catalyst was performed by TEM. Fig. 5 clearly exposed that  $\text{Fe}_3\text{O}_4$  nanoparticles have been successfully covered by the polymer shell. The dark core corresponds to magnetic nanoparticles while the light shell attributes to polymer shell. Also, the TEM images showed that the spherical Pd particles have been dispersed in MNP/HPG-CA.

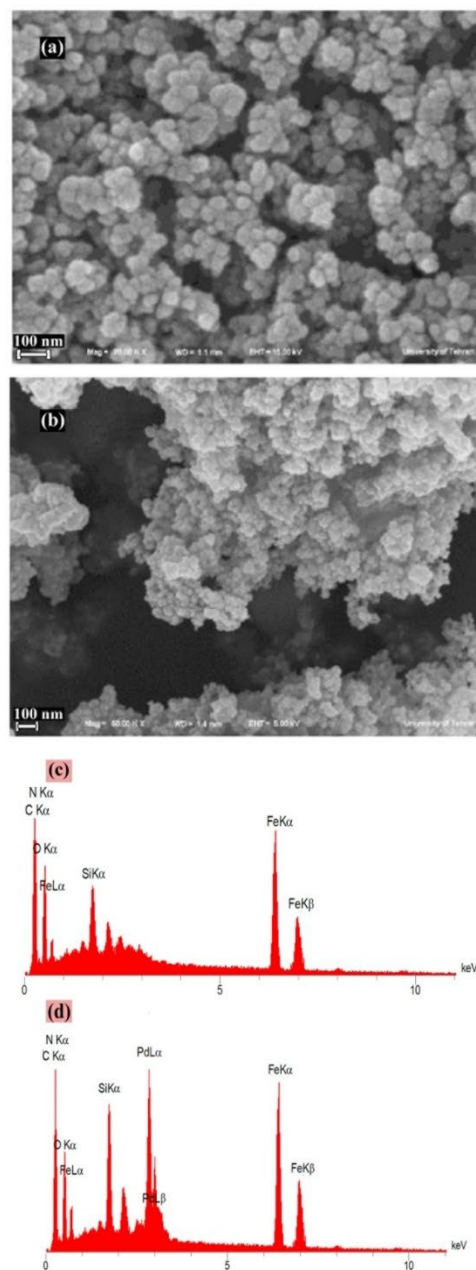


Fig. 4. (a) and (b) FE-SEM images of MNP/HPG-CA/Pd and EDS spectrum of (c) MNP/HPG-CA and (d) MNP/HPG-CA/Pd

#### *Suzuki-Miyaura cross-coupling of aryl halides with arylboronic acids*

Initially, the reaction parameters such as kind of solvent, temperature, kind of base and amount of catalyst were optimized in the Suzuki-Miyaura cross-coupling of 4-iodotoluene with phenylboronic acid. The results are summarized in Table 1. The model reaction was first performed in the presence of different organic and inorganic

