

Open air O-arylation reaction of phenols with aryl halides catalyzed by polymer-anchored copper(II) complexes

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Abstract Two copper complexes were synthesized from macroporous chloromethylated polystyrene beads. The first one was prepared by sequential attachment of imidazole and copper acetate with chloromethylated polystyrene-divinyl benzene copolymer, and the second one was prepared from 4-vinylpyridine and copper acetate with chloromethylated polystyrene-divinyl benzene copolymer. These catalysts showed excellent catalytic activity in O-arylation reaction of aryl halides with phenol in dimethylsulfoxide using potassium carbonate at 130 °C under open air conditions to give diaryl ethers in high yields. Less reactive aryl bromides and aryl chlorides have also been shown to react with phenols to give good yields of the diaryl ethers. The effects of various parameters such as solvent, catalyst from different copper salt and base on the reaction system were studied. The reaction is applicable to a wide variety of substituted aryl halides and phenols with different steric and electronic properties. These catalysts were recovered by simple filtration, and the reusability experiments showed that these catalysts can be used five times without much loss in the catalytic activity.

Introduction

Diaryl ethers are not only important structures in biological systems, but also common moieties in pharmaceutical research and materials interest [1, 2]. The Ullmann ether formation reaction, in which an aryl bromide or iodide

reacts with a phenol under basic conditions in the presence of copper salt catalysts, has been the focus of a number of recent studies because it provides very direct access to diaryl ethers [3–8]. Diaryl ethers have also been prepared from the cross-coupling reaction of aryl halides with phenol (transition-metal catalyzed O-arylation reaction of phenol) in the presence of palladium compounds as catalysts. Palladium compounds are very active and have high catalytic activity, but the high costs of Pd compounds have lowered their popularity, particularly for large-scale reactions [9]. Hartwig et al. and Buchwald et al. have greatly contributed to novel Pd-catalyzed arylation of phenols [10, 11], but their systems still suffer from the expensive price of palladium and ligand sources. As a result, much of the recent literature has focused on the continuing evolution of Ullmann's original copper-based diaryl ether formations [12, 13]. Recent work in Buchwald's group with copper(II) triflate catalyst has made it possible to carry out these reactions under milder conditions with a wider variety of substrates in good yields [14]. Due to the relatively high cost of copper triflate and its air sensitivity, it is still desirable to develop more robust and more cost-effective processes for this important reaction. Although recent progress in palladium-catalyzed ether formation reactions has solved some problems in this area [15, 16], copper catalysts still hold the advantage of low cost for large-scale industrial applications.

Copper metal has been employed as catalyst for various organic reactions such as oxidation [17, 18], amination [19, 20], cyanation [21] and Sonogashira [22, 23], etc. The O-arylation reaction generally proceeds in the presence of homogeneous copper catalysts that possess high efficiency and are suitable for the study of the reaction mechanism, but their higher susceptibility to drastic reaction conditions and the difficulties associated with their isolation from the

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product mixture restrict their reusability. This is a great disadvantage in this coupling reaction using homogeneous catalysts. Also, recycling of catalysts is a task of great economic and environmental importance in the chemical and pharmaceutical industry, especially when expensive or toxic heavy metal complexes are employed [24]. These disadvantages can be overcome by anchoring the metal on suitable supports. These studies confirm that the anchoring of a metal on a 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 of immobilizers such as Cu- or Pd-catalytic systems [25–29]. 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 [30–33]. 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 of polymer-supported copper catalysts and illustrate their application in a number of cross-coupling reactions between aryl halides and phenols. Our strategy was to attach a ligand to a polymer support and then allow it to bind to copper through ligand exchange. The resulting binding interaction also needs to be strong enough to prevent the copper from dissociating from the polymer support under the reaction conditions. The experimental results reveal that polymer-anchored copper(II) catalysts can be recycled more than five times without much loss in the activity.

Result and discussion

Preparation of catalysts

The outline for the preparation of the polymer-anchored Cu(II) catalysts is given in Scheme 1.

Characterization of the polymer-anchored Cu(II) catalysts

Elemental analysis

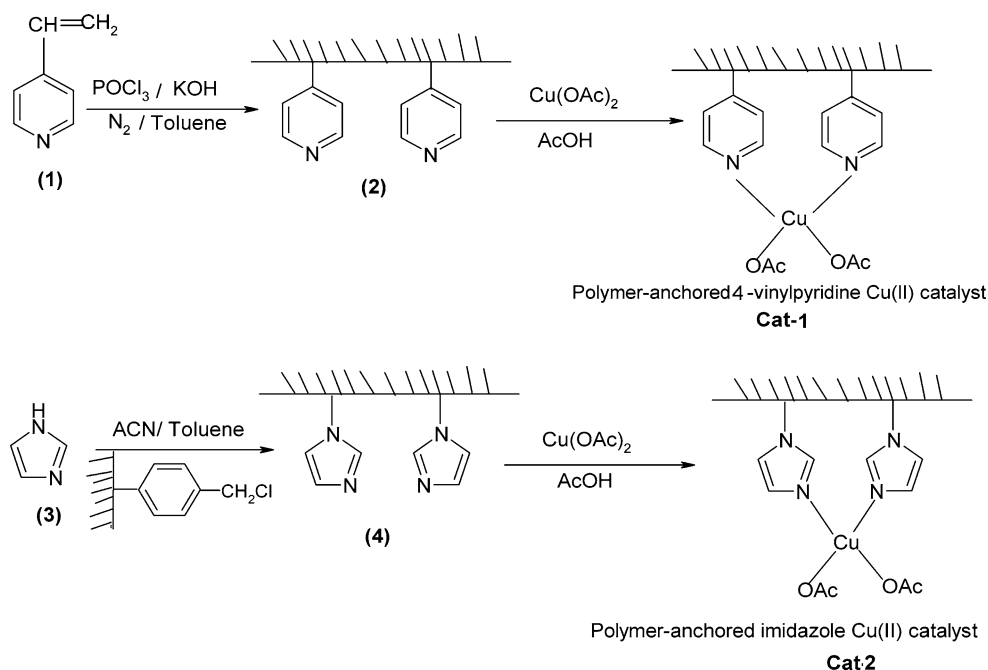
Elemental analysis for polymer-anchored 4-vinylpyridine ligand, polymer-anchored imidazole ligand, Cat-1 and Cat-2 was carried out, and the data are tabulated in Table 1. Amount of metal was determined by stripping the bound metal from the support and analysis by using atomic absorption spectrophotometer. Copper content in the

