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Article

# Recyclable hydrophobic copper (II) phthalocyanine catalyzed *N*-arylation of imidazoles in dimethylsulfoxide

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ABSTRACT

Copper (II) phthalocyanine (CuPc) was used as a catalyst for the *N*-arylation of imidazoles with aryl iodides or bromides. The catalyst showed high activity and could be reused 3 times without any significant loss in activity. The catalyst was characterized by Fourier transform infrared spectroscopy, X-ray photoelectron spectroscopy, and ultraviolet-visible spectroscopy.

## 1. Introduction

Phthalocyanine transition metal complexes are important industrial pigments and are considered to be potential oxidation catalysts because of their cheap and facile preparation on large scale and in particular their chemical and thermal stability [1–3]. For example, Rezaeifard and coworkers [1] used copper (II) phthalocyanine (CuPc) for the aqueous heterogeneous oxygenation of hydrocarbons. However, few reports exist about other reactions by metal phthalocyanine [3,4]. Shinu and coworkers [3] reported a novel highly stereoselective multi-component synthesis of *N*-substituted-$\beta$-amino ketone derivatives using CuPc as a reusable catalyst. However, the low solubility of metallophthalocyanines is perhaps the most serious limitation in their application as catalysts although it may be overcome by sulfonation and carboxylation at the periphery of the molecule to give water-soluble derivatives [5]. Unfortunately, the separation of water-soluble catalysts from solutions is also difficult leading to recycling problems.

*N*-arylated azoles (e.g., arylpyrroles, arylpyrazoles, arylimidazoles, aryltriazoles, arylindoles, arylcarbazoles, etc.) have important applications in the medicinal and material fields [6–8]. The transition-metal-catalyzed cross-coupling of aryl halides with amines, amides, and *N*-heterocyclic nucleophiles has become a powerful strategy for these reactions [9–12]. Some homogeneous and heterogeneous catalysts for the catalytic *N*-arylation coupling reaction have been reported [10,13–15]. However, not much research has been done on the *N*-arylation reaction catalyzed by metal phthalocyanines.

We thus report the first efficient CuPc system for the *N*-arylation of imidazoles with aryl halides. Although homogeneous catalysis under mild reaction conditions is characterized by higher catalytic activity than heterogeneous catalysis, homogenous catalysts are difficult to separate and recycle. Therefore, the use of homogeneous catalysts in industrial production is limited [16,17]. CuPc is soluble in dimethylsulfoxide

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(DMSO) but not in water. Therefore, in our experiment, DMSO was used as the solvent and was involved in the reaction. CuPc played a homogeneous role in the reaction process because of its excellent solubility in DMSO, which had the remarkable advantage of homogeneous catalysis under mild conditions. Additionally, this material was precipitated by adding water to the reaction system, and isolated by simple centrifugation. Therefore, this reaction has the advantages of both heterogeneous and homogeneous catalysis.

## 2. Experimental

### 2.1. Materials and characterization

CuPc was synthesized according to the literature [18]. The structure of the CuPc catalyst is shown in Fig. 1. All reagents were purchased from commercial suppliers and used without further purification. The catalyst was characterized by Fourier transform infrared spectroscopy (FT-IR, Nicolet 6700 FT-IR, USA), X-ray photoelectron spectroscopy (XPS, Kratos XSAM-800, UK) and ultraviolet-visible spectroscopy (UV-Vis, Shimadzu UV-2550, JP).

### 2.2. General procedure for the N-arylation of imidazoles with aryl halides

In a typical experiment, imidazole (1.2 mmol), aryl halide (1.0 mmol), catalyst, and base (2.0 mmol) were added to a hydrothermal reactor (20 mL). The mixture was heated to the desired temperature with stirring. After the completion of the reaction and cooling to room temperature, the reaction mixture was diluted with water and extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were dried with anhydrous $Na_2SO_4$ and the obtained product was purified by column chromatography on silica gel using dichloromethane: methanol (100:1, v/v) as the eluent.

### 2.3. Recycling experiment

The recyclability of the synthesized catalyst was investigated using the coupling reaction between iodobenzene and imidazole. After the completion of each reaction the material was precipitated by adding water to the reaction system and the CuPc composite was removed by centrifuging and washing with 3 mL ethyl acetate. The collected catalyst was dried under vacuum at 70 °C, and reused for a subsequent reaction.

