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ARTICLE TYPE

Palladium supported on magnetic microgel: an efficient and recyclable catalyst for Suzuki and Heck reactions in water

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A novel heterogeneous Pd catalyst was synthesized by anchoring palladium (II) onto poly (undecylenic acid-co-*N*-isopropylacrylamide-co-potassium 4-acryloxyoylpyridine-2,6-dicarboxylate)-coated Fe_3O_4 (Fe_3O_4@PUNP) magnetic microgel. The catalyst (Fe_3O_4@PUNP-Pd) was characterized by FT-IR, TEM, VSM, XRD and XPS, and the loading level of Pd in Fe_3O_4@PUNP-Pd catalyst was measured to be 0.330 mmol g^{-1} by AAS. This catalyst exhibits excellent catalytic activity for the Suzuki and Heck reactions in water. In addition, the Fe_3O_4@PUNP-Pd catalyst can be easily separated and recovered with an external permanent magnet, and the reuse experiment shows that it can be used consecutively six times without significant loss in catalytic activity.

1 Introduction

Palladium-catalyzed Suzuki and Heck cross-coupling reactions constitute important methods for C-C bond formation in organic synthesis and industrial processes.[1,2] Currently the Heck and Suzuki reactions are performed mostly in organic solvents with homogeneous palladium salts and complexes, which bring about concerns of high cost and environmental issues at large scale. Therefore, it is highly desirable to develop reusable heterogeneous palladium catalysts which can be easily separated from the reaction systems. In addition, from the viewpoint of green chemistry, it is preferable to use water to replace toxic organic solvents as the reaction medium. However, many developed heterogeneous catalytic systems suffer from the drawbacks of low catalytic activity and selectivity, and are not suitable to be used to catalyze the reactions in aqueous media because most organic substrates dissolve poorly in water. How to solve these problems is now a major issue to chemists working in this area.[3]

Polymers are commonly used as supports for catalyst loading. Among these systems, microgels, with the advantages of nanometer scale, large surface area, and easy functionalization, has attracted widespread attention.[4,5] The microgels modified by introducing a specific ligand can be uniformly dispersed in reaction media, and as a catalyst support, they can increase the probability of contact of the reactants with the active sites of catalyst, and thus improve the latter's catalytic activity.[6,7] Biffis and his co-workers synthesized 4-vinyl pyridine-functionalized microgel-supported-Pd catalyst and applied it to the Suzuki reaction in DMA/H_2O.[8] Zhang et al.[9] prepared pH-responsive polymeric microsphere-immobilized palladium-iminodiacetic acid catalyst for the Suzuki and Heck reactions in aqueous solution. While satisfactory results were obtained in these works, but the recovery of catalyst needs cumbersome and time-consuming centrifugation and filtration.

Recently, the magnetic nanoparticles have been widely applied as solid supports for catalyst.[10-12] The magnetic nanoparticle-supported catalysts can be simply and efficiently separated from the reaction system by an external permanent magnet and thus avoid cumbersome operating process.[13,14] The organic polymer coated-magnetic nanoparticles can be stabilized in reaction media by the prevention of nanoparticle aggregation. In addition, as it is easier to functionalize the polymers by introducing various kinds of ligands, the immobilization of metal catalysts can be greatly facilitated.[15] Recently, Stevens and his co-workers[16] prepared the polystyrene coated-γ-Fe_2O_3 nanoparticle-supported-Pd catalyst, and used it for the Suzuki reaction of iodo- and bromoaromatics in DMF/H_2O. The catalyst can be easily recovered and reused by an external permanent magnet. Amorin and his coworkers[17] synthesized a very efficient dendritic Pd (II) catalyst grafted on γ-Fe_2O_3/polymer nanoparticles, which showed high reactivity and recoverability for the Sonogashira coupling in water.

On continuation of our research interest in developing heterogeneous transitional metal catalysts loaded on hydrogels and magnetic nanoparticles,[18,19] we endeavored to combine the high catalytic activity of microgel supported-catalyst with the advantages of easy separation and recycling of magnetic nanoparticles supported-catalyst by preparing a novel magnetic microgel supported-Pd catalyst (Fe_3O_4@PUNP-Pd). This catalyst shows high catalytic activity for the Suzuki and Heck reactions in water, and could be used six times without significant loss in catalytic activity. Herein we wish to report this work in detail.

2 Experimental

2.1 Materials

N-isopropylacrylamide (NIPAM, ≥ 99%) was purchased from J&K Chemicals and purified by recrystallization from hexane before use. *N*, *N*'-methylenebisacrylamide (BIS, ≥ 98%) was purchased from Sinopharm Chemical Reagent Co., Ltd. and used as received. Potassium persulfate (KPS, ≥ 99.5%) was obtained from Xi'an Chemical Reagent Factory and was purified by recrystallization from water. The chelidamic acid-functionalized monomer of potassium 4-acryloxyoylpyridine-2,6-dicarboxylate (PAP) was synthesized as described elsewhere.[19] Palladium (II) chloride ($PdCl_2$, ≥ 59.5%) was provided by Shenyang Keda Reagents Company. Tetrabutyl ammonium bromide (TBAB, ≥ 99%) was purchased from Tianjin Guangfu Fine Chemicals and used as received. Other reagents were all in analytical grade and used without further purification. Deionized water was used in the present experiments.

