蒙脱土负载 Cu^+ 催化含氮杂环化合物的 *N*-芳基化反应綦晓龙¹, 周丽梅^{1,a}, 蒋晓慧^{1,b}, 范红伟¹, 付海燕², 陈 华²¹ 四川省化学合成与污染控制重点实验室, 西华师范大学化学化工学院, 四川南充 637002² 四川大学化学学院有机金属络合催化研究所, 四川成都 610064

摘要: 通过简单的离子交换法制备出蒙脱土 (MMT) 负载 Cu^+ 催化剂, 采用 X 射线衍射, X 射线光电子能谱, 扫描电子显微镜和 X 射线能量色散谱等技术对催化剂样品进行了表征。结果表明, Cu^+ 已经成功的插入到蒙脱土层间。在芳基氯或芳基溴与含氮杂环化合物的 *N*-芳基化反应中, 催化剂显示出高的催化活性, 且可通过简单的过滤分离出该催化剂, 重复使用 4 次其活性无明显降低。

关键词: 铜; 蒙脱土; *N*-芳基化反应; 芳基卤; 多相催化剂

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^a通讯联系人. 电话: (0817)2568081; 电子信箱: cwnuzhoulimei@163.com

^b通讯联系人. 电话: (0817)2568081; 电子信箱: jxh2314508@163.com

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Montmorillonite-Supported Copper(I) for Catalyzing *N*-Arylation of Nitrogen HeterocyclesQI Xiaolong¹, ZHOU Limei^{1,a}, JIANG Xiaohui^{1,b}, FAN Hongwei¹, FU Haiyan², CHEN Hua²¹ Chemical Synthesis and Pollution Control Key Laboratory of Sichuan Province, China West Normal University, Nanchong 637002, Sichuan, China² Institute of Homogeneous Catalysis, College of Chemistry, Sichuan University, Chengdu 610064, Sichuan, China

Abstract: Montmorillonite-supported copper (I) catalyst has been prepared by a simple ion exchange method. The resulting catalyst was characterized by X-ray diffraction, X-ray photoelectron spectroscopy, scanning electron microscopy, and energy dispersive X-ray spectrometry, with results showing that Cu^+ had been successfully intercalated into the interlayer of Montmorillonite. The catalyst showed high levels of activity towards the *N*-arylation of nitrogen heterocycles with aryl chlorides or bromides. Furthermore, the catalyst could be reused up to four times without any significant loss in activity.

Key words: copper; montmorillonite; *N*-arylation reaction; aryl halides; heterogeneous catalyst

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^aCorresponding author. Tel: +86-817-2568081; E-mail: cwnuzhoulimei@163.com

^bCorresponding author. Tel: +86-817-2568081; E-mail: jxh2314508@163.com

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N-Arylheterocycles represent an attractive class of chemicals that are widely used in the preparation of agro-

chemicals, pharmaceuticals, and *N*-heterocyclic carbenes [1,2]. Traditionally, *N*-arylheterocycles have been predomi-

nantly prepared using the Ullmann cross-coupling reaction [3–7]. These reactions, however, are greatly limited by their requirement for harsh conditions (>200 °C) and the use of a stoichiometric amount of copper. During the course of the last two decades, significant progress has been made towards the development of C–N coupling reactions using homogeneous catalysts [8–10]. Unfortunately, however, the industrial application of these processes still remains challenging because of difficulties associated with the recovery of the homogeneous catalysts from the reaction medium, which can lead to the loss of the catalyst, as well as heavy metal contamination of the reaction product. Furthermore, the majority of the ligands required of these processes are expensive. These disadvantages can be overcome by anchoring the metal catalyst onto a suitable support that would allow for the catalyst to be easily separated and recycled with minimal contamination of the product with metal. Several different solid supports have recently been reported with copper anchored to their surfaces, including fluorapatite [11], SiO₂ [12], hydrotalcite [13], NaY zeolite [14], cellulose [15], cation-exchanger resin [16], and a several other polymers [17–19]. These studies confirmed that the anchoring of a metal to a solid support not only provided a material that exhibited improved catalyst activity, stability, and selectivity but they also demonstrated that the catalysts themselves could be easily recovered and reused.