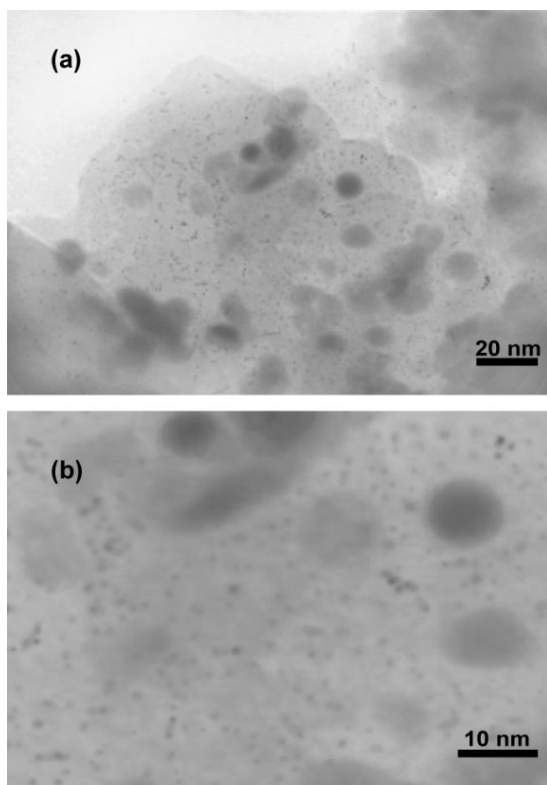


Fig. 5. TEM images of MNP/HPG-CA/Pd

bases including DBU, Et<sub>3</sub>N, NaOH, NaHCO<sub>3</sub>, K<sub>3</sub>PO<sub>4</sub> and K<sub>2</sub>CO<sub>3</sub>. Among the screened bases,

K<sub>2</sub>CO<sub>3</sub> was found to be the most appreciate base. Then, the same reaction was carried out in different single and mixed solvents. Among the solvents examined, DMF/H<sub>2</sub>O (3:1) was proved to be the best reaction medium. Also, the model reaction was conducted at different temperatures. Base on the obtained results, the optimum reaction temperature was found to be 50 °C. The effect of the amount of catalyst on the model reaction was also explored. As can be seen from Table 1, the best result was obtained in the presence of 0.05 mol% of Pd catalyst. Therefore, we concluded that 0.05 mol% of the catalyst in DMF/H<sub>2</sub>O (3:1) at 50 °C are the most appropriate reaction conditions for the Suzuki–Miyaura cross-coupling reaction. It is noteworthy that the model reaction was also carried out under argon and oxygen atmosphere; the results were comparable to that obtained in an open system (Table 1, entries 16 and 17), which obviously reveals that MNP/HPG-CA/Pd is a stable and oxygen-insensitive catalyst.

Under the optimized reaction conditions, Suzuki–Miyaura cross-coupling of aryl halides with arylboronic acids in the presence of MNP/HPG-CA/Pd was investigated. The results, shown in Table 2, indicated that MNP/HPG-CA/Pd is an efficient catalyst for the Suzuki–Miyaura cross-coupling reaction, and that the biphenyl derivatives

Table 1. Optimization of Suzuki–Miyaura cross-coupling of 4-iodotoluene with phenylboronic acid catalyzed by MNP/HPG-CA/Pd<sup>a</sup>

| Entry           | Catalyst (mol% Pd) | Base                           | Solvent                    | T (°C) | Time (min) | Yield (%) <sup>b</sup> |
|-----------------|--------------------|--------------------------------|----------------------------|--------|------------|------------------------|
| 1               | 0.05               | NEt <sub>3</sub>               | DMF                        | 50     | 25         | 30                     |
| 2               | 0.05               | DBU <sup>c</sup>               | DMF                        | 50     | 25         | 44                     |
| 3               | 0.05               | NaHCO <sub>3</sub>             | DMF                        | 50     | 25         | 60                     |
| 4               | 0.05               | NaOH                           | DMF                        | 50     | 90         | 58                     |
| 5               | 0.05               | K <sub>3</sub> PO <sub>4</sub> | DMF                        | 50     | 50         | 64                     |
| 6               | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 50     | 25         | 70                     |
| 7               | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (1:1) | 50     | 25         | 76                     |
| 8               | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 50     | 10         | 93                     |
| 9               | 0.05               | K <sub>2</sub> CO <sub>3</sub> | Toluene                    | 50     | 140        | 51                     |
| 10              | 0.05               | K <sub>2</sub> CO <sub>3</sub> | MeCN                       | 50     | 120        | 45                     |
| 11              | 0.05               | K <sub>2</sub> CO <sub>3</sub> | H <sub>2</sub> O           | 50     | 120        | 65                     |
| 12              | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | RT     | 120        | 77                     |
| 13              | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 80     | 10         | 94                     |
| 14              | 0.03               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 50     | 30         | 72                     |
| 15              | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 50     | 10         | 91                     |
| 16 <sup>d</sup> | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 50     | 10         | 92                     |
| 17 <sup>e</sup> | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF/H <sub>2</sub> O (3:1) | 50     | 10         | 93                     |

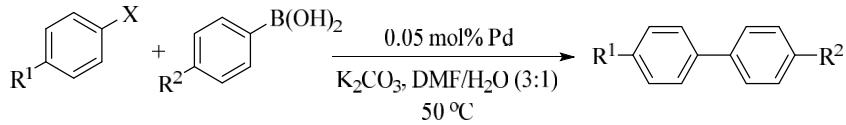
<sup>a</sup> Reaction was performed using 4-iodotoluene (1 mmol), phenylboronic acid (1 mmol) and base (1 mmol) in 2 mL solvent.

