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Magnetic Nanoparticles-Supported Palladium: A Highly Efficient and Reusable Catalyst for the Suzuki, Sonogashira, and Heck Reactions

Pinhua Li,[a,b] Lei Wang,[a,c,*] Lei Zhang,[a] and Guan-Wu Wang[b,*]

[a] Department of Chemistry, Huaibei Normal University, Huaibei, Anhui 235000, People's Republic of China
Fax: (+86)-561-3090-518; phone: (+86)-561-3802-069; e-mail: leiwang@chnu.edu.cn
[b] Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, People's Republic of China
E-mail: gwang@ustc.edu.cn
[c] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, People's Republic of China

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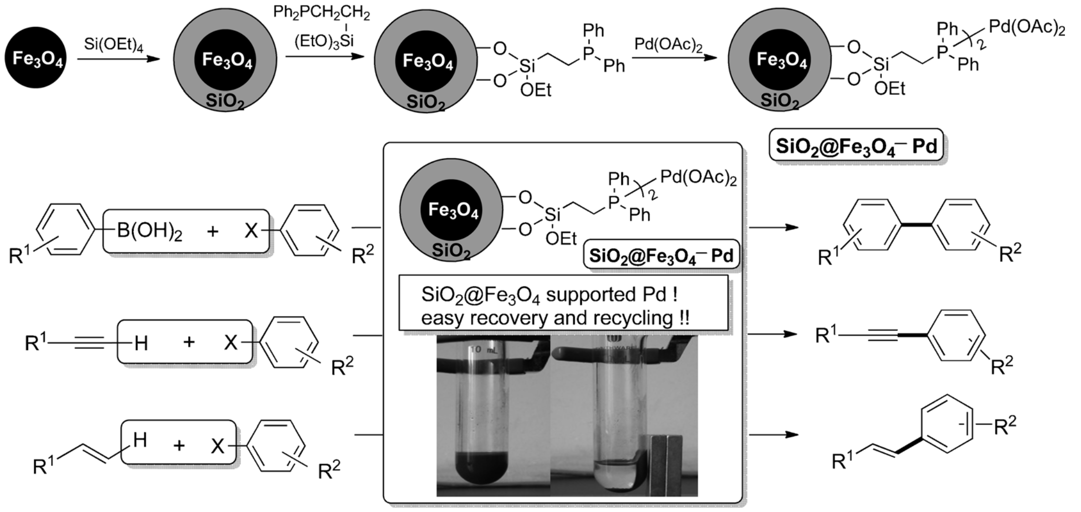
Abstract: A highly efficient, air- and moisture-stable and easily recoverable magnetic nanoparticle-supported palladium catalyst has been developed for the Suzuki, Sonogashira and Heck reactions. A wide range of substrates was coupled successfully under aerobic conditions. In particular, the performance of the magnetic separation of the catalyst was very efficient, and it is possible to recover and reuse it at least eight times without significant loss of its catalytic activity.

Keywords: Heck reaction; magnetic nanoparticles-supported palladium; reusable catalyst; Sonogashira reaction; Suzuki coupling

Introduction

Transition metal-catalyzed cross-coupling reactions have contributed greatly to the facile and efficient construction of carbon-carbon and carbon-heteroatom bonds,[1] and they have emerged as powerful tools for advanced organic synthesis in both academic[2] and industrial laboratories.[3] It is well known that the palladium-catalyzed Suzuki coupling, Sonogashira reactions and Heck reactions are all very important and powerful strategies for the formation of carbon-carbon bonds, and the 2010 Nobel Prize in chemistry was awarded to three scientists, Heck, Negishi and Suzuki for their work on palladium-catalyzed cross-couplings in organic synthesis.[4] In the past decades, significant progress in this area has been achieved with a variety of homogeneous palladium catalysts.[5] However, homogeneous catalysis suffers from the problematic separation of the expensive catalyst. Furthermore, homogeneous catalysis might result in heavy metal contamination of the desired isolated product. These problems are of particular environmental and economic concern in large-scale syntheses. Heterogenization of the existing homogeneous catalysts, especially expensive and/or toxic heavy metal complexes could be an attractive solution to these problems.[6] There has been considerable interest in the development of supported catalytic systems that can be efficiently recycled and reused whilst keeping the inherent catalytic activity. Various inorganic and organic supports have been explored, such as mesoporous silica,[7] ionic liquids[8] and polymers.[9] It is pleasing to find that the covalent grafting of such supports with homogeneous catalysts often provides good catalytic activity together with the possible recovery of the catalyst system by a simple process.

Magnetic nanoparticles have been studied widely for various biological and medical applications,[10] and most recently, they have emerged as smart and promising supports with great industrial potential for immobilization because the magnetic nanoparticles-supported catalysts can be easily separated from the reaction medium by application of an external permanent magnet, which achieves simple separation of the catalysts without filtration.[11] During recent years, magnetic nanoparticles-supported palladium catalysts have been developed for the carbon-carbon bond formation reactions. In 2005, Gao and his co-workers have prepared super-paramagnetic nanoparticles-supported NHC-Pd complexes, which were efficient cata-



Scheme 1. Preparation of the magnetic nanoparticle-supported palladium catalyst and its applications in Suzuki, Sonogashira and Heck reactions.

lysts for Suzuki, Heck, and Sonogashira cross-coupling reactions.[12] Subsequently, Zhu et al. have also developed a magnetic nanoparticles-supported ultra small palladium catalyst for Suzuki couplings and Heck reactions, but merely moderate to good yields of the desired products were obtained.[13] In 2008, Xia and his colleagues have developed a magnetically-separable palladium catalyst for carbonylative Sonogashira reactions in the synthesis of α,β-alkynyl ketones.[14] It is worth noting that Manorama et al. have developed a magnetically separable palladium catalyst, which was highly active in Suzuki and Heck coupling reactions with a range of aryl halides, moreover, the catalyst was equally active towards the chloro derivatives.[15] Most recently, Thiel and his co-workers have reported the synthesis of a magnetically recoverable palladium(II)-phosphine catalyst for the Suzuki reactions, however, the preparation of the supported catalyst was not convenient.[16] More importantly, all the above-mentioned supported catalysts could be easily separated from the reaction mixture by simple magnetic attraction, and no significant loss of the catalytic activity was observed after several consecutive reaction cycles. It is thus desirable to develop more efficient and simple magnetic nanoparticles-supported palladium catalysts for the carbon-carbon bond formation reactions.