Montmorillonite (MMT) is a type of naturally occurring clay that can be structurally defined as layers of negatively charged two-dimensional silicate sheets. A variety of different metal ions can be introduced into the narrow interlayers by simple ion exchange methods [20]. Recently, Borah et al. [21] prepared Cu nanoparticles in the nanopores of modified MMT and investigated the catalytic activity of the material in a series of 1,3-dipolar cycloaddition reactions between azides and terminal alkynes in the synthesis of 1,2,3-triazoles [21].

In the current study, Cu⁺ was introduced into the interlayer of MMT by a simple ion exchange method. The resulting catalyst was used in an Ullmann cross-coupling reaction for the *N*-arylation of nitrogen heterocycles with aryl chlorides or bromides. This catalyst showed high levels of activity in this reaction and could be reused up to four times.

1 Experimental

1.1 Preparation of catalyst

CuI (0.213 mmol) and MMT (0.5 g) were added to an oven-dried round-bottomed flask (50 ml) under an atmosphere of cooled nitrogen. The round-bottomed flask was then sealed with a septum and purged by three cycles of

evacuation and back-filling with pure and dry nitrogen. Deionized water (15 ml) was then added to the flask through a syringe and the resulting mixture was magnetic stirred at 50 °C for 24 h. The mixture was then cooled to ambient temperature and filtered. The resulting filter-cake was washed thoroughly with deionized water before being collected and dried in a vacuum oven at 60 °C for 12 h to give the desired product, which was ground into powder and subsequently denoted as Cu⁺-MMT. The amount of Cu⁺ present in the Cu⁺-MMT catalyst was 2.7% according to the formula ($c(\%) = m_{\text{Cu}} / (m_{\text{support}} + m_{\text{Cu}}) \times 100\%$). The MMT supported Cu²⁺ catalyst (Cu²⁺-MMT) was prepared according to a similar procedure.

The MMT supported Cu⁰ catalyst (Cu⁰-MMT) was prepared according to the following procedure: CuCl₂ (0.213 mmol), MMT (0.5 g), and deionized water (15 ml) were added to a round-bottomed flask (50 ml) and the resulting mixture was heated with magnetic stirring at 50 °C for 24 h. The mixture was then cooled to ambient temperature and then 5.0 ml NaBH₄ solution ($n(\text{NaBH}_4):n(\text{Cu}) = 10:1$) was added dropwise into the aforementioned mixture within 2 h. The resulting mixture was then filtrated and the filter-cake was washed thoroughly with deionized water before being collected and dried in a vacuum oven at 60 °C for 12 h to give the desired product which was then ground into powder and subsequently denoted as Cu⁰-MMT.

1.2 Characterization of the Cu⁺-MMT catalyst

The Cu⁺-MMT catalyst was characterized by scanning electron microscopy (SEM, AJEOL JSM-6510LV, Japan), X-ray photoelectron spectroscopy (XPS, Kratos XSAM-800, UK) and X-ray diffraction (XRD, D/MAX Ultima IV, Japan).

1.3 General procedure for the *N*-arylation of nitrogen heterocycles with aryl halides

In a typical experiment, a nitrogen-containing heterocycle, catalyst and base were added to an oven dried tube under nitrogen. The tube was then sealed with a septum and purged with nitrogen by three cycles of evacuation and back-filling with pure and dry nitrogen. Then solvent and aryl halide were then added to the reaction tube through a syringe and the tube was sealed and heated to the desired temperature with stirring under nitrogen. Upon completion of the reaction (reaction monitored by TLC), the mixture was centrifuged to remove the solid catalyst. The reaction mixture was then diluted with water and extracted three times with ethyl acetate. The combined organic extracts were dried with anhydrous Na₂SO₄ before being distilled to dryness. The resulting crude residue was purified by column

chromatography on silica gel to afford the product with high purity.

