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Recyclable and reusable nano-$CuFe_2O_4$ catalyzed C-O cross-coupling

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ABSTRACT

An efficient protocol was developed and validated for the synthesis of biaryl/aryl alkyl ethers using $CuFe_2O_4$ nano powder as a recyclable catalyst *via* the reaction between aryl halides and phenols/alcohols. Variety of aryl ethers were synthesized efficiently in the presence of catalytic amount of $CuFe_2O_4$, KOH as base, under ligand free conditions in nitrogen atmosphere with DMSO as solvent at 120 °C. The catalyst is air-stable, inexpensive, magnetically separable and recyclable up to four cycles.

1. Introduction

Diaryl ethers constitute a very important class of organic compounds that are finding widespread applications in numerous fields such as life sciences, chemical, pharmaceutical, polymer and material industries [1-9]. Biaryl ethers are found in variety of natural compounds such as antifungal peperazinomycin and combretastatin D-2, antiviral cyclic peptide K-13, glycopeptides antibiotics vancomycin [10-12] (Figure 1). The transition metal catalyzed cross-coupling of aryl halides with phenols is the most straight forward and regular method for the synthesis of biaryl ethers [13]. Despite palladium catalyzed methods to achieve diaryl ether structural scaffold, Hartwig *et al* reported the synthesis of biaryl ethers using sodium phenoxide and electron-deficient aryl bromides in the presence of ligand (dppf) [14]. Buchwald and co workers reported the C-O coupling reaction between aryl halides and phenols by using palladium as a catalyst [15-19]. In recent past palladium based complexes, [20-22] were explored for the synthesis of biaryl ethers. However, these methods use the expensive palladium in more than stoichiometric amounts and tedious work up procedure involved in the synthesis of phosphine ligands, would limit its applications to large (or) industrial-scale production [23-29]. To widen the applicability of this reaction in all facets, explorations were carried out towards the classical Ullmann type copper [30], catalyzed reactions for the synthesis of biaryl ethers, however these reactions also suffer from limitations such as high catalyst loadings, requirement of high reaction temperature (>220 °C) [31]. During the last decade tremendous research work has been carried out on copper catalyzed reactions and showed that certain additives in combination with copper source enhanced the reaction rate under mild reaction conditions.

Thus neocuproine [32], tripod ligands [33], ethylene glycol diactate [34], 1-naphthoic acid [35], 2,2,6,6-tetramethyl heptane-3,5-dione [36], β-keto ester [37], triphenyl phosphine [38], 2-pyridyl acetone [39], were successfully employed as additives. It is thought that these additives increase the efficiency of the catalyst by increasing the solubility of the copper salts and by preventing their aggregation [40]. These metal/ligand based systems suffer from certain limitations, such as high catalyst loading of ligand and require high reaction temperature etc. Dewei Ma and co-workers reported that the *N*,*N*-dimethyl glycine promoted Ullmann coupling reaction of phenols with aryl halides at 90 °C [41]. Recently, few studies have focused on the use of copper [42-44], zinc [45], nickel [46], copper/iron [47] and iron [48], based catalytic systems for the synthesis of biaryl ethers by using the cross-coupling of aryl halide and phenol. However, these aforementioned protocols have one (or) more drawbacks such as use of various well designed ligands, lack of recyclability, high cost of ligands etc. Marc Taillefer *et al.* reported an efficient, inexpensive and practical copper-catalyzed method to cross-couple various phenols with aryl bromides under very mild conditions [49]. Sekar and co-workers developed an efficient, general, mild and intermolecular Ullmann type synthesis of biaryl and alkyl aryl ethers catalyzed by diol-copper(I) complex [50-51]. However, most of these metal-catalyzed reactions involve expensive catalysts/co-catalysts causing major problems such as commercialization to the plant scale and recovery of the catalyst.

In the recent past, heterogeneous catalysis has received a paramount attention in view of improved efficacy due to recyclability and reusability of the process. Heterogeneous catalysts have become more significant both economically and industrially when compared to homogeneous catalytic systems. B. H. Lipshutz, *et al.* reported copper-on-charcoal (Cu/C) as a heterogeneous catalyst to the synthesize biaryl ethers from aryl bromides with phenol [52]. Now days, chemistry of nanoparticles is more fascinating as these metal nanoparticles offer active sites with extended surface area, recyclability and reusability without the loss of catalytic activity.

