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# Palladium nanoparticles supported on cysteine-functionalized MNPs as robust recyclable catalysts for fast *O*- and *N*-arylation reactions in green media

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#### Abstract

A magnetically robust recyclable nanocatalyst was fabricated by immobilizing of Pd onto the surface of cysteine-functionalized magnetic nanoparticles (MNPs@Cys-Pd). This nanocatalyst was characterized using various techniques such as FT-IR, XRD, TEM, SEM, EDX, VSM, and ICP. The application of catalyst (MNPs@Cys-Pd) was investigated for *O*-arylation and *N*-arylation reactions. This phosphine-free complex was found as highly efficient heterogeneous catalyst in green media and mild reaction conditions. In addition, it gave excellent recyclability without significant deactivation after ten cycles.

Keywords: Cysteine, palladium, magnetic nanoparticles, O-arylation, N-arylation reactions

#### Introduction

Transition metal catalysis is a powerful methodology to construction of aryl-nitrogen and aryloxygen bonds; therefore, development of catalytic systems and investigation of their applications in organic transformations are so interesting [1]. Currently, palladium is the most popular transition-metal which widely used as catalyst in carbon–carbon and carbon–heteroatom bond formation reactions [2-10]. Homogeneous catalytic systems have attractive properties such as high activity and selectivity but reusability of these systems limits their usage in industrial and synthetic applications. So, studies have been focused on development of heterogeneous Pd catalysts using different supports [11-14].

However, compared with their homogeneous counterparts, the immobilized catalyst often suffer from lower activity and selectivity [15, 16]. In the last few decades nanomaterial-based catalysts are attracted a great deal of attention due to their high densities of active sites and high specific surface area which increase their catalytic activity [17]. In this context, wide variety of solid supports such as metal oxides [18] and carbon based [19], mesoporous and amorphous silica [20-26], polymers [27] and zeolites [28, 29] have been used for stabilizing of metal nanoparticles. Among these, magnetic nanoparticles, besides easy separation by an external permanent magnet [30], can stabilize metal nanoparticles using simple organic compounds such as silanes [31-38], carboxylic acids [39-41] and phosphonic acids [42-44].

L-cysteine is an amino acid with a SH functional group which a range of metals can bind to it [45, 50]. Some application of cysteine derivatives as catalyst in organic transformations are available such as aldol condensation reaction reported by Li et al [51] and one-pot synthesis of 2-amino-4H-chromene-3-carbonitriles introduced by Khalafi-Nezhad et al [52].

In continues of our previous experience on using heterogonous catalyst for cross coupling reaction [53-61]. We decided to employing cysteine to preparing palladium catalyst (MNPs@Cys-Pd) and study its efficiency in O-arylation and N-arylation reactions.

#### **Results and Discussion**

#### Preparation and characterization of the catalyst

The synthetic route for the preparation of MNPs@Cys-Pd is depicted in Scheme 1. The magnetic nanoparticles (MNPs) were prepared by co-deposition method according to the reported procedure [62] and subsequently coated by a silica layer upon reaction with tetraethyl orthosilicate (TEOS). Then, 3-iodopropyl trimethoxysilane was added to the dispersed Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub> in a nitrogen atmosphere to generate the iodo-functionalized MNPs. In this study, the modified silica was applied in order to graft cysteine moiety on magnetic nanoparticles. Afterwards, palladium acetate has immobilized onto the magnetic support in ethanol to obtain the MNPs@Cys-Pd as final catalyst.

The catalytic system was well characterized using various techniques including FT-IR, TEM, SEM, DLS, XRD, EDX, VSM and ICP. The progress of functionalization of magnetic nanoparticles was confirmed by FT-IR spectroscopy (Figure 1).



Scheme 1. The nanocatalyst preparation

The signal observed at 578 cm<sup>-1</sup> is attributed to the Fe–O stretching vibration of Fe<sub>3</sub>O<sub>4</sub> [63]. In the spectra of Fe<sub>3</sub>O<sub>4</sub>/SiO<sub>2</sub> nanoparticles (curve b), a strong broad peak at 1090 cm<sup>-1</sup> is corresponding to the Si–O–Si vibration, being revealing of the presence of a SiO<sub>2</sub> layer around the Fe<sub>3</sub>O<sub>4</sub> nanoparticles [64]. A comparison between the FT-IR spectra of Fe<sub>3</sub>O<sub>4</sub>, Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub> and cysteine-modified nanoparticle (curve c) clearly revealed the successful immobilization of cysteine moiety on the surface of magnetic nanoparticles [65]. For study in forming of complexes of the Pd-species with cysteine moieties, the spectra of final catalyst was compared with those of pure cysteine. As can be seen in supplemental data, in spectra of pure cysteine stretching vibration of C-S and C-N are appeared at 1584 and 1342 cm<sup>-1</sup>, while in the spectra of final catalyst these bonds shifted to 1670 and 1440 cm<sup>-1</sup>, respectively.

