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Copper oxide nanoparticles-catalyzed direct N-alkylation of amines with alcohols

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ABSTRACT

This paper describes the direct N-alkylation of amines with alcohols through oxidation/imination/reduction sequence using a catalytic amount of nanocrystalline CuO as a recyclable catalyst and K_2CO_3 as the base in toluene at 110 °C. This method is found to be applicable for wide range of amines and alcohols. The operational simplicity and the mild reaction conditions add to the value of this method as a practical alternative to the N-alkylation of amines with alcohols.

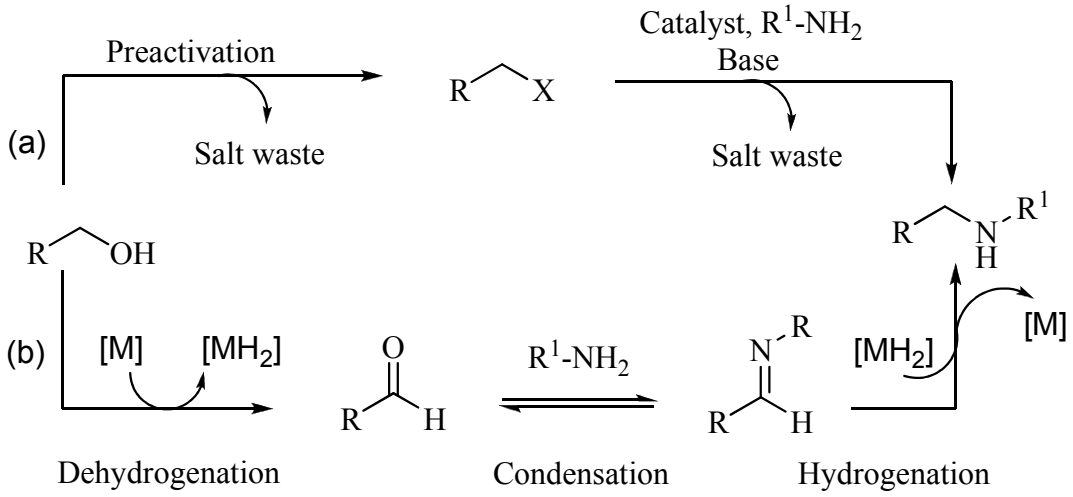
Key words: N-alkylation, benzyl alcohols, amines, CuO nanoparticles, reusability.

INTRODUCTION

Amines and their derivatives are of fundamental importance as naturally occurring bio-active compounds such as alkaloids, amino acids and nucleotides contain amino groups, which are particularly useful for the development of new pharmaceuticals and agrochemicals.[1] Consequently, the development of improved methods for the synthesis of amines continues to be an intense focus of research.[2]

Traditionally, the alkylation of amines is achieved using conventional alkylating agents, such as alkyl halides. There can be selectivity problems in such reactions when control of multiple alkylation can be difficult and many alkyl halides have toxic or even mutagenic properties and an alternative to using such reagents is therefore advantageous.[3] Alternatively, in recent years a number of reports on the hydroamination[4] or hydroamino-methylation of olefins or alkynes[5] for the synthesis of amines have been reported. Compared to the frequently applied N-alkylations with alkyl halides and reductive aminations, an economically and environmentally attractive method is the N-alkylation of amines using primary and secondary alcohols. This domino reaction sequence involves in situ dehydrogenation of the alcohol to give the corresponding carbonyl compound, which on subsequent imination followed by reduction with the initially produced hydrogen leads to the formation of the N-alkylated amine (Scheme 1). The advantages of this method are the ubiquitous availability of alcohols and high atom efficiency, for example,

no salt formation and water as the only by-product. Moreover, compared to reductive aminations, it is possible to run these reactions in the absence of hydrogen pressure.

