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Copper(II) *trans*-bis-(glycinato): an efficient heterogeneous catalyst for cross coupling of phenols with aryl halides

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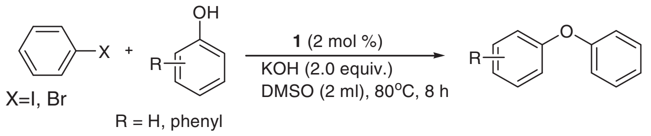
Copper(II) *trans*-bis-(glycinato) complex, easily prepared by the solid state reaction of copper(II) acetate and glycine (*trans*-[Cu(glyo)$_2$·H$_2$O]) was found to be an efficient, recyclable, and high yielding catalyst for the Ullmann type synthesis of diaryl ethers via the cross coupling of phenols with aryl halides without using any additives at relatively low reaction temperature. The catalyst could easily be recovered by simple filtration and was reused for several runs with consistent catalytic activity.

Diaryl ethers are valuable structural motifs which are widely used in the synthesis of numerous synthetically challenging and biologically active molecules.[1] Conventionally, these compounds are prepared by intermolecular reaction between aryl halide and phenol using copper or palladium as catalyst.[2,3] However, harsh reaction conditions, use of stoichiometric quantities of the copper catalyst, and the low yields have significantly limited the effectiveness of this reaction. Therefore, improved coupling methodologies using catalytic amounts of a copper precursor in the presence of various ligands such as 1,10-phenanthroline,[4] 2,2,6,6-tetramethylheptane-3,5-dione,[5] triphenylphosphine,[6] phosphazene,[7a] ethylene glycol,[7b] neocuproine,[8] *N*-methyl glycine,[7c,d] oxime-phosphine oxide ligand,[7e] a tripod ligand,[7f] benzotriazole,[7g] 1,2-diaminocyclohexane,[7h] L-proline,[7i] 8-hydroxyquinoline,[9] (2-pyridyl)acetone,[10] and 1-naphthoic acid[2a] under relatively mild reaction conditions are receiving increasing interest in recent years. However, the use of expensive, less conveniently available reagents or additives and homogeneous protocols is the major drawback associated with most of the existing methods. In the recent years, the utilization of heterogeneous catalysts in organic synthesis has been increased due to their facile recovery and recycling ability of the catalysts. In this context, various heterogeneous copper catalysts including nanoparticulate CuO,[11a] nano CuI,[3a,b] Cu_2O,[4] and Cu nanoparticles[11b] have been used for Ullmann type coupling. Since the reported catalysts are difficult to synthesize, require excess ligands/additives, and are economically less affordable, there is a need to develop a convenient and cost effective catalyst system. In continuation of our interest toward developing new methodologies for coupling reactions, herein we report an efficient, cheap, easily accessible, and reusable heterogeneous catalyst copper(II) *trans*-bis-(glycinato) **1** for the Ullmann type synthesis of diaryl ethers via cross coupling of phenols with aryl halides without any additive at relatively low reaction temperature (Scheme 1).

The required catalyst was easily synthesized via the grinding of $Cu(CH_3COO)_2{\cdot}H_2O$ and glycine in a 1:2 molar ratio as following the literature procedure.[12,13] The values of elemental analyses suggested the proposed formula of complex is *trans*-[Cu(gly)$_2$(H$_2$O)] **1**. Further, a strong band at 1699 cm^{-1} in IR spectra corresponding to carboxyl group of glycine revealed the successful formation of adduct **1**. The stability of the complex was determined by the thermo gravimetric analysis (TGA) under oxygen atmosphere. The TG curve of the complex **1** showed two-step decomposition pattern (Supplementary Fig. 1). In the first stage, weight loss was observed in the temperature range of 50–150 °C, which is probably due to the loss of coordinated water molecule. The second stage



Scheme 1. Copper-catalyzed Ullmann coupling.

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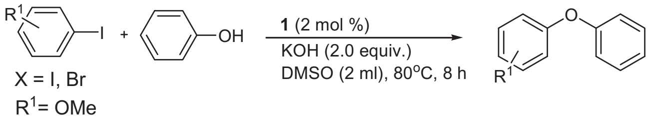
decomposition was taken place in the temperature range between 250 and 500 °C with the final formation of CuO.

