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Nano-magnetic Fe_3O_4@TiO_2/Cu_2O composite: a simple, effective and reusable heterogeneous catalyst for ligand-free *N*-arylation of amines and nitrogen heterocycles

Firouzeh Nemati[1] · **Ali Elhampour**[1]

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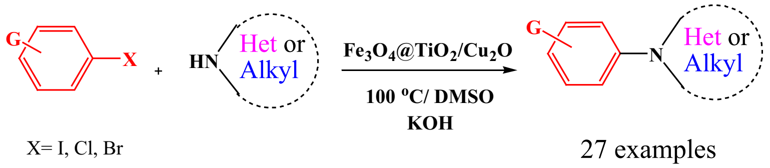
Abstract A practical and mild synthetic strategy has been investigated for the arylation of aromatic amines and nitrogen heterocycles using nano-magnetic-Fe_3O_4@TiO_2/Cu_2O composite and KOH as the base. The protocol does not require the use of expensive ligands. Notably, the catalyst is easily recoverable and reused by magnetic separation up to five runs without appreciable loss of catalytic activity.

Graphical Abstract



Keywords Nano-chemistry · Nano-magnetic · Green chemistry · Heterogeneous catalyst · *N*-Arylation

Introduction

Transition metal-catalyzed cross-coupling reactions are one of the most efficient and powerful tools in organic synthesis for the connection of two fragments through C–C or C–N bond formation. The development of an efficient methodology for C–N

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✉ Firouzeh Nemati
fnemati@semnan.ac.ir

[1] Department of Chemistry, Semnan University, Semnan, Iran

bond formation is one of the most important reactions since the resultant *N*-arylated heterocyclic products play an important role in a wide range of pharmaceuticals and biologically active compounds and natural products [1]. Among the many reported C–N coupling reactions such as Ullmann coupling, Chan–Lam coupling [2] and Buchwald–Hartwig amination [3], the Ullmann-type coupling reactions are particularly attractive because they often allow the usage of low-cost starting materials and readily available copper complexes. The Ullmann-type coupling reactions can be mediated by palladium, nickel or copper catalysts with different coordinating ligands [4–8]. In this context, various types of ligands have been developed to facilitate the copper-catalyzed *N*-arylation reaction under different conditions. Although these catalysts and ligands or many copper/ligand combinations are used in low loading, they are very expensive and the toxicity caused by the presence of metal in the products is a serious disadvantage of these reactions. Therefore, development of new methodology taking into consideration a decrease of reaction time, minimum metal contamination of products, a simple catalyst system involving easy isolation and reusability of catalysts, and ligand-free conditions is highly desirable.

Magnetic nanoparticles are particularly attractive structures since they are favorable as one of the most powerful heterogeneous catalysts in organic synthesis, for their high surface area, more active sites, low density, hybrid functionalities and ease of handling that result in improving the efficiency, selectivity and yields of the catalytic process [9, 10]. As important, the magnetic separation technique as one of the advantages of magnetic nanoparticles has major significance for nano-sized structures in which the conventional filtration method results in the loss of catalyst particles and product contaminations [11, 12].

In recent years, titanium dioxide (TiO_2) nanoparticles have been extensively considered in various applications, including purification of wastewater, hydrogen production [13], sensors [14] and organic pollutant degradation [15], due to its high photocatalytic activity, chemical stability, low cost, non-toxicity and environmentally friendly advantages. Despite their wide use in photocatalytic activity, much less attention has been focused on the catalytic behavior of titanium dioxide nanoparticles in organic transformations because of the difficult separation of them from products for recycling [16, 17]. In this regard, a variety of nanostructures have been designed, such as core/shell, mesoporous, nanotube, and hollow sphere structures, providing an excellent chance to explore their unique surface properties [15, 18–20]. Among the various structures, an interesting nanoparticle system is that of core/shell structure nanoparticles in which the magnetic core is coated with a layer of a nonmagnetic, antiferromagnetic, or ferro/ferri-magnetic shell. In this regard, TiO_2 can be considered as a shell due to its unique surface properties, its high chemical and thermal stability, non-toxicity, as well as its great accessibility and moderate cost [21, 22]. Furthermore, the inclusion of an Fe_3O_4 core into TiO_2 nanospheres makes them easy to be recovered [23].

