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Palladium nanoparticles supported on agarose-functionalized magnetic nanoparticles of Fe_3O_4 as a recyclable catalyst for C–C bond formation *via* Suzuki–Miyaura, Heck–Mizoroki and Sonogashira–Hagihara coupling reactions†

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In this paper, the preparation of palladium nanoparticles supported on agarose-functionalized magnetic nanoparticles of Fe_3O_4 is described. The new material was characterized by EDX, TEM, TGA, FT-IR, VSM, AAS, and solid UV-visible analysis. This magnetic material has been successfully applied as a highly efficient, magnetically recoverable and air-stable catalyst for the Suzuki–Miyaura, Heck–Mizoroki and Sonogashira–Hagihara coupling reactions. Using this material as a catalyst, a wide range of substrates was employed for carbon–carbon bond formation in wet PEG 200.

Introduction

Transition metals play an important role in organic reactions as catalysts.[1] Among different types of transition metal catalysts, palladium has become a significant catalyst due to its ability to catalyze important carbon–carbon and carbon–heteroatom bond formation reactions. Palladium-catalyzed Suzuki–Miyaura,[2] Heck–Mizoroki[3] and Sonogashira–Hagihara[4] coupling reactions are important and powerful strategies for the formation of carbon–carbon bonds. In recent years, both homogeneous and heterogeneous palladium catalysts have been employed for the above mentioned coupling reactions.[5] However, palladium metal and its compounds are expensive, and homogeneous palladium catalysis suffers from a problem associated with its separation from the reaction mixture. In addition, using homogeneous palladium catalysts might result in contamination of the coupling products with palladium species, especially problematic when they are used for biologically active natural products and pharmaceuticals. Using heterogeneous catalysts can overcome those difficulties. However, despite the simple handling of heterogeneous catalysts, they are typically less effective than their homogeneous counterparts. Moreover, many heterogeneous catalysts encounter difficulties in their separation from the reaction mixture by filtration and centrifugation. This problem could be solved by preparation of magnetic catalysts which can be separated by an external magnet from the reaction system.[6] In recent years, extensive attention has been paid to the use of Fe_3O_4 nanoparticles as a magnetically recoverable solid support for transition metals such as palladium,[7] copper,[8] nickel,[9] and gold.[10] The advantages of magnetic nanocatalytic systems are their easy separation by an external magnet, high reactivity, and an enormous surface area to volume ratio and morphology of the catalysts. In addition, the magnetic property of these catalysts causes their flocculation or dispersion being reversibly controlled by a static magnetic field. Consequently, magnetic nanoparticles can be well-dispersed in the reaction medium for their reuse in the absence of an external magnetic field.

Nowadays, most efforts on development of magnetic nanoparticle-supported catalysts are focused on two aspects: the synthesis of size-controlled and monodispersed magnetic nanoparticles (MNPs),[11] and surface stabilization of nanoparticles by simple organic compounds such as silanes,[12] carboxylic acids,[13] and phosphonic acids.[14] This surface modification is often performed through a process that involves the exchange of stabilizing ligands or the coating of the magnetic core with an organic/inorganic polymer shell.[15] Also, apart from the surface modification of MNPs, several researchers have combined MNPs with activated carbon fiber,[16] carbon nanotubes,[17] and graphene.[18]

Very recently, we have introduced agarose as an inexpensive and bioorganic ligand and support for palladium nanoparticles and its application in different carbon–carbon bond formation reactions.[19] Also, preparation of magnetically recoverable

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heteropolyacids–chitosan–Fe_3O_4 (HSiW–CS–Fe_3O_4) and its successful application in the acetalization reaction of benzaldehyde with ethylene glycol has been reported.[20] In the present report, we describe a newly developed material composed of magnetic Fe_3O_4 nanoparticles modified with agarose-supported palladium nanoparticles; this combination is referred to as Pd@agarose–Fe_3O_4 throughout the text of this article. Characterization of this material was performed by SEM, EDX, TEM, TGA, FT-IR, VSM, AAS, and solid UV-visible spectrum. This new material has been applied as a magnetically separable and recyclable catalyst for C–C bond formation with success *via* Suzuki–Miyaura, Heck–Mizoroki and Sonogashira–Haghihara reactions.

Results and discussion

Fe_3O_4 nanoparticles were prepared without using any capping agent or surfactant *via* conventional co-precipitation of iron(II) chloride and iron(III) chloride according to a reported procedure.[21] After sonication, Fe_3O_4 nanoparticles were treated with agarose in the presence of $Pd(OAc)_2$ and citric acid as a reducing agent in aqueous media. After drying the resulting material, the initial investigation was focused on the characterization of the resulting new solid material. Based on the atomic absorption spectroscopy (AAS) analysis, the amount of Pd in Pd@agarose–Fe_3O_4 was found to be 0.0075 mmol Pd g^{-1}.