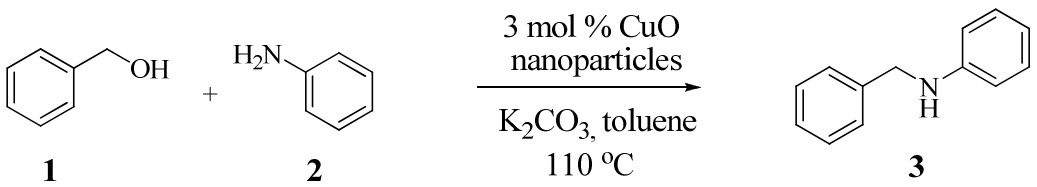


Scheme 1. N-Alkylation of amines with alcohols by (a) preactivation and (b) catalytic hydrogen transfer reactions.

Amination reactions of alcohols, which proceed via oxidation/imination/reduction sequence,[3] have been studied using several catalytic systems such as ruthenium,[6] rhodium,[7] platinum,[8] and iridium catalysts[9] under homogeneous conditions. Although the reported catalysts are active for this reaction, they are significantly more expensive and not recoverable. Industry favours the catalytic process induced by a heterogeneous catalyst over the homogeneous one in view of its ease of handling, simple workup and regenerability. Recently, Likhar et al. have reported the amination of alcohols using copper-aluminium hydrotalcite as the catalyst under heterogeneous conditions.[10] However, heterogenized catalyst generally require tedious preparation and/or separation procedures. In view of the above, there is a need to find new materials with speciality properties in order to overcome these limitations.

Recently, organic reactions catalyzed by metal/metal oxide nanoparticles has attracted much attention. The notable advantages of this novel family of heterogeneous catalysts, such as high catalytic activity, good recyclability and improved selectivity, extend to a wide-range of applications in various organic reactions.[11] Recently, copper oxide nanoparticles (CuO NPs) has been employed as a heterogeneous catalyst for various organic transformations.[12] This inspired us to focus on the aspect of CuO NPs catalysis for the N-alkylation of amines using primary alcohols.

We report herein, our investigations on the application of CuO NPs [13] for the practical and atom-economic N-alkylation of amines using primary alcohols through oxidation/imination/reduction sequence in the presence of K_2CO_3 as the base (Scheme 2).



Scheme 2

MATERIALS AND METHODS

All chemicals were purchased from Sigma-Aldrich and S.D Fine Chemicals, Pvt. Ltd. India and used as received. ACME silica gel (100–200 mesh) was used for column chromatography and thin-layer chromatography was performed on Merck-precoated silica gel 60-F_{254} plates. All the other chemicals and solvents were obtained from commercial sources and purified using standard methods. The IR spectra of all compounds were recorded on a Perkin-Elmer, Spectrum GX FTIR spectrometer. The IR values are reported in reciprocal centimeters (cm^{-1}).

The ^{1}H, ^{13}C NMR spectra were recorded on a Varian- 400 MHz, Bruker-Avance 300 MHz Spectrometer. Chemical shifts (δ) are reported in ppm, using TMS (δ =0) as an internal standard in $CDCl_3$. ESI mass spectra were recorded on a Finnigan LCQ Advantagemax spectrometer. EI mass spectra were recorded on a GC-MS QP2010 Plus (Shimadzu).

Typical procedure for the N-alkylation of amines with alcohols: A mixture of amine (1 mmol) alcohol (1.2 mmol), K_2CO_3 (1.5 mmol) and CuO NPs (3 mol %) in toluene (3 mL) was stirred at 110 ^{o}C temperature for 12 h. After completion of the reaction as indicated by TLC, the reaction mixture was centrifuged to separate the catalyst, the solid residue was washed with EtOAc to make the catalyst free of organic matter, and the reaction mixture was diluted with water and then extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo* and purified by column chromatography on silica gel to afford the pure product. All products were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopic techniques.

Spectroscopic data for the representative examples:

1. Benzyl-phenyl-amine: (Table 2, entry 1): IR (neat): 3418, 2923, 1735, 1601, 1505, 1252, 1069, 749 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93 (brs, 1H), 4.31 (brs, 2H), 6.56 (d, 2H, *J* = 7.8 Hz), 6.65 (t, 1H, *J* = 7.2 Hz), 7.11 (d, 2H, *J* = 7.5 Hz), 7.21 – 7.35 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.26, 112.70, 117.5, 127.2, 127.4, 128.6, 129.2, 139.4, 148. ESI MS (*m/z*): 184 (M + H).

