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Cu-Oxide Nanoparticles Catalyzed Synthesis of Nitriles and Amides from Alcohols and Ammonia in Presence of Air

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The synthesis and functionalization of nitrogen-containing compounds continue to be important due to their wide applications. In particular, the preparation of nitriles and amides applying cost-effective and green methodologies is of central importance because these products represent valuable fine and bulk chemicals and serve as key precursors and central intermediates in organic synthesis and drug discovery as well as materials. Here, the preparation of nitriles and primary amides from alcohols and ammonia by a heterogeneous Cu-catalyzed aerobic oxidation process is reported. The optimal catalyst for this synthesis is based on supported copper oxide-nanoparticles, which are prepared by the impregnation and pyrolysis of simple copper nitrate on carbon. Applying these reusable nanoparticles, various simple, substituted, and functionalized aromatic, heterocyclic, and aliphatic nitriles are synthesized starting from inexpensive and easily accessible alcohols and ammonia in the presence of air. In addition, the synthesis of selected primary amides in a water medium is also performed using these Cu nanoparticles.

1. Introduction

The development of cost-effective and sustainable catalytic methodologies for the synthesis and functionalization of nitrogen-containing compounds, which represent highly valuable and widely used products, continues to be important.[1–11] Among N-containing compounds, nitriles[3–7] and amides[8–11] constitute valuable fine and bulk chemicals, which are used as precursors and intermediates for essential chemical products, pharmaceuticals, agrochemicals, and biomolecules as well as materials. Noteworthy, nitrile and amide functionalities serve as vital motifs in many life science molecules.[5–13] Regarding the synthesis of nitriles, simple ones are produced industrially by ammoxidations, which in general are performed in the gas phase at drastic conditions (>300 °C).[12–14] Unfortunately, these reactions cannot be applied to the synthesis of structurally challenging nitriles.[12–14] On the other hand, the preparation of functionalized nitriles still relies on nucleophilic cyanation reactions of aryl or alkyl halides using toxic and waste-generating reagents such as HCN or metal cyanides.[15,16] For a sustainable point of view, the synthesis of functionalized and structurally diverse nitriles from inexpensive and easily accessible starting materials using green and more abundant reagents is highly beneficial and scientifically interesting. In this regard, the preparation of nitriles from alcohols and ammonia by catalytic aerobic oxidations is considered to be an appropriate and green methodology.[17–28]

In general, the creation of an amide bond is of fundamental importance in organic synthesis, medicine, and biology.[8–11] Classically, primary amides are prepared by the reaction of activated carboxylic acid derivatives such as chlorides and anhydrides with ammonia or from carboxylic acids with ammonia in presence of coupling agents.[11,29–31] However, these methodologies employ stoichiometric quantities of activating reagents, which generate significant amounts of wastes and are low atom-efficient reactions. Notably, the catalytic synthesis of primary amides starting from alcohols and ammonia in water represents a convenient and green methodology.[18,32–34]

Noteworthy, alcohols serve as potential feedstocks to produce various chemicals because they are easily accessible and inexpensive as well as some of them can be obtained from renewable resources.[35–37] Hence, alcohols are considered as suitable starting materials for the synthesis of nitriles and amides.[17–29,32–34] The other starting, ammonia is an abundant and green chemical, which is produced in >175 million tons per year scale.[38,39] Noteworthy, this bulk chemical is extensively used to produce urea and other fertilizers as well as various fine and bulk chemicals.[38,39] In order to synthesize nitriles

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and amides from alcohols, the use of an oxidant is essential. Among various oxidants, the air is "ideal" because it is more abundant, inexpensive, green, safer to use, and produces only water as the by-product.[40]

To carry out aerobic oxidation of alcohols to prepare nitriles and amides the applicability of catalysts is crucial. In the past, catalysts based on heterogeneous Au, Ru, Fe, Co, Mn, and V,[17–28] as well as homogeneous Fe-[23] and Cu-[22] based ones have been successfully applied for the synthesis of various nitriles from alcohols and ammonia; most of these utilize molecular oxygen as oxidant. For the synthesis of primary amides from alcohols and ammonia Mn, Co, V, and Au-[18,28,32–34] based systems are reported.

Despite these achievements, the development of appropriate catalysts, which should work in a selective and efficient manner, especially in the presence of air, is still desired. Regarding potential catalysts, earth-abundant metal-based ones are desirable due to their relatively low costs and availability. More specifically, heterogeneous materials are in general preferable for sustainable and cost-efficient chemical synthesis.[41–50] Here, we report the preparation of carbon-supported copper nanoparticles, which constitute excellent aerobic oxidation catalysts for the synthesis of aromatic, heterocyclic, and aliphatic nitriles starting from alcohols and ammonia. Moreover, using these Cu-nanoparticles the synthesis of primary amides directly from alcohols and ammonia in water is also performed.

2. Results and Discussion

2.1. Preparation and Catalytic Evaluation of Cu-Based Nanoparticles

Among heterogeneous catalysts, supported nanoparticles are more desirable due to their advantages such as tunable activities and selectivities as well as stability and convenient recycling and reusability.[41–50] In recent years we focused on the development of such nanostructured materials for organic synthesis.[18,47–50] As a result, Fe-, Co- and Ni-based nanoparticles-based catalysts have been prepared and applied for the hydrogenation, amination, and oxidation reactions involving functionalized and structurally complex molecules.[18,47–50] However, until now, we have not developed related Cu-based nanocatalysts for essential organic reactions.

In this regard, we turned our interest to prepare Cu-nanoparticles-based catalysts for the synthesis of nitriles and amides using air. To prepare these nanoparticles, we applied a general and commonly used impregnation and pyrolysis method (**Figure 1**). In a typical experiment, $Cu(NO_3)_2.3H_2O$ was dissolved in DMF by stirring at 150 °C for 30 min. To this solution, Vulcan XC-72R (as carbon powder) was added and stirred for 4 h at 150 °C. Next, DMF was evaporated slowly and dried to obtain immobilized solid materials. Finally, this material was pyrolyzed at different temperatures under argon to obtain carbon-supported copper oxide nanoparticles (Figure 1).

