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# Efficient Ullmann C-X coupling reaction catalyzed by a recoverable functionalized-chitosan supported copper complex

Xuemin Liu<sup>a</sup>, Shuo Chang<sup>a</sup>, Xinzhi Chen<sup>b</sup>, Xin Ge<sup>a\*</sup> and Chao Qian<sup>b\*</sup>

<sup>a</sup> School of Chemical and Material Engineering, Jiangnan University, Wuxi, P.R China

<sup>b</sup> Zhejiang Provincial Key Laboratory of Advanced Chemical Engineering Manufacture

Technology, College of Chemical and Biological Engineering, Zhejiang University, Hangzhou, P.R

#### China.

**Abstract:** The three different types of functionalized-CS were prepared and anchored copper salts to employed as the catalyst for Ullmann C-X coupling reaction. The Schiff-basic chitosan supported copper complex (PCCS@CuI) has the highest catalytic activity. The structure of the catalyst was characterized by FTIR, TG, XRD, SEM, EDS and XPS. This catalyst exhibited high applicability for the C-N and C-S coupling reactions, in which the good to excellent yields were obtained. Its easy separation, good reusability and stability were noticeable.

Keywords: Schiff-basic chitosan, copper, Ullmann coupling, supported catalysis Graphical Abstract



\* Corresponding author. Xin, Ge, E-mail: <u>gexin@jiangnan.edu.cn</u> and Chao Qian, E-mail: <u>gianchao@zju.edu.cn</u>

# 1. Introduction

The copper-catalyzed Ullmann coupling reaction is one of the most important strategies for the construction of C-X bond, which plays a fundamental role in pharmaceutical and agrochemical industry.<sup>1</sup> However, the prototypical Ullmann reaction suffers from some disadvantages, such as high temperature, excessive usage of copper catalyst, limited substrate scope and moderate yield, which hinder its wide application.<sup>2</sup> Up until 2001, important breakthroughs just started to be achieved in developing novel efficient catalytic systems by introducing ligands.<sup>3</sup> More specifically, various ligands, e.g. diamines,<sup>3-4</sup> glycol,<sup>5</sup> Schiff base,<sup>6</sup> amino acids,<sup>7</sup> diketones,<sup>8</sup> phenanthroline,<sup>9</sup> 2,2'-bipyridine,<sup>10</sup> carbohydrates,<sup>11</sup> oxalamic acid<sup>12</sup> and diamide,<sup>13</sup> have been explored for efficiently promoting the C-X coupling. Although these efficient ligands have made great achievements in improving Ullmann reaction, the recovery of catalysts remains challenging. The entrapment and coordination of transition metal complexes in heterogeneous supports, which could enable the easy separation of the products and reusability of the catalyst, therefore have gained enormous attention. Up to now, various organic and inorganic materials, e.g., alumina,<sup>14</sup> zeolites,<sup>15</sup> polymers<sup>16</sup> and magnetic materials,<sup>17</sup> have been evaluated, whereas their applications were still limited from its instability in basic conditions, high energy-consuming and time-demanding, during the preparation process. Therefore, the exploration of new green, renewable, environmental friendly and low-cost materials for Ullmann reaction is becoming an urgent and interesting issue.

Due to its biodegradable, renewable and eco-friendly characteristics, polysaccharides are becoming the most popular bio-resources in recent years.<sup>18</sup> Moreover, they have enormous potential in variation and optimization for possessing many functional groups on the backbone.<sup>19</sup> Among those kinds of polysaccharides, chitosan (CS) has many outstanding properties such as antibacterial, high "metal affinity" and water solubility. In 2014, Shen *et al.*<sup>20</sup> successfully applied an unmodified chitosan-Cu catalyst for Ullmann C-S coupling, nevertheless the CS in the form of powders lack adequate catalytic activity and absorption capacity. Owning to its abundance in amino groups, amenable for chemical modification,<sup>21</sup> various CS derivatives and microspheres have also been prepared to chelate different metals, e.g. Pd, Cu, Rh and Au, and have been used as efficient and green catalysts for organic reactions, e.g. Sonogashira cross-coupling,<sup>22</sup>