The quantitative determination of the palladium content was determined by ICP as 0.47 mol%. The XRD spectrum was also performed. As shown in Figure 2, the characteristic diffraction peaks clearly considered cubic spinel phase of Fe<sub>3</sub>O<sub>4</sub> {JCPDS 01-075-0033},  $2\theta = 30.1^{\circ}$  (220),  $35.5^{\circ}$  (311),  $43.1^{\circ}$  (400),  $47.2^{\circ}$  (331),  $53.5^{\circ}$  (422),  $57.0^{\circ}$  (511),  $62.6^{\circ}$  (440),  $75.1^{\circ}$  (622),  $82.0^{\circ}$  (551),  $86.8^{\circ}$  (642) and  $89.8^{\circ}$  (731). The wide diffraction peak at  $2\theta = 23^{\circ}$  attributed to silica coated magnetite particles {Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>} and other peaks in the sample at 20 of  $39.9^{\circ}$ ,  $46.4^{\circ}$ ,  $67.7^{\circ}$ ,  $81.6^{\circ}$  can be well indexed to the diffraction of (111), (200), (220), (311) crystal planes of Pd (0). The scanning electron microscopy (SEM) images was illustrated spherical external morphologies of the catalyst. The EDX spectrum showed the elemental composition after grafting reaction, confirming the presence of C, N, O, Si, S, Pd and Fe in the catalyst (Figure 3).



Figure 1. FT-IR spectra of (a) MNPs, (b) MNPs@SiO<sub>2</sub>, (c) MNPs@Cys-Pd

As displayed in Figure 4, TEM micrographs of the fresh catalyst reveals that nanoparticles are in spherical shape with an average of 14 nm and good monodispersity. The magnetization curve of the catalyst in comparison with pure MNPs and MNPs@SiO<sub>2</sub> (the VSM spectra was given in supplemental data, Figure 2S), represents the magnetic behavior of the catalyst and contact of organic moieties on MNPs (Figure 5).



Figure 2. The XRD pattern of catalyst



Figure 3. SEM photographs and the EDX spectrum of catalyst



Figure 4. The TEM images and histogram representing the size distribution of catalyst



Figure 5. The vibrating sample magnetometer (VSM) of the catalyst

After synthesis and characterization of catalyst, its catalytic performance in the *O*-arylation coupling between a various types of alcohols and aryl halides was studied. In order to obtain suitable conditions, the reaction of iodobenzen with phenol was selected as the model reaction. The efficiency of various parameters such as base, solvents, different temperature and several amount of catalyst were examined (Table 1). The initial experiments were performed by running the model reaction in the presence of KOH, 10 mg of catalyst at 100 °C under aerobic conditions in various reaction times. After founding the best reaction time, different solvent effect was studied. Among different solvents, EtOH was chosen as the most effective solvent. In the next step, to obtain the proper base, the effect of several types of bases was investigated. The KOH gave rise to the most suitable effect. To optimum temperature of the reaction, the performance of reaction was also checked by acting the model reaction at different temperatures while keeping the other parameters fixed. The O-arylation reaction proceeds efficiently at 60 °C, thus this temperature was selected as optimum. The optimized amount of catalyst found as 5 mg.

With these favored reaction conditions in hand, the scope and generality of this procedure in the O-arylation reaction for commercially available alcohols with some aryl halides was explored. As clearly shown in Table 2, both aromatic and aliphatic alcohols can be coupled efficiently under the defined reaction conditions. To our delight, the various substituted aryl iodides, bromides and chlorides bearing both electron-rich and electron-poor groups were converted effectively to desired products in good to excellent yields. It was also observed that increasing steric hindrance of ortho-substituted phenols gave lesser yield than those obtained with parasubstituted ones.