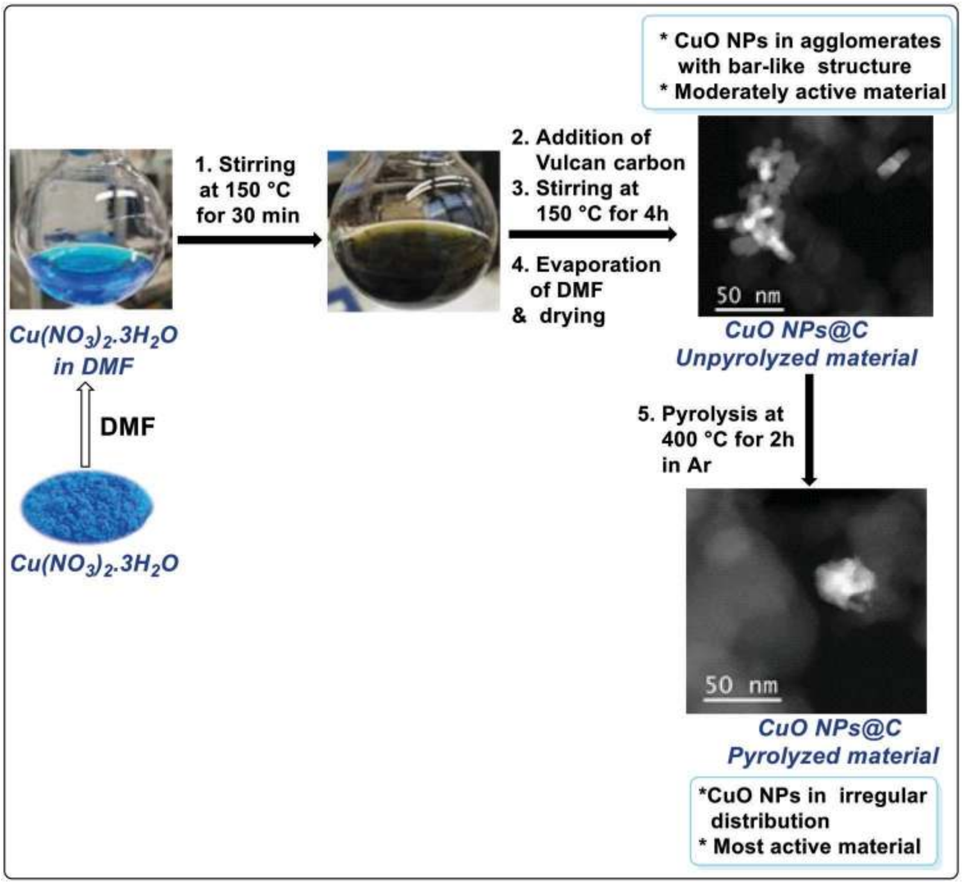
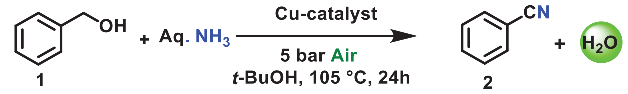


Figure 1. Preparation of carbon-supported CuO nanoparticles.

Table 1. Cu-catalyzed synthesis of benzonitrile from benzyl alcohol and ammonia in the presence of air: Evaluation of catalytic activities.



Entry	Catalyst	Conv. [%]	Yield [%]
1	$Cu(NO_3)_2.3H_2O$	3	2
2	$Cu(NO_3)_2$-carbon	37	33
3	CuO@C unpyrolyzed	67	60
4	CuO@C-300	75	70
5	CuO@C-400	>99	98
6	CuO@C-600	85	83
7	CuO@C-800	83	79

Reaction conditions: 0.5 mmol alcohol, 200 µL aq. NH_3 (28–30% in water), 30 mg heterogeneous catalyst (3-4 mol% of Cu), 5 bar air, 2 mL *t*-butanol, 105 °C, 24 h. Conversions and yields were determined by GC using n-hexadecane as standard. In the case of homogeneous catalysis conditions 4 mol% of $Cu(NO_3)_2.3H_2O$ was used.

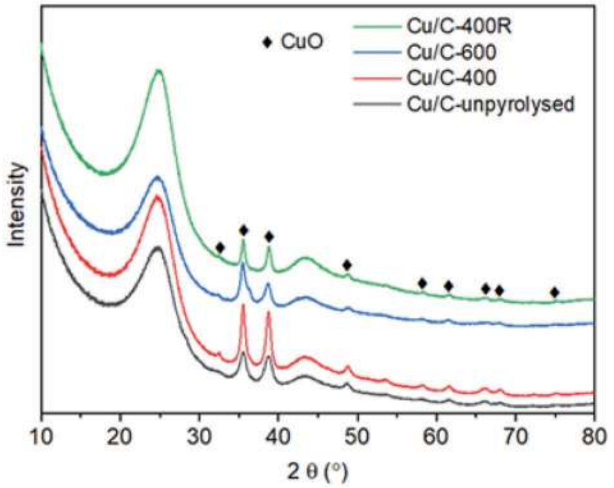


Figure 2. XRD patterns of Cu-based materials.

In order to select the optimal Cu-based catalyst, all the prepared materials were tested for the synthesis of benzonitrile from benzyl alcohol and aqueous ammonia in the presence of air as the model reaction. First, $Cu(NO_3)_2.3H_2O$ was tested and found that it was not active (**Table 1**, entry 1). Next, the mixture of copper nitrate and Vulcan carbon powder was tested and some activity from this system was observed (37% Conv., 33% yield; Table 1, entry 2). To our surprise, the impregnated, non-pyrolyzed material, CuO@C, produced 60% of the desired product (Table 1, entry 3). After pyrolysis of this CuO@C material, we observed a further increase in the activity. As a result, materials pyrolyzed at different temperatures (CuO@C-300-800; 300-800 indicates the applied pyrolysis condition in °C) were tested and the one pyrolyzed at 400 °C was found to be the most active and selective catalyst (Table 1, entries 4–7). From this material (CuO@C-400), complete conversion of benzyl alcohol took place and produced 98% of the desired product, benzonitrile (Table 1, entry 5). On the other hand, the materials pyrolyzed at 600 (CuO@C-600) and 800 °C (CuO@C-800) also exhibited good activities, but less compared to CuO@C-400.

2.2. Characterization of Cu-Oxide Nanoparticle-Based Catalysts

To know the structural features and the varying catalytic activities, these novel Cu-based materials were characterized using state-of-the-art analytical techniques such as X-ray diffraction (XRD), scanning transmission electron microscopy (STEM), energy-dispersive X-ray spectroscopy (EDX), electron energy-loss spectroscopy (EELS) and X-ray photoelectron spectroscopy (XPS). XRD patterns of both unpyrolyzed (CuO@C) and pyrolyzed catalysts (CuO@C-400 and CuO@C600) as well as recycled ones (CuO@C-400R), showed the presence of mainly CuO particles (**Figure 2**).

