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Magnetic graphitic carbon nitride: application in C-H activation of amines

Sanny Verma[a†], R. B. Nasir Baig[a†], Changseok Han[b], Mallikarjuna N. Nadagouda[b] and Rajender S. Varma[a]*

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Magnetic graphitic carbon nitride, Fe@g-C₃N₄, has been synthesized by adorning graphitic carbon nitride (g-C₃N₄) support with iron oxide via non-covalent interaction. The magnetically recyclable catalyst showed excellent reactivity for expeditious C-H activation and cyanation of amines.

The chemical industry caters to the daily needs of humanity ranging from drugs for the treatment of various diseases to materials used in technological advancements. However, there is close association of generated toxic waste and the release of hazardous chemicals in to the environment with chemical enterprises.[1] The heightened awareness of the importance of environmental protection has resulted in stringent laws for handling and disposition of toxic waste.[2-4] Pollution prevention and the eventual elimination of the generation of hazardous waste is the ideal way to save the environment.[5] Thus, there is tremendous interest in developing clean, sustainable and environmentally benign methods for the synthesis of pharmaceutical and industrially important products.[6]

α-Aminonitriles are important intermediates in organic synthesis.[7] They have been widely used for the synthesis of bioactive natural products, unnatural α-amino acids and heterocyclic compounds.[8-9] Their synthesis often entails the use of stoichiometric amount of reagents.[10-14] The catalytic variant of these reagents has lately been emphasized via C-H activation of amines using transition metal catalysts.[15-18] Although the catalytic methods have abetted in reducing the waste generation, the homogeneous nature of the catalyst does not allow recycling and reuse of the reagents; waste

generated, even in catalytic systems, becomes prominent on large scale industrial use. Consequently, research shave realized that the use of heterogeneous systems is the way forward to address the environmental issues that diminish the toxic waste generation. There have been some successful efforts to develop a heterogeneous variant of these catalysts.[19-24] Most of these reagents involve the use of toxic metals and suffer from catalyst poisoning or deactivation thus limiting the recyclability and reuse of these reagents. Engaged in the development of benign and sustainable methods in organic synthesis and nano-catalysis,[25-28] herein, we report a simple and efficient method for the synthesis of a magnetic-graphitic carbon nitride, a magnetically retrievable and inexpensive iron-based catalyst and its application in C-H activation and α-cyanation of secondary and tertiary amines.

The synthesis of catalyst, Fe@g-C₃N₄, involves two steps: preparation of graphitic carbon nitride (g-C₃N₄) support and deposition of magnetic ferrites over the layers of graphitic carbon nitride.[29-32] The graphitic carbon nitride (g-C₃N₄) was synthesized by calcination of urea at 500 °C for 2 h. The highly porous graphitic material was dispersed in a 10% solution of polyethylene glycol (PEG-400) in water by sonication. The FeSO₄.7H₂O was added to this solution and the stirring was continued for 8 hours; sodium borohydride (NaBH₄) was finally added to reduce the iron sulfate to magnetic ferrites and the stirring was continued for another 8 hours (Scheme 1). The ensuing material, magnetic ferrites nanoparticles deposited on layers of graphitic carbon nitride, was then separated using an external magnet, washed with water followed by methanol and dried under vacuum at 50 °C. Catalyst characterization by SEM, transmission electron microscopy (TEM), EDX and X-ray diffraction (XRD) (Fig. 1a, 1b, 1c and 1d) confirmed the formation of single-phase nanoparticles; graphitic carbon nitride-nano-ferrite (Fe@g-C₃N₄) catalyst exhibits spherical morphology and a size range of 5-30 nm.

a. Sustainable Technology Division, National Risk Management Research Laboratory, U. S. Environmental Protection Agency, MS 443, Cincinnati, Ohio 45268, USA. Fax: 513- 569-7677; Tel: 513-487-2701.E-mail:varma.rajender@epa.gov
b. WQMB,WSWRD, National Risk Management Research Laboratory, U. S. Environmental Protection Agency, MS 443, Cincinnati, Ohio 45268, USA
† Equal contribution
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