In continuation of our efforts to develop economical and eco-friendly synthetic pathways for organic transformations from the viewpoint of green chemistry,[17] here we wish to report the synthesis of a simple, highly efficient, air- and moisture-stable and magnetically recoverable palladium-phosphine catalyst for the Suzuki, Sonogashira and Heck reactions under aerobic conditions (Scheme 1). The catalyst shows a high catalytic activity in the above-mentioned classic carbon-carbon bond formation reactions. In particular, easy catalyst recovery and excellent recycling efficiency of the catalyst make it an ideal system for these reactions under mild reaction conditions. We demonstrated that it is possible to recover and reuse the grafted catalyst at least eight times without significant loss of its catalytic activity.

Results and Discussion

The magnetic nanoparticles-supported palladium catalyst was synthesized according to the procedure summarized in Scheme 1. The silica-coated Fe_3O_4 ($SiO_2@Fe_3O_4$) was prepared according to the literature method:[11c,16,18] commercially available Fe_3O_4 nanoparticles, with an average diameter of 10 nm after sonication, were coated with a thin layer of silica using a sol-gel process to give silica-coated Fe_3O_4. TEM images of the $SiO_2@Fe_3O_4$ showing the structure of the particles and the silica coating, which has a thickness of about 10 nm, are presented in Figure 1. The phosphine can be anchored easily onto the surface of the $SiO_2@Fe_3O_4$ by using 2-(diphenylphosphino)ethyltriethoxysilane $[Ph_2P(CH_2)_2Si(OEt)_3]$[19] under reflux in toluene for 24 h, with a loading of 0.18 mmol of phosphine per gram, which was quantified *via* CHN microanalysis on the basis of the carbon content determination. The supported Pd catalyst (Figure 1) was obtained by simply dissolving $Pd(OAc)_2$ in THF and treating it with the above phosphine-functionalized $SiO_2@Fe_3O_4$, with a loading of 0.049 mmol of palladium per gram determined *via* inductively coupled plasma atomic emission spectrometry (ICP-AES). XRD measurements of the supported catalyst are shown in Figure 2

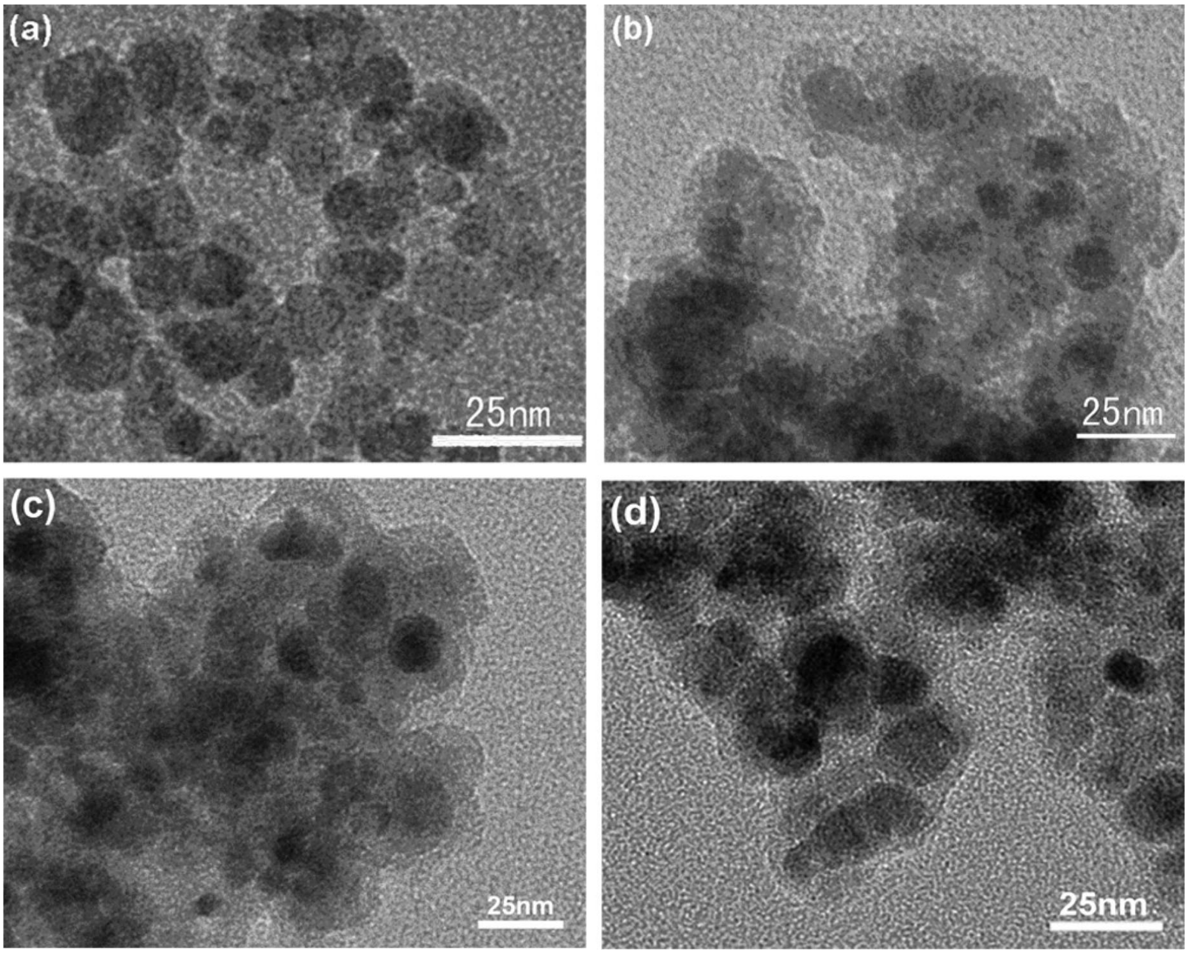


Figure 1. TEM images: (**a**) Fe_3O_4 nanoparticles; (**b**) $SiO_2@Fe_3O_4$; (**c**) $SiO_2@Fe_3O_4$–Pd catalyst; (**d**) recycled $SiO_2@Fe_3O_4$–Pd catalyst.