In the case of unpyrolyzed material, (CuO@C-unpyrolyzed), the agglomeration of particles in bar-like oxidic structures in the range of 20 to 180 nm is observed (**Figure 3**a,b and Figures S1 and S2, Supporting Information). Scanning transmission electron microscopy (STEM) of the most active material CuO@C-400 showed the formation of CuO particles in an irregular shape with sizes ranging from about 20 to 130 nm (see Figure 3c,d). Electron energy-loss spectroscopy (EELS) of CuO@C-400 revealed the presence of both Cu(II)- and Cu(I)-oxide nanoparticles (see Figure S3, Supporting Information). The material obtained at higher pyrolysis temperature (CuO@C-600) also contained CuO particles in an irregular shape with sizes ranging from about 4 to 150 nm (Figure 3e,f). In CuO@C-600, we also observed some extent of agglomeration of CuO particles. The sample obtained after one run, CuO@C-400R, looks very similar to CuO@C-400, but the size range of particles is larger (from about 3 to 300 nm) and is less compact (Figure 3g,h). This is again supported by the XRD patterns, where less intense and broader reflections are observed for Cu@C-400R. In the unpyrolyzed material, agglomerations of bar-like structures can be seen, while more compact oxidic copper can be observed in the pyrolyzed catalysts. Among these Cu-materials, the one pyrolyzed at 400 (CuO@C-400) is more active compared to the catalysts pyrolyzed at higher temperatures >600 (CuO@C-600-800). This varying activity is due to the formation and distribution of Cu-oxide nanoparticles. In case of CuO@C-400, particles are not agglomerated and are well defined. On the other hand, the particles in CuO@C-600 are in agglomeration, which could be the reason for the less activity of this material.

Further analysis of the catalyst surface by X-ray photoelectron spectroscopy (XPS) showed the presence of C, O, Cu, and N elements (**Table 2**). Additionally, small amounts of Si and S can be found which may be originated from the support (Vulcan XC-72R). The Cu 2p spectra in **Figure 4** reveal the presence of peaks at 933.6 eV and 954.0 eV, which are corresponding to Cu $2p_{3/2}$ and Cu $2p_{1/2}$. The strong satellite features around 942.5 and 962.5 eV together with the binding energy of the Cu $2p_{3/2}$ peak clearly prove CuO as the main oxidation state.[51] The unpyrolyzed catalyst as well CuO@C-400 and CuO@C-600 show very similar Cu 2p spectra and the same oxidation state (Figure 4a–c) with decreasing concentration of Cu

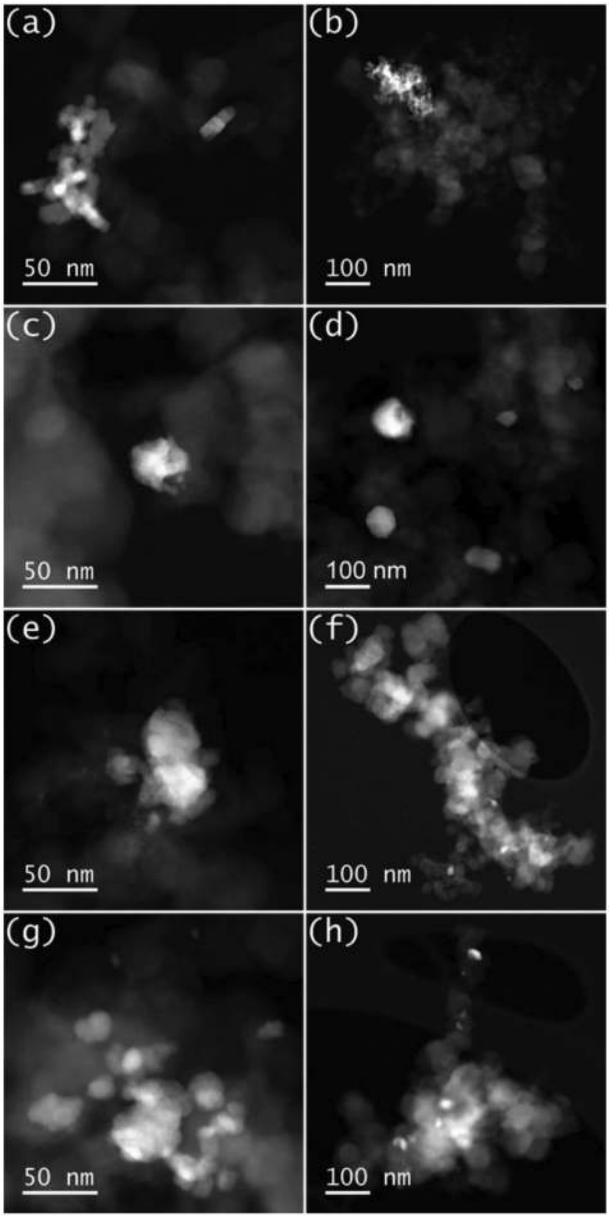


Figure 3. STEM images of copper-based nanocatalysts. STEM-HAADF images of a,b) CuO@C-unpyrolyzed, c,d) CuO@C-400, e,f) CuO@C-600, and g,h) CuO@C-400R-recycled.

Table 2. Amount of C, O, N, and Cu (in %) on the surface of Cu-materials obtained by XPS.

Catalyst	C	O	N	Cu
CuO@C unpyrolyzed	96.0	2.3	0.3	0.7
CuO@C-400	97.0	1.7	0.2	0.5
CuO@C-600	97.5	1.6	–	0.3
CuO@C-400R	95.6	2.1	1.6	0.7

Reaction conditions: 0.5 mmol alcohol, 200 µL aq. NH_3 (28–30% in water), 30 mg CuO@C-400 (3.3 mol% Cu), 80 mg of radical quenching /trapping agent, 5 bar air, 2 mL *t*-BuOH, 105 °C, 24 h, conversions, and yields were determined by GC yields using n-hexadecane as standard.