2.2 Characterizations

Transmission electron microscopy (TEM) images were obtained with a Tecnai-G2-F30 (FEI, USA) transmission electron microscopy operating at 300 kV. At least 50 particles were measured to obtain the average diameter of the nanoparticles. Fourier transform infrared spectra (FT-IR) were measured on a NEXUS670 (Nicolet, USA) spectrophotometer using KBr pellets of samples. X-ray diffraction (XRD) of the samples were recorded on a Shimadzu XRD-6000 spectrometer using Nicker-filter Cu K_α radiation (λ=0.15418 nm). The magnetic properties of nanoparticles were measured on a Model 7304 (Lake Shore, USA) vibrating sample magnetometer (VSM) at room temperature. The N_2 adsorption–desorption isotherms were measured at 76 K using a Micromeritics ASAP 2020M instrument. The specific surface area was calculated by the Brunauer–Emmett–Teller (BET) method. The quantity of leaching Pd was detected using an AA240 (Varian Corporation, USA) atomic absorption spectroscopy (AAS). X-ray photo-electron spectroscopy (XPS) measurements were performed on a Thermon Scientific ESCALAB250xi electron spectrometer with contaminated C as internal standard (C_{1s}=284.8 eV). The ^1H NMR (400 MHz) and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Bruker AVANCE III 400 NMR spectrometer with TMS as internal reference.

2.3 Synthesis of the Fe_3O_4@PUNP magnetic microgel

Fe_3O_4@Poly (undecylenic acid-co-*N*-isopropylacrylamide-co-potassium 4-acryloxyoylpyridine-2,6-dicarboxylate) (Fe_3O_4@ PUNP) magnetic microgel was synthesized in a two-step procedure:

Firstly, undecylenic acid-coated magnetic nanoparticles (Fe_3O_4@UA) were prepared according to a previous report by chemical co-precipitation method.[20] As a typical procedure, 0.86 g of $FeCl_2$ and 2.35 g of $FeCl_3$ were dissolved in 40 mL of deionized water, and then the solution was degassed for 30 min. After the solution was heated to 80 °C, a solution of 0.1 g of undecylenic acid in 5 mL of acetone was added, followed by 5 mL of 28% (w/w) $NH_3\cdot H_2O$. Then 1.0 g (5 × 0.2 g) of undecylenic acid was added into the mixture. The mixture was stirred vigorously for 30 min at 80 °C, and was then cooled slowly to room temperature. The mixture was precipitated with mixed solvent of acetone and MeOH (1:1 by volume), and the precipitates were isolated from the solvent by magnetic separation method. Finally, the precipitates were washed with the same mixed solvent for five times to remove the excessive undecylenic acid. The prepared Fe_3O_4@UA was dried under vacuum.

Next, In a 100 mL four-neck round-bottomed flask, 20 mg Fe_3O_4@UA was mixed with 30 mL of aqueous solution containing NIPAM (2 mmol), PAP (0.32 mmol) and BIS (0.147 mmol). After being degassed under argon gas for 30 min., the solution was heated up to 80 ºC, and 0.18 mL of 0.05 g mL^{-1} KPS solution was injected in to initiate the polymerization. After the polymerization process maintained for 4 h under argon gas with vigorous stirring, the final product was collected by magnetic separation, washed with deionized water for 5 times, and finally dried under vacuum.

2.4 Synthesis of Fe_3O_4@PUNP-Pd catalyst

Fe_3O_4@PUNP-Pd catalyst was prepared in a typical procedure as follows: Fe_3O_4@PUNP (3 mg) and $PdCl_2$ (0.001 mmol) were added into a screw-capped vial, where the molar ratio of the ligand of PAP to Pd was 3:1. The mixture was stirred at room temperature for 12 h. During the period the color of the solution turned into transparent from light yellow. The obtained catalyst was washed with deionized water to remove the excessive Pd^{2+}, and then was used directly in the coupling reaction.

2.5 General procedure for Suzuki reaction in water

To a 10 mL overpressure screw-capped vial were added sequentially aryl halide (1 mmol), arylboronic acid (1.5 mmol), K_2CO_3 (3 mmol), the Fe_3O_4@PUNP-Pd catalyst (0.1 mol% Pd based on Aryl halide) and 2 mL deionized water. The mixture was degassed under argon gas for 10 min, and then vigorously stirred at 90 ºC for 1 h. After being cooled to room temperature, the solution was diluted with deionized water, and the catalyst was separated by using an external permanent magnet. The crude product was extracted with diethyl ether (3×10 mL). (for substrates containing –OH or -COOH, the solution was diluted with deionized water, acidified with 1 mol L^{-1} HCl and then extracted with diethyl ether.) The organic phase was washed with brine, dried with $MgSO_4$, and then the solvent was evaporated under reduced pressure. The resulting residual was chromatographed on silica gel (hexane/ ethyl acetate) to give pure product which was analyzed by ^1H and ^{13}C NMR spectra.

For kinetics study, to a 10 mL overpressure screw-capped vial were added sequentially 4-iodoanisole (1 mmol), arylboronic acid (1.5 mmol), K_2CO_3 (3 mmol), the Fe_3O_4@PUNP-Pd catalyst (0.1 mol % Pd based on Aryl halide) and 2 mL deionized water. The mixture was degassed under argon gas for 10 min, and then vigorously stirred at 90 ºC for the indicated time. The reaction mixture was then treated following the aforementioned procedure, and the yield was determined according to the isolated product.

