Fe_3O_4-nanoparticles catalyzed an efficient synthesis of nitriles from aldehydes

Pranab Ghosh, Bittu Saha, Gyan Chandra Pariyar, Abiral Tamang, Raju Subba

PII: S0040-4039(16)30804-8
DOI: http://dx.doi.org/10.1016/j.tetlet.2016.06.125
Reference: TETL 47852

To appear in: *Tetrahedron Letters*

Received Date: 12 May 2016
Revised Date: 26 June 2016
Accepted Date: 27 June 2016

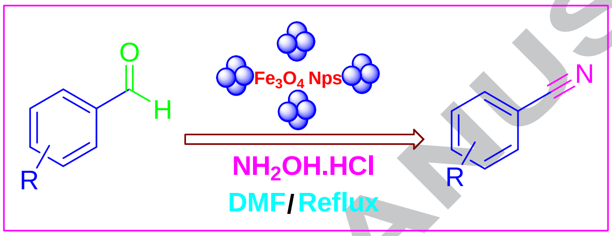
Please cite this article as: Ghosh, P., Saha, B., Pariyar, G.C., Tamang, A., Subba, R., Fe_3O_4-nanoparticles catalyzed an efficient synthesis of nitriles from aldehydes, *Tetrahedron Letters* (2016), doi: http://dx.doi.org/10.1016/j.tetlet.2016.06.125

Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Fe_3O_4-nanoparticles catalyzed an efficient synthesis of nitriles from aldehydes

Pranab Ghosh[a*], Bittu Saha[a], Gyan Chandra Pariyar[a], Abiral Tamang[b] and Raju Subba[a]



Tetrahedron Letters
journal homepage: www.elsevier.com

Fe_3O_4-nanoparticles catalyzed an efficient synthesis of nitriles from aldehydes

Pranab Ghosh[a*], Bittu Saha[a], Gyan Chandra Pariyar[a], Abiral Tamang[b] and Raju Subba[a]

[a]*Department of Chemistry, University of North Bengal, District Darjeeling-734013, West Bengal, India.*
[b]*Department of Physics, Jadavpur University, Jadavpur, Kolkata-700032, India.*
Tel.: +91 (0353) 2776381; fax: +91 (0353) 2699001.
E-mail address: pizy12@yahoo.com (P. Ghosh).

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Aldehydes
Nitriles
Fe_3O_4-CTAB NPs
DMF
Reflux

ABSTRACT

Fe_3O_4-CTAB NPs have been applied as a competent catalyst for one-pot synthesis of nitriles directly from aldehydes. The present investigation describes the synthesis of nitriles by combination of aromatic/aliphatic/heterocyclic aldehydes and hydroxylamine hydrochloride in the presence of iron oxide nanocatalyst in DMF under reflux condition. Fe_3O_4-CTAB NPs were prepared by reported method and characterized by FE-SEM, TEM and XRD analysis. The amount of Fe in Fe_3O_4-CTAB was quantified by Atomic Absorption Spectroscopy (AAS). The protocol endow with excellent yield of products along with simple reaction set up and economically adept alternative approach.

Introduction

Suitably design organonitrile derivatives are widely documented as bioactive molecules[1] (**fig. 1**). Nitriles are also regarded as prominent intermediate for the production of various pharmaceuticals, agrochemicals, polymers, pigments and dyes.[2] It's applications in heterocyclic compound synthesis and functional group transformations are well established from the long time.[3] Classically adopted methods for nitrile synthesis are Sandmeyer reaction,[4] ammoxidation of aldehydes,[5] Kolbe nitrile synthesis,[6] hydrocyanation of alkenes,[7] and Rosenmund–von Braun reaction.[8] Moreover, various methodologies for single step preparation of nitriles from the substrates like alcohols,[9] amines,[10] amides,[11] azides[12] and oximes[13] are known. The other alternative approaches are olefinic bond cleavage of alkene,[14] cyanation of aryl halides,[15] oxidative rearrangement of alkene,[16] methyl arenes[17] and benzyl or allyl halides.[18] Preparation of nitriles from aldehydes is one of the interesting and advantageous approach because the number of carbon in reactant and final product will remain same. The main features of one-pot transformations are valuable strategic way in terms of economic and environmental aspects. One-pot reactions usually consist of two or more than two steps that has to be done in a single step without isolation of intermediate, which in turn, substantially help to reduces the energy consumption, solvent waste and reaction time. Focusing on these advantages of one-pot synthesis, we planned to accomplish single step transformation of aldehydes into nitriles by means of minimum energy, chemicals waste and small time outlay. The literature survey reveals that diverse catalytic systems have been applied for one-pot transformation of aldehydes into nitriles[19] but most of them are suffers from various constrain such as harsh reaction conditions, longer reaction time, low yield, work-up difficulties and waste of toxic metal salt or solvents into the environment. In view of our attempt to develop an efficient and environment friendly protocol, we have chosen Fe_3O_4-CTAB NPs catalyst for our present investigation. We believe that our investigation will definitely robust the synthetic approach and fulfil the paucity of sustainable development.