and exhibit diffraction peaks corresponding to the typical spinel maghemite structure whereas the diffraction peak of the layered amorphous silica was not obvious, and no peaks characteristic for palladium(0) nanoparticles were observed, which proves the excellent dispersion of the palladium sites on the magnetic nanoparticles. The structure of supported palladium catalyst was also verified by X-ray photoelectron spectroscopy (XPS) determination. The electron binding energy analysis shown in Figure 3 indicates that the oxidation state of palladium in freshly prepared catalyst was Pd(II), which coordinated to two phosphorus atoms.[11d,16] However, the state of palladium in the used catalyst was mainly Pd(0), which could be coordinated to four P-ligands.

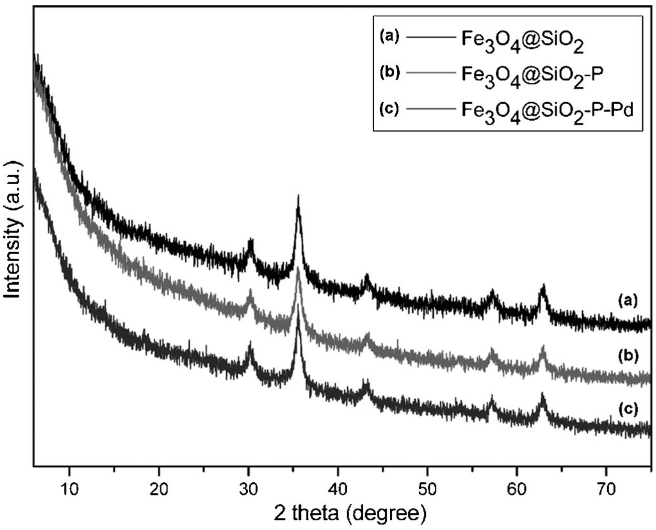


Figure 2. XRD of the supported Pd catalyst.

First, the Suzuki coupling reaction was investigated in the presence of the magnetic nanoparticle-supported catalyst. Initial experiments with 4-bromoanisole and phenylboronic acid were performed to optimize the reaction conditions (base, solvent, and reaction temperature, see Table 1 in the Supporting Information for details). For the base, K_3PO_4 gave better conversions than other bases, such as Na_3PO_4, K_2CO_3, Na_2CO_3, Cs_2CO_3, KOH, KF, NaOAc, Et_3N and DBU.

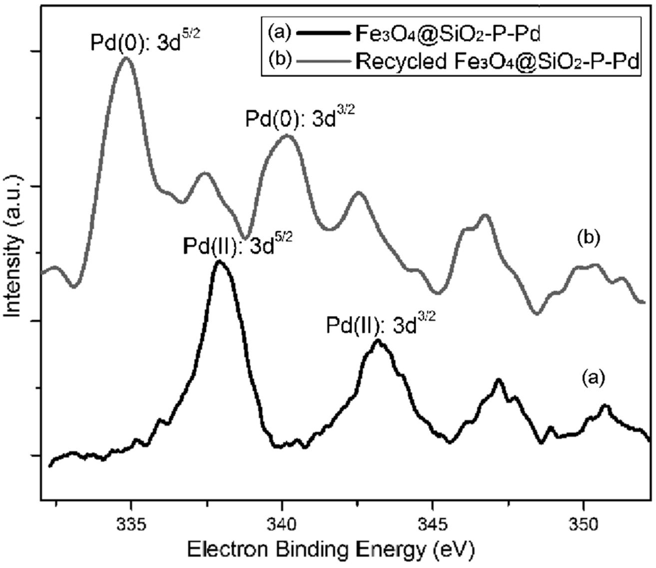


Figure 3. XPS of the supported Pd catalyst

On the other hand, for the solvent, methanol is the first choice among a series of other solvents, such as ethanol, *i*-PrOH, CH_3CN, DMF, DMA, DMSO, THF, dioxane, NMP, DCE, toluene, benzene, hexane, H_2O and $MeOH/H_2O$ (1/1, v/v), and for the temperature, 60 °C is the best choice. The coupling reaction could be catalyzed by $PdCl_2$, $Pd(OAc)_2$, $Pd(PPh_3)_2Cl_2$, or $Pd(PPh_3)_4$, but, their catalytic activities are inferior to that of $Fe_3O_4@SiO_2$–Pd. The reactions were generally complete within 1–2 h at 60 °C. It was worthy of note that the reactions could also be completed in 12 h at room tempreture. We have also screened the amount of supported palladium catalyst, and a 0.50 mol% loading of palladium in $SiO_2@Fe_3O_4$-Pd was found to be optimal.

With the optimized reaction conditions (0.50 mol% loading of palladium, K_3PO_4, MeOH, 60 °C, 1.5 h), we examined the scope of the supported palladium-catalyzed Suzuki coupling reactions on a series of different substrates (Table 1). A wide array of electronically diverse aryl bromides, and chlorides in the reaction with phenylboronic acid was examined. As can be seen from Table 1, aryl bromides bearing electron-withdrawing and electron-donating groups, as well as 1-bromonaphthalene, coupled efficiently with phenylboronic acid, and generated the corresponding products in excellent yields at 60 °C within 1.5 h (Table 1, entries 1–11). And also, 2-bromopyridine, 3-bromopyridine and 3-bromoquinoline were also able to undergo the coupling reactions with phenylboronic acid smoothly and generate the desired cross-coupling products in excellent yields under the present reaction conditions (Table 1, entries 12–14). Notably, 1,4-dibromobenzene (1.0 equiv.) could also undergo the coupling reaction with arylboronic acid (2.4 equiv.) to generate the corresponding di-coupled products in 90% yields (Table 1, entry 15).