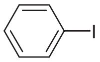
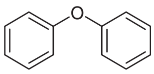
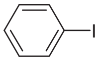
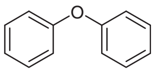
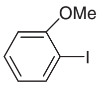
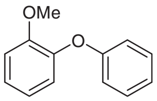
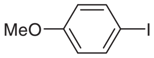
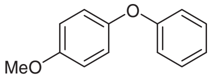
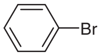
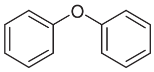
At first, we studied the coupling of phenol with various aryl halides mediated with KOH in the presence of catalytic amount of **1** (2 mol %) at 80 °C in dimethyl sulfoxide without using any additive.[14] The results of these experiments are summarized in Table 1. As shown in the results, both aryl iodides and bromides were found to be efficient and provided moderate to high yield of the product. However, the steric hindrance of aryl halides such as 2-iodoanisole was found to disfavor this reaction and provided comparatively lower yield of the desired product (Table 1, entry 3). It was found that the reaction did occur promisingly at 80 °C in dimethyl sulfoxide in comparison to the other solvents such as acetonitrile, THF, and dichloroethane under similar reaction conditions (Table 1, entry 1). Next, we carried out the Ullmann coupling of different phenols/naphthols with phenyl iodide/ bromide with the use of **1** (2 mol %) in the presence of KOH in DMSO under similar reaction conditions. The results are summarized in Table 2. As shown, all the substrates were found to be effective and afforded moderate to high yields of the corresponding diaryl ethers. In all cases, the products were confirmed by GC/MS analysis and their identity was established by comparing their spectral data with those of reported compounds. Among the various phenols, those substituted with electron donating groups were found to be more reactive substrates as compared to those having electron withdrawing groups (Table 2, entries 13–18). The sterically hindered phenols such as 2-methoxyphenol, 2,4-dimethoxyphenol also provided moderate yield of the product under the described reaction conditions (Table 2, entries 5,9,10–11). The use of 1-naphthol and 2-naphthol in place of phenol also provided comparable results under the described reaction conditions (Table 2, entries 19 and 20). The developed protocol is advantageous over the reported method[7c,d] in many ways; (i) it does not require excess ligand during the reaction; (ii) catalyst is heterogeneous which can easily be recovered by simple filtration; (iii) simple work-up and offers high product yield. Furthermore, the reaction of phenol with chlorobenzene did not give any coupling product under described experimental conditions. We compared the potential of the developed catalyst with some of the already reported copper catalysts for the coupling of phenols with aryl halides. These results are presented in Table 1 (entries 2 and 5). The higher product yield in comparatively lesser reaction times in the absence of additional additive clearly indicates the superiority of the developed methodology.

Next, we tested the recycling of the developed catalyst by choosing the coupling of phenol with iodobenzene under described experimental conditions. After completion of the reaction, the catalyst could easily be recovered by simple filtration and used for the subsequent experiments (7 runs). The results of these experiments are summarized in Table 3. As shown, the yield of the product and reaction time remained almost same in all cases, establishing the efficient recycling of the catalyst as well as heterogeneous nature of the developed methodology. Further we also analyzed the recovered catalyst by Inductive Coupled Plasma-Atomic Emission Spectroscopy (ICP-AES) analysis and the value of copper was found to be same as in fresh catalyst, ascertaining that the reaction is truly heterogeneous in nature.

In summary, we have developed an efficient, cost-effective, easily accessible, and recyclable catalyst for carrying out the Ullmann diaryl ether synthesis without using any additive under mild reaction conditions. The key advantages of the developed method are: (i) facile synthesis of the catalyst, (ii) low reaction temperature (iii) tolerance to various functional groups, (iv) facile recovery, and recycling of the catalyst. Further applications of the developed catalyst as well as mechanistic studies, are currently in progress in our laboratory.