2 Results and discussion

2.1 Characterization of the Cu^+ -MMT catalyst

The morphologies of the Cu^+ -MMT catalyst and MMT support were investigated with an SEM equipped with an energy dispersive X-ray spectrometer (EDS). The results showed that there were not many morphologic differences observed between the Cu^+ -MMT and MMT materials (Fig. 1(a) and (b)). The EDS analyses confirmed that the copper had been successfully loaded onto the MMT surface (Fig. 1(c) and (d)).

The catalyst was also characterized by XRD. Based on the results of the XRD analysis (Fig. 2), the basal spacing of MMT was determined to be 1.55 nm, whereas the spacing in the Cu^+ -MMT material was reduced to 1.47 nm. The main cations in the MMT interlayer were Na^+ and Ca^{2+} . Exchanging of the interlayer Na^+ and Ca^{2+} in MMT with Cu^+ led to reduction in the interlayer space because the ionic radius of Cu^+ is smaller than those of Na^+ and Ca^{2+} . A similar result to this has also been reported in the literature [22]. It is noteworthy that there were characteristic copper peaks at 42.4° , 50.1° , and 77.2° in the pattern of Cu^+ -MMT [21]. In light of these data, it appeared that the Cu^+ had been successfully intercalated into the MMT interlayer by the ionic exchange method.

The XPS spectrum of the Cu^+ -MMT catalyst is shown in

Fig. 2. XRD patterns of MMT and Cu^+ -MMT.

Fig. 3(a). The $\text{Cu } 2p_{3/2}$ peak at 932.8 eV was assigned to Cu^+ [23]. Furthermore, the $\text{Cu } 2p_{3/2}$ peak at 934.7 eV suggested the presence of a Cu^{2+} component, which probably resulted from the oxidation of the Cu^+ upon exposure to air. The ratio of $\text{Cu}^+/\text{Cu}^{2+}$ was around 0.59. We also investigated the XPS spectrum of Cu^{2+} -MMT and Cu^0 -MMT catalysts (Fig. 3(b) and (c), respectively). As seen in Fig. 3(b), the XPS spectrum displayed a single $\text{Cu } 2p_{3/2}$ peak at 935.0 eV, which was assigned to Cu^{2+} . In view of the close proximity of the binding energies of Cu^0 and Cu^+ [21], the $\text{Cu } 2p_{3/2}$ peak at 932.3 eV was attributed to Cu^0 (Fig. 3(c)). The $\text{Cu } 2p_{3/2}$ peak at 934.6 eV suggested the presence of a Cu^{2+} component in the Cu^0 -MMT catalyst (Fig. 3(c)).

2.2 Catalytic results for *N*-arylation of nitrogen heterocycles with aryl halides

Fig. 1. SEM images and EDS analyses of the MMT support (a, c) and Cu^+ -MMT catalyst (b, d).

Fig. 3. XPS spectra of the catalysts. (a) Cu^+ /MMT; (b) Cu^{2+} /MMT; (c) Cu^0 /MMT.

A series of experiments were initially conducted using imidazole and bromobenzene as model substrates to evaluate and optimize the most efficient catalytic system (Table 1). We observed that without a copper source, the MMT support provided only a poor level of conversion in the reaction (Table 1, entry 1). In a separate control experiment, we established that unsupported CuI effectively promoted the model reaction, but required relatively large amounts of CuI (Table 1, entry 2). In contrast, we were pleased to find that Cu^+ -MMT effectively promoted the model reaction (87.6%, Table 1, entry 12). We also investigated the effect of the valence state of the copper on the outcome of the model reaction. Of the Cu^{2+} -MMT, Cu^+ -MMT, and Cu^0 -MMT catalysts, Cu^+ -MMT provided the best yield (Table 1, entries 3–5). Several different bases were also tested

