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Stable and Reusable Nanoscale Fe₂O₃-catalyzed Aerobic Oxidation Process for Selective Synthesis of Nitriles and Primary Amides

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Sustainable introduction of nitrogen moiety in the form of nitrile or amide functionality in synthetic molecules is of fundamental interest because nitrogen-containing motifs are found in a large number of life science molecules, natural products and materials. Hence, the synthesis and functionalization of nitriles and amides from easily available starting materials using cost-effective catalysts and green reagents is highly desired. In this regard, herein we report nanoscale iron oxide-catalyzed environmentally benign synthesis of nitriles and primary amides from aldehydes and aqueous ammonia in presence of 1 bar O2 or air. Under mild reaction conditions, this iron-catalyzed aerobic oxidation process proceeds for the synthesis of functionalized and structurally diverse aromatic, aliphatic and heterocyclic nitriles. Further, applying this iron-based protocol, primary amides have also been prepared in water medium.

1. Introduction

The development of iron-catalyzed reactions for the modern state-of-the-art organic synthesis is an actual goal of chemical $\ensuremath{\mathsf{research}}^{\ensuremath{\mathsf{1}}\xspace^{\ensuremath{\mathsf{1}}\xspace^{\ensuremath{\mathsf{2}}\xspace}}$ Remarkably, more abundance, cheaper price and less toxicity of iron makes it an ideal metal for catalysis applications,¹⁻² and can be suitable candidate for the replacement of existing precious metal-based catalysts. Compared to homogeneous iron complexes, heterogeneous catalysts based on nanostructured iron materials constitute more practical and cost-efficient catalytic systems due to their ease of separation, reusability and stability.^{1d, 2a, 3} In order to realize more environmentally benign synthesis, iron catalyzed reactions should exploit the use of green and renewable reagents under mild reaction conditions. 1c-d, 4-7 Clearly, ironcatalyzed synthesis utilizing atmospheric O_2 or air $^{1\text{c-d},\ 4\text{-7}}$ and ammonia⁸ demonstrating exquisite selectivity constitutes more sustainable process that is crucial for the advancement of academic research and industrial production. Therefore, the development of iron catalyzed aerobic oxidation reactions are highly desired for the production of valuable chemicals, especially nitriles and amides. Noteworthy, nitriles and amides represent major building blocks and central intermediates for advanced chemicals, life science molecules and materials 9-13. Further, these structural motifs have been found as the integral parts of bio-active molecules and natural products.¹³⁻¹⁷

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While simple nitriles have been prepared by industrial ammoxidation processes under drastic conditions (>300 °C in gas phase) ¹⁸, functionalized and structurally diverse ones still rely on toxic cyanation reactions.¹⁹ However, the limitations of ammoxidation and drawbacks of cyanation processes inspired to look for alternative sustainable routes for the synthesis of nitriles from suitable starting materials. In this regard, catalytic oxidative conversion of alcohols ²⁰ or aldehydes ^{20a}, ²¹ using ammonia represents green methodology to produce various nitriles.

Complementary to alcohols are aldehydes, which represent easily available fine and bulk chemicals, and serve as suitable starting materials for the preparation of various chemicals such as amines,²² carboxylic acids,²³ alcohols,²⁴ esters²⁵ and heterocycles²⁶ as well as in C-C bond forming reactions that enabled the preparation of array of interesting molecules^{24a-c,} ²⁷. Particularly, recently reported Fe-^{23a} and Cu-^{23b} catalyzed oxidative conversions of aldehydes to carboxylic acids are quite interesting. Regarding the synthesis of nitriles from aldehydes, few methods have been reported using different nitrogen sources such as hexamethyldisilazane (HMDS),²⁸ hydroxylamine²⁹, NaN₃ 30 , and K₃[Fe(CN)₆]³¹ and ammonia,^{20a,} as nitrogen sources using different catalysts. Unfortunately, all of these reagents either toxic or produce stoichiometric amount of wastes. Therefore, ammonia is considered to be the green and abundant nitrogen source for the preparation of nitrogen containing compounds. With regards to the utilization of ammonia for the synthesis of nitriles from aldehydes, various oxidants and catalysts have already been disclosed. 20a,b,21,34 Among these, iodine and iodine containing compounds were commonly employed.³² However these reagents are not only sensitive and hazardous, but also produce significant amount of wastes. Hence these