Entry	Reaction time (h)	Solvent	Base	T(°C)	Cat (mg)	Yield <sup>b</sup>
1	6	<b>DMSO</b>	KOH	<mark>60</mark>	<mark>10</mark>	<mark>96</mark>
2	<mark>3</mark>	<b>DMSO</b>	KOH	<mark>60</mark>	<mark>10</mark>	<mark>97</mark>
<mark>3</mark>	<mark>0.5</mark>	<mark>DMSO</mark>	KOH	<mark>60</mark>	10	<mark>96</mark>
<mark>4</mark>	<mark>0.25</mark>	<mark>DMSO</mark>	KOH	<mark>60</mark>	10	<mark>84</mark>
5	0.5	EtOH	КОН	60	10	98
6	0.5	Toluene	КОН	100	10	91
7	0.5	DMF	КОН	100	10	95
8	0.5	DMSO	КОН	100	10	96
9	0.5	EtOH	K <sub>2</sub> CO <sub>3</sub>	60	10	91
10	0.5	EtOH	K <sub>3</sub> PO <sub>4</sub>	60	10	89
11	0.5	EtOH	КОН	25	10	33
12	0.5	EtOH	КОН	40	10	91
13	0.5	EtOH	кон	60	5	97
14	0.5	EtOH	КОН	60	15	<mark>95</mark>

**Table 1**. Effect of different parameters in O-arylation reaction<sup>a</sup>

<sup>a</sup>Reaction conditions: iodoobenzene (1 mmol), phenol (1.2 mmol), base (2 mmol), solvent (5 ml). <sup>b</sup>Isolated yield.

Encouraged by these results, we decided to apply our designed catalyst in the N-arylation reaction of various types of aryl halides with different amines. The N-arylation reaction between iodobenzene and morpholine was chosen as a model to evaluate optimum reaction conditions by employing different solvents, bases, temperatures and catalyst loading (Table 3). In our first set of experiments, the effect of the different solvent in this transformation was studied. The results showed that the yield of product was enhanced to 96% when the reaction was carried out in solvent-free conditions.

			X Alcohol MNPs@Cys-Pd		Ether	
		ĸŢ	Optimized	conditions		$\mathbf{C}$
Entry	R	Х	Alcohol	Yield <sup>b</sup>	TON <sup>c</sup>	$TOF(h^{-1})^d$
1	Н	Ι	phenol	98	3.6×10 <sup>3</sup>	$7.2 \times 10^{3}$
2	Н	Ι	2,3,6-trimethylphenol	72	$2.7 \times 10^{3}$	5.3×10 <sup>3</sup>
3	Н	Ι	(4-chlorophenyl)methanol	95	$3.5 \times 10^{3}$	$7.0 \times 10^{3}$
4	Н	Ι	2-chloro-6-nitrophenol	88	$3.2 \times 10^{3}$	<mark>6.5×10<sup>3</sup></mark>
5	Н	Ι	phenol	97	$3.6 \times 10^{3}$	$7.2 \times 10^{3}$
6	Н	Ι	5bromo-2-hydroxybenzaldehyde	86	$3.2 \times 10^{3}$	$6.5 \times 10^{3}$
7	Н	Ι	3,5-dinitrophenol	100	$3.7 \times 10^{3}$	$7.4 \times 10^{3}$
8	Н	Ι	resorcinol	73	$2.7 \times 10^{3}$	$5.4 \times 10^{3}$
9	4-Me	Ι	2,6-dimethylphenol	71	$2.6 \times 10^{3}$	$5.2 \times 10^{3}$
10	Н	Br	4-hydroxybenzaldehyde	92	$3.4 \times 10^{3}$	6.8×10 <sup>3</sup>
11	Н	Br	naphthalen-1-ol	76	2.8×10 <sup>3</sup>	5.6×10 <sup>3</sup>
12	$4-NO_2$	Br	(4-chlorophenyl)methanol	90	3.3×10 <sup>3</sup>	<mark>6.6×10<sup>3</sup></mark>
13	Н	Cl	(4-chlorophenyl)methanol	93	$3.4 \times 10^{3}$	<mark>6.8×10<sup>3</sup></mark>

Table 2. O-arylation of aryl halides and different alcohols

Y

<sup>a</sup>Reaction conditions: aryl halide (1 mmol), alcohols (1.2 mmol), KOH (2 mmol), EtOH (4 ml), catalyst (5 mg), 60 °C in 0.5 h; <sup>b</sup>Isolated yield;

<sup>c</sup>(Mol product/mol palladium); <sup>d</sup>(Mol product/mol palladium) (h<sup>-1</sup>

Then, the type of base was changed and the best result is obtained when KOH is used as base. The 60 °C was found as the best considering to good yield and energy safe aims. Moreover, efficient amount of catalyst was selected as 5 mg. To specify the scope and generality of this procedure for obtained aryl amine derivatives, a various types of aryl halides have reacted with some commercially available amines under optimized reaction conditions. As depicted in Table 4, N-arylation reaction of various substrates (iodo-, bromo- and chloro- derivatives) and

substituents (electron-rich and electron-poor), provided very good to excellent yields of coupling products.