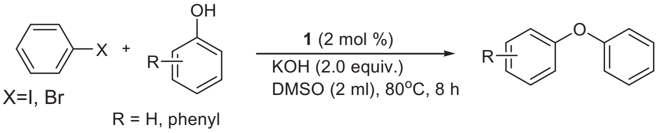
Table 1
Ullmann coupling of phenol with different aryl/alkyl halides[a]

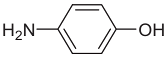
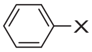
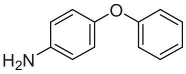
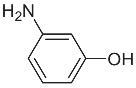
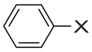
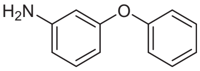
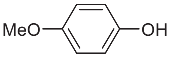
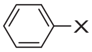
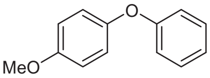
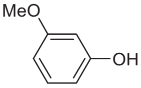
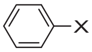
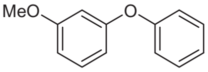
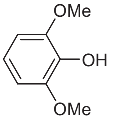
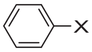
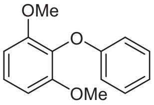
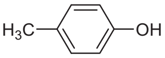
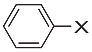
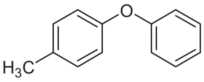
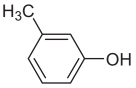
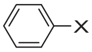
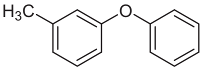
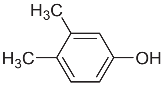
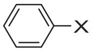
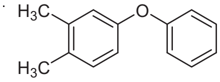
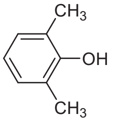
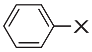
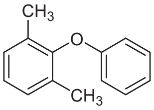
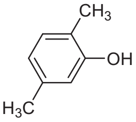
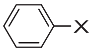
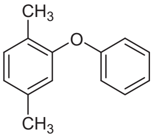
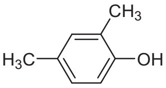
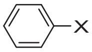
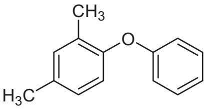
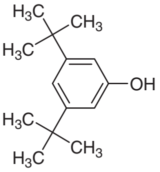
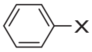
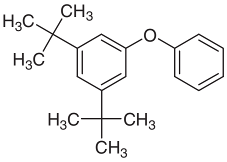
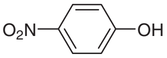
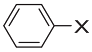
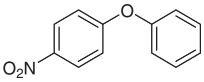
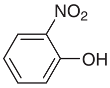
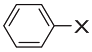
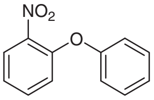
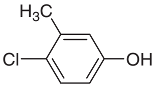
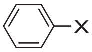
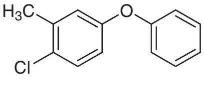


Entry	Aryl/alkyl halide	Product	Solvent	Time (h)	Yield[b] (%)
1			DMSO CH_3CN, THF, $ClCH_2CH_2Cl$	8 12 24 24	98[a] 65[c] 40[d] 40[e]
2			DMSO	18	84[f]
3			DMSO	12	44
4			DMSO	8 8	98[a] 95[g]
5			DMSO	8 18[f]	88[a] 88[f]

[a] Reaction conditions: phenol (2 mmol), aryl/alkyl halide (2 mmol), KOH (2 equiv), catalyst (2 mol %), DMSO (5 ml) at 80 °C.
[b] Isolated yields.
[c] Using CH_3CN.
[d] THF.
[e] Dichloroethane.
[f] Ref. 2c.
[g] Ref. 10.