Table 1 Chemical composition of polymer-anchored ligands and complexes

Compound	Color	C%	H%	N%	Cu%
2	Light-orange	80	6.76	13.39	–
4	White	78.26	6.45	15.21	–
Cat-1	Yellowish-green	55.74	4.13	7.23	1.33 1.33 ^a
Cat-2	Greenish-blue	61.59	4.77	10.27	1.28 1.27 ^a

^a Used catalyst

Scheme 1 Synthesis of the polymer-anchored Cu(II) catalysts



catalysts determined by AAS suggests 1.33 wt% Cu in the Cat-1 and 1.28 wt% Cu in the Cat-2. Copper content remained almost unchanged even after recycling the catalyst for five cycles.

Infrared spectral studies

The modes of attachment of metals onto the support were confirmed by comparison of the FTIR spectral bands of the metal catalyst over the polymer in various steps of its synthesis. For the Cat-1, infrared spectra of the complex are identical to those of the polymers in the region 4,000–1,000 cm^{-1} [34]. The characteristic stretching of pyridine rings for pure polymer-anchored 4-vinylpyridine ligand occurs at ca. 1,600 cm^{-1} , which is shifted to 1,616 cm^{-1} in copper complex (Cat-1), suggesting coordination between the pyridinic nitrogen atoms and the copper metallic center [35, 36]. In the metal complex, a medium or weak band is observed at 547 cm^{-1} , which can be attributed to the metal with pyridine nitrogen mode [37]. Monodentate acetate usually shows two bands at 1,630 and 1,310 cm^{-1} due to antisymmetric and symmetric stretching, respectively [38]. In Cat-1, a band observed at 1,313 cm^{-1} suggests the monodentate coordination of the acetate groups [39]. The Cat-1 exhibits a single peak at 430 cm^{-1} ($\text{Cu}-\text{O}_{\text{acetate}}$), indicating the presence of the coordination of acetate group with copper metal [38].

Chloromethylated polystyrene exhibits a peak at 1,263 cm^{-1} attributed to $-\text{CH}_2\text{Cl}$ and imidazole shows $\nu\text{N}-\text{H}$ around 3,124 cm^{-1} . The intensity of the first peak was reduced ($\nu-\text{CH}_2\text{Cl}$), and the second peak was not found in Cat-2, indicating that hydrogen of (N–H) imidazole is lost consequent to functionalization and it is bonded to the polymer support through nitrogen [40]. In this metal complex, a medium or weak band is observed at 542 cm^{-1} , which can be attributed to the metal with imidazole nitrogen mode [37]. Cat-2 exhibits a medium intensity band at 1,315 cm^{-1} consistent with monodentate coordination of the acetate groups [39] and a single peak at 432 cm^{-1} ($\text{Cu}-\text{O}_{\text{acetate}}$), indicating the presence of the coordination of acetate group with copper metal [38].

UV–vis spectral studies

The electronic spectrum of the polymer-anchored Cu(II) complexes were recorded in diffuse reflectance spectrum mode as $\text{MgCO}_3/\text{BaSO}_4$ disks due to their solubility limitations in common organic solvents. The spectrum for Cat-1 exhibits three spectral bands at ca. 325, 360–380 and 525–530 nm. The peak at 325 nm is due to $\pi-\pi^*$ [41] transition of the pyridine moiety. The band at the range 360–380 nm is assigned to ligand to metal charge transfer [42]. The d–d bands were observed for Cat-1 in the range

of 525–530 nm [43]. The spectrum for Cat-2 exhibits two bands at ca. 365–375 and 390–410 nm. The UV spectrum in the 390–410 nm regions has been widely highlighted in order to identify the imidazole contribution to the coordination chemistry [44]. The charge transfer spectra for the interaction between copper(II) and imidazole nitrogen appeared at 365–375 nm [42]. The expected d–d bands are not observed in the polymer-anchored copper catalyst. Possibly low loading of the complex on the polymer matrix has prevented observation of the d–d band, which is a low-energy and eventually less-intense band [45].

SEM studies

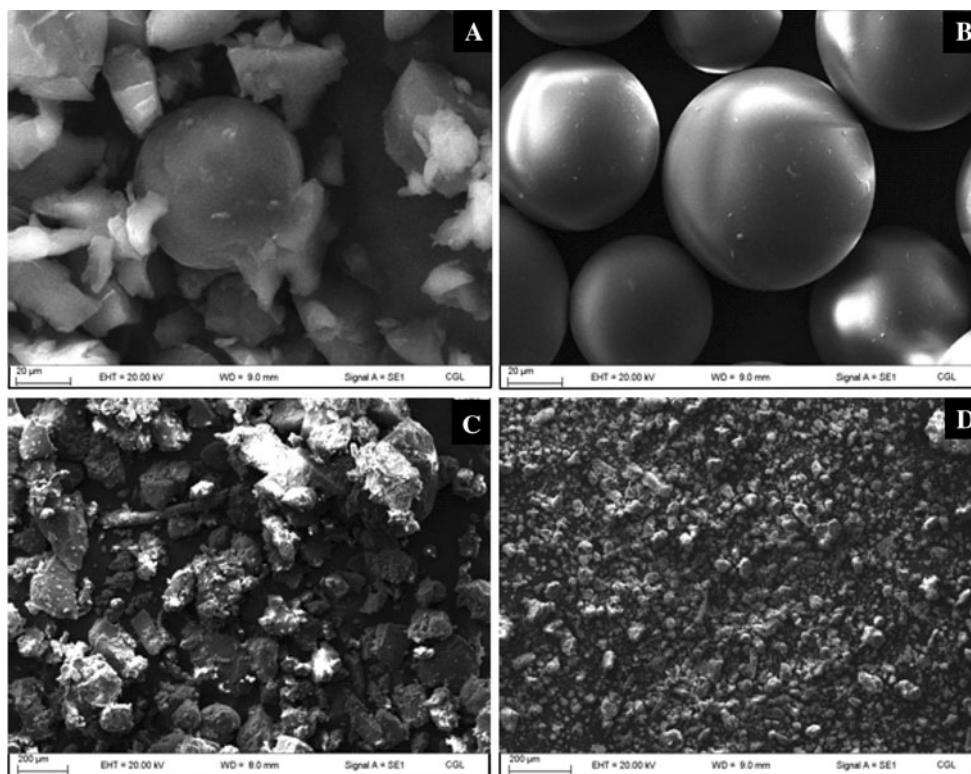
The morphology of the Cat-1 and Cat-2 were studied using Scanning Electron Microscope. The micrographs of the polymer-anchored imidazole ligand, 4-vinylpyridine ligand, Cat-2 and Cat-1 obtained from the scanning electron microscope are presented in Fig. 1a–d, respectively. The morphological changes in the polymer-anchored ligands and immobilized copper(II) complexes are quite evident from these images and suggest the loading of copper metal on the surface of the polymer matrix. Energy-dispersive spectroscopy analysis of X-rays (EDAX) data for the anchored imidazole ligand, 4-vinylpyridine ligand, Cat-2 and Cat-1 are given in Fig. 2a–d. The EDX data also inform the attachment of copper on the surface of the polymer matrix.

