

Synthetic Application of Magnetic Nanocomposite Fe₃O₄@PEG-Au as a Heterogeneous and Reusable Nanocatalyst in The Suzuki Coupling Reactions

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ABSTRACT

In the present study, we carried out chemical synthesis and characterization of Fe₃O₄@PEG-Au as a magnetic nanocomposite in aqueous solution by chemical co-precipitation of Fe³⁺ and Fe²⁺ ions and encapsulated by poly (ethylene glycol) (PEG) in order to enhancing hydrophilicity, biocompatibility and immobilizing gold ions in the presence of NaBH₄ as a reducing agent. Nanostructures were characterized again with FESEM and TEM. The nanoparticles with their spherical shape and dimensions of approximately 12 nm were used as a heterogeneous catalyst for Suzuki coupling reactions whilst in mild conditions. The high efficiency of the catalytic reaction was affirmed by the good yields of products, easy work-up, and absence of leached gold from the support and the smooth recovery of the catalyst.

Keywords: Nanocatalyst, Suzuki, Magnetic, PEG, Gold NPs

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INTRODUCTION

A most valuable and practical method in the organic synthesis has been recently focused on via the catalysis of carbon-carbon cross-coupling reactions using palladium. [1-4]Accordingly, the most efficient method for the synthesis of biaryls has been proceeded through the Suzuki-Miyaura reaction between aryl halides and organoboranes. [5] Biaryls are commonly thought to have partial structures in polymers, natural products, pharmaceuticals, and generally material science. [6-8].

For industrial applications, fundamental

research on catalysts and catalytic reactions has drawn much attention. [9] To produce water-soluble catalysts, homogeneous palladium complexes as the main catalysts for the Suzuki-Miyaura coupling reaction are directed toward phosphine ligands. The catalyst, as well as frequently unstable and toxic ligands, is recovered by such catalytic systems, thus being a major disadvantage. [10-18] Due to their increased recyclability properties, heterogeneous catalysts show greater efficiency compared to their homogeneous counterparts. [19, 20] However, because of leaching from the support, certain heterogeneous catalysts of palladium have low reactivity. [21, 22] This would make the structures of the new heterogeneous catalysts

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capable of retaining the behaviors and selectivities of homogeneous catalysts crucial. [23].

As an alternative, supported Magnetic Nanoparticles (MNPs) have been efficiently applied as heterogeneous catalysts. The main advantage of this application for a catalytic system can be the efficient separation of MNPs from the reaction mixture after completion via a simple magnetic isolation process. [24].

On the other hand, MNPs serve as an efficient alternative support for the immobilization of homogeneous catalysts. [25,26] Due to their high surface areas and unique magnetic properties, these nanoparticles are widely used in different scientific fields, including biomedicine, biotechnology, and physics, and as catalysis supports in material science.[27-29] MNP-supported catalysts further represent high degrees of dispersion, reactivity, and chemical stability. Varied catalysts and ligands are immobilized on MNPs due to these advantages over other supporting materials.[30].

In this regard, we synthesized and characterized an inorganic-organic hybrid ($Fe_3O_4@PEG$ -Au) nanocomposite as a heterogeneous catalyst in Suzuki-Miyaura cross-coupling reactions.

RESULT AND DISCUSSION

The chemicals were purchased from Merck Chemical Company. The reagents and solvents were obtained from Sigma-Aldrich and Merck and used without further purification.

Preparation of Magnetic Fe_3O_4 Nanoparticles (MNPs)

Fe^{2+} and Fe^{3+} ions with a molar ratio of 2:1 were chemically co-precipitated to prepare naked Fe_3O_4 nanoparticles. Typically, $FeCl_2 \cdot 4H_2O$ (2.147 g, 0.0108 mol) and $FeCl_3 \cdot 6H_2O$ (5.838 g, 0.0216 mol) were dissolved in 100 ml of deionized water and vigorously stirred (500 rpm) at 85°C under nitrogen atmosphere. Then, 10 ml (one portion) of 25% NH_4OH was quickly added to the reaction mixture (Fe^{2+}/Fe^{3+} salt solution), while a black precipitate of MNPs was immediately formed. After another 25 min, the mixture was cooled to room temperature. Consequently, the ultrafine magnetic particles treated by magnetic separation were washed with deionized water several times.

