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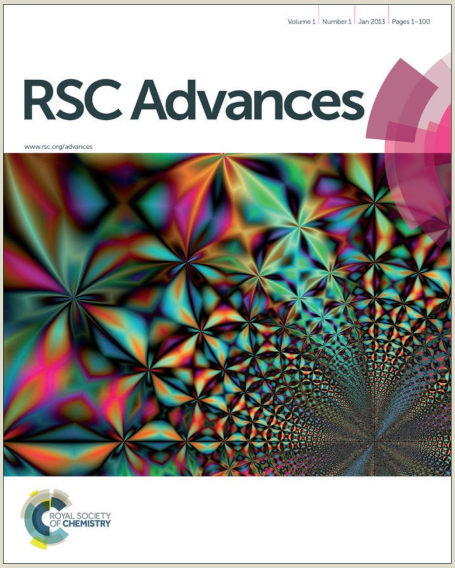

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Journal Name

ARTICLE

Cu(0)@Al_2O_3/SiO_2 NPs: Efficient Reusable Catalyst for the Cross Coupling Reactions of Aryl Chlorides with Amines and Anilines

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The C-N cross coupling reaction of aryl chlorides with various alkyl/aryl amines catalyzed by copper nanoparticles impregnated on alumina/silica support (Cu(0)@Al_2O_3/SiO_2) was investigated. The prepared catalyst was characterized for its intrinsic physico-chemical and textural properties using XRD, XPS, HR-TEM, BET surface area, SEM-EDAX, H_2-TPR and ICP-AES techniques. The catalyst exhibits excellent reactivity and efficacy in the cross-coupling of a wide range of alkyl/aryl amines including challenging anilines with aryl chlorides. The catalyst offers significant advantages such as brevity, milder reaction conditions, excellent yields and high functional group tolerance for C-N cross coupling when compared with the other reported methods. Moreover, this atom-economical methodology does not require an additional ligand or co-catalyst/activator. The Cu(0)@Al_2O_3/SiO_2 catalyst was efficiently applied to a gram scale synthesis of 7-chloro-4-(4-(2-nitrophenyl)piperazin-1-yl)quinolone (**2k**). The robustness of the catalyst was examined by reusing it for five consecutive runs.

Introduction

The metal catalyzed construction of Carbon–Nitrogen bond has perhaps received more attention than any other covalent bond formation in synthetic organic chemistry. Nitrogen containing organic compounds not only possess diverse biological activities,[1-3] but also serve as a building block for various macromolecules and novel materials.[4] Since the pioneering work of Ullmann and Goldberg at the beginning of 20th century wherein stoichiometric amounts of Cu salts were used for the cross-coupling of aryl halides and amines, albeit under harsh conditions, many methodologies have been developed to improve the synthetic utility of the C-N cross-coupling reactions.[5] Buchwald and Hartwig developed palladium based catalysis for the coupling of aryl chlorides and amines.[6] This methodology has some inherent advantages over other transition metal catalyzed C-N bond forming reactions such as high tolerance of functional groups, coupling of challenging substrates, mild reaction conditions.[7] However, the use of precious and rare Pd metal along with an additional ligand, besides the need of an inert atmosphere and generation of hazardous by-products constraints the wide usage of palladium in C-N cross-coupling. Other transition metals (Ru, Rh Ir etc.) that have been explored for the C-N cross-couplings also suffer from such drawbacks, which in turn, again put the focus on the inexpensive Cu based catalysts.

However, the Cu-catalyzed Ullmann-type reactions suffer with the limitations of poor substrate scope, requirement of stoichiometric amounts of copper and harsh reaction conditions. The use of copper nano-catalysts can overcome many such limitations. Copper based nanoparticles have gained much importance in organic synthesis due to their ease of preparation, cost-effectiveness and low toxicity while offering better reactivity leading to various substrate scope, low catalyst loading, high yield and short reaction time. Recently copper based nanoparticles[8] and Cu metal organic framework (MOF) catalytic system[9] were shown to catalyze the carbon-heteroatom bond formation using -bromo or -iodo arenes as starting materials. More recently, efforts to incorporate metal nanoparticles on heterogeneous support and their use for successful organic transformations have also been reported.[10] This approach is significant due to the inherent benefits such as ease of separation/purification of the products and recyclability of the catalyst. Use of mixed oxides as a heterogeneous catalyst-support has many advantages like higher surface area, stronger surface acidity/basicity and favourable thermal stability compared to respective single metal oxides.[11] Alumina/silica mixed oxides have been reported as a promoter/catalyst for many organic reactions.[12] Amorphous alumina/silica materials are highly suitable acidic components for the preparation of supported metal catalysts.[13] Towards this end, and in continuation of our efforts to develop novel catalysts for the important organic conversions,[14] we synthesized copper nanoparticles impregnated on commercially available alumina/silica (Al_2O_3/SiO_2, Sasol, Germany) support and successfully applied it for the C-N cross couplings by employing inexpensive and more challenging aryl chlorides instead of aryl bromides and iodides with aliphatic, aromatic and *N*-heterocyclic amines.

