

# Synthesis and Characterization of Polymer Anchored Cu(II) Complexes: Heterogeneous Catalysts for Preparation of Diaryl Ethers

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Polymer anchored Cu(II) Schiff base complexes have been prepared and characterized by using scanning electron microscope (SEM), elemental analysis, atomic absorption spectroscopy (AAS), thermogravimetric analysis (TGA), spectrometric methods like diffuse reflectance spectra of solid (DRS) and fourier transform infrared spectroscopy (FTIR). These catalysts show excellent catalytic activity in the *O*-arylation reaction of aryl halides with phenol in acetonitrile using  $\text{Cs}_2\text{CO}_3$  at 70 °C under an open air condition to give diaryl ethers in high yields. The effects of various parameters such as solvent, catalyst from different copper salt and base on the reaction system have been studied. The reaction is applicable to a wide variety of substituted aryl halides and phenols with different steric and electronic properties. These catalysts are recovered by simple filtration and the reusability experiments show that these catalysts can be used five times without much loss in the catalytic activity.

**Keywords** polymer anchored Cu(II) Schiff base catalyst, *O*-arylation, aryl halides, diaryl ethers, open air, reusability

## Introduction

Diaryl ethers are valuable intermediates in organic synthesis<sup>1</sup> and are found in a variety of naturally occurring and biologically important compounds. They play an important role in chemical industries and also have wide applications in the production of fragrances, cosmetics, pharmaceuticals and polymer materials.<sup>2</sup>

These compounds are prepared from the cross-coupling reaction of aryl halides with phenol (transition metal catalyzed *O*-arylation reaction of phenol) in presence of palladium or copper compounds as catalysts. Palladium compounds are very active and have high catalytic activity, but the high costs of Pd-compounds lowered its popularity, particularly for large scale reactions.<sup>3</sup> Hartwig *et al.* and Buchwald *et al.* have greatly contributed to novel Pd-catalyzed arylation of phenols,<sup>4</sup> but their systems still suffer from the expensive price of palladium and ligand sources. In the meantime, a catalytic version of Cu-mediated Ullmann coupling of aryl halides and phenols was successfully developed and so offered a cheaper alternative to Pd.<sup>5</sup>

Thus, important efforts were invested to provide the most efficient Cu-ligand system in terms of softening reaction conditions and widening functional tolerance.<sup>6</sup> Nowadays there are many Cu-catalyzed *O*-arylation of phenols with aryl halides in the presence of a variety of P—, N—, and O-based ligands or additives.<sup>7–11</sup> There

are many compounds of the oxime and Schiff base types serving as powerful ligands in the copper catalyzed arylation of pyrazoles and phenols with aryl halides.<sup>12</sup>

Nowadays solid-phase technique has gained much importance in this cross-coupling reaction. Homogeneous catalysts have some disadvantages, for example, they may easily be destroyed during the course of the reaction and they cannot be easily recovered after the reaction for reuse. These disadvantages can be overcome by anchoring metal on suitable supports. These studies confirm that the anchoring of metal on solid support not only exhibits improved catalyst activity, stability and selectivity of the product but also enables easy recovery and reuse of the catalyst. There are many examples for immobilizing such Cu- or Pd-catalytic systems.<sup>13–16</sup> To date, few reports described reusable copper catalytic systems for this C—O coupling that allowed the recycling of active metal, nevertheless only some reported leaching measurements of metal toxic residues in final products.<sup>17,18</sup> This feature is of high importance for purity requirements especially in pharmaceutical industries. Therefore, mild, simple and low-cost reusable methods are highly desirable to avoid toxicity.

Herein, we report the synthesis and characterization of the new polymer anchored copper(II) Schiff base catalysts and illustrate their application in a number of diaryl ether coupling reactions between aryl halides and

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phenols. We also studied the effects of solvent and base to obtain the optimized reaction condition. Then using the optimized reaction conditions, we compared the reactivity of phenols and aryl halides. The present work further revealed that the polymer anchored Cu(II) Schiff base catalyst has potential applications in the diaryl ether coupling reactions and gives better results than other homogeneous catalysts. Our polymer anchored Cu(II) Schiff base catalyst has gained attention because of its inert, non-toxic, insoluble and recyclable properties. The experimental results reveal that the polymer anchored Cu(II) Schiff base catalyst can be recycled more than five times without much loss in the activity.

## Experimental

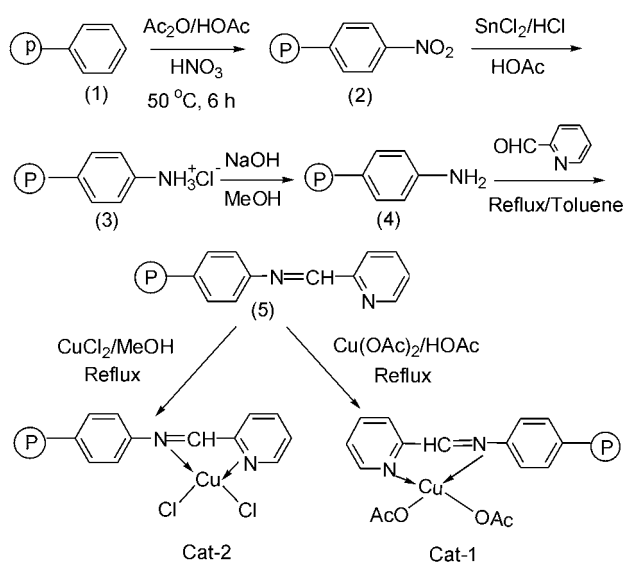
### Materials

Analytical grade reagents and freshly distilled solvents were used throughout the experiment. All reagents and substrates were purchased from Merck. Liquid substrates were predistilled and dried by appropriate molecular sieve and solid substrates were recrystallized before use. Distillation, purification of the solvents and substrates were done by standard procedures.<sup>19</sup> Macroporous polystyrene beads cross linked with 2% divinylbenzene and 2-pyridinecarboxaldehyde were purchased from Aldrich Chemical Company (USA). Copper salts were purchased from Merck and used without further purification.