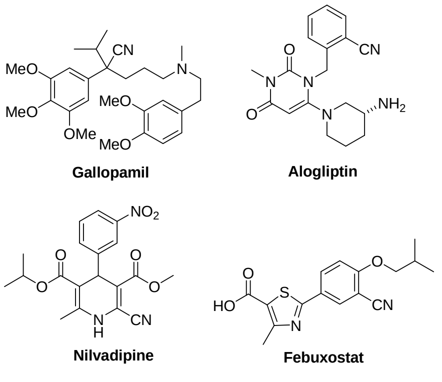


Fig.1: Potent bioactive organonitrile derivatives

As iron oxide NPs are well documented in catalysis and medicinal chemistry.[20] The versatile catalytic activity, magnetic recyclability, low toxicity and useful in medicinal chemistry made it environmentally and economically advantageous.[21] Easy accessibility and relatively low toxicity made iron NPs a desirable nanocatalysts in present time. In our endeavour to develop efficient protocol for nitrile synthesis, we report herein, Fe_3O_4-CTAB NPs catalyzed one-pot synthesis of organonitriles from aldehydes and hydroxylamine hydrochloride in DMF under reflux condition (**Scheme 1**).

Result and discussion

In continuation of our work for one-pot nitrile synthesis from aldehydes and hydroxylamine hydrochloride,[22] we used Fe_3O_4-CTAB NPs as catalyst for our present investigation. Fe_3O_4-CTAB NPs were synthesized by reported method[23] (see supporting information). The synthesized Fe_3O_4-CTAB NPs were then characterized by Field Emission Scanning Electron Microscope (FE-SEM, INSPECT F50, FEI), Transmission Electron Microscope (TEM, JEOL, JEM 2100, 200 kV) and X-ray Diffraction (XRD, Advance D8, Bruker) analysis. FE-SEM images (**fig. 2a**) reveal that the Fe_3O_4 NPs are 20-35 nm in size which is further confirmed by the TEM images (**fig.2b**). TEM images also reveal that the Fe_3O_4 NPs are in crystalline cubical shape. XRD spectra shows the standard peaks of the Fe_3O_4 are unhindered by the CTAB presence although peak broadening has occurred due to the nano-size of the Fe_3O_4. Moreover, we have compared XRD pattern of freshly prepared Fe_3O_4-CTAB NPs (fig.2c [B]) with literature XRD pattern of pure Fe_3O_4 magnetite NPs (fig.2c [A]) and found exactly similar XRD pattern with Fe_3O_4 magnetite NPs. X-ray diffraction pattern of Fe_3O_4-CTAB also confirm the purity of magnetite via the absence of other phases of iron oxide such as maghemite or hematite in product. The quantification of Fe in Fe_3O_4-CTAB has been evaluated by Atomic Absorption Spectroscopy (AAS) using Fe standard solution as supplied by Sigma Aldrich. **Fig.2d** depicts the plot of absorbance versus concentration of Fe in Fe_3O_4-CTAB Nps. The concentration of Fe used during the calibration was 0, 2, 4, 6 ppm. The solution of Fe_3O_4-CTAB NPs in water was prepared by taking 5 mg of the sample in 100 ml water and the absorbance of the sample were taken. From the absorbance data, the concentration of Fe in Fe_3O_4-CTAB has been found to be 3.7 ppm (blue) and the percentage of Fe in Fe_3O_4-CTAB has been found to be 74% by weight.