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Remarkably, the catalyst prepared in this course has shown high catalytic activity for the coupling of chlorobenzenes, a challenging substrate for metal-catalyzed cross couplings, showing better TON and TOF values in comparison to previously reported copper based catalysts.[8a,17-19] Furthermore, this new class of eco-friendly metal-catalyst can be easily recovered and reused in the subsequent runs, even for the gram scale reactions, making it amenable for industrial use as well.

Results and discussion

Preparation of Cu(0)@Al_2O_3/SiO_2

The copper nanoparticles on alumina/silica (Cu(0)@Al_2O_3/SiO_2) was impregnated in four steps.

1. 33.35 g of copper nitrate was dissolved in 500 mL of doubly deionized water and to this solution 100 g of alumina/silica support (Al_2O_3/SiO_2) was added and stirred at 60 °C for 12 h to obtain blue slurry of Cu(II)@Al_2O_3/SiO_2.
2. The copper impregnated support (Cu(II)@Al_2O_3/SiO_2) was filtered, washed thoroughly with double deionised water and dried at 110 °C for 12 h to obtain 130 g of Cu(II)@Al_2O_3/SiO_2 as pale blue powder.
3. 100 g of Cu(II)@Al_2O_3/SiO_2 was taken in a crucible and calcined in the presence of air at a ramping temperature of 150 °C/1 h and 800 °C/3 h. The calcined catalyst was then cooled to room temperature to obtain 85 g of grey coloured CuO@Al_2O_3/SiO_2.
4. 5 g of CuO@Al_2O_3/SiO_2 was then taken in SS (stainless steel) reactor and reduced in the presence of hydrogen flow with optimized following parameters, temperature 250 °C, hydrogen pressure 10 bar with a flow rate of 1L/h to obtain 4.8 g black coloured Cu(0)@Al_2O_3/SiO_2.

Characterization of Cu(0)@Al_2O_3/SiO_2

The copper loading on alumina/silica support (Cu(0)@Al_2O_3/SiO_2) was found to be 2.06 wt% by SEM-EDAX elemental analysis (ESI, Figure S4), while Al and Si were found to be 53.78 and 0.55 wt% respectively. Figure 1 shows the powder XRD spectrum of Cu(II)Al_2O_3/SiO_2 [A], CuO@Al_2O_3/SiO_2 [B], Cu(0)@Al_2O_3/SiO_2 [C, Fresh] and Cu(0)@Al_2O_3/SiO_2 [D, reused]. The XRD pattern of Cu(0) nanoparticles (Figure 1) contains peaks that are not clearly distinguishable. This could be due to low loading and well dispersion of copper nanoparticles.[15a] Further, the copper metal percentage and the oxidation states were confirmed by SEM- EDAX (ESI Figure S4), ICP-AES and XPS analysis.

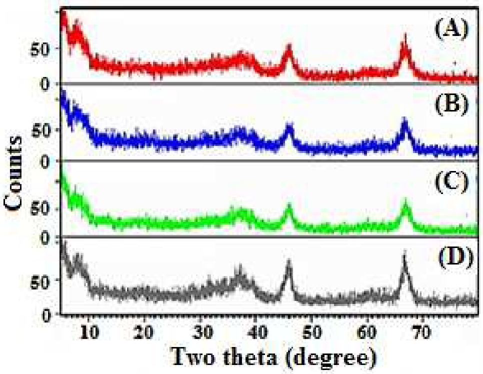

Figure 1. PXRD of Cu(II)@Al_2O_3/SiO_2 [A], CuO@Al_2O_3/SiO_2 [B], Cu(0)@Al_2O_3/SiO_2 [C, fresh], and Cu(0)@Al_2O_3/SiO_2 [D, 5th run].

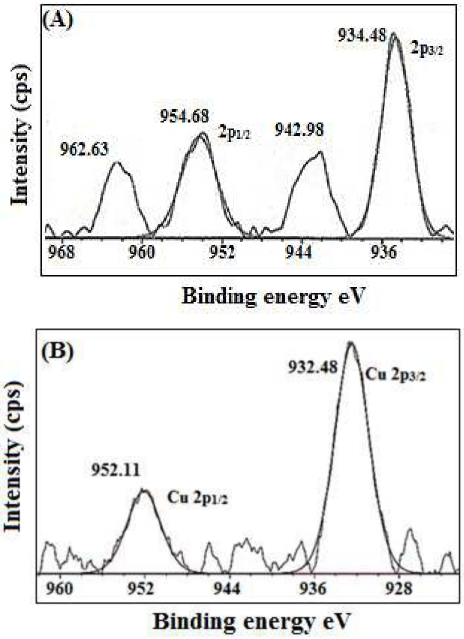

Figure 2. XPS spectra of CuO@Al_2O_3/SiO_2[A] and Cu(0)@Al_2O_3/SiO_2[B].