in the model reaction, with KOH providing the best results (Table 1, entries 5–7). The evaluation of several different solvents revealed that CH_3CN and DMF were less effective than DMSO (Table 1, entries 7–9). The effect of reaction temperature on the catalytic activity of the Cu^+ -MMT catalyst was also investigated (Table 1, entries 10–13). From these data, it was clear that an increase in the reaction temperature promoted the model reaction. When the temperature was increased from 80 to 110 °C, the yield was significantly increased from 26.4% to 87.5%. Increases in the temperature beyond 120 °C, however, provided no further increase in the yield and the optimal reaction temperature was therefore determined to be 110 °C. The reaction time was also established to be an important factor, as demonstrated by a comparison of entries 17 and 18 with 12 (Table

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

Entry	Catalyst	Cu (%)	Solvent	Base	Time (h)	Temperature (°C)	Isolated yield (%)
1	MMT	—	DMSO	KOH	24	110	8.3
2	CuI	2.5	DMSO	KOH	24	110	56.1
3	Cu^{2+} -MMT	0.8	DMSO	K_2CO_3	24	100	31.5
4	Cu^0 -MMT	0.8	DMSO	K_2CO_3	24	100	45.5
5	Cu^+ -MMT	0.8	DMSO	K_2CO_3	24	100	51.3
6	Cu^+ -MMT	0.8	DMSO	Cs_2CO_3	24	100	50.6
7	Cu^+ -MMT	0.8	DMSO	KOH	24	100	82.2
8	Cu^+ -MMT	0.8	CH_3CN	KOH	24	100	8.8
9	Cu^+ -MMT	0.8	DMF	KOH	24	100	70.0
10	Cu^+ -MMT	0.8	DMSO	KOH	24	80	26.4
11	Cu^+ -MMT	0.8	DMSO	KOH	24	90	40.1
12	Cu^+ -MMT	0.8	DMSO	KOH	24	110	87.6
13	Cu^+ -MMT	0.8	DMSO	KOH	24	120	85.3
14	Cu^+ -MMT	0.4	DMSO	KOH	24	110	84.0
15	Cu^+ -MMT	0.2	DMSO	KOH	24	110	83.1
16	Cu^+ -MMT	0.1	DMSO	KOH	24	110	30.9
17	Cu^+ -MMT	0.8	DMSO	KOH	12	110	78.6
18	Cu^+ -MMT	0.8	DMSO	KOH	18	110	80.0

Reaction conditions: bromobenzene (1.0 mmol), imidazole (1.2 mmol), base (2.0 mmol), and solvent (2 ml) under N_2 atmosphere.

Table 2 Cu^+ -MMT catalyzed *N*-arylation of imidazole with differentially substituted aryl halides

$\text{X} = \text{I}, \text{Br}, \text{Cl}$

Entry	ArX	Product	Isolated yield (%)
1			92.3
2			87.6
3			90.1
4			95.1
5			45.0
6			71.0 ^a
7			43.1, 71.3 ^b
8			74.5, 80.1 ^b
9			87.1
10			62.1 ^c

Reaction conditions: aryl halides (1.0 mmol), imidazole (1.2 mmol), Cu^+ -MMT (0.2 mol%), KOH (2.0 mmol), and DMSO (2 ml) under a N_2 atmosphere at 110 °C for 24 h; ^a130 °C, Cu^+ -MMT (0.4 mol%), 48 h; ^b120 °C; ^c130 °C.

1). Finally, we investigated the effect of the amount of copper on this reaction (Table 1, entries 12, 14–16). When the amount of copper was decreased from 0.8 mol% to 0.2 mol%, there was no discernible impact on the yield. Taken together, these data indicated that the optimum conditions were as follows: Cu^+ -MMT catalyst (0.2 mol%), KOH as base (2.0 equiv.), and DMSO as solvent at 110 °C under an atmosphere of nitrogen.

With the optimized reaction conditions in hand, we proceeded to investigate the reaction scope of this Cu^+ -MMT catalytic system and its functional group tolerance for the reaction of functionalized aryl halides with imidazole (Table 2).