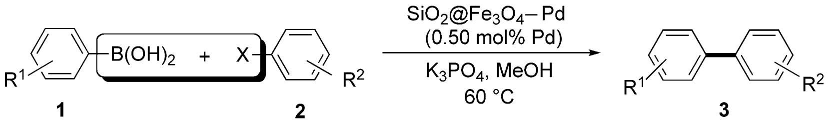
Moreover, the less reactive and less expensive aryl chlorides also showed moderate reactivity in the presence of the supported palladium catalyst $SiO_2@Fe_3O_4$–Pd: 4-cyanochlorobenzene and 4-nitrocholorobenzene reacted with phenylboronic acid to generate the corresponding cross-coupling products in moderate yields, but the reaction of 4-choloroanisole with phenylboronic acid gave a poor result (Table 1, entries 16–18). On the other hand, arylboronic acids bearing electron-withdrawing and electron-donating groups on the aryl rings, also coupled efficiently with 4-bromoanisole, 2-bromoanisole and bromobenzene, and the excellent yields of the corresponding products were obtained (Table 1, entries 19–24).

It is important to note that the supported palladium-catalyzed Suzuki cross-coupling could tolerate *ortho*-substituted aryl halides, as well as arylboronic acid (Table 1, entries 2, 20 and 22–24). The reactions of 2-bromoanisole with phenylboronic acid, 2-chlorophenylboronic acid with 4-bromoanisole, 2-methoxyphenylboronic acid with 4-bromoanisole, 2,4-dimethoxyphenylboronic acid with bromobenzene, and 2-methoxyphenylboronic acid with 2-bromoanisole, were carried out under the present reaction conditions, and the desired products were obtained in excellent yields (Table 1, entries 2, 20 and 22–24).

Next, we examined the Sonogashira coupling reaction of various aryl iodides and bromides with terminal alkynes in the presence of the supported catalyst $SiO_2@Fe_3O_4$–Pd (Table 2). Gratifyingly, we were able to perform the efficient copper-free Sonogashira coupling reactions of aryl iodides and activated aryl bromides under the optimized reaction conditions (1.0 mol% loading of palladium, K_2CO_3, DMF, 100 °C, 6 h, see Table 2 in the Supporting Information for details), and most of the coupling reactions proceeded completely and generated the corresponding products in good to excellent yields (Table 2, entries 1–8, 10–12, and 14–19), while with an *ortho*-substituted aryl iodide, a relatively lower yield was isolated under the present reaction conditions (Table 2, entry 2 *vs.* 4). For the Sonogashira cross-coupling of a neutral aryl bromide with terminal alkyne, for example, the coupling of bromobenzene and 1-bromonaphthalene with phenylacetylene, generated the corresponding products in 71 and 79% yields under the optimized conditions respectively, which is inferior to the reactions of aryl iodides and activated aryl bromides with phenylacetylene (Table 2, entries 9 and 13 *vs.* 1–8 and 10–12).

However, this catalytic system was no longer effective for the couplings of aryl chlorides with terminal alkynes. No desired Sonogashira coupling product was obtained for the reactions of aryl chlorides with phenylacetylene, and the starting materials were recovered unchanged under the present reaction condi-

Table 1. Suzuki coupling reactions of aryl halides with arylboronic acids.[a]



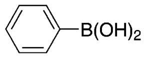
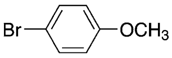
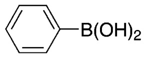
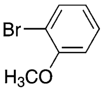
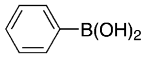
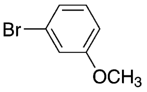
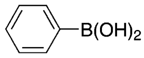
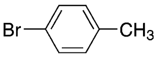
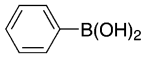
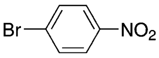
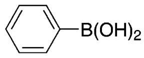
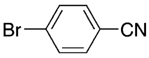
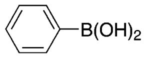
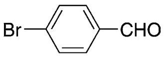
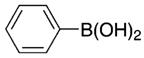
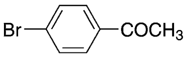
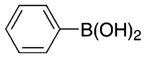
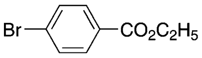
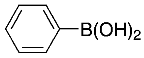
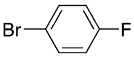
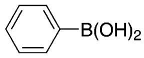
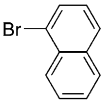
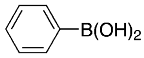
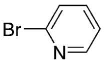
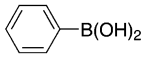
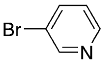
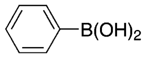
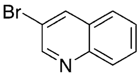
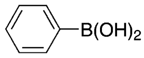
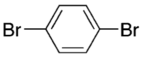
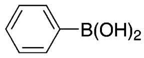
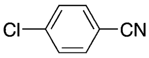
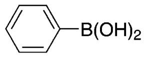
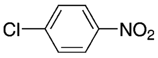
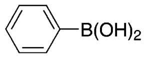
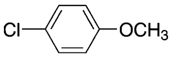
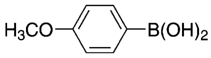
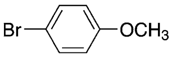
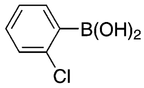
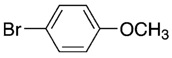
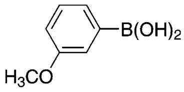
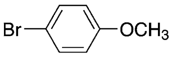
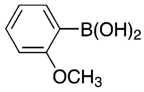
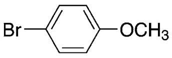
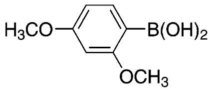
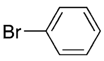
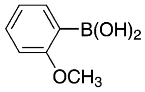
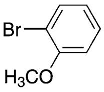
Entry	Arylboronic acid	Aryl halide	Product **3**	Yield[b] [%]
1			**3a**	99
2			**3b**	99
3			**3c**	99
4			**3d**	99
5			**3e**	99
6			**3f**	99
7			**3g**	98
8			**3h**	99
9			**3i**	98
10			**3j**	99
11			**3k**	97
12			**3l**	92
13			**3m**	99
14			**3n**	95
15[c]			**3o**	90
16[d]			**3f**	52
17[d]			**3e**	41
18[d]			**3a**	26
19			**3p**	99
20			**3q**	94
21			**3r**	99
22			**3s**	98