The X-ray photoelectron spectroscopic analysis of freshly prepared CuO@Al_2O_3/SiO_2 and Cu(0)@Al_2O_3/SiO_2 was carried out to evaluate the oxidation state of copper nanoparticles on alumina/silica (Cu(0)Al_2O_3/SiO_2). As shown in Figure. 2, The binding energies of CuO@Al_2O_3/SiO_2 were observed at 934.48 and 954.69 eV corresponding to $Cu2p_{3/2}$ and $Cu2p_{1/2}$ with satellite peaks at 942.98 and 962.63 eV which confirmed the Cu 2p core level in +2 oxidation state. In the case of Cu(0)@Al_2O_3/SiO_2, the binding energies were observed at 932.48, 952.11 eV which corresponds to Cu $2p_{1/2}$, Cu $2p_{3/2}$ and confirms the copper in metallic phase, disappearance of satellite peaks at corresponding positions also strongly confirms the reduction of Cu(II) to Cu(0) state.[15,16]

The HR-TEM Images of Cu(0)@Al_2O_3/SiO_2 catalyst with a Cu loading of 2.06 wt% are shown in Figure 3. The majority of NPs

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are spherical in shape with size in range of 4 to 6 nm and well dispersed in the mixed oxide support. The selected area electron diffraction (SAED) pattern obtained from the Copper nanoparticles depicts the characteristic Scherrer ring patterns of the face centered cubic (fcc) Copper (figure 3D).

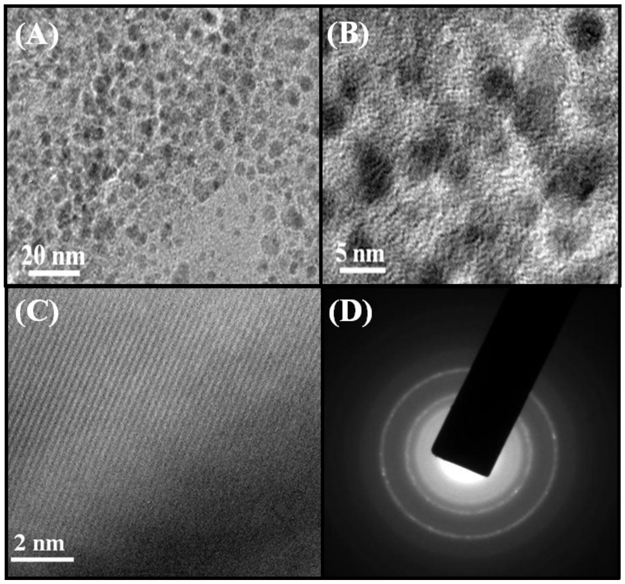
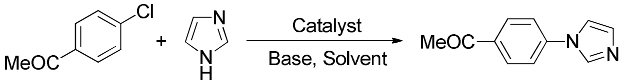


Figure 3. Low to high magnified HR-TEM images of Cu(0)@Al_2O_3/SiO_2[A, B and C] with SAED pattern[D].

The temperature programmed reduction (H_2-TPR) analysis was performed for Cu(0)@Al_2O_3/SiO_2 (fresh) and reused Cu(0)@Al_2O_3/SiO_2 (recovered after 5th run) catalysts to confirm the zero oxidation state of copper. The results revealed that no oxidation of copper nanoparticles (Cu(0)@Al_2O_3/SiO_2) was observed even after five successive runs, whereas Cu(II)@Al_2O_3/SiO_2 and CuO@Al_2O_3/SiO_2 showed reduction of Cu(II) to Cu(0) (ESI, Figure S2). Further the surface area of Alumina/Silica (Al_2O_3/SiO_2) and Cu(0)Al_2O_3/SiO_2 were determined by BET analysis. The increase in surface area of Al_2O_3/SiO_2 to Cu(0)@Al_2O_3/SiO_2 was found to be 220 and 240 m^2/g.

As shown in table 1, for the C-N cross coupling between *p*-chloroacetophenone and imidazole, various catalysts were screened to find an effective catalytic system for a successful conversion. Initially copper oxide nanoparticles impregnated on various supports like Al_2O_3, SiO_2, MgO, Al_2O_3/SiO_2 and hydrotalcite were prepared and screened for their catalytic ability. CuO NPs, CuO/Al_2O_3 and CuO/MgO (Table 1, entry 1-3) gave low yields. In case of Cu_2O and Cu-Al/HT and CuO/SiO_2 (Table 1, entry 4-6) the yields were moderate but increase in yields up to 80% was observed with CuO on Al_2O_3/SiO_2 (Table 1, entry 8). Recently, Cu(0) NPs have been reported for successful C-C cross-coupling reactions.[16] So, in order to check the veracity of Cu(0) in the present C-N cross-coupling reaction, Cu(0) NPs impregnated on Al_2O_3/SiO_2 were prepared. Amusingly, screening of Cu(0)@Al_2O_3/SiO_2 gave sharp increase in the yield (up to 96%, table 1, entry 14). As evident from Table 1, best results were obtained by using Cu(0)@Al_2O_3/SiO_2 catalyst with K_2CO_3 as a base and DMF as solvent. Additionally, the catalyst loading was halved (entry 15), but it was found that 5 mol% catalyst will suffice for an efficient reaction.