In our continuing efforts towards the development of efficient and environmentally benign synthetic methodologies [24–30], very recently, we have reported on the preparation and characterization of a new Fe_3O_4@TiO_2/Cu_2O magnetic composite, which demonstrated an efficient catalysis for the synthesis of 1,2,3-

triazoles [31]. The catalyst was readily prepared through a simple method and composed of micro-sized Cu_2O in Fe_3O_4@TiO_2 core/shell magnetic particles.

In this report, we would like to disclose our findings towards the development of ligand-free amination of aryl halides, in which *N*-arylated amines were synthesized in high yields, promoted by the heterogeneous Fe_3O_4@TiO_2/Cu_2O magnetic composite as a catalyst. The magnetic composite could be easily separated from the crude reaction mixture and recycled in five consecutive runs without significant loss of catalytic activity.

Materials and methods

Chemical reagents in high purity were purchased from Merck and Sigma-Aldrich and were used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded using a Bruker DRX-400 spectrometer at 400 and 100 MHz, respectively. The progress of the reaction was monitored by thin layer chromatography (TLC) on commercial aluminum-backed plates of silica gel 60 F254, visualizing using ultraviolet light.

Preparation of nano-magnetic Fe_3O_4@TiO_2/Cu_2O composite

The nano-magnetic composite was prepared in accordance to our earlier report (For details, see ESI) [31]. We explored that the most appropriate ratio of nano-Fe_3O_4@TiO_2:Cu_2O was 80:20 % (Table S1). Therefore, the optimal weight ratio of Fe_3O_4@TiO_2:Cu_2O, 8:2, was selected for the *N*-arylation of aryl iodides.

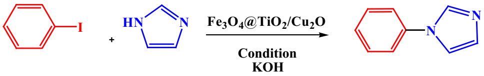
General procedure for the *N*-arylation of aryl iodide

A mixture of aryl iodide (1.0 mmol), Het-NH (1.2 mmol), KOH (2 mmol), nano-magnetic Fe_3O_4@TiO_2/Cu_2O (0.010 g equal to 1.4 mol% Cu_2O) and anhydrous DMSO (2 mL) was stirred at 100 °C. After completion of the reaction as indicated by TLC, the reaction mixture was cooled to room temperature and diluted by ethyl acetate and the catalyst was separated by an external magnet from the mixture, washed with acetone, dried in an oven at 80 °C for 3 h and re-used for a consecutive run under the same reaction conditions. The combined ethyl acetate layer was washed with water and dried over anhydrous $MgSO_4$. The residue was purified by recrystallization or short column chromatography on silica gel to afford the target products in excellent yield.

Results and discussion

To access the catalytic activity of Fe_3O_4@TiO_2/Cu_2O, it was applied in the model reaction for *N*-arylation of aryl halides. In order to find out the appropriate conditions, the reaction of iodobenzene **1a** (1 mmol) and imidazole **2a** (1.2 mmol) was studied, (Table 1), in which the effects of solvents, loading of catalyst and temperature were evaluated (Table 1).

Table 1 Optimization of the model reaction



Entry	Catalyst (g)	Conditions	Time/h	Yield/%
1	$Fe_3O_4@TiO_2$ (0.02)	DMSO/100 °C	2	23
2	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	DMSO/25 °C	2	Trace
3	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	DMSO/80 °C	2	87
4	**$Fe_3O_4@TiO_2/Cu_2O$ (0.01)**	**DMSO/100 °C**	**2**	**92**
5	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	DMSO/100 °C	5	91
6	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	DMSO/110 °C	2	93
7	$Fe_3O_4@TiO_2/Cu_2O$ (0.015)	DMSO/100 °C	2	90
8	$Fe_3O_4@TiO_2/Cu_2O$ (0.02)	DMSO/100 °C	2	83
9	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	Water/reflux	2	Trace
10	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	Ethanol/reflux	2	49
11	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	CH_2Cl_2/Reflux	5	53
12	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	Toluene/100 °C	2	62
13	$Fe_3O_4@TiO_2/Cu_2O$ (0.01)	Solvent free/100 °C	2	Trace
14	–	DMSO/100 °C	6	Trace