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hydroformylation,<sup>23</sup> cyclopropanation<sup>24</sup> and olefin oxidation<sup>25</sup>. However, so far as reported, there were only a few examples using functional chitosan for Ullmann reaction. Importantly, the functional chitosan anchored metal has been found to be more potential than chitosan metal complex.<sup>26</sup>

Thus, following the interests in fine-tuning and design of carbohydrate structure,<sup>27</sup> we report a recoverable functionalized-chitosan supported copper complex for Ullmann C-X coupling reaction. To accomplish this, three different types of functionalized-CS by introducing various functional groups onto its backbone (in Figure 1) were studied and their catalytic activities for Ullmann reaction were evaluated. The Schiff-basic chitosan supported copper complex was characterized and the stability of this catalyst was tested.



Figure 1. Preparation of the functionalized-chitosan supported copper complex

## **2** Experimental Section

#### 2.1 General

Chitosan powder (MW: 10,000-50,000, deacetylation degree 95%, purchased from Aladdin reagent (Shanghai) Co., Ltd.) was used without further purification. Pyridine-2-carboxaldehyde,

2-hydroxybenzaldehyde and *N,N'*-carbonyldiimidazole were purchased from Damas-beta, 2-Pyridinecarboxylic acid was purchased from Sinopharm Chemical Reagent Co. Ltd. Aryl halides, imidazole and sulfinate salts were purchased from Alfa Aesar. Melting points were determined on an X4-Data microscopic melting point apparatus and were uncorrected. Nuclear magnetic resonance (NMR) spectra were measured at 400 MHz (<sup>1</sup>H) or at 100 MHz (<sup>13</sup>C) with CDCl<sub>3</sub> as solvent on a Bruker Avance DRX-400 spectrometer. All reactions were monitored by analytical thin-layer chromatography (TLC) from Merck with detection by UV. The products were purified by column chromatography through silica gel (300-400 mesh). All reagents and solvents were general reagent grade unless otherwise stated.

#### 2.2 Preparation of Functional Chitosan.

As a linear polysaccharide of D-glucosamine unit, CS possesses a number of amino groups. In this work, the amino groups in CS were modified by introducing pyridine-2-carboxaldehyde, 2-hydroxybenzaldehyde and 2-pyridinecarboxylic acid, to synthesize PCCS, HBCS and PACS, respectively. Based on this design, recyclable functionalized-chitosan supported copper complex was prepared and used for Ullmann reaction. It was achieved by suspending the functionalized-chitosan in the solution of copper salts, subsequently was separated by using centrifuge and dried under vacuum at 50 °C.

*The preparation of PCCS.* Chitosan (2.0 g, equivalent to 12.4 mmol  $NH_2$  group), pyridine-2-carboxaldehyde (4.72 mL, 49.6 mmol) and acetic acid (10 mL) were added to methanol (75 mL). Then the mixture was refluxed for 12 h at 65 °C. After the resultant mixture was cooled to 0 °C, the solid was separated by filtration, washed with ethanol and then dried under vacuum at 50 °C for 12 h.

*The preparation of HBCS.* Chitosan (2.0 g, equivalent to 12.4 mmol  $NH_2$  group) and 2-hydroxybenzaldehyde (7.58 g, 62.1 mmol) were added to ethanol (100 mL), meanwhile 10 mL acetic acid was added. The mixture was refluxed for 12 h at 70 °C, then cooled with ice water to 0 °C. The solid was separated by filtration, and finally dried under vacuum at 50 °C for 12 h.

*The preparation of PACS. N*,*N*'-Carbonyldiimidazole (3.24 g, 20 mmol) and 2-Pyridinecarboxylic acid (1.85 g, 15 mmol) were heated to 60 °C in THF (100 mL) with stirring. After adding chitosan (1.61 g, 10 mmol), the mixture was stirred at 60 °C for 12 h. The product was crystallized by adding ice water and dried under vacuum at 50 °C for 12 h.