Table 1. Optimization study for *N*-arylation of imidazole with *p*-chloroacetophenone.[a]



Entry	Catalysts (mmol)	Solvents	Bases	Time [h]	Yield [%][b]
1	CuO NPs (5)	DMF	K_2CO_3	8	37
2	CuO/Al_2O_3 (5)	DMF	K_2CO_3	8	36
3	CuO/MgO (5)	DMF	K_2CO_3	8	24
4	Cu_2O (5)	DMF	K_2CO_3	8	50
5	Cu-Al HT (5)	DMF	K_2CO_3	8	42
6	CuO/SiO_2	DMF	K_2CO_3	8	57
7	CuO@Al_2O_3/SiO_2 (5)	DMSO	K_2CO_3	8	70
8	CuO@Al_2O_3/SiO_2 (5)	DMF	K_2CO_3	8	80
9	CuO@Al_2O_3/SiO_2 (5)	Dioxane	K_2CO_3	8	45
10	CuO@Al_2O_3/SiO_2 (5)	NMP	K_2CO_3	8	67
11	CuO@Al_2O_3/SiO_2 (5)	Xylene	K_2CO_3	8	52
12	Cu(0)@Al_2O_3/SiO_2(5)	NMP	K_3PO_4	4	60
13	Cu(0)@Al_2O_3/SiO_2 5)	DMSO	K_2CO_3	4	90
14	Cu(0)@Al_2O_3/SiO_2(5)	DMF	K_2CO_3	3	96
15	Cu(0)@Al_2O_3/SiO_2 (2.5)	DMF	K_2CO_3	4	75

[a] Reaction conditions: *p*-chloroacetophenone (1.0 mmol), imidazole (1.1mmol), catalyst (0.05 mmol), K_2CO_3 (1.5 mmol) and DMF (2 mL) were stirred under N_2 at 150 °C for appropriate time. [b] Isolated yield

A variety of substituted halo benzenes were coupled with imidazole, benzimidazole and triazoles in the presence of Cu(0)@Al_2O_3/SiO_2 catalyst leading to corresponding *N*-arylated products in good to excellent yields (Table 2, entries **1a**-**1s**). As expected, electron-withdrawing groups containing chloroarenes such as –$COCH_3$, -CN and –NO_2 gave excellent yields in shorter reaction times (Table 2, entries **1a**-**1f**) in comparison to halobenzenes having electron-donating groups (Table 2, **1g**-**1h** and **1j**-**1k**). Also, it was noticed that electron withdrawing groups such as –NO_2 or –CN present at *ortho*-position to the halide (leaving group) increased the yield of corresponding *N*-arylated products compared to the *meta*- and *para*- substituents (Table 2, entries **1a**-**1e**). Coupling of chlorobenzenes with benzimidazole and triazole was also performed and gave good results but 1*H*-benzimidazole was relatively difficult to react with, when compared to imidazole (Table 2, entries **1a** and **1r**). The expediency of this method was also checked with electron-deficient heteroaryl chlorides