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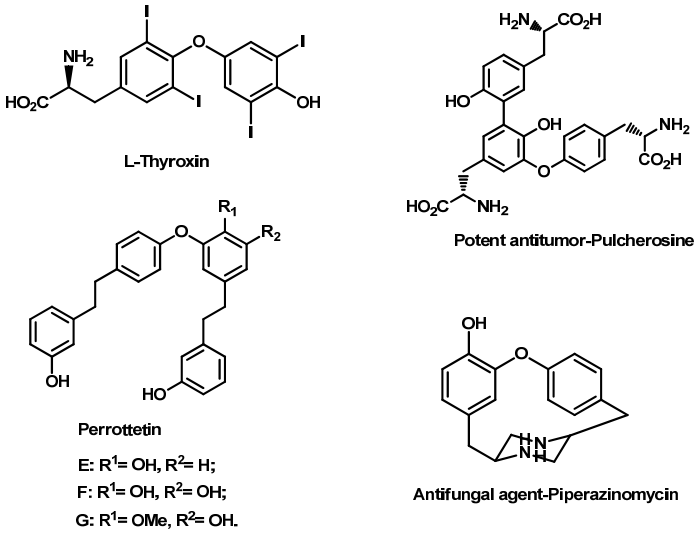


Figure 1. Some of the biologically active molecules containing ether linkage.

These prominent features of nanoparticles led us to focus on the aspect of $CuFe_2O_4$ nanoparticles [53], as catalyst for the formation of carbon-oxygen bond. In general, nano scale heterogeneous catalysts provide greater advantages in organic reactions, as they offer higher surface area and lower coordination sites [54-55], which are responsible for higher catalytic activity and increase the reaction rates. Nano-CuO [56-57] and CuI [58] were used as active catalysts for the cross-coupling of aryl halides with phenols under ligand free conditions.

However, till now investigation of nanoparticles as catysts has been utilized in various organic transformations. In this regard, we envisaged the application of commercially available, inexpensive $CuFe_2O_4$ nanoparticle as a catalyst for the formation of carbon-oxygen bonds. Herein, we wish to report a general, mild and efficient magnetically separable $CuFe_2O_4$ nanoparticle as catalyst for C-O cross-coupling processes. To test the efficiency of the catalytic system, we chose to focus our initial studies on the cross-coupling of phenol with iodobenzene as model substrates under ligand free conditions.

2. Experimental

2.1. Instrumentation

$CuFe_2O_4$ (purity ≥ 98.0%) was purchased from Sigma Aldrich. All experiments were carried out under nitrogen atmosphere. Column chromatography was carried out with 60-120 sized mesh silica gel using ethyl acetate and hexane as eluent. Analytical thin layer chromatography (TLC) was performed with silica gel plates and the products were visualized by UV detection. ^{1}H NMR and ^{13}C NMR (Avance 300, Innova 400 MHz and Brucker Gemini 200 MHz) spectra were recorded in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are reported in ppm, and spin-spin coupling constants (J) are in Hz. Melting points were determined on a Fischer-Johns melting point apparatus. IR and MS were recorded on a Thermo Nicolet Nexus 670 FT-IR spectrometer and Finnegan MAT 1020 mass spectrometer operating at 70 eV.

2.2. Synthesis

Representative experimental procedure for the synthesis of biaryl ethers by using heterogeneous nano-$CuFe_2O_4$ as a catalyst: Phenol (1.0 mmol), iodobenzene (0.1 mL, 1.0 mmol), nano-$CuFe_2O_4$ (6 mol%, 143 mg), KOH (2.0 equiv.), and were charged in a 25 mL round-bottomed flask with a condenser, under nitrogen atmosphere, followed by the addition of dry DMSO (2.0 mL) and the reaction mixture was heated at 120 ^{o}C under nitrogen atmosphere for 20 h, The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate (3x10 mL). The combined organic layers were dried with anhydrous Na_2SO_4. The solvent was evaporated under vacuum to give the crude product, which was purified by column chromatography with hexane as eluent to yield the expected product **3a** (159 mg, 94%) as yellowish oil. The purity of the product was confirmed by ^{1}H, ^{13}C, Mass, and IR spectroscopy.