#### 2.3 The preparation of functionalized-chitosan supported copper complex

Three modified chitosan supported copper salt was synthesized according to the following procedure: the catalyst was prepared by suspending modified chitosan in a solution of copper salt for 3 h under neutral conditions at 50 °C (For CuI, the solvent was acetonitrile. For CuSO<sub>4</sub> and Cu(OAc)<sub>2</sub>, water was used as solvent). After adsorption of the copper, the solid was preconditioned by washing thoroughly to remove any loose Cu compounds and dried under vacuum at 50 °C overnight to give the catalyst. After complexation with CuI, CuSO<sub>4</sub> and Cu(OAc)<sub>2</sub>, the colors of these catalyst are as follows: PCCS@CuI is reddish brown, PCCS@ CuSO<sub>4</sub> is green, PCCS@Cu(OAc)<sub>2</sub> is green, HBCS@CuI is yellow, HBCS@CuSO<sub>4</sub> is yellow, HBCS@Cu(OAc)<sub>2</sub> is blue.

#### 2.4 General procedure for Ullmann reaction catalyzed by the PCCS@CuI

To a stirred solution of DMSO (3 mL) were added aryl halide (1.0 mmol), nucleophile (1.2 mmol), PCCS@CuI and Cs<sub>2</sub>CO<sub>3</sub> (2 mmol) at room temperature. Then the reaction mixture was heated to 110 °C under air and stirred for 24 h. After cooling to room temperature, the catalyst PCCS@CuI was separated by centrifugation. The reaction mixture was partitioned by adding the ethyl acetate (20 mL) and water (20 mL). Subsequently, the organic phase was separated and the aqueous phase was extracted with ethyl acetate (20 mL) twice. The combined organic phases were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. Then the crude product was purified by column chromatography through silica gel, eluting with petroleum ether/ethyl acetate solvent mixture, to give the pure product.

### 3. Results and Discussion

Performances of these functionalized-chitosan supported copper complexes were evaluated in the Ullmann C-N reaction of iodobenzene with imidazole. More details on the screening of catalysts and optimization of the reaction conditions were summarized in Table 1. Initially, the model reaction catalyzed by unmodified-chitosan@Cu was studied (Table1, entries 1-3), in which CS@Cu(OAc)<sub>2</sub> exhibited the highest activity. This result was consistent with previous report.<sup>20</sup> A preliminary comparison of the reaction catalyzed by functionalized-chitosan@Cu with unmodified-chitosan@Cu indicated that the fine-tuning on the backbone of chitosan promoted the activity of copper. Functionalized-chitosan@Cu showed higher catalytic activity than unmodified-chitosan@Cu (Table1, entries 4-12). For functionalized-chitosan@Cu, various copper sources, i.e. CuI, CuSO<sub>4</sub> and Cu(OAc)<sub>2</sub>, were examined in this process, among which PCCS@CuI was found to be the most effective catalyst, achieving an excellent yield (up to 99%). In addition, a various of bases, e.g. Na<sub>2</sub>CO<sub>3</sub>, KOH, NaOH, K<sub>2</sub>CO<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub>, NaOAc and NaHCO<sub>3</sub>, were tested, and it was found that Cs<sub>2</sub>CO<sub>3</sub> was the most ideal base (Table1, entries 5, 13-18). The mixture solvent, i.e. DMSO, DMF and MeOH were studied, among which the reaction carried out in foremost gave the highest yield (Table1, entries 17,19-20), while trying the reaction using water as a solvent, the yield of the product is only 30% (Table1, entry 21). Other reaction temperature including 70 °C was screened, the yield was decreased from 99% to 75% (Table1, entry 22). In summary, the optimum conditions for Ullmann C-N reaction were demonstrated as below: using Cs<sub>2</sub>CO<sub>3</sub> as base, DMSO as solvent, and PCCS@CuI as catalyst, under which condition the yield of iodobenzene coupling with imidazole could reach up to 99%.

Table 1. The coupling reaction catalyzed by functionalized-chitosan supported copper complex <sup>a</sup>

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	+	HZ Z	Catalyst Solvent, Base 110 °C, 12h, under air	N N
1a		2a		20