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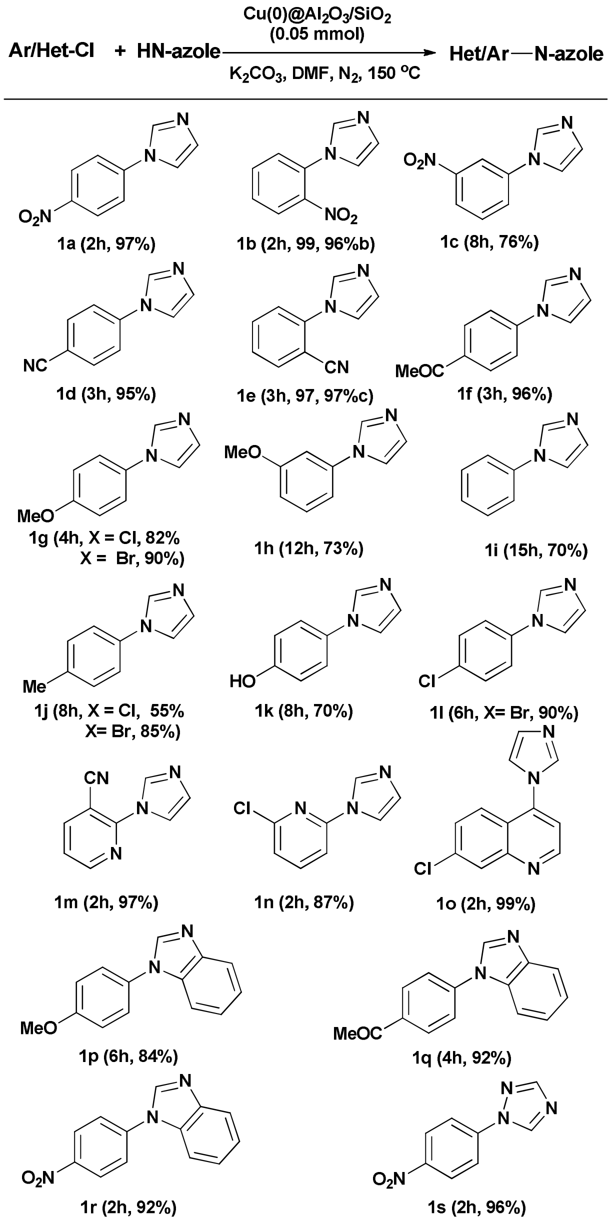
(Table 2, entries **1m**-**1o**). To our delight, the cross-coupling reaction with electron-deficient heteroaryl chlorides such as pyridine and quinoline has also shown excellent to good yields (87-99%)

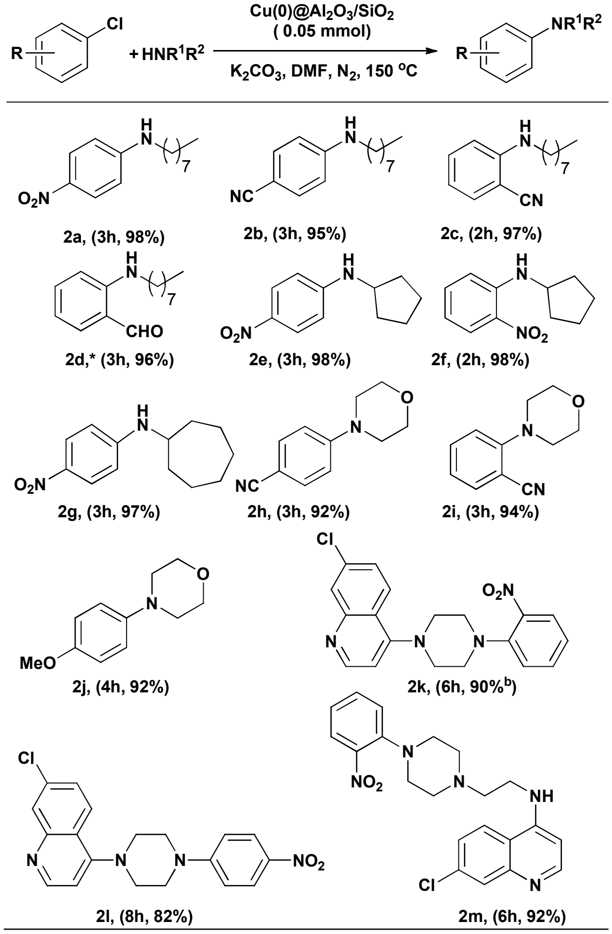
Table 2. Cu(0)@Al_2O_3/SiO_2 catalyzed *N*-arylation of heterocyclic amines with aryl chlorides[a]



[a]Reaction conditions: halo benzene (1 mmol), amine (1.1 mmol), Cu(0)@Al_2O_3/SiO_2 (0.05 mmol), K_2CO_3 (1.5 mmol) and DMF (2 mL) were stirred under N_2 at 150 °C for appropriate time; [b] Yield after fifth cycle; [c] Scaled up by factor 10 and isolated yield.

In order to study the versatility of the prepared catalyst, various aryl chlorides were successfully coupled with a variety of aliphatic primary and secondary amines under the optimized set of conditions. As observed before, the reactivity of aryl chlorides decreases as the electron-withdrawing nature of substituted groups decreases (Table 3, entries **2a**-**2j**). Presence of the electron-withdrawing groups at *ortho*-position of the aryl chlorides gave higher yields with shorter reaction-times compared to the corresponding *para*-substituted aryl chlorides (Table 3, entries **2b**-**2c** and **2e**-**2f**). It was also observed that the formyl substituent was oxidized to a carboxylic group during the reaction (Table 3, entry **2d**). which offers a method for the preparation of N-substituted amino-benzoic acids in a single step. The coupling of different chloroarenes with cycloalkylamines (cyclopentylamine and cyloheptylamine) and secondary cyclic amines (morpholine and *N*-substituted piperazines) was performed and reactions with the latter occurred at a relatively lower reaction time compared to reported methods and the results are summarized in Table 3 (Table 3, entries **2e**-**2m**).