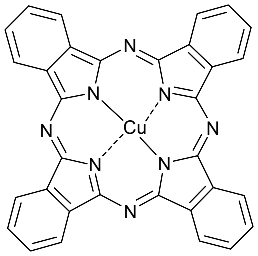


**Fig. 1.** Structure of the CuPc catalyst.

**Fig. 2.** Dispersity of CuPc in different solvents. (a) A mixture of DMSO and water ($V_{DMSO}$:$V_{H2O}$ = 1:2); (b) DMSO.

## 3 Results and discussion

### 3.1. Characterization of the catalyst

The effective dispersity of the CuPc catalyst in the solvent seems to be the most important factor that affects its catalytic performance in this reaction. First, the dispersibility of the catalyst was investigated in different solvents, as shown in Fig. 2. The result indicated that the CuPc catalyst was insoluble and hydrophobic in a mixture of DMSO and water ($V_{DMSO}$:$V_{H2O}$ = 1:2), whereas it was uniformly dispersed in DMSO. Therefore, the reaction could be carried out in a homogeneous system using CuPc as the catalyst. After the completion of each reaction we reused the CuPc catalyst after centrifugation. Therefore, the reaction has the advantages of both heterogeneous and homogeneous catalysis.

Figure 3 shows FT-IR spectrum of the CuPc catalyst. The as-fabricated CuPc sample has several absorption peaks around 724, 901, 1091, 1120, and 1636 $cm^{-1}$, which can be assigned to the phthalocyanine skeletal and metal-ligand vibrations, respectively [19]. This is consistent with structure of a typical CuPc material.

To further confirm the valence state of the copper complex, an XPS spectrum of the catalyst was obtained and is shown in Fig. 4. The characteristic Cu 2*p* peak and the satellite peaks are very typical of a stable CuPc layer. The XPS spectrum shows a single Cu $2p_{3/2}$ peak at 934.8 eV, which can be assigned to $Cu^{2+}$ [20–22]. Therefore, divalent copper was immobilized in the CuPc material without other valence states being present.

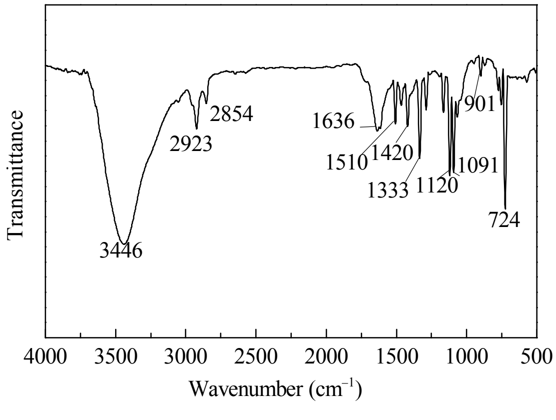


**Fig. 3.** FT-IR spectrum of the CuPc catalyst.

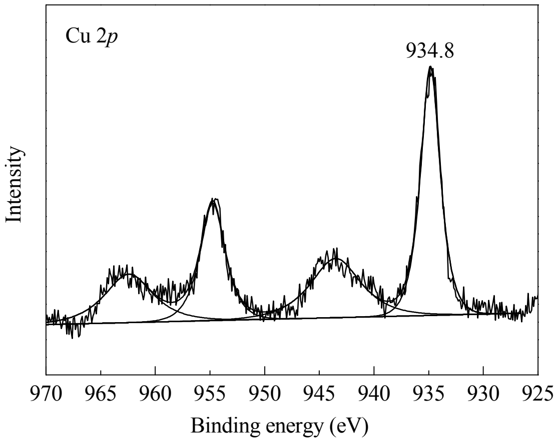
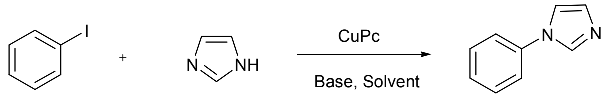