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reagents are not suitable from green chemistry perspective. Next, Ru-based catalysts were used at drastic conditions (130 °C, 6 bar air).^{20a,b} In addition to ruthenium, Cu, ²¹ Ni, ^{33a} and Mg-Mn $^{\rm 33b}$ based systems are also catalyzed aldehyde and ammonia reaction to obtain nitriles. Among these, Cu/TEMPO/bipyridin catalyst system works under mild reaction conditions (25 $^{\circ}$ C, 1 bar O₂) to produce nitriles. ^{21a} Even though this catalyst works under mild reaction conditions, it is a homogeneous catalyst and cannot be recycled. ^{21a} In addition, the use of NaOH additive and fewer substrate scope have hindered its practical utility for sustainable synthesis of nitriles.^{21a} Furthermore, other oxidants/catalysts such as trichloroisocyanuric acid (TCCA),^{34a} tetrabutylammonium tribromide (TBATB)^{34b} chloramine-T (CAT) ^{34c} and ceric ammonium nitrate (CAN)^{34d} have also been used for the preparation of nitrile from aldehydes and ammonia. Again these compounds led to the formation of significant amount of wastes and hence they are not considered as green oxidants. Nevertheless, most of these methodologies have disadvantages regarding the use of toxic and waste generating reagents, or poor selectivity and less substrate scope for the synthesis of functionalized and structurally diverse nitriles. Hence, more green and efficient methodologies for the synthesis of advanced nitriles from aldehydes using heterogeneous iron-based catalysts under mild reaction conditions are highly required. In this regard, herein we report the application of reusable iron oxide catalyst for the synthesis of a variety of nitriles starting from aldehydes and aqueous ammonia under mild reaction conditions. Compared to previously reported catalysts (Fig. 1), our ironbased catalyst is more advantageous and empowers the synthesis of functionalized and structurally diverse nitriles. Noteworthy, the synthetic utility and practical applicability of this catalyst have been presented by performing gram-scale synthesis and catalyst recycling. In addition to the synthesis of nitriles, more green protocol for the preparation of amides using iron-based catalyst starting from aldehydes and ammonia is also demonstrated in water medium.



Fig. 1. Synthesis of nitriles from aldehydes and ammonia using different catalysts/oxidants: Comparison of our method with those of previously reported methods.

2. Results and discussion

2.1 Preparation of nanoscale Fe_2O_3 -based catalysts (Fe_2O_3 -N/C).

In 2013, we have developed nanoscale Fe₂O₃-based particles activated by nitrogen doped graphene layers for catalysis applications (Fe₂O₃-N/C).^{2a} Motivated by these materials and based on our objective to develop iron-based sustainable chemical processes, herein we demonstrate the synthesis of all kinds of aromatic, heterocyclic and aliphatic nitriles as well as primary amides starting from aldehydes and aqueous ammonia using 1 bar of molecular oxygen or air. Notably, this Fe_2O_3 -based catalyst has been prepared (Fig. 2) bv impregnation of in situ generated Fe(II)(1,10phenanthroline)₃(OAc)₂ complex on commercial carbon (Vulcan XC 72R) and subsequent pyrolysis at 800 °C for 2 h in argon atmosphere (Fe-Phen/C-800; Phen = 1.10phenanthroline).^{2a} The detailed preparation and characterization of this material by transmission electron microscopy (TEM), X-ray photoelectron spectroscopy (XPS), electron paramagnetic resonance (EPR), and Mössbauer spectroscopy has been reported in our previously published paper.^{2a} (see also supporting information) The Fe-Phen/C-800 catalyst system was characterized by the formation of nanoscale Fe₂O₃ particles (2-5 and 20-80 nm), which are surrounded by 3-5 nitrogen doped graphene layers (Fig. S1A). In contrast to the active material, the inactive material, Fe(OAC)₂/C-800 prepared without phenanthroline ligand contained much larger and well facetted big Fe₂O₃ particles of 100-800 nm size. In this case there is no formation of graphene layer and hence these particles are not surrounded by graphene layers.