Table 3: Cu(0)@Al_2O_3/SiO_2 catalysed amination of aryl chlorides with primary and secondary amines[a]



[a]Reaction conditions: halo benzene (1 mmol), amine (1.1 mmol), Cu(0)@Al_2O_3/SiO_2 (0.05 mmol), K_2CO_3 (1.5 mmol), DMF (2 mL) were stirred under N_2 at 150 °C for appropriate time, [b]scaled up by gram scale and isolated yield, *carbonyl group gets oxidised to carboxylic acid.

Further, in view of biological importance of anilines as intermediates for the synthesis of various active drug ingredients, the present methodology was explored for the synthesis of antimalarial aminoquinoline intermediates (Table 3, entries **2k**-**2m**). The gram scale reaction of 7-chloro-4-

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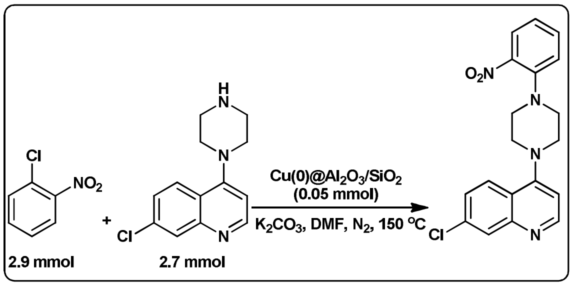
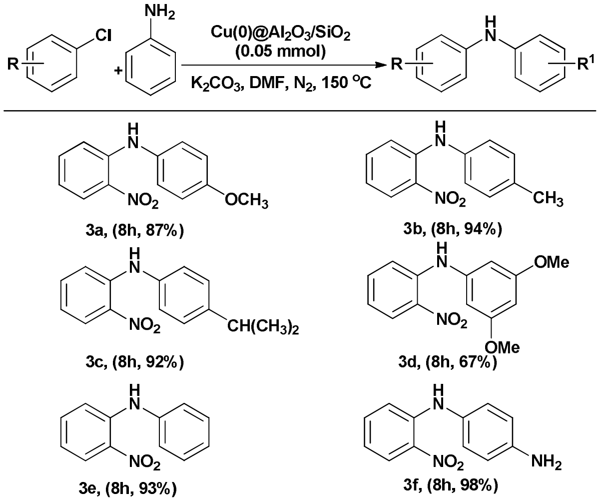
(piperazin-1-yl)quinoline (1 g, 2.7 mmol) with 1-chloro-2-nitrobenzene (0.45 g 2.9 mmol) offered desired 7-chloro-4-(4-(2-nitrophenyl)piperazin-1-yl)quinolone (**2k**) in 90% yield (Scheme 1).



Scheme 1. Gram scale synthesis of 7-chloro-4-(4-(2-nitrophenyl)piperazin-1-yl)quinoline (**2k**).

Next, we extended the scope of the catalyst by coupling different substituted anilines with 1-chloro-2-nitrobenzene. The electron-rich *p*-phenylenediamine gave excellent yield (98%, Table 4, entry **3f**). While the reaction with anilines containing electron-donating substituents (-methoxy, -methyl and -isopropyl) was satisfactory with 87-94% yields (Table 4, entries **3a**-**3c**), with 3,5-dimethoxyaniline, the yield was lower which can be attributed to the cumulative effect of the two methoxy groups present *meta*- to the aniline-group (Table 4, entry **3d**).

Table 4. $Cu(0)@Al_2O_3/SiO_2$ catalysed *N*-arylation of aryl chlorides with aniline[a]



[a] Reaction conditions: halo benzene (1 mmol), aniline (1.1 mmol), $Cu(0)@Al_2O_3/SiO_2$ (0.05 mmol), K_2CO_3 (1.5 mmol) and DMF (2mL) were stirred under N_2 at 150 °C for appropriate time, [b] Isolated yield.

The catalyst prepared during the course of study showed good catalytic activity for the C-N cross coupling reactions with a wide range of amines, anilines and heteroaromatic amines. Compared with other recent copper-based heterogeneous catalysts, the turnover number (TON) and turnover frequency (TOF) of the present catalyst exhibited higher values (19.8 and 9.9, Table 5). This, along with the amenability of the present catalyst towards gram scale synthesis of imidazole and quinoline analogues (**1d** and **2k**), proves the superiority of $Cu(0)@Al_2O_3/SiO_2$ over other copper based heterogeneous systems for C-N cross couplings.