**Fig. 4.** XPS spectrum of the CuPc catalyst.

### 3.2. N-arylation catalyzed by the CuPc catalyst

A series of experiments were initially conducted using imidazole and iodobenzene as model substrates to evaluate and optimize the most efficient catalytic system (Table 1). Poor conversion was achieved in the reaction in the absence of the catalyst (Table 1, entry 1). In the presence of the catalyst, the yield of product increased significantly. Different bases were then evaluated using the model reaction, and the best result was achieved when using KOH as the alkali (Table 1, entries 2–5). We then investigated the effect of catalyst amount on this reaction (Table 1, entries 5–8). When the amount of CuPc was increased from 5 to 15 mol%, the product yield increased. A nearly equivalent conversion ratio was achieved using 10 and 15 mol% of the catalyst. Therefore, from an economic point of view the 10 mol% catalyst loading is most appropriate. The effect of reaction temperature on the catalytic activity of the CuPc catalyst was also investigated (Table 1, entries 6, 8–10). When the reaction temperature was increased from 90 to 110 °C no significant change in yield was observed. However, a significant decrease in the yield was observed when the temperature was decreased to 80 °C. Therefore, the optimal reaction temperature was determined to be 90 °C. Finally, the reaction time was also found to be an important factor as is shown by a comparison between entries 9, 11, and 12 in Table 1. The most appropriate reaction time was found to be 24 h. Therefore, the optimum conditions were: CuPc catalyst (10 mol%), KOH as base (2.0 mmol), and DMSO as solvent at 90 °C for 24 h.

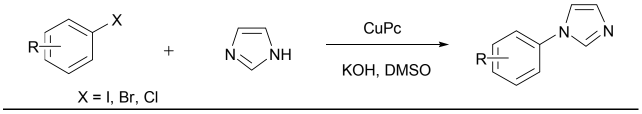
**Table 1**
Screening reaction conditions for the N-arylation of imidazole with iodobenzene.

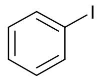
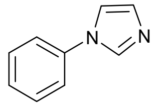
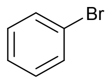
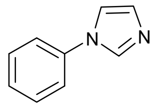
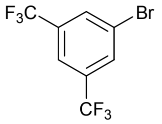
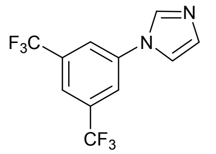
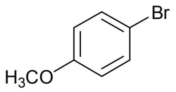
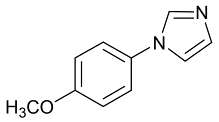
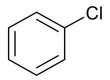
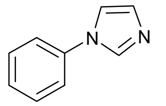
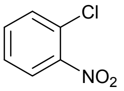
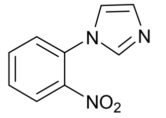
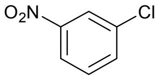
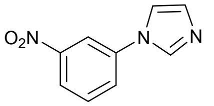
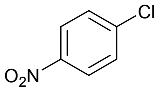
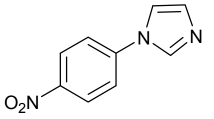
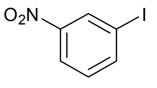
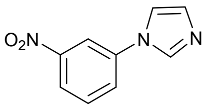
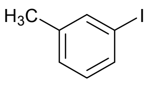
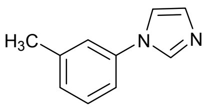


| Entry | Base | Temperature (°C) | Time (h) | Catalyst (mol%) | Yield (%) |
|---|---|---|---|---|---|
| 1 | KOH | 90 | 24 | — | 4.5 |
| 2 | $CsCO_3$ | 110 | 24 | 5 | 16.8 |
| 3 | $K_3PO_4$ | 110 | 24 | 5 | 24.0 |
| 4 | NaOH | 110 | 24 | 5 | 42.2 |
| 5 | KOH | 110 | 24 | 5 | 75.2 |
| 6 | KOH | 110 | 24 | 10 | 95.5 |
| 7 | KOH | 110 | 24 | 15 | 97.3 |
| 8 | KOH | 100 | 24 | 10 | 93.5 |
| 9 | KOH | 90 | 24 | 10 | 92.6 |
| 10 | KOH | 80 | 24 | 10 | 51.0 |
| 11 | KOH | 90 | 20 | 10 | 75.7 |
| 12 | KOH | 90 | 16 | 10 | 66.9 |