Oxydibenzene [24] (**3a**) (Table 1, entry 1): Yield: 94%. Colour: Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.35-7.24 (4H, m, ArH), 7.10-6.93 (6H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 157.4, 129.9, 123.1, 118.8. IR: 3442, 2950, 1637, 1480, 752. MS (EI, *m/z*): 170.

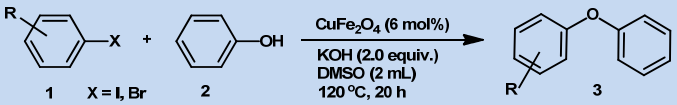
1-Fluoro-4-phenoxybenzene [47] (**3b**) (Table 1, entry 2): Yield: 89%. Colour: Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.60 (1H, d, J = 8.9 Hz, ArH), 7.37-7.20 (2H, m, ArH), 7.12-6.88 (4H, m, ArH), 6.78-6.64 (2H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 160.6, 157.5, 153.0, 138.6, 129.8, 123.3, 120.6, 120.4, 118.5, 116.5, 116.2. FT-IR (KBr, cm^{-1}): 3450, 2930, 2858, 1598, 1216, 841, 780, 690. MS (EI, *m/z*): 188.

1-Phenoxy-4-(trifluoromethyl)benzene [38] (**3c**) (Table 1, entry 3): Yield: 85%. Colour: Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.56 (2H, d, J = 8.5 Hz, ArH), 7.45-7.32 (2H, m, ArH), 7.23-7.10 (3H, m, ArH), 7.01 (2H, d, J = 8.5 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 160.8, 155.7, 130.5, 129.9, 127.0, 124.3, 124.1, 119.9, 119.4, 117.9. FT-IR (KBr, cm^{-1}): 3445, 2930, 2850, 1485, 1225, 848, 765. MS (EI, *m/z*): 238.

1-Chloro-4-phenoxybenzene [47] (**3d**) (Table 1, entry 4): Yield: 88%. Colour: Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.36-7.22 (4H, m, ArH), 7.11-7.04 (1H, m, ArH), 7.01-6.88 (4H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.0, 156.3, 129.9, 129.7, 123.5, 129.1, 119.3. FT-IR (KBr, cm^{-1}): 3448, 2930, 2858, 1583, 1465, 1089, 840, 758, 695. MS (EI, *m/z*): 204.

1-Bromo-4-phenoxybenzene [60] (**3e**) (Table 1, entry 5): Yield: 88%. Colour: Yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.40 (1H, d, J = 8.9 Hz, ArH), 7.33-7.23 (3H, m, ArH), 7.10-7.03 (2H, m, ArH), 6.97 (2H, d, J = 7.9 Hz, ArH), 6.86 (1H, d, J = 8.9 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.2, 156.5, 132.6, 129.9, 129.6, 123.8, 123.1, 120.5, 119.0, 118.8, 115.3.

Table 1. Reaction of aryl halides with phenol using nano copper iron oxide as a catalyst[a].



Entry	Arylhalide	Nucleophile	Product	Yield (%) [b]
1	Iodobenzene	Phenol	3a	94
2	1-Fluoro-4-iodobenzene	Phenol	3b	89
3	1-Iodo-4-(trifluoromethyl)benzene	Phenol	3c	85
4	1-Chloro-4-iodobenzene	Phenol	3d	88
5	1-Bromo-4-iodobenzene	Phenol	3e	88
6	1-Iodo-4-methoxybenzene	Phenol	3f	80
7	1-Iodo-4-methylbenzene	Phenol	3g	78
8	1-Tert-butyl-4-iodobenzene	Phenol	3h	73
9	1-Iodo-3-methoxybenzene	Phenol	3i	79
10	1-Iodo-3,5-dimethylbenzene	Phenol	3j	78
11	1-Iodonaphthalene	Phenol	3k	70
12	2-Iodonaphthalene	Phenol	3l	76
13	1-Iododecane	Phenol	3m	75
14	1-Iodooctane	Phenol	3n	79
15	Bromobenzene	Phenol	3a	76
16	1-Bromo-4-fluorobenzene	Phenol	3b	70
17	1-Bromo-4-chlorobenzene	Phenol	3e	69
18	1-Bromo-4-methoxybenzene	Phenol	3f	60

[a] Reaction conditions: 1 (1.0 mmol), 2 (1.0 mmol), $CuFe_2O_4$ (6 mol% , 143 mg), N_2, 20 h.
[b] Isolated yield.