Table 5. Comparison of $Cu(0)@Al_2O_3/SiO_2$ with reported catalysts for the synthesis of **1b**

S.no	Catalyst	Time [h]	Yield [%]	TON	TOF [h^{-1}]	Ref.
1	CuFAP	3	100	13.6	4.56	17
2	Nano-CuO	4	86	8.6	2.15	18
3	CuI, Indion-770	20	92	9.2	0.46	19
4	CuNPs/Mag-Si	18	87	8.1	0.47	8(a)
5	$Cu(0)@Al_2O_3/SiO_2$	2	99	19.8	9.9	Present

Recyclability study of $Cu(0)@Al_2O_3/SiO_2$

To check the robustness and re-usability of the catalyst after completion of the reaction, catalyst was separated by centrifugation and washed several times with ethyl acetate to remove organic impurities and re-used it for subsequent runs. Further, we examined the heterogeneity of catalyst by hot filtration method. The reaction was stopped and filtered at 50% conversion of starting materials and allowed to stir for further reaction time, no change in progress of the reaction indicating active catalyst was not leaching from the support. ICP-AES analysis of re-used catalyst also shown no leaching of Cu(0) from Al_2O_3/SiO_2.

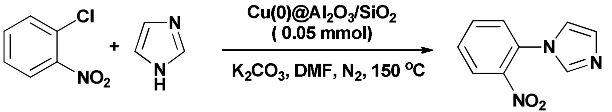


Table 6. Recyclable yields of **1b** up to five successive runs[a].

Yields of isolated product (%)					
Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
99	99	98	96	97	96

[a] Reaction conditions: *o*-chloro nitrobenzene (1 mmol), imidazole (1.1 mmol), $Cu(0)@Al_2O_3/SiO_2$ (150 mg, 0.05 mmol), K_2CO_3 (1.5 mmol) and DMF (2 mL) were stirred under N_2 at 150 °C for appropriate time.

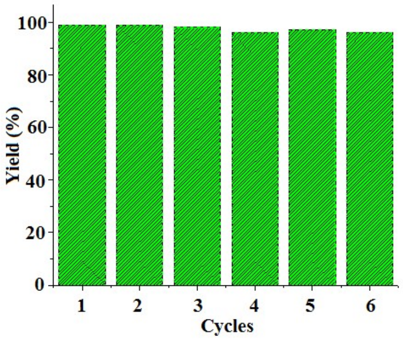


Figure 3. Recyclability of catalyst for synthesis of **1b** up to five successive runs.

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Experimental section

An oven dried 10 mL round bottom flask was charged with Dry DMF (2 mL), K_2CO_3 (1.5 mmol) and the catalyst (150 mg, 5 mol% of Cu(0)) and stirred for about 0.5 h under nitrogen, to this amine (1.1 mmol) and aryl chloride were added (1 mmol) and stirred further for about 0.5h under nitrogen atmosphere. The reaction flask is then transferred to a pre heated 150 ^{o}C oil bath and continued stirring for an appropriate reaction time. After completion of the reaction (progress was monitored by TLC at different time intervals) the reaction mixture was cooled to room temperature and the catalyst was recovered by centrifugation. The solid catalyst is washed several times with ethyl acetate to make the catalyst free of all the organic matter, the organic layers were dried over on Na_2SO_4 and then subjected to column chromatography (silica gel 100-200 mesh) using ethyl acetate and hexane as eluents to afford the desired *N*-alkylated/arylated product in excellent yields. The spectroscopic characterization of the product(s) is in conformation with the literature precedents.

Spectral data of selected compounds

7-chloro-4-(4-(2-nitrophenyl)piperazin-1-yl)quinoline (2k): Yellow solid, mp 177-179 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 5.04 Hz, 1H), 8.07 (d, *J* = 2.29 Hz, 1H), 7.99 (d, *J* = 8.70 Hz,1H), 7.82 (dd, *J* = 8.24 Hz, *J* = 1.83 Hz, 1H), 7.59-7.53 (m, 1H), 7.45 (dd, *J* = 8.70 Hz, *J* = 1.83 Hz, 1H), 7.30-7.27 (m, 1H), 7.18-7.11 (m, 1H), 6.91 (d, J = 5.04 Hz, 1H), 3.42-3.33 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 152.0, 150.1, 145.6, 144.0, 134.9, 133.5, 128.9, 126.3, 125.8, 124.9, 122.7, 121.8, 121.4, 109.3, 52.2, 51.8; IR (cm^{-1}, Film): 2924, 2850, 1595, 1498, 1320, 1237, 1115, 754; ESI-HRMS (m/z) Anal. Calcd. for $C_{19}H_{18}ClN_4O_2$: 369.1113 (MH)$^+$; Found: 369.1119 (MH)$^+$.