To determine the scope of the practical use of the CuPc catalyst, N-arylations of various substituted aryl halides were carried out under optimal conditions (Table 2). As shown in Table 2, it is clear that the activity of the aryl halides in this reaction

**Table 2**
CuPc catalyzed N-arylation of imidazole with different substituted aryl halides.

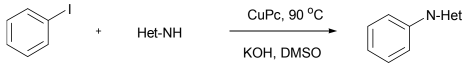


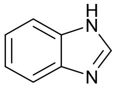
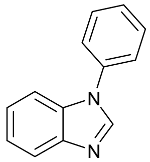
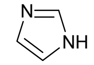
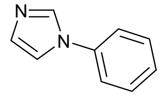
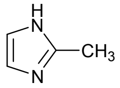
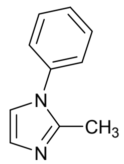
| Entry | ArX | Product | Isolated yield (%) |
|---|---|---|---|
| 1 |  |  | 92.6 |
| 2 |  |  | 31.3 |
| 3 |  |  | 86.5 |
| 4 |  |  | 31.8 |
| 5 |  |  | 5.5 |
| 6 |  |  | 75.1 |
| 7 |  |  | 77.3 |
| 8 |  |  | 88.3 |
| 9 |  |  | 94.4 |
| 10 |  |  | 38.8 |

Reaction conditions: aryl halides 1.0 mmol, imidazole 1.2 mmol, CuPc 10 mol%, KOH 2.0 mmol, DMSO 2 mL, 90 °C, 24 h.

**Table 3**

CuPc catalyzed *N*-arylation of heterocycles with iodobenzene.



| Entry | Het-NH | Product | Isolated yield (%) |
|---|---|---|---|
| 1 |  |  | 53.8 |
| 2 |  |  | 92.6 |
| 3 |  |  | 71.9 |

Reaction conditions: iodobenzene 1.0 mmol, azoles 1.2 mmol, CuPc 10 mol%, KOH 2.0 mmol, DMSO 2 mL, 90 °C, 24 h.

increase as follows: iodobenzene > bromobenzene > chlorobenzene (Table 2, entries 1, 2, 5). Furthermore, the electron-deficient aryl halides afforded the corresponding *N*-aryl imidazole products in better yields than the electron-rich aryl halides (Table 2, entries 3, 4, 9, 10). Interestingly, steric hindrance had little impact on the outcome of the reaction (Table 2, entries 6–8).

To further evaluate the scope of the catalytic system, the *N*-arylation of iodobenzene was investigated with a variety of nitrogen-containing heterocycles (Table 3). It is clear that benzimidazole and 2-methylimidazole were successfully coupled with iodobenzene to give the corresponding *N*-arylated products in satisfactory yields (Table 3, entries 1 and 3). These results thus show the versatility of the current catalytic system.

### 3.3. *Recycling the catalyst*

A series of experiments were also carried out to evaluate the recyclability of the catalyst. The results are listed in Table 4. The catalyst was recovered by centrifugation and reused 3 times without significant loss of activity. The yield was lower in the fourth recycle but we obtained a yield of 90.3% when prolonging the reaction time. To explain the reasons for this decrease in catalyst activity, we characterized fresh and used 5 times CuPc catalyst by UV-Vis spectroscopy (Fig. 5).

**Table 4**

CuPc catalyst recycling for the *N*-arylation of imidazole and iodobenzene.

| Run | Yield (%) |
|---|---|
| 1 | 93.1 |
| 2 | 89.3 |
| 3 | 88.7 |
| 4 | 75.3 |
| 5* | 90.3 |

Reaction conditions: iodobenzene 2.0 mmol, imidazole 2.4 mmol, CuPc 10 mol%, KOH 4.0 mmol, DMSO 3 mL, 90 °C, 24 h (*30 h).