<sup>b</sup> Isolated yield.

<sup>c</sup> 1,8-Diazabicyclo[5.4.0]undec-7-ene

<sup>d</sup> Reaction was performed under an oxygen atmosphere.

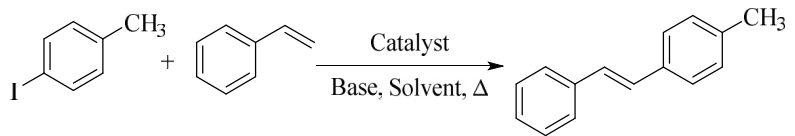
<sup>e</sup> Reaction was performed under an argon atmosphere.

Table 2. Suzuki–Miyaura cross-coupling of aryl halides with arylboronic acid catalyzed by MNP/HPG-CA/Pd<sup>a</sup>


| Entry | R <sup>1</sup>    | R <sup>2</sup> | X  | Time (min) | Yield (%) <sup>b</sup> |
|-------|-------------------|----------------|----|------------|------------------------|
| 1     | H                 | H              | I  | 10         | 95                     |
| 2     | H                 | 4-MeO          | I  | 10         | 92                     |
| 3     | 4-MeO             | H              | I  | 10         | 91                     |
| 4     | 4-MeO             | 4-MeO          | I  | 10         | 94                     |
| 5     | 4-CH <sub>3</sub> | H              | I  | 10         | 95                     |
| 6     | 4-Ac              | H              | Br | 15         | 91                     |
| 7     | 4-Ac              | 4-MeO          | Br | 15         | 94                     |
| 8     | H                 | H              | Br | 15         | 90                     |
| 9     | H                 | 4-MeO          | Br | 15         | 95                     |
| 10    | 4-CH <sub>3</sub> | H              | Br | 20         | 93                     |
| 11    | 4-MeO             | H              | Br | 20         | 92                     |
| 12    | H                 | H              | Cl | 100        | 85                     |
| 13    | H                 | 4-MeO          | Cl | 100        | 81                     |
| 14    | 4-Ac              | H              | Cl | 100        | 83                     |
| 15    | 4-Ac              | 4-MeO          | Cl | 100        | 87                     |

<sup>a</sup> Reaction conditions: aryl halide (1 mmol), arylboronic acid (1 mmol), K<sub>2</sub>CO<sub>3</sub> (1 mmol), catalyst (0.05 mol% Pd), DMF/H<sub>2</sub>O (3:1, 2 mL), 50°C.

<sup>b</sup> Isolated yield.

Table 3. Optimization of the conditions in the Heck reaction of 4-iodotoluene with styrene catalyzed by MNP/HPG-CA/Pd<sup>a</sup>


| Entry | Catalyst (mol% Pd) | Base                           | Solvent                    | T (°C) | Time (min) | Yield (%) <sup>b</sup> |
|-------|--------------------|--------------------------------|----------------------------|--------|------------|------------------------|
| 1     | 0.08               | Piperidine                     | DMF                        | 80     | 75         | 32                     |
| 2     | 0.08               | DBU                            | DMF                        | 80     | 75         | 41                     |
| 3     | 0.08               | NEt <sub>3</sub>               | DMF                        | 80     | 75         | 25                     |
| 4     | 0.08               | NaHCO <sub>3</sub>             | DMF                        | 80     | 75         | 62                     |
| 5     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 80     | 60         | 94                     |
| 6     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF:H <sub>2</sub> O (3:1) | 80     | 75         | 53                     |
| 7     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | EtOH                       | 80     | 120        | 48                     |
| 8     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | H <sub>2</sub> O           | 80     | 120        | 50                     |
| 8     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | Toluene                    | 80     | 120        | 35                     |
| 9     | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 80     | 75         | 94                     |
| 10    | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 50     | 120        | 62                     |
| 11    | 0.08               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 100    | 60         | 92                     |
| 12    | 0.05               | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 80     | 90         | 82                     |
| 13    | 0.1                | K <sub>2</sub> CO <sub>3</sub> | DMF                        | 80     | 75         | 93                     |