		<u> </u>			
Entry	Reaction time (h)	Solvent	Base	T(°C)	Yield <sup>b</sup>
1	<mark>6</mark>	H <sub>2</sub> O	КОН	100	22
2	<mark>3</mark>	H <sub>2</sub> O	КОН	100	20
3	<mark>0.5</mark>	H <sub>2</sub> O	КОН	100	20
4	0.25	H <sub>2</sub> O	КОН	100	11
5	<mark>0.5</mark>	CH <sub>3</sub> CN	кон	80	43
6	<mark>0.5</mark>	DMF	КОН	110	86
7	<mark>0.5</mark>	Solvent free	КОН	110	95
8	<mark>0.5</mark>	Solvent free	K <sub>3</sub> PO <sub>4</sub>	110	81
9	<mark>0.5</mark>	Solvent free	K <sub>2</sub> CO <sub>3</sub>	110	84
10	<mark>0.5</mark>	Solvent free	кон	60	93
11	0.5	Solvent free	КОН	25	36

Table 3. Effect of different parameters in N-arylation reaction<sup>a</sup>

<sup>a</sup>Reaction conditions: iodobenzene (1 mmol), morpholine (1.2 mmol), base (2 mmol), in 0.5 h. <sup>b</sup>Isolated yield.

The hot filtration test was accomplished for *N*-arylation as same as the *O*-arylation reaction. After removal of catalyst, using an external magnetic bar, no further progress in product yield was determined. The ICP analysis of resultant supernatant only showed 0.03 ppm palladium in solution, it indicated heterogeneously nature of our catalytic system. The recyclability of catalyst was investigated in model reaction of O-arylation (the reaction of iodobenzen with phenol) and no significant decrease in catalytic activity was observed until the ten runs (Table 5).

		Δmi	MNPs@Cys-Pd	Products		
	R	+ 700	Optimized conditions			
Entry	R	Х	Amine	Yield <sup>b</sup>	TON <sup>c</sup>	TOF(h <sup>-1</sup> ) <sup>d</sup>
1	Н	Ι	morpholine	93	$3.4 \times 10^{3}$	6.9×10 <sup>3</sup>
2	Н	Br	morpholine	94	$3.5 \times 10^{3}$	6.9×10 <sup>3</sup>
3	4-NO <sub>2</sub>	Br	diphenylamine	81	$3.0 \times 10^{3}$	6.0×10 <sup>3</sup>
4	4-NO <sub>2</sub>	Cl	diphenylamine	79	2.9×10 <sup>3</sup>	$5.8 \times 10^{3}$
5	2,4-di-NH <sub>2</sub>	Cl	morpholine	72	2.7×10 <sup>3</sup>	5.3×10 <sup>3</sup>
6	4-OMe	Br	morpholine	87	3.2×10 <sup>3</sup>	6.4×10 <sup>3</sup>
7	Н	Br	propan-1-amine	trace	•	-
8	2-NO <sub>2</sub>	Br	morpholine	81	3.0×10 <sup>3</sup>	6.0×10 <sup>3</sup>
9	Н	Br	N-methylbenzenamine	93	3.4×10 <sup>3</sup>	$6.0 \times 10^{3}$
10	4-NO <sub>2</sub>	Br	N-methylbenzenamine	98	<mark>3.6×10<sup>3</sup></mark>	$7.2 \times 10^{3}$
11	4-Br	Br	morpholine	92	3.4×10 <sup>3</sup>	$3.4 \times 10^{3}$
12	4-NO <sub>2</sub>	Cl	morpholine	87	3.2×10 <sup>3</sup>	6.4×10 <sup>3</sup>
13	Н	Cl	morpholine	80	2.9×10 <sup>3</sup>	5.9×10 <sup>3</sup>
14	9-bromophenanthrene	Br	morpholine	86	3.2×10 <sup>3</sup>	<mark>6.4×10<sup>3</sup></mark>
15	3- COCH <sub>3</sub>	Br	morpholine	trace	•	-

Table 4. N-arylation of aryl halides and different amines

<sup>a</sup>Reaction conditions: aryl halide (1 mmol), amine (1.2 mmol), KOH (2 mmol), catalyst (5 mg), 60 °C; in 0.5 h.