Table 1. (Continued)

Entry	Arylboronic acid	Aryl halide	Product **3**	Yield[b] [%]
23			**3t**	97
24			**3u**	91

[a] *Reaction conditions:* aryl halide (0.50 mmol), arylboronic acid (0.60 mmol), $SiO_2@Fe_3O_4$–Pd catalyst (50 mg, containing Pd 0.0025 mmol), K_3PO_4 (1.0 mmol) in MeOH (2.0 mL) at 60 °C for 1.5 h.

[b] Isolated yields.

[c] 1,4-Dibromobenzene (0.25 mmol), 4-methoxyphenylboronic acid (0.60 mmol), $SiO_2@Fe_3O_4$–Pd catalyst (50 mg, containing Pd 0.0025 mmol) in MeOH (2.0 mL) at 60 °C for 6 h.

[d] Aryl chloride (0.50 mmol), arylboronic acid (0.60 mmol), $SiO_2@Fe_3O_4$–Pd catalyst (100 mg, containing Pd 0.005 mmol) in DMF (2.0 mL) at 110 °C for 10 h.

tions. To the terminal alkynes, regardless of their electronic characters, both aromatic alkynes and aliphatic alkynes could be coupled smoothly with iodobenzene, as well as 4-iodoanisole to produce the desired products in good to excellent yields, and the reactions of aromatic alkynes with 4-iodoanisole gave the superior yields of the products to that of aliphatic alkynes with 4-iodoanisole (Table 2, entries 14–16 *vs.* 18 and 19).

Encouraged by the above satisfactory results of Suzuki and Sonogashira reactions, the synthetic potential of the supported palladium catalyst, $SiO_2@Fe_3O_4$–Pd was then evaluated for the Heck reaction. The Heck reactions of a variety of aryl iodides and activated aryl bromides with vinyl substrates were performed in the presence of $SiO_2@Fe_3O_4$–Pd (1.0 mol%) in DMF at 100 °C, see Table 3 in the Supporting Information for details). The coupling reactions proceeded smoothly and generated the corresponding products in good to excellent yields (Table 3, entries 1–21). Meanwhile, the reaction of bromobenzene with *n*-butyl acrylate, *p*-bromotoluene with styrene, and *p*-bromoanisole with styrene, gave the corresponding products in 73, 64, and 51% yields, respectively (Table 3, entries 10, 20 and 21). However, no Heck reaction product was detected when aryl chlorides were used as one of the substrates in reactions with methyl acrylate under the standard reaction conditions. The scope of this catalytic system with vinyl substrates including methyl acrylate, ethyl acrylate, *n*-butyl acrylate, *tert*-butyl acrylate, acrylonitrile and styrene was also examined. Good to excellent results were obtained when the reactions of the above vinyl substrates with aryl iodides and activated aryl bromides were carried out under the identical reaction conditions (Table 3, entries 1–9, and 11–19).

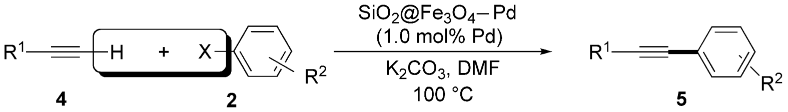
For investigations on the recyclability of the catalyst, it was recovered by magnetic separation, washed with ethanol, H_2O, ethanol and diethyl ether respectively, dried in air and reused for the next reaction. More than 99% of the catalyst could simply be recovered by fixing a magnet near to the reaction vessel. For the model reactions of Suzuki coupling, Heck reaction and Sonogashira reaction, the supported palladium catalyst $SiO_2@Fe_3O_4$–Pd could be recycled and reused for 8 consecutive trials without loss of its catalytic activity (Table 4). Moreover, palladium leaching in $SiO_2@Fe_3O_4$–Pd catalyst was determined and ICP analyses of the methanol solution (3.0 mL) of a Suzuki reaction, the DMF solutions (3.0 mL) of Heck and Sonogashira cross-coupling reactions indicated that the Pd contents were less than 0.20 ppm in the above solutions, respectively. It is indicated that more than 99.64 wt% of Pd was recovered after the Suzuki reaction, and more than 99.79 wt% of Pd was recovered after the Heck or Sonogashira cross-coupling reaction. Meanwhile, iron leaching in $SiO_2@Fe_3O_4$–Pd catalyst was also determined and analysis of the reaction solution (3.0 mL) of Suzuki, Heck or Sonogashira cross-couplings indicated that the Fe content was less than 0.10 ppm in the solution, which also demonstrated that there was almost no corrosion on the silica layer of the supported catalyst in the anhydrous weak basic reaction medium.[20]