3a

Entry	Catalyst	Base	Solvent	Yiled/% <sup>b</sup>
1	CS@CuSO <sub>4</sub>	Na <sub>2</sub> CO <sub>3</sub>	DMSO	70
2	CS@CuI	Na <sub>2</sub> CO <sub>3</sub>	DMSO	72
3	CS@Cu(OAc) <sub>2</sub>	Na <sub>2</sub> CO <sub>3</sub>	DMSO	85
4	PCCS@CuSO4	Na <sub>2</sub> CO <sub>3</sub>	DMSO	95
5	PCCS@CuI	Na <sub>2</sub> CO <sub>3</sub>	DMSO	97
6	PCCS@Cu(OAc) <sub>2</sub>	Na <sub>2</sub> CO <sub>3</sub>	DMSO	88
7	PACS@CuSO4	Na <sub>2</sub> CO <sub>3</sub>	DMSO	88
8	PACS@CuI	Na <sub>2</sub> CO <sub>3</sub>	DMSO	85
9	PACS@Cu(OAc) <sub>2</sub>	Na <sub>2</sub> CO <sub>3</sub>	DMSO	86
10	HBCS@CuSO4	Na <sub>2</sub> CO <sub>3</sub>	DMSO	95
11	HBCS@CuI	Na <sub>2</sub> CO <sub>3</sub>	DMSO	72
12	HBCS@Cu(OAc) <sub>2</sub>	Na <sub>2</sub> CO <sub>3</sub>	DMSO	80
13	PCCS@CuI	КОН	DMSO	86
14	PCCS@CuI	K <sub>2</sub> CO <sub>3</sub>	DMSO	85
15	PCCS@CuI	NaHCO <sub>3</sub>	DMSO	90
16	PCCS@CuI	NaOH	DMSO	96
17	PCCS@CuI	$Cs_2CO_3$	DMSO	99

18	PCCS@CuI	NaOAc	DMSO	95
19	PCCS@CuI	Cs <sub>2</sub> CO <sub>3</sub>	MeOH	50
20	PCCS@CuI	$Cs_2CO_3$	DMF	80
21	PCCS@CuI	$Cs_2CO_3$	$H_2O$	30
22	PCCS@CuI	$Cs_2CO_3$	DMSO	75 <sup>c</sup>
a D	1			1 1 1 1

<sup>a</sup> Reaction conditions: iodobenzene **1a** (1.0 mmol), imidazole **2a** (1.2 mmol), base (2.0 mmol) and catalyst (0.05 mmol based on copper) in the solvent (3 mL), 110 °C for 12 h. <sup>b</sup> Isolated yield, <sup>c</sup> reaction was performed at 70 °C.

Catalyst PCCS@CuI were characterized by Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TG), X-ray diffraction (XRD), scanning electron microscope (SEM), energy disperse spectroscopy (EDS) and X-ray photoelectron spectroscopy (XPS). FTIR spectra of CS, PCCS and PCCS@CuI are shown in Figure 2. For CS, the characteristic absorption peaks appeared at 3400 cm<sup>-1</sup> (O-H stretching vibration), 2873 cm<sup>-1</sup> (C-H stretching vibration), 1591 cm<sup>-1</sup> (N-H bending vibration), 1375 cm<sup>-1</sup> (C-H bending vibration), 1150 cm<sup>-1</sup> (C-O-C stretching vibration) and 1025 cm<sup>-1</sup> (C-O stretching vibration). Compared with the FTIR spectra of CS, a new band at 1649 cm<sup>-1</sup> emerged in PCCS, which might be due to the C=N stretching vibration. In addition, the peaks at 1569-1472 cm<sup>-1</sup> and 792 cm<sup>-1</sup> were foud, which can be attributed to the bending vibration and stretching vibration of pyridine ring skeleton, respectively. These above changes implied that pyridine-2-carboxaldehyde was introduced to CS by the formation of Schiff base. Differences were also found in the FTIR spectra of PCCS and PCCS@CuI: the band at 1649 cm<sup>-1</sup> (C=N stretching vibration) was changed to 1644 cm<sup>-1</sup> and turned broader, resulting from coordination of the imine group and copper. Besides, the band of pyridine at 1600-1500 cm<sup>-1</sup> and 900-700 cm<sup>-1</sup> became weaker, which could be also attributed to complexation of copper with pyridine.

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Figure 2. FTIR spectra of CS (a), PCCS (b) and PCCS@CuI (c)

TG curves of CS, PCCS and PCCS@CuI were shown in Figure3. It was obvious that they had two different mass loss stages. The first stage was at the range of 50-100 °C, which might be caused by the loss of water. In the second stage of mass loss, the decomposition of these materials was occurred from 250 °C to 350 °C. Notably, the mass loss of PCCS@CuI was lower than the others, due to the formation of Schiff base and coordination with the copper. Importantly, PCCS@CuI was stable at up to 200 °C.