2.6 General procedure for Heck reaction in water

To a 10 mL overpressure screw-capped vial were added aryl halide (1 mmol), acrylic acid (1.5 mmol), K_2CO_3 (3 mmol), Fe_3O_4@PUNP-Pd catalyst (0.1 mol% Pd) and 2 mL deionized water. The mixture was degassed under argon gas for 10 min., and then vigorously stirred at reflux temperature (94 ºC) for 12 h. After being cooled to room temperature, the solution was diluted with deionized water, and the catalyst was separated by using an external permanent magnet. The reaction solution was acidified with 1 mol L^{-1} HCl. The solid product was filtered, washed with cold water, and then recrystallized from water and ethanol. Their structures were analyzed by ^1H and ^{13}C NMR spectra.

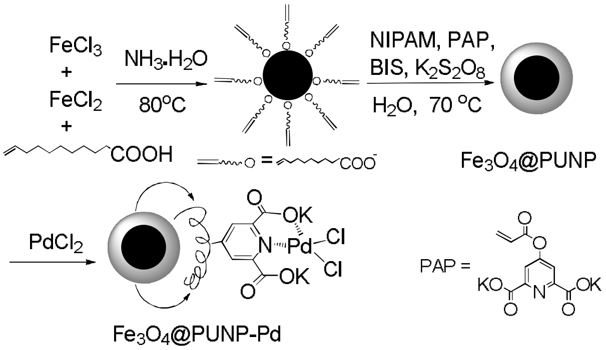
2.7 Reusability of the Fe_3O_4@PUNP-Pd catalyst

The reusability of the Fe_3O_4@PUNP-Pd catalyst was examined by applying it to the Suzuki coupling of 4-bromoacetophenone with arylboronic acid. After the first run completed, the Fe_3O_4@PUNP-Pd catalyst was separated with an external permanent magnet and washed with deionized water and diethyl ether alternately. Then the recovered catalyst was reused directly in the next run of the reaction. This process was repeated multiple times.

3 Result and Discussions

3.1 Synthesis and characterization of Fe_3O_4@PUNP magnetic microgel and Fe_3O_4@PUNP-Pd catalyst

Using well designed microgel as catalyst scaffold is advantageous in that they can be uniformly dispersed in the reaction medium, and thus the contact of reactants with active sites of the catalyst can be greatly improved.[6] On the other hand, when the magnetic nanoparticles act as supports for catalyst, they can be easily separated and recycled by an external permanent magnet, obviating the cumbersome operating process of precipitation or centrifugation.[21] We envisioned that if magnetic nanoparticles coated with functionalized microgels are used to load catalyst, the advantages of both microgels and magnetic nanoparticles would be combined. In this view, we prepared a novel Fe_3O_4@PUNP magnetic microgel via radical polymerization in water.



Scheme 1 Preparation of Fe_3O_4@PUNP magnetic microgel and Fe_3O_4@PUNP-Pd catalyst

As shown in Scheme 1, the Fe_3O_4@PUNP magnetic microgel was synthesized in two steps from commercially available stuffs. In the first step, the undecylenic acid-coated magnetic nanoparticles (Fe_3O_4@UA) were prepared by chemical co-precipitation. The purpose of this operation was to introduce onto the surface of Fe_3O_4 nanoparticles the C=C bond which would find use in the subsequent copolymerization. Next, the copolymerization of Fe_3O_4@UA with NIPAM and PAP was realized in water by using $K_2S_2O_8$ as the radical initiator. It was expected that thus formed Fe_3O_4@PUNP would bind Pd^{2+} favorably as PAP possesses excellent capacity for anchoring Pd^{2+} [19]. As such, Fe_3O_4@PUNP was then treated with an aqueous solution of $PdCl_2$ to afford the designed Fe_3O_4@PUNP-Pd catalyst. The content of Pd^{2+} in Fe_3O_4@PUNP-Pd was determined to be 0.330 mmol g^{-1} by AAS.

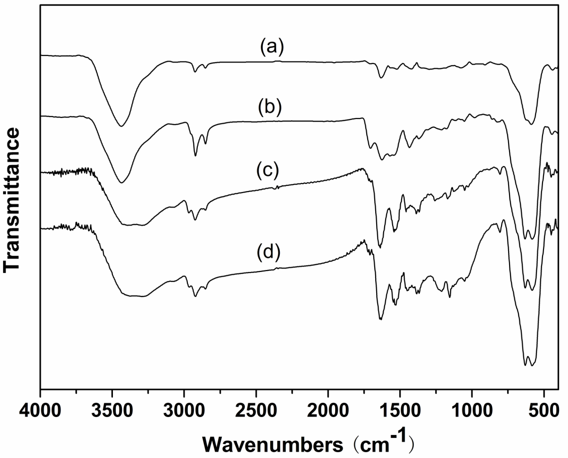


Fig. 1 FT-IR spectra of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP, (c) fresh Fe_3O_4@PUNP-Pd and (d) Fe_3O_4@PUNP-Pd after six runs