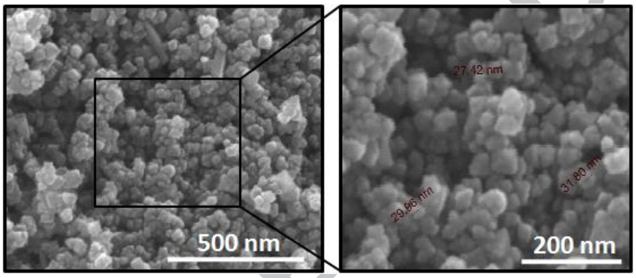


Fig. 2a: FE-SEM images of Fe_3O_4-CTAB NPs

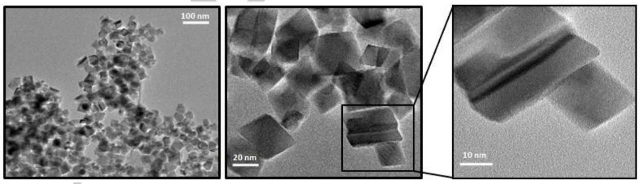


Fig. 2b: TEM images of Fe_3O_4-CTAB NPs

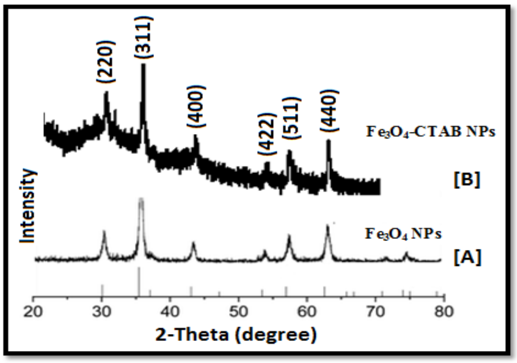


Fig. 2c: Comparison of XRD pattern of Fe_3O_4-CTAB NPs [B] with literature XRD pattern of pure Fe_3O_4 NPs [A]

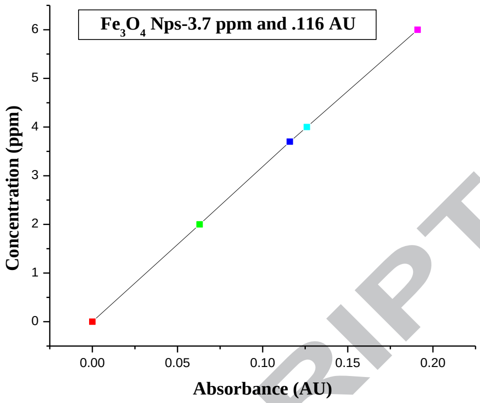
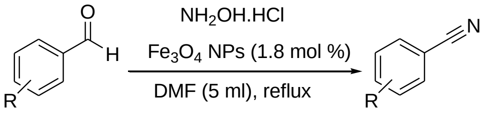


Fig 2d: AAS plot of absorbance versus concentration

In an endeavor to begin our present investigation we have taken vanillin as our model compound. The model reaction comprising vanillin (0.5 mmol), hydroxylamine hydrochloride (0.75 mmol) and Fe_3O_4 NPs (7.4 mol %) in dry DMF (5 ml). The reactions were screened from room temperature to high temperature (table 1). The excellent yield was found only at high temperature (entry 6, table 1). The reaction at the temperature range between 50-70 °C furnish only oxime derivative and at 80-90 °C offered a mixture of oxime and nitriles derivatives.

After reaching satisfactory result under reflux condition in short reaction time (table 1), the catalytic potential of Fe_3O_4-CTAB NPs was tested by reducing the amount of catalyst in similar reaction condition (table 2). Finally we could be able to optimize the reaction condition and isolate 96 % yield of nitrile in minimum reaction time (entry 5, table 2). Further reduction of amount of catalyst or changing the reaction time could not produce a good result (entry 6-9, table 2). The % of yield depends on both amount of catalyst and reaction temperature. The combination of aldehyde (0.5 mmol), hydroxylamine hydrochloride (0.75 mmol) and Fe_3O_4 NPs (1.8 mol %) in dry DMF (5 ml) under reflux condition found to be optimized reaction condition for desired transformation (entry 5, table 2). For the generalization of our scheme, aldehydes **1-15** were successfully converted into corresponding nitriles under optimized condition[24] (table 3).