Figure 3. TG analysis of CS (a), PCCS (b) and PCCS@CuI (c)

As shown in Figure 4, the distinct morphologies of CS, PCCS and PCCS@CuI were recorded via SEM. Compared with the relatively smooth surface of CS, the surface of PCCS became more rough, due to the outcome of modification on the CS by grafting pyridine-2-carboxaldehyde (in Figure 4a and 4b). Further, the bright spot in Figure 4c suggested that CuI was chelated to PCCS. Moreover, the copper of PCCS@CuI was measured by EDS (in Figure 4g), and a content of 2.05 mmol g<sup>-1</sup> was detected by ICP analysis. Therefore, it was demonstrated that copper was successfully chelated to PCCS. The XRD patterns of CS, PCCS and PCCS@CuI were shown in Figure 5. Obviously, the major characteristics of chitosan were the two peaks at 11.2° and 20.2° (in Figure 5a), which was consistent with the literature reported previously <sup>28</sup>. Furthermore, as shown in Figure 5b, the peak at 11.2° disappeared and the peak at range of 20° became sharper, possibly due to the formation of Schiff base and the decrease of free amino groups. Figure 5c exhibited deposition of the composite film from a dispersion of CuI in PCCS, in which PCCS@CuI has (111), (220) and (311) diffraction peaks of CuI film.



Figure 4. SEM images of CS (a), PCCS (b), PCCS@CuI (c), recovered PCCS@CuI after the second run (d), recovered PCCS@CuI after the third run (e), recovered PCCS@CuI after the fifth run (f) and EDS of PCCS@CuI (g)



Figure 5. X-ray diffraction of CS (a), PCCS (b) and PCCS@CuI (c)



Figure 6. XPS spectra of PCCS and PCCS@CuI (a), Cu 2p peaks of PCCS@CuI and recovered

PCCS@CuI after the second run (b), N 1s pattern of PCCS (c) and PCCS@CuI (d)

XPS spectra has been used to analyze the existence of different elements and to identify the different valence of the same element. All peaks were corrected by taking the peak of C 1s at 284.6 eV. Figure 6a reveals the full spectrum of PCCS and PCCS@CuI, which appears two new elements. The XPS peaks at 620 ev and 631 ev correspond to I  $3d_{5/2}$  and  $3d_{3/2}$  and at about 932.3 ev and 952.1 ev correspond to Cu  $2p_{3/2}$  and  $2p_{1/2}$ ,<sup>29</sup> which in accordance with the results of EDS. However, the absence of shake-up satellite peak in the Cu 2p claims the +1 oxidation state of Cu is present in the active catalyst in Figure 6b. With the weak of the peak of the Cu 2p and the appearance of the noise peaks, which indicates that the copper ion has slightly lost after the second run. The infrared analysis show that three forms of nitrogen: -NH<sub>2</sub>, -N=, N on the pyridine ring. In Figure 6c and 6d, the typical N 1s XPS spectra of PCCS before and after Cu<sup>+</sup> adsorption is presented. Before adsorption, the peak at 399.3 eV, 398.6 ev and 398.2 ev were attributed to -NH-, -N=H and the N of pyridine in Figure 6c.<sup>30</sup> After copper was chelated to PCCS, as shown in Figure 6d, the peaks at 399.6 ev, 399.2 ev and 398.6 ev were attributed to -NH-,-N= and N of pyridine, simultaneously, it also exhibited a new N 1s binding energy at 400.3 ev, this phenomenon demonstrates the formation of Cu...N-complexes,<sup>31</sup> which is in accordance with the results of FTIR.