2. (4-Methoxy-benzyl)-phenyl-amine (Table 2, entry 2): Pale yellow oil; R_f = 0.7 (in hexane/ethyl acetate 90:10). IR (neat): 749, 1032, 1175, 1244, 1507, 1604, 2835, 3415 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H), 3.83 (brs, 1H), 4.21 (s, 2H), 6.56 (d, 2H, *J* = 7.6 Hz), 6.64 (t, 1H, *J* = 7.4 Hz), 6.81 (d, 2H, *J* = 8.5 Hz), 7.11 (m, 2H), 7.24 (d, 2H, *J* = 8.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.7, 55.2, 112.7, 113.9, 117.4, 128.7, 129.2, 131.3, 148.1, 158.8. ESI MS (*m/z*): 214 (M + H).

3. (4-Methyl-benzyl)-phenyl-amine (Table 3, entry 3): IR (neat): 3418, 2920, 1603, 1507, 1322, 1255, 1179, 749 cm^{-1} ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.34 (s, 3H), 3.86 (brs, 1H), 4.23 (s, 2H), 6.54 (d, 2H, *J* = 7.6 Hz), 6.64 (t, 1H, *J* = 7.4 Hz), 7.06 – 7.14 (m, 4H), 7.20 (d, 2H, *J* = 7.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 48.1, 112.8, 117.5, 127.5, 129.2, 136.3, 136.8, 148.2. ESI MS (*m/z*): 198 (M + H).

4. (4-Bromo-benzyl)-phenyl-amine (Table 2, entry 4): IR (neat): 3417, 1735, 1601, 1505, 1231, 750 cm^{-1} ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (brs, 1H), 4.29 (s, 2H), 6.60 (d, 2H, *J* = 8.7 Hz), 6.72 (t, 1H, *J* = 7.3 Hz), 7.17 (m, 2H), 7.25 (d, 2H, *J* = 8.1 Hz), 7.46 (d, 2H, *J* = 8.1 Hz). ^{13}C

NMR (75 MHz, $CDCl_3$): δ 47.8, 113.2, 118.1, 129.1, 129.3, 129.9, 138.2, 147.2. ESI MS (*m/z*): 262 (M^+), 264 (M + 2).

5. 4-Phenylaminomethyl-phenol (Table 2, entry 5): IR (KBr): 3386, 1603, 1510, 1236 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 4.21 (s, 2H), 4.50 (brs, 1H), 5.28 (s, 1H), 6.56 (d, 2H, *J* = 7.6 Hz), 6.67 (t, 1H, *J* = 7.2 Hz), 6.73 (d, 2H, *J* = 8.6 Hz), 7.11 (2H, t, *J* = 7.3 Hz), 7.20 (d, 2H, *J* = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.8, 113.1, 115.4, 117.7, 128.9, 129.2, 131.2, 148, 154.7. ESI MS (*m/z*): 200 (M + H)

6. Benzo[1,3]dioxol-5-ylmethyl-phenyl-amine (Table 2, entry 6): IR (KBr): 3410, 1602, 1497, 1443, 1429, 1035, 746 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.96 9 (brs, 1H), 4.20 (s, 2H), 5.91 (s, 2H), 6.61 (d, 2H, *J* = 7.7 Hz), 6.68 – 6.85 (m, 4H), 7.16 (t, 2H, *J* = 7.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.8, 100.7, 107.8, 108.1, 112.7, 117.4, 120.4, 129.1, 133.2, 146.5, 147.7, 147.9. ESI MS (*m/z*): 228 (M + H).

7. **Phenyl-thiophen-2-ylmethyl-amine (Table 2, entry 7):** Yellow oil; R_f = 0.4 (in hexane/ethyl acetate 95:5). IR (KBr): 696, 750, 1258, 1315, 1504, 1601, 2923, 3409 cm^{-1}.^1H NMR (300 MHz, $CDCl_3$): δ 3.38 (brs, 1H), 4.47 (s, 2H), 6.60 (d, 2H, *J* = 7.5 Hz), 6.68 (t, 1H, *J* = 7.5 Hz), 6.91 (t, 1H, *J* = 3.0 Hz), 6.96 (s, 1H), 7.07-7.14 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.4, 113.1, 114.2, 118.1, 124.5, 125.0, 126.7, 129.2. EI MS (*m/z*): 189 (M^+).