The solid UV-Vis spectrum of the obtained material shows complete conversion of Pd(II) to Pd(0) by the absence of the peak at 420 nm which belongs to Pd(II) species (Fig. 1). In addition, increase of the absorption in the visible region for the catalyst indicates that the Pd(0) nanoparticles are formed.[22]

The FT-IR spectrum of Pd@agarose–Fe_3O_4 did not show a carbonyl group absorption band, which confirms that the –OAc anion has been removed after the process of reduction of Pd(II) to Pd(0). The characteristic absorption bands of Fe_3O_4 nanoparticles at 630, 578 and 442 cm^{-1} are attributed to the presence of Fe–O bonds.[23] These results prove the existence of magnetic Fe_3O_4 nanoparticles in the new solid material (see ESI†).

To get information about the size of metal particles distributed in the agarose mass, the TEM image of the material (Fig. 2) was studied. The image shows that the particles are mostly spherical and have an average diameter of about 10–15 nm. However, the amount of palladium NP on the surface of the material is very low and therefore, differentiation of Pd NP from Fe_3O_4 NP is not so easy.

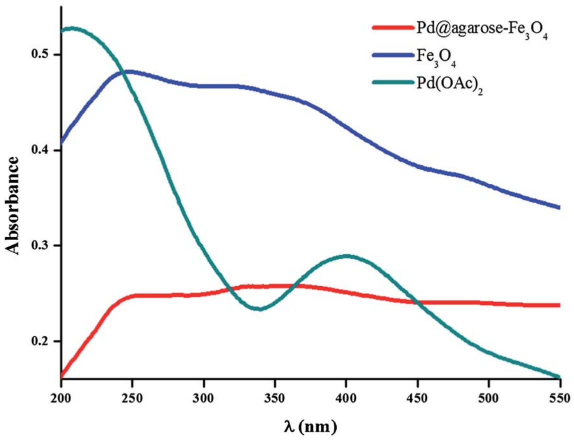


Fig. 1 Solid UV-Vis spectrum of $Pd(OAc)_2$, Fe_3O_4 and Pd@agarose–Fe_3O_4.

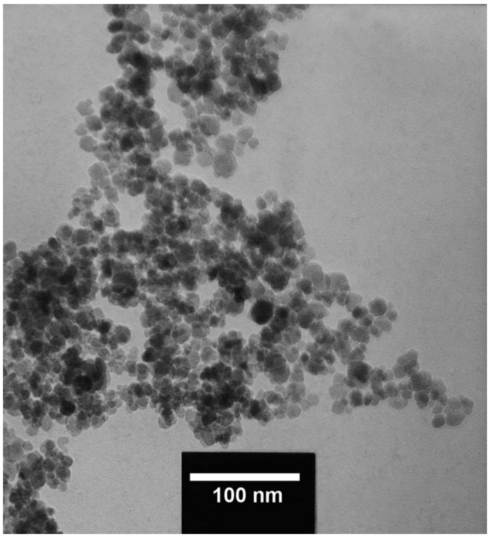


Fig. 2 TEM image of Pd@agarose–Fe_3O_4 with the average spherical particle size 10–15 nm.

The EDX study of Pd@agarose–Fe_3O_4 (see ESI†) confirms the presence of palladium and iron nanoparticles in the structure of the material.

The thermo-gravimetric analysis (TGA) of Pd@agarose–Fe_3O_4 shows that the prepared composites have high thermal stability and negligible agarose leaching up to 200 °C (Fig. 3).

The superparamagnetic[24] behavior of Pd@agarose–Fe_3O_4 was confirmed using magnetization curves of Fe_3O_4 NPs and Pd@agarose–Fe_3O_4 at room temperature (Fig. 4). The two samples show zero coercivity and remanence on the magnetization loop. The absence of a hysteresis loop shows the superparamagnetic property and the ability of the material to be separated from the reaction mixture by an external magnet (Fig. 5). In addition, the decrease in the magnetization value of the composite (65.8 emu g^{-1}) in comparison with Fe_3O_4 NPs

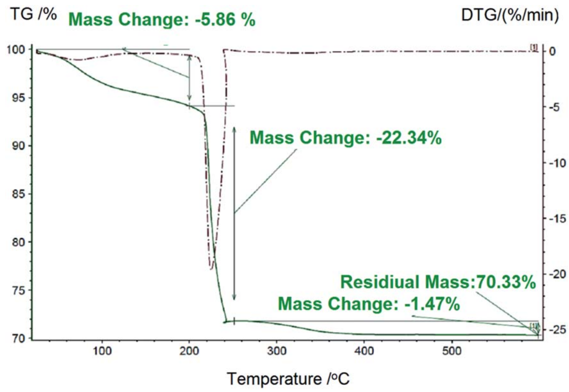


Fig. 3 Thermo-gravimetric diagram of Pd@agarose–Fe_3O_4.