<sup>b</sup>Isolated yield.

<sup>°</sup>(Mol product/mol palladium);

<sup>d</sup>(Mol product/mol palladium) (h<sup>-1</sup>)

TEM images of recycled catalyst (after ten runs) was shown in Figure 6, in comparison with fresh catalyst no significant change was done. The comparison between the XRD spectra of fresh and reused catalyst also indicated that the state of Pd was kept during the reaction progress (Figure 6).

Run	Yield <sup>a</sup> (%)	Run	Yield <sup>a</sup> (%)				
1	98	69	96				
2	98	7	95				
3	97	8	95				
4	97	9	94				
5	96	10	90				

 Table 6. Reusability of the catalyst

<sup>a</sup>Isolated yield



Figure 6. TEM image and XRD pattern of the recovered catalyst

A comparison study between efficiency of MNPs@Cys-Pd with some reported heterogeneous Pd-catalysts in O-arylation and N-arylation reactions was given in Table 6. It can be obviously seen that the current MNPs@Cys-Pd is superior to others in terms of catalytic efficiency. Our efficient heterogeneous palladium catalytic system gave high catalytic activity in short time while green media and mild reaction conditions was applied.

**Table 6.** Comparison of catalytic activity of nanocatalyst with literature examples for *O*-arylation and N-arylation reactions

Entry[ref.]	Catalyst	Conditions	Yield (%)	TON	-TOF(h <sup>-1</sup> )
		+ OH catalyst, Base Solvent	-0-		
1 [66]	Pd/ZnO	K <sub>2</sub> CO <sub>3</sub> , DMF, 120 °C, 5 h	98	3.6×10 <sup>6</sup>	$7.2 \times 10^{5}$
2 [67]	PdCl <sub>2</sub> , SDPP	NaOH, Bu <sub>4</sub> NOH, 70 °C	98	$5.4 \times 10^{3}$	$1.8 \times 10^{3}$
3 [68]	$[Pd(P_3S_4)(dba)]$	Cs <sub>2</sub> CO <sub>3</sub> , isopropanol	83	$2.7 \times 10^{2}$	$1.35 \times 10^{3}$
5(This work	) MNPs@Cys-Pd	KOH, EtOH, 0.5 h, 60 $^\circ\mathrm{C}$	98	3.6×10 <sup>3</sup>	$7.2 \times 10^{3}$
		+ Catalyst, Base Solvent		)	
7 [69]	Pd/Nf-G DM	SO, tBuONa, 12 h, 110 °C	93	4.6×10 <sup>2</sup>	<mark>3.9</mark>
8 [70]	$[Pd(pp_3S_4)(dba)]$	Cs <sub>2</sub> CO <sub>3</sub> , Isopropanol, 24 h	80	$5.2 \times 10^{3}$	$2.2 \times 10^{2}$
9 [71]	PFG-Pd	NaOtBu, toluene,12 h, 110	°C 90	$4.8 \times 10^{2}$	4.0×10
10 [This wo	rk] MNPs@Cys-Pc	KOH, solvent-free, 0.5 h	a, 60 °C 93	$3.4 \times 10^{3}$	6.9×10 <sup>3</sup>

#### Experimental

#### Chemical, instrumentation and analysis

All chemical reagents were purchased from Merck and Aldrich chemical companies and were used without further purification. <sup>1</sup>H-NMR was recorded on a Brucker (250 MHZ) Avance DRX in pure CDCl<sub>3</sub> solvent with tetramethylsilane (TMS) as internal standards. FT-IR spectra were obtained as KBr pellets on a JASCO 680- Plus spectrophotometer. Magnetic measurement was done by vibrating sample magnetometer (VSM) in 0.0001-50 emu. The transmission electron microscopy (TEM) using TEM device (Zeiss–EM10C–80 KV) and scanning electron microscopy [MIRA3 TESCAN] were acquired for characterization of the catalyst. The X-ray diffraction (XRD, D8, Advance, Bruker, axs) was engaged. The reaction monitoring was

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accomplished by TLC or gas chromatography (GC) (BEIFIN 3420 gas chromatograph equipped with a Varian CP SIL 5CB column: 30 m, 0.32 mm, 0.25 mm). Column chromatography was carried out on columns of silica gel 60 (70–230 mesh).