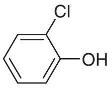
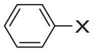
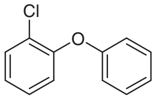
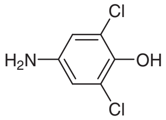
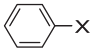
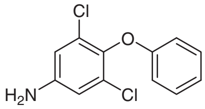
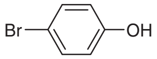
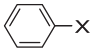
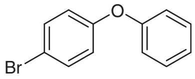
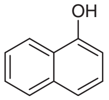
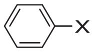
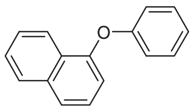
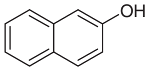
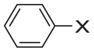
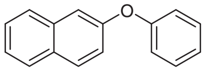
Table 2
Heterogeneous copper-catalyzed Ullmann coupling of phenols/naphthols[a]



Entry	Substrate	Aryl halide	Product	Yield[b] (%)
1				98 (X = I) 95 (X = Br)
2				95 (X = I) 93 (X = Br)
3				90 (X = I) 87 (X = Br)
4				92 (X = I) 85 (X = Br)
5				92 (X = I) 85 (X = Br)
6				98 (X = I) 96 (X = Br)
7				86 (X = I) 82 (X = Br)
8				97 (X = I) 94 (X = Br)
9				82 (X = I) 76 (X = Br)
10				90 (X = I) 86 (X = Br)
11				92 (X = I) 88 (X = Br)
12				94 (X = I) 90 (X = Br)
13				55 (X = I) 48 (X = Br)
14				62 (X = I) 50 (X = Br)
15				84 (X = I) 80 (X = Br)

(continued on next page)

Table 2 (*continued*)

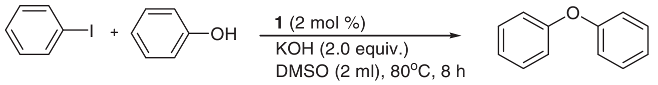
Entry	Substrate	Aryl halide	Product	Yield[b] (%)
16				80 (X = I) 74 (X = Br)
17				70 (X = I) 66 (X = Br)
18				62 (X = I) 55 (X = Br)
19				90 (X = I) 80 (X = Br)
20				89 (X = I) 82 (X = Br)

[a] Reaction conditions as mentioned in the text.

[b] Isolated yields.

Table 3

Results of recycling experiments



Run	1	2	3	4	5	6	7
Yield	98	98	97	98	97	97	97

Acknowledgment

We are thankful to the Director, IIP for his kind permission to publish these results. S.V. acknowledges CSIR, New Delhi for the award of his Research Fellowship. Analytical division of the Institute is kindly acknowledged for providing the analysis (GC–MS, IR &^{1}H NMR) of the products.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.06.071.