### Preparation of catalysts

The preparation for the polymer anchored Cu(II) Schiff base catalysts is shown in Scheme 1.

**Scheme 1** Synthesis of the polymer anchored Cu(II) Schiff base catalysts



### Preparation of *p*-nitro-polystyrene (2)

A suspension of macroporous polystyrene beads (1, 5.0 g) in a mixture of acetic anhydride (20 mL), nitric

acid (*ca.* 70%, 2 mL) and glacial acetic acid (4 mL) was stirred for 30 min at 5 °C followed by 5 h at 50 °C.<sup>20</sup> The corresponding *p*-nitro polystyrene (2) was washed successively with acetic acid, water and methanol and finally dried under vacuum.

### Preparation of *p*-amino-polystyrene (4)

A mixture of acetic acid (20 mL), stannous chloride (5.0 g), concentrated hydrochloric acid (6 mL) and *p*-nitro polystyrene (2, 5.0 g) was stirred for 72 h at room temperature to reduce the nitro-compound to the corresponding aminehydrochloride (3).<sup>20</sup> The residue was washed several times with hydrochloric acid (12 mol·L<sup>-1</sup>) and glacial acetic acid (*V* : *V* = 1 : 4) mixture and then with methanol. The product on repeated treatment with dilute alcoholic NaOH (5%) produced the corresponding free amine (4). This was washed with alcohol and dried under vacuum.

### Preparation of the polymer anchored Schiff base ligand (5), P-[C<sub>6</sub>H<sub>4</sub>N=CHPy]

The suspension of macroporous amino polystyrene (4, 2.0 g) in toluene (25 mL) was taken in a 100 mL round bottom flask and stirred for 30 min. 2-Pyridinecarboxaldehyde (5 mL) was added drop-wise to the reaction mixture. The suspension was changed its color from pale yellow to yellowish brown. The reaction mixture was refluxed for 48 h at 120 °C. After cooling it to room temperature, the brown polymer anchored Schiff base ligand (5) was filtered out, washed thoroughly with methanol and dried under vacuum.

### Preparation of the polymer anchored Cu(II) Schiff base catalyst, P-[(C<sub>6</sub>H<sub>4</sub>N=CHPy)Cu(OAc)<sub>2</sub>] (Cat-1)

Polymer anchored Schiff base ligand (5) (2.0 g) was added in acetic acid (20 mL) placed in a round bottom flask. Copper acetate (0.05 g) in acetic acid (5 mL) was added to the above suspension with constant stirring and then refluxed on an oil bath for 24 h. After cooling the reaction mixture to room temperature, the separated deep brown color solid was filtered out, washed thoroughly with methanol and dried under vacuum.

### Preparation of the polymer anchored Cu(II) Schiff base catalyst, P-[(C<sub>6</sub>H<sub>4</sub>N=CHPy)Cu(Cl)<sub>2</sub>] (Cat-2)

Polymer anchored Schiff base ligand (5, 2.0 g) was added in methanol (20 mL) taken in a round bottom flask. Copper chloride (0.05 g) in methanol (5 mL) was added to the above suspension with constant stirring and then refluxed on an oil bath for 24 h. After cooling the reaction mixture to room temperature, the separated brown color solid was filtered out, washed thoroughly with methanol and dried under vacuum.

### Characterization of the catalysts

Surface morphology and particle size of the samples were analyzed by using a Scanning Electron Microscope (SEM) (ZEISS EVO40, England) equipped with EDX facility. Thermogravimetric analysis (TGA) of the

immobilized catalyst was determined using a Mettler Toledo TGA/SDTA 851. The FTIR spectra were recorded on a Perkin-Elmer FTIR 783 spectrophotometer using KBr pellets. Diffuse reflectance UV-Vis spectra were taken using a Shimadzu UV-2401PC doubled beam spectrophotometer having an integrating sphere attachment for solid samples. A Perkin-Elmer 2400C elemental analyzer was used to collect microanalytical data (C, H and N). Copper content in the catalyst was determined using a Varian AA240 atomic absorption spectrophotometer (AAS).

### Representative procedure for *O*-arylation reaction of phenols with aryl halides

Polymer anchored Cu(II) Schiff base catalyst (0.05 g, Cat-1: 1.56 mmol, Cat-2: 1.29 mmol) in 5 mL ACN was placed in a 100 mL R.B. flask and stirred at room temperature for 10 min. Then aryl halide (1 mmol), phenol (1 mmol), tetrabutylammonium bromide (*t*-Bu<sub>4</sub>NBr) (0.1 mmol), Cs<sub>2</sub>CO<sub>3</sub> (1 mmol), dihexyl ether (5 mL) and ACN (5 mL) were added to it. The final reaction mixture was refluxed for 12 h at 70 °C under an open air condition. The products were collected at different time intervals and identified by GCMS and quantified by GC using dihexyl ether as an internal standard. After cooling to room temperature, the reaction was extracted with ethyl acetate (20 mL × 3) and the combined organic layers were dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>. The filtrate was concentrated by vacuum and the resulting residue was purified by column chromatography on silica gel to provide the desired product. The product was purified by column chromatography and its identity confirmed by comparison of color, m.p. and NMR spectra with those reported in the literature or authentic samples from our laboratories.