FT-IR (KBr, cm^{-1}): 3450, 2928, 1598, 1490, 1213, 850, 758. MS (EI, *m/z*): 247.

1-Methoxy-4-phenoxybenzene [24] (**3f**) (Table 1, entry 6): Yield: 80%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.36-7.12 (5H, m, ArH), 6.90-6.82 (2H, m, ArH), 6.77-6.68 (2H, m, ArH), 3.79 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm):159.5, 155.7, 150.4, 129.7, 122.3, 121.2, 118.1, 116.4, 115.1, 55.3. FT-IR (KBr, cm^{-1}): 3448, 2956, 1362, 1179, 758, 693. MS (EI, *m/z*): 200.

1-Methyl-4-phenoxybenzene [51] (**3g**) (Table 1, entry 7): Yield: 78%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.31-7.22 (2H, m, ArH), 7.19-6.83 (5H, m, ArH), 6.81-6.73 (2H, m, ArH), 2.33 (3H, s, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 157.8, 154.8, 132.7, 130.2, 129.6, 122.8, 119.6, 118.2, 20.5. FT-IR (KBr, cm^{-1}): 3443, 2899, 1591, 1298, 765, 699. MS (EI, *m/z*): 184.

1-Tert-butyl-4-phenoxybenzene [24] (**3h**) (Table 1, entry 8): Yield: 73%. Colour: White solid. M.p.: 52-53 °C. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.34-7.22 (4H, m, ArH), 7.06-6.86 (5H, m, ArH), 1.33 (9H, s, $(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.1, 154.4, 145.2, 129.2, 126.3, 123.2, 118.5, 34.3, 31.2. FT-IR (KBr, cm^{-1}): 3450, 2960, 1593, 1498, 1368, 754, 695. MS (EI, *m/z*): 226.

3-Methoxy-4-phenoxybenzene [47] (**3i**) (Table 1, entry 9): Yield: 79%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.35-7.24 (2H, m, ArH), 7.21-7.11 (1H, m, ArH), 7.09-6.96 (3H, m, ArH), 6.61-6.50 (3H, m, ArH), 3.75 (3H, s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm):161.1, 158.5, 157.3, 130.1, 129.5, 123.3, 119.1, 110.9, 108.8, 104.8. FT-IR (KBr, cm^{-1}): 3448, 2959, 1590, 1178, 850, 753, 698. MS (EI, *m/z*): 200.

1,3-Dimethyl-5-phenoxybenzene [24] (**3j**) (Table 1, entry 10): Yield: 78%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.30-7.19 (2H, m, ArH), 7.08-6.91 (2H, m, ArH), 6.84-6.76 (2H, m, ArH), 6.71-6.56 (2H, m, ArH), 2.28 (6H, s, $(CH_3)_2$). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 158.3, 157.1, 139.4, 132.2, 129.8, 127.6, 124.7, 122.8, 121.8, 120.1, 118.8, 116.8, 21.5. FT-IR (KBr, cm^{-1}): 3446, 2860, 2495, 1640, 1486, 1245. MS (EI, *m/z*): 198.

1-Phenoxynaphthalene [57] (**3k**) (Table 1, entry 11): Yield: 70%. Colour: Colorless oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 8.15 (1H, d, *J* = 7.9 Hz, ArH), 7.81 (1H, d, *J* = 7.9 Hz, ArH), 7.55 (1H, d, *J* = 7.6 Hz, ArH), 7.50-7.41 (2H, m, ArH), 7.35-7.22 (3H, m, ArH), 7.10-6.89 (4H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 157.8, 153.1, 135.1, 129.8, 128.2, 127.7, 126.6, 125.8, 125.6, 123.3, 123.1, 122.4, 118.9, 118.5, 113.4. FT-IR (KBr, cm^{-1}): 3445, 2928, 1600, 1485, 1238, 1165. MS (EI, *m/z*): 220.