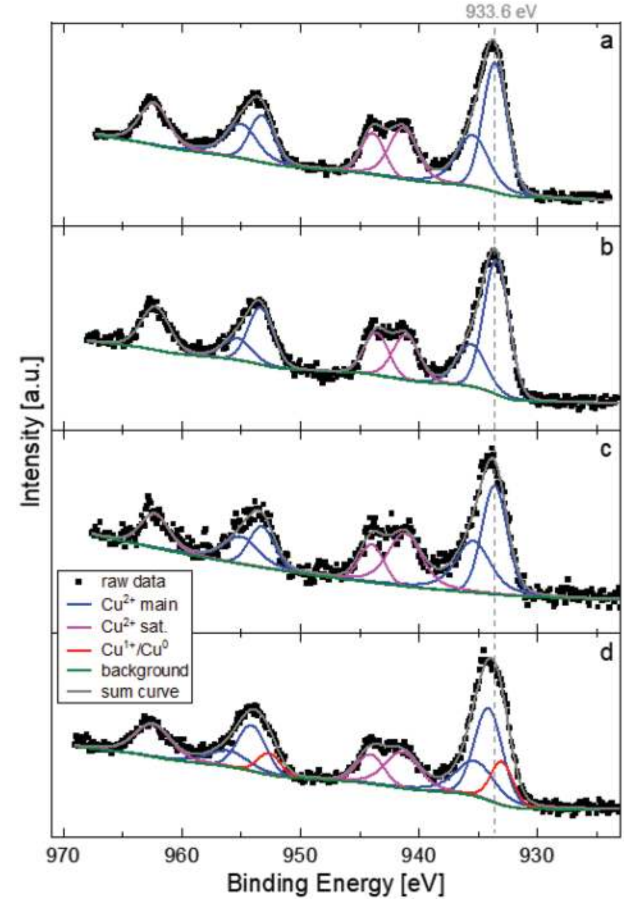


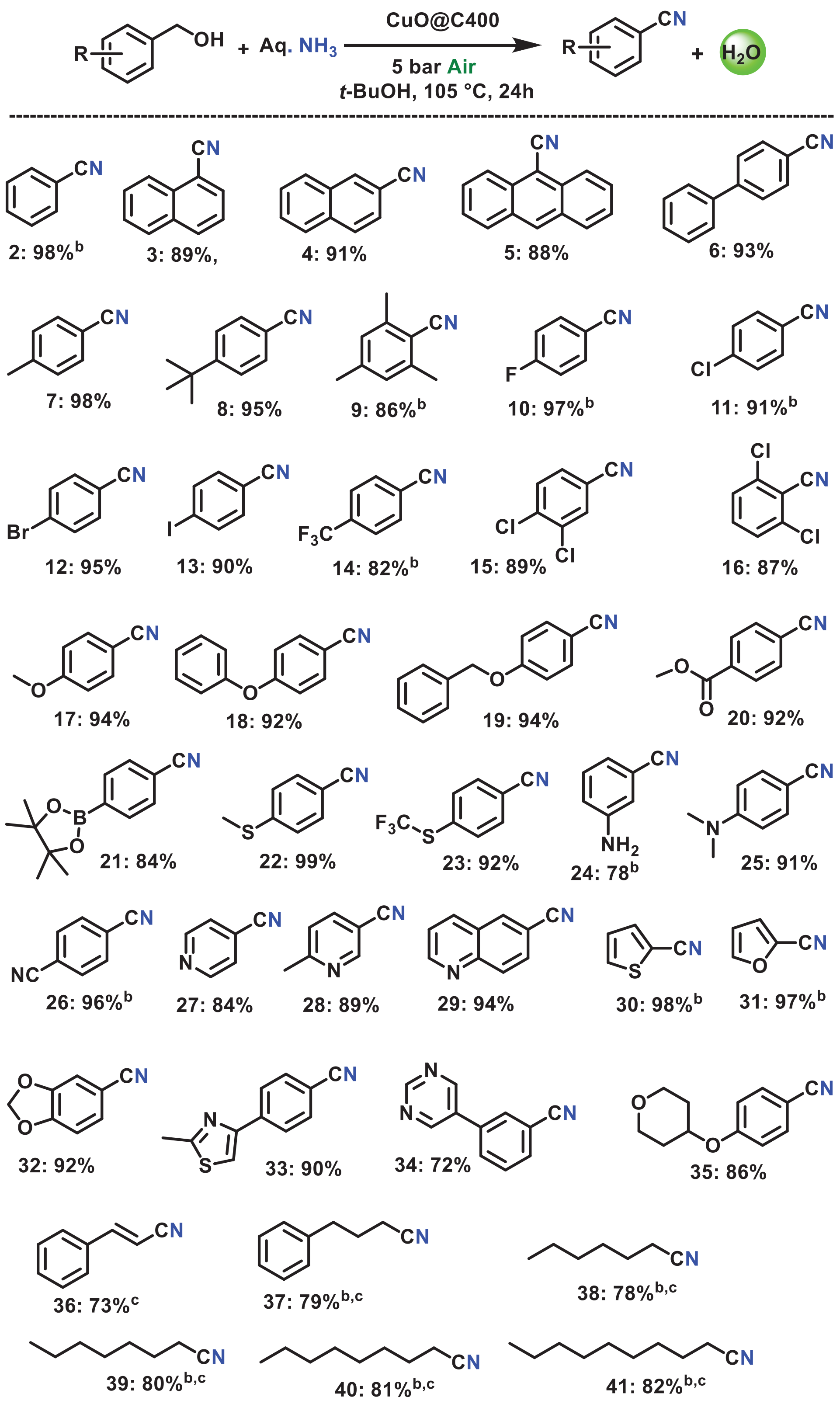
Figure 4. Deconvoluted XPS Cu 2p spectra of a) CuO@C-unpyrolyzed, b) CuO@C-400, c) CuO@C-600, and d) CuO@C-400R.

at the surface. However, for the recycled catalyst CuO@C-400R a slightly higher amount of Cu can be observed as well as differences in the Cu 2p spectra. Here, the satellite features are not as pronounced and a peak at lower binding energy (around 932.7 eV) appears. This indicates the presence of Cu^+/Cu^0, which cannot be distinguished, as the second oxidation state to a minor extent.[51]

The N 1s spectra of catalysts reveal the presence of pyrrolic-N (≈399.4 eV)[52] as the main component (Figure S4, Supporting Information) with a low total concentration of N (Table 2). However, in the recycled catalyst CuO@C-400R a slightly higher N concentration can be observed, also showing pyridinic and graphitic nitrogen to a minor extent (Figure S4, Supporting Information).