Further extensive study focused on expanding the substrate scope for PCCS@CuI catalyzed Ullmann C-N coupling reaction. Relative details were summarized in Table 2. It was shown that electron withdrawing and donating effect of the groups substituted on aryl halide had much influence on the C-N coupling with imidazole. When the electron-donating substituents, *e.g.* 4-OMe (3b), 4-Me (3c), 4-OEt (3d) and 4-OCF<sub>3</sub> (3g) were present at the aryl halide, the yields were much better as compared to the ones with electron-withdrawing substituents, *e.g.* 4-F (3h), 4-Cl (3i), 4-NO<sub>2</sub> (3j) and 4-Ac (3k). In addition, aryl halide at *ortho*-substituents, e.g. OMe (3e) and Me (3f), were well tolerated and the desired products were obtained with 85% and 83% yield, respectively. In our previous report, substituent at *ortho*-position catalyzed by  $\beta$ -CD@CuI, had poor reactivity <sup>27a</sup>. Thus, the catalytic activity of PCCS@CuI was impressive. Meanwhile, the reactivities of different aryl halides were examined, and the order of corresponding reactivities was PhI > PhBr > PhCl. Furthermore, different nucleophiles coupling with aryl halide were performed, and several heterocycles, e.g. pyrrolidine (3i), *n*-butylamine (3m), 2-Pyrrolidinone (3n),

1*H*-benzoimidazole (30), 4-methyl-1*H*-imidazole (3p) and 5-nitroindole (3q) gave the corresponding products with good yields.

Table 2. The C-N coupling reaction catalyzed by PCCS@CuI<sup>a</sup>



<sup>a</sup> Reaction conditions: aryl halides 1 (1.0 mmol), nitrogen nucleophiles 2 (1.2 mmol),  $Cs_2CO_3$  (2.0 mmol) and PCCS@CuI (25 mg, loading 5 mol%) in the DMSO (3 mL) at 110 °C for 24 h.

The PCCS@CuI-catalyzed protocol was expanded to the Ullmann C-S coupling reaction of aryl halides with sulfinate salts, and the results were shown in Table 3. To our delight, aryl sulfinate could react efficiently with iodobenzene, and targeted product was obtained with excellent yields. Moreover, it was notable that the aryl iodide with electron-donating substituents were more reactive than the ones with electron-withdrawing substituents. Besides, the steric hindrance by *ortho*-substituents decreased the efficiency of this reaction. In addition, the reactivities of aryl chloride and aryl bromide with sulfinate salts were lower than the one of aryl iodide. For sulfinates, neither electron donating nor withdrawing groups substituted on the ring showed obvious influences on the yields.

Table 3. The C-S coupling reaction catalyzed by PCCS@CuI<sup>a</sup>



<sup>a</sup> Reaction conditions: aryl halides 1 (1.0 mmol), aryl sulfinate 4 (1.2 mmol), Cs<sub>2</sub>CO<sub>3</sub> (2.0 mmol) and PCCS@CuI (25 mg, loading 5 mol%) in the DMSO (3 mL) at 110°C for 24 h.



Figure 7. Recycling and reuse of PCCS@CuI as catalyst

As a further advantage of PCCS@CuI, it can be easily separated from the reaction mixture and reused. Herein, PCCS@CuI was removed from the reaction mixture by centrifugal filtration, and then the separated catalyst was washed by 6 times using the deionized water, and dried at 50°C under vacuum, to reuse it directly again. In addition, the reusability of PCCS@CuI was studied by the above Ullmann C-N model reaction. The results of reusable catalyst were shown in Figure 7. It was obvious that the catalyst had excellent catalytic effect after being reused five times. Moreover, the SEM of PCCS@CuI after being reused was shown in Figure 4d-4f, in which there are bright spots. These bright spots indicate the copper ions were attached to the complex. Compared Figure 4c with Figure 4d, there is no significant loss of copper ions after the catalyst being reused twice. Although some copper ions are missing after the catalyst being reused fifth run, there are still much copper ions on the surface. Therefore, it gave obvious evidences to its structural stability. The copper of recovered catalyst was measured by EDS (see the ESI in Figure S3), and a content of 1.89 mmol g<sup>-1</sup> was detected by ICP analysis.

# 4. Conclusions

In summary, we have successfully designed and prepared a green and efficient copper catalyst based on the Schiff-base chitosan. Schiff-base chitosan was synthesized by the condensation of pyridine-2-carboxaldehyde and amino group on chitosan. The applicability of the catalyst was proved by Ullmann reaction, in which good to excellent yields of C-N and C-S coupling reaction were obtained. In addition to high catalytic activity, the functionalized-chitosan supported copper complex is easily recoverable and reused stably.