Scheme 1. Fe_3O_4 NPs catalyzed synthesis of nitriles from aldehydes

Table 1

Screening of catalytic activity of Fe_3O_4-CTAB NPs[a]

Entry	Fe_3O_4-CTAB (mg)	Fe_3O_4 (mol %)[b]	Temp (° C)	Time (h)	Yield (%)[c]
1	23.1	7.4	r.t	4	nil
2	-	-	50	4	-
3	-	-	70	4	-
4	-	-	80	3	25
5	-	-	90	3	36
6	-	-	reflux	2	97

[a] Reaction of vanillin (0.5 mmol), hydroxylamine hydrochloride (0.75 mmol) and Fe_3O_4-CTAB NPs (23.1 mg,) in dry DMF (5 ml) at different temperature. [b] Amount of Fe_3O_4 NPs in Fe_3O_4-CTAB quantified by AAS. [c] Isolated yield.

Table 2

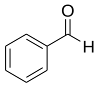
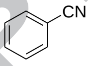
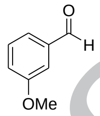
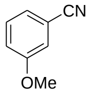
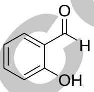
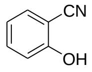
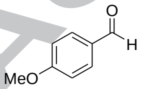
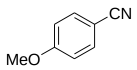
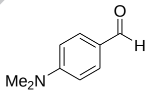
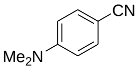
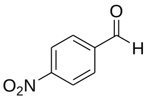
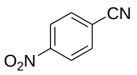
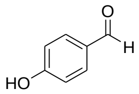
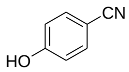
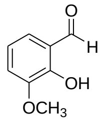
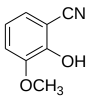
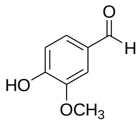
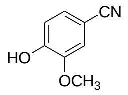
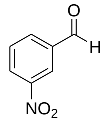
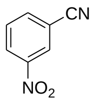
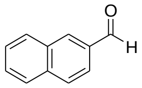
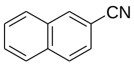
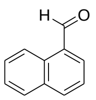
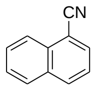
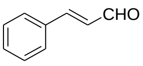
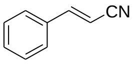
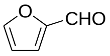
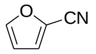
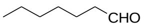
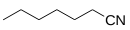
Optimization of catalyst[a]

Entry	Fe_3O_4-CTAB (mg)	Fe_3O_4 (mol %)[b]	Time (h)	Yield (%)[c]
1	23.1	7.4	1.5	97
2	11.5	3.7	2	-
3	5.7	1.8	2	96
4	5.7	1.8	1.5	-
5	**5.7**	**1.8**	**1**	**96**[d]
6	5.7	1.8	0.5	91
7	3.4	0.9	2.5	88
8	2.3	0.6	4	83
9	1.1	0.3	4	78

[a] Reaction of vanillin (0.5 mmol), hydroxylamine hydrochloride (0.75mmol) and Fe_3O_4-CTAB NPs in dry DMF (5 ml) under reflux condition. [b] Amount of Fe_3O_4 NPs in Fe_3O_4-CTAB quantified by AAS. [c] Isolated yield. [d] Optimized reaction condition.

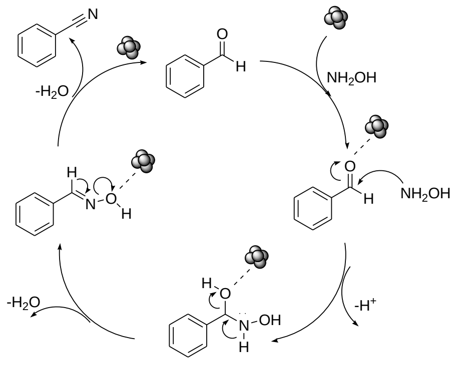
Table 3

Fe_3O_4 NPs catalyzed synthesis of nitriles

Entry	Aldehydes	Time (h)	Products	Yield (%)[b]
1		1		97
2		1		93
3		1.5		94
4		1.5		92
5		1.5		86
6		1		89
7		1.5		87
8		1		94
9		1		96
10		1.5		86
11		2		91
12		2		93
13		2		91
14		1.5		87
15		2		76

[b] Isolated yield.