2-Phenoxynaphthalene [57] (**3l**) (Table 1, entry 12): Yield: 76%. Colour: White solid. M.p.: 47-48 °C. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.85-7.62 (3H, m, ArH), 7.45-7.19 (6H, m, ArH), 7.12-6.96 (3H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm):157.2, 155.1, 134.3, 129.8, 129.7, 127.6, 127.2, 126.4, 124.5, 123.2, 120.1, 119.1, 118.8, 114.2. FT-IR (KBr, cm^{-1}): 3445, 2923, 1596, 1496, 1245, 1160, 1046. MS (EI, *m/z*): 220.

Decyloxybenzene [57] (**3m**) (Table 1, entry 13): Yield: 75%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.26-7.15 (2H, m, ArH), 6.90-6.79 (3H, m, ArH), 3.91 (2H, d, *J* = 6.9 Hz, CH_2), 1.77 (2H, d, *J* = 6.6 Hz, *J* = 7.9 Hz, CH_2), 1.51-1.23 (14H, m, $(CH_2)_7$), 0.91 (3H, d, *J* = 6.9 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.2, 129.3, 120.4, 114.6, 67.7, 31.8, 29.7, 29.5, 29.3, 26.1, 22.8, 14.2. FT-IR (KBr, cm^{-1}): 3445, 2929, 1597, 1239, 1175. MS (EI, *m/z*): 234.

Octyloxybenzene (**3n**) (Table 1, entry 14): Yield: 79%. Colour: Yellowish oil. ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.26-7.16 (2H, m, ArH), 6.91-6.78 (3H, m, ArH), 3.91 (2H, d, *J* = 6.6 Hz, CH_2), 1.76 (2H, d, *J* = 6.6 Hz, *J* = 7.9 Hz, CH_2), 1.52-1.23 (10H, m, $(CH_2)_5$), 0.91 (3H, d, *J* = 6.6 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 159.1, 129.2, 120.4, 114.5, 67.6, 31.8, 29.6, 29.4, 29.2, 26.2, 22.8, 14.2. FT-IR (KBr, cm^{-1}): 3444, 2921, 1598, 1498, 1245, 1145. MS (EI, *m/z*): 206.

3. Results and discussion

Here, we report a highly efficient, reusable nano-$CuFe_2O_4$ catalyzed *O*-arylation of phenols/alcohols with aryl halides in dry DMSO as a reaction medium in presence of nitrogen atmosphere at 120 °C. The reaction of iodo benzene with phenol was selected as a preliminary model reaction for C-O cross-coupling (Scheme 1). Here, the reaction conditions were optimized by taking into consideration of parameters such as temperature, solvent, base. No product formation was seen in the presence of $CuFe_2O_4$ (6 mol %) at room temperature, while lower yield was observed at 70 °C. Temperature has a significant effect on product control, as temperature increases the yield is also slowly increases to 94% at 120 °C (Table 2, entries 1-4). As a part of optimization studies, several solvents were screened in the reaction, among these, toluene, dioxane, NMP, DMF were less effective compared to DMSO (Table 2, entries 4-8).

Table 2. Nano copper ferrite nanoparticle catalyzed cross coupling of iodobenzene with phenol [a].

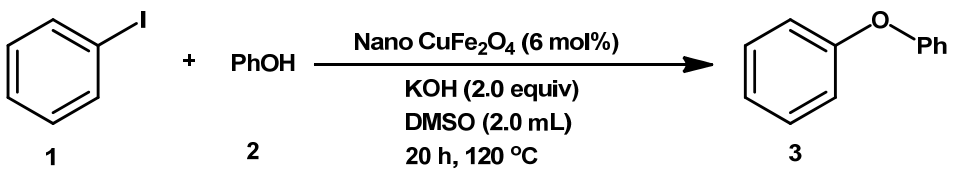
Entry	Solvent	Base (2 equiv.)	Temperature (°C)	Yield (%)[b]
1	DMSO	KOH	R.t.	-
2	DMSO	KOH	70	50
3	DMSO	KOH	100	80
4	Toluene	KOH	120	94
5	Toluene	KOH	120	65
6	NMP	KOH	120	60
7	DMF	KOH	120	58
8	DMSO	KOH	120	70
9	DMSO	K_2CO_3	120	60
10	DMSO	Cs_2CO_3	120	62
11	DMSO	NaO^{t}Bu	120	52
12	DMSO	KO^{t}Bu	120	50
13	DMSO	K_3PO_4	120	54

[a] Reaction conditions: 1 (1.0 mmol), 2 (1.0 mmol), $CuFe_2O_4$ (6 mol% , 143 mg), N_2, 20 h.
[b] Isolated yield.