Catalytic activity

The polymer-anchored Cat-1 and Cat-2 have been investigated as catalysts in the O-arylation reaction of aryl halides with equimolar amount of phenols using tetrabutylammonium bromide ($t\text{Bu}_4\text{NBr}$) at 130 °C for 12 h. The O-arylation reaction gives diaryl ether as a main product in yields of up to 96%. The Cat-1 and Cat-2 are comparable in their activities, but Cat-1 is superior due to its higher metal loading (Table 1). To optimize the conditions for the O-arylation reaction, we have chosen the reaction between iodobenzene and phenol as a model reaction (Scheme 2) using copper catalysts and various parameters, such as solvent and base to get maximum product.

Our initial screening experiments were carried out by the polymer-supported copper catalysts using iodobenzene and phenol. In the presence of K_2CO_3 in DMSO medium, the Ullmann diaryl etherification can be catalyzed by either Cu(I) or Cu(II) in the absence of any palladium. However, no reaction occurred in the absence of copper catalyst. As can be seen from Table 2, polymer-anchored Cu(II) catalysts were superior. Among polymer-supported Cu(II) catalysts, which were prepared from different copper(II) sources, polymer-supported Cu(II) catalyst from copper(II)

Fig. 1 FE SEM images of the polymer-anchored imidazole ligand (a), Cat-2 (b), 4-vinylpyridine ligand (c), Cat-1 (d)



acetate was found to be the most effective one (entries 7–8). Next, the reaction was carried out with different amounts of copper catalysts over the range of 0.025–0.065 g, and it was found that 0.05 g of copper catalyst was the most effective catalytic system (Table 2, entries 9–14).

We tested several different bases for the Ullmann coupling reactions catalyzed by the polymer-supported copper(II) catalysts in DMSO. K_2CO_3 was found to be the most effective. Other bases such as KOH, Cs_2CO_3 , Na_2CO_3 , Et_3N and K_3PO_4 were substantially less effective (Table 3, entries 1–6). Solvents such as dimethyl sulphoxide (DMSO), N-methyl pyrrolidinone (NMP), acetonitrile (CAN), methanol (MeOH), dimethyl formamide (DMF), toluene (PhMe) and water were investigated, and it was found that moderate polar solvents were more favored. With DMSO, NMP, ACN, DMF, MeOH and water yields were comparatively good (Table 3, entries 1, 7–11). By contrast, the catalytic performance was not acceptable when the non-polar solvent toluene was employed (Table 3, entry 12). Consequently, DMSO was chosen as the medium of choice for this coupling reaction. This arylation was also found to be highly sensitive to the reaction temperature and time. At lower temperatures (60 °C) and with lower reaction time (6 h), only low to moderate yields were obtained (Table 3, entries 13, 14). A reaction temperature of 130 °C and reaction time of 12 h

were found to be optimal. From the above discussions, it can be seen that the best yield was obtained by using K_2CO_3 (1 mmol) in DMSO solvent at 130 °C for 12 h under open air. Now the optimized reaction conditions were used to examine C–O bond formations involving functionalized coupling partners. Reactivity comparisons were made by interrupting the reactions after 12 h.

On the basis of the above results, the coupling reactions catalyzed by Cat-1 and Cat-2 were tested with several different aryl iodides and phenols, and the results are summarized in Table 4. Both electron-rich and electron-deficient aryl iodides were suitable substrates for this reaction to provide the corresponding diaryl ethers in good to excellent yields. A variety of functional groups of aryl iodides were known to tolerate this reaction condition, which include nitro, methyl, ketomethyl and cyano groups. Phenols with electron-rich and iodobenzene with electron-deficient groups made very good pairings for this coupling reaction (entries 5–7). Some tolerance of electron-withdrawing groups on the phenols was observed, as the reactions with 4-bromophenol (entry 8) gave reasonable to good yields. Phenols with extremely strong electron-withdrawing groups do not undergo the desired ether formation (entry 9). This might be due to the decreased nucleophilicity of phenols induced by the nitro group [46]. The steric hindrance of phenols was slightly disfavored for this reaction. For example, when 2-methylphenol and