Preparation of $Fe_3O_4@PEG400$

1 g of Fe_3O_4 NPs was dispersed in 200 mL

of water and sonicated for 20 min. Then, 3 g of PEG400 dissolved in 10 mL of water was added to the solution and sonicated for 10 min again. Using an external magnet, the suspended substance yielded after mechanical agitation at 25°C for 24 h was separated to be washed with water and ethanol. After synthesizing PEG400-functionalized Fe_3O_4 ($Fe_3O_4@PEG400$), the NPs were dried at 50°C for 12 h.

Preparation of $Fe_3O_4@PEG400/Au$

200 mg of $Fe_3O_4@PEG$ was dispersed in 50 mL of water and sonicated for 20 min. After the addition of 20 mL of 10⁻² M $AuNO_3$ solution to the reaction mixture and stirring for 2 h, 25 mL of a freshly prepared aqueous $NaBH_4$ solution (5×10⁻² M) was added at one portion to be stirred at room temperature for 30 min. Ultimately, using an external magnetic field, the as-prepared nanocomposite was separated and washed with deionized water several times. The prepared nanocomposite was found to have an Au loading of 0.10 mmol/g using ICP measurement.

Suzuki-Miyaura coupling reaction

In a typical reaction, 20 mg of $Fe_3O_4@PEG$ -Au (0.002 mmol Au) was poured into a 25 mL Schlenk tube. Then, a mixture of 1 mmol of aryl halide and 3 mL of water/ethanol (1:1) was added to 0.134 g (1.1 mmol) of phenyl boronic acid and 0.276 mg of K_2CO_3 (2 mmol). The whole mixture was stirred at 40°C for a desired time. Monitoring of the reaction was followed through Thin Layer Chromatography (TLC). Finally, 5 mL of ethanol was added after the reaction was completed. Now, the catalyst could be removed by an external magnet. Further purification was done via column chromatography (n-hexane-acetone; 4:1). To identify the products, ¹H NMR and ¹³C NMR spectroscopy was utilized.

As a part of our ongoing research program to develop new synthetic methodologies, after successful fabrication of the catalyst [31], we have investigated again the morphology surface by SEM and TEM images (Figure 1). The FESEM image (right) of the synthesized $Fe_3O_4@PEG$ -Au was confirmed that the catalyst was made up of uniform nanometer-sized particles. The TEM image of the $Fe_3O_4@PEG$ -Au catalyst (left) revealed that the Au nanoparticles with nearly

spherical morphology were formed on the surface of the modified Fe_3O_4 nanoparticles with PEG. In the transmission electron microscopy images, iron oxide nanoparticles of 10-15 nm in diameter and Au nanoparticles of ~3 nm entrapped in iron oxide are observed.

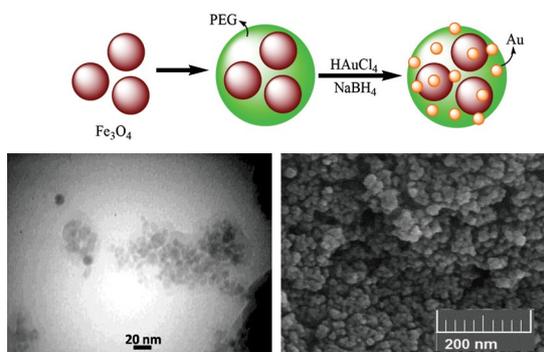
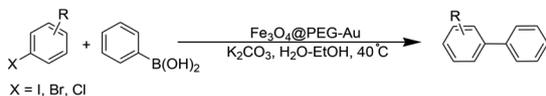


Fig. 1. Preparation of $Fe_3O_4@PEG-Au$ and its SEM and TEM images.

Encouraged by our previous work on C-C-coupling reactions,[32] we aimed to test the catalytic activity of the $Fe_3O_4@PEG-Au$ in the Suzuki-Miyaura coupling reaction under ligand-free conditions in the present study (Scheme 1).



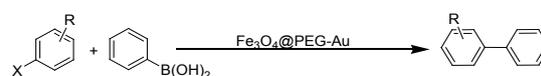
Scheme. 1. The catalytic activity of $Fe_3O_4@PEG-Au$ catalyst in the Suzuki coupling reaction.

We investigated several representative coupling reactions based on various aryl halides (I, Br, and Cl) and phenyl boronic acid after establishing a standard set of reaction conditions, i.e., 0.2 mol% of the supported gold catalyst, suitable K_2CO_3 and $H_2O-EtOH$ applications, and a temperature of $25^\circ C$, the results of which are displayed in Table 1.