Bold value indicates the optimized condition

[a] Reaction conditions: imidazole (1.2 equiv.) and iodobenzene (1 equiv.) and $Fe_3O_4@TiO_2/Cu_2O$ as catalyst

[b] Isolated yield

In our initial screening experiments, we carried out the model reaction in DMSO at 100 °C in the presence of 20 mg of $Fe_3O_4@TiO_2/Cu_2O$ magnetic composite as a catalyst and only 23 % conversion was obtained even after 4 h. It seems noteworthy to mention that the reaction was not successful in the absence of a base. Thus, to promote the initial abstraction of the activated proton of imidazole **1a**, the addition of several bases such as KOH, NaOH, Na_2CO_3, K_2CO_3, Et_3N and pyridine to the reaction mixture was examined. The screening of bases revealed that inorganic bases due to more basicity were more efficient than the soluble organic bases for this coupling reaction. Thus, the reaction yield was improved up to 92 % when 2 mmol KOH was added.

A further increase in the base amount to 3 mmol did not provoke any improvements of the reaction time or yield. Moreover, the reaction did not occur in the absence of the catalyst after a prolonged reaction time (Table 1, entry 14). According to the reported literature, Cu_2O could catalyze the synthesis of 1-phenyl-1H-imidazole **3a** for 24 h in the presence of KOH in DMSO under Ar atmosphere [32]. The model reaction was performed using 20 mg of $Fe_3O_4@TiO_2$, in which no desired product was observed. Hence, it established the synergetic effect of Cu_2O and magnetic-$Fe_3O_4@TiO_2$ in this system. The catalyst loading for this reaction could be reduced from 20 to 10 mg without affecting the product yields. Hence, 10 mg of nanocomposite Fe_3O_4@TiO_2/Cu_2O is optimum and sufficient for this reaction during 2 h.

Having determined the optimum base and loading of catalyst for the reaction, investigation pertaining to the choice of an appropriate solvent was performed. From the data in Table 1, it was found that DMSO is a suitable solvent to give the desired product in high yield; while others solvents such as water, ethanol, CH_2Cl_2 and toluene and even solvent-free conditions gave relatively low yields (Table 1, entries 9–13). Furthermore, the reaction temperature exerted an impact on this coupling reaction. As indicated in Table 1, it was noted that at lower temperature (25–80 °C) the reaction gave the product in low yield and the best temperature was found to be 100 °C.

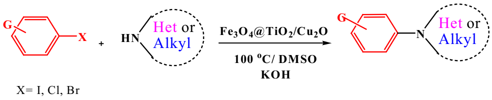
Thus, the best condition was found to be Fe_3O_4@TiO_2/Cu_2O (0.01 g) as the catalyst, DMSO (2 ml) as the solvent, KOH (2 mmol) as the base, ligand-free and conducting the reaction at 100 °C. The reaction proceeds smoothly and the corresponding product resulted in high yields without observing any side-product. Encouraged by these results, and in order to expand the scope of this methodology, we initiated our investigation into the variety of substituted aryl halide derivatives with heterocyclic amines in this cross-coupling reaction, and the results are reported in Table 2. As shown in Table 2 (entries 1–9 and 19–27), the coupling reactions were performed well by the reaction of heterocyclic amines with various aryl halides, and the desired products were isolated in moderate to excellent yields. Notably, when the reaction was carried out with iodobenzene, the expected products were obtained in high yields, in accordance with the bond reactivity order of C–I > C–Br > C–Cl (Table 2).

Generally, the aryl halides containing electron-withdrawing and electron-donating groups are reacted with imidazole to afford the corresponding *N*-arylated products in good to excellent yields. Electron-deficient *p*-substituted aryl iodides were found to proceed in higher yields than those with electron-donating substituent groups (e.g. Table 2, entries 2 and 3). Instead of imidazoles, other nitrogen-containing heterocycles such as 2-methyl imidazoles, benzo[a]imidazoles, pyrrole and indole could be used in the arylation process with use of aryl iodide and good results were obtained (Table 2, entries 6–9). Owing to the excellent results obtained in the *N*-arylation of aryl iodides with nitrogen-containing heterocycles, a similar protocol was employed with aliphatic and aromatic amines, and only with increasing the reaction time, the corresponding products were obtained in high to good yields (Table 2, entries 10–14).