X-ray photoelectron spectra for N1s electrons (Fig. S3A) of Fe₂O₃-N/C (Fe-Phen/C-800) catalyst has been revealed that there are three N1s peaks occur at 398.3 eV, 399.3 eV and 401.0 eV. The first two peaks are assigned to pyridinic nitrogen and Fe-N centers respectively. The peak observed at at 401.0 eV, is assigned to nitrogen in a grapheme-like structure. The XPS for Fe2P electrons, two peaks corresponding to Fe species in the near-surface region were observed (Fig. S3B). The first one (major) appeared at 712.4 eV and the second one (minor) at 709.9 eV. The first peak is due to the presence of Fe^{+3} species (more likely Fe_2O_3) while the second one is assigned to Fe⁺² species. Fe⁺² species are in minor proportion compared to Fe⁺³. By XPS analysis, in Fe-Phen/C-800 catalyst both Fe⁺³ (major) and $\mathrm{Fe}^{^{+2}}$ (minor) species are presented on the surface of the material. However, the bulk composition is somewhat different from the surface composition. In the bulk, we could see the presence of mainly the $\mathrm{Fe}^{^{+3}}$ species (in the form of Fe_2O_3). The presence of Fe_2O_3 in bulk composition has confirmed by EPR and Mössbauer spectral analysis (Figs. S4 and S5; See supporting information for more details). Based on reactivity and detailed spectroscopic characterization of the active (Fe-Phen/C-800) and non-active (Fe(OAc)/C-800) catalysts, the active site of the catalyst consists mainly nanoscale Fe₂O₃ particles, which are surrounded by nitrogen species of the graphene layers. Both the nano-sized particles

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and the Fe-N interactions are responsible for the remarkable activity of this catalyst. Thus, the active sites appear to be Fe- N_x centers that govern the catalytic acticities.



Fig. 2. Preparation of nitrogen doped graphene activated nanoscale ${\sf Fe}_2{\sf O}_3\text{-}$ particle supported on carbon.

2.2. Reaction design for the synthesis of nitriles

Using our Fe-Phen/C-800 catalyst (Fe₂O₃-N/C), we started to investigate the preparation of nitriles from suitable starting materials using aqueous ammonia in presence of 1 bar molecular oxygen under mild temperature (<50 °C) in conventional apparatus (in glass vial using balloon); without the use of any special equipment or autoclave. Under these conditions, first we tested benzyl alcohol at 40 $^{\circ}$ C with 1 bar O₂ in presence of Fe_2O_3 -N/C-catalyst and found that no reaction was occurred to produce desired benzonitrile. However, to our surprise the reaction of benzaldehyde gave selectively benzonitrile in 96% yield (Table 1, entry 6). Obviously homogeneous catalyst systems based on iron acetate or iron acetate/phenanthroline were found to be inactive (Table 1 entries 1-2). Similarly, the unpyrolyzed Fe-Phen@C material, pyrolyzed simple iron acetate on carbon (Fe(OAc)₂@C-800) and bulk Fe₂O₃ were also not active (Table 1 entries 3-5). After having excellent results using Fe₂O₃-N/C-catalyst and a set of mild reaction conditions established, we explored the applicability of this methodology for the preparation of nitriles from aldehydes and aqueous ammonia. As seen from schemes 1-3, structurally diverse and functionalized aromatic, heterocyclic and challenging aliphatic nitriles have been synthesized from various aldehydes.