## Results and discussion

### Characterization of the polymer anchored Cu(II) Schiff base catalysts

Due to insolubilities of the polymer anchored Cu(II) complexes in all common organic solvents, their structural investigation were limited to the physicochemical properties, chemical analysis, SEM, EDAX, IR, TGA-DTA and UV-Vis spectral data only.

#### Elemental analysis

Table 1 provides the data of elemental analysis of different functionalized polymer and the complexes. Copper content in the catalysts determined by AAS suggests  $w(\text{Cu}) = 1.98\%$  in the Cat-1 and  $w(\text{Cu}) = 1.64\%$  in the Cat-2.

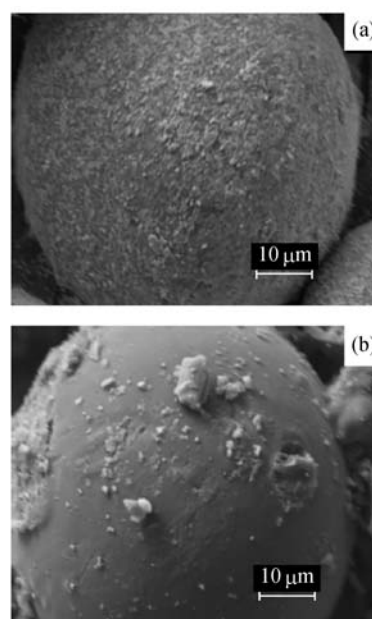
#### Scanning electron microscope (SEM) analysis

The morphology of the Cat-1 was studied using scanning electron microscope. The micrographs of the polymer anchored Schiff-base ligand and the Cat-1 obtained from the scanning electron microscope is pre-

**Table 1** Chemical analysis of different compounds

Compound	Color	Cl/%	C/%	H/%	N/%	Cu/%
1	Colorless	—	92.50	7.60	—	—
2	Light yellow	—	74.10	5.69	6.01	—
3	Yellow	13.25	72.01	6.72	5.81	—
4	Pale yellow	—	84.12	7.34	6.72	—
5	Brown	—	83.23	6.28	9.07	—
Cat-1	Deep-Brown	—	67.80	5.46	6.62	1.98(1.96) <sup>a</sup>
Cat-2	Brown	8.65	69.51	5.24	7.60	1.64

<sup>a</sup> Used catalyst.

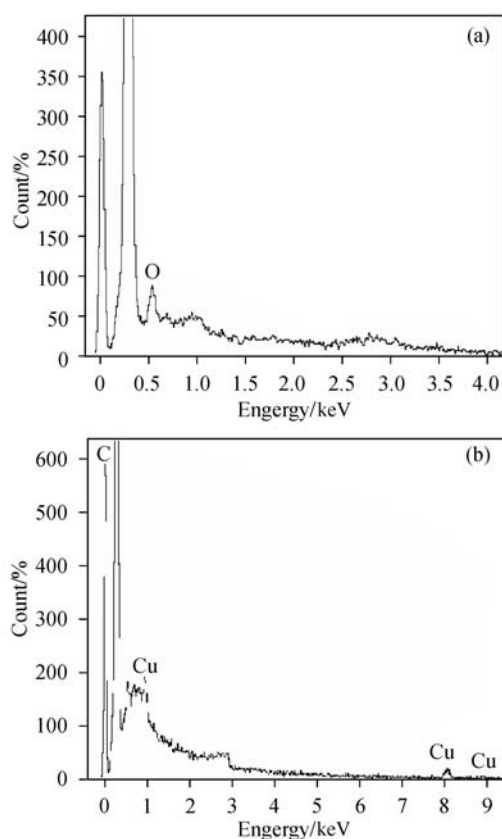


**Figure 1** FE SEM images of polymer anchored Schiff base ligand (a) and Cat-1 (b).

sented in Figures (1a) and (1b), respectively. The morphological change in the polymer anchored Schiff base ligand and the immobilized copper(II) complex (Cat-1) is quite evident from these images and suggesting the loading of copper metal on the surface of the polymer matrix. Energy dispersive spectroscopy analysis of X-rays (EDAX) data for the polymer anchored Schiff base ligand and the Cat-1 is given in Figures (2a) and (2b), respectively. The EDX data also inform the attachment of copper metal on the surface of the polymer matrix.

#### FT-IR studies

The IR spectra of the various functionalized polystyrenes and the corresponding metal complex are presented in Table 2. The presence of Schiff base moiety in the ligand is indicated by the appearance of absorption band at 1639 cm<sup>-1</sup> due to C=N stretching vibration of azomethine group. This on complexation with Cu shifted at 1614 cm<sup>-1</sup>, while the bands at 1583 and 1453 cm<sup>-1</sup> have been assigned to the aromatic skeletal vibration.<sup>21,22</sup> The lowering in frequency of C=N peak is indicative of the formation of the metal-ligand bonding.