We examined a wide electronic mixture of aryl iodides, bromides, and chlorides with phenyl boronic acid. As indicated in Table 1, the corresponding good-to-excellent products were yielded within a short-time reaction after an efficient coupling of aryl iodides bearing electron-withdrawing and electron-donating groups with phenyl boronic acid (Table 1, entries of 1, 4, 7, 10, 12, and 14). The desired products were moderately

produced by the coupling reaction of aryl chlorides with phenyl boronic acid after an extended reaction time compared to aryl iodides and bromides (Table 1, entries of 3, 6, and 9). Also, under the optimized reaction conditions, good yields of the desired biaryls were provided by the reactions of sterically hindered ortho-position halides and bulky 1-bromo naphthalene with phenyl boronic acid (Table 1, entries of 14 and 15).

Table 1. Heterogeneous Suzuki-Miyaura reaction of aryl halides with phenyl boronic acid catalyzed by $Fe_3O_4@PEG-Au$ catalyst.^a



Entry	RC6H4X	X	Time (h)	Yield (%) ^b
1	H	I	1	98
2	H	Br	2	90
3	H	Cl	24	50
4	4-CH ₃	I	1	96
5	4-CH ₃	Br	2	92
6	4-CH ₃	Cl	24	45
7	4-COCH ₃	I	2	92
8	4-COCH ₃	Br	5	90
9	4-COCH ₃	Cl	24	55
10	4-CH ₃ O	I	1	96
11	4-CH ₃ O	Br	4	88
12	4-Cl	I	2	92
13	4-Cl	Br	5	90
14	2-CH ₃ O	I	4	90
15	2-CH ₃ O	Br	6	82

Using a hot filtration test, analysis of the leaching of Au nanoparticles from the solid catalyst was performed. The reaction of bromobenzene with phenyl boronic acid was conducted in the presence

of $\text{Fe}_3\text{O}_4@$ PEG-Au catalyst by using K_2CO_3 in H_2O -EtOH as the solvent at room temperature. Thus, a solid precipitate was formed when 2 mL of ethanol was added, which was then recollected via centrifugation. The solid-free filtrate reaction was allowed to continue for another 60 min under similar conditions. The prepared catalyst stability and minimal leaching of Au species from the solid support were concluded since no enhanced amount of the product was observed. Moreover, Au content in the solution was corroborated by the atomic absorption spectroscopy of the filtrate to be under the detection limit of 0.1 ppm. This was indicative of the heterogeneity of the catalyst and its maintenance on the support at elevated temperatures during the reaction.

A vital concern for coupling reactions is related the catalyst recovery. Fortunately, the reaction efficiency can be significantly enhanced through the easy separation and recycling of catalysts in successive batch operations. Using the reaction of bromobenzene and phenyl boronic acid, the present heterogeneous nanocatalyst reusability was studied in the Suzuki cross-coupling reaction (Figure 2). Upon completion of the reaction, the catalyst was washed with ethyl acetate and then acetone to be dried under a lowered pressure at 40°C after being separated by an external magnet. Afterwards, appropriate proportions of the substrates were further added to the recovered catalyst under optimal reaction conditions to be applied in the next run. An unchanged catalytic behavior up to 6 reactions

was displayed by the catalyst. Thus, the high stability of the heterogeneous catalyst under the reaction conditions without degeneration was verified.

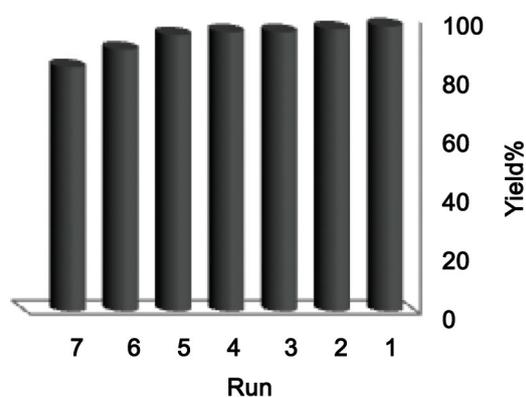


Fig. 2. Recycling of $\text{Fe}_3\text{O}_4@$ PEG-Au catalyst for the Suzuki coupling reaction under similar conditions.