Table.1. Preparation of benzonitrile from benzaldehyde and aqueous ammonia using iron catalysts: comparison of catalytic activity

	CHO Fe-catalyts	
1 bar O ₂ (Balloon) t-Amyl alcohol, 40 ^o C		
Entry	Catalyst	Yield of benzonitrile (%)
1 ^a	Fe(OAC) ₂	<1
2 ^a	Fe(OAC) ₂ +Phen	<1
3 ^b	Fe-Phen@C	<1
4 ^b	Fe(OAC) ₂ @C-800	<3
5 ^b	Bulk Fe ₂ O ₃	<1
6 ^b	Fe-Phen@C-800	96

Carbon=Vulcan XC72R, Phen= phenanthroline, materials were pyrolyzed at 800 °C for 2h under argon, Bulk Fe₂O₃ obtained commercially (>96% Fe basis). Reaction conditions: ^a Homogeneous catalysis conditions: 0.5 mmol benzaldehyde, 300 µL aq. NH₃ (28-30% NH₃ basis), 0.015 mmol Fe(OAC]₂, 0.045 mmol phenanthroline, 1 bar O₂ (balloon), 2 mL t-amyl alcohol, 40 °C, 24 h, GC yields using 100 µL nhexadecane as standard. ^a Heterogeneous catalysis conditions: 0.5 mmol benzaldehyde, 300 µL aq. NH₃ (28-30% NH₃ basis), weight of catalyst corresponds to 3 mol% Fe, 1 bar O₂ (balloon), 2 mL t-amyl alcohol, 40 °C, 24 h, GC yields using 100 µL n-hexadecane as standard.

2.3. Synthesis of structurally diverse aryl nitriles

Aryl nitriles, which are an important motifs found in a majority of nitrile containing life science molecules, especially in central nervous system CNS, cardiovascular and anti-HIV drugs ¹⁴ were obtained in good to excellent yields (Scheme 1). Interestingly, halogenated benzonitriles, which encounter selectivity problem by typical cyanation reactions, were prepared in 89-97% yields (Scheme 1). The resulting halogenated benzonitriles serve as precursors for agrochemicals, pesticides and engineering materials. As an example, 2, 6-dichlorobenzonitrile (DCBN) is an herbicide and a key intermediate in the preparation of various potential pesticides and high thermal resistant engineering plastics, was obtained in 94% yield (Scheme 1; product 11). This particular reaction is of high commercial significance and is also very challenging topic in the field of heterogeneous catalysis under gas phase conditions due to steric hindrance (i.e. due to substitution of two deactivating chlorine atoms in ortho positions).



Scheme 1. Fe₂O₃-N/C-catalyzed synthesis of structurally diverse and functionalized benzonitriles^{*a*}. ^aReaction conditions : 0.5 mmol aldehyde, 200-300 μ L aq. NH₃ (28-30% NH₃ basis), 30 mg catalyst (3 mol% Fe), 1 bar O₂ (balloon), 2 mL t-amyl alcohol, 40 °C, 24 h, isolated yields. ^bYields were determined by GC using 100 μ L n-hexadecane as standard.)

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The yield of DCBN achieved through the present study is much higher compared to the state of the art (Y_{DCBN} = ca. 80% only). Further, functionalized benzaldehydes underwent selective reaction to produce challenging benzonitriles up to 97% (Scheme 1).

2.4. Synthesis of heterocyclic nitriles

Next, cyano-substituted heterocycles and aryl nitriles bearing heterocyclic backbones were synthesized in 84-96% yields (Scheme 2). In general heterocyclic nitriles have been found to be key starting materials for the preparation of various active subunits of medicinal and biological molecules.



Scheme 2. Preparation of cyano-heterocycles using Fe₂O₃-N/C-Catalyst^{*a*}. (^aReaction conditions: 0.5 mmol aldehyde, 200-300 μ L aq. NH₃ (28-30% NH₃ basis), 30 mg catalyst (3 mol% Fe), 1 bar O₂ (balloon), 2 mL t-amyl alcohol, 40 °C, 24 h, isolated yields. ^bYields were determined by GC using 100 μ L n-hexadecane as standard.)

2.5. Synthesis of challenging aliphatic nitriles

In subsequent efforts, various aliphatic aldehydes, that are difficult to react, have been chosen as potential substrates to produce their corresponding nitriles in good to excellent yields (up to 96%; scheme 3). More interestingly the allylic nitriles, important starting compounds for allylic amines, were obtained without further oxidation of olefinic group (Scheme 3).