**Figure 2** EDAX data of polymer anchored Schiff base ligand (2A) and Cat-1 (2B).

**Table 2** IR spectral data ( $\text{cm}^{-1}$ ) of the compounds

Compd.	$\delta_{\text{NH}_2}$	$\nu_{\text{NH}_2/\text{Cl}}$	$\nu_{\text{NO}_2}$	$\nu_{\text{C}=\text{N}}^a$	$\nu_{\text{C}=\text{N}}^b$	$\nu_{\text{Cu}-\text{N}}^c$	$\nu_{\text{Cu}-\text{N}}^d$	$\nu_{\text{Cu}-\text{O}}$	$\nu_{\text{Cu}-\text{Cl}}$
2			1520(s)						
			1350(s)						
3		2550	1520(w)						
			1350(w)						
4	1625		1520(w)						
			1350(w)						
5			1520(w)	1639	1594				
			1350(w)						
Cat-1			1520(w)	1614	1600	462	545	430	
			1350(w)						
Cat-2			1520(w)	1614	1600	462	545		360
			1350(w)						

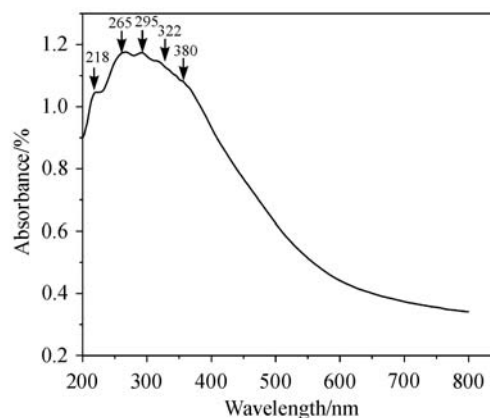
<sup>a</sup> Azomethine group; <sup>b</sup> pyridine moiety; <sup>c</sup> azomethine nitrogen; <sup>d</sup> nitrogen in the pyridine moiety.

The absorption signal at  $1594 \text{ cm}^{-1}$  can be assigned with stretching frequency of  $\text{C}=\text{N}$  ( $\nu$ ,  $\text{C}=\text{N}$ ) of pyridine ring in the Schiff base ligand which on complexation with Cu shifted at  $1600 \text{ cm}^{-1}$ .<sup>23</sup> In the metal complex, a medium or weak band is observed at  $545 \text{ cm}^{-1}$  which can be attributed to the metal with pyridine nitrogen mode<sup>24</sup> and absorption frequency appeared at  $462 \text{ cm}^{-1}$  can be attributed to the metal with azomethine nitrogen mode.<sup>25</sup> In Cat-1 a medium intensity band observed at  $1318 \text{ cm}^{-1}$  suggests the monodentate coordi-

nation of the acetate groups.<sup>26</sup> Monodentate acetate usually shows two bands at  $1630$  and  $1310 \text{ cm}^{-1}$  due to antisymmetric and symmetric stretching respectively.<sup>27</sup> Since absorption of Schiff base moiety [ $\nu(\text{C}=\text{N})$ ] also appeared in this region, the band at  $1630 \text{ cm}^{-1}$  could not be located. The acetate oxygen involved in the complexation with copper in Cat-1 which is clearly evident from the appearance of a new medium intensity band at  $430 \text{ cm}^{-1}$  assignable to [ $\nu(\text{Cu}-\text{O})$ ] in the IR spectra.<sup>27</sup> Also chlorine involved in the complexation with copper in Cat-2 which is clearly evident from the appearance of a new band at  $360 \text{ cm}^{-1}$  assignable to [ $\nu(\text{Cu}-\text{Cl})$ ] in the IR spectra.<sup>28</sup>

### Electronic spectral studies

The electronic spectrum of the polymer anchored Cu(II) Schiff base catalyst was recorded in diffuse reflectance mode as a  $\text{MgCO}_3/\text{BaSO}_4$  disc due to their solubility limitations in common organic solvents. In Figure 3, electronic spectrum for the Cat-1 is shown. The spectrum exhibits five spectral bands at ca. 218, 265, 295, 322 and 380 nm. The first two peaks in the UV region can be assigned to intraligand  $\pi-\pi^*$  transitions. The two bands at 295 and 322 nm arise due to  $n-\pi^*$ <sup>29</sup> and  $\pi-\pi^*$ <sup>24</sup> transitions of pyridine moiety. The peak appeared at 380 nm may be due to ligand to metal charge transfer.<sup>30</sup> The expected d-d bands are not observed in the polymer anchored copper catalyst. Possibly poor loading of the complex on the polymer matrix has prevented the exhibit of the d-d band, which is a low energy and eventually less intense band.<sup>31</sup>



**Figure 3** DRS-UV-visible absorption spectra of Cat-1.

### Thermogravimetric analysis (TGA)

Thermal stability of Cat-1 and Cat-2 was investigated using TGA-DTA at a heating rate of  $10 \text{ }^\circ\text{C}/\text{min}$  in air over a temperature range of  $30-600 \text{ }^\circ\text{C}$ . Both the catalysts are stable up to  $300 \text{ }^\circ\text{C}$  and above this temperature they decomposed. Thermogravimetric study suggests that the polymer anchored Cu(II) complexes degrade at a slightly higher temperature.

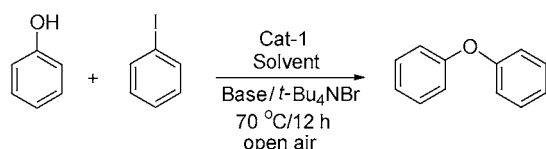
From the different spectral and microanalytical data,

the probable structure of the polymer anchored Cat-1 and Cat-2 may be proposed, according to Scheme 1.