<sup>a</sup> Reaction was performed using 4-iodotoluene (1 mmol), styrene (1 mmol) and base (1 mmol) in 2 mL solvent.

<sup>b</sup> Isolated yield.

are produced in good to excellent yields. As expected, iodobenzenes are more reactive than bromobenzenes.

It is noteworthy to mention that aryl chlorides usually are cheaper, more readily accessible and practical but less reactive than aryl iodides and bromides. Due to lower reactivity, the coupling reactions with aryl chlorides have been generally investigated using a higher amount of catalyst and under harsh conditions [60–65]. In order to further

explore the applicability of this method, the cross-coupling of aryl chlorides with arylboronic acids was also checked under the same conditions. As shown, reaction of aryl chlorides with phenylboronic acid and 4-methoxyphenylboronic acid (Table 2, entries 12–15) proceeded smoothly in the presence of the same catalyst amount as used for aryl iodides and bromides (0.05 mol% Pd) at 50 °C, resulting in the desired cross-coupling products in high yields (81–87%) within 100 min.

**Heck reaction of aryl halides with styrene**

The high efficiency of this catalyst in the Suzuki-Miyaura cross-coupling reactions encouraged us to investigate the potential of the catalyst in the Heck reaction of aryl halides with styrene. To find the optimal experimental conditions in the Heck reaction of aryl halides with styrene catalyzed by MNP/HPG-CA/Pd catalyst, the reaction of 4-iodotoluene with styrene was considered as a model reaction. The effect of base and solvent, temperature and catalyst amount were carefully examined. The results, summarized in Table 3, showed that the highest yield is obtained using 4-iodotoluene (1 mmol), styrene (1 mmol),  $K_2CO_3$  (1 mmol) and MNP/HPG-CA/Pd (0.08 mol% Pd) in DMF at 80 °C.

Under the optimized reaction conditions, the catalyst was applied in the reaction of different aryl halides with styrene, and the corresponding stilbene derivatives were obtained in good to excellent yields (Table 4). As expected, aryl iodides and bromides were more reactive than aryl chlorides.

**Sonogashira coupling reaction of aryl halides with alkyne**

In other part of this study we evaluated the catalytic activity of this catalyst in the copper-free Sonogashira reaction. Traditionally, the Sonogashira reaction is carried out in the presence

of palladium and copper as well, to contribute in the catalysis. [15-19]

Over the last years, many efforts have been made to study such C-C coupling in the absence of copper. Furthermore, while Sonogashira couplings in polar mixed aqueous medium, in the presence of organic bases and under inert atmosphere are common, in this paper, we describe a novel method that allows amine-free condition in water alone [45, 66-69]. Sonogashira coupling was investigated to perform under amine- and copper-free condition using commercially available reagents.

To find the optimal reaction conditions, we examined the Sonogashira cross-coupling reaction between iodobenzene and phenylacetylene in the presence of the MNP/HPG-CA/Pd catalyst in  $H_2O$  as a model reaction. In this regard, the effects of the reaction conditions such as the type of base, temperature and catalyst amount were screened and a summary of the optimization experiments is provided in Table 5. Initially, some bases including  $K_2CO_3$ ,  $Na_2CO_3$ ,  $Et_3N$ , NaOH and  $K_3PO_4$  were tested in the model reaction and  $K_2CO_3$  was selected as the best one. Also, the effects of the amount of catalyst were also explored; while with increasing the amount of the catalyst, the yield of the desired product did not further increase (Table 5, entry 6), the yield decreased obviously with decreasing this parameter, (Table 5, entry 7).