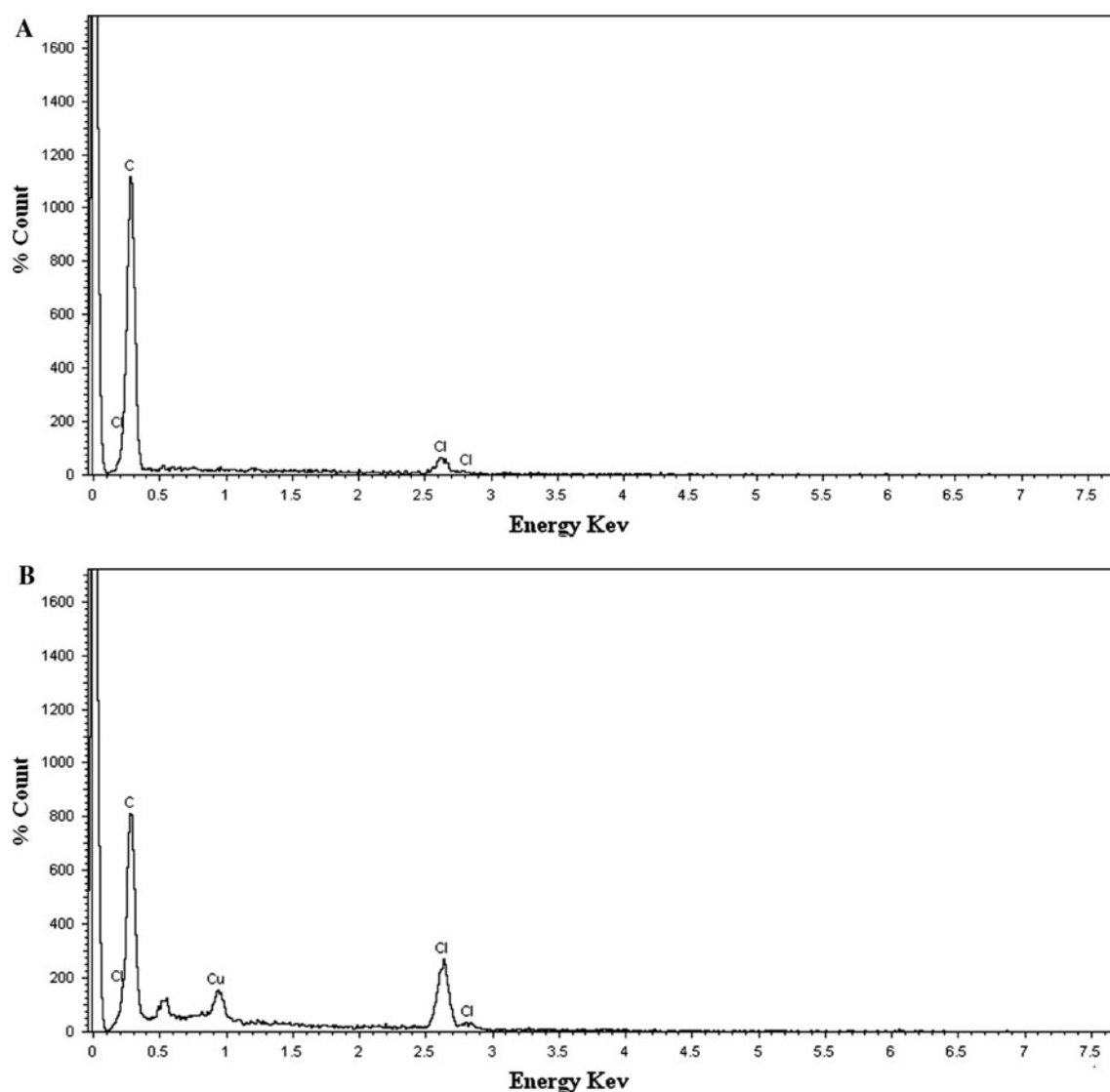


Fig. 2 EDAX data for the polymer-anchored imidazole ligand (a), Cat-2 (b), 4-vinylpyridine ligand (c) and Cat-1 (d)

2-methoxyphenol were used as the substrate, the reaction gave considerably lower yield in comparison with that of less-hindered phenol (entries 10, 11). However, the steric hindrance of aryl iodides was highly disfavored for this reaction (entries 12, 13). As shown in Table 4, the present catalytic system was also effective for the coupling reaction of aryl bromides and phenols. High yields were obtained for the aryl bromides with an electron-withdrawing group such as nitro and cyano groups (entries 15 and 16). The reaction of 4-methylphenyl bromide with phenol, which was a difficult case for the classical Ullmann coupling method, gave the coupling product in 56 and 48% (entry 17) yield for the Cat-1 and Cat-2, respectively. Furthermore, 1-bromo-4-nitrobenzene successfully coupled with 4-methoxyphenol with an excellent yield (entry 18). Because of their low cost and ready availability, aryl chlorides are much more attractive substrates for the

industrial production and laboratory preparation of diaryl ethers [47]. We further investigated the potential catalytic efficiency of the present catalytic system for the coupling between aryl chlorides and phenols. In some cases, higher temperature and higher reaction time were used to promote the reaction. As summarized in Table 4, Cat-1 and Cat-2 successfully promoted the coupling reaction with good or moderate yields. The electron-deficient aromatic chlorides tested gave good yields under the catalysis at 160 °C (Table 4, entries 20–21).

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

We compared the activity of the Cat-1 and Cat-2 in the O-arylation reaction with the other reported copper catalysts (Table 5). The reaction using the present heterogeneous