From Table 2, it is clear that the activity of the aryl halides in this reaction followed the trend of iodobenzene > bromobenzene > chlorobenzene (Table 2, entries 1, 2, and 6). 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 3–5). Steric hindrance also had an impact on the outcome of the reaction, with *ortho*- and *meta*-substituted substituents having an adverse effect on the yield of the reaction (Table 2, entries 7, 8, and 9). Interestingly, however, the adverse impact of the steric hindrance could be overcome by increasing the temperature of the reaction from 110 to 120 °C (Table 2, entries 7 and 8). In another interesting observation, only one of the chloride moieties in 1,4-dichlorobenzene was observed participate in the coupling reaction (Table 2, entry 10). This observation was attributed to the electron-donating properties of the 4-chloroimidazolylbenzene product relative to the starting material, suggesting that the reaction preferred electron deficient substrate. Similar results to this have also been reported in the literature [24]. Remarkably, the chlorobenzene tested gave particularly encouraging results, with the corresponding coupling product being isolated in 71.0% yield (Table 2, entry 6).

To further demonstrate the utility of the Cu^+ -MMT catalyst in the *N*-arylation reaction of imidazole and chlorobenzene, the catalyst was compared with several other reported heterogeneous catalysts [11, 13, 15, 16, 25] (Table 3). From Table 3, it is clear that the current catalytic system exhibited higher yields compared with the other reported systems and also required a smaller charge of copper.

To further evaluate the scope of the catalytic system, the *N*-arylation of bromobenzene was investigated with a variety of different nitrogen-containing-heterocycles (Table 4). From the results, it is clear that benzimidazole and pyrrole were successfully coupled with bromobenzene to give the corresponding *N*-arylated products in satisfying yields (Table 4, entries 1 and 2). It is noteworthy that the sterically hindered 2-methylimidazole gave a yield of 72.4% (Table 4, entry 3). Taken together, these results provide a good dem-

Table 3 Comparison of several different heterogeneous copper catalysts in the *N*-arylation reaction of imidazole and chlorobenzene

Entry	Catalyst	Reaction conditions	Isolated yield (%)	Reference
1	Cu-FAP	7.3 mol% Cu, 120 °C, DMF, 36 h	60	[11]
2	Cu-Al-HTB	2.5 mol% Cu, 100 °C, DMF, 18 h	n.r.	[13]
3	Cellulose-Cu(0)	1.84 mol% Cu, 130 °C, DMSO, 48 h	20	[15]
4	Cu-indion-770 resin	10 mol% Cu, 125 °C, DMSO, 48 h	<8	[16]
5	Cu^0 -nitrogen-rich copolymeric microspheres	10 mol% Cu, 120 °C, DMSO	67.7	[25]
6	Cu^+ -MMT	0.4 mol% Cu, 130 °C, DMSO, 48 h	71.0	this study

Table 4 Cu⁺-MMT catalyzed *N*-arylation of heterocycles with bromobenzene

$\text{C}_6\text{H}_5\text{Br} + \text{Het-NH} \xrightarrow[\text{DMSO, KOH}]{\text{Cu}^+\text{-MMT, 110 } ^\circ\text{C}} \text{C}_6\text{H}_5\text{-N-Het}$			
Entry	Het-NH	Product	Isolated yield (%)
1			76.1
2			53.0
3			72.4

Reaction conditions: bromobenzene (1.0 mmol), azoles (1.2 mmol), Cu⁺-MMT (0.2 mol%), KOH (2.0 mmol), and DMSO (2 ml) at 110 °C under N₂ atmosphere for 24 h.

Fig. 4. Recyclability studies of the Cu⁺-MMT catalyst for *N*-arylation of imidazole with bromobenzene. Reaction conditions: bromobenzene (3.0 mmol), azoles (3.6 mmol), Cu⁺-MMT (0.2 mol%), KOH (6.0 mmol), and DMSO (6 ml) under an N₂ atmosphere for 24 h.

onstration of the versatility of the current catalytic system.