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The deposition and percentage of nanoferrites was confirmed using EDX and ICP-AES analysis; the wt. percentage of iron was found to be 9.87 (0.17 mol/g). The XRD pattern of Fe@g-C$_3$N$_4$ (Fig. 1d) clearly indicates that the product is enriched with FeO/Fe$_2$O$_3$. This was confirmed by X-ray photoelectron spectra (XPS) analysis of sample (ESI Fig.S1a and S1b). The binding energy of Fe 2p$_{3/2}$ in Fe^{2+} is about 709 eV and about 711 eV for Fe^{3+}; binding energy of elements increases with the increase in the oxidation state.[33] The X-ray photoelectron spectra (ESI Fig S1b) signal for Fe 2p region and the peak of Fe 2p$_{3/2}$ at 709 eV indiace that Fe^{2+} in the form of FeO. The disapearance of peak at 711 eV confirms the absence of Fe$_3$O$_4$. The setalite peak at 718 eV is a charectorstic peak of Fe^{3+} in γ-Fe$_2$O$_3$, suggesting that that the catalyst is a mixture of FeO/ γ-Fe$_2$O$_3$.
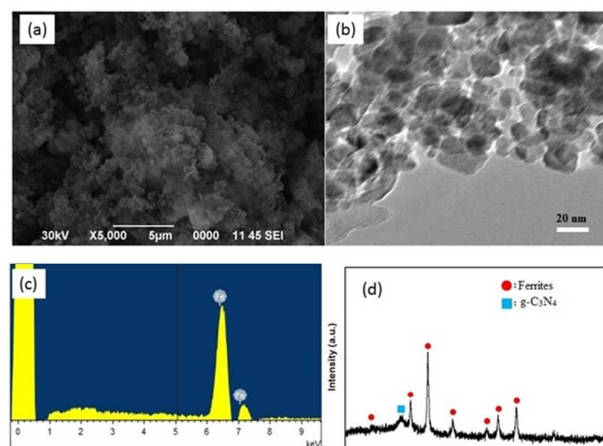
Figure 1: (a) SEM of the magnetic g-C$_3$N$_4$; (b) TEM of the magnetic g-C$_3$N$_4$; (c) EDX of the magnetic g-C$_3$N$_4$; (d) XRD of the magnetic g-C$_3$N$_4$

Graphitic carbon nitide (g-C$_3$N$_4$)   Graphitic carbon nitride-nano-ferrite (Fe@g-C$_3$N$_4$)
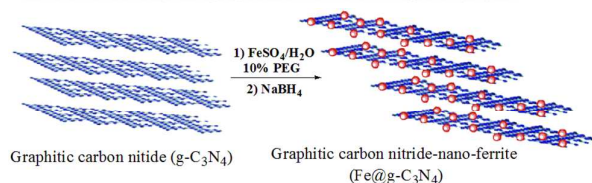
Scheme 1:Synthesis of magnetic graphitic carbon nitride-nano-ferrite

Initially, experiments were performed to optimize the reaction conditions for the cyanation of *N, N*-dimethylaniline. First, the reaction was conducted using graphitic carbon nitride (g-C$_3$N$_4$) at room temperature; no product formation was observed under these conditions (Table 1, entry 1).

Table 1: Reaction condition optimization

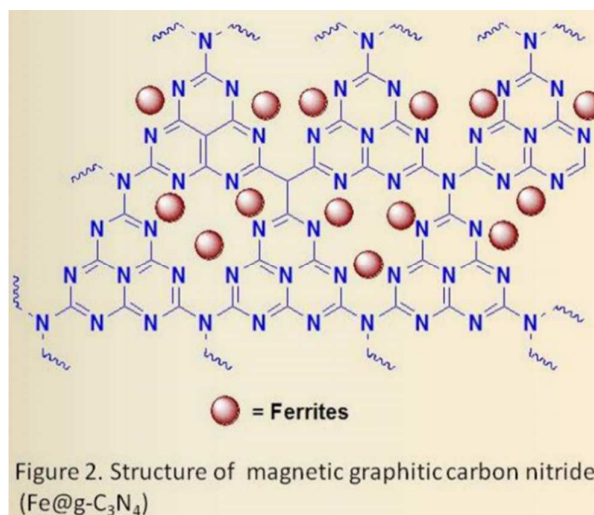| Entry	Catalyst	Condition	Time	Product Yield[a]
1	g-C$_3$N$_4$	AcOH:MeOH	24 h	0%
2	Fe$_3$O$_4$	AcOH:MeOH	24 h	20%
3	FeO-Graphene	AcOH:MeOH	2.5 h	90%[b]
4	Fe@g-C$_3$N$_4$	AcOH:MeOH	90 min	92%
5	Fe@g-C$_3$N$_4$	AcOH:H$_2$O	25 min	97%

a) Isolated Yield; b) Ref 34.