Scheme 3. Synthesis of challenging aliphatic nitriles using Fe₂O₃-N/C-catalyst⁸. (^aReaction conditions: 0.5 mmol aldehyde, 200-300 μ L aq. NH3 (28-30% NH3 basis), 30 mg catalyst (3 mol% Fe), 1 bar O₂ (balloon), 2 mL t-amyl alcohol, 40 °C, 24 h, isolated yields. ^bYields were determined by GC by using 100 μ L n-hexadecane as standard.)

2.6. Green Synthesis of primary amides

The creation of amide functionality³⁵⁻³⁷ is highly important in chemistry, medicine and biology because it plays a major role in the amplification and configuration of life science molecules, peptides, proteins and as well as materials^{13, 16-17}. In general, primary amides have been prepared by the reaction of carboxylic acids or their activated derivatives such as acid chlorides, anhydrides with ammonia. Nevertheless for the synthesis of this important class of amides, more environmentally benign procedures are required. In addition to alcohols,^{37a,b} the synthesis of primary amides from aldehydes and ammonia was also been carried out using manganese oxide,^{37a} Rh^{38a} KMnO₄^{38b} and lodine.^{38c}. However, the use of iron-based heterogeneous catalysts for the synthesis of primary amides is obviously more advantageous.



Scheme 4. Nanoscale Fe₂O₃-N/C -catalysed synthesis of amides from aldehydes and aqueous ammonia^a. ^{(a}Reaction conditions: 0.5 mmol aldehyde, 100 μ L aq. NH₃ (28-30% NH₃ basis), 50 mg catalyst (5.0 mol% Fe), 10 bar air 3 mL H₂O, 120 °C, 24 h, isolated yields.)

After having successfully demonstrated the preparation of important nitriles, we have further extended the potential of Fe_2O_3 -N/C-catalyst for direct and one-pot synthesis of primary amides from benzaldehyde and aqueous ammonia. Interestingly, this catalyst is also observed to be active and

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selective for the preparation of even primary amides (Scheme 4). However, to achieve sufficient activity and selectivity, the reaction temperature and pressure had to be raised to a certain extent and also the reaction conditions need to be adjusted accordingly. In water medium, we were able to convert aldehydes into primary amides using aqueous ammonia and air in up to 91 % yield (Scheme 4).

The reaction pathway for the formation of nitriles and amides is presented in Scheme 5. In the first step, the formation intermediate, primary imine was took place from aledehyde and ammonia. In presence of Fe₂O₃-N/C-catalyst, this unstable imine underwent oxidation to produce nitrile. In the final step, in presence of water and ammonia the formed nitrile was hydrolyzed to produce primary amide. The production of amide from nitrile requires higher temperature to proceed under forcing conditions. In order to confirm the formation mechanism of amide, we performed the reaction of benzonitrile in water at 120 °C in presence of ag. ammonia and catalyst. In this case formation of benzamide in 80% yield was observed. This result clearly evidenced that water is required for the formation of amide from aldehyde and ammonia. Due to the involvement of two step reaction, the obtained yields of amides are somewhat lower than that of nitriles. In this case the unreactive nitrile was observed as the other product.



Scheme 5. Reaction pathway for the Fe₂O₃-N/C -catalyzed synthesis of nitriles and amides from aldehydes and ammonia.

2.7. Scale up studies for gram scale synthesis

In order to demonstrate the synthetic and practical utility of this approach using our iron-catalyzed synthetic protocol, we further performed the gram scale (i.e. 1 to 5 g) reactions. In the direction of scale up, a few grams of some selected aldehydes have been converted to their corresponding nitriles under identical reaction conditions. The yields of desired nitriles obtained from these tests are very much comparable and quite consistent with those obtained from 0.5 mmol (small) scale tests (Scheme 6).