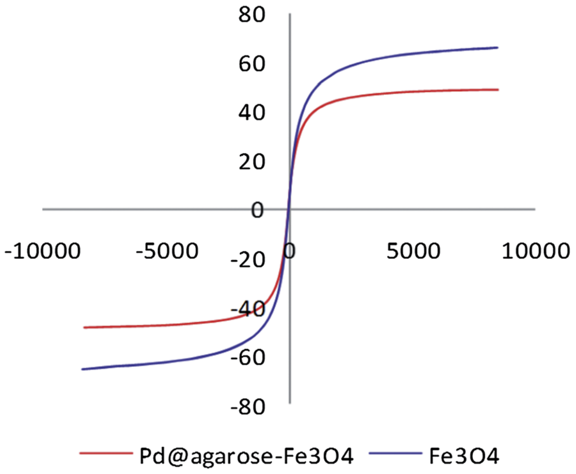
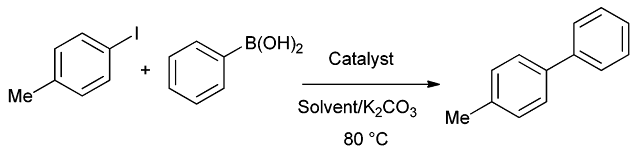


Fig. 4 The magnetization curves of nanoparticles of Fe_3O_4 NP and Pd@agarose–Fe_3O_4.

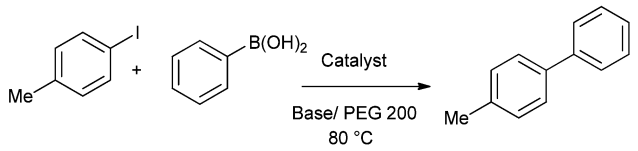
Fig. 5 Photograph showing the magnetic separation of Pd@agarose–Fe_3O_4 catalyst from the PEG phase by an external magnet.

Table 1 Screening of different solvents for the reaction of 4-iodotoluene with phenylboronic acid catalyzed by Pd@agarose–Fe_3O_4



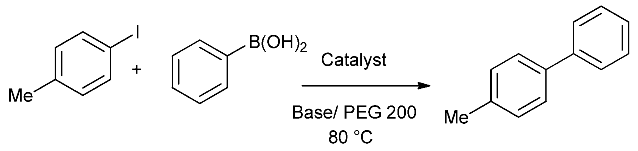
Entry	Solvent	Base	Yield
1	Toluene	0.5	N.R
2	Water	0.5	52
3	EtOH	0.5	60
4	PEG 200	0.5	94
5	DMF	0.5	40

Table 2 Screening of different bases for the reaction of iodotoluene with phenylboronic acid in the presence of Pd@agarose–Fe_3O_4



Entry	Base	Base amount	Yield (%)
1	NaOH	0.5	90
2	K_2CO_3	0.5	94
3	Morpholine	0.5	20
4	Et_3N	0.5	45
5	None	0.5	17

Table 3 Effect of different amounts of Pd@agarose–Fe_3O_4 for the reaction of 4-iodotoluene with phenylboronic acid



Entry	Pd@agarose–Fe_3O_4	Base	Yield (%)
1	0	0.05	N.R
2	0.005	0.05	50
3	0.01	0.05	80
4	0.02	0.05	94

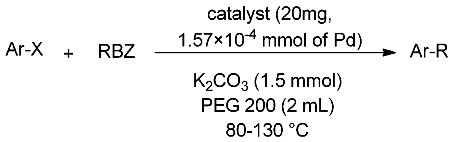
(48.7 emu g^{-1}) confirms that the surface of Fe_3O_4 NPs is covered by the attachment of agarose molecules through their bond formation *via* their hydroxyl functional groups.

After characterizing Pd@agarose–Fe_3O_4, we investigated the catalytic properties of Pd@agarose–Fe_3O_4 for C–C bond formation *via* a Suzuki–Miyaura coupling reaction. For this purpose, the reaction of 4-iodotoluene (1.0 mmol) with phenylboronic acid (1.5 mmol) as a model reaction in the presence of K_2CO_3 (1.5 mmol) and 20 mg of Pd@agarose–Fe_3O_4 (this optimized amount of the catalyst was found through a study as shown in Table 3 and contains 1.5×10^{-4} mmol of Pd as determined by ICP analysis) in different solvents at 80 °C was studied (Table 1). The results of this experiment showed that wet PEG 200 was the most suitable solvent for this reaction.

The effect of different bases was also studied using the reaction of 4-iodotoluene with phenylboronic acid. Among the studied bases, NaOH and K_2CO_3 were found to be suitable; however, K_2CO_3 was selected as the most efficient base for the reaction, as shown in Table 2.

The optimized reaction condition was then applied to the reaction of varieties of aryl halides with arylboronic acids. Aryl iodides were reacted efficiently with phenylboronic acid, 4-fluorophenylboronic acid and pinacol vinylboronate. The reactions proceeded smoothly to produce the desired biphenyl and phenylvinyl products in excellent yields. Also, the reactions of aryl bromides under the optimized conditions proceeded successfully to give the desired biphenyl and phenylvinyl products in high to excellent yields. However, under the optimized reaction conditions, the reactions of aryl chlorides proceeded sluggishly. Therefore, the temperature of the reaction was raised to 130 °C; at this temperature, the aryl chlorides reacted more

Table 4 Reaction of different aryl halides (I, Br, Cl) with organoborons catalyzed by Pd@agarose–Fe_3O_4