Table 3. Optimization studies of aryl halide and phenol by using different nano catalysts [a].

Entry	Arylhalide	Nucleophile	Diaryl ether	Nano catalyst (6 mol%)	Yield (%)[b]
1	Iodobenzene	Phenol	3a	Sb_2O_3	55
2	Iodobenzene	Phenol	3a	Y_2O_3	70
3	Iodobenzene	Phenol	3a	YFe_2O_4	65
4	Iodobenzene	Phenol	3a	Bi_2O_3	53
5	Iodobenzene	Phenol	3a	$CuFe_2O_4$	94
6	Iodobenzene	Phenol	3a	Co_3O_4	58
7	Iodobenzene	Phenol	3a	SnO_2	54
8	1-iodo-4-methoxybenzene	Phenol	3f	Sb_2O_3	44
9	1-iodo-4-methoxybenzene	Phenol	3f	Y_2O_3	56
10	1-iodo-4-methoxybenzene	Phenol	3f	YFe_2O_4	45
11	1-iodo-4-methoxybenzene	Phenol	3f	Bi_2O_3	42
12	1-iodo-4-methoxybenzene	Phenol	3f	$CuFe_2O_4$	80
13	1-iodo-4-methoxybenzene	Phenol	3f	Co_3O_4	43
14	1-iodo-4-methoxybenzene	Phenol	3f	SnO_2	45

[a] Reaction conditions: Aryl halide (1.0 mmol), phenol (1.0 mmol), $CuFe_2O_4$ (6 mol% , 143 mg), N_2, 20 h.
[b] Isolated yield.



Scheme 1

We have then examined the different bases, KOH, K_2CO_3, Cs_2CO_3, NaO^{t}Bu, KO^{t}Bu, and K_3PO_4 (Table 2, entries 9-13). Of these, KOH provided biaryl ether in excellent yield.

Next we turned our attention to test different metal oxide nanoparticles such as Sb_2O_3, Y_2O_3, YFe_2O_4, Bi_2O_3, $CuFe_2O_4$, Co_3O_4 and SnO_2 towards C-O cross-coupling reaction with aryl halide and phenol under ligand free conditions and the results are summarized in Table 3.

After having optimized the reaction parameters for *o*-arylation of phenol with aryl halides, the proposed catalytic system was employed to cross-couple wide range of commercially available aryl halides/alkyl halides with phenols under ligand free conditions. All the reactions were clean and the corresponding cross-coupled products were obtained in excellent yields and as shown in Table 1. In the case of aryl halide, substitutions on the aromatic ring played a pivotal role in governing the C-O cross coupling reaction. The substitution of electron withdrawing groups at *para*-position of aryl halide gave the high yield when compared to electron donating groups (Table 1, entries 2-8). Next, the electron donating groups at *para* to *meta*-position of aryl halide decreased the yield (Table 1, entries 9-10). In case of aliphatic aryl halides, as the carbon chain length increases, a slight decrease in the product yield was observed (Table 1, entries 13-14). Aryl bromides were less reactive than the corresponding aryl iodides and good yields were obtained (Table 1, entries 15-18).

In order expand and explore the scope of this catalytic system various phenols/alcohols were treated with iodo benzene under optimized reaction conditions and the results are represented in Table 4. Satisfactory yields were obtained in the case of electron donating and withdrawing substitutions at *para* and *meta*-position of phenols (Table 4, entries 1-5). In the case of alcohols, as the carbon chain was increased, a slight decrease in the product yield was observed (Table 4, entries 8-9). We were then interested in investigating the recyclability of the nano-$CuFe_2O_4$ catalyst. After completion of the C-O cross coupling reaction, the reaction mixture was cooled to room temperature and the catalyst was recovered with the help of magnetic bar and washed with ethyl acetate and acetone, air dried and used directly for the cycles without any further purification and the results are summarized in Table 5. The catalyst maintained its high level of activity even after the fourth cycle in C-O cross-coupling reaction.