7-chloro-N-(2-(4-(2-nitrophenyl)piperazin-1-yl)ethyl)quinolin-4-amine (2m): Yellow solid, mp 103-105; ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ = 8.41 (s, 1H), 8.05 (s, 1H), 7.92 (d, *J* = 8.70 Hz, 1H), 7.79-7.75 (m, 1H), 7.53-7.47 (m, 1H), 7.38 (d, *J* = 8.70 Hz, 1H), 7.17 (d, *J* = 8.24 Hz, 1H), 7.07 (t, *J* = 7.79 Hz, 1H), 6.43 (d, *J* = 4.58 Hz, 1H), 3.73 (brs, 1H, *NH*), 3.51-3.44 (m, 2H), 3.18-3.10 (m, 4H), 2.90 (t, *J* = 5.50 Hz, 2H), 2.78-2.71(m, 4H); ^{13}C NMR (100 MHz, DMSO): δ = 151.9, 149.9, 149.0, 134.1, 133.3, 131.5, 128.7, 127.5, 125.6, 124.8, 124.1, 123.9, 117.3, 98.7, 56.5, 54.3, 45.6; IR (cm^{-1}, Film): 3360, 3011, 2923, 2852, 1668, 1607, 1578, 1520, 1484, 1217, 744; ESI-HRMS (m/z) Anal. Calcd. for $C_{21}H_{23}ClN_5O_2$: 412.1535 (MH)$^+$; Found: 412.1549 (MH)$^+$.

N-(4-isopropylphenyl)-2nitroaniline (Table 4, Entry 3c): Thick oil; ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.48 (brs, 1H, N*H*), 8.19 (dd, *J* = 8.70 Hz, *J* = 1.83 Hz, 1H), 7.37-7.32 (m, 1H), 7.30-7.25 (m, 2H), 7.22-7.16 (m, 3H), 6.77-6.71 (m, 1H), 3.00-2.88 (m, 1H), 1.32-1.24 (d, *J* = 6.87 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.6, 143.6, 136.1, 135.6, 132.7,127.6, 126.5, 124.7, 117.0, 115.9, 33.6, 23.9; IR (cm^{-1}, Film): 3355, 3022, 2961, 2964, 2858, 1611, 1574, 1503, 1406, 1348, 1261, 747; ESI-HRMS (m/z) Anal. Calcd. For $C_{15}H_{17}N_2O_2$: 257.1285 (MH)$^+$; Found: 257.1281 (MH)$^+$.

3,5-dimethoxy-N-(2-nitrophenyl)aniline (Table 4, Entry 3d): Brown solid, mp 85-87; ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.41 (brs, 1H, *NH*), 8.19 (d, *J* = 8.39 Hz, 1H), 7.42-7.30 (m, 2H), 6.78 (t, *J* = 7.63 Hz, 1H), 6.43 (d, *J* = 2.29 Hz, 2H), 6.33 (t, *J* = 2.29 Hz, 1H), 3.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.6, 142.5, 140.4, 135.6, 133.3, 126.5, 117.6, 116.6, 102.1, 97.5, 54.4; IR (cm^{-1}, Film): 3355, 3018, 2927, 2852, 1600, 1504, 1469, 1270, 1213, 1157, 751; ESI-HRMS (m/z) Anal. Calcd. For $C_{14}H_{15}N_2O_4$: 275.1026 (MH)$^+$; Found: 275.1056 (MH)$^+$.

N1-(2-nitrophenyl)benzene-1,4-diamine (Table 4, Entry 3f): Brown solid mp 111-113; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (brs, 1H, *NH*), 8.21-8.15 (m, 1H), 7.33-7.27 (m, 1H), 7.05 (d, *J* = 8.39 Hz, 1H), 6.97 (d, *J* = 8.39 Hz, 1H), 6.73 (d, *J* = 8.39 Hz, 2H), 6.71-6.65 (m, 1H), 3.74 (brs, 2H, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.9, 135.6, 132.1, 129.0, 127.3,126.5, 116.3, 115.9, 115.8, 102.3; IR (cm^{-1}, Film): 3358, 3021, 1619, 1507, 1412, 1351, 1260, 1215, 745; ESI-HRMS (m/z) Anal. Calcd. For $C_{12}H_{12}N_3O_2$: 230.0924 (MH)$^+$; Found: 230.0924 (MH)$^+$.

Conclusion

We have developed a simple, efficient, environmentally-benign and cost-effective heterogeneous copper catalytic system for the efficient C-N cross coupling of different chlorobenzenes with a variety of amines, anilines and heterocyclic amines under ligand-free conditions at relatively mild conditions. The present work provides an improved protocol that obviates the need of high stoichiometric amounts of Cu-catalyst for C-N bond formation reactions. Moreover, this recyclable heterogeneous catalyst viz. Cu(0)@Al_2O_3/SiO_2 offers several advantages including simplicity in handling, easy purification, and high yields in relatively shorter reaction times. Furthermore the use of Al_2O_3/SiO_2 as support for impregnation of copper paves a way for the industrial use of copper in the synthesis of amines with challenging aryl chlorides, the catalyst was recyclable which makes this approach efficacious and atom-economical To the best of our knowledge Al_2O_3/SiO_2 support is used fist time for the amines synthesis.

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