### Catalytic activity of the polymer anchored Cu(II) Schiff base catalyst in the *O*-arylation reaction

The polymer anchored Cat-1 and Cat-2 are investigated as a catalyst in the *O*-arylation of aryl halides with equimolar amount of phenols using tetrabutylammonium bromide (*t*-Bu<sub>4</sub>NBr) at 70 °C for 12 h. The *O*-arylation reaction gives diarylether as a main product up to yield 95%. The Cat-1 and Cat-2 are comparable in their activities but Cat-1 is superior due to its higher metal loading (Table 1). The detailed catalytic investigations are made with Cat-1 due to its highest efficiency (Table 3). To optimize the reaction conditions, we have chosen the reaction between iodobenzene and phenol as a model reaction (Scheme 2) using Cat-1 and various parameters, such as solvent and base being varied to get maximum product.

**Scheme 2** Copper catalyzed *O*-arylation of iodobenzene with phenol



### Effect of solvent

Table 4 illustrates the effect of solvent in the *O*-arylation reaction of phenol with iodobenzene using Cat-1. Acetonitrile (ACN), dimethylformamide (DMF),

toluene and dimethylsulfoxide (DMSO) are used as a solvent keeping the other parameters constant. *O*-Arylation reaction conducted in ACN is faster than those conducted in DMF, DMSO and toluene. The decreasing order of solvent in the *O*-arylation reaction is given below: ACN > DMF > DMSO > Toluene.

**Table 4** Effect of solvent on the coupling of phenol with iodobenzene<sup>a</sup>

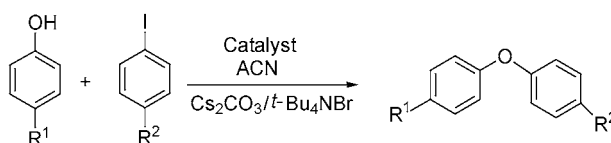
Entry	Solvent	Temperature/°C	Conversion <sup>b</sup> /%	Yield <sup>b</sup> /%
1	ACN	70	96	92
2	DMF	120	82	72
3	DMSO	115	77	65
4	Toluene	100	70	60

<sup>a</sup> Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenol, 1 mmol Cs<sub>2</sub>CO<sub>3</sub>, Cat-1 (0.05 g, 1.56 mmol), solvent (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, open air, 12 h. <sup>b</sup> Conversion and yield refers to GC and GC-MS analysis using dihexyl ether as internal standard.

### Effect of base

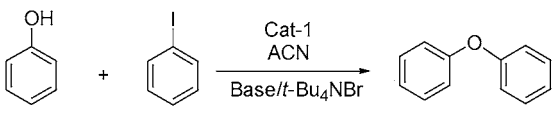
Table 5 illustrates the effect of base in the *O*-arylation reaction of phenol with iodobenzene using Cat-1. Cesium carbonate (Cs<sub>2</sub>CO<sub>3</sub>), potassium carbonate (K<sub>2</sub>CO<sub>3</sub>), sodium carbonate (Na<sub>2</sub>CO<sub>3</sub>), potassium hydroxide (KOH) and triethylamine (Et<sub>3</sub>N) are used as a base keeping the other parameters constant. Cesium carbonate is particularly effective as a base in *O*-aryla-

**Table 3** Comparison of catalytic activities of Cat-1 and Cat-2 using phenols with aryl halides<sup>a</sup>



Entry	Phenol	Aryl halide	Product	Catalyst	Conversion <sup>b</sup> /%	Yield <sup>b</sup> /%
1				Cat-1	96	92
				Cat-2	85	80
2				Cat-1	90	88
				Cat-2	81	77
3				Cat-1	98	95
				Cat-2	89	85

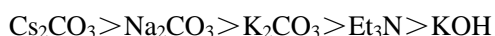
<sup>a</sup> Reaction conditions: 1 mmol of aryl halides, 1 mmol of phenols, 1 mmol Cs<sub>2</sub>CO<sub>3</sub>, 50 mg catalyst, ACN (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, 70 °C, open air, 12 h. <sup>b</sup> Conversion and yield refers to GC and GC-MS analysis using dihexyl ether as internal standard.

**Table 5** Effect of base on the coupling of phenol with iodobenzene<sup>a</sup>


Entry	Base	Conversion <sup>b</sup> /%	Yield <sup>b</sup> /%
1	Cs <sub>2</sub> CO <sub>3</sub>	96	92
2	Na <sub>2</sub> CO <sub>3</sub>	82	75
3	K <sub>2</sub> CO <sub>3</sub>	80	73
4	Et <sub>3</sub> N	65	58
5	KOH	63	51

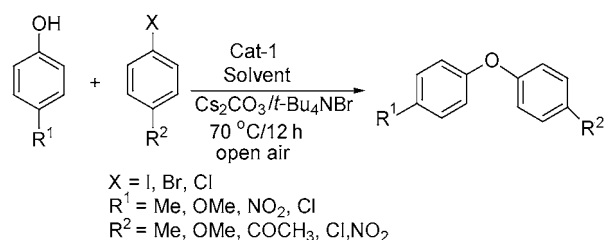
<sup>a</sup> Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenol, 1 mmol base, Cat-1 (0.05 g, 1.56 mmol), ACN (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, 70 °C, open air, 12 h. <sup>b</sup> Conversion and yield refers to GC and GC-MS analysis using dihexyl ether as internal standard.