The results obtained in our studies support the oxidative addition/reductive elimination type of reaction mechanism for C-O cross-coupling reaction (Scheme 2). Initially the ArX oxidatively adds on to the nano-$CuFe_2O_4$ catalyst and forms a complex **A** followed by replacement of X with a nucleophile in the presence of base forming complex **B** and reductive elimination affords the O-arylated product. The newly regenerated heterogeneous nano-$CuFe_2O_4$ catalyst is released to complete the catalytic cycle.

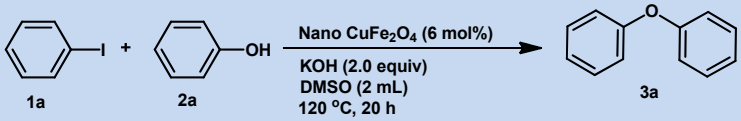
The FT-IR spectroscopic analysis of the $CuFe_2O_4$ nanoparticles, indicated that the significant bands, obtained in range of 680-400 cm^{-1}, proved the presence of $CuFe_2O_4$ peaks.

Table 4. Reaction of aryl halides with phenol using heterogeneous copper as a catalyst[a].

Entry	Aryliodide	Nucleophile	Product	Yield (%) [b]
1	Iodobenzene	4-Chlorophenol	3d	87
2	Iodobenzene	4-Bromophenol	3e	85
3	Iodobenzene	*p*-Cresol	3g	80
4	Iodobenzene	4-*tert*-Butylphenol	3h	79
5	Iodobenzene	3-Methoxyphenol	3i	85
6	Iodobenzene	Naphthalen-1-ol	3k	75
7	Iodobenzene	Naphthalen-2-ol	3l	80
8	Iodobenzene	Decan-1-ol	3m	78
9	Iodobenzene	Octan-1-ol	3n	80

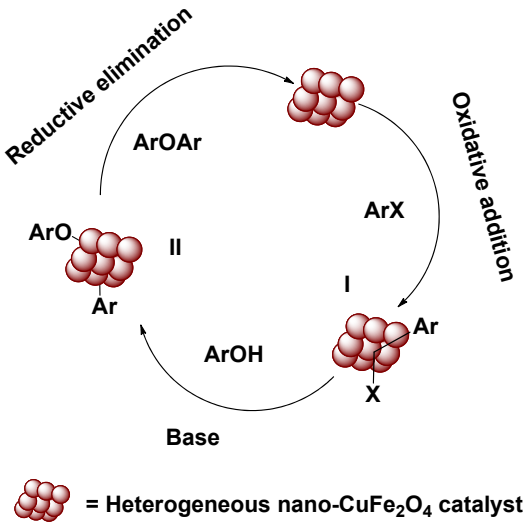
[a] Reaction conditions: Aryl iodide (1 mmol), phenol/alcohol (1 mmol), $CuFe_2O_4$ (6 mol%, 143 mg), base (2.0 equiv.), DMSO (2 mL), 120 °C, 20 h.
[b] Isolated yield.

Table 5. Recyclability of nano copper iron oxide as a catalyst[a].



Cycle	Product isolated yield (%)	Catalyst recovery (%)
Native	98	94
1	91	92
2	85	89
3	83	81

[a] Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), $CuFe_2O_4$ (6 mol %, 143 mg), KOH (2.0 equiv.), DMSO (2 mL), 120 °C, 20 h.



Scheme 2

These significant peaks appeared both in fresh and reused catalyst (Supplementary Figure S1). In addition, the powder X-ray diffraction analysis, [59] showed identical peaks for both the fresh and recovered $CuFe_2O_4$ nanoparticles (Supplementary Figure S2).