2.3. CuO-Nanoparticles Catalyzed Synthesis of Nitriles

With the most active catalyst (CuO@C-400) in hand, we demonstrated its general applicability for the synthesis of different kinds of nitriles, which are of commercial and industrial interest, starting from various alcohols and ammonia (**Scheme 1**). Among cyano-compounds, benzonitriles constitute integral parts of advanced products and pharmaceuticals



Scheme 1. Synthesis of nitriles from alcohols and ammonia by CuO@C-400 catalyzed aerobic oxidation[a]. Reaction conditions: [a]0.5 mmol alcohol, 200 µL aq. NH_3 (28-30% in water), 30 mg CuO@C-400 (3.3 mol% Cu), 5 bar air, 2 mL *t*-butanol, 105 °C, 24 h, isolated yields. [b]GC yield using n-hexadecane as standard. [c]0.5 mmol alcohol, 400 µL aq. NH_3 (28–30% in water), 45 mg CuO@C-400 (4.9 mol%), 5 bar air, 2 mL *t*-butanol, 130 °C, 36 h.

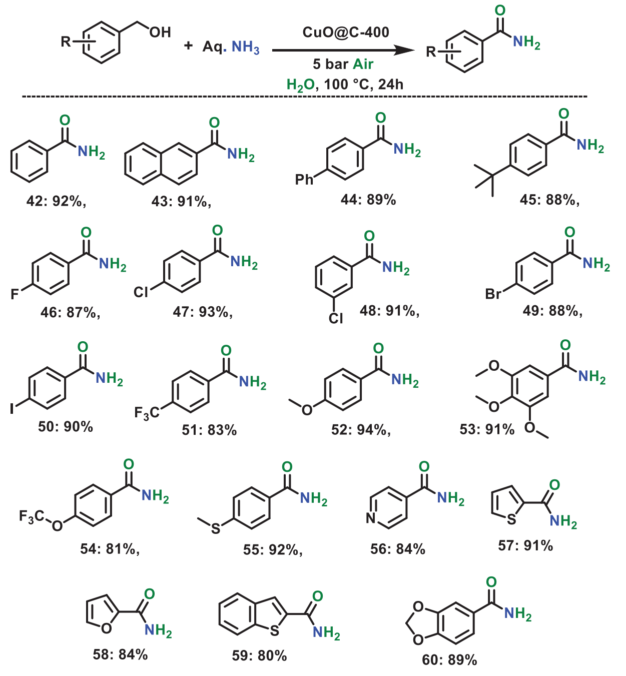
and play significant roles in their physical, chemical, and bioactivities.[14] In addition, aryl nitrile-containing compounds have been developed as selective enzyme inhibitors for the treatment of estrogen-dependent diseases.[14]

Noteworthy, applying CuO@C-400, substituted and functionalized benzonitriles were prepared in good to excellent yields (Scheme 1, products 2-26). Simple and substituted benzonitriles were obtained in up to 95% yield (Scheme 1, products 2-8). The sterically hindered, 2,4,6-trimethyl benzyl alcohol, which is difficult to react, was successfully proceeded to give 86% of the corresponding nitrile (Scheme 1, product 9). Interestingly, halogenated benzonitriles (their synthesis is problematic in both ammoxidation and nucleophilic cyanation reactions), were conveniently obtained in up to 97% yield (Scheme 1, products 10-16). Notably, such functionalized aryl halides are of interest in organic synthesis because these compounds can easily undergo various reactions to access different types of value-added products. Among these, 2,6-dichlorobenzonitrile (DCBN), is a special product that is considered as a potential herbicide as well as serves as a key intermediate in the production of pesticides and the thermally resistant plastics. Again, the preparation of this compound by traditional methods is highly challenging. However, starting from inexpensive and commercial 2,6-dichlorobenzyl alcohol, DCBN was obtained with 87% yield. (Scheme 1, product 16). In synthetic organic chemistry and drug discovery, the preparation and reaction of functionalized compounds are of central importance. In this regard, different functionalized benzonitriles were synthesized. As an example, ether-, ester-, boronic-ester-, thio-ether-, primary amine-, *N,N*-dimethylamine- and cyano-substituted benzonitriles were selectively prepared starting from corresponding alcohols (Scheme 1, products 17-26).

Heterocycles are an essential class of compounds and are of increasing interest in medicinal and biological chemistry. Among these, cyano-heterocycles are specifically important in organic synthesis as well as drug discovery. Applying our Cu-based catalyst, different heterocyclic nitriles such as cyno-pyridine, cyano-quinoline-, cyano-thiophene-, and cyano-furan as well as dioxole-, thiazole- and tetrahydro pyran-based nitriles were prepared in up to 98% (Scheme 1, products 27-86). As an example of allylic nitrile, cinnamonitrile was accessed from cinnamyl alcohol in a 73% yield (Scheme 1, product 36). Among alcohols, aliphatic ones in general are difficult to react and require highly active catalysts or drastic conditions. Nevertheless, CuO@C-400 catalyst is also active for the aliphatic substrates; albeit requires higher temperature and longer reaction time. As a result, 4-phenylbutane *n*-heptane, *n*-octane, *n*-nonane, and *n*-decane nitriles were prepared in up 81% yield (Scheme 1, products 36-41).

2.4. CuO-Nanoparticles Catalyzed Synthesis of Primary Amides in Water

After the successful preparation of nitriles, we turned our interest in the synthesis of primary amides using CuO@C-400. As shown in **Scheme 2**, 19 primary amides were prepared in good to excellent yields from benzylic and heterocyclic alcohols and ammonia in presence of air in water. Interestingly, F-, Cl-, Br-, and I-substituted benzylic alcohols were smoothly reacted and provided corresponding halogenated primary amides (Scheme 2, products 46-50). In addition, trifluoromethyl-, ether, thio-ether substituted primary amides were obtained in up to 93% yield (Scheme 2, products 51-54). Further, different heterocyclic amides such as isonicotinamide (product 56), thiophene-2-carboxamide (product 57), furan-2-carboxamide (product 58, benzothiophene-2-carboxamide (product 59), and benzodioxole-5-carboxamide (product 60) were prepared in up to 91% yield. Unfortunately, CuO@C-400 did not show sufficient activity for the synthesis of aliphatic primary amides, although it showed good activity to access aliphatic nitriles.



Scheme 2. CuO@C-400 catalyzed synthesis of primary amides from alcohols and ammonia in water. Reaction conditions: 0.5 mmol alcohol, 300 µL aq. NH_3 (28–30% in water), 30 mg CuO@C-400 (3.3 mol% Cu), 5 bar air, 2 mL H_2O 100 °C, 24 h, isolated yields.