tion reaction because cesium phenoxides are indeed more dissociated and more soluble in organic solvents than their potassium and sodium counterparts.<sup>32</sup> The decreasing order of the base in the *O*-arylation reaction is given below:



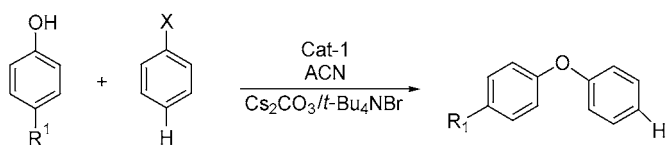
From the above discussions, it can be seen that the best yield is obtained by using Cs<sub>2</sub>CO<sub>3</sub> (1 mmol) in acetonitrile solvent (10 mL) in presence of Cat-1 (0.05 g, 1.56 mmol) at 70 °C for 12 h. The optimized reaction conditions for *O*-arylation reaction is shown in Scheme 3.

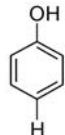
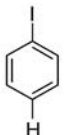
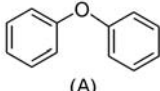
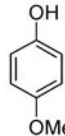
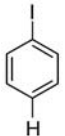
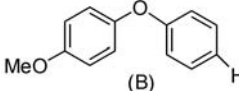
Now the optimized reaction conditions are used to examine C—O bond formations involving functionalized coupling partners. Reactivity comparisons are made by interrupting the reactions after 12 h.

**Scheme 3** Copper catalyzed *O*-arylation of aryl halides with phenols

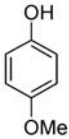

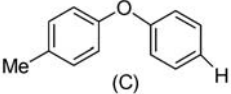
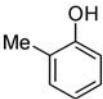
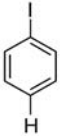
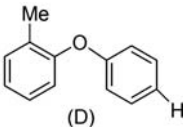

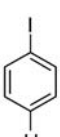
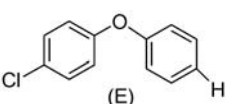

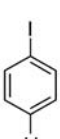
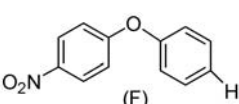
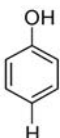
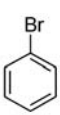
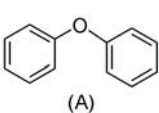
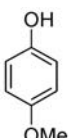

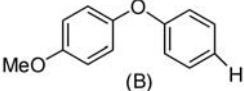
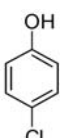

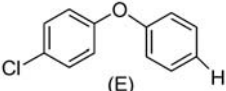
### Reactivity comparison of phenols with aryl halides using Cat-1

Table 6 shows the reactivity comparison of phenols with iodobenzene using Cat-1. The conversion is varies with *para*-substituted and *ortho*-substituted phenols. It is observed that the yield obtained with electron-donating groups in the *para* position of phenol is greater than with electron-withdrawing groups in the *para* position of phenol. Probably phenols with electron-donating groups (such as methoxy and methyl) in the *para* position behave as a good nucleophile and give higher yield than unsubstituted phenol (Entries 2 and 3). *ortho*-Substituted phenol gives much lower yield due to steric effect (Entry 4). 4-Chlorophenol proved to be a significantly less effective coupling partner, due to its poor nucleophilicity (Entry 5), while 4-nitrophenol, which bears a strong electron-withdrawing group, does not undergo the desired *O*-arylation reaction, even at high temperature (Entry 6). After achieving excellent results with iodobenzene, we further applied this catalytic system to the *O*-arylation of phenols with bromobenzene. The reaction of phenol with bromobenzene gives 78% yield of diarylether (Entry 7). 4-Methoxyphenol and 4-chlorophenol give 80% (Entry 8) and 38% (Entry 9) yield of the desired product respectively when reacts with bromobenzene.

**Table 6** Reactivity comparison of phenols with aryl halides using Cat-1<sup>a</sup>


Entry	Phenol	Aryl halide	Product	Conversion <sup>b</sup> /%	Isolated yield <sup>c</sup> /%
1			 (A)	96	92
2			 (B)	98	95

Continued

Entry	Phenol	Aryl halide	Product	Conversion <sup>b</sup> /%	Isolated yield <sup>c</sup> /%
3				96	93
4				84	66
5				78	55
6				10	2
7				85	78
8				89	80
9				42	38

<sup>a</sup> Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenols, 1 mmol Cs<sub>2</sub>CO<sub>3</sub>, Cat-1 (0.05 g, 1.56 mmol), ACN (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, 70 °C, open air, 12 h. <sup>b</sup> Conversion refers to GC and GC-MS analysis using dihexyl ether as internal standard. <sup>c</sup> Isolated yield after column chromatography.

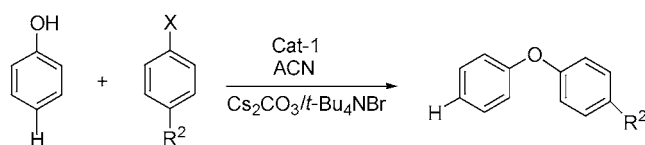
### Reactivity comparison of aryl halides with phenol using Cat-1

Table 7 shows the reactivity comparison of aryl halides with phenol using Cat-1. There is very little electronic effect observed when phenol is submitted to coupling with *para*-substituted iodobenzene. It is noted that iodobenzene with electron-donating groups in *para* position such as methyl and methoxy groups decrease slightly the yield (%) (Entries 2 and 3) and with electron-withdrawing groups in *para* position such as *tert*-methyl, chloro and nitro groups increase the yield (Entries 4–6). 2-Iodobenzene, as usually observed in the literature with hindered aryl halides, gives lower conversions after 12 h and the arylation reaction re-

quired longer reaction times to go to completion (Entry 7). Significant electronic effects are observed for substituted aryl bromides. As for bromoarenes, electron-deficient (Entries 8 and 9) ones are good substrates for this reaction, providing the desired diaryl ethers in moderate to good yields. But the reaction with electron-rich bromoarenes (Entry 10) is slightly difficult, and lower yield of the desired product is obtained.