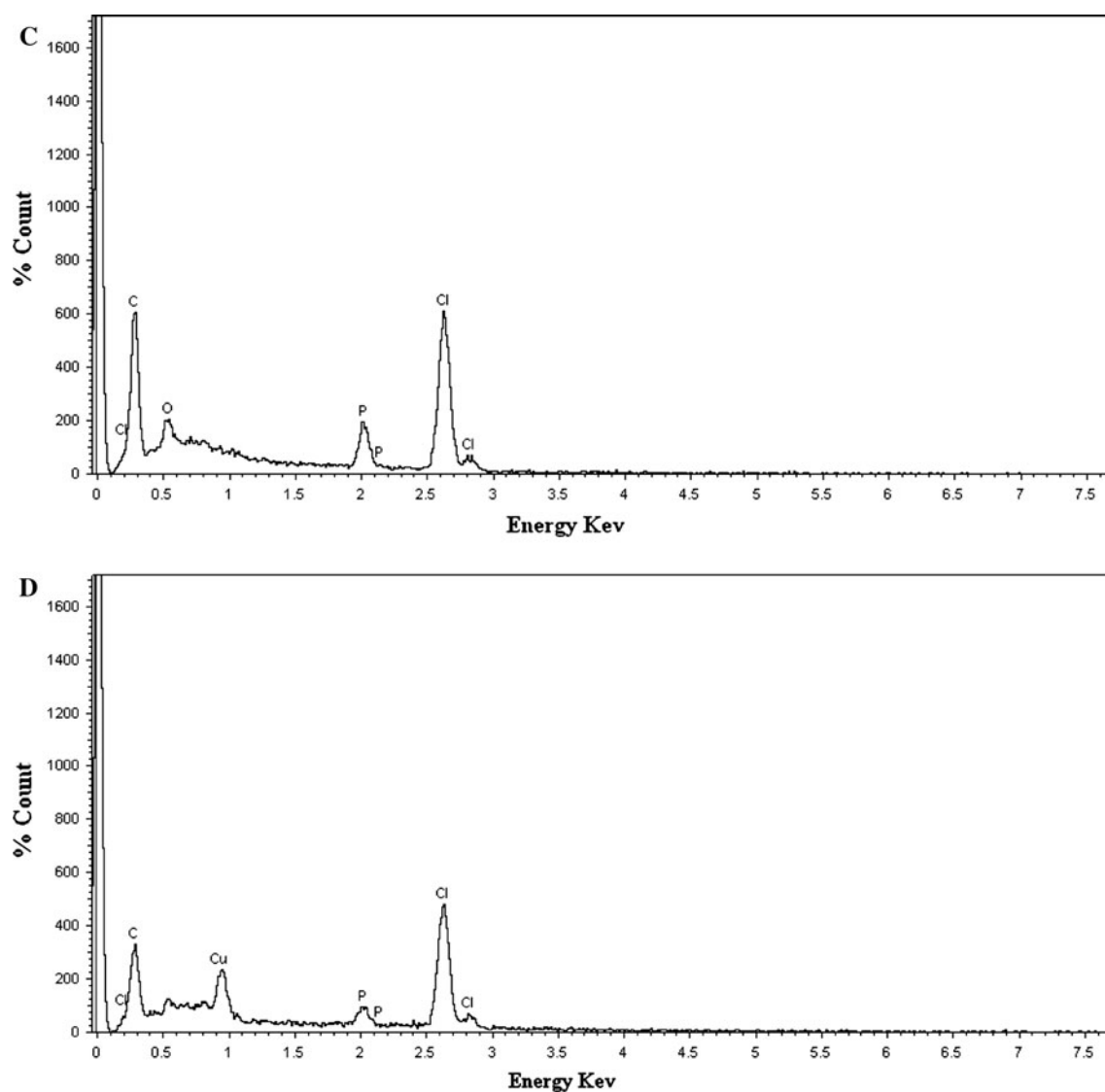
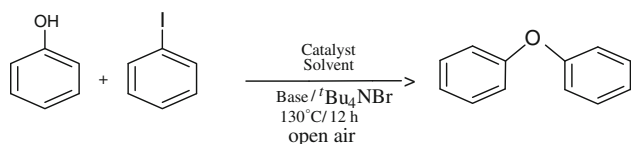


Fig. 2 continued



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

Cat-1 and Cat-2 with phenol and iodobenzene in DMSO medium at 130°C for 12 h results in 95 and 92% yields, respectively, while the other reported copper catalysts such as CuI with *N,N*-dimethylglycine HCl salt [49], BINAM-Cu(OTf)₂ catalyst [56], Cu(OAc)₂·H₂O [57] and Cu(bpy)₂BF₄ [58] gave yields of only 86, 70, 78 and 85%, respectively. From Table 5, it can be also seen that the present catalytic systems work better at shorter reaction time.

Catalyst reuse and stability

The stabilities of the copper complex catalysts were studied by performing repeated O-arylation reactions using the same reaction conditions as described earlier. Phenol and iodobenzene were used as model substrates. At the end of each reaction cycle, the catalyst was recovered by filtration and washed with DMSO and acetone, dried and reused. The yield (%) was almost identical up to the 5th recycle (Fig. 3). Copper content of the recycled catalysts remained almost unaltered, indicating no leaching of the metal from the polymer-support complexes (Table 1). No evidence for leaching of copper or decomposition of the complex catalysts were observed during the catalysis reaction, and no copper could be detected by atomic absorption spectroscopic

Table 2 Effect of copper source/amount on the O-arylation reaction

Entry	Copper source/amount	Yield ^a (%)
1.	None	No reaction
2.	CuI (0.05 g)	53
3.	CuCl ₂ (0.05 g)	67
4.	Cu(OAc) ₂ (0.05 g)	79
5.	Polymer-supported Cu(I) ^b 4-vinylpyridine (0.05 g)	77
6.	Polymer-supported Cu(II) ^c 4-vinylpyridine (0.05 g)	82
7.	Polymer-supported Cu(II) ^d imidazole (0.05 g)	92
8.	Polymer-supported Cu(II) ^d 4-vinylpyridine (0.05 g)	96
9.	Polymer-supported Cu(II) ^d imidazole (0.025 g)	66
10.	Polymer-supported Cu(II) ^d 4-vinylpyridine (0.025 g)	68
11.	Polymer-supported Cu(II) ^d imidazole (0.04 g)	78
12.	Polymer-supported Cu(II) ^d 4-vinylpyridine (0.04 g)	81
13.	Polymer-supported Cu(II) ^d imidazole (0.065 g)	93
14.	Polymer-supported Cu(II) ^d 4-vinylpyridine (0.065 g)	96

Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenol, 1 mmol of K₂CO₃, 0.1 mmol of ^tBu₄NBr, DMSO (10 mL), 130 °C, 12 h, open air

^a Yield determined by GC and GCMS analysis using dihexyl ether as internal standard

^b Catalyst prepared from CuI

^c Catalyst prepared from CuCl₂

^d Catalyst prepared from Cu(OAc)₂

Table 3 Effect of solvent, base, temperature, reaction time on the O-arylation reaction