# 5. Acknowledgements

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## References

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- (1) (a) Carroll, M. P.; Guiry, P. J. Chem. Soc. Rev 2014, 43, 819(b) Bariwal, J.; Van der Eycken, E. Chem. Soc. Rev 2013, 42, 9283(c) Enugala, R.; Carvalho, L. C. R.; Pires, M. J. D.; Marques, M. M. B. Chem-Asian J 2012, 7, 2482(d) Monnier, F.; Taillefer, M. Angew. Chem. Int. Ed 2008, 47, 3096.
- (2) (a) Beletskaya, I. P.; Cheprakov, A. V. Coord. Chem. Rev 2004, 248, 2337(b) Hassan, J.;
   Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Chem. Rev 2002, 102, 1359.
- (3) Klapars, A.; Antilla, J. C.; Huang, X. H.; Buchwald, S. L. J. Am. Chem. Soc 2001, 123, 7727.
- (4) (a) Klapars, A.; Huang, X. H.; Buchwald, S. L. J. Am. Chem. Soc 2002, 124, 7421(b) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. J. Org. Chem 2004, 69, 5578(c) Surry, D. S.; Buchwald, S. L. Chem. Sci 2010, 1, 13.
- (5) (a) Kwong, F. Y.; Klapars, A.; Buchwald, S. L. Org. Lett 2002, 4, 581(b) Yang, B.; Mao, Z. X.;
   Zhu, X. H.; Wan, Y. Q. Catal. Commun 2015, 60, 92.
- (6) (a) Cristau, H. J.; Cellier, P. P.; Spindler, J. F.; Taillefer, M. Chem.eur. J 2004, 10, 5607(b)

Wang, Y.; Gao, J. Y.; Zhao, M. D.; Li, J. M. Chem Res Chinese U 2015, 31, 549.

- (7) (a) Ma, D. W.; Cai, Q. Synlett 2004, 128(b) Tang, J. M.; Xu, B. Q.; Mao, X.; Yang, H. Y.;
   Wang, X. X.; Lv, X. J. Org. Chem 2015, 80, 11108.
- (8) (a) Shafir, A.; Buchwald, S. L. J. Am. Chem. Soc 2006, 128, 8742(b) de Lange, B.;
  Lambers-Verstappen, M. H.; van de Vondervoort, L. S.; Sereinig, N.; de Rijk, R.; de Vries, A. H. M.; de Vries, J. G. Synlett 2006, 3105.
- (9) Altman, R. A.; Buchwald, S. L. Org. Lett 2006, 8, 2779.
- (10) Zhang, C.; Huang, B.; Bao, A. Q.; Li, X.; Guo, S.; Zhang, J. Q.; Xu, J. Z.; Zhang, R.; Cui, D.
   M. Org. Biomol. Chem 2015, 13, 11432.
- (11) (a) Cheng, D. P.; Gan, F. F.; Qian, W. X.; Bao, W. L. *Green Chem* 2008, *10*, 171(b) Wen, M.;
  Shen, C.; Wang, L. F.; Zhang, P. F.; Jin, J. Z. *RSC Adv* 2015, *5*, 1522(c) Suresh, P.; Pitchumani,
  K. J. Org. Chem 2008, *73*, 9121.
- (12) (a) Zhang, Y.; Yang, X. Y.; Yao, Q. Z.; Ma, D. W. Org. Lett 2012, 14, 3056(b) Wang, Y. B.;
   Zhang, Y.; Yang, B. B.; Zhang, A.; Yao, Q. Z. Org. Biomol. Chem 2015, 13, 4101.
- (13) Zhou, W.; Fan, M. G.; Yin, J. L.; Jiang, Y. W.; Ma, D. W. J. Am. Chem. Soc 2015, 137, 11942.
- (14) Handzlik, J.; Ogonowski, J.; Stoch, J.; Mikolajczyk, M. Catal. Lett 2005, 101, 65.
- (15) (a) Gu, L.; Ma, D.; Yao, S.; Wang, C.; Shen, W.; Bao, X. Chem. Commun 2010, 46, 1733(b)
   Iwasaki, M.; Shinjoh, H. Chem. Commun 2011, 47, 3966.
- (16) Lei, Z. Q. React. Funct. Polym 2000, 43, 139.
- (17) (a) Polshettiwar, V.; Luque, R.; Fihri, A.; Zhu, H.; Bouhrara, M.; Basset, J. M. Chem. Rev **2011**, 111, 3036(b) Baig, R. B. N.; Varma, R. S. Chem. Commun **2012**, 48, 2582(c) Ayad, M. M.; Amer, W. A.; Kotp, M. G. Mol. Catal **2017**, 439, 72(d) Doustkhah, E.; Rostamnia, S.; Gholipour, B.; Zeynizadeh, B.; Baghban, A.; Luque, R. Mol. Catal **2017**, 434, 7.
- (18) Marques, M. M.; Queda, F.; Carvalho, L.; Santos, C. t. Chem Asian J 2016, 11.
- (19) (a) Sudheesh, N.; Sharma, S. K.; Khokhar, M. D.; Shukla, R. S. J. Mol. Catal. A: Chem 2011, 339, 86(b) Zhao, X.; Wei, Z.; Zhao, Z.; Miao, Y.; Qiu, Y.; Yang, W.; Jia, X.; Liu, Z.; Hou, H. ACS Appl Mater Inter 2018.
- (20) Shen, C.; Xu, J.; Yu, W. B.; Zhang, P. F. Green Chem 2014, 16, 3007.
- (21) Xu, D.; Hein, S.; Wang, K. Mater. Sci. Technol 2013, volume 24, 1076.
- (22) (a) Frindy, S.; Primo, A.; Lahcini, M.; Bousmina, M.; Garcia, H.; El Kadib, A. Green Chem