The FT-IR spectra of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP and (c) fresh Fe_3O_4@PUNP-Pd are shown in Fig. 1. In Fig. 1a, two bands located at 2925 cm^{-1} and 2853 cm^{-1} can be attributed to the aliphatic C-H stretching vibrations, and the bands at 1638 cm^{-1} and 991 cm^{-1} are assigned to the C=C stretching vibration and the C=C out-of-plane bend vibration respectively. The band at 910 cm^{-1} is assigned to the C-H out-of-plane bend vibration for the $=CH_2$ group, and the band at 588 cm^{-1} can be attributed to Fe-O stretching vibration. These characteristic bands of Fe_3O_4@UA are consistent with those reported by Shen et al.[22] In Fig. 1b, the band at 1706 cm^{-1} corresponds to the C=O stretching vibration for the PAP groups. The bands at 1625 cm^{-1}, 1570cm^{-1}, 1436 cm^{-1} can be attributed to the C=O stretching vibration (amide I band), N-H deformation vibration (amide II band), and the methyl group asymmetric bending vibrations in the PNIPAM segments respectively. The band at 582 cm^{-1} is consistent with the Fe-O stretching vibration. All the characteristic bands in the FT-IR spectrum (Fig. 1b) demonstrate that the Fe_3O_4@PUNP magnetic microgel has been successfully prepared. On complexation with Pd(II) (Fig. 1c), the intensity of the band at about 1710 cm^{-1} become obviously weaker than that of Fe_3O_4@PUNP, consistent with the formation of a metal-ligand bond.

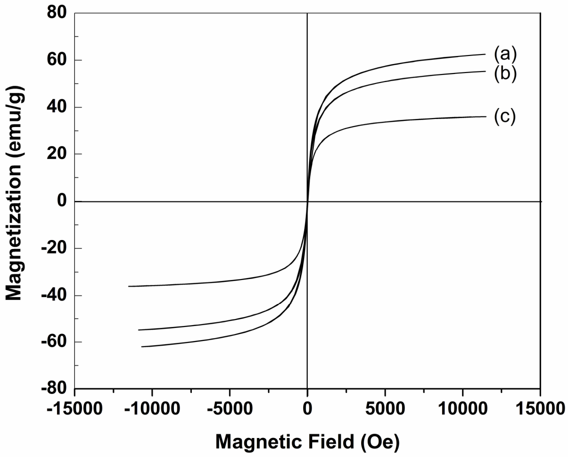


Fig. 2 Magnetic hysteresis curves of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP and (c) fresh Fe_3O_4@PUNP-Pd.

The magnetic property of magnetic materials was investigated with a vibrating sample magnetometer (VSM) at 300 K. As shown in Fig. 2, the magnetic hysteresis curves of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP and (c) fresh Fe_3O_4@PUNP-Pd reveal that they possess superparamagnetic behavior, and their saturation magnetization values are 62.5, 55.3 and 36.0 emu g^{-1} respectively, indicating that these magnetic materials can be efficiently separated by an external permanent magnet.

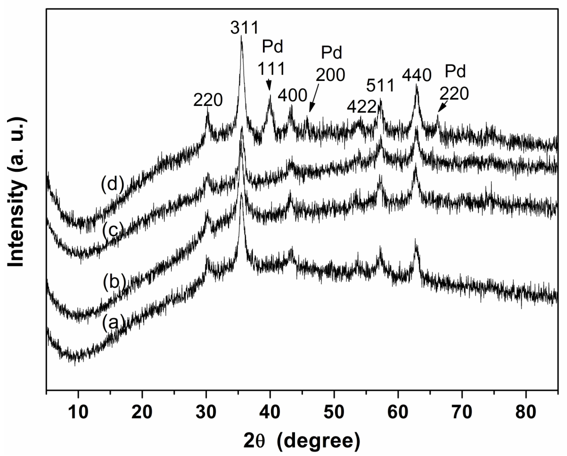


Fig. 3 XRD patterns of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP, (c) fresh Fe_3O_4@PUNP-Pd and (d) Fe_3O_4@PUNP-Pd after six runs.

The XRD patterns of the (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP and (c) fresh Fe_3O_4@PUNP-Pd are presented in Fig. 3. The characteristic diffraction peaks in the samples at 2θ of 30.2º, 35.5º, 43.3º, 53.8º, 57.2º, and 62.8º correspond to the diffraction of (220), (311), (400), (422), (511), and (440) of the Fe_3O_4. All the diffraction peaks match with the magnetic cubic structure of Fe_3O_4 (JCPDS 65-3107).[23]

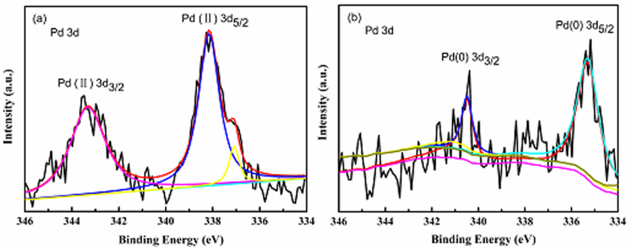


Fig. 4 XPS Pd 3d spectra of (a) fresh Fe_3O_4@PUNP-Pd and (b) Fe_3O_4@PUNP-Pd after one run.