To show the superiority of the present method over previous ones, we compared our results with some other results reported in the literature (Table 3). For example, the $CuFe_2O_4$ was used as a catalyst for amination of aryl iodides (Table 3, entry 12). It has some merits including being ligand and additive-free, using a recyclable media and magnetically separable catalyst.

As shown in Table 3, Fe_3O_4@TiO_2/Cu_2O magnetic composite as a simple catalyst has some other advantages such as short reaction times, excellent yields, simple recovery of the magnetic catalyst and avoiding the separation of other ligands or media in the reaction system.

Table 2 *N*-Arylation of various heterocyclic, aliphatic and aryl amines with aryl halides



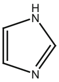
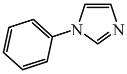
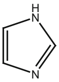
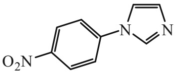
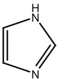
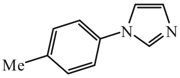
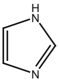
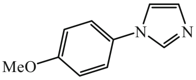
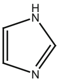
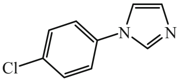
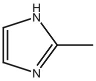
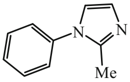
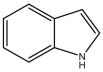
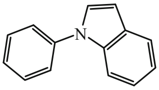
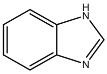
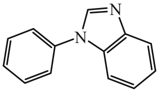
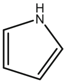
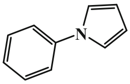
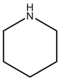
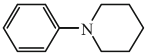
Entry	X	G	Amine	Product	Time h:min	Yield[a] (%)	M.P.C [References]
1	I	H		 **3a**	2	93	Yellow oil [33]
2	I	*p*-NO_2		 **3b**	1:25	94	199–201 (200–202) [33]
3	I	*p*-CH_3		 **3c**	6:40	77	Colorless oil [33]
4	I	*p*-OCH_3		 **3d**	7:50	86	120–122 (120–122) [34]
5	I	*p*-Cl		 **3e**	5	92	Colorless oil [33]
6	I	H		 **3f**	11:30	79	Yellow oil [35]
7	I	H		 **3g**	6	58	Yellow oil [34]
8	I	H		 **3h**	7	55	91–93 (93–95) [33]
9	I	H		 **3i**	5	85	62–64 (64–66) [33]
10	I	H		 **3j**	2	84	Colorless oil [34]

Table 2 continued

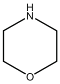
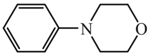
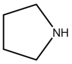
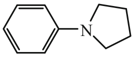
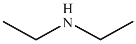
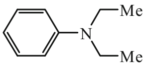
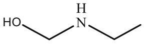
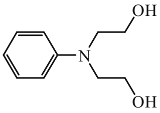
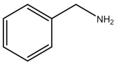
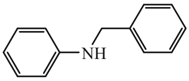
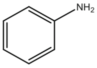
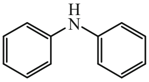
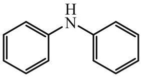
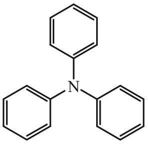
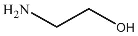
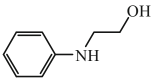
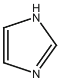
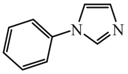
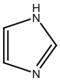
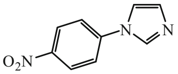
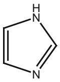
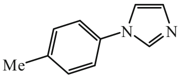
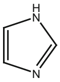
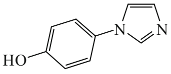
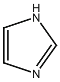
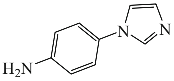
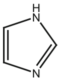
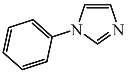
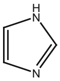
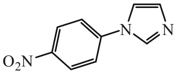
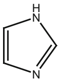
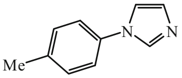
Entry	X	G	Amine	Product	Time h:min	Yield[a] (%)	M.P.C [References]
11	I	H		 **3k**	2	87	53–55 (53–54) [34]
12	I	H		 **3l**	2:40	73	Colorless liquid [36]
13	I	H		 **3m**	4:15	69	Colorless liquid [36]
14	I	H		 **3n**	3	94	55–57 (56–58) [37]
15[b]	I	H		 **3o**	1:30	90	33–35 (33–34) [34]
16[b]	I	H		 **3p**	18	30	50–52 (50–52) [38]
17	I	H		 **3q**	18	61	126–128 (128–130) [39]
18	I	H		 **3r**	5:30	81	Yellow oil [10]
19	Br	H		 **3a**	9	87	Yellow oil [33]
20	Br	p-NO_2		 **3b**	2:25	93	199–201 (200–202) [33]
21	Br	p-CH_3		 **3c**	9	82	Colorless oil [33]