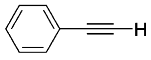
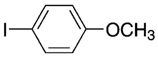
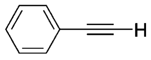
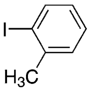
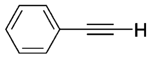
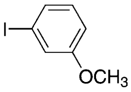
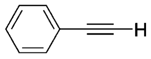
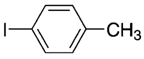
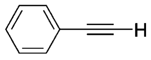
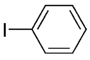
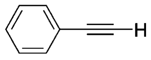
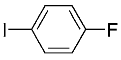
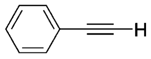
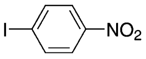
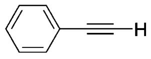
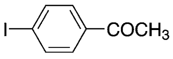
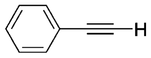
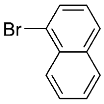
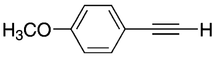
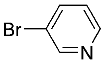
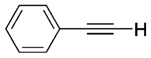
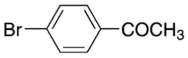
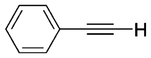
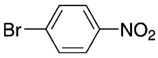
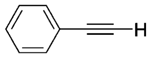
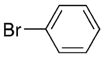
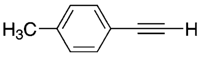
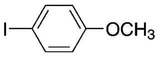
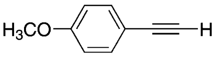
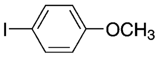
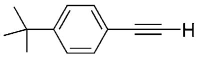
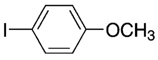
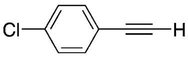
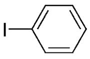
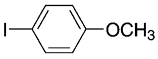
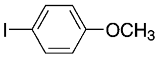
Although the Suzuki coupling reaction could be carried out in the presence of a palladium catalyst down to a level of ppm, the leached palladium in the solution failed to catalyze the reaction under the present reaction conditions. The key to the success of the ultra-low palladium method was the use of tetrabutylammonium bromide and using controlled microwave heating.[21]

Conclusions

In summary, we have developed a highly active, air- and moisture-stable and easily recoverable magnetic nanoparticle-supported palladium catalyst for the

Table 2. Sonogashira coupling reaction of aryl halides with terminal alkynes[a].



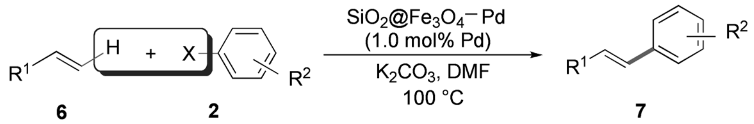
Entry	Alkyne	Aryl halide	Product **5**	Yield[b] [%]
1			**5a**	95
2			**5b**	85
3			**5c**	94
4			**5d**	93
5			**5e**	95
6			**5f**	91
7			**5g**	97
8			**5h**	96
9			**5i**	71
10			**5j**	89
11			**5h**	87
12			**5g**	85
13			**5e**	79
14			**5k**	94
15			**5l**	92
16			**5m**	96
17			**5n**	93
18	$n\text{-}C_6H_{13}{\equiv}H$		**5o**	85
19	$n\text{-}C_4H_9{\equiv}H$		**5p**	82

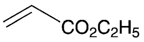
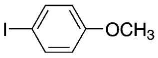
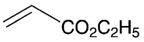
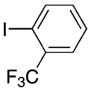
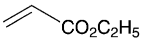
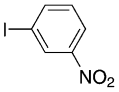
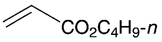
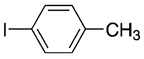
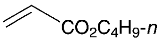
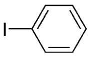
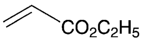
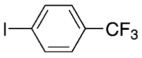
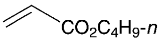
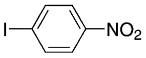
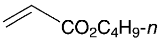
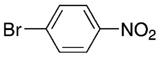
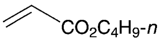
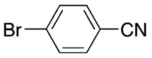
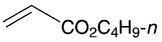
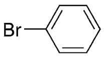
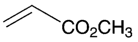
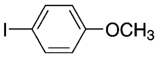
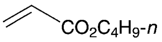
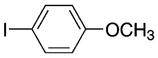
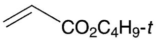
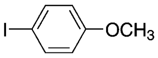
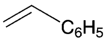
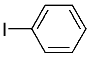
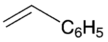
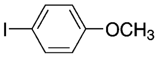
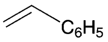
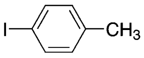
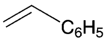
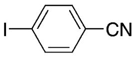
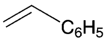
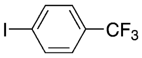
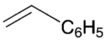
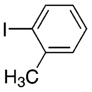
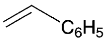
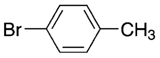
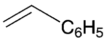
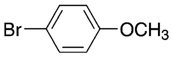
[a] Reaction conditions: aryl halide (0.50 mmol), terminal alkyne (0.60 mmol), $SiO_2@Fe_3O_4$–Pd catalyst (100 mg, containing Pd 0.0050 mmol), K_2CO_3 (1.0 mmol) in DMF (2.0 mL) at 100 °C for 6 h.

[b] Isolated yields.

Suzuki, Sonogashira and Heck reactions. A wide range of substrates was coupled successfully under aerobic conditions. In particular, the performance of the catalyst was fully retained during the reuse process, and it is possible to recover and reuse at least eight times without significant loss of catalytic activity. It should represent a more simple, efficient, reusable and widely applicable magnetic nanoparticles-supported palladium catalyst for the classic carbon-carbon bond formation reactions through the cross-coupling reactions in comparison with the recent reported literature.[12–16]

Table 3. Heck reaction of aryl halides with alkenes.[a]



Entry	Alkene	Aryl halide	Product **7**	Yield[b] [%]
1			**7a**	98
2			**7b**	97
3			**7c**	98
4			**7d**	98
5			**7e**	97
6			**7f**	98
7			**7g**	98
8			**7g**	90
9			**7h**	88
10			**7e**	73
11			**7i**	98
12			**7j**	97
13			**7k**	96
14			**7l**	95
15			**7m**	90
16			**7n**	93
17			**7o**	98
18			**7p**	97
19			**7q**	88
20			**7n**	64
21			**7m**	51