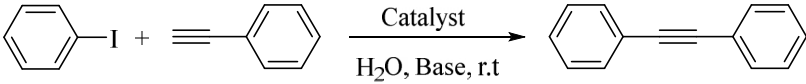
Table 4. Heck reaction of aryl halides with styrenes catalyzed by MNP/HPG-CA/Pd<sup>a</sup>

| Entry | R <sup>1</sup> | R <sup>3</sup> | X  | Time (min) | Yield (%) <sup>b</sup> |
|-------|----------------|----------------|----|------------|------------------------|
| 1     | H              | H              | I  | 60         | 95                     |
| 2     | H              | 4-Me           | I  | 60         | 93                     |
| 3     | 4-Me           | 4-Me           | I  | 60         | 95                     |
| 4     | 4-Me           | H              | I  | 60         | 94                     |
| 5     | 4-Ac           | 4-Me           | I  | 60         | 91                     |
| 6     | H              | H              | Br | 75         | 90                     |
| 7     | H              | 4-Me           | Br | 75         | 92                     |
| 8     | 4-MeO          | 4-Me           | Br | 80         | 93                     |
| 9     | 4-F            | H              | Br | 80         | 91                     |
| 10    | 4-F            | 4-Me           | Br | 80         | 90                     |
| 11    | 4-Me           | H              | Br | 75         | 93                     |
| 12    | 4-Ac           | 4-Me           | Br | 70         | 95                     |
| 13    | 4-Ac           | H              | Br | 70         | 92                     |
| 14    | 4-CHO          | H              | Br | 75         | 90                     |
| 15    | H              | H              | Cl | 75         | 92                     |
| 16    | 4-MeO          | H              | Cl | 100        | 89                     |
| 17    | 4-Ac           | H              | Cl | 100        | 88                     |
| 18    | 4-Ac           | 4-Me           | Cl | 100        | 91                     |
| 19    | 4-CHO          | H              | Cl | 100        | 88                     |

<sup>a</sup> Reaction conditions: aryl halide (1 mmol), styrene (1 mmol),  $K_2CO_3$  (1 mmol), catalyst (0.08 mol% Pd), DMF (2 mL).

<sup>b</sup> Isolated yield.



Table 5. Optimization of the conditions in the sonogashira reaction of iodobenzene with phenylacetylene catalyzed by MNP/HPG-CA/Pd<sup>a</sup>


| Entry          | Catalyst (mol% Pd) | Base                            | Time (h) | Yield (%) <sup>b</sup> |
|----------------|--------------------|---------------------------------|----------|------------------------|
| 1              | 0.05               | NEt <sub>3</sub>                | 24       | 75                     |
| 2              | 0.05               | Na <sub>2</sub> CO <sub>3</sub> | 9        | 65                     |
| 3              | 0.05               | NaOH                            | 18       | 23                     |
| 4              | 0.05               | K <sub>3</sub> PO <sub>4</sub>  | 12       | 41                     |
| 5              | 0.05               | K <sub>2</sub> CO <sub>3</sub>  | 5        | 93                     |
| 6              | 0.08               | K <sub>2</sub> CO <sub>3</sub>  | 5        | 93                     |
| 7              | 0.03               | K <sub>2</sub> CO <sub>3</sub>  | 6        | 85                     |
| 8 <sup>c</sup> | 0.05               | K <sub>2</sub> CO <sub>3</sub>  | 6        | 90                     |

<sup>a</sup> Reaction conditions: iodobenzene (1 mmol), phenylacetylene (1.1 mmol), base (1 mmol), H<sub>2</sub>O (2 mL), room temperature.

<sup>b</sup> Isolated yield.

<sup>c</sup> Reaction was performed at 80 °C.