It is important to note that sulfur-containing compounds create a common poisoning effect for heterogeneous catalysts. However, favorably, our Cu-based nanocatalyst is well tolerated and exhibited good to excellent activity for the preparation of several sulfur-containing products (Schemes 1 and 2, products 22, 23, 30, 33, 55, 57, 59).

2.5. Catalyst Recycling and Reusability

In the context of practical and cost-effective synthetic processes, recycling and reusability of a given catalyst are key factors. As shown in **Figure 5**, the catalyst can be conveniently recycled and reused up to 3 runs without any significant loss of activity or selectivity. However, after the 4th run the activity of catalyst decreased, which is due to the leaching of Cu-particles from the catalyst (wt% of Cu in the fresh catalyst = 3.5% and in the recycled catalyst after 4th run = 2.5%).

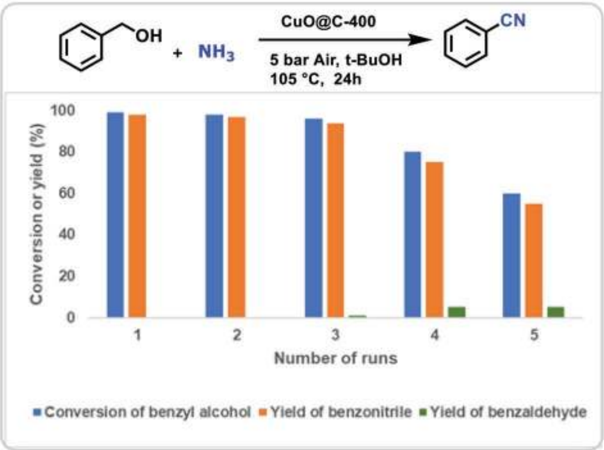


Figure 5. Recycling and reusability of CuO@C-400 for the synthesis of benzonitrile. Reaction conditions: 1 mmol alcohol, 400 µL Aq. NH_3 (28-30% in water), 60 mg CuO@C-400 (3.3 mol% Cu), 5 bar air, 4 mL *t*-butanol, 105 °C, 24 h, GC yields using n-hexadecane as standard.

2.6. Kinetic and Mechanistic Investigations

After having demonstrated the synthetic applicability, we performed mechanistic investigations and monitored the reaction profile. For the model reaction, we studied the effect of (a) reaction time, (b) amount of catalyst, (c) reaction temperature, and (f) substrate (benzyl alcohol) concentration (**Figure 6**). Increasing the reaction time, temperature, and amount of catalyst the yield of benzonitrile was increased, and the best result was achieved at 105 °C with 30 mg of catalyst for 24 h. In contrast, varying the concentration of benzyl alcohol (substrate) the yield of benzaldehyde was decreased, indicating that the higher amount of the starting material on the surface hinders the reaction.

To identify the formation of possible reactive oxygen species (ROS) during this CuO@C-400 catalyzed synthesis of benzonitrile, we conducted radical quenching/trapping experiments. For this purpose, under standard conditions, we tested the reaction in presence of PBQ (*p*-benzoquinone, NaN_3, and *i*-PrOH, which are generally used as radical quenchers/trapping agents for superoxide ($O_2^{\bullet-}$), singlet oxygen ($^{[1]}O_2$) and hydroxyl radical ($^{\bullet}OH$) (**Table 3**) respectively. These experiments showed that the reaction has been inhibited in presence of 80 mg PBQ. On the other hand, there is no effect on the reaction after adding NaN_3 or *i*-PrOH. These observations infer the formation of superoxide ($O_2^{\bullet-}$) species is more likely during this Cu-catalyzed nitriles synthesis protocol. Next, we also conducted an experiment to trap superoxide ($O_2^{\bullet-}$) species using butylated hydroxytoluene (BHT) (**Figure 7**). In absence of benzyl alcohol, the reaction was performed using 30 mg of Cu@C-400 and 0.5 mmol BHT in presence of 1 bar of air at 80 °C in 2 mL n-heptane for 24 h and detected the formation of BHT-OOH by GC MS analysis (Figure 7).

Further, in situ electron paramagnetic resonance (EPR) studies for the aerobic oxidation of benzyl alcohol over CuO@C-400 catalyst in *t*-butanol were carried out in the presence of 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) as a spin trap. The EPR spectrum of the reaction mixture shows a six-line signal at $g = 2.006$, which can be simulated with $A_N = 18.28$ MHz and $A_{\beta H} = 55.98$ MHz characteristic for DMPO-R spin adduct.

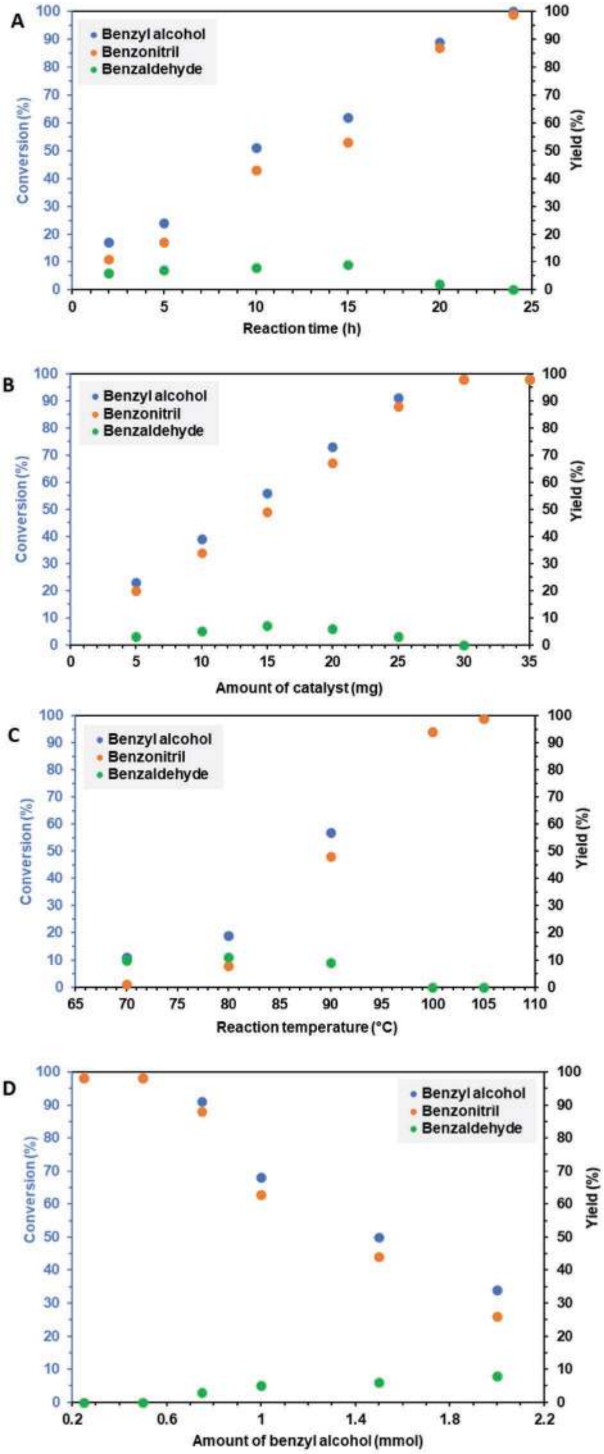
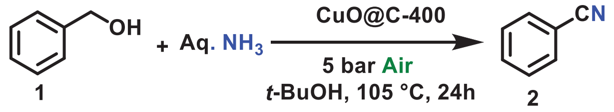