Entry	Base	Solvent	Temperature (°C)	Time (h)	Yield ^a (%)	
					Cat-1	Cat-2
1	K ₂ CO ₃	DMSO	130	12	96	92
2	CS ₂ CO ₃	DMSO	130	12	85	82
3	Na ₂ CO ₃	DMSO	130	12	76	68
4	K ₃ PO ₄	DMSO	130	12	79	75
5	Et ₃ N	DMSO	130	12	66	60
6	KOH	DMSO	130	12	57	55
7	K ₂ CO ₃	ACN	80	14	81	78
8	K ₂ CO ₃	DMF	140	14	88	83
9	K ₂ CO ₃	NMP	120	14	78	74
10	K ₂ CO ₃	MeOH	70	18	56	48
11	K ₂ CO ₃	Water	70	18	55	51
12	K ₂ CO ₃	Toluene	130	14	34	30
13	K ₂ CO ₃	DMSO	60	12	72	69
14	K ₂ CO ₃	DMSO	130	6	65	61

Reaction conditions: Cat-1 (0.05 g, 0.0104 mmol) and Cat-2 (0.05 g, 0.0101 mmol), 1 mmol of iodobenzene, 1 mmol of phenol, solvent (10 mL), 1 mmol of base, 0.1 mmol of ^tBu₄NBr, open air

^a Yield determined by GC and GCMS analysis using dihexyl ether as internal standard

measurement of the liquid reaction mixture after each catalytic reaction.

Heterogeneity tests

To determine whether the catalysts were actually functioning in a heterogeneous manner, a hot-filtration test was performed in the O-arylation reaction of phenol with

iodobenzene. The solid catalyst was filtered out after the reaction had proceeded for 6 h and the yield determined by GC was 65% for the Cat-1 and 61% for the Cat-2. 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 yield was determined to be still 65 and 61% for the Cat-1 and Cat-2, respectively. 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 DMSO remains completely colorless on addition of the Cu(II) catalysts. These results also suggested that the Cu was not being leached out from the catalyst during the O-arylation reactions.

Conclusion

The current procedure enhances the utility of copper-catalyzed coupling reactions of phenols with aryl halides. 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. 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) catalyst systems.

In summary, we have developed a cheap and simple way to carry out the Ullmann diaryl ether synthesis, which is

Table 4 Polymer-supported copper(II) catalyzed O-arylation reaction of aryl halides with phenols

Entry	Phenols	Aryl halides	Products	Isolated yield (%)	
				Cat-1	Cat-2
1	C ₆ H ₅ OH	C ₆ H ₅ I	C ₆ H ₅ OH ₅ C ₆ (4a)	95	92
2	C ₆ H ₅ OH	p-NO ₂ C ₆ H ₄ I	p-NO ₂ C ₆ H ₄ OH ₅ C ₆ (4b)	96	94
3	C ₆ H ₅ OH	p-CNC ₆ H ₄ I	p-CNC ₆ H ₄ OH ₅ C ₆ (4c)	96	93
4	C ₆ H ₅ OH	p-MeC ₆ H ₄ I	p-MeC ₆ H ₄ OH ₅ C ₆ (4d)	88	86
5	p-OMeC ₆ H ₄ OH	p-CNC ₆ H ₄ I	p-OMeC ₆ H ₄ OH ₄ C ₆ CN-p (4e)	97	94
6	p-MeC ₆ H ₄ OH	p-COMeC ₆ H ₄ I	p-MeC ₆ H ₄ OH ₄ C ₆ COMe-p (4f)	94	93
7	p-OMeC ₆ H ₄ OH	p-NO ₂ C ₆ H ₄ I	p-OMeC ₆ H ₄ OH ₄ C ₆ NO ₂ -p (4g)	97	95
8	p-BrC ₆ H ₄ OH	p-NO ₂ C ₆ H ₄ I	p-BrC ₆ H ₄ OH ₄ C ₆ NO ₂ -p (4h)	88	85
9	p-NO ₂ C ₆ H ₄ OH	C ₆ H ₅ I	p-NO ₂ C ₆ H ₄ OH ₅ C ₆ (4b)	45	38
10	o-MeC ₆ H ₄ OH	C ₆ H ₅ I	o-MeC ₆ H ₄ OH ₅ C ₆ (4i)	65	60
11	o-OMeC ₆ H ₄ OH	C ₆ H ₅ I	o-OMeC ₆ H ₄ OH ₅ C ₆ (4j)	68	65
12	C ₆ H ₅ OH	o-MeC ₆ H ₄ I	o-MeC ₆ H ₄ OH ₅ C ₆ (4i)	57	51
13	C ₆ H ₅ OH	o-OMeC ₆ H ₄ I	o-OMeC ₆ H ₄ OH ₅ C ₆ (4j)	55	54
14	C ₆ H ₅ OH	C ₆ H ₅ Br	C ₆ H ₅ OH ₅ C ₆ (4a)	88	85
15	C ₆ H ₅ OH	p-NO ₂ C ₆ H ₄ Br	p-NO ₂ C ₆ H ₄ OH ₅ C ₆ (4b)	90	88
16	C ₆ H ₅ OH	p-CNC ₆ H ₄ Br	p-CNC ₆ H ₄ OH ₅ C ₆ (4c)	89	88
17	C ₆ H ₅ OH	p-MeC ₆ H ₄ Br	p-MeC ₆ H ₄ OH ₅ C ₆ (4d)	56	48
18	p-OMeC ₆ H ₄ OH	p-NO ₂ C ₆ H ₄ Br	p-OMeC ₆ H ₄ OH ₄ C ₆ NO ₂ -p (4g)	92	91
19 ^a	C ₆ H ₅ OH	C ₆ H ₅ Cl	C ₆ H ₅ OH ₅ C ₆ (4a)	58	55
20 ^a	C ₆ H ₅ OH	p-NO ₂ C ₆ H ₄ Cl	p-NO ₂ C ₆ H ₄ OH ₅ C ₆ (4b)	77	76
21 ^a	C ₆ H ₅ OH	p-CNC ₆ H ₄ Cl	p-CNC ₆ H ₄ OH ₅ C ₆ (4c)	74	70

Reaction conditions: Cat-1 (0.05 g, 0.0104 mmol) and Cat-2 (0.05 g, 0.0101 mmol), 1 mmol of aryl halides, 1 mmol of phenols, 1 mmol K₂CO₃, DMSO (10 mL), 0.1 mmol ^tBu₄NBr, 130 °C, open air, 12 h