Table 2 continued

Entry	X	G	Amine	Product	Time h:min	Yield[a] (%)	M.P.C [References]
22	Br	*p*-OH		 **3s**	9	58	138–143 (138–139) [34]
23	Br	*p*-NH_2		 **3t**	10	78	200–203 (202–205) [33]
24	Cl	C_6H_5		 **3a**	14	88	Yellow oil [33]
26	Cl	*p*-NO_2		 **3b**	3:30	84	199–201 (200–202) [33]
27	Cl	*p*-CH_3		 **3c**	24	59	Colorless oil [33]

Reaction condition: Het–NH (1.2 mmol) or aliphatic amine (4 mmol), aryl halide (1 mmol), KOH (2 mmol), and $Fe_3O_4@TiO_2/Cu_2O$ (0.010 g) in DMSO (2 mL) at 100 °C

[a] Isolated yield

[b] Under the same conditions, but aromatic amine and benzylamine (1 mmol) was used

In order to check that the catalyst is heterogeneous, the model reaction was performed at 100 °C and after 45 min, the catalyst was immediately separated under hot conditions. After that, the reaction was continued without the catalyst, for a further 2 h at the same temperature. However, the yield of the reaction was only 45 %, indicating that no homogeneous catalyst was involved.

Finally, we carried out the recovery and reusability testing of the nano-magnetic $Fe_3O_4@TiO_2/Cu_2O$ catalytic system in the C–N coupling reaction of 1-phenyl-1H-imidazole **3a**. After the reaction was completed, the catalyst system was recovered by using an external magnet (the saturation magnetization of the core/shell composite was 24.11 emu/g) [31], washed with acetone, followed by distilled water and ethanol, then dried in a desiccator and subjected to the next run. Hence, the catalyst can be used for five times with almost consistent activity. Even at the end run, the yield of *N*-arylated product is 88 %, indicating a good reusability and chemical stability of the catalyst. The slight decrease in the yield could probably be due to the gradual loss of the catalyst during washing. The performance of the recycled heterogeneous catalyst in *N*-arylation reactions for five successive runs was: 92, 92, 90, 89, 88 which demonstrates the practical and excellent recyclability of this catalyst. Additionally, the field emission scanning electron microscopy (FE-

Table 3 Comparison of catalytic activity of Fe_3O_4@TiO_2/Cu_2O with various reported catalysts for *N*-arylation of iodobenzene and imidazole