To establish the oxidation state of Pd in Fe_3O_4@PUNP-Pd, XPS analysis was conducted, and the result is shown in Fig. 4. The binding energy of Pd $3d_{5/2}$ and $3d_{3/2}$ for the fresh Fe_3O_4@PUNP-Pd is found to be 338.2 and 343.2 eV (Fig. 4a), indicating that the loaded palladium is in its II state.[24]

The TEM images of (a) Fe_3O_4@UA, (b) Fe_3O_4@PUNP and (c) fresh Fe_3O_4@PUNP-Pd catalyst are presented in Fig. 5. The obtained Fe_3O_4@UA nanoparticles have an average diameter of 9.05 ± 1.91 nm (Fig. 5a). Fe_3O_4@PUNP microgels have the average diameter of 10.85±2.52 nm (Fig. 5b). After the loading of Pd^{2+} (Fig. 5c), the fresh Fe_3O_4@PUNP-Pd catalyst had an average diameter of 11.55±2.14 nm. The nitrogen adsorption–desorption measurement indicates that the catalyst had a specific surface area of 31.9 m^2 g^{-1} (see ESI, Fig. S1).

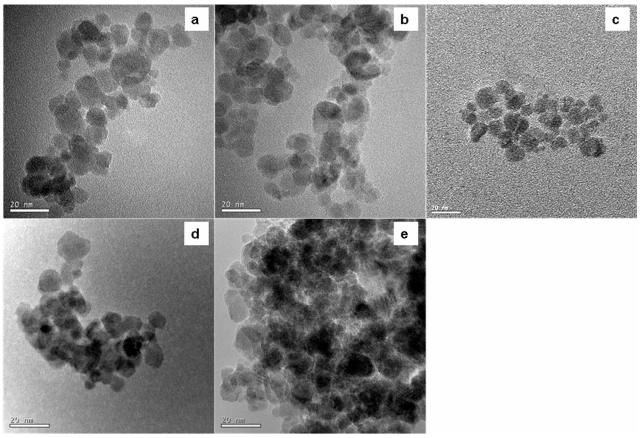
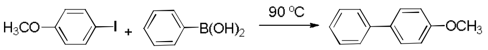


Fig. 5 TEM images of (a) Fe_3O_4@ UA, (b) Fe_3O_4@PUNP, (c) fresh Fe_3O_4@PUNP -Pd, (d) Fe_3O_4@PUNP-Pd after one run and (e) Fe_3O_4@PUNP-Pd after six runs.

3.2 Fe_3O_4@PUNP-Pd catalyzed Suzuki reaction in water

Following the successful preparation of Fe_3O_4@PUNP-Pd, its effectiveness for the Suzuki coupling reaction was examined next. It is known that the Suzuki reaction is largely effected by the type of alkaline and the amount of catalyst used.[25-29] Therefore, firstly the reaction of 4-iodoanisole with phenylboronic acid was used as a model reaction for the screening of bases, and the results were summarized in Table 1 (entries 1-5). With the amount of catalyst fixed as 0.1 mol %, the reaction proceeded well when organic bases such as triethylamine and piperidine were used, affording the desired coupling product in excellent yields (entries 1 and 2),. However, the yield was considerable lower with tributylamine as the base (entry 3). The decrease in yield with tributylamine is probably because the solubility of tributylamine is low in water. Excellent result was also obtained when inorganic base K_2CO_3 (entry 5) was used. By comparison, $NaHCO_3$, a weaker inorganic base, was less effective for the reaction (entry 4). As K_2CO_3 was the most efficient base for the present catalytic system, it was chosen for subsequent investigations. Further experiments showed that 0.1 mol% amount of catalyst were sufficient to guarantee a clean and complete conversion. When the amount of catalyst was reduced to 0.05 mol% under the otherwise same conditions as shown in entry 5, Table 1, the yield decreased to 72% (entry 6). On the other hand, using 0.2 mol% catalyst didn't increase the yield significantly (entry 7).

Table 1 Optimization of the reaction conditions for Suzuki reaction of 4-iodoanisole with phenylboronic acid catalyzed by Fe_3O_4@PUNP-Pd [a]



Entry	Base	Catalyst (mol %)	Yield (%) [b]
1	Et_3N	0.1	95
2	Piperidine	0.1	93
3	t-Bu_3N	0.1	80
4	$NaHCO_3$	0.1	85
5	K_2CO_3	0.1	96
6	K_2CO_3	0.05	72
7	K_2CO_3	0.2	97

[a] Reaction conditions: 1 mmol 4-iodoanisole, 1.5 mmol phenylboronic acid, 3 mmol base, Fe_3O_4@PUNP-Pd catalyst, 2 mL deionized water and argon atmosphere. [b] Isolated yield.