2015, 17, 1893(b) Hu, D.; Cui, Y.; Dong, X.; Fang, Y. React. Funct. Polym 2000, 48, 201.

- (23) Makhubela, B. C. E.; Jardine, A.; Smith, G. S. Green Chem 2012, 14, 338.
- (24) Xia, C. G.; Sun, W.; Wang, H. W. New J. Chem 2002, 26, 755.
- (25) Lei, X.; Zhou, D. J.; Li, T.; Ji, X. F.; Huang, M. Y.; Jiang, Y. Y. *React. Funct. Polym* 2004, 58, 117.
- (26) Anuradha; Kumari, S.; Pathak, D. D. Tetrahedron Lett 2015, 56, 4135.
- (27) (a) Chen, L.; Wang, C.; Zhou, L.; Sun, J. Adv. Synth. Catal 2014, 356, 2224(b) Iwasaki, F.;
  Onomura, O.; Mishima, K.; Kanematsu, T.; Maki, T.; Matsumura, Y. Tetrahedron Lett 2001, 42, 2525(c) Nugent, T. C.; El-Shazly, M. Adv. Synth. Catal 2011, 353, Cp6(d) Nugent, T. C.;
  El-Shazly, M. Adv. Synth. Catal 2010, 352, 753.
- (28) Zhang, H.; Dang, Q.; Liu, C.; Cha, D.; Yu, Z.; Zhu, W.; Fan, B. ACS Appl Mater Inter 2017, 9, 11144.
- (29) (a) Saha, S.; Das, S.; Sen, D.; Ghorai, U. K.; Mazumder, N.; Gupta, B. K.; Chattopadhyay, K. K. J. Mater. Chem C 2015, 3, 6786(b) Kumar, M.; Bhatt, V.; Nayal, O. S.; Sharma, S.; Kumar, V.; Thakur, M. S.; Kumar, N.; Bal, R.; Singh, B.; Sharma, U. Catal. Sci. Technol 2017, 7, 2857.
- (30) (a) Tong, J.; Li, Z.; Xia, C. J. Mol. Catal A :Chem 2005, 231, 197(b) Zeng, L.; Chen, Y.; Zhang, Q.; Guo, X.; Peng, Y.; Xiao, H.; Chen, X.; Luo, J. Carbohydr. Polym 2015, 130, 333(c) Teng, S. X.; Wang, S. G.; Liu, X. W.; Gong, W. X.; Sun, X. F.; Cui, J. J.; Gao, B. Y. Colloids Surf. A 2009, 340, 86.
- (31) Zhou, Y. T.; Branford-White, C.; Nie, H. L.; Zhu, L. M. Colloids Surf. B 2009, 74, 244.