Figure 6. Kinetic investigations on the CuO@C-400-catalyzed synthesis of benzonitrile from benzyl alcohol and ammonia in the presence of air. A) Yield versus reaction time, B) yield versus amount of catalyst, C) yield versus reaction temperature, and D) yield versus concentration of benzyl alcohol (substrate).

Table 3. Effect of different radical quenching/trapping agent on CuO@C-400 catalyzed conversion benzyl alcohol benzonitrile.



Entry	Radical quenching/ trapping agent	Reactive oxygen species	Conv. [%]	Yield [%]
1	–	–	>99	98
2	PBQ	Superoxide ($O_2^{\bullet-}$)	5	3
3	NaN_3	Singlet oxygen ($^1O_2$)	96	94
4	*i*-PrOH	Hydroxyl radical ($^{\bullet}OH$)	94	92

These results indicate that the reaction mechanism involves the formation of carbon radical intermediate with the interaction of superoxide radical species (**Figure 8**).

Regarding the reaction pathway (**Scheme 3**) for the preparation of nitrile (D), first the oxidation of alcohol to aldehyde (B) takes place in presence of CuO@C-400 and air. Then, the aldehyde couples with ammonia and generates primary imine (c). This intermediate is unstable and undergoes oxidation in presence of CuO@C-400 to produce the corresponding nitrile. For the synthesis of amides, two pathways are possible: a) the aldehyde formed by the oxidation of alcohol can react with ammonia and generates hemiaminal as the intermediate, which could be then converted to the corresponding primary amide, or b) the benzonitrile produced from alcohol which can undergo hydrolysis to form the primary amide in presence of water.

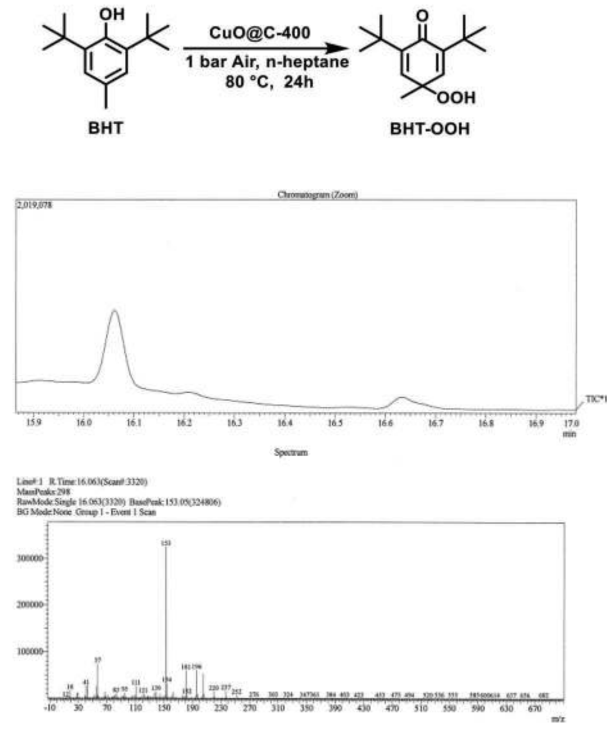


Figure 7. Trapping of super oxide ($O_2^{\bullet}$-) using butylated hydroxytoluene (BHT) and mass spectrum BHT-OOH.

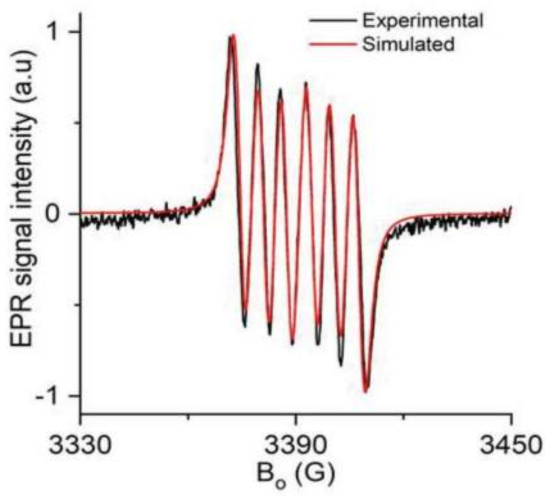
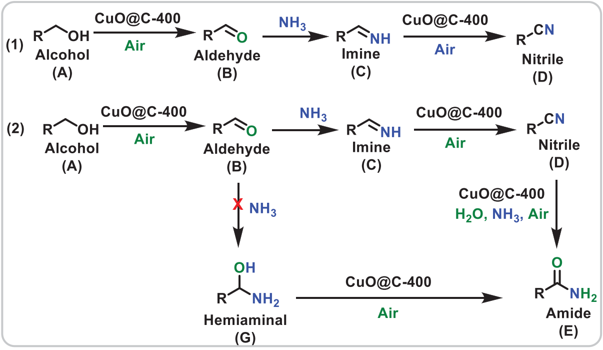


Figure 8. EPR spectra of CuO@C-400 (10 mg) + benzyl alcohol (20 µL) + DMPO (10 µL) in *t*-BuOH (0.5 mL) were measured at 20 °C after heating the suspension at 80 °C for 2 min under O_2 (black experimental and red simulated spectra).