Entry	Catalyst	Phase-transfer catalyst	Ligand	Conditions	Time (h)	Yield (%)	[Reference]
1	Fe_3O_4@TiO_2/Cu_2O (1.4 mol % Cu_2O)[a]	Free	Free	KOH, DMSO, 100 °C	2	93	This work
2[a]	$Cu(OAc)_2\cdot H_2O$ (15 mol %)	Free	8-Hydroxyquinoline	K_2CO_3, DMF, 130 °C	24	99	[40]
3	$CuSO_4\cdot 5H_2O$ (0.01 mol %)	Free	Dimethylglyoxime	Cs_2CO_3, H_2O, 100 °C	24	85	[41]
4	CuO/MWCNT (0.98 mol %)	Free	Dimethylacetamide	K_2CO_3, Free, 120 °C	24	96	[42]
5	CuI/MNP-3 (10 mol %)	Free	Free	Cs_2CO_3, DMF, 110 °C	24	98	[43]
6	Activated/Cu (10 mol %)	TBAB	Free	LiOH, H_2O, 100 °C	24	81	[44]
7	CuFAP (12.5 mol %)	Free	Free	K_2CO_3, DMSO, 110 °C	4	85	[45]
8	Cu_2O(10 mol %)	Free	Ninhydrin	KOH, DMSO, 110 °C	24	92	[46]
9	CuBr (5 mol %)	PEG-400	DPPhen	KOH, H_2O, 110 °C	21	97	[47]
10	CuO (1 mol %)	TBAB	Oxalyldihydrazide (5 mol %) hexane-2,5-dione	$K_3PO_4\cdot H_2O$, H_2O, 120 °C	48	50	[48]
11	Cu (0.5 mol %)	TBAB	2-(2-Tertbutylhydrazinecarbonyl) pyridine *N*-oxide	KOH, H_2O, 120 °C	24	75	[49]
12	Cu_2O (0.05 mmol)	Free	–	KOH, DMSO/H_2O, 110 °C, Ar	24	99	[32]
13	$CuFe_2O_4$	–	–	K_3PO_4, PEG-400, 100 °C	12	85[b]	[8]

It should be noted that reaction times vary considerably

[a] This work

[b] Aryl halide is 4-iodoanisole and amine is benzylamine

SEM) of fresh and recovered composite and X-ray diffraction (XRD) of recycled catalyst were also investigated and revealed that there was no change in the morphology of the composite after the coupling reactions (Figs. 1, 2).

Based on reports in the literature [50], a plausible mechanism for *N*-arylation is proposed in Scheme 1. In the first step, the intermediate II was formed from the aryl halide and magnetic composite. Then, the imidazole could be deprotonated using

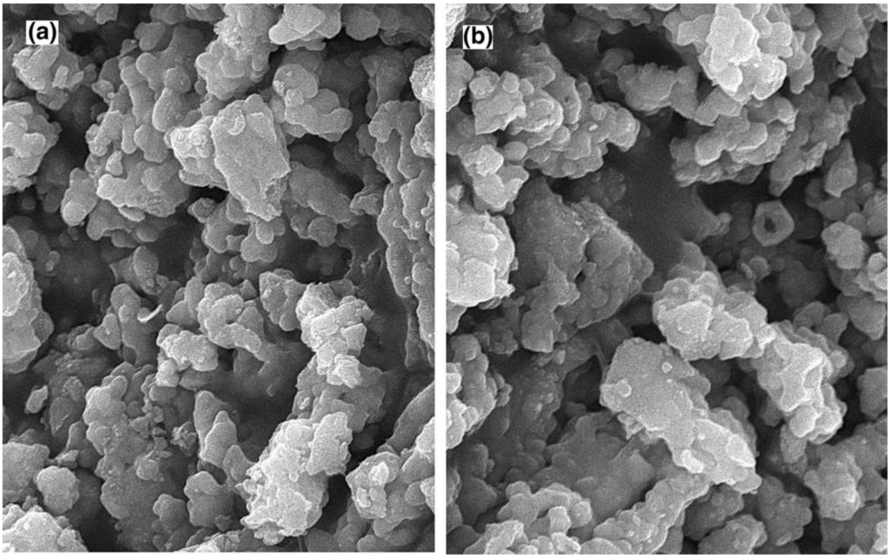


Fig. 1 FE-SEM of nano-Fe_3O_4@TiO_2/Cu_2O (**a**) fresh (**b**) recycled after five times