The SEM images of the nano-$CuFe_2O_4$ catalyst before and after the cycles were recorded and it was observed that the morphology and size of the nanoparticle did not change considerably, even after the last cycle (Figure 2). The X-ray photoelectron spectroscopic [60-62] (XPS) study of the fresh and used nano-$CuFe_2O_4$ catalyst at the Cu 2p level shows the $2p_{3/2}$ lines at 934.6 and 934.8 eV respectively and the Fe 2p level shows the $2p_{3/2}$ lines at 710.7 and 710.8 eV respectively, which indicates that Cu is in the +2 and Fe is in +3 oxidation state before and after the reaction. The X-ray photoelectron spectroscopic (XPS) study of the fresh and used nano-$CuFe_2O_4$ catalyst at the Cu 2p level shows the $2p_{1/2}$ lines at 954.7 and 954.9 eV respectively and the Fe 2p level shows the $2p_{1/2}$ lines at 724.7 and 724.9 eV respectively, which indicates that Cu is in the +2 and Fe is in +3 oxidation state before and after the reaction (Figure 3). From these experimental data, we can conclude that there was no significant change in the catalytic activity of nano-$CuFe_2O_4$, before and after the reaction.

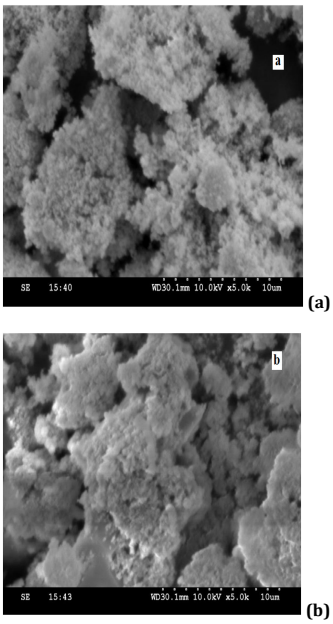


Figure 2. SEM analysis of (a) native nano-$CuFe_2O_4$ catalyst and (b) reused nano-$CuFe_2O_4$ catalyst.

4. Conclusions

In summary, we have developed a simple, general and efficient procedure for the synthesis of biaryl ethers by using aryl halides/alkyl halides with phenols/alcohols as substrates employing heterogeneous nano-$CuFe_2O_4$ as a catalyst in DMSO

[63] as solvent. The catalyst is air-stable, inexpensive, easily recoverable and recyclable.

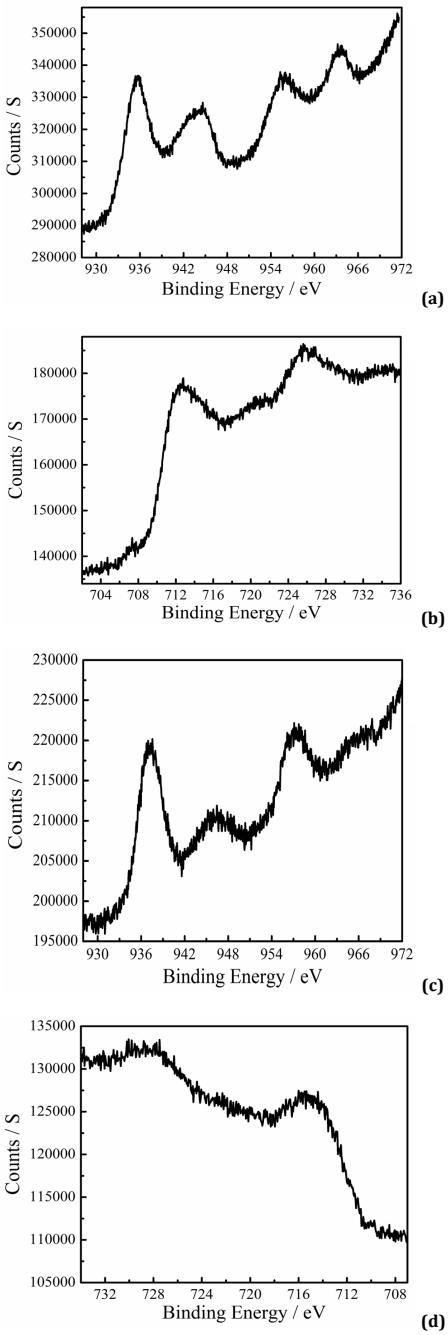


Figure 3. XPS profiles of (a) Cu 2p orbital of native nano-$CuFe_2O_4$ catalyst (b) Fe 2p orbital of native nano-$CuFe_2O_4$ catalyst (c) Cu 2p orbital of reused nano-$CuFe_2O_4$ catalyst (d) Fe 2p orbital of reused nano-$CuFe_2O_4$ catalyst.

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