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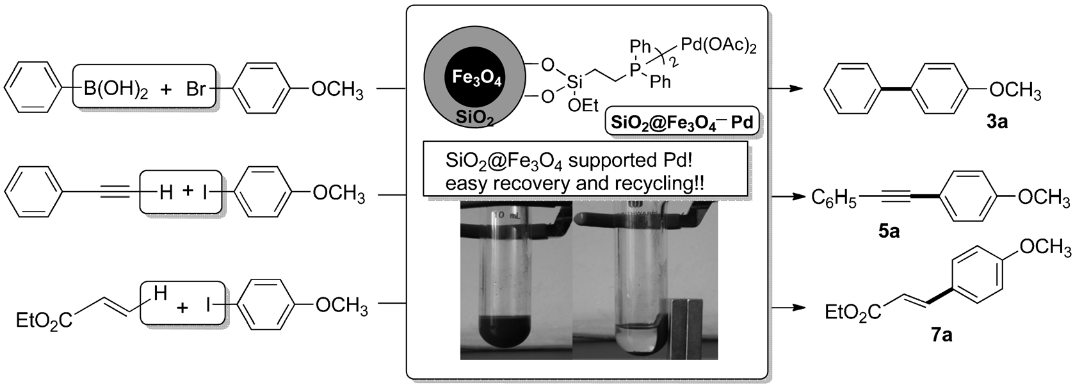
[a] *Reaction conditions:* aryl halide (0.50 mmol), vinyl substrate (0.60 mmol), $SiO_2@Fe_3O_4$–Pd catalyst (100 mg, containing Pd 0.0050 mmol), K_2CO_3 (1.0 mmol) in DMF (2.0 mL) at 100 °C for 8 h.

[b] Isolated yields.

Table 4. Successive trials by using recoverable $SiO_2@Fe_3O_4$–Pd catalyst.[a]



Trial	Yield [%] of **3a**[b]	Yield [%] of **5a**[b]	Yield [%] of **7a**[b]
1	99	95	98
2	99	93	94
3	97	93	95
4	95	91	96
5	96	90	93
6	95	91	93
7	95	89	91
8	94	90	92

[a] *Reaction conditions for Suzuki coupling:* 4-bromoanisole (94 mg, 0.50 mmol), phenylboronic acid (72 mg, 0.60 mmol), reused $SiO_2@Fe_3O_4$–Pd catalyst (50 mg, containing Pd 0.0025 mmol), K_3PO_4 (212 mg, 1.0 mmol) in MeOH (2.0 mL) at 60 °C for 1.5 h. *Reaction conditions for Heck reaction:* 4-iodoanisole (118 mg, 0.50 mmol), ethyl acrylate (86 mg, 1.0 mmol), reused $SiO_2@Fe_3O_4$–Pd catalyst (100 mg, containing Pd 0.005 mmol), K_2CO_3 (138 mg, 1.0 mmol) in DMF (2.0 mL) at 100 °C for 8 h. *Reaction conditions for Sonogashira coupling reaction:* 4-iodoanisole (118 mg, 0.50 mmol), phenylacetylene (56 mg, 0.60 mmol), reused $SiO_2@Fe_3O_4$–Pd catalyst (100 mg, containing Pd 0.005 mmol), K_2CO_3 (138 mg, 1.0 mmol) in DMF (2.0 mL) at 100 °C for 6 h.

[b] Isolated yields.

Experimental Section

General Remarks

The chemicals were purchased from commercial suppliers (Aldrich, USA and Shanghai Chemical Company, China) and were used without purification prior to use. All ^1H NMR spectra were recorded at 400 MHz on Bruker FT-NMR spectrometers. Chemical shifts are given as δ values with reference to tetramethylsilane (TMS) as internal standard. The CHN analysis was performed on a Vario El III elementar. The Pd content was determined by a Jarrell-Ash 1100 ICP analysis. Transmission electron micrograph (TEM) images were obtained with a JEOL-2010 transmission electron microscope. X-ray diffraction (XRD) measurements were carried out at room temperature using a Bruker D8 Advance X-ray powder diffractmeter. Infrared (IR) spectra were measured on a Nicolet 6700 FT-IR spectrophotometer using KBr pellets. Products were purified by flash chromatography on 200–300 mesh silica gel, SiO_2.

Synthesis of the Silica-Coated Magnetic Nanoparticles ($SiO_2@Fe_3O_4$)

Fe_3O_4 particles (0.50 g, with an average diameter of 20 nm, purchased from Aldrich) were diluted with 5.0 mL of deionized water and 50 mL of 2-propanol, and the mixture was sonicated for approximately 30 min. To this well dispersed magnetic nanoparticles solution, 2.0 mL of $NH_3{\cdot}H_2O$ followed by 1.6 g of tetraethoxysilane were slowly added and stirred for further 4 h at room temperature. The material was washed repeatedly with water until the solution was neutral, then the solid material was magnetically separated, washed with ethanol and diethyl ether, respectively, and dried under vacuum. The silica-coated magnetic nanoparticles, $SiO_2@Fe_3O_4$ (1.36 g) was thus obtained. IR (KBr): $\nu_{O-H} = 3397$, $\nu_{Si-O} = 1082\ cm^{-1}$.

Synthesis of Phosphine-Functionalized $SiO_2@Fe_3O_4$

According to the similar procedure,[19] 2-(diphenylphosphino)ethyltriethoxysilane (0.38 g) dissolved in 5.0 mL of dry toluene, was added to a suspension of 1.0 g of $SiO_2@Fe_3O_4$ in 30.0 mL of dry toluene. The mixture was then shaken at 100 °C under a nitrogen atmosphere for 24 h. Then the solid material ($SiO_2@Fe_3O_4$–P) was magnetically separated, washed repeatedly with toluene and CH_2Cl_2 to remove any unanchored species and dried under vacuum. The phosphine-functionalized $SiO_2@Fe_3O_4$ (brown nanoparticles) was obtained; yield: 1.05 g. The loading of phosphine was quantified *via* CHN microanalysis and found to be 0.18 mmol g^{-1} based on the carbon content determination. IR (KBr):

$\nu_{O-H}=3396$, $\nu_{C-H}=2925$, 2863, $\nu_{Ar,C-C}=1518$, 1469, $\nu_{Si-O}=1081\ cm^{-1}$.