8. **Cyclohexyl methyl-phenyl-amine (Table 2, entry 8):** IR (KBr): 747, 1506, 1603, 3418, 2923, 1603, 1506, 747 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.88-0.90 (m, 11H), 3.58 (brs, 1H), 6.50 (d, 2H, *J* = 7.5Hz), 6.60 (t, 1H, *J* = 7.5Hz), δ 7.09 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.9, 26.5, 31.2, 37.5, 50.5, 112.5, 116.8, 129.1, 148.5. EI MS (*m/z*): 189 (M^+).

9. Butyl-phenyl-amine (Table 2, entry 9): IR (neat): 3410, 2957, 1603, 1506, 1320, 747 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, 3H, *J* = 7.1 Hz), 1.38 – 1.50 (m, 2H), 1.56 - 1.65 (m, 2H), 3.10 (t, 2H, *J* = 6.9 Hz), 3.47 (brs, 1H), 6.52 (d, 2H, *J* = 7.7 Hz), 6.61 (t, 1H, *J* = 7.4 Hz), 7.06 – 7.12 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 20.3, 31.6, 43.6, 112.6, 116.9, 129.1, 148.5. ESI MS (*m/z*): 150 (M + H).

10. Isobutyl-phenyl-amine (Table 3, entry 10): IR (neat): 3418, 2957, 1603, 1507, 1320, 1259, 748 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.99 (d, 6H, *J* = 6.6 Hz), 1.82 – 1.96 (m, 1H), 2.92 (d, 2H, *J* = 6.8 Hz), 3.66 (brs, 1H), 6.52 (d, 2H, *J* = 7.5 Hz), 6.61 (t, 1H, *J* = 7.2 Hz), 7.09 (t, 2H, *J* = 7.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 28.1, 51.8, 112.7, 117.1, 129.1, 148.5. ESI MS (*m/z*): 150 (M + H).

11. N,N'-(1,4-phenylenebis(methylene))dianiline (Scheme 3): White solid; R_f = 0.3 (hexane/ethyl acetate 90:10). IR (KBr): 3448, 2919, 1603, 1507, 1324, 1174, 748 cm^{-1}.^1H NMR (300 MHz, $CDCl_3$): δ 3.93 (s, 2H), 4.31 (s, 4H), 6.58 (d, 4H, *J* = 7.8 Hz), 6.68 (t, 2H, *J* = 7.8 Hz), 7.11 – 7.14 (m, 4H), 7.33 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.3, 112.9, 117.5, 127.6, 129.4, 1383, 148.2. ESI MS (*m/z*): 289 (M+H).

12. Benzyl-(4-chloro-phenyl)-amine (Table 3, entry 1): IR (KBr): 3412, 2831, 1618, 1506, 1419, 1321, 1072, 791 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.95 (brs, 1H), 4.28 (s, 2H), 6.49 (d, 2H, *J* =8.8 Hz), 7.06 (d, 2H, *J* = 8.8 Hz), 7.23 – 7.31 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.3, 113.9, 122.1, 127.4, 128.7, 129.1, 138.9, 146.7. ESI MS (*m/z*): 218 (M + H).

13. Benzyl-(4-fluoro-phenyl)-amine (Table 3, entry 2): IR (neat): 3414, 2930, 1616, 1512, 1457, 1236, 1033 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.84 (brs, 1H), 4.26 (s, 2H), 6.50 (d, 2H, *J* = 8.8 Hz), 6.83 (d, 2H, *J* = 8.8 Hz), 7.22 – 7.32 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.8, 113.6, 115.4, 115.7, 127.4, 128.6, 139.2, 144.4, 157.3. ESI MS (*m/z*): 202 (M + H).