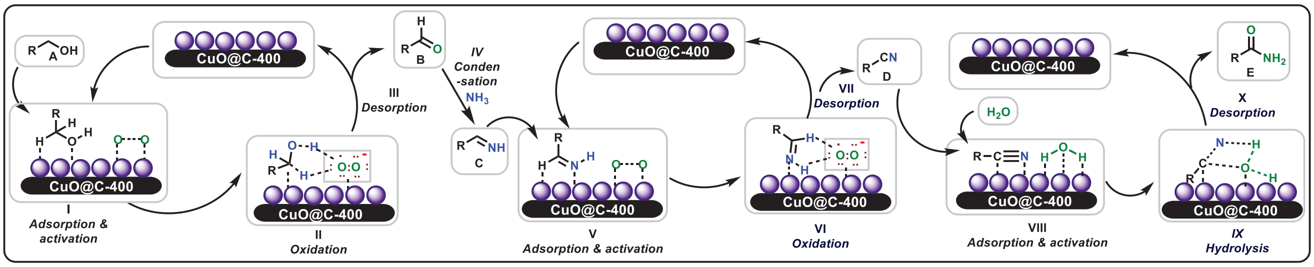
To confirm the formation of primary amide, the reaction of benzonitrile in presence of ammonia and air using CuO@C-400 was conducted at 100 °C for 24 h in water. This reaction provided benzylamide in a 90% yield (Figure S10, Supporting Information), which confirmed that the formation of amide occurs mainly by the hydration of benzonitrile. The catalytic hydration of nitriles is also another green method to prepare amides.[53,54]

Compared to nitriles, the formation of amides from alcohols is challenging because it involves a two-step reaction. In particular, the hydrolysis of aliphatic nitriles is difficult compared to aromatics ones and hence this might be the reason that using CuO@C-400 catalyst was very poor or no yield of aliphatic nitriles was observed.

Based on reaction pathways and obtained results, we propose the plausible reaction mechanism of the Cu-catalyzed aerobic oxidation process to prepare nitriles and primary amides in **Scheme 4**. First, on the surface of CuO@C-400 catalyst, adsorption and activation of both alcohol and oxygen take place



Scheme 3. Reaction pathways for the Cu-nanoparticle catalyzed synthesis of nitriles and primary amides from alcohols and ammonia in presence of air.



Scheme 4. Proposed mechanism for the CuO@C-400-catalyzed synthesis of nitriles and amides from alcohols and ammonia in presence of air.

with the generation of superoxide as oxygen reactive species (I). Next, oxidation of activated alcohol proceeds using superoxide species (II). Further, the desorption of aldehyde with the regeneration of catalyst (III) occurs. The formed aldehyde condenses with ammonia and forms imine as an intermediate (IV). In the next catalytic cycle imine undergoes adsorption and activation on the catalyst (V) surface followed by oxidation (VI). Finally, the nitrile desorbs with the regeneration of catalyst (VII). For the formation of amide, the nitrile and water adsorb and activate on catalyst surface (VIII) and then hydrolysis occurs (IX). Finally, desorption of amide takes place with the regeneration of catalyst (X).

3. Conclusion

Pyrolysis of simple copper nitrate on carbon generated efficient and selective copper oxide nanoparticles-based aerobic alcohol oxidation catalysts (CuO@C-400). Applying optimal CuO-based nanocatalyst, ammoxidation of various alcohols with ammonia in presence of air has been performed and produced various simple, substituted, and functionalized aromatic, heterocyclic, and aliphatic nitriles in good to excellent yields. In addition, this Cu-based aerobic oxidation protocol has been used for the synthesis of primary amides in a water medium. Superoxide ($O_2^{\bullet-}$) radical species are identified as the reactive oxygen species in this Cu-NPs catalyzed aerobic oxidation process. Finally, reaction pathways and plausible mechanism for the CuO-NPs catalyzed synthesis of nitriles and amides from alcohols and ammonia in presence of air have been proposed.

4. Experimental Section

Procedure for the Preparation of CuO NPs-Based Catalysts: In a 50 mL round-bottomed flask, 142 mg of $Cu(NO_3)_2.3H_2O$ and 25 mL of DMF were added and the mixture was stirred at 150 °C for 30 min. Then, 885 mg of Vulcan XC 72R carbon powder was added and the whole reaction mixture was stirred again at 150 °C for 4 h fixing a reflux condenser to the round-bottomed flask. Then after, the reflux condenser was removed and the round-bottomed flask containing the reaction mixture was allowed to stand for 24 h at 150 °C for the slow evaporation of DMF to obtain Cu-carbon based solid material. After the evaporation of the solvent and drying, the solid material was cooled to room temperature and ground to a fine powder. Finally, the powdered material was pyrolyzed at different temperatures (300–800 °C) for 2 h under argon atmosphere. Elemental analysis of optimal catalytic material CuO@C-400 (wt%): C = 88.5, N = 0.76, Cu = 3.5% H = 0.25%.

Elemental analysis recycled catalyst CuO@C-400R (after 4th run): C = 85.4, N = 1.26, Cu = 2.57%, H = 0.20%.

Procedure for the Synthesis of Nitriles and Amides: To a glass vial (8 mL), the magnetic stirring bar and 0.5 mmol alcohol were added and then 2 mL *t*-butanol as solvent (in case of amides synthesis, 2 mL water was used as solvent) were added. Then, 30 mg CuO@C-400 catalyst was added followed by the addition of 200 µL aq. NH_3 (in case of amides synthesis 230 µL aq. NH_3 was used). Afterward, the reaction vial was fitted with a septum, cap, and needle. The reaction vials (8 vials with different substrates) were placed into a 300 mL autoclave and the autoclave was pressurized with 5 bar air. The autoclave was placed into a preheated aluminum block at 115 °C (110 °C in case of amides synthesis) and reactions were allowed to progress under stirred conditions for 24 h. During the reaction, the inside temperature of the autoclave is measured to be 105 °C (100 °C in case of amides synthesis) and this temperature has been considered as the reaction temperature. After the completion of the reactions, the autoclave was cooled down to room temperature and the remaining air was slowly discharged. The catalyst was filtered-off, and washed with ethyl acetate. The products were purified by column chromatography and analyzed by GC, GC-MS, and NMR spectroscopy. In the case of yields determined by GC, 100 µL *n*-hexadecane was added to the reaction vial containing products and diluted with ethyl acetate. Then, the crude mixture containing catalyst and products was filtered through a plug of silica and the filtrate containing products were analyzed by GC.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

aerobic oxidation, alcohols, amides, ammonia, Cu nanoparticles, nitriles

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