Plausible mechanism for Fe_3O_4-CTAB NPs catalyzed one-pot synthesis of nitriles from aldehydes is shown in **Sheme 2**. Fe_3O_4-CTAB NPs activate carbonyl carbon for nucleophilic attack by hydroxylamine. Subsequent deprotonation followed by loss of water molecule gives rise to the formation of oxime derivatives. Finally, Fe_3O_4-CTAB NPs participate in expulsion of water molecule from oxime to give desire product and itself get regenerated at the end of reaction for consecutive cycle.



Scheme 2. Plausible mechanism for the transformation of aldehyde into nitrile

Conclusion

In conclusion, we have developed Fe_3O_4-CTAB NPs catalyzed an efficient protocol for one-pot conversion of aldehydes into nitriles from aldehydes (0.5 mmol), hydroxylamine hydrochloride (0.75 mmol) in dry DMF (5ml) under reflux condition. Advantage of this protocol includes the use of inexpensive and relatively less toxic nanocatalyst, excellent yield, easy reaction setup and easy work-up process.

Acknowledgement

One of the authors (B.S) is thankful to BSR, UGC-New Delhi for financial support.

Supplementary Material

Supplementary data associated with this article can be found, in the online version, at xxxxxxxxxxxxxxxxxxxx

References

1. Fleming, F. F.; Yao, L.; Ravikumar, P. C.; Funk, L.; Shook, B. C. *J. Med. Chem.* **2010**, *53*, 7902-7917; (b) Sweeney, A. M.; Grosche, P.; Ellis, D.; Combrink, K.; Erbel, P.; Hughes, N.; Sirockin, F.; Melkko, S.; Bernardi, A.; Ramage, P.; Jarousse, N.; Altmann, E. *ACS Med. Chem. Lett.* **2014**, *5*, 937-941; (c) Frizler, M.; Lohr, F.; Furtmann, N.; Kläs, J.; Gutschow, M. *J. Med. Chem*. **2011**, *54*, 396-400; (d) Chuck, C-P.; Chen, C.; Ke, Z.; Wan, D. C.; Chow, H-F.; Wong, K-B. *Eur. J. Med. Chem*. **2013**, *59*, 1-6.
2. (a) Larock, R. C. Comprehensive Organic Transformations; VCH: New York **1989**, 819; (b) Houben-Weyl, C.; Grundmann, Methodender Organischen Chemie. Falbe; J. Ed. Georg Thieme Verlag: Stuttgart, **1985**, E5, 1313.
3. (a) Battilocchio, C.; Hawkins, J. M.; Ley, S. V. *Org. Lett.* **2014**, *16*, 1060-1063; (b) Muñoz, J. M.; Alcázar, J.; Hoz, A.; Díaz-Ortiz, A. *Tetrahedron Lett*. **2011**, *52*, 6058-6060; (c) Caddick, S.; Haynes, A. K. K.; Judd, D. B.; Williams, M. R. V. *Tetrahedron Lett*. **2000,** *41*, 3513-3516; (d) Heller, B.; Sundermann, B.; Buschmann, H.; Drexler, H-J.; You, J.; Holzgrabe, U.; Heller, E.; Oehme, G. *J. Org. Chem*. **2002**, *67*, 4414-4422; (e) Bosch, L.; Vilarrasa, J. *Angew. Chem. Int. Ed*. **2007**, *46*, 3926-3930; (f) Aureggi, V.; Sedelmeier, G.; *Angew. Chem. Int. Ed*. **2007**, *46*, 8440-8444; (g) Aldhoun, M.; Massi, A.; Dondoni, A. *J. Org. Chem*. **2008**, *73*, 9565-9575; (h) Bokach, N. A.; Kuznetsov, M. L.; Haukka, M.; Ovcharenko, V. I.; Tretyakov, E. V.; Kukushkin, V. Y. *Organometallics*. **2009**, *28***,** 1406-1413; (i) Cohen, M. A.; Sawden, J. N.; Turner, J. *Tetrahedron Lett*. **1990,** *31*, 7223-7226; (j) Bhattacharyya, S.; Pathak, U. *Synthesis*. **2015**, 3553-3560.