14. Benzyl-p-tolyl-amine (Table 3, entry 3): IR (neat): 3419, 3019, 1609, 1512, 1473, 1355, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 3.80 (brs, 1H), 4.28 (s, 2H), 6.49 (d, 2H, *J* = 8.5 Hz), 6.99 (d, 2H, *J* = 8.5 Hz), 7.21 – 7.35 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 48.5, 112.9, 126.5, 127.0, 127.4, 128.5, 129.6, 139.5, 145.8. ESI MS (*m/z*): 198 (M +H).

16. Benzyl-o-tolyl-amine (Table 3, entry 4): IR (neat): 3068, 3019, 2831, 1612, 1512, 1430, 1279 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H), 3.81 (brs, 1H), 4.38 (s, 2H), 6.58 (d, 1H, *J* = 7.6 Hz), 6.63 (t, 1H, *J* = 7.6 Hz), 7.01 – 7.07 (m, 2H), 7.25 – 7.38 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.2, 109.9, 117.1, 121.8, 127.1, 127.5, 128.6, 130.0, 139.4, 146.0. ESI MS (*m/z*): 198 (M +H).

17. Benzyl-(4-methoxy-phenyl)-amine (Table 3, entry 5): IR (KBr): 3375, 2944, 1629, 1511, 1456,1236, 1033, 820 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.72 (s, 3H), 4.24 (s, 2H), 6.52 (d, 2H, *J* = 9.0 Hz), 6.70 (d, 2H, *J* = 9.0 Hz), 7.21 – 7.35 9 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 48.9, 55.5, 113.8, 114.6, 126.9, 127.3, 128.4, 139.5, 142.2, 151.9. ESI MS (*m/z*): 214 (M + H).

18. 4-Benzylamino-phenol (Table 3, entry 6): IR (KBr): 3381, 2920, 1614, 1507, 1239,1072 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.88 (brs, 2H), 4.24 (s, 2H), 6.48 (d, 2H, J = 8.0 Hz), 6.62 (d, 2H, J = 8.7 Hz), 7.20 – 7.33 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.5, 114.8, 116.3, 127.2, 127.7, 128.6, 139.4, 141.9, 148.2. ESI MS (*m/z*): 200 (M +H).

19. *N*-benzyl-4-(benzyloxy) aniline (Table 3, entry 7): IR (KBr): 3392, 2922, 1723, 1511, 1452, 1234, 1020, 820, 736, 694, 584 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.65 (brs, 1H), 4.25 (s, 2H), 4.95 (s, 2H), 6.52 (d, 2H, *J* = 8.6 Hz), 6.76 (d, 2H, *J* = 8.8 Hz) 7.15-7.44 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 49.4, 70.7, 113.9, 116.0, 127.1, 127.4, 127.7, 128.4, 128.5, 137.5, 139.6, 142.6. ESI MS (*m/z*): 290 (M+H).

20. 4-(Benzylamino)benzoic Acid (Table 4, Entry 4): ^1H NMR (300 MHz, CDCl3): *δ* 8.10 (d, *J* = 8.4 Hz, 2 H), 7.40–7.25 (m, 5H), 6.55 (d, *J* = 8.4 Hz, 2 H), 4.75 (br. s, 1 H), 4.40 (s, 2 H). 13C NMR (75 MHz, CDCl3): *δ* = 170.3, 153.1, 138.2, 137.3, 130.2, 128.9, 127.2, 126.3, 117.4, 111.2, 47.5 ppm. EI-MS (*m/z*): 228 $[M + H]^+$.

RESULTS AND DISCUSSION

In our initial studies, an assortment of bases in combination with different solvents were investigated using CuO NPs as the catalyst, benzyl alcohol and aniline as model substrates for the synthesis of N-alkylated amines (Table 1). The conditions were optimized and the best condition was found to be 3 mol % of CuO NPs, 1.5 eq of K_2CO_3 with toluene as the solvent and the results are summarized in Table 1, entry 1. By virtue of these optimized conditions, the reaction afforded the desired product in 88 % yield. The reaction with $CsCO_3$, Li_2CO_3, $NaHCO_3$ and CH_3COONa gave the product in moderate yield (Table 1, entries 3-6). However, the reaction with other bases such as Na_2CO_3, KO^{t}Bu and NaO^{t}Bu gave the desired product in good yield (Table 1, entries 2, 7-8). Subsequently, the reaction conditions were optimized by employing different solvents. Thus, various polar and non polar solvents were examined and it