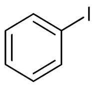
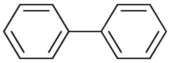
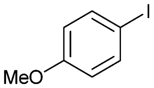
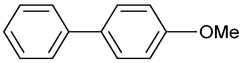
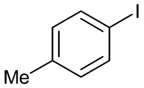
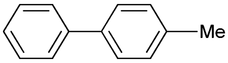
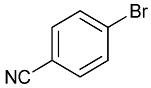
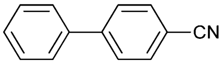
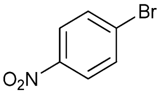
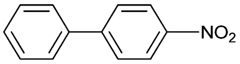
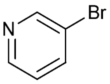
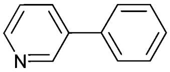
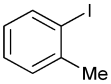
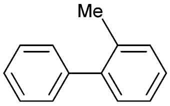
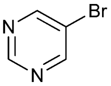
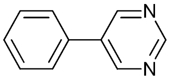
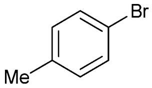
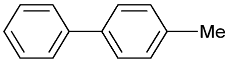
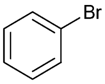
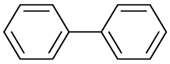
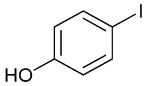
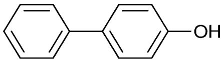
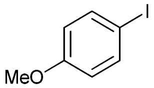
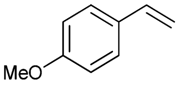
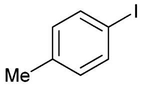
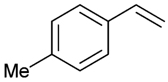
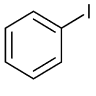
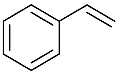
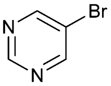
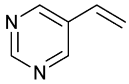
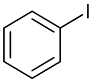
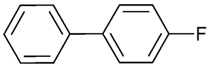
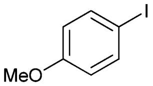
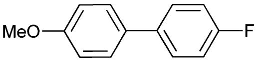
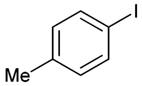
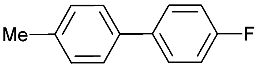
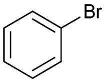
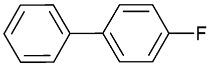
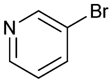
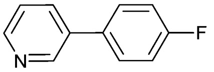
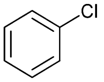
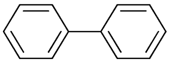
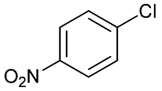
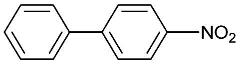
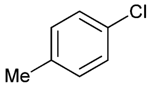
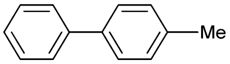
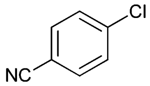
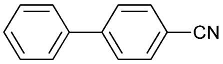
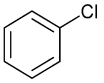
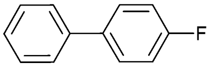
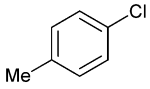
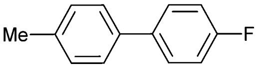
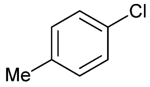
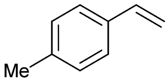
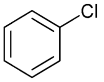
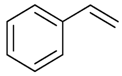
Entry	Aryl halide	RBZ	Time (h)	Product	Isolated yield%
1		$PhB(OH)_2$	0.5		97
2		$PhB(OH)_2$	0.5		95
3		$PhB(OH)_2$	0.5		94
4		$PhB(OH)_2$	0.5		90
5		$PhB(OH)_2$	0.5		90
6		$PhB(OH)_2$	6		93
7		$PhB(OH)_2$	4		92
8		$PhB(OH)_2$	3.5		87
9		$PhB(OH)_2$	0.5		93
10		$PhB(OH)_2$	0.75		92
11		$PhB(OH)_2$	0.5		90
12		Pinacol vinylboronate	2		85
13		Pinacol vinylboronate	2		80
14		Pinacol vinylboronate	1.5		90
15		Pinacol vinylboronate	6		80

Table 4 (*Contd.*)

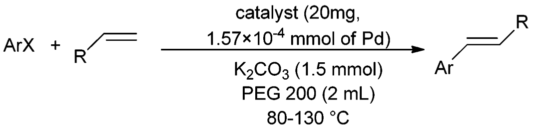
$$\text{Ar-X} + \text{RBZ} \xrightarrow[\substack{\text{K}_2\text{CO}_3\text{ (1.5 mmol)}\\ \text{PEG 200 (2 mL)}\\ 80\text{-}130\ ^\circ\text{C}}]{\substack{\text{catalyst (20mg,}\\ 1.57\times10^{-4}\text{ mmol of Pd)}}} \text{Ar-R}$$

Entry	Aryl halide	RBZ	Time (h)	Product	Isolated yield%
16		4-Fluorophenylboronic acid	0.5		95
17		4-Fluorophenylboronic acid	0.5		93
18		4-Fluorophenylboronic acid	0.5		93
19		4-Fluorophenylboronic acid	0.5		92
20		4-Fluorophenylboronic acid	6.5		90
21		$PhB(OH)_2$	24		73
22		$PhB(OH)_2$	24		86
23		$PhB(OH)_2$	24		75
24		$PhB(OH)_2$	24		89
25		4-Fluorophenylboronic acid	24		70
26		4-Fluorophenylboronic acid	24		72
27		Pinacol vinylboronate	24		67
28		Pinacol vinylboronate	24		70

efficiently and afforded the corresponding biphenyl and phenylvinyl products in 67–89% isolated yields (Table 4).