4. Beletskaya, I. P.; Sigeev, A. S.; Peregudov,A. S.; Petrovskii, P. V. *J. Orgm. Chem.* **2004**, *689*, 3810-3812.
5. Ellis, G. P.; Romney-Alexander, T. M. *Chem. Rev*. **1987**, *87*, 779-794.
6. Friedman, L.; Shechter, H. *J. Org. Chem.* **1960**, *25*, 877-879.
7. Bini, L.; Muller, C.; Wilting, J.; Chrzanowski, L.; Spek, A. L.; Vogt, D. *J. Am. Chem. Soc.* **2007**, *129*, 12622-12623.
8. Lindley, J. *Tetrahedron* **1984**, *40*, 1433-1456.
9. (a) Yin, W.; Wang, C.; Huang, Y. *Org. Lett*. **2013**, *15*, 1850-1853; (b) Rad, M. N. S.; Khalafi-Nezhad, A.; Behrouz, S.; Faghihi, M. A. *Tetrahedron Lett.* **2007**, *48*, 6779-6784; (c) Chen, F-E.; Li, Y-Y.; Xu, M.; Jia, H-Q. *Synthesis* **2002**, 1804-1806.
10. (a) Yamaguchi, K.; Mizuno, N. *Angew. Chem. Int. Ed*. **2003**, *42*, 1480-1483; (b) Ghorbani-Vaghei, R.; Veisi, H. *Synthesis* **2009**, 945-950.
11. Zhou, S.; Junge, K.; Addis, D.; Das, S.; Beller, M. *Org. Lett*. **2009**, *11*, 2461-2464.
12. (a) Lamani, M.; Prabhu, K. R. *Angew. Chem. Int. Ed*. **2010**, *49*, 6622-6625; (b) He, J.; Yamaguchi, K.; Mizuno, N. *J. Org. Chem.* **2011**, *76*, 4606-4610.
13. (a) Song, Y.; Shen, D.; Zhang, Q.; Chen, B.; Xu, G. *Tetrahedron Lett*. **2014**, *55*, 639-641; (b) Li, D.; Shi, F.; Guo, S.; Deng, Y. *Tetrahedron Lett.* **2005**, *46*, 671-674; (c) Rad, M. N. S.; Khalafi-Nezhad, A.; Behrouz, S.; Amini, Z.; Behrouz, M. *Synth. Commun.* **2010**, *40*, 2429-2440; (d) Yadav, L. D. S.; Srivastava, V. P.; Patel, R. *Tetrahedron Lett.* **2009**, ***50*****,** 5532-5535; (e) Augustine, J. K.; Kumar, R.; Bombrun, A.; Mandal, A. B. *Tetrahedron Lett.* **2011**, ***52*****,** 1074-1077; (f) Tambara, K.; Pantos, G. D. *Org. Biomol. Chem*. **2013**, *11*, 2466-2472; (g) Sengupta, R.; Weinreb, S. M. *Synthesis* **2012**, 2933-2937.; (h) Rad, M. N. S; Behrouz, S.; Nekoei, A-R. *Synlett* **2012**, 1191-1198; (i) Jiang, N.; Ragauskas, A. J. *Tetrahedron Lett.* **2010**, *51*, 4479-4481.
14. Xu, S.; Cai, T.; Yun, Z. *Synlett* **2016**, 221-224.
15. Yeung, P. Y.; So, C. M.; Lau, C. P.; Kwong, F. Y. *Org. Lett.* **2011**, *13*, 648-651.
16. Qin, C.; Jiao, N. *J. Am. Chem. So***c. 2010,** *132*, 15893-15895.
17. Zhou, W.; Zhang, L.; Jiao, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 7094-7097.
18. Zhou, W.; Xu, J.; Zhang, L.; Jiao, N. *Org. Lett*. **2010**, *12*, 2888-2891.