Isolated yield after column chromatography

^a Reaction temperature = 160 °C, reaction time = 18 h

Table 5 Comparison of activity of different copper catalysts in the O-arylation reaction of phenol with iodobenzene

Entry	Catalyst	Reaction conditions	Yield (%)	References
1	Cat-1	DMSO, K ₂ CO ₃ , 130 °C, 12 h	95	This study
	Cat-2		92	
2	0.04 mmol of CuI and 0.15 mmol of <i>N,N</i> -dimethylglycine HCl salt	Dioxane, Cs ₂ CO ₃ , 90 °C, 16 h	86	[49]
3	BINAM, Cu(OTf) ₂ catalyst	Dioxane, Cs ₂ CO ₃ , 110 °C, 18 h	70	[56]
4	Cu(OAc) ₂ ·H ₂ O	NMP, K ₃ PO ₄ , 180 °C, 22 h	78	[57]
5	Cu(bpy) ₂ BF ₄	DMF, K ₃ PO ₄ , 90 °C, 24 h	85	[58]

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 the two new polymer-anchored Cu(II) catalysts that can be successfully applied in a number of cross-coupling reactions and give better results than other reported copper catalysts. These two catalysts can be recycled up to five cycles without appreciable loss of activity. The easy workup procedure provides a method that is well suited

toward the synthesis of parallel libraries based upon this type of transformation.

Experimental

Analytical-grade reagents and freshly distilled solvents were used throughout. All reagents and substrates were purchased from Merck. Liquid substrates were predistilled and dried by appropriate molecular sieve, and solid substrates were

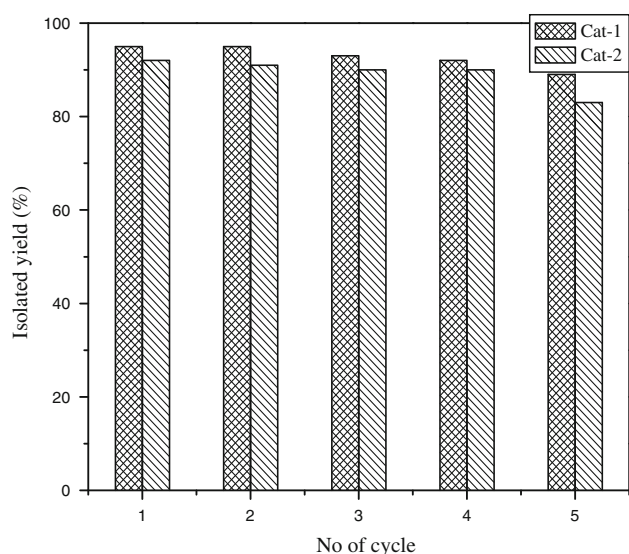


Fig. 3 Recycling activity of the Cat-1 and Cat-2 toward the O-arylation reaction of phenol with iodobenzene. Reaction conditions: 1 mmol of iodobenzene, 1 mmol of phenol, 1 mmol K_2CO_3 , 0.05 g catalyst, DMSO (10 mL), 0.1 mmol tBu_4NBr , 130 °C, 12 h, open air

recrystallized before use. Distillation, purification of the solvents and substrate were done by standard procedures [48]. Chloromethylated polystyrene, 200–400 mesh (Art. No. 63863-50G) and 4-vinyl pyridine were supplied by Aldrich Chemical Company, U.S.A. Copper acetate and imidazole were purchased from Merck and used as such without further purification.

Preparation of the polymer-anchored 4-vinylpyridine ligand (2)

The monomer was refluxed over solid KOH pellets and distilled under nitrogen at a pressure of 6 mmHg. $POCl_3$ (3 g) was added to a toluene solution of the monomer (100 mL, 2 M) and the mixture was stirred for 20 h at 30 °C under nitrogen. Addition of the mixture to a larger volume of light petroleum produced a pale-yellow precipitate that was dried and purified by precipitating several times from ethanol by light petroleum (b.p. 40–60 °C).

Preparation of the polymer-anchored imidazole ligand (4)

Chloromethylated polystyrene (3 g) was stirred with a 1:1 mixture of acetonitrile and toluene for 30 min. Then imidazole (1.2 g) was added to the above solution of the polymer, and the mixture was refluxed for 24 h at 60 °C. The white polymer-anchored ligand (2) was filtered out, washed thoroughly with methanol and dried under vacuum.

Preparation of the polymer-anchored 4-vinylpyridine copper(II) catalyst (Cat-1)

Polymer-anchored 4-vinylpyridine ligand (2 g) was added to acetic acid (20 mL). Copper acetate (50 mg) in acetic acid (5 mL) was added to the above suspension with constant stirring and then refluxed for 24 h. After cooling the reaction mixture to room temperature, the separated yellowish-green color solid was filtered out, washed thoroughly with methanol and dried under vacuum.

Preparation of the polymer-anchored imidazole copper(II) catalyst (Cat-2)

Polymer-anchored imidazole ligand (2 g) was added to acetic acid (20 mL). Copper acetate (0.05 g) in acetic acid (5 mL) was added to the above suspension with constant stirring and then refluxed for 24 h. After cooling the reaction mixture to room temperature, the separated green solid was filtered out, washed thoroughly with methanol and dried under vacuum.

Instrumentation

Surface morphology and particle size of the samples were analyzed by using a scanning electron microscope (SEM) (ZEISS EVO40, England) equipped with EDX facility. 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 double-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 Varian AA240 atomic absorption spectrophotometer (AAS).

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

Cu-catalyst (0.05 g) in DMSO (5 mL) was taken 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 (tBu_4NBr) (0.1 mmol), K_2CO_3 (1 mmol), dihexyl ether (5 mL) and DMSO (5 mL) were added. The final reaction mixture was refluxed for 12 h at 130 °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 internal standard. After cooling to room temperature, the reaction was extracted with ethyl acetate (3×20 mL), and the combined organic layers were dried with anhydrous Na_2SO_4 by vacuum. 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 and NMR spectra with those reported in the literature or authentic samples from our laboratories.