Along with the expansion of the application of the catalyst, the Heck–Mizoroki reaction was also studied under similar optimized reaction conditions as mentioned above. For this purpose, reactions of a variety of aryl halides with styrene, butyl acrylate and 1-octene in the presence of 20 mg of the catalyst and K_2CO_3 in PEG 200 at 80 °C were studied. However, the reactions of aryl bromides and chlorides with alkenes were found to be inefficient at 80 °C. Therefore, the reaction

Table 5 Reaction of different aryl halides (I, Br, Cl) with styrene and butyl acrylate in the presence of the catalyst



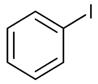
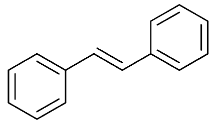
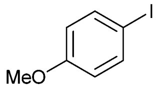
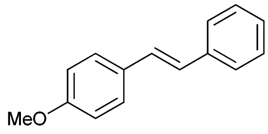
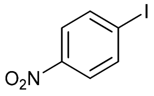
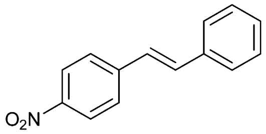
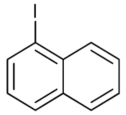
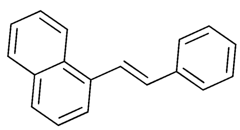
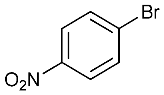
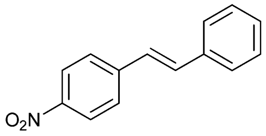
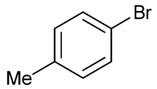
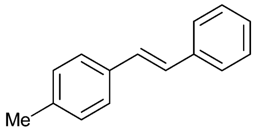
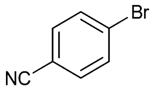
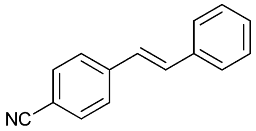
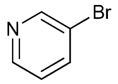
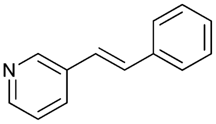
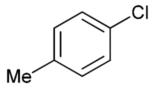
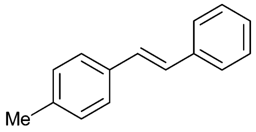
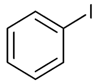
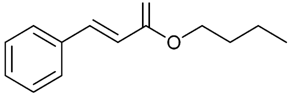
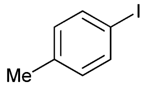
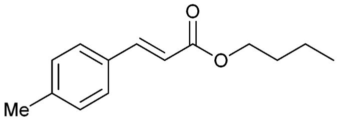
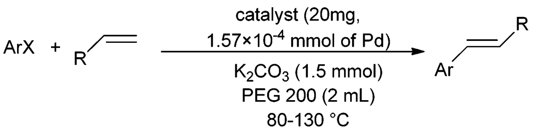
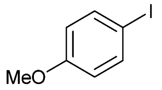
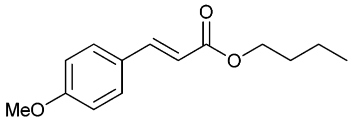
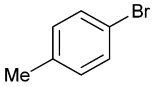
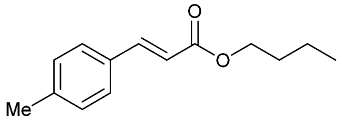
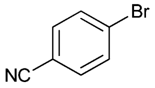
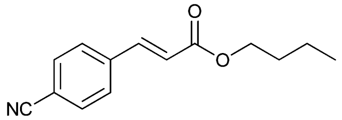
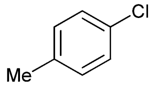
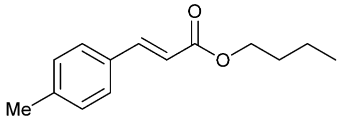
Entry	ArX	Alkene	T (°C)	Time (h)	Product	Yield%
1		Styrene	80	1(1)[a]		94(89)
2		Styrene	80	4		92
3		Styrene	80	1		94
4		Styrene	80	18		67
5		Styrene	120	20		20
6		Styrene	120	14		93
7		Styrene	120	16		87
8		Styrene	120	20		85
9		Styrene	130	24		87
10		Butyl acrylate	80	1		94
11		Butyl acrylate	80	1		94

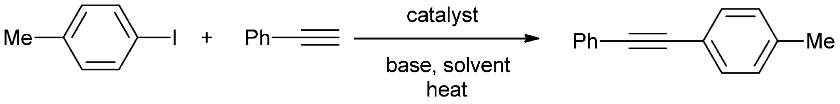
Table 5 (*Contd.*)



Entry	ArX	Alkene	T (°C)	Time (h)	Product	Yield%
12		Butyl acrylate	80	1		92
13		Butyl acrylate	120	14		60
14		Butyl acrylate	120	10		88
15		Butyl acrylate	130	24		76

[a] In parentheses, time and the isolated yield of the large-scale reaction using 10 mmol of iodobenzene and 20 mmol of styrene are indicated.