#### **Catalyst preparation**

#### Synthesis of 3-iodopropyltrimethoxysilane

To a solution of anhydrous sodium iodide (5 mmol) in dry acetone (50 mL), 3chloropropyltrimethoxysilane (5 mmol) was added and the mixture was refluxed for 24 h under a nitrogen atmosphere. After that, the solvent was removed under vacuum. The residue was then diluted in  $CH_2Cl_2$ , filtered and washed twice with  $CH_2Cl_2$ .

#### Preparation of MNPs@Cys-Pd catalyst

Magnetic nanoparticles were prepared via co-precipitation of Fe (III) and Fe (II) ions according to a reported procedure.<sup>27</sup> After sonication, to a mixture containing 1 g of Fe<sub>3</sub>O<sub>4</sub>, 20 mL water, 80 mL ethanol, 3 mL ammonia and 3 mL tetraethyl orthosilicate (TEOS) were added. The solution was refluxed to obtain MAGNPS-Silica core–shell materials.<sup>30</sup> Afterward, 1 g of prepared SiO<sub>2</sub>coated Fe<sub>3</sub>O<sub>4</sub> nanoparticles were suspended in dry toluene by sonication for 30 min, and 3iodopropyltriethoxysilane was then added. The solution was refluxed for 24 h under nitrogen atmosphere. After being cooled to room temperature, the product was collected and washed with toluene and acetone several times. For the synthesis of MNPs@Cys-Pd, 2 mmol of l-cysteine and 3 mmol K<sub>2</sub>CO<sub>3</sub> were added in to a prepared solution containing 1g of iodo-functionalized  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> in 30 mL acetonitrile. The mixture was then refluxed for 24 h under nitrogen atmosphere. The resulting precipitate was collected by external magnetic field, washed with water and ethanol. To a mixture of magnetic cysteine -functionalized chitosan (MNPs@Cys) (0.5 g) in ethanol (20 mL),  $Pd(OAc)_2$  (0.05 g) was added and stirred for 24 h in room temperature. Then, the catalyst was separated from the mixture and washed with acetone several times. The final catalyst was obtained as a black powder.

#### General procedure for coupling of N-arylation

In a round-bottomed flask equipped with mechanical stirrer, aryl halide (1 mmol), amine (1.2 mmol), catalyst (5 mg) and KOH (2 mmol) were stirred in ethanol (5 ml) under air atmosphere at 60 °C for 0.5 h. The progress of the reaction was monitored by TLC and GC. After completion of the reaction,  $CH_2Cl_2$  (15 ml) was added and the catalyst was separated using an external magnet. The organic layer was washed with water (3 × 10 ml) and dried over anhydrous MgSO<sub>4</sub>. The product was isolated by column chromatography (n-hexane–ethyl acetate, 5:1) to afford the corresponding products. The products were characterized by their physical properties, melting points, and FT-IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR [69-71].

### **General procedure for O-arylation**

In a round-bottomed flask equipped with mechanical stirrer, aryl halide (1 mmol), phenol (1.2 mmol), catalyst (3 mg) and KOH (2 mmol) were stirred in solvent-free conditions under air atmosphere at 60 °C for 0.5 h. The progress of the reaction was monitored by TLC (eluent: n-hexane–ethyl acetate, 5:1) and GC. After completion of the reaction,  $CH_2Cl_2$  (15 ml) was added and the catalyst was separated using an external magnet. The organic layer was washed with water (3 × 10 ml) and dried over anhydrous MgSO<sub>4</sub>. The product was isolated by column chromatography (n-hexane–ethyl acetate, 5:1) to afford the corresponding products. The

products were characterized by their physical properties, melting points, and FT-IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR [66-68].

#### Conclusions

In conclusion; herein, efficient heterogeneous palladium catalytic system was synthesized via immobilizing of Pd-NPs on the surface of magnetic cysteine material and its application in O-arylation and N-arylation reactions was investigated. Addition to a high catalytic activity in green media and mild reaction conditions, it exhibited excellent reusability.

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# ACCEPTED MANUSCRIPT

## Table of content

This work provides an active magnetically separable catalyst based palladium nanoparticle supported on cysteine functionalized magnetic nanoparticle for the *O*-arylation and *N*-arylation reactions in mild condition.



# Highlights

- A heterogeneous catalyst, MNPs@Cys-Pd, was synthesized by anchoring a palladium (0) on cysteine-functionalized magnetic nanoparticle.
- The catalytic activity of these catalytic systems was evaluated for the Oarylation in ethanol and N-arylation in solvent-free media under phosphinefree conditions.
- This nanocatalyst could be easily recovered from the reaction mixture and also exhibited good reusability.