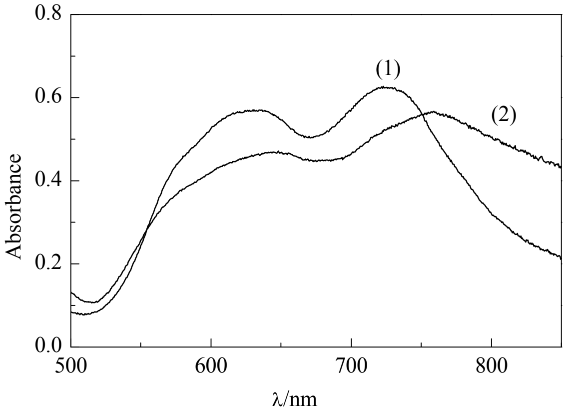


**Fig. 5.** UV-Vis spectra of fresh (1) and after 5 runs (2) CuPc in DMSO.

Generally, the aggregation of CuPc is the main factor that caused catalyst deactivation [23]. As shown in Fig. 5, typical dimer absorption peak was observed at 630 nm, and the broad absorption around 730 nm in the near-infrared region is believed to originate from the Q-band of the benzene ring structure [24]. However, we found that the amount of dimer did not evidently increase before and after the reaction, which indicates that CuPc was stabilized in DMSO. Therefore, the aggregation of CuPc did not lead to low catalytic activity. However, Q-band of the used catalyst moved toward the longer-wavelength side. Therefore, a new species might be generated via an interaction between CuPc and imidazole.

Furthermore, the conditions of this CuPc catalyzed *N*-arylation reaction are mild compared with the systems listed in Table 5. High product yields were achieved at 90 °C in 24 h, which is better than that of the other heterogeneous catalysts. A salen-Cu(II) complex has also shown good catalytic performance during *N*-arylation reactions but this catalyst could not be recycled from the homogeneous system [26]. In our previous research, the $Cu^+$-MMT catalyst gave good performance but a high temperature was still required in this system [27]. The catalyst thus has an obvious advantage in terms of its outstanding performance and utilization value.

## 4. Conclusions

In conclusion, we used hydrophobic divalent CuPc as a catalyst for the *N*-arylation reaction. Good yields were achieved when using CuPc under mild conditions. The CuPc catalyst was

**Table 5**

Comparison of the activity of different heterogeneous catalysts in the *N*-arylation of imidazole with iodobenzene.

| Catalyst | Reaction conditions | Isolated yield (%) | Ref. |
|---|---|---|---|
| CuI | 10 mol%, 120 °C, DMSO, NaH, 24 h | 95 | [9] |
| CuI/PEG | 10 mol%, 110 °C, $K_2CO_3$, 24 h | 91 | [10] |
| $Cu_2O$ | 10 mol%, 120 °C, KOH, DMSO, 24 h | 92 | [25] |
| Salen-Cu(II) complex | 10 mol%, 100 °C, DMSO, NaOH, 12 h | 98 | [26] |
| $Cu^+$-MMT | 0.2 mol%, 110 °C, DMSO, KOH, 24 h | 92 | [27] |
| CuPc | 10 mol%, 90 °C, DMSO, KOH, 24 h | 93 | this study |

## Graphical Abstract

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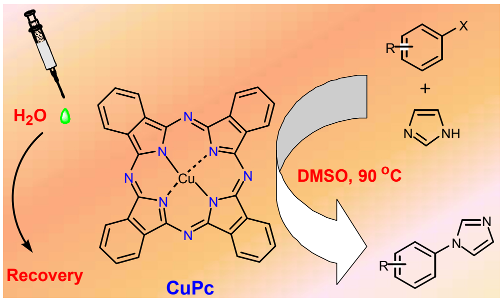
**Recyclable hydrophobic copper (II) phthalocyanine catalyzed *N*-arylation of imidazoles in dimethylsulfoxide**

Qiang Huang, Limei Zhou *, Xiaohui Jiang, Xiaolong Qi, Zhonghua Wang, Wencheng Lang
*China West Normal University*



The copper (II) phthalocyanine (CuPc) catalyst catalyzed the *N*-arylation of imidazoles with aryl iodides or bromides under mild conditions and was reused 3 times without any significant loss in activity.

used 3 times without significant loss of activity. This catalytic system has the advantages of homogeneous and heterogeneous catalysis, which could be potentially useful in industrial applications. Work is in progress to further broaden the scope of this catalytic system and the results will be reported in due course.

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