Scheme 6. Demonstrating gram scale reactions for synthesis of some selected nitriles over Fe₂O₃-N/C catalyst. (Reaction conditions: 2-5 g substrate, weight of catalyst corresponds to 3 mol% Fe, 200 μ L Aq. NH₃ for every 0.5 mmol substrate, 40 °C, 10-50 mL *t*-amyl alcohol, 1 bar O₂ (balloon), 24-30 h. Isolated yields.)

2.8. Stability and Recycling of Fe_2O_3 -N/C-catalyst.

In general, stability, recycling and reusability features of any catalyst are very important features for the advancement of

sustainable industrial processes. Noticeably, our Fe₂O₃-N@C catalyst is highly stable and conveniently recycled up to 5 times without any significant loss of catalytic activity and selectivity (Fig. 3). The recycled catalyst has been subjected to ICP analysis and found that there is no leaching of iron in the recycled catalyst.



Fig. 3. Recycling of Fe_2O_3 -N/C-catalyst for the synthesis of benzonitrile. (Reaction conditions: 1 mmol benzalydehyde, 60 mg catalyst (3.2 mol% Fe), 400 μ L aq. NH₃ (28-30% NH₃ basis), 1 bar O₂ (balloon), 4 mL t-amyl alcohol, 40 °C, 24 h, yields were determined by GC using n-hexadecane standard.)

Further the stability of catalyst was also tested by performing kinetic studies (Fig. S6). The effect of ammonia concentration, reaction time, amount of catalyst, concentration of substrate (benzaldehyde) and pressure of O_2 on the yield of benzonitrile was performed (Fig. S6). Noticeably, the catalyst is stable and exhibited similar catalytic activity in presence of excess of ammonia (1mL), with prolonged reaction time and at high pressure of O_2 (5 bar). As seen from the kinetic plots (Fig. S6), on increasing the reaction time, catalyst amount and ammonia concentration, the yeild of benonitrile was increased and observed highest yeld for 24 h with 30mg of catalyst, in presence of 200 microl Aq. ammonia and one bar O_2 .

3. Experimental section

3.1. Procedure for the reparation of $Fe_2O_3\text{-}N/C$ (Fe-Phen/C-800) catalyst (1 g) $^{[2a]}$

Appropriate amounts of $Fe(OAc)_2$ and 1,10-phenanthroline corresponds to 3 wt% of Fe in 1:3 molar ratio of Fe to phenathroline were stirred in ethanol for 30 minutes at room temperature. Then, carbon powder (VULCAN® XC72R, Cabot Corporation Prod. Code XVC72R; CAS No. 1333-86-4) was added and the whole reaction mixture was stirred at 60 °C for 12-15 hours. The reaction mixture was cooled to room temperature and the ethanol was removed in vacuo. The solid material thus obtained was dried at 60 °C for 12 hours, after which it was grinded to a fine powder. Then, the powdered material was pyrolyzed at 800 °C for 2 hours under an argon atmosphere and then cooled to room temperature.

Elemental analysis of Fe2O3-N/C (pyrolyzed Fe-phen/C at 800 $^{\circ}$ C) (Wt%): C = 91.1, H = 0.19, N = 2.69, Fe = 2.95.

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The 8 mL oven dried glass vial was charged with magnetic stirrer bar and 0.5 mmol corresponding aldehyde and then 2 mL t-amyl alcohol was added. Next, 30 mg Fe₂O₃-N/C (i.e. Fe-Phen/C-800) catalyst (3 mol% Fe) was added followed the by the addition of 200-300 μL aq. NH_3 (28-30% NH_3 basis). The glass vial was fitted with septum and screw cap. Then 1 bar O₂ containing balloon was connected to the reaction vial though needle and then the reaction was allowed to proceed for 24 hrs at 40 °C under continuous stirring. After completion of the reaction, the reaction vial was cooled down to room temperature and the excess O₂ was gradually discharged. Then, the catalyst was filtered-off, and washed with ethyl acetate. The solvent from the filtrate containing the reaction products and unreacted substrate (if any?) was removed in vacuo and the target nitrile was purified by column chromatography. In case of yields determined by GC, 100 µL nhexadecane was added to the reaction vial containing products and diluted with ethyl acetate. Then, filtered through plug of silica and the filtrate containing products was analysed by GC (HP-6890, column HP-5 (30 m x 250 mm x 0.25 μm) equipped with FID. Conversion and yields were determined on the basis of GC area counts using pre-calibrations. All products were analyzed by GC, GC-MS and NMR analysis.