### Comparison of activity of different copper catalysts in the *O*-arylation reaction

We compared the activity of the Cat-1 in the *O*-arylation reaction with other reported copper catalysts (Table 8). From Table 8, it can be seen that the activity

**Table 7** Reactivity comparison of aryl halides with phenol using Cat-1<sup>a</sup>

Entry	Phenol	Aryl halide	Product	Conversion <sup>b</sup> /%	Isolated yield <sup>c</sup> /%
1				96	92
2				90	88
3				87	84
4				94	93
5				96	95
6				97	95
7 <sup>d</sup>				80	76
8				90	82
9				86	79



Continued

Entry	Phenol	Aryl halide	Product	Conversion <sup>b</sup> /%	Isolated yield <sup>c</sup> /%
10				67	42

<sup>a</sup> Reaction conditions: 1 mmol of aryl halides, 1 mmol of phenol, 1 mmol Cs<sub>2</sub>CO<sub>3</sub>, Cat-1 (0.05 g, 1.56 mmol), ACN (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, 70 °C, open air, 12 h. <sup>b</sup> Conversion refers to GC and GC-MS analysis using dihexyl ether as internal standard. <sup>c</sup> Isolated yield after column chromatography. <sup>d</sup> Reaction time 24 h.

**Table 8** Comparison of activity of different copper catalysts in the *O*-arylation reaction

Entry	Catalyst	Reaction condition	Yield/%	Reference
1	P-[(C <sub>6</sub> H <sub>4</sub> N=CHPy)Cu(OAc) <sub>2</sub> ], (Cat-1)	ACN, Cs <sub>2</sub> CO <sub>3</sub> , 70 °C, 12 h	92	This study
2	0.04 mmol of CuI and 0.15 mmol of <i>N,N</i> -dimethylglycine HCl salt	Dioxane, Cs <sub>2</sub> CO <sub>3</sub> , 90 °C, 16 h	86	34
3	BINAM, Cu(OTf) <sub>2</sub> catalyst	Dioxane, Cs <sub>2</sub> CO <sub>3</sub> , 10 °C, 18 h	70	37
4	Cu(OAc) <sub>2</sub> •H <sub>2</sub> O	NMP, K <sub>3</sub> PO <sub>4</sub> , 180 °C, 22 h	78	38
5	Cu(bpy) <sub>2</sub> BF <sub>4</sub>	DMF, K <sub>3</sub> PO <sub>4</sub> , 90 °C, 24 h	85	39

of Cat-1 is more than the other reported systems. Also, the present system requires lower temperature (70 °C) and mild solvent ACN, which are other advantages.

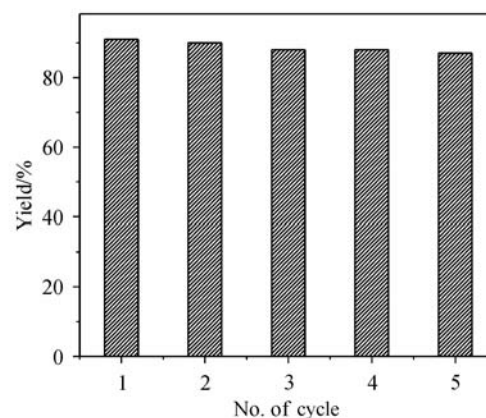
### Heterogeneity tests

To determine whether the catalyst was actually functioning in a heterogeneous manner, a hot-filtration test<sup>33</sup> was performed in the *O*-arylation reaction of phenol with iodobenzene. The solid catalyst was filtered out after the reaction had proceeded for 4 h and the conversion determined by GC was 56% and the liquid phase of the reaction mixture was collected at the reaction temperature. Atomic absorption spectrometric analysis of the liquid phase of the reaction mixtures collected by filtration confirmed that Cu was absent from the reaction mixture. The obtained filtrate was stirred under the reaction conditions. After 12 h the conversion was determined to be still 56%. This result indicated that the catalytic reaction was caused by the solid catalyst. Cu was also not detected in the liquid phase of the reaction mixture after the completion of the reaction. It is noteworthy that the ACN remains completely colorless on addition of Cu(II) catalyst. These results also suggested that the Cu was not being leached out from the catalyst during the *O*-arylation reactions.

### Catalyst recycling

The best advantage of the heterogeneous catalysis was the possibility of recovering and reusing the catalyst during the reaction. The capability of recycling of the Cat-1 was confirmed after five consecutive *O*-arylation reactions in ACN medium. After first run, the catalyst was separated by filtration, washed, dried under vacuum and then subjected to the second run under the same conditions. The catalytic run was repeated with further addition of substrates in appropriate amount

under optimum reaction conditions and the nature and yield of the final products were comparable to that of the original one. The results summarized in Figure 4, demonstrate that there was almost no change in catalytic activity even after fifth recycle. Metal content of the recycled catalyst remained unaltered indicating no leaching of the metal from the polymer support (Table 1). The nature of the recovered catalyst has been followed by IR and UV-Vis spectra. The results indicated that the catalyst after reusing several times, showed no change in its IR and UV-Vis spectra.