Table 6 Optimization of conditions for the Sonogashira–Hagihara reaction for the reaction of 4-iodotoluene and phenylacetylene using Pd@agarose–Fe_3O_4



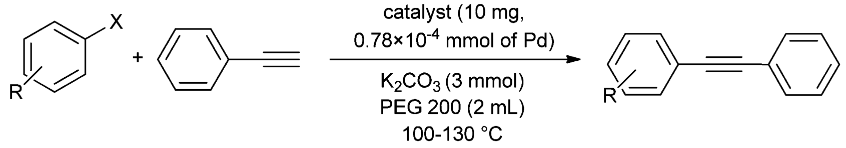
Entry	Catalyst (g)	Solvent	Base	Temp. (°C)	Time (h)	Isolated yields (%)
1	0.02	PEG 200	K_2CO_3	100	1	60[a]
2	0.02	PEG 200	KOAc	100	1	40
3	0.02	PEG 200	n-Pr_3N	100	1	10
4	0.02	PEG 200	None	100	1.5	N.R
5	0.02	DMSO	K_2CO_3	100	1	44
6	0.02	EtOH	K_2CO_3	100	1	25
7	0.02	NMP	K_2CO_3	100	1	50
8	0.02	DMF	K_2CO_3	100	1	30
9	0.02	EG	K_2CO_3	100	1	10
10	0.03	PEG 200	K_2CO_3	100	0.5	50
11	0.01	PEG 200	K_2CO_3	100	3	73
12	None	PEG 200	K_2CO_3	100	5	10
13	0.01	PEG 200	K_2CO_3	110	1.5	65
14	0.01	PEG 200	K_2CO_3	120	1	60
15	0.01	PEG 200	K_2CO_3/TBAB	100	3	70
16	0.01	None	K_2CO_3/TBAB	100	1.5	N.R
17	0.01	PEG 200	K_2CO_3	100	1.5	94[b]

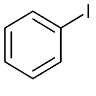
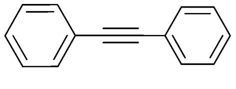
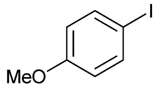
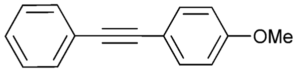
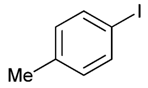
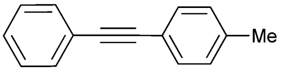
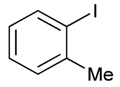
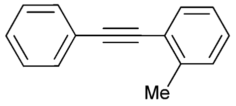
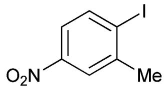
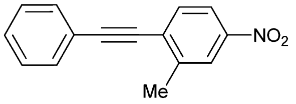
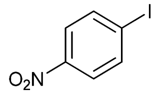
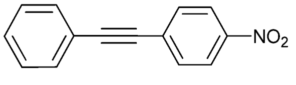
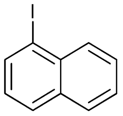
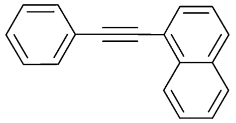
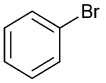
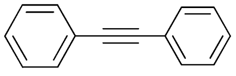
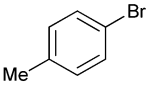
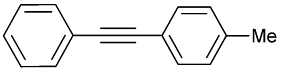
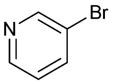
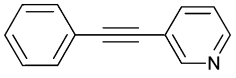
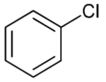
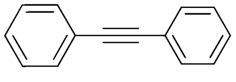
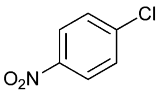
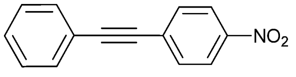
[a] Conversion was 100% under the defined condition. [b] Reaction proceeded in the presence of 3 mmol of K_2CO_3.

temperature was increased to 120 °C for aryl bromides and to 130 °C for aryl chlorides. The results show that the catalyst was suitable and efficient for Heck–Mizoroki reactions using structurally different aryl halides and alkenes to give the desired alkene compounds in good to excellent isolated yields (Table 5).