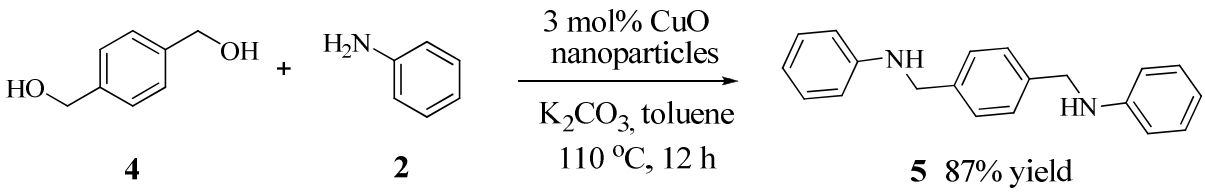
was found that the product was obtained in moderate yield with 1, 4 dioxane and all other solvents had negative influence on the reaction and no product was formed (Table 1, entry 9-10).

Table 1. Solvent and base screening for the CuO NPs catalyzed N-alkylation of aniline with benzyl alcohol.[a]

entry	solvent	base	yield (%)
1	toluene	K_2CO_3	88
2	toluene	Na_2CO_3	80
3	toluene	$CsCO_3$	60
4	toluene	Li_2CO_3	52
5	toluene	$NaHCO_3$	65
6	toluene	CH_3COONa	50
7	toluene	NaO^tBu	80
8	toluene	KO^tBu	85
9	1,4 dioxane	K_2CO_3	60
10	THF, ACN DMF, DMSO	K_2CO_3	trace

[a]*Reaction conditions: aniline (1 mmol), benzyl alcohol (1.2 mmol), CuO NPs (3 mol %), solvent (3mL) and base (1.5 equiv) at 110 ^oC for 12 h.*

Under the optimized reaction conditions, the scope of the reaction was explored with structurally and electronically diverse alcohols with wide range of amines. The alcohols used for this study included examples of benzylic, aliphatic and heterocyclic. As shown in the Table 2, irrespective of the electronic nature of the substituent, benzyl alcohols reacted smoothly to give the corresponding products in good yields even with a benzyl alcohol bearing a substituent at ortho-position. (Table 2, entries 1-6). Whereas, heteroaromatic alcohol (thiophen-2-ylmethanol) gave the corresponding product in moderate yield (Table 2, entry 7).



Scheme 3

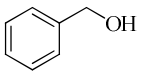
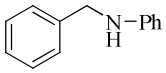
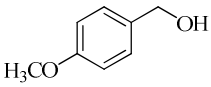
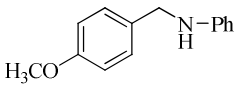
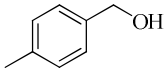
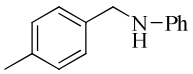
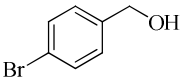
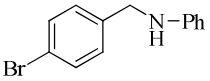
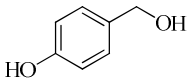
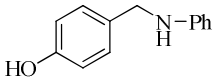
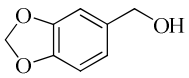
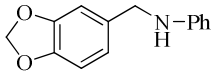
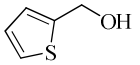
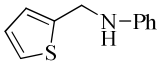
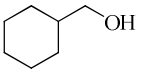
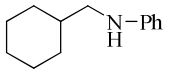
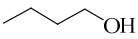
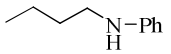
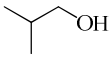
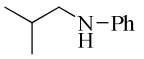
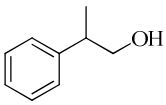
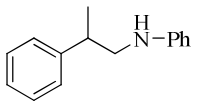
On the other hand, aliphatic alcohols regardless of whether they are linear or branched underwent the reaction smoothly and gave the N-alkylated products in good yields (Table 2, entries 8-10).

To show the convenience of our approach for the synthesis of multivalent structures, 1,4-phenylenedimethanol and aniline were reacted under the optimized reaction conditions to afford N,N'-(1,4-phenylenebis(methylene))dianiline in high yield, showing the versatility of the catalytic system for generating multivalent structures (Scheme 3).