With the optimized reaction conditions in hand, the scope of the Fe_3O_4@PUNP-Pd-catalyzed Suzuki reactions was investigated by

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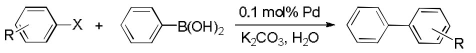
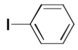
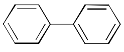
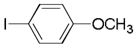
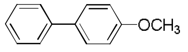
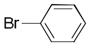
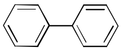
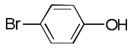
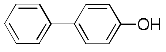
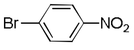
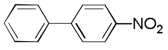
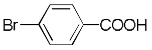
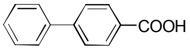
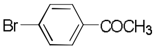
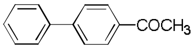
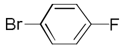
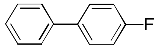
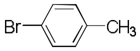
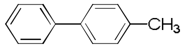
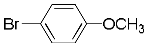
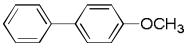
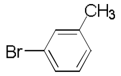
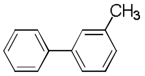
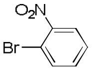
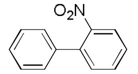
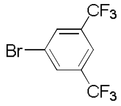
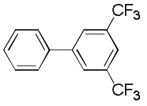
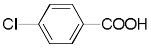
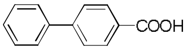
employing various substituted aryl halides to react with arylboronic acid. The results are summarized in Table 2. With iodobenzene and 4-iodoanisole as the reactants, the reaction finished in 1 h, forming the corresponding coupling products in yields of 98% and 96% (entries 1 and 2) respectively. The reaction of substituted bromobenzenes, such as p-OH, p-NO_2, p-COOH, p-$COCH_3$ as well as bromobenzene, also afforded satisfactory yields (95-97%) in 1 h (entries 3-7). The yield was a little lower when 4-bromofluorobenzene was used as the substrate (entry 8). The reaction of 4-bromotoluene with phenylboronic acid was not complete in 1 h, but when the reaction time was extended to 3 h, the coupling product was obtained in 91% yield (entry 9). On the other hand, the Suzuki reaction of 4-bromoanisole with phenylboronic acid proceeded poorly under the same conditions, and only 10 % yield was obtained. However, when TBAB was added to the reaction mixture, a satisfactory yield of 90% was achieved in 1 h (entry 10). Similar phenomena were also observed when the protocol was applied to the *ortho*- and *meta*-substituted aryl halides (entries 11 and 12). The beneficial effect of TBAB was exhibited the most in the case of 3,5-ditrifluoromethyl bromobenzene, where the reaction hardly took place without TBAB, but proceeded very well in its presence (entries 13). It is noteworthy that hydrophilic 4-chlorobenzoic acid could also react with phenylboronic acid by the action of 0.1 mol% Fe_3O_4@PUNP-Pd to afford the coupling product in 68% yield (entry 14), albeit that elevated temperature (reflux) and longer time (5 h) were required.

Mechanistically, the Suzuki coupling reactions start with the oxidative addition of C-X bond to Pd (0), and under all the circumstances, the active catalyst is Pd (0). In cases where Pd (II) is used as the catalyst, it has to be firstly reduced *in situ* to Pd (0). During the preparation of Fe_3O_4@PUNP-Pd, we did not use any reductant to reduce Pd (II) to Pd (0). In deed, the XPS analysis of the freshly prepared Fe_3O_4@PUNP-Pd indicates that there is no Pd (0) species on its surface. Therefore, there must be some species in the reaction system responsible for the generation of Pd (0). One possibility is that phenylboronic acid could act as the reductant, as proposed by Köhler et al.[30] On the other hand, Veinot et al.[31] recently reported a solid palladium catalyst (II) supported on iron/iron oxide nanoparticles which are also effective for the Suzuki coupling reactions. They believed that the iron/iron oxide nanoparticles themselves could reduce palladium (II). Considering the relevance of these studies to ours, we think that both of these mechanisms might explain the high catalytic capacity of Fe_3O_4@PUNP-Pd. Evidence to support the hypothesis was provided by the XPS study of the catalyst after reaction. As shown in Fig. 4b, the XPS Pd 3*d* spectrum of the recovered Fe_3O_4@PUNP-Pd shows the binding energies of Pd $3d_{5/2}$ and Pd $3d_{3/2}$ at about 335.2 and 340.6 eV respectively, which can be attributed to the Pd (0) species.[31,32] This result confims tha formation of Pd (0) during the reaction process.

Table 2 Fe_3O_4@PUNP-Pd-catalyzed Suzuki reactions in water [a]



Entry	Aryl halide	Product	Temp. (ºC)	Time (h)	Yield [b] (%)
1			90	1	98
2			90	1	96
3			90	1	95
4			90	1	96
5			90	1	97
6			90	1	96
7			90	1	96
8			90	1	80
9			90	1 3	40 91
10			90	1 1	10 90 [c]
11			90	1 1	40 92 [c]
12			90	1 5 5	28 53 83 [c]
13			90	1 3	Trace 90 [c]
14			reflux	1 5	Trace 68

[a] Reaction conditions: 1 mmol aryl halide, 1.5 mmol phenylboronic acid, 0.1 mol% Fe_3O_4@PUNP-Pd catalyst, 3 mmol K_2CO_3, 2 mL deionized water and argon atmosphere. [b] Isolated yield. [c] 2 mmol TBAB was used.

In order to evaluate the efficiency of the Fe_3O_4@PUNP-Pd catalyst, the present catalytic system was compared with some other magnetic nanoparticles-supported catalysts. As shown in Table 3, for the reaction of bromobenzene with phenylboronic acid, Fe_3O_4@PUNP-Pd was the most efficient catalyst, with the highest apparent turnover frequencies (TOF) of 950 h^{-1} (entry 1). In addition, with Fe_3O_4@PUNP-Pd as the catalyst, the reaction can be realized in water which is not only cheap and readily available, but also non-toxic and non-flammable.