The application of the catalyst was also extended to C–C bond formation *via* the Sonogashira–Hagihara reaction by studying the reaction of structurally different aryl iodides, bromides and chlorides with phenylacetylene. First, we performed optimization of the reaction conditions with respect to

Table 7 Sonogashira–Hagihara reaction of aryl halides with phenylacetylene catalyzed by Pd@agarose–Fe_3O_4

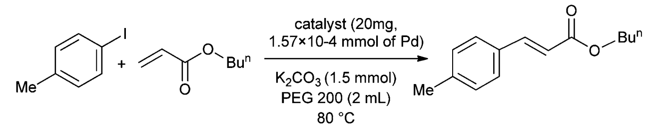


Entry	Aryl halide	Product	Time (h)	Isolated yield (%)
1			1	95
2			6	84
3			1.5	94
4			3	85
5			3.5	68
6			2.5	94
7			3	89
8			1	60
9			10	78
11			5	90
12			24	53[a]
13			24	62[a]

[a] Reaction temperature was 130 °C.

solvents, bases, temperature, and the amounts of the catalyst for the reaction of 4-iodotoluene (1.0 mmol) with phenylacetylene (1.5 mmol). These reactions were carried out using 10 mg of the catalyst in the presence of K_2CO_3 (2 mmol) in different solvents at 100 °C. The results showed that PEG 200 and K_2CO_3 were the most suitable solvent and the base for the reaction. Under these conditions, the yield of the product was found to be only 60%, even though the reaction was completed with respect to the reactants in the appropriate reaction time (Table 6, Entry 1). This observation induced us to study the effect of the amounts of the catalyst on the reaction. By increasing the amount of the catalyst from 10 to 30 mg, an increase in the byproduct formation was observed (Table 7, Entries 10 and 11). Thus the amount of the catalyst was kept at 10 mg. Then the effect of increasing the temperature was investigated. The results showed that increasing the temperature from 100 °C to 120 °C was accompanied with a decrease of the reaction time, but the amount of unwanted products increased (Table 6, Entries 13 and 14). Finally, we decided to increase the amount of K_2CO_3 from 2 mmol to 3 mmol in the presence of 10 mg of the catalyst in wet PEG 200. By this change, the desired product was obtained in 94% isolated yield (Table 6, Entry 17).

Table 8 Recycling of Pd@agarose–Fe_3O_4 for the reaction of 4-iodotoluene with *n*-butyl acrylate



No. of runs	Yield (%)
1	94
2	94
3	92
4	90
5	87
6	86

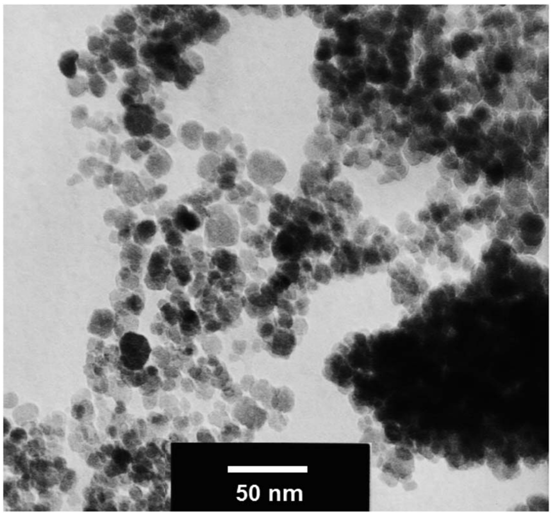


Fig. 6 TEM image of the catalyst after the 2nd run of recycling.

Then the optimized reaction condition was applied to the reaction of structurally different halides with phenyl acetylene. The reaction of aryl iodides and bromides proceeded smoothly and the desired aryl alkynes were obtained in 60–95% isolated yields (Table 7, Entries 1–11). In the case of aryl chlorides, the reaction needed harsher conditions; therefore, the reaction temperature was raised to 130 °C. At this temperature, aryl chlorides did react and the corresponding aryl alkynes were obtained in 53–62% isolated yields (Table 7, Entries 12 and 13).

Finally, recycling of the catalyst was tested for the reaction of 4-iodotoluene with *n*-butyl acrylate employing 20 mg of the catalyst in the presence of K_2CO_3/PEG 200 at 80 °C. After completion of the reaction, the reaction mixture was diluted with ethyl acetate. The catalyst was separated by an external magnet (Fig. 5), washed with ethyl acetate, water and dried under vacuum. The resulting solid catalyst was used directly for the next run. The yield of the desired product dropped from 94% after the first run to 86% after the sixth run, which shows a negligible loss in activity of the catalyst (Table 8).

As shown in Table 8, no considerable change in the reaction yield was observed during six consecutive runs. This observation indicates that the amounts of leaching of Pd into the reaction mixture must not be significant; this has also been quantitatively supported by ICP analysis. The analysis showed that after six recycling runs of the catalyst, only 7% of Pd was leached.

The TEM image of the recycled catalyst shows that the catalyst preserves its structure with little aggregation of the nanoparticles after the second run (Fig. 6).

Conclusion

In this study, we have introduced a new magnetically separable material: Pd@agarose–Fe_3O_4. In this composite, palladium nanoparticles are supported on an agarose hydrogel which is attached to magnetic Fe_3O_4 nanoparticles. This new compound was characterized by different techniques, such as EDX, TEM, TGA, FT-IR, VSM, AAS, and solid UV-visible analysis. Pd@agarose–Fe_3O_4 shows good magnetic properties and has been successfully applied as a catalyst for Suzuki–Miyaura, Heck–Mizoroki and Sonogashira–Hagihara reactions of structurally different aryl halides in wet PEG 200. The recyling of the catalyst was successfully tested in the Heck–Mizoroki reaction for six consecutive runs. The TEM images of the recycled catalyst shows that agglomeration of the nanoparticles in the catalyst was negligible and that the size of the particles was reasonably preserved during the reaction. The ICP analysis of the reaction mixture shows that the amounts of the Pd species leached into the reaction mixture was not significant and after six consecutive runs in a Heck reaction, only 7% of Pd was leached into the reaction media.