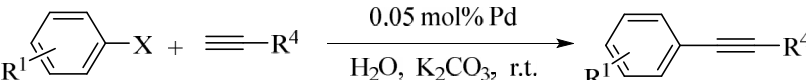
Furthermore, rising the reaction temperature to 80 °C did not affect the reaction time. Therefore, we concluded that 0.05 mol% of the catalyst, K<sub>2</sub>CO<sub>3</sub> as the base, in H<sub>2</sub>O at room temperature, is the most convenient reaction condition for this transformation.

To survey the scope and versatility of MNP/HPG-CA/Pd in the Sonogashira reaction, diverse aryl halides were coupled with aromatic and aliphatic terminal alkynes under the optimal reaction conditions. As shown in Table 6, aryl iodide and bromide gave desired products in high yields and in reasonable reaction times (5-12 h) (entries 1-7). Moreover, this is an appropriate method for activated and deactivated aryl chlorides in reaction with aryl acetylenes to give desired products in 81–90% yields (Table 6, entries 9-11) under the same conditions, however these reactions required longer times.

To show the efficiency and the reactivity of MNP/HPG-CA/Pd catalytic system compared to some of those reported using Pd-based nanoparticle catalysts.

The comparison of MNP/HPG-CA/Pd with some reported nanocatalytic systems for the Sonogashira reaction is presented in Table 7. As shown in Table 7, our method is superior to some results from the literature in terms of the reaction condition, reaction time, yield and turnover frequency (TOF).

The importance of using heterogeneous catalysts is due to their application in industry. Additionally, the recycling and reusability of heterogeneous catalysts are very important from practical, economical and environmental points of view. Therefore, the recovery and reusability of the novel magnetic supported catalyst, was examined in the Sonogashira reaction of iodobenzene with phenylacetylene as model reaction. In each cycle, the catalytic system can be easily recovered and separated from the reaction mixture by using a magnet, and used in the next run after washing with water, diethyl ether and drying. The results showed that the catalyst could be reused for several times

Table 6. Sonogashira cross-coupling of aryl halides with aromatic or aliphatic alkynes catalyzed by MNP/HPG-CA/Pd<sup>a</sup>


| Entry | X  | R <sup>1</sup> | R <sup>4</sup>                     | Time (h) | Yield (%) <sup>b</sup> |
|-------|----|----------------|------------------------------------|----------|------------------------|
| 1     | I  | H              | Ph                                 | 5        | 93                     |
| 2     | I  | 2-Me           | Ph                                 | 5        | 93                     |
| 3     | I  | 4-MeO          | Ph                                 | 5        | 85                     |
| 4     | I  | 4-MeO          | Butyl                              | 5        | 85                     |
| 5     | Br | 4-Ac           | Pentyl                             | 7        | 92                     |
| 6     | Br | Ac             | Ph                                 | 6        | 94                     |
| 7     | Br | 4-Ac           | Butyl                              | 7        | 87                     |
| 8     | Br | H              | Pentyl                             | 7        | 85                     |
| 9     | Cl | H              | Ph                                 | 18       | 90                     |
| 10    | Cl | 4-Ac           | 3-MeOC <sub>6</sub> H <sub>4</sub> | 18       | 81                     |
| 11    | Cl | 4-MeO          | Ph                                 | 18       | 84                     |

<sup>a</sup> Reaction conditions: aryl halide (1 mmol), aryl or alkyl acetylene (1.1 mmol), K<sub>2</sub>CO<sub>3</sub> (1 mmol), MNP/HPG-CA/Pd (0.05 mol% Pd), H<sub>2</sub>O (2 mL), room temperature.

<sup>b</sup> Isolated yield based on aryl halide.