Characterization of the used catalyst

Characterization of the used catalyst was done by IR and UV–vis spectroscopic data. The FTIR spectrum of the used catalyst was identical to that of the original catalyst. Thus, for the used Cat-1, peaks at $1,618\text{ cm}^{-1}$ (for pyridine ring), $1,313\text{ cm}^{-1}$ ($\nu\text{C-O}$, coordinated), a weak peak at 547 cm^{-1} ($\nu\text{Cu-N}$) and a Cu–O stretching vibration at 431 cm^{-1} were all present in the spectrum. In Cat-2, a peak at $1,250\text{ cm}^{-1}$ (for $-\text{CH}_2\text{Cl}$), $1,312\text{ cm}^{-1}$ ($\nu\text{C-O}$, coordinated), a weak peak at 542 cm^{-1} ($\nu\text{Cu-N}$) and a Cu–O stretching vibration at 433 cm^{-1} were all present in the spectrum of the used Cat-2. The UV–vis spectra of the used catalysts were also very similar to those of the original catalysts. From the spectroscopic data, we conclude that the structures of the used catalysts are identical with those of the original.

Characterization of the products

All ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. The characterizations of the products were carried out by ^1H NMR spectroscopy using Bruker DPX-400 in CDCl_3 with TMS as internal standard. Chemical shifts are given as δ values with reference to tetramethylsilane (TMS) as the internal standard. The reaction products were quantified (GC data) by 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. Standardization of the products was done by calibration using dihexyl ether as internal standard. Color, ^1H and ^{13}C NMR data of all the products are given below.

Diphenylether (4a). Colorless liquid [49]. ^1H NMR (CDCl_3 , 400 MHz) δ : 7.07–7.14 (m, 4H), 7.13–7.20 (m, 2H); 7.41–7.45 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 116, 124.4, 128.7, 157.0.

4-Nitro-diphenylether (4b). Yellow solid [50]. ^1H NMR (CDCl_3 , 400 MHz) δ : 6.98–7.00 (m, 2H), 7.04–7.10 (m, 2H), 7.20–7.28 (m, 1H), 7.41–7.44 (m, 2H), 8.14–8.20 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 117.4, 121.2, 125.7, 127, 129.4, 142.2, 153.9, 163.2.

4-Phenoxybenzotrile (4c). Oil [51]. ^1H NMR (CDCl_3 , 400 MHz) δ : 7.57 (d, $J = 8.6\text{ Hz}$, 2H), 7.42 (t, $J = 7.9\text{ Hz}$, 2H), 7.25 (t, $J = 7.6\text{ Hz}$, 1H), 7.0 (d, $J = 7.9\text{ Hz}$, 2H), 6.89 (d, $J = 8.8\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 160.4, 151.1, 135.8, 131.5, 123.0, 118.4, 116.5, 120.3, 101.5.

4-Methyl-diphenylether (4d). Colorless liquid [49]. ^1H NMR (CDCl_3 , 400 MHz) δ : 2.41 (s, 3H), 7.00 (d, $J = 8.0\text{ Hz}$, 2H), 7.03–7.3 (m, 2H), 7.10–7.17 (m, 1H), 7.24 (d, $J = 8.4\text{ Hz}$, 2H), 7.35 (t, $J = 8.4\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 20.4, 118.3, 119.6, 122.8, 129.8, 130.1, 133.0, 154.2, 157.9.

4-Cyano-4-methoxy-diphenylether (4e). White solid [52]. ^1H NMR (CDCl_3 , 400 MHz) δ : 3.76 (s, 3 H), 6.84–6.87 (m, 4H), 6.91–6.94 (m, 2H), δ 7.47–7.51 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 55.7, 105.4, 115.2, 117.31, 119.15, 122, 134.2, 148, 157.2, 162.5.

4'-Methyl-4-phenoxy-phenylacetate (4f). White Solid [53]. ^1H NMR (CDCl_3 , 400 MHz) δ : 8.00–8.04 (2H, d, $J = 8.4$), 7.18–7.20 (2H, d, $J = 8.3$), 6.95–6.96 (4H, m), 3.88 (3H, s) and 2.34 (3H, s); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 166.7, 162.6, 153.0, 134.0, 131.6, 130.7, 124.5, 120.3, 117.1, 52.0, 21.0.

1-(4-nitrophenoxy)-4-methoxybenzene (4g). Off-white solid [54]. ^1H NMR (CDCl_3 , 400 MHz) δ : 3.84 (s, 3H), 6.91 (d, $J = 8.8\text{ Hz}$, 2H), 7.05 (d, $J = 10.3\text{ Hz}$, 2H), 7.10 (d, $J = 8.8\text{ Hz}$, 2H), 8.16 (d, $J = 8.1\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 55.6, 113.3, 117.7, 118.1, 119.0, 139.4, 149.3, 153.8, 163.0.

1-(4-nitrophenoxy)-4-bromobenzene (4h). Yellow solid [54]. ^1H NMR (CDCl_3 , 400 MHz) δ : 6.98 (d, $J = 8.9\text{ Hz}$, 2H), 7.00 (d, $J = 9.3\text{ Hz}$, 2H), 7.51 (d, $J = 8.9\text{ Hz}$, 2H), 8.22 (d, $J = 9.1\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 113.0, 118.4, 120.1, 121.0, 139.2, 155.4, 163.3.

2-Methyl-diphenylether (4i). Colorless liquid [49]. ^1H NMR (CDCl_3 , 400 MHz) δ : 2.19 (s, 3H), 6.87–6.91 (m, 3H), 6.97–7.07 (m, 2H), 7.12–7.165 (m, 1H), 7.19–7.30 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 16.1, 117.6, 119.7, 122.0, 124.0, 127.3, 129.6, 130.1, 131.2, 154.7, 158.0.

2-Methoxy-diphenylether (4j). Colorless liquid [55]. ^1H NMR (CDCl_3 , 400 MHz) δ : 3.77 (s, 3H), 6.81–6.90 (m, 3H), 6.91–6.94 (m, 1H), 6.96–7.02 (m, 2H), 7.03–7.10 (m, 1H), 7.16–7.25 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ : 56, 112.9, 117.3, 121.1, 121.2, 122.6, 124.9, 129.6, 145.1, 151.6, 158.

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