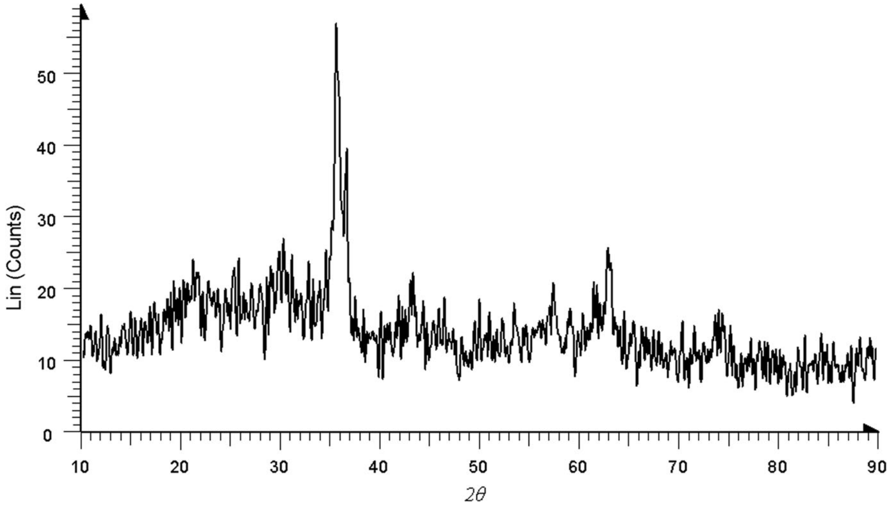
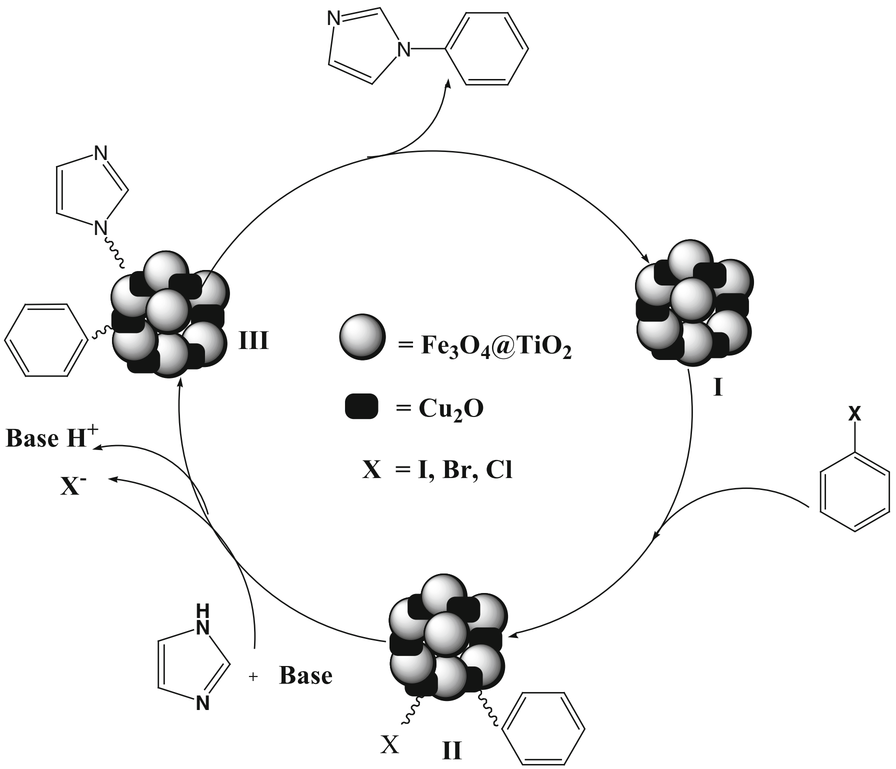


Fig. 2 XRD of recycled catalyst after five times



Scheme 1 The proposed mechanism

the base and instantly replaced with halide anion leading to intermediate III. Finally, the intermediate III is converted to the desired product and the catalyst would be regenerated, completing the catalyst cycle.

Representative spectral data

1-phenyl-1H-imidazole **3a** [31]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.37–7.31 (m, 3H), 7.20 (d, J = 7.8 Hz 1H), 7.12 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 139.3, 138.6, 133.0, 132.7, 129.0, 120.2, 117.3 ppm.
1-(4-nitrophenyl)-1H-imidazole **3b** [31]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35–8.31 (m, 2H), 8.03 (s, 1H), 7.63–7.53 (m, 2H), 7.30 (s, 1H), 7.09 (d, J = 8.8 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 146.3, 142.0, 135.4, 131.7, 125.8, 121.0, 117.8 ppm.
1-(4-methylphenyl)-1H-imidazole **3c** [31]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.28–7.25 (m, 5H), 7.16 (s, 1H), 2.41 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 137.5, 135.6, 133.9, 130.3, 130.2, 121.5, 118.3, 20.9 ppm.