Table 7. Comparison of the results of Sonogashira coupling reactions catalyzed by MNP/HPG-CA/Pd and reported results with some other Pd catalysts

| Entry | Catalyst  | Condition   | Time (h) (Yield (%)) <sup>a</sup> | TOF (h <sup>-1</sup> ) | Ref.      |
|-------|---|---|-----------------------------------|------------------------|-----------|
| 1     | MNP/HPG-CA/Pd (0.05 mol%)                                 | K <sub>2</sub> CO <sub>3</sub> , H <sub>2</sub> O, r.t.   | 5 (93)                            | 372                    | This work |
| 2     | DAB dendr/Pd(OAc) <sub>2</sub> , G <sup>2b</sup> (1 mol%) | NEt <sub>3</sub> , N <sub>2</sub> , 25 °C                 | 40 (100)                          | 2.5                    | 29        |
| 3     | PNP-SSS <sup>c</sup> (1.2 mol%)                           | K <sub>2</sub> CO <sub>3</sub> , H <sub>2</sub> O, reflux | 3 (95)                            | 26.4                   | 30        |
| 4     | Polymer NHC-Pd complex (1 mol%) <sup>d</sup>              | CS <sub>2</sub> CO <sub>3</sub> , 60 °C                   | 3 (85)                            | 28.3                   | 16        |
| 5     | Pd(OAc) <sub>2</sub> (3 mol %)                            | TBAB, EtOH, K <sub>2</sub> CO <sub>3</sub> , 80 °C        | 6 (90)                            | 5                      | 31        |

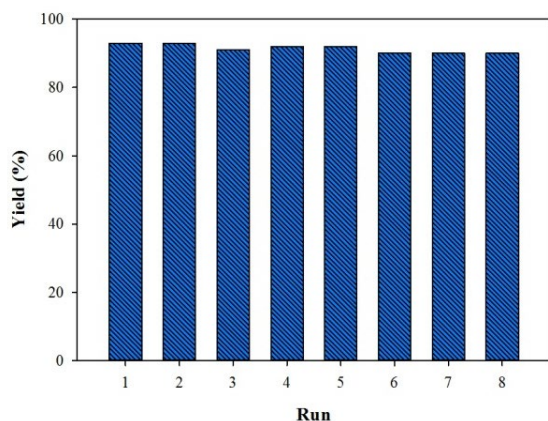
<sup>a</sup> Isolated yield.<sup>b</sup> Diaminobutanedendrimer/Pd(OAc)<sub>2</sub>.<sup>c</sup> Immobilization of Pd nanoparticles on a silica-starch substrate.<sup>d</sup> NHC = *N*-heterocyclic carbene.

Fig. 6. Reusability of the MNP/HPG-CA/Pd catalyst in the Sonogashira reaction of iodobenzene, phenylacetylen

without a significant loss of activity (Fig. 6). The analysis of palladium leaching from the catalyst by ICP indicated that only a trace amount of palladium has been leached out from the catalyst surfaces after eight cycles. The amount of palladium leached was determined by ICP-OES. The result of ICP analysis for the reaction showed no palladium species.

To establish the heterogeneity of the C-C cross coupling reaction, a hot filtering test was performed for the Heck reaction between 4-iodotoluene and styrene at 80 °C as model reaction [70]. The MNP/HPG-CA/Pd was isolated by magnet at 80 °C after 30 min and mixture of reaction was stirred, but no further progress was observed.

## CONCLUSIONS

In summary, we have demonstrated a novel phosphine-free magnetic support for immobilization of the Pd nanoparticles. The catalytic system is air- and moisture-stable, oxygen-insensitive and highly reusable. Also, because of the numerous functional

groups of support, compared to other magnetic Pd-loaded catalyst reported in literature, MNP/HPG-CA/Pd showed greatly high loading capacity of the Pd nanoparticles with extraordinary dispersion. The catalyst showed high catalytic activity for the C-C cross-coupling reactions under mild and green conditions. In particular, the catalyst can be easily recovered by using an external magnet and reused for several times, with negligible Pd leaching to the solution. Compared to the conventional separation procedures used for the recovery of solids, such as filtration and centrifugation, this method is an economic and environmentally-benign process. Besides, this system avoided the use of phosphine ligands which are dangerous for environment. We expect that this novel catalyst has more wide applications in Pd-catalyzed reactions. Additionally, these magnetic supports can be also utilized as a highly efficient adsorbent for various species such as metal ions and dyes, thus they will also find important applications in environmental technology and biotechnology.

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