The SEM and TEM images (Fig. 3) of the catalyst after the 5 runs indicated the preservation of the catalyst's nanostructure. The TEM image of reused catalyst also exhibited that the Fe_3O_4 NPs were still well spread and no clear aggregation of NPs was observed.

A contrast of the behavior of multiple catalysts with $\text{Fe}_3\text{O}_4@$ PEG-Au in the Suzuki coupling reaction released in the literature is recorded in Table 2. From Table 2, it is visible that the current catalyst exhibited more conversions and yields in comparison to the other listed system.

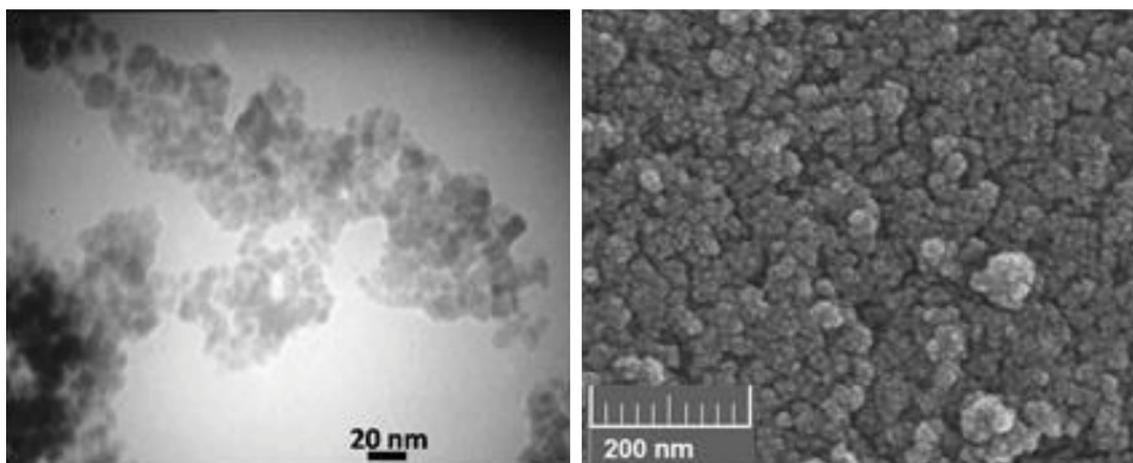


Fig. 3. TEM and SEM images of reused catalyst after the 5 runs.

Table 2. Catalytic performance of different catalysts in the coupling reaction of iodobenzene and bromobenzene with phenylboronic acid.

Entry	Catalyst (mol%)	Conditions	X	Time (h)	Yield (%)	Refs.
1	Bis(oxamato)palladate(II) complex (5)	Et ₃ N, <i>n</i> -Bu ₄ NBr, 120°C	I Br	2.0 2.0	78 65	[33]
2	NHC-Pd(II) complex (0.2)	K ₃ PO ₄ ·3H ₂ O, H ₂ O, TBAB, 40°C	I Br	5.0 6.0	98 90	[34]
3	SiO ₂ -pA-Cyan-Cys-Pd (0.5)	K ₂ CO ₃ , H ₂ O, 100°C	I Br	5.0 5.5	95 88	[35]
4	Pd ₃ (dba) (1)	K ₃ PO ₄ , THF, 80°C	Br	24	77.7	[36]
5	Pd-BOX (2)	K ₂ CO ₃ , DMF, 70°C	I	6.0	100	[37]
6	γ-Fe ₂ O ₃ -acetamidine-Pd (0.12)	Et ₃ N, DMF, 100°C	I Br	0.5 0.5	96 96	[38]
7	Pd-isatin Schiff base-γ-Fe ₂ O ₃ (0.5, 1.5)	Et ₃ N, Solvent-free, 100°C	I Br	0.5 0.7	95 90	[39]
8	Fe ₃ O ₄ @PEG-Au	K ₂ CO ₃ , H ₂ O/EtOH, 40°C	I Br	1.0 2.0	96 90	this work

CONCLUSION

In the current study, a nanosized Fe₃O₄@PEG-Au catalyst was successfully synthesized with high magnetic and excellent dispersibility characteristics. The magnetic catalyst provided a decent reactivity and reusability in the Suzuki reaction of aryl halides with phenylboronic acids. Furthermore, it could be easily recovered by an external magnet and reused 6 times without significant loss of its activity. Hence, due to its low Au leaching after several cycles, the new magnetic catalyst can be considered to be more economical and environment-friendly.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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