3.3. General procedure for the preparation of amides

A magnetic stirrer bar and the corresponding aldehydes were transferred to 8 mL glass vial and then the 3 mL H₂O was added. Later on, 50 mg Fe₂O₃-N/C (i.e. Fe-Phen/C-800) catalyst (5 mol% Fe) was added followed by the addition of 100 μ L ag. NH₃. Then, the vial was fitted with septum, cap and needle. The reaction vials (i.e. 8 vials in each test) were placed into a 300 mL autoclave (PARR Instrument Company, USA) and then autoclave was pressurized with 10 bar of air. The autoclave was placed into an aluminium block and the temperature of the aluminium block was set to measure 120 $^{\circ}$ C inside the autoclave and reactions were allowed to progress under continuous stirring for required time at 120 °C. In this set-up the temperature of the aluminium block was set more than 120 °C (130-140 °C) in ordered to attain exactly 120 °C inside the autoclave). After completion of the reaction, the excess air remained in the autoclave was slowly depressurized and then the samples were removed from the autoclave. Afterwards, the catalyst was filtered-off, washed with methanol. The solvent from the filtrate containing the reaction products was removed in vacuo and the corresponding amide was purified by column chromatography. All products were analyzed by GC-MS and NMR analysis.

3.4. Procedure for the gram scale reactions

The reactions were performed similar to the procedure mentioned in section 3.2 in 100 or 300 mL glass fitted autoclave with the conditions, 2-5 g aldehyde, corresponds to 3 mol% Fe, 200 μ L Aq. NH₃ for every 0.5 mmol substrate, 40 °C, 10-50 mL t-amyl alcohol, 24-30 h. After completion of the reaction, the autoclave was cooled to room temperature and remaining air was discharged. The catalyst from the reaction mixture was filtered off and washed with ethyl acetate. The

solvent from the filtrate containing reaction products was removed in vacuo. The corresponding nitrile was purified by column chromatography (silica; n-hexane-ethyl acetate mixture). All products were analyzed by GC-MS and NMR analysis.

3.5. Procedure for catalyst recycling

The recycling of the catalyst was carried out for the synthesis of benzonitrile under the same procedure given in the section 3.2 under reaction conditions: 1 mmol benzalydehyde, 60 mg Fe₂O₃-N/C (Fe-Phen/C-800) (3% Fe), 400 μ L aq. NH₃, 1 bar O₂, 4mL t-amyl alcohol, 40 °C, 24 hrs, yields were determined by GC using 100 μ L n-hexadecane standard. In each run, after the reaction the catalyst was separated by centrifugation, washed thoroughly with ethyl acetate and dried by vacuum. Then, the dried catalyst was used further, without any purification or reactivation. The recycled catalyst and centrifugate containing reaction products were subjected to ICP analysis. This analysis showed that the content of Fe in recycled catalysts has not been decreased (2.94) and also not detected in centrifuate.

Conclusions

In conclusion, we have demonstrated green methodology for preparation nitriles and primary amides starting from easily accessible various aldehydes by make use of combination of earth abundant Fe-based nano-catalyst and green reagents such as atmospheric O_2 or air and inexpensive aqueous ammonia. Under operationally simple and mild reaction conditions, this iron-based catalyst is highly reactive and selective for the synthesis of series of functionalized and structurally diverse aromatic, heterocyclic and aliphatic nitriles. Further, this aerobic green oxidative methodology has been applied for the preparation of primary amides. Moreover synthetic utility and and practical applicability of this methodology were demonstrated by up scaling the reactions to gram scales (1-5 g scale) and recycling of the catalyst.

Conflicts of interest

There are no conflicts to declare.

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