**Figure 4** Recycling activity of Cat-1 towards the *O*-arylation reaction of phenol with iodobenzene. Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenol, 1 mmol Cs<sub>2</sub>CO<sub>3</sub>, 50 mg Cat-1, ACN (10 mL), 0.1 mmol *t*-Bu<sub>4</sub>NBr, 70 °C, open air, 12 h.

### Characterization of the products

Melting points were recorded on a melting point apparatus. All <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 400 and 100 MHz, respectively. The characterizations

of the products were carried out by  $^1\text{H}$  NMR spectroscopy using Bruker DPX-400 in  $\text{CDCl}_3$  with TMS as internal standard. Chemical shifts were given as  $\delta$  value with reference to tetramethylsilane (TMS) as the internal standard. The reaction products were quantified (GC data) using a Varian 3400 gas chromatograph equipped with a 30 m CP-SIL8CB capillary column and a flame ionization detector and identified (GC-MS) by Trace DSQ II GC-MS equipped with a 60 m TR-50MS capillary column. Standardized of the products were done by calibration using dihexyl ether as internal standard. Color, m.p. and  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of all the products are given below:

Diphenylether<sup>34</sup> (a): colorless liquid;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.09–7.15 (m, 4H), 7.16–7.22 (m, 2H); 7.39–7.46 (m, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 119, 123.4, 129.9, 157.4.

4-Methoxy-diphenylether<sup>35</sup> (b): Colorless liquid;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 3.73 (s, 3H), 6.78–6.82 (m, 2H), 6.85–6.92 (m, 4H), 6.93–6.98 (m, 1H), 7.16–7.24 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 55.8, 115, 117.8, 121, 122.6, 129.7, 150.3, 156.1, 158.7.

4-Methyl-diphenylether<sup>34</sup> (c): Colorless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 2.42 (s, 3H), 7.01 (d,  $J=8.0$  Hz, 2H), 7.05–7.1 (m, 2H), 7.12–7.18 (m, 1H), 7.21 (d,  $J=8.4$  Hz, 2H), 7.38 (t,  $J=8.4$  Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 20.8, 118.5, 119.3, 122.9, 129.8, 130.4, 133.0, 154.9, 157.9.

1-Methyl-diphenylether<sup>34</sup> (d): Colorless liquid;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.23 (s, 3H), 6.87–6.92 (m, 3H), 6.98–7.08 (m, 2H), 7.12–7.18 (m, 1H), 7.22–7.31 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 16.3, 117.4, 119.9, 122.4, 124.1, 127.3, 129.8, 130.1, 131.6, 154.6, 158.1.

4-Chloro-diphenylether<sup>36</sup> (e): Colorless liquid;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.82–6.87 (m, 2H), 6.89–6.93 (m, 2H), 7.01–7.06 (m, 1H), 7.15–7.21 (m, 2H), 7.22–7.28 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 119.1, 120.2, 123.8, 128.3, 129.8, 130, 156.1, 157.

4-Nitro-diphenylether<sup>36</sup> (f): Yellow solid; m.p. 57–60 °C (Lit.<sup>36</sup> 60 °C);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.99–7.02 (m, 2H), 7.05–7.10 (m, 2H), 7.22–7.29 (m, 1H), 7.40–7.44 (m, 2H), 8.16–8.21 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 117.2, 120.6, 125.5, 126, 130.4, 142.7, 154.8, 163.4.

4-Acetyl-diphenylether<sup>36</sup> (g): White solid; m.p. 47 °C (Lit.<sup>36</sup> 49–51 °C);  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.94 (d,  $J=10.4$  Hz, 2H), 7.39 (m, 2H), 7.20 (t,  $J=7.2$  Hz, S10 1H), 7.07 (d,  $J=7.8$  Hz, 2H), 7.00 (d,  $J=9.0$  Hz, 2H), 2.57 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 196.7, 161.9, 155.5, 131.9, 130.6, 130.0, 124.6, 120.2, 117.3, 26.4.

## Conclusion

The current procedure enhances the utility of copper catalyzed coupling reactions of phenols with aryl hal-

ides. The reactions are, in general, more efficient with respect to quantity of catalyst required and the yields obtained and a much wider range of substrates can be utilized including electron-rich, electron-deficient and electronically neutral aryl halides and phenols. The mild base cesium carbonate is effective in a large majority of these reactions and low polar solvent ACN is used as a solvent. We are currently working to improve the scope and generality of copper-catalyzed diaryl ether formation. We anticipate that existing difficulties with homogeneous catalyst will be overcome through the development of new polymer anchored Cu(II) Schiff base catalyst systems.

In summary, we have developed a cheap and simple way to carry out the Ullmann diaryl ether synthesis, which is applicable to a wide variety of substrates with different functional groups. The application of this method to the synthesis of more complex diaryl ethers, as well as mechanism studies, is in progress. We have developed a new polymer anchored Cu(II) Schiff base catalyst which can be successfully applied in a number of cross-coupling reactions and gives better results than other reported copper catalysts. The polymer anchored Cu(II) Schiff base catalyst can be recycled with minimal loss of activity and it is able to promote the reaction catalytically. The easy workup procedure provides a method that is well suited toward the synthesis of parallel libraries based upon this type of transformation.

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