A series of experiments were also conducted to evaluate the recyclability of the catalyst. The results have been presented in Fig. 4. The catalyst was recovered by centrifugation and reused up to four times without significant loss of activity.

3 Conclusions

In summary, we have developed a simple, highly efficient, and inexpensive protocol for the *N*-arylation of a variety of different nitrogen-containing-heterocycles with aryl chlorides or bromides in DMSO with a cheap base using a novel Montmorillonite-supported copper (I) catalyst. Remarkably, this catalyst effectively catalyzed the *N*-arylation of imidazole with the relatively inactive chlorobenzene to give the

desired product in good yield. In addition, the catalyst can be easily recovered and reused. We believe this catalytic system could find potential industrial applications once it has been adapted for large scale manufacture, where it could provide significant economic benefits by minimizing processing times and improving overall product quality and throughput.

References

- Kison C, Opatz T. *Chem Eur J*, 2009, **15**: 843
- Kantam M L, Yadav J, Laha S, Sreedhar B, Jha S. *Adv Synth Catal*, 2007, **349**: 1938
- Evano G, Blanchard N, Toumi M. *Chem Rev*, 2008, **108**: 3054
- Monnier F, Taillefer M. *Angew Chem, Int Ed*, 2008, **47**: 3096
- Ma D, Cai Q. *Acc Chem Res*, 2008, **41**: 1450
- Lindley J. *Tetrahedron*, 1984, **40**: 1433
- Kunz K, Scholz U, Ganzer D. *Synlett*, 2003: 2428
- Klapars A, Antilla J C, Huang X, Buchwald S L. *J Am Chem Soc*, 2001, **123**: 7727
- Zhu L, Li G, Luo L, Guo P, Lan J, You J. *J Org Chem*, 2007, **74**: 2200
- Xi Z, Liu F, Zhou Y, Chen W. *Tetrahedron*, 2008, **64**: 4254
- Choudary B M, Sridhar C, Kantam M L, Venkanna G T, Sreedhar B. *J Am Chem Soc*, 2005, **127**: 9948
- Likhar P R, Roy S, Roy M, Kantam M L, De R L. *J Mol Catal A*, 2007, **271**: 57
- Sreedhar B, Arundhathi R, Reddy P L, Reddy M A, Kantam M L. *Synthesis*, 2009, **15**: 2517
- Kantam M L, Rao B P C, Choudary B M, Reddy R S. *Synlett*, 2006: 2195
- Reddy K R, Kumar N S, Sreedhar B, Kantam M L. *J Mol Catal A*, 2006, **252**: 136
- Amal Joseph P J, Priyadarshini S, Lakshmi Kantam M, Maheswaran H. *Catal Sci Technol*, 2011, **1**: 234
- Kantam M L, Roy M, Roy S, Bojja S, Lal De R. *Catal Commun*, 2008, **9**: 2226
- Arundhathi R, Kumar D C, Sreedhar B. *Eur J Org Chem*, 2010: 3621
- Islam S M, Mondal S, Mondal P, Roy A S, Tuhina K, Salam N, Mobarak M. *J Organomet Chem*, 2012, **696**: 4264
- Mitsudome T, Nose K, Mori K, Mizugaki T, Ebitani K, Jitsukawa K, Kaneda K. *Angew Chem, Int Ed*, 2007, **46**: 3228
- Borah B J, Dutta D, Saikia P P, Barua N C, Dutta D K. *Green Chem*, 2011, **13**: 3453
- Holesova S, Kulhankova L, Martynkova G S, Kukutschova J, Capkova P. *J Mol Struct*, 2009, **923**: 85
- Shuai M, Liao L, Lu H B, Zhang L, Li J C, Fu D J. *J Phys D*, 2008, **41**: 135010/1
- Son S U, Park I K, Park J, Hyeon T. *Chem Commun*, 2004: 778
- Huang Z, Li F, Chen B, Xue F, Chen G, Yuan G. *Appl Catal A*, 2011, **403**: 104