Experimental

All reactants were purchased from Acros, Merck and Sigma Aldrich and were used without further purification. ^{1}H NMR spectra were recorded at 250 and 400 MHz, and ^{13}CNMR spectra were recorded at 62.9 and 100 MHz in $CDCl_3$ using TMS as an internal standard. Thin layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka. Column chromatography was carried out on silica gel 60 Merck (230–240 mesh) in glass columns (2 or 3 cm diameter) using 15–30 grams of silica gel per one gram of the crude mixture. Thermo-gravimetric analysis was conducted from room temperature to 800 °C in an oxygen flow using a NETZSCH STA 409 PC/PG instrument. The structures of the prepared materials were observed by transmission electron microscopy (Philips CM-120). FT-IR spectra were obtained using a Shimadzu FTIR-8300 spectrophotometer. UV-Vis spectra were recorded on a Perkin Elmer Lambda 25, UV-Vis spectrometer.

Gram-scale preparation of Pd@agarose–Fe_3O_4

Agarose (1.00 g) was dissolved in water (100 mL) and heated to 80 °C for 15 min. To this solution, the synthesized Fe_3O_4 nanoparticles (4.00 g), which had been sonicated in H_2O (25 mL) for 15 min, were added. The resulting mixture was stirred for 4 h at 80 °C. Then an acidic solution of $Pd(OAc)_2$ (0.022 g, 1.0 mM) was added. After that, a solution of citric acid (20 mL, 4.0 mM) was added and the mixture was stirred for 12 h at 80 °C. Upon stirring, a black gel mass of the hydrogel was formed, which was separated from the mixture by an external magnet. The resulting solid Pd@agarose–Fe_3O_4 was washed with cold water (3 × 15 mL) and ethanol (3 × 15 mL), and dried under vacuum to give Pd@agarose–Fe_3O_4 composite.

General procedure for Suzuki–Miyaura reaction of aryl halides catalyzed by Pd@agarose–Fe_3O_4 in PEG 200

To a flask containing the catalyst (20 mg, containing 1.57×10^{-4} mmol of Pd species as determined by ICP analysis) in PEG 200 (2 mL), were added aryl halide (1.0 mmol), organoborane (1.5 mmol) and K_2CO_3 (2.0 mmol, 0.276 g), and the mixture was stirred at 80 °C for the appropriate reaction time. After completion of the reaction (monitored by GC or TLC), the catalyst was separated from the reaction mixture by an external magnet. Then H_2O (10 mL) was added to the mixture and the product was extracted with ethyl acetate (3 × 10 mL). The organic extracts were combined and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded the crude desired product, which was purified by column chromatography on silica gel using *n*-hexane or different mixtures of *n*-hexane–ethyl acetate as the eluents to afford the highly pure products in 80–97% yields (Table 4).

General procedure for the Heck–Mizoroki reaction of aryl halides and styrene in the presence of Pd@agarose–Fe_3O_4 in PEG 200

Aryl halide (1.0 mmol) and alkene (2.0 mmol) were added to a flask containing the catalyst (20 mg, containing 1.57×10^{-4} mmol of Pd) and K_2CO_3 (2.0 mmol) in PEG 200 (2 mL). The mixture was stirred at appropriate temperature for the appropriate reaction time (Table 5). Progress of the reaction was monitored by GC or TLC. After completion of the reaction, the catalyst was separated by an external magnet. Then, H_2O (10 mL) was added to the mixture and extracted with ethyl acetate (3 × 10 mL). The organic portions were combined and dried over anhydrous $MgSO_4$ and filtered. The resulting solution was evaporated under vacuum to give the crude product. The column chromatography of the crude product on silica gel using *n*-hexane or different mixtures of *n*-hexane–ethyl acetate as the eluents afforded the highly pure product (Table 5).

General procedure for Sonogashira–Hagihara reaction of aryl halides in the presence of Pd@agarose–Fe_3O_4 in PEG 200

A round-bottom flask was charged with phenylacetylene (1.5 mmol, 0.153 g), K_2CO_3 (3.0 mmol, 0.414 g), PEG 200 (2 mL), and aryl halide (1.0 mmol). To this mixture, the catalyst (10 mg, containing 0.78×10^{-4} mmol of Pd) was added. The mixture was stirred at 100 °C under an argon atmosphere; the progress of the reaction was monitored by GC or TLC. After completion of the reaction, the catalyst was removed by an external magnet. To the resulting mixture H_2O (10 mL) was added followed by extraction with ethyl acetate (3 × 10 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and filtered. The organic solvent was evaporated under diminished pressure to give the desired crude product. Purification of the crude product was performed by column chromatography on silica using *n*-hexane or different mixtures of *n*-hexane–ethyl acetate as the eluents to afford the product in a high purity in 53–95% isolated yields (Table 7).

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