19. (a) An, X-D.; Yu, S. **2015**, *17*, 5064-5067.; (b) Shargi, H.; Sarvari, M. H. *Synthesis* **2003**, 243-246; (c) Zhu, J- L.; Lee, F-Y.; Wu, J-D.; Kuo, C-W.; Shia, K-S. *Synlett* **2007**, 1317-1319; (d) Augustine, J. K.; Atta, R. N.; Ramappa, B. K.; Boodappa, C. *Synlett* **2009**, 3378-3382; (e) Sridhar, M.; Reddy, M. K. K.; Sairam, V. V.; Raveendra, J.; Godala, K. R.; Narsaiah, C.; Ramanaiah, B. C.; Reddy, C. S. *Tetrahedron Lett.* **2012**, *53*, 3421-3424; (f) Coşkun, N.; Arikan, N. *Tetrahedron*. **1999**, *55*, 11943-11948; (g) Erman, M. B. J.; Snow, W.; Williams, M. J. *Tetrahedron Lett.* **2000**, *41*, 6749-6752; (h) Carmeli, M.; Shefer, N.; Rozen, S. *Tetrahedron Lett*. **2006**, 47, 8969-8972; (i) Telvekar, V. N.; Patel, K. N.; Kundaikar, H. S.; Chaudhari, H. K. *Tetrahedron Lett.* **2008**, *49*, 2213-2215; (j) Sharghi, H.; Sarvari, M. H. *Tetrahedron* **2002**, *58*, 10323-10328; (k) Reddy, K. R.; Maheswari, C. U.; Venkateshwar, M.; Prashanthi, S.; Kantam, M. L. *Tetrahedron Lett.* **2009**, *50*, 2050-2053.
20. (a) Chen, H-P.; Chen, M-H.; Tung, F-I.; Liu,T-Y.; *J. Med. Chem*. **2015**, *58*, 3704-3719; (b) Wei, H.; Insin, N.; Lee, J.; Han, H-S.; Cordero, J. M.; Liu, W.; Bawendi, M. G. *Nano Lett*. **2012,** *12*, 22-25; (c) Jiang, S.; Eltoukhy, A. A.; Love, K. T.; Langer, R.; Anderson, D. G. *Nano Lett*. **2013**, *13*, 1059-1064; (d) Lee, N.; Choi, Y.; Lee, Y.; Park, M.; Moon, W. K.; Choi, S. H.; Hyeon, T. *Nano Lett*. **2012**, *12*, 3127-3131; (e) Hultman, K. L.; Raffo, A. J.; Grzenda, A. L., Harris, P. E.; Brown, T. R.; O'Brien, S. *Acs. Nano*. **2008**, *2*, 477-484.; (f) Cantillo, D.; Moghaddam, M. M.; Kappe, C. O. *J. Org. Chem*. **2013**, *78*, 4530-4542; (g) Riente, P.; Yadav, J.; Pericas. M-A. *Org. Lett*. **2012**, *14*, 3668-3671; (h) Sonnenberg, J. F.; Coombs, N.; Dube, P. A.; Morris. R. H. *J. Am. Chem. Soc*. **2012**, *134*, 5893-5899; (i) Basavegowda, N.; Mishra, K.; Lee. Y. R. *Rsc. adv*. **2014**, *4*, 61660-61666.
21. (a) Trost, B. M. *Science* **1991**, *254*, 1471-1477; (b) Jenck, J. F.; Agterberg, F.; Droescher, M. J. *Green Chem.* **2004**, *6*, 544-556.
22. Ghosh, P.; Subba, R. *Tetrahedron Lett*. **2013**, *54*, 4885-4887.
23. Tan, W.L.; Abu Bakar, M. *J. Phys. Sci.* **2006**, *17*, 37-50.
24. *General procedure for the synthesis of nitrile from aldehyde*: Aldehyde (0.5 mmol) and hydroxylamine hydrochloride (0.75 mmol) were added successively to a solution of Fe_3O_4-CTAB NPs (5.7 mg) i.e Fe_3O_4 (1.8 mol%) in 5 ml dry DMF. The mixture was reflux for appropriate time (table 3). The progress of the reaction was monitored by TLC. After completion of the reaction, the solution was poured into 100 ml water and extract with ethyl acetate, washed several times with water. The combined organic

mixture was dried over anhydrous Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel 60-120 mesh using petroleum ether/ethyl acetate (95:5) as eluent to afford the pure nitrile. All the products were characterized by IR, ^{1}H NMR and ^{13}C NMR.

HIGHLIGHTS OF OUR WORK:

1. Easy reaction set up.
2. Simple and easy workup procedure.
3. Economically benefited.