Table 3 Performance of different magnetic nanoparticle-supported Pd catalysts for the reaction of bromobenzene with phenylboronic acid

Entry	Pd catalyst (mol%)	Time (h)/ Temp (°C)	Medium	Yield [a] (%)	TOF [b] (h^{-1})	Ref
1	Fe_3O_4@PUNP-Pd (0.1)	1/90	H_2O	95	950	This work
2	Pd-Fe_3O_4@C (1)	2/60	EtOH	99	46.2	32
3	Pd-Fe_3O_4@C (6)	1/reflux	EtOH	98	16.3	33
4	Xerogel g1-MNPs (1)	5 /60	MeOH	89	17.8	34
5	Fe_3O_4-Bpy-$Pd(OAc)_2$ （2）	12/80	Toluene	> 99	4.2	35
6	Pd@Mag-MSN (1)	6/80	Dioxane	77	12.8	36
7	Fe@Fe_xO_y/Pd (0.5)	4/ R.T	H_2O/EtOH (1:1)	95	47.5	31
8	Pd/$NiFe_2O_4$-300 (0.08)	12/80	NMP/H_2O （5:2）	97	101	37
9	Pd/Fe_3O_4 (1)	24/reflux	DME/H_2O （3:1）	70	2.9	38
10	Pd/$NiFe_2O_4$ (1)	0.5/ 90	DMF/H_2O (1:1)	98	196	39

[a] Isolated yield. [b] The apparent TOF value was measured as moles of product with per mole of Pd catalyst per hour.

Furthermore, the reaction kinetics of Suzuki reaction of 4-iodoanisole with phenylboronic acid with 0.1 mol% Fe_3O_4@PUNP-Pd as catalyst was investigated, and the result is shown in Fig. 6a. The yield of 4-methoxybiphenyl increased quickly with reaction time until it reached 96% at 60 min. The high efficiency of Fe_3O_4@PUNP-Pd catalyst can be attributed to the uniformly dispersion Fe_3O_4@PUNP-Pd in the reaction medium and its large surface area. Both factors would increase the probability of contact between reactants and the active sites of Fe_3O_4@PUNP-Pd, and thus improve the catalyst's performance.[40]

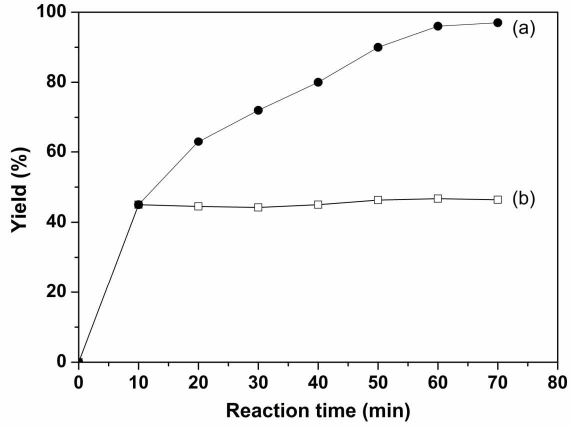
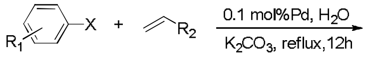


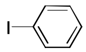
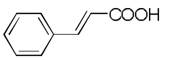
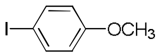
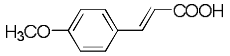
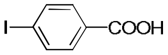
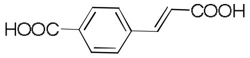
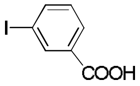
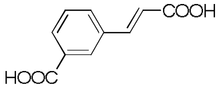
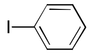
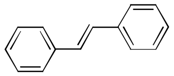
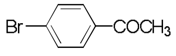
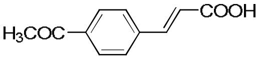
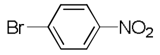
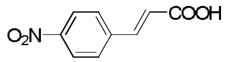
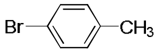
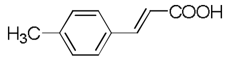
Fig. 6 The kinetic plots of Suzuki reaction of 4-iodoanisole with phenylboronic acid. (a) Normal reaction kinetics; (b) Reaction kinetics after the catalyst being removed from the reaction at 10 minutes. Reaction conditions: 1 mmol 4-iodoanisole, 1.5 mmol phenylboronic acid, 0.1 mol% Fe_3O_4@PUNP-Pd catalyst, 3 mmol K_2CO_3, 2 mL deionized water and argon atmosphere. The yields are isolated yields.

3.3 Fe_3O_4@PUNP-Pd catalyzed Heck reaction in water

Encouraged by the satisfactory results with the Suzuki reaction, the Fe_3O_4@PUNP-Pd catalyst was applied to the Heck reaction next. Toward this end, 0.1 mol% of Fe_3O_4@PUNP-Pd was used to effect in the reaction of aryl halides with vinyl substrates in water. As shown in Table 4, the Heck reactions of various aryl iodides with hydrophilic acrylic acid proceeded well in H_2O at reflux temperature, resulting in the formation of cinnamic acids in yields of 91-96 % (entries 1-4). The substituents at the phenyl ring of aryl iodides had no significant effect on the reaction consequence. Iodobenzene did not react with hydrophobic styrene in H_2O, but when a mixed solvent of H_2O/DMF (1:1 by volume) was used, the reaction took place, and a satisfactory yield of 95% was achieved in 8 h (entry 5). This protocol is also applicable to aryl bromides. Both electron-withdrawing and electron-donating group substituted aryl bromides, such as 4-bromoacetophenone, 4-nitroacetophenone and 4-bromotoluene, can be smoothly converted to the corresponding coupling products in high yields (entries 6-8).

Table 4 Fe_3O_4@PUNP-Pd-catalyzed Heck reactions in water [a]



Entry	Aryl halide	Product	Time (h)	Yield [b] (%)
1			12	96
2			12	91
3			12	94
4			12	96
5			12 8	trace 95 [c]
6			12	89
7			12	90
8			12	91

[a] Reaction conditions: 1 mmol aryl halide, 1.5 mmol vinyl substrates, 0.1 mol% Fe_3O_4@PUNP-Pd, 3 mmol K_2CO_3, 2 mL deionized water and argon atmosphere. [b] Isolated yield. [c] A mixed solvent of H_2O/DMF (1:1 by volume) was used.

3.4 The reusability of the Fe_3O_4@PUNP-Pd catalyst

The reusability of the Fe_3O_4@PUNP-Pd catalyst was evaluated by using the Suzuki coupling of 4-bromoacetophenone with phenylboronic acid as the model reaction. The procedure is simple: the Fe_3O_4@PUNP-Pd catalyst was firstly applied to the reaction, and then recovered after reaction complete by separating it from the reaction mixture with an external permanent magnet, washing it with H_2O and diethyl ether alternatively. It was reused directly for the next cycle without further treatment. Our recycling experiment showed that the yield maintained in the range of 94-96% before the fifth run, and still reached 88% at the sixth run (Table 5).

Subsequently, the leaching of Pd after the sixth run was analyzed by AAS, which gave the values of 0.24 ppm and 0.47 ppm in the diethyl ether and aqueous phases respectively. The result indicates that the Fe_3O_4@PUNP-Pd catalyst are stable under the experiment conditions. A few catalytic tests were further

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conducted to assess the impact of palladium leaching: (1) the magnetic catalyst was removed from the reaction system after 10 minutes and the reaction kinetics was monitored from then on. As shown in Fig. 6b, after the catalyst was removed, the yield stopped to increase, remaining almost constant (44-47%); (2) as mentioned above, there was 0.47 ppm of Pd detected leaching into the supernatant during the course of the reaction. Correspondingly, a control experiment was conducted with the same equivalent of $PdCl_2$ (0.47 ppm) as the catalyst. We found that only a tiny amount of product (2%, GC yield) formed after one hour, with most of the reactant remained. From these analyses we concluded that effect of palladium leaching was negligible for the present catalyst system.

Table 5 Reusability of Fe_3O_4@PUNP-Pd catalyst in the Suzuki reaction 4-bromoacetophenone with phenylboronic acid[a]

Runs	1	2	3	4	5	6
Yield[b] (%)	96	95	96	94	90	88

[a] Reaction conditions: 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, 0.1 mol% Fe_3O_4@PUNP-Pd, 3 mmol K_2CO_3, 2 mL deionized water and argon atmosphere. [b] Isolated yield.

To gain a deep insight on the stability of Fe_3O_4@PUNP-Pd, its structure was analyzed by FT-IR, XRD and TEM after being recovered from reaction mixture. Fig. 1d shows the FT-IR spectrum of Fe_3O_4@PUNP-Pd after three runs. The weak band at about 1710 cm^{-1} indicates that the metal-ligand bond still exists in the reused Fe_3O_4@PUNP catalyst. Fig. 3d shows that the XRD image of Fe_3O_4@PUNP-Pd after the six run, from which we can see that the crystalline phase of Fe_3O_4 did not change during the reaction. Compared with Fig. 3c, new peaks appear at 2θ of 40.1 °, 46.0 ° and 67.3°. These peaks are due to the (111), (200), and (220) reflections of the face-centred cubic Pd lattice,[41] revealing that Pd (0) nanoparticles were formed during the reaction.[30,31] The TEM images of the recycled Fe_3O_4@PUNP-Pd shows that after the first run, there were a part of palladium (0) nanoparticles dispersed onto the surface of the magnetic nanoparticles support (Fig. 5d). After six cycles (Fig. 5e), Pd nanoparticles have aggregated into bigger particles on the surfaces of the matrices.[19] The aggregation of Pd probably led to the reduction in catalytic activity after multiple runs.[35]

4 Conclusions

In summary, a novel heterogeneous Pd catalyst has been developed by supporting Pd (II) onto the Fe_3O_4@PUNP magnetic microgel. This Fe_3O_4@PUNP-Pd catalyst not only exhibits impressive catalytic capacity to effect the Suzuki and Heck reactions in water, but also possesses high stability. It can be used for at least six consecutive runs without significant loss of its catalytic activity. In addition, as magnetic nanoparticles were used as the solid support, the present catalyst can be simply recovered from the reaction mixture by an external permanent magnet, and then put to use again after washing with water and ethyl ether. The merits associated with Fe_3O_4@PUNP-Pd hopefully will render it a valuable catalyst in practical synthesis.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [BET surface analysis, ^1H and ^{13}C NMR spectra data of the products]. See DOI: 10.1039/b000000x/

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