References and notes

1. (a) Boeger, D. L.; Patane, M. A.; Zhou, J. *J. Am. Chem. Soc.* **1994**, *116*, 8544; (b) Zhu, J. *Synlett* **1997**, 133; (c) Nicolaou, K. C.; Boddy, C. N. C.; BrDse, S.; Winssinger, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 2096; (d) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054.
2. (a) Marcoux, J.-F.; Doye, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 10539; (b) Ouali, A.; Spindler, J.-F.; Cristau, H.-J.; Taillefer, M. *Adv. Synth. Catal.* **2006**, *348*, 499; (c) Zhang, J.; Zhang, Z.; Wang, Y.; Zheng, X.; Wang, Z. *Eur. J. Org. Chem.* **2008**, 5112; (d) Cristau, H.-J.; Cellier, P. P.; Hamada, S.; Spindler, J.-F.; Taillefer, M. *Org. Lett.* **2004**, *6*, 2004; (e) Sawyer, J. S. *Tetrahedron* **2000**, *56*, 5045; (f) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954.
3. (a) Shen, G.; Lv, X.; Qian, W.; Bao, W. *Tetrahedron Lett.* **2008**, *49*, 4556; (b) Sreedhar, B.; Arundhathi, R.; Reddy, P. L.; Kantam, M. L. *J. Org. Chem.* **2009**, *74*, 7951; (c) Fernandez Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 2180; (d) Fernandez Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. *Chem. Eur. J.* **2006**, *12*, 7782.
4. (a) Hosseinzadeh, R.; Tajbakhsh, M.; Mohadjerani, M.; Alikarami, M. *Synlett* **2005**, 1101; (b) Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315; (c) Goossen, L. J.; Rodríguez, N.; Melzer, B.; Linder, C.; Deng, G.; Levy, L. M. *J. Am. Chem. Soc.* **2007**, *129*, 4824.
5. Buck, E.; Song, Z. J.; Tschaen, D.; Dormer, P. G.; Volante, R. P.; Reider, P. J. *Org. Lett.* **2002**, *4*, 1623.
6. Gujadhur, R. K.; Venkataraman, D. *Synth. Commun.* **2001**, *31*, 2865.
7. (a) Palomo, C.; Oiarbide, M.; Lopez, R.; Gomez-Bengoa, E. *Tetrahedron Lett.* **2000**, *41*, 1283; (b) Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 3517; (c) Deng, W.; Zou, Y.; Wang, Y.-F.; Liu, L.; Guo, Q.-X. *Synlett* **2004**, *7*, 1254; (d) Ma, D.; Cai, Q. *Org. Lett.* **2003**, *5*, 3799; (e) Zhu, D.; Xu, L.; Wu, F.; Wan, B. *Tetrahedron Lett.* **2006**, *47*, 5781; (f) Chen, Y.-J.; Chen, H.-H. *Org. Lett.* **2006**, *8*, 5609; (g) Verma, A. K.; Singh, J.; Chaudhary, R. *Tetrahedron Lett.* **2007**, *48*, 7199; (h) SanMartin, M. R.; Dominguez, E.; Tellitu, I. *Chem. Eur. J.* **2007**, *13*, 5100; (i) Zhang, H. K.; Cao, W.; Ma, D. *Synth. Commun.* **2007**, *37*, 25.
8. Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 2803.
9. (a) Fagan, P. J.; Hauptman, E.; Shapiro, R.; Casalnuovo, A. *J. Am. Chem. Soc.* **2000**, *122*, 5043; (b) Corbet, J.-P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651.
10. Zhang, Q.; Wang, D.; Wang, X.; Ding, K. *J. Org. Chem.* **2009**, *74*, 7187–7190.
11. (a) Rout, L.; Jammi, S.; Punniyamurthy, T. *Org. Lett.* **2007**, *9*, 3397; (b) Kidwai, M.; Mishra, N.; Bansal, V.; Kumarb, A.; Mozumdar, S. *Tetrahedron Lett.* **2007**, *48*, 8883.
12. (a) Jia, D. Z.; Xin, X. Q. *Acta Chim. Sinica* **1993**, *51*, 358; (b) Wang, L.; Lang, L.; Dianzeng, J.; Yali, C.; Xinquan, X. *Chin. Sci. Bull.* **2005**, *50*, 758.
13. *Synthesis of copper(II) trans-bis-(glycinato) complex*[12]: Reagent grade copper(II) acetate monohydrate {Cu(OCOCH$_3$)$_2$·H$_2$O} and glycine were used. Copper acetate monohydrate and glycine were taken in a 1:2 molar ratio and ground for 5–10 min in an agate mortar respectively for mixing. The mixture was ground for 60 min and the reaction was checked by infrared spectrum as it showed the reduction of the free amino band of the glycine. At the end of the reaction (absence of free amino band in IR spectrum), the synthesized complex was washed twice with ethanol and dried. Anal. Calcd for $C_4H_{10}N_2O_5Cu$ (%): C, 20.91; H, 4.39; N, 12.20%. Found: C 20.78, H 4.46, N 12.86%.
14. *Experimental procedure for the synthesis of diaryl ether*: To a stirred solution of iodo benzene (1.0 mmol) and phenol (1.0 mmol) in dry DMSO (2.0 ml) were added Cu catalyst 1 (0.02 mmol) and KOH (2.0 equiv) and the reaction mixture was heated at 80 °C for 8 h. The progress of the reaction was monitored by TLC. After being cooled the reaction mixture at room temperature, the precipitated catalyst was separated by simple filtration and filtrate so obtained was diluted with ethyl acetate (10 ml). The organic layer was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum to give the crude product, which was purified by column chromatography with hexane as eluent to yield the expected product as yellowish oil. The products were analyzed by GC–MS, IR, ^{1}H & ^{13}C NMR analysis.