In light of these excellent results, to evaluate the usefulness of the present N-alkylation system, various anilines were subjected to the N-alkylation with benzyl alcohol, in order to explore the

scope of amine substrates (Table 3). Chloro, fluoro, methoxy, methyl, hydroxy, acetyl substituents were tolerant in the present reaction system.

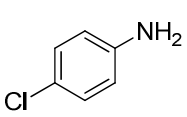
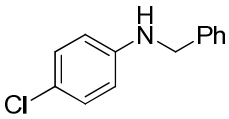
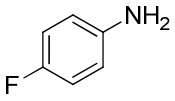
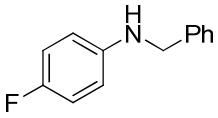
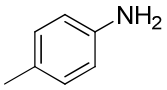
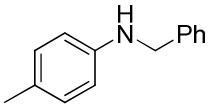
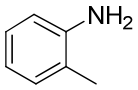
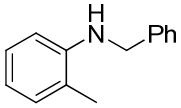
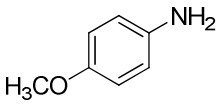
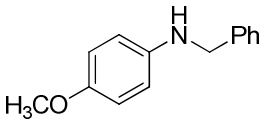
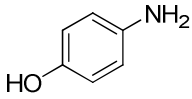
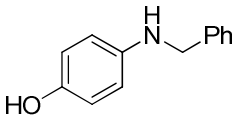
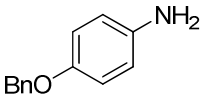
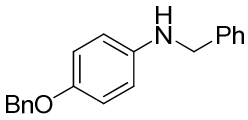
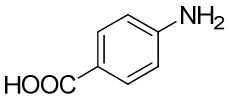
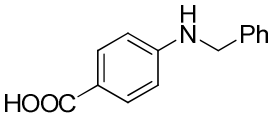
Table 2. Direct N-alkylation of aniline with different substituted benzyl alcohols and aliphatic alcohols.[a]

entry	alcohol	product	yield (%)
1			88
2			85
3			94
4			90
5			87
6			90
7			60
8			90
9			86
10			84
11			92

[a]*Reaction conditions as exemplified in typical experimental procedure.*

All of these reactions resulted in the selective formation of mono-alkylated arylamines in good to excellent yields. Even with *o*-toluidine bearing a substituent at ortho-position, the reaction proceeded in an excellent yield (Table 3, entry 4). In the reaction with 4-amino benzoic acid having electron- withdrawing substituent acetyl group, gave the product in moderate yield (Table 3, entry 8).

Table 3. Direct N-alkylation of different amines with benzyl alcohol.[a]

Entry	Aniline	Product	Yield (%)
1			87
2			85
3			92
4			84
5			87
6			81
7			86
8			72

[a]*Reaction conditions as exemplified in typical experimental procedure.*

Table 4. Recovery and reuse of CuO NPs for the N-alkylation of aniline with benzyl alcohol[a]

Entry	Run	Yield (%)
1	1	88
2	2	85
3	3	86
4	4	82

[a]*Reaction conditions: aniline (5 mmol), benzyl alcohol (6 mmol), CuO NPs (3 mol %), K_2CO_3 (1.5 equiv) and toluene (10 mL) at 110 ^oC for 12 h.*

To check the recyclability of the catalyst, as can be seen from the Table 4, after the reaction of aniline with benzyl alcohol had reached completion, the catalyst was recovered from the reaction

mixture by centrifugation and reused up to four times without significant loss of catalytic activity.

CONCLUSION

In conclusion, we have developed a CuO NPs catalyzed direct N-alkylation of amines with alcohols under ligand-free conditions. The present new catalytic system can provide an environmentally benign and versatile protocol for the synthesis diverse range of N-alkyl amines in good to excellent yields. The catalyst can be easily recovered and reused for several times without any significant loss of activity.

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[13] CuO nano particles (mean particle size, 33 nm, surface area, 29 m^2/g and purity, 99.99%) were purchased from Sigma Aldrich.