Synthesis of $SiO_2@Fe_3O_4$–Pd

To a sealable reaction tube, palladium acetate (22.4 mg, 0.10 mmol) and THF (15.0 mL) were added. The solution was shaken at room temperature under an inert atmosphere for 10 min, and then 2.0 g of the above phosphine-functionalized magnetic nanoparticles ($SiO_2@Fe_3O_4$–P) were added. The mixture was shaken at room temperature for 4 h, then the solid catalyst was magnetically separated, and the solid was washed thoroughly with THF, and dried under vacuum at 50 °C for 3 h. The supported Pd catalyst, $SiO_2@Fe_3O_4$–Pd (brown nanoparticles) was obtained with a loading of 0.049 mmol of palladium per gram determined *via* inductively coupled plasma atomic emission spectrometry (ICP-AES); yield: 2.01 g. IR (KBr): $\nu_{O-H}=3397$, $\nu_{C-H}=2978$, 2896, $\nu_{Ar,C-C}=1650$, 1521, $\nu_{Si-O}=1080\ cm^{-1}$.

General Procedure for the Suzuki Coupling Reaction

Aryl halide (0.5 mmol), arylboronic acid (0.6 mmol), K_3PO_4 (212 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$–Pd, 50 mg, containing Pd 0.0025 mmol) were mixed in MeOH (2.0 mL). The mixture was shaken at 60 °C in an air atmosphere for 1.5 h. After magnetic separation of the catalyst, the organic material was twice extracted with diethyl ether. The organic phase was evaporated under reduced pressure. The product was purified by short-column chromatography on silica gel. All the products have been previously reported, and their identities were confirmed by comparison of their ^1H and ^{13}C NMR spectral data with the values of authentic samples.

General Procedure for the Sonogashira Coupling Reaction

Aryl halide (0.50 mmol), terminal alkyne (0.60 mmol), K_2CO_3 (138 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$–Pd, 100 mg, containing Pd 0.0050 mmol) were mixed in DMF (2.0 mL). The mixture was shaking at 100 °C in an air atmosphere for 6 h. After magnetic separation of the catalyst, the organic material was twice extracted with diethyl ether. The organic phase was evaporated under reduced pressure. The product was purified by short-column chromatography on silica gel. All the products have been previously reported, and their identities were confirmed by comparison of their ^1H and ^{13}C NMR spectral data with the values of authentic samples.

General Procedure for the Heck Reaction

Aryl halide (0.50 mmol), vinyl substrate (1.0 mmol), K_2CO_3 (138 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$–Pd, 100 mg, containing Pd 0.0050 mmol) were mixed in DMF (2.0 mL). The mixture was shaken at 100 °C in an air atmosphere for 8 h. After magnetic separation of the catalyst, the organic material was twice extracted with diethyl ether. The organic phase was evaporated under reduced pressure. The product was purified by short-column chromatography on silica gel. All the products have been previously reported, and their identities were confirmed by comparison of their ^1H and ^{13}C NMR spectral data with the values of authentic samples.

Typical Procedure for Catalyst Recovery and Palladium Leaching of $SiO_2@Fe_3O_4$-Pd in the Suzuki Reaction

In a reaction vessel, 4-bromoanisole (94 mg, 0.50 mmol), phenylboronic acid (72 mg, 0.60 mmol), K_3PO_4 (212 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$–Pd, 50 mg, containing Pd 0.0025 mmol) were mixed in MeOH (2.0 mL). The mixture was shaken at 60 °C in an air atmosphere for 1.5 h. The supported catalyst was magnetically separated, and washed with ethanol (2.0 mL), H_2O (2.0 mL), ethanol (2.0 mL) and diethyl ether (2.0 mL × 2) respectively, then dried, and used directly for the next run. In addition, palladium leaching from the $SiO_2@Fe_3O_4$–Pd catalyst was determined. ICP analysis of the methanol solution (3.0 mL) of a Suzuki reaction indicated that Pd contents were less than 0.20 ppm.

Typical Procedure for Catalyst Recovery and Palladium Leaching of $SiO_2@Fe_3O_4$-Pd in the Heck Reaction

In a reaction vessel, 4-iodoanisole (118 mg, 0.50 mmol), ethyl acrylate (86 mg, 1.0 mmol), K_2CO_3 (138 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$-Pd, 100 mg, containing Pd 0.0050 mmol) were mixed in DMF (2.0 mL). The mixture was shakeng at 100 °C in an air atmosphere for 8 h. The supported catalyst was magnetically separated, and washed with ethanol (2.0 mL), H_2O (2.0 mL), ethanol (2.0 mL) and diethyl ether (2.0 mL × 2) respectively, then dried, and used directly for the next run. In addition, palladium leaching from the $SiO_2@Fe_3O_4$–Pd catalyst was determined. ICP analysis of the DMF solution (3.0 mL) of a Heck reaction indicated that Pd contents were less than 0.20 ppm.

Typical Procedure for Catalyst Recovery and Palladium Leaching of $SiO_2@Fe_3O_4$-Pd in the Sonogashira Reaction

In a reaction vessel, 4-iodoanisole (118 mg, 0.50 mmol), phenylacetylene (56 mg, 0.60 mmol), K_2CO_3 (138 mg, 1.0 mmol), and the supported palladium catalyst ($SiO_2@Fe_3O_4$-Pd, 100 mg, containing Pd 0.0050 mmol) were mixed in DMF (2.0 mL). The mixture was shaken at 100 °C in an air atmosphere for 6 h. The supported catalyst was magnetically separated, and washed with ethanol (2.0 mL), H_2O (2.0 mL), ethanol (2.0 mL) and ethyl ether (2.0 mL × 2), respectively, then dried, and used directly for the next run. In addition, palladium leaching in the $SiO_2@Fe_3O_4$–Pd catalyst was determined. ICP analysis of the DMF solution (3.0 mL) of a Sonogashira reaction indicated that Pd contents were less than 0.20 ppm.

Supporting Information

Optimization of the reaction conditions for Suzuki reaction, Sonogashira reaction, and Heck reaction (Table 1, Table 2 and Table 3), general procedure for the recycling of the supported palladium catalyst, and ^{1}H and ^{13}C NMR data of all products are available in the Supporting Information.

Acknowledgements

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