1-(4-Chlorophenyl)imidazole **3e** [31]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.51–7.22 (m, 5H), 7.16 (s, 1H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$): 137.8, 136.1, 130.3, 125.7, 123.3, 120.0, 112.0 ppm.

1-Phenyl-2-methyl-1H-imidazole **3f** [33]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.35–7.03 (m, 6H), 2.35 (s, 3H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$): 147.1, 139.1, 129.3, 128.0, 127.2, 123.6, 118.7, 14.3 ppm.

1-Phenyl-1H-indole **3g** [32]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, $J = 8.8$ Hz, 1H), 7.71–7.60 (m, 1H), 7.46–7.42 (m, 4H), 7.31–7.26 (m, 2H), 7.24–7.20 (m, 2H), 6.90–6.89 (m, 1H) ppm, ^{13}C NMR (100 MHz, $CDCl_3$): 144.0, 141.3, 130.1, 129.3, 129.0 127.4, 125.5, 124.6, 123.3, 119.6, 113.7, 108.5 ppm.

1-Phenyl-1H-benzimidazole **3h** [31]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.91–7.85 (m, 1H), 7.61–7.25 (m, 6H), 7.27–7.20 (m, 2H) ppm, ^{13}C NMR: 148.4, 146.3, 135.5, 134.3, 134.0, 129.3, 124.7, 124.0, 123.6, 120.3, 112.7 ppm.

N-Phenylmorpholine **3k** [10]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.31 (m, 2H), 6.87–6.81 (m, 3H), 3.78 (t, $J = 7.8$ Hz, 4H), 3.18 (t, $J = 7.8$ Hz, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 151.5, 129.3, 120.9, 114.7, 57.2, 49.6 ppm.

N-Phenylpyrrolidine **3l** [10]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (t, $J = 7.8$ Hz, 2H), 6.92 (t, $J = 7.8$ Hz, 1H), 6.54–6.50 (m, 2H), 3.35 (d, $J = 8.4$ Hz, 4H), 1.96 (d, $J = 8.4$ Hz, 4H) ppm.

N,N-Diethylaniline **3m** [34]; ^{1}H NMR [$(CD_3)_2SO$, 400 MHz]: δ 7.22–7.18 (m, 2 H), 6.60 (d, $J = 7.6$ Hz, 2 H), 6.33 (t, $J = 8$ Hz, 1 H), 3.29 (q, $J = 7.5$ Hz, 4 H), 1.02 ppm (t, $J = 7.5$ Hz, 6 H). ^{13}C NMR [$(CD_3)_2SO$, 100 MHz]: 147.3, 128.5, 117.8, 112.0, 43.6, 12.3 ppm.

N-Phenylbenzylamine **3o** [10]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.28 (m, 5H), 7.21–7.16 (m, 2H), 6.68–6.50 (m, 3H), 4.19 (s, 2H), 3.91 (br, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): 148.3, 135.5, 129.3, 128.8, 128.1, 127.3, 118.8, 112.8, 46.6 ppm.

Triphenylamine **3q** [37]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.50 (m, 6H), 7.36–7.29 (m, 6H), 7.13–6.97 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 157.8, 127.4, 124.2, 123.0 ppm.

Conclusions

In conclusion, nano-magnetic Fe_3O_4@TiO_2/Cu_2O composite as a cheap, air-stable and highly active reusable heterogeneous green catalyst was used for the C–N cross-coupling reaction of heterocycles and aliphatic or aromatic amines with a variety of aryl halides. Most importantly, the protocol was simple, general, ligand-free and efficient to afford the cross-coupled products in high yield in short reaction times. The nano-magnetic Fe_3O_4@TiO_2/Cu_2O as an inexpensive heterogeneous catalyst can be easily separated from the reaction mixture as well as reused for five cycles without significant loss of activity.

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