= Ferrites

Figure 2. Structure of magnetic graphitic carbon nitride (Fe@g-C$_3$N$_4$)

The reaction with pure FeO was sluggish as it did not proceed to completion even after 12 hours of stirring at room temperature (Table 1, entry 2). It was found that immobilization of iron oxide over grapheme oxide surface increases its activity (Table 1, entry 3).[34] In order to avoid the use of complex and costly graphene oxide, which requires toxic chemicals for its synthesis, we planned to study the effect of readily available graphitic carbon nitride surface on the activity of nanoferrite for the C-H activation of amines and its applications in the synthesis of α-aminonitriles. The graphitic carbon nitride supported iron oxides was exceptionally active toward the cyanation of amine and the reaction was completed within 1.5 hr in methanol (Table 1, entry 4). The activity of the catalyst may be attributed to the presence of nitrogen in the graphitic frame work and the cage structure of the support (Figure 2). It was interesting to observe that the change of solvent from methanol to water increases the rate of reaction and yields the cyanation product in less than half an hour (Table1, entry 5).

After optimization of the amount of active magnetic graphitic carbon nitride (Fe@g-C$_3$N$_4$) catalyst, the scope of the reaction was explored and its synthetic prowess was demonstrated. The treatment of various amines with Fe@g-C$_3$N$_4$ under optimized conditions gave the corresponding α-amino nitriles (Table 2). Tertiary and secondary amines react efficaciously to afford the corresponding amino nitrile in very good yield. Although the electronic nature of the substituents had minimal effect on the rate of reaction and product outcome; it is obvious from table 1 that the rate of the reaction with electron donating substituent has an edge over the substrate with electron withdrawing substituents.

The plausible mechanism of the reaction entails the formation of reactive oxo-Iron(IV) species which upon its reaction with tertiary amine results in the formation of iminium ion;[35-36] this intermediate reacts with in-situ generated HCN providing the desired α-aminonitrile (Figure 3).[37]
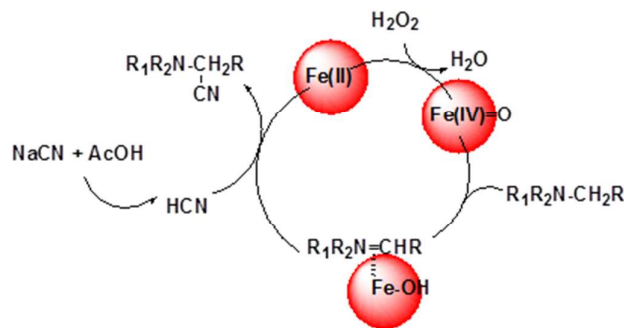
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Figure 3. Plausible mechanism of cyanation of amines

Table 2: Fe@g-C$_3$N$_4$ catalyzed α-cyanation of secondary and tertiary amines

Entry	Substrate	Time	Product	Yield[a,b]
1		25min		98%
2		25 min		97%
3		25 min		98%
4		25min		91%
5		35min		95%
6		35min		93%
7		60min		88%
8		60min		87%

a) Reaction condition: 1 mmol Amines, 1 mmol H$_2$O$_2$, 1.1mmol NaCN, 10 mg of Catalyst (0.017 mmol of Fe) 4 mL 50% Acetic acid, r.t; b) Isolated Yield

In terms of industrial applications, the lifetime and the recyclability of catalysts are very important. A set of experiments was conducted for the cyanation of *N, N*-dimethylaniline. After completion of the first reaction, the catalyst was recovered magnetically, washed with methanol, and dried at 50 °C. A new reaction was then performed with fresh reactants, under the similar conditions. The magnetic graphitic carbon nitride (Fe@g-C$_3$N$_4$) could be recycled at least 5 times without any loss in its activity.

The metal leaching was studied by ICP-AES analysis of the catalyst. The concentration of Fe was found to be 9.87 % before reaction and 9.85% after the reaction. The SEM and TEM images of the catalyst taken after the fifth cycle of the reaction did not show significant change in the morphology

and/or nature of iron oxide nanoparticles (ESI, Fig.S2 and Fig.S3); No iron was detected in the reaction solvent after completion of the reaction. This confirms the fact that the graphitic carbon nitride cage holds the iron metal tightly which minimizes leaching and facilitates the efficient recycling.

Conclusions

A simple, efficient and sustainable aqueous protocol for the C-H activation leading to α-cyanation of amines has been developed using magnetically retrievable active Fe@g-C$_3$N$_4$ catalyst. The formation of α-amino nitriles occurs expeditiously in less than an hour. The unprecedented activity is due to the non-covalent interaction of nanoferrites with nitrogenous framework and cage structure. The recovery of Fe@g-C$_3$N$_4$ using an external magnet eliminates the requirement of catalyst filtration after completion of the reaction; the magnetic catalysts could be readily recycled with minimal loss of catalytic activity.

Disclaimer

The U.S. Environmental Protection Agency, through its Office of Research and Development, funded and managed, the research described herein. It has been subjected to the Agency's administrative review and has been approved for external publication. Any opinions expressed in this paper are those of the author(s) and do not necessarily reflect the views of the Agency, therefore, no official endorsement should be inferred. Any mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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