CHAPTER II

$FeCl_3$-silica: A novel approach for the synthesis of nitriles from oximes

II.A. Introduction

II.A.1. Nitriles

Nitriles are organic compounds having –CN as functional group. When inorganic compounds are attached to -CN, it is called cyanide but in case of organic compound it is called nitriles. Here, we have dealt with synthesis of organic compounds having –CN functional group.

Organonitrile derivates are widely used as an intermediate for the production of agrochemicals, pharmaceuticals, polymers, pigments and dyes.

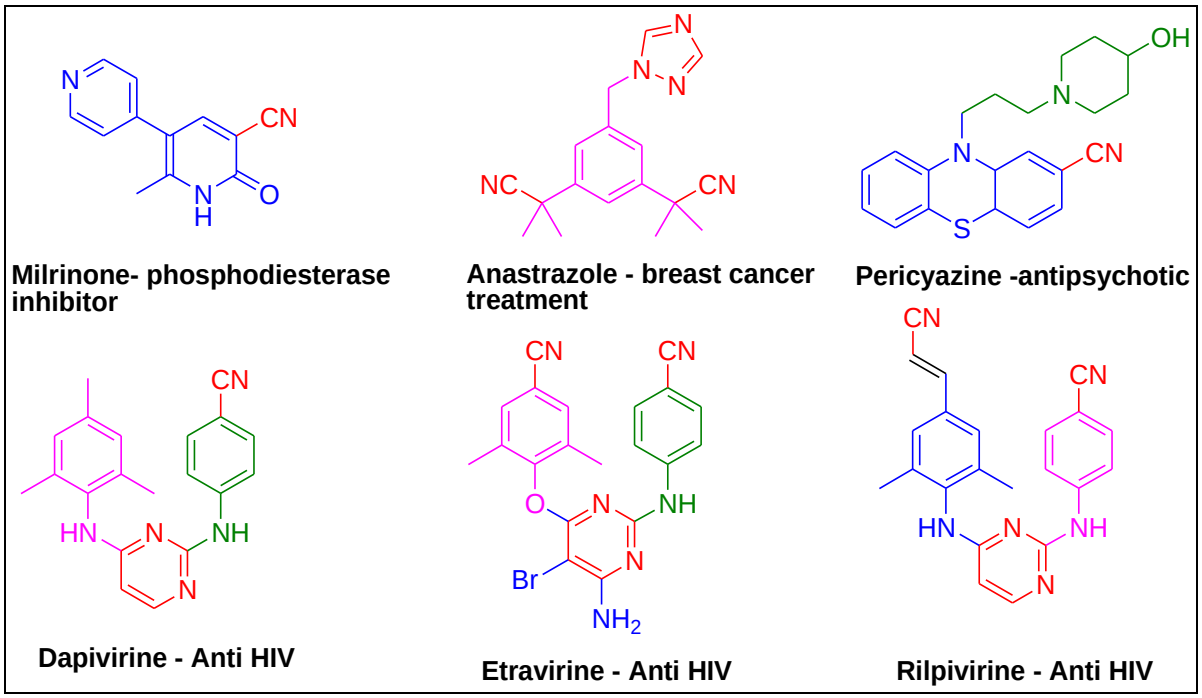


Figure II.1. Biologically active molecules containing nitrile moiety

In spite of that, nitriles are broadly used starting materials for the wide range of organic synthesis such as amines, amides, aldehydes, ketones, carboxylic acids and esters.

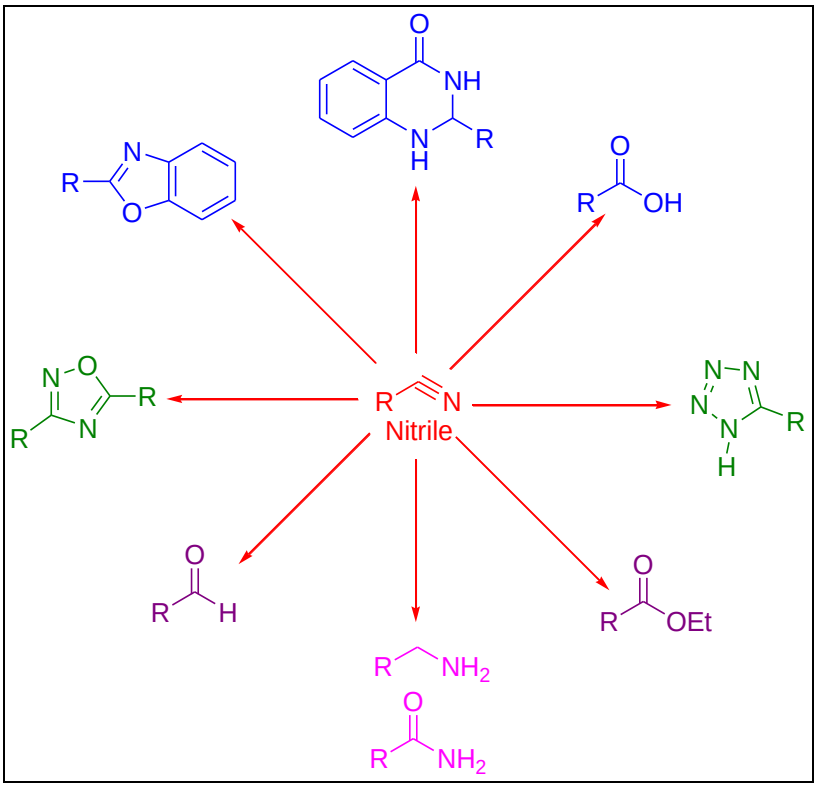


Figure II.2 Organic synthesis of different compounds from nitrile

II.A.2. Historical Background

It was in the year of 1782 when Scheele was first able to prepare hydrogen cyanide.[1] But unfortunately he died while attempting to isolate the anhydrous material. Later on during the year of 1811, Gay-Lussac successfully prepared the pure acid [2] and he was also able to establish its constitution. The first synthesis of nitriles dates back in the year around 1832 when Friedrich Wholer and Justus von Leibig reported the synthesis of benzoyl cyanide or benzonitrile.[3] But since the yield obtained was very small, the physical or chemical properties were not established then. Théophile-Jules Pelouze in the year 1834 synthesized propionitrile.[4] 1844 marks to be an important year in the history of nitrile because it was this year when Hermann Fehling was able to synthesize benzonitrile by heating ammonium benzoate and this time the yield was enough to initiate chemical research. Fleming was able to establish the structure of this newly found substance. He gave this compound the name “nitrile” which later on became the name for these types of compound.

Then a century followed but significant contribution of research in nitrile chemistry became a rare sight. Though contribution was made but people became more reluctant to put their effort due to toxic hazards associated with it.

Only after the beginning of 1920 major contributions started pouring in and since then nitrile chemistry never ever looked back. Ever more important, the last decades witness the metamorphosis of organic nitriles from laboratory interest to large scale chemicals of commerce. Adiponitriles (synthetic fibres), acrylonitriles (plastics, synthetic fibres, synthetic rubber), cyanohydrins (plastics), phthalonitrile (dyes) trichloroacetonitrile (fumigant) are only a few examples which has witness large scale production. Other examples includes insecticides, synthetic resins, solvents and not to forget intermediates for the synthesis of vitamins, pharmaceuticals, plastics etc.

II.A.3. Natural occurrence

Occurrences of nitriles are usually low in nature. But they have been found, though in minor amount, to be present in a large number of plants. Most commonly they are present as glycosides of malanonitrile. One of the best known examples is amygdalin, a cyanogenic glycoside as shown in Fig.II.1. In pangium edule leaves, the concentration of hydrogen cyanide reaches upto 1 percent of its dry weight. Rosenthaler has reported that small amounts of hydrogen cyanide are found in leaves, roots, fruits, seeds, flowers and stem of about 360 varieties of 41 cyanogenetic plant family which includes ferns, trees, legumes, flowers, mushrooms, etc.[5] Certain reducing sugar may get oxidized in presence of atmospheric oxygen and ammonia to hydrogen cyanide and urea and hence partially explains the formation of cyanogenic glycosides as proposed by Parrod.[6] 3-Phenylpropionitrile and phenylacetonitrile was shown to be present in essential oils.[7-8] Acetonitrile can be isolated from gas tar [9] and coal tar. Butyronitrile, propionitrile, valeronitrile and few higher homologues has been isolated from bone oil.[10]

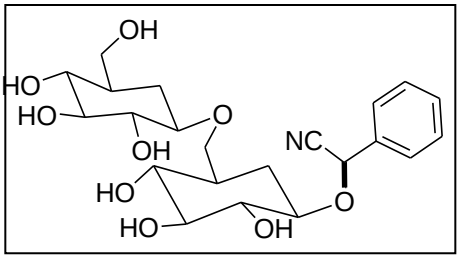
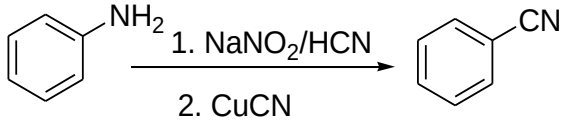


Figure II.3. Cyanogenic glycoside

II.A.4. Synthesis of nitriles using classical methods

II.A.4.1. Sandmeyer reaction

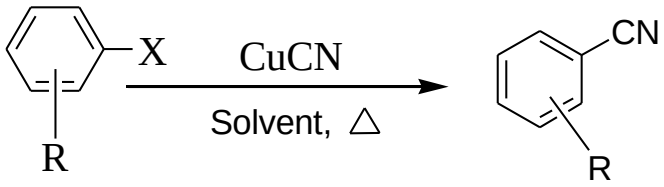
Swiss chemist T. Sandmeyer[11] was the first person to introduce this reaction in 1884. Aryl nitrile was synthesized by this method by cyanation of a cold solution of azobenzene using cuprous cyanide. However the process was not of much importance due to toxicity involved with metal cyanides, less selectivity and harsh reaction conditions (Scheme II.1).



Scheme II.1. Synthesis of nitrile using Sandmeyer reaction

II.A.4.2. Rosenmund-von Braun reaction

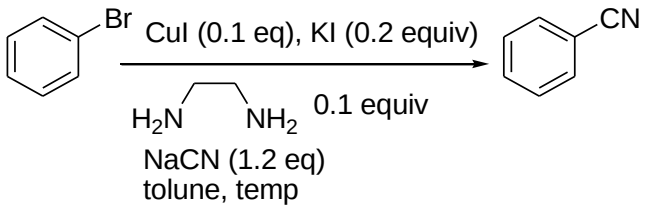
In presence of excess of copper (I) cyanide, this process involves cyanation of aryl halides to prepare aryl nitriles using high boiling polar solvents such as nitrobenzene, DMF, pyridine under reflux conditions (Scheme II.2).[12]



Scheme II.2. Rosenmund-von Braun reaction

However purification of product was difficult in this case due to use of high boiling polar solvents and excess of copper cyanide involved during this reaction. In addition lower functional group tolerance was reported at such elevated reaction temperature (up to 200 ^{o}C). Also the method was not satisfactory with aryl bromides compared to aryl iodides.

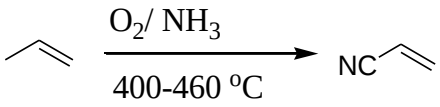
The reaction was modified by S. A. Buchwald *et al.*[13] recently using much milder reaction conditions. With the use of copper(I) cyanide in stoichiometric amount and non polar solvent, the isolation and purification process was greatly improved (Scheme II.3).



Scheme II.3. S. A. Buchwald *et al.* method for synthesis of aryl nitrile

II.A.4.3. Ammoxidation reaction

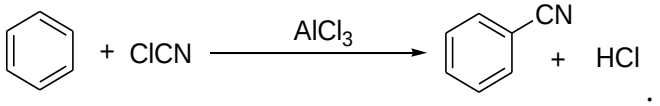
Using ammonia and oxygen, nitriles are industrially produced by this reaction. The substrate involved usually is alkenes. Production of acrylonitriles is an important application of this process (Scheme II.4).[14]



Scheme II.4. Ammoxidation reaction for the synthesis of acrylonitrile

II.A.4.4. Friedel-Crafts-Karrer synthesis

In 1878, Friedel and Crafts[15] implemented their method for acetylation of aromatic hydrocarbons and included cyanogens chloride along with anhydrous aluminum chloride for the synthesis of benzonitrile (Scheme II.5).



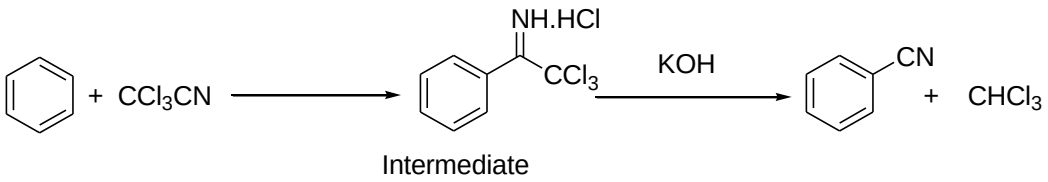
Scheme II.5. Friedel-Crafts synthesis of benzonitrile

However, the yield of benzonitrile obtained was very poor and of high-boiling complexes in considerable amounts were formed as by-products. Karrer[16] in the year of 1919 modified this reaction. By using freshly prepared cyanogens bromide and finally ground aluminium chloride, he was able to obtain 69 % yield of benzonitrile.

II.A.4.5. Houben-Fischer synthesis

Houben and Fischer, in the year of 1929[17] introduced a method for the synthesis of aromatic nitriles in a very simple way (Scheme II.6). These authors, while investigating the formation of

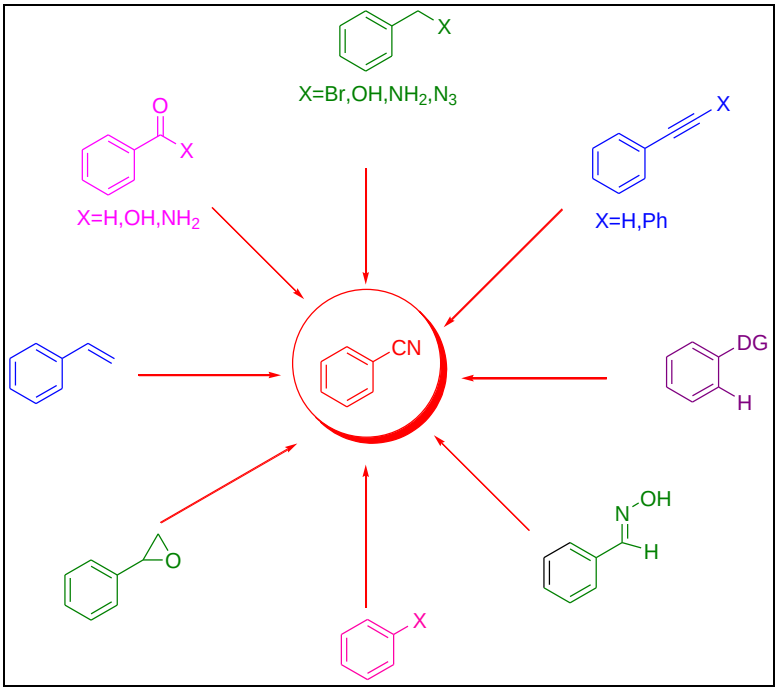
aryl ketones from nitriles, noted that trichloroacetonitrile lead to the expected intermediate, the ketimine hydrochloride. When the intermediate was hydrolyzed using potassium hydroxide, excellent yield of aromatic nitrile was obtained.



Scheme II.6. Houben-Fischer synthesis of aromatic nitrile

II.A.5. Modern methods for synthesis of nitriles

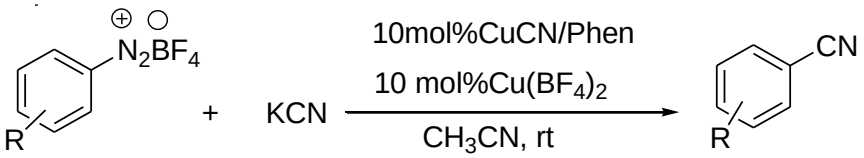
The classical methods of nitrile synthesis was not sufficient enough to meet the modern criteria of environmental friendly strategy and sustainable synthesis due to the production of heavy metal waste and numerous other pollutants. This led to the modern methods of synthesis of nitriles which was greener, eco friendly and simpler. Here a few methods of approaches towards nitrile synthesis are discussed (Scheme II.7).



Scheme II.7. Approaches towards synthesis of nitriles

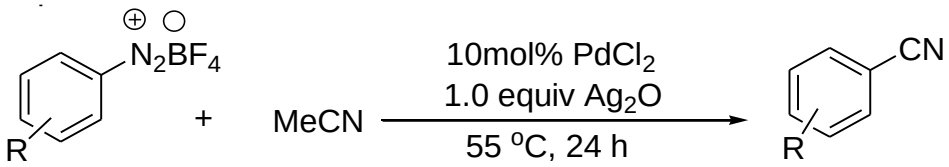
II.A.5.1. Synthesis of nitriles from aryl diazonium salts

Due to high reactivity and easy availability, aryl diazonium salts has been highly explored as arylating reagent in organic synthesis.[18a-c] Sandmeyer reaction being one of the earlier synthetic route. In the past decades, much work has been done to improve the drawbacks associated with this reaction. I.P. Beletskaya *et al.*[19] employed $Cu(BF_4)_2$ as a co-catalyst and got a good yield of nitriles with aryl diazonium salts having electron withdrawing groups(Scheme II.8). However they could not eliminate use of highly toxic KCN in stoichiometric amount.



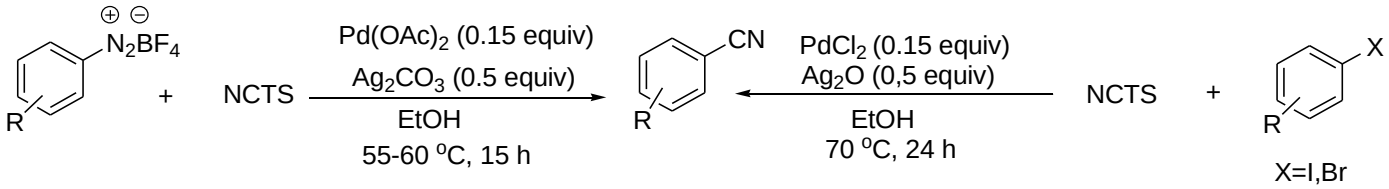
Scheme II.8. Cu-catalyzed cyanation of aryldiazonium salt

J. Li *et al.*[20a] recently have reported cyanation of aryldiazonium tetrafluoroborates using palladium catalyst and hence avoided the use of toxic CuCN. Acetonitrile was used as a non-metal -CN source as well as a cheap solvent (Scheme II.9).



Scheme II.9. Pd-catalyzed cyanation of aryldiazonium salt

NCTS was also explored as a non toxic cyanating reagent by J. Li. *et al.*[20b] along with palladium catalyst under mild conditions (Scheme II.10). However limited substrate scope and low yield were the main drawbacks of these synthesis.



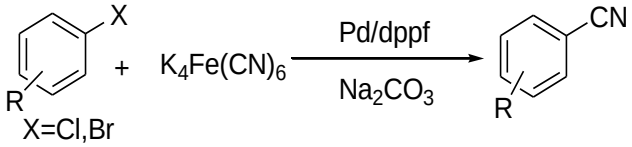
Scheme II.10. Pd-catalyzed cyanation using NCTS as cyanation reagent

Later S. Dughera *et al.*[21] reported transition metal catalyst free cyanation of diazonium salt which was supposed to be a rare case of Sandmeyer reation. Here aryldiazonium *o*-benzene disulfonimide was supposed to have played an important role as electron transfer agent (Scheme II.11**)**.

Scheme II.11. Transition metal catalyst free Sandmeyer reaction

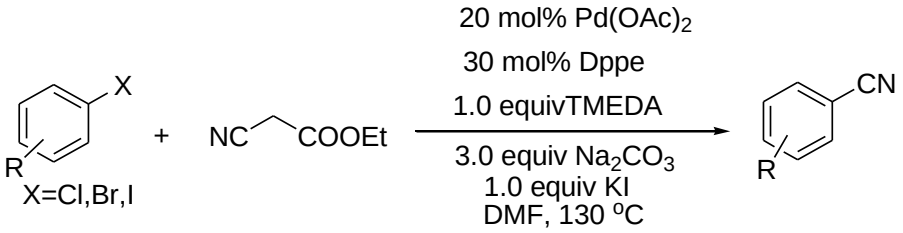
II.A.5.2. Synthesis of nitriles using aryl halides and pseudohalides

Cross-coupling reactions using transition-metal catalyst as been considered as an important tool in carbon-hetero and carbon-carbon bond formation reactions.[22] In this cross-coupling reaction, aryl halides and aryl pseudohalides are basically used as electrophilic associates. K. Takagi *et al.*[22] in 1973 reported the synthesis of nitriles from aryl halides using Pd (II)-catalyst and KCN as the cyanating agent. Following this synthesis, intense efforts are reported to be made in order to improve the cyanating reagents using an array of catalysts. Since metalloid-bound cyanides such are KCN, NaCN, CuCN , $Zn(CN)_2$ were considered to be generally toxic due to the formation of hydrogen cyanide, search of non toxic cyanide source was one of the main aim for these reactions. Finally in the year 2004, M. Beller *et al.*[24] reported cyanation of aryl halides using potassium hexacyanoferrate(II) as a cyanating agent (Scheme II.12).



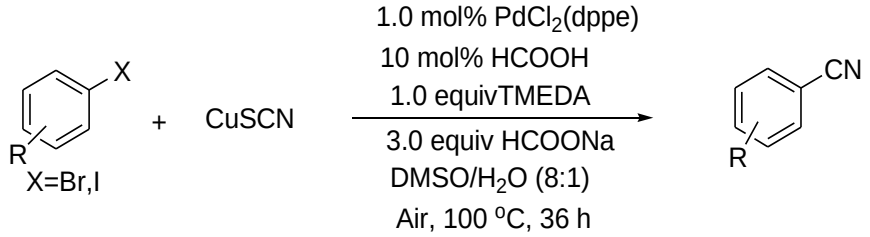
Scheme II.12. Synthesis of nitriles using potassium hexacyanoferrate(II)

In 2012, Z. Shen *et al.*[25] reported the cyanation of aryl halides using ethyl cyanoacetate and palladium catalyst (Scheme II.13). However, formation of by-products like arylacetonitrile and dimer of ethyl cyanoacetate was the major drawback of this reaction.



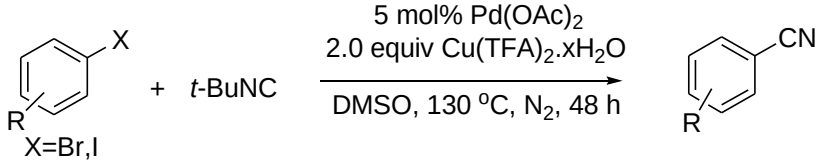
Scheme II.13. Cyanation using ethyl cyanoacetate

J. Cheng *et al.*[26] then introduced cuprous thiocyanate (CuSCN) as a cyanation reagent in 2013 which promised a protocol with good functional group tolerance and good yield (Scheme II.14).



Scheme II.14. Cyanation using cupous thiocyanate

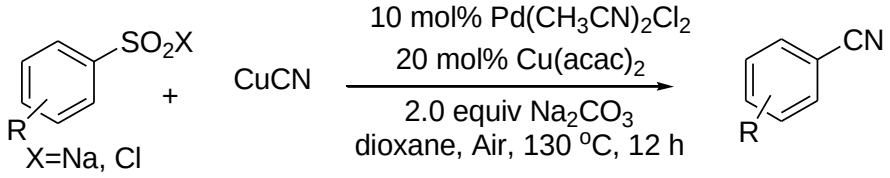
Recently, S.-J. Ji *et al.*[27] reported cyanation of aryl iodides using *tert*-butyl isocyanide as the source of cyano group to be a convenient protocol with wide range of aryl and hetero aryl substrates (Scheme II.15).



Scheme II.15. Cyanation using *tert*-butyl isocyanide

II.A.5.3. Synthesis of nitriles using arylsulphonyl chlorides

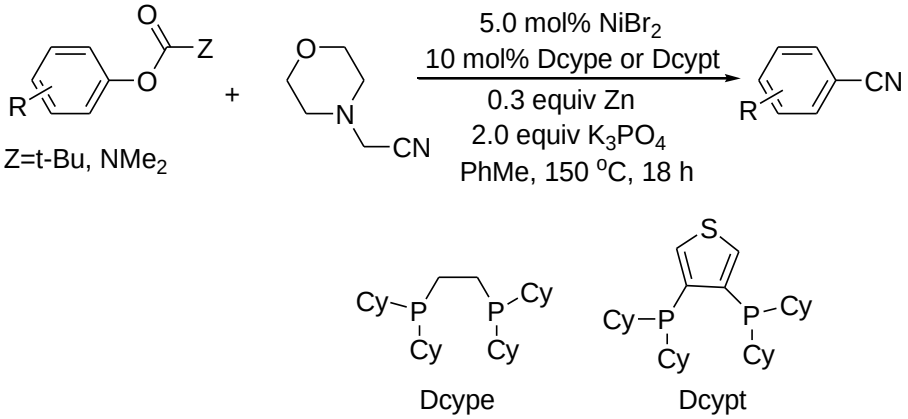
In 2012, J. Cheng *et al.*[28] introduced arylsulfonyl chlorides as a substrate for the synthesis of nitriles using palladium catalyst. Various functional groups including acetamido, phenyl, methoxy, acetyl, nitro and *tert*-butyl and halo groups attached to aryl sulphonyl chloride were compatible for this reaction giving excellent yield (Scheme II.16).



Scheme II.16. Synthesis of nitriles from arylsulphonyl chlorides

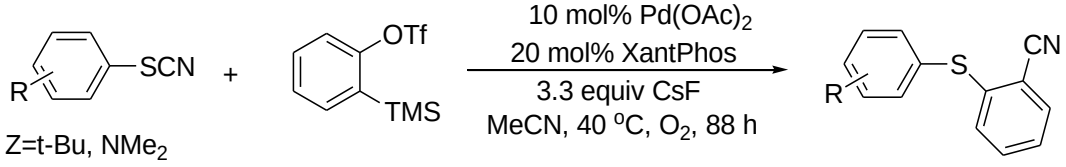
II.A.5.4. Synthesis of nitriles using phenol derivatives

Phenol derivatives are inexpensive and easily available for synthetic purpose. These benefits led to the wide range exploration of phenol derivatives. Nickel catalyzed synthesis of nitriles from phenol derivatives (Scheme II.17) was recently reported by K. Itami *et al.*[29a]



Scheme II.17. Ni-catalyzed cyanation of phenol derivatives

Palladium catalyzed carbon-sulfur bond activation for generation of 1, 2-thiobenzonitriles was reported by D.B. Werz *et al.*[29b] in 2016. Cyanation and simultaneous sulfenylation of aryne gave an excellent yield for variety of 1, 2-thiobenzonitriles (Scheme II.18).

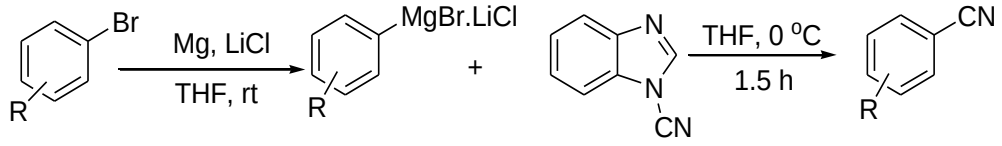


Scheme II.18. Pd- catalyzed cyanation of phenol derivatives

II.A.5.5. Synthesis of nitriles using organometallic reagent

Though, considerable advancement has been achieved in the synthesis of nitriles using transition metal catalysts, toxicity associated with the methodologies always encourage developments of

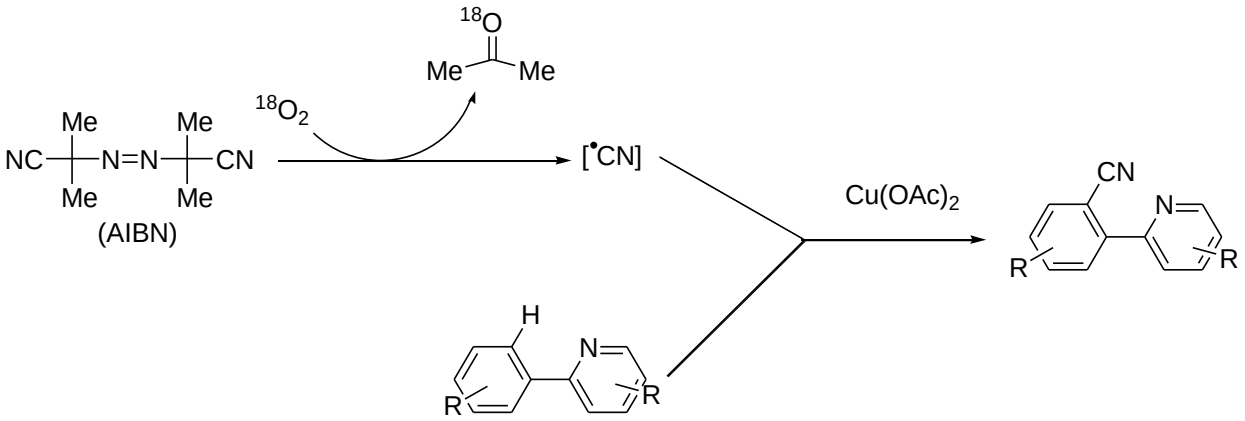
new protocols .Cyanation using organometallic reagents thus provide an alternative way for aryl nitrile synthesis. P. Knochel *et al.*[30] were able to report the synthesis of aryl and heteroaryl nitriles using Grignard reagent (Scheme II.19).



Scheme II.19. Electrophilic cyanation of Grignard reagent

II.A.5.6. Synthesis of nitriles by cyanation of aromatic C-H bonds

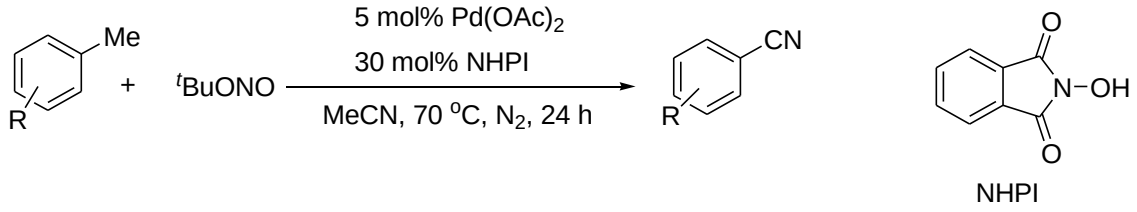
F.-S. Han *et al.*[31] in 2013 reported copper mediated cyanation of aryl C-H bond using AIBN as a free radical CN source (Scheme II.20).



Scheme II.20. Cyanation of aromatic C-H bond

II.A.5.7. Synthesis of nitriles from methylarenes

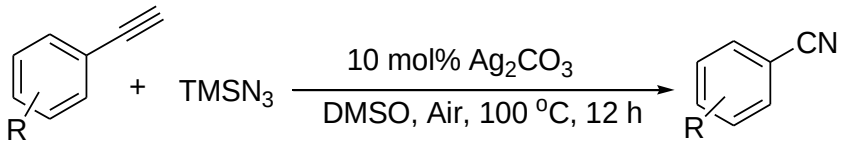
J. Wang *et al.*[32] reported direct transformation of arene methyl group to cyano group via palladium catalyzed reaction using *tert*-butyl nitrite as a source of nitrogen as well as an oxidant (Scheme II.21).



Scheme II.21. Palladium-catalyzed transformation of methyl arenes into nitriles

II.A.5.8. Synthesis of nitriles from aryl-substituted alkynes

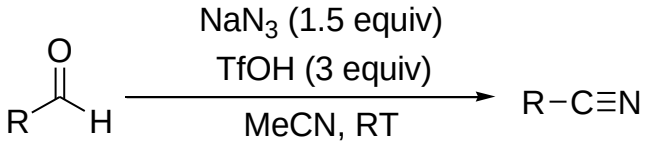
N. Jiao *et al.*[33] developed a silver-catalyzed synthetic route for the direct conversion of germinal aryl alkynes into nitriles. The protocol was reported to have mild reaction conditions and gave good yield with sufficient functional group tolerance (Scheme II.22).



Scheme II.22. Synthesis of nitriles from aryl alkenes

II.A.5.9. Synthesis of nitriles from aldehydes

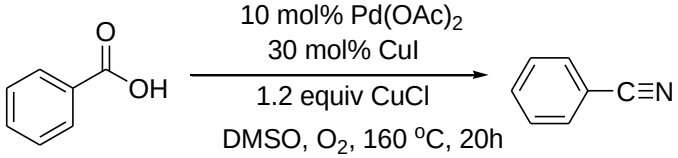
Aldehydes can be readily converted into nitriles from Schmidt reaction using sodium azide. K. R. Prabhu *et al.*[34] have developed synthesis of nitriles from aldehydes in presence of TfOH. The reaction is supposed to proceed via the formation of in situ hydrazoic acid (Scheme II.23).



Scheme II.23. Synthesis of nitriles from aldehydes

II.A.5.10. Synthesis of nitriles from carboxylic acids

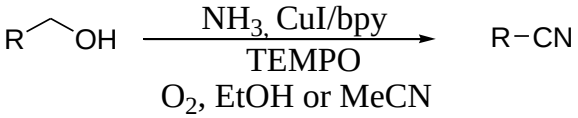
Recently, H. Cai *et al.*[35] reported the conversion of carboxylic acids to nitriles using Palladium catalyst in presence of $K_4[Fe(CN)_6]$. Several carboxylic acids including heteroaryl carboxylic acid was being converted into nitriles using this protocol which furnished excellent yield and showed good functional group tolerance (Scheme II.24).



Scheme II.24.Synthesis of nitriles from carboxylic acids

II.A.5.11. Synthesis of nitriles from benzyl alcohols

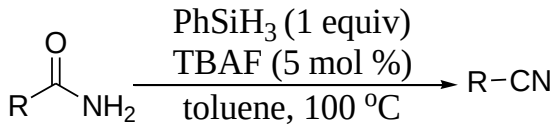
Y Haung *et al.*[36] reported one pot synthesis of nitriles from various aliphatic/aromatic alcohols via CuI-bpy catalyst using TEMPO as an oxidant (Scheme II.25).



Scheme II.25 Synthesis of nitriles from benzyl alcohols

II.A.5.12. Synthesis of nitriles from amides

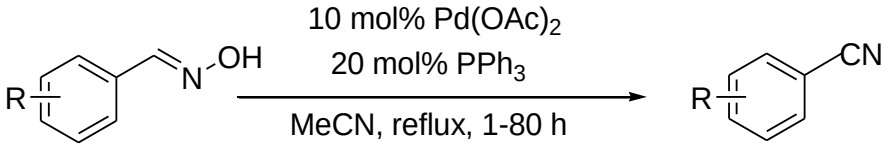
With catalytic amount of tetra-butyl ammonium fluoride (TBAF) and using silanes, M. Beller *et al.*[37] was able to convert aliphatic/aromatic amides into nitriles. The synthetic method showed high degree of selectivity under mild condition (Scheme II.26).



Scheme II.26. Synthesis of nitriles from amides

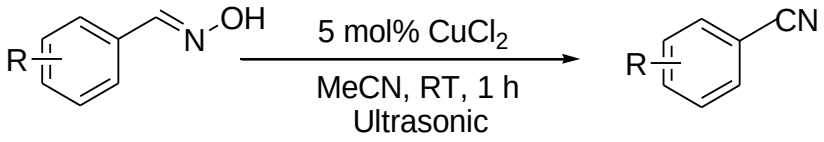
II.A.5.13.Synthesis of nitriles from oximes

One of the most widely used methods for the synthesis of nitriles has been reported to be the dehydration of oximes (Scheme II.27). Oximes are prepared very much easily from the corresponding aldehydes using ammonia or hydroxylamine. With the advantages like simple reaction procedure, environmentally friendly, high yield etc, this methodology has widely being explored in the recent past. Common dehydrating agents like conc. H_2SO_4 or P_2O_5 may be used in the synthesis. But due to low selectivity, it has not been employed for industrial purposes. N. Kim *et al.*[38] in 2009 reported the synthesis of nitriles from aldoximes using palladium catalyst.



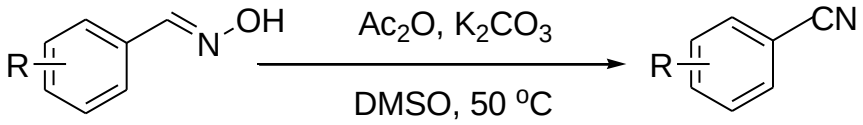
Scheme II.27. palladium-catalyzed synthesis of nitriles from oximes

J. Ragauskas *et al.*[39] also has reported copper-catalyzed ultrasonic-promoted synthesis of nitriles from oximes in good yield where minimal purification procedure was required (Scheme II.28).



Scheme II.28. Copper-catalyzed synthesis of nitriles from oximes

G. Hu *et al.*[40] reported synthesis of oximes from nitriles using acetic anhydride as the dehydrating agent. Wide range of aromatic aldoximes, aliphatic aldoximes and hetercyclic oximes has been successfully transformed into nitriles with good yield by this protocol (Scheme II.29).

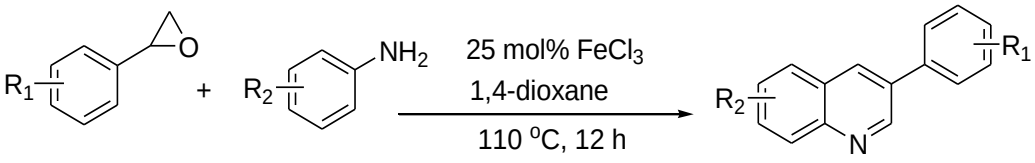


Scheme II.29. Synthesis of nitriles from oximes using acetic anhydride

II.A.6. Organic synthesis catalyzed by $FeCl_3$

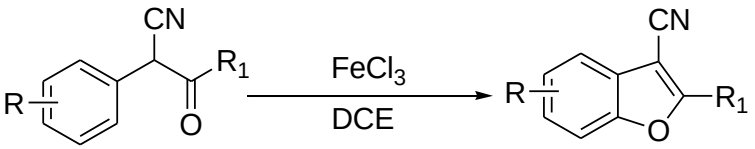
A number of reasons can be given for the choice of iron as a catalyst. After aluminum, it is the most abundant metal found in the earth crust. With the decrease in availability of the transition metals or rare earth metals and subsequent increase in their price over the past decade has demanded for other cheap alternatives. Iron catalyst seems to fit in nicely as an alternative. Regarding efficiency, iron still lags behind palladium. However, protocols using iron as a catalyst is gaining importance. Being a non toxic cheap metal, many publications using iron as catalyst have surfaces in the past years and are likely to continue.

$FeCl_3$ catalyzed reactions were known since long time back. One such example is Friedel-Craft reaction. Recently L. Wang *et al.*[41] has reported the synthesis of quinolines from anilines using $FeCl_3$ as catalyst via tandem reaction with styrene oxide (Scheme II.30).



Scheme II.30. Synthesis of quinolines using $FeCl_3$ as catalyst

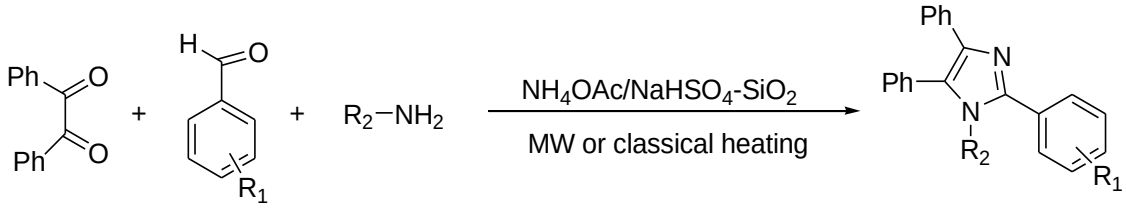
In 2009, K. Zhao *et al.*[42] reported the synthesis of 3-functionalized Benzo[*b*]furans by ring closure of α-Aryl ketones using $FeCl_3$ as a catalyst where oxidative aromatic C-O bond formation took place (Scheme II.31).



Scheme II.31. Synthesis of 3-functionalized Benzo[*b*]furans using $FeCl_3$ as catalyst

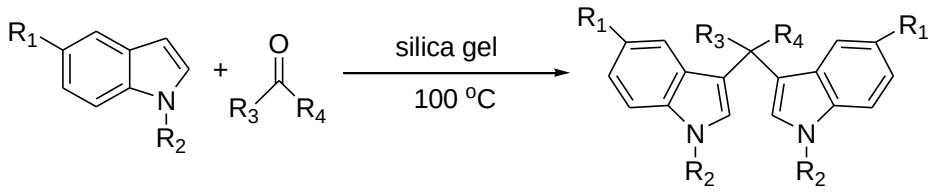
II.A.7. Silica gel supported organic synthesis

Environment pollution has become one of the major concerns today. During organic synthesis a number of factors are responsible to spread chemicals which are toxic and can cause pollution. Solvents plays a major role during synthesis but it may also cause environmental hazards. An alternative solvent which may be benign towards environment is always a boon. In recent year, silica is being used as a reaction medium for many organic syntheses in order to avoid hazardous solvents. Silica gel is known to be non toxic and has a high thermal and chemical stability. A. R. Karimi *et al.*[43]. have reported synthesis of tetra-substituted imidazoles using $NaHSO_4$–SiO_2 as a solid support in the year 2006(Scheme II.32).



Scheme II.32. Synthesis of imidazole using $NaHSO_4$–SiO_2 as a solid support

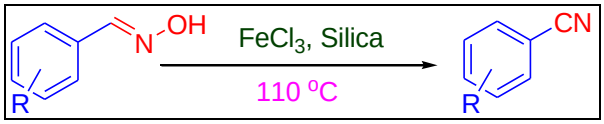
R. G. Jacob *et al.*[44] in 2012 reported synthesis of bis (indolyl)methanes by the reaction of indoles with cyclohexanone using silica as a solid recyclable surface under solvent free condition (Scheme II.33). Silica was reported to be recovered and reutilized without loss of activity in his methodology.



Scheme II.33. Synthesis of bis (indolyl)methanes using silica as surface

II.C. Present Work

Here we report the synthesis of nitriles from various oximes using $FeCl_3$ as a catalyst. The reaction was carried out under solvent free condition in presence of silica. With this methodology, good yield of the products were obtained.

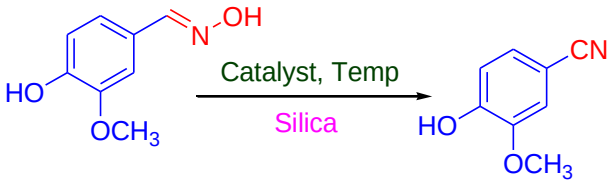


Scheme II.34. Synthesis of nitriles from oximes

II.C.1. Result and discussion

To standardize the reaction protocol, vanillin oxime was treated as the starting material. The model reaction comprising vanillin oxime (1 mmol) and silica gel (1 g) at 50 °C on a magnetic stirrer for 5 h furnished no yield. After raising the temperature up to 100 °C, it yielded only carbonyl compound instead of the nitrile. The next reaction was then set up by combining vanillin oxime (1 mmol), silica gel (1 g), and 10 mol% anhydrous $FeCl_3$. The reaction was monitored from room temperature to 100 °C but only 18% desired product could be isolated at 100 °C in 5 h (Table II.1). The quantity of $FeCl_3$ and the reaction temperature was then raised. The isolated product at 110 °C and 20 mol% $FeCl_3$ in 5 h was only 32% (Table II.1). With same reaction condition and time, at 40 mol% $FeCl_3$, the isolated product was 56% (Table II.1). The sharp increase in the quantity of nitrile with the increase in amount of $FeCl_3$ at the same reaction condition clearly indicates the requirement of more $FeCl_3$ for excellent transformation whereas no such outcome was observed by lengthening the reaction time (entry 6, Table II.1). When the reaction was carried out with 75 mol% $FeCl_3$, the yield of the desired product was more than 90%. Finally the reactant and $FeCl_3$ ratio was put at 1:1 in silica (1 g), which furnished 98% desired product (entry 8, Table II.1).

Table II.1. Optimization of reaction condition[a]



Entry	$FeCl_3$ (mol %)	Temp (^oC)	Time (h)	Yield (%)[b]
1	Nil	50	5	Nil
2	-	90	5	Nil
3	10	100	5	18
4	20	110	5	32
5	40	110	5	56
6	40	-	6.5	56-57
7	75	-	5	>90
8	100	-	-	98
9	-	-	4	-
10	-	-	3	-
11	-	-	2	-
12	-	-	1.5	98[c]
13	-	-	1	93

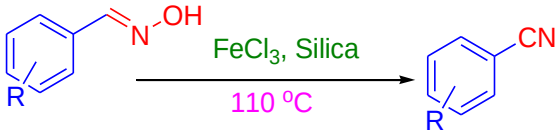
[a] Reaction of vanillin oxime (0.5 mmol), anhydrous $FeCl_3$ (0-90 mol %) and silica gel 60-120 mesh (1.00 g) on a magnetic stirrer in different time interval at 110 ^oC.

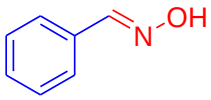
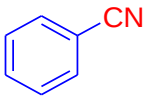
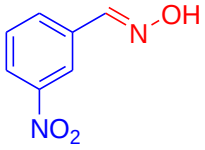
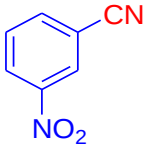
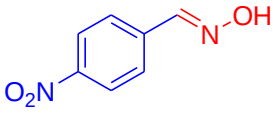
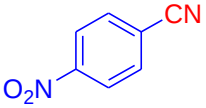
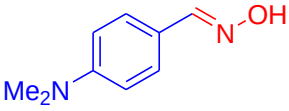
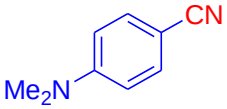
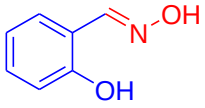
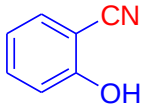
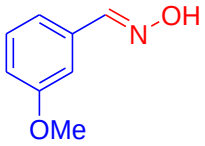
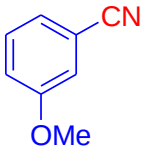
[b]Isolated yield.

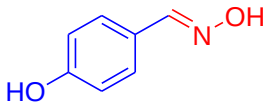
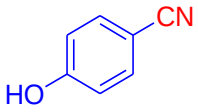
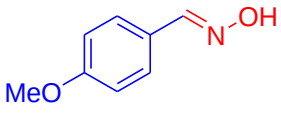
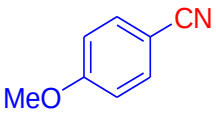
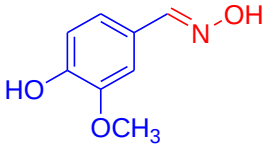
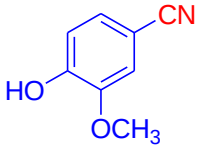
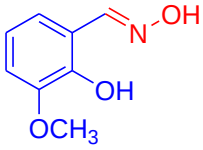
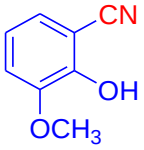
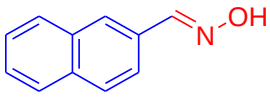
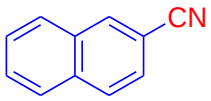
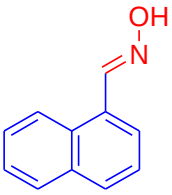
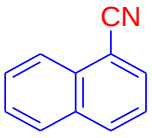
[c]Optimized reaction condition.

Again, maintaining all parameters similar, an excellent yield was found by shortening the reaction time (2 h) (entry 12, Table II.1). Again, the decrease in yield was observed when the time was shortened from 2 h to 1 h (entry 13, Table II.1). Finally, optimization of the reactant ratio and condition showed aldoxime (1 mmol), anhydrous $FeCl_3$ (1 mmol), and silica gel 60–120 mesh (1 g) at 110 °C to be the best combination to furnish maximum yield of the desired product (98%) in 2 h (entry 12, Table II.1). For the generalization of our scheme, the aldoximes **1a–l** were successfully converted to the corresponding nitriles **2a–l** under optimized condition (Table III.2).

Table II. 2. $FeCl_3$-silica mediated synthesis of nitriles



Entry	Aldoximes (**1**)	Time (h)	Product (**2**)	Yield%[b]
a		3		95
b		5		81
c		5		79
d		5		90
e		4		87
f		5		90

g		5		89
h		4.5		88
i		5		98
j		5		97
k		5		87
l		5		86

[b]Isolated yield.

The oximes having various substituents have been converted into nitriles. Those having electron-releasing groups such as –OH, -OCH_3, and -$N(CH_3)_2$ furnished an excellent yield whereas oximes having electron-withdrawing groups offered comparatively lower yield with minimal difference (Table. III.2). Increasing hydrophobic moiety to neutral oximes provide a lower yield of the desired product (entries 1a, 1k, 1l, Table II.2). The overall applicability of the protocol is

highly suitable for the desired conversion under the aspects of sustainable development and green chemistry.

II.C. Conclusion

In conclusion, we have developed a solvent-free and environmentally benign protocol for the single-step facile synthesis of nitriles from aldoximes by using anhydrous $FeCl_3$ on silica gel. The reaction protocol includes the use of an inexpensive and less toxic reagent, gives one-pot excellent yield of the desired products and has simple and easy reaction conditions and workup process.

II.D. Experimental

II.D.1. General Information

All the products were purified by column chromatography on 60−120 mesh silica gel (SRL, India). For TLC, Merck plates coated with silica gel 60, IR spectra were recorded on using KBr pellets for solid compounds and under neat condition for liquid compounds in the range 4000-400 cm^{-1} on Shimadzu FT-IR 8300 Spectrometer. The ^{1}H & ^{13}C NMR spectra were recorded at 300 MHz, 500 MHz and 75 MHz, 125 MHz respectively on Bruker AV 300 spectrometer in $CDCl_3$. Splitting patterns of protons were described as s (singlet), d (doublet), t (triplet), br (broad) and m (multiplet). All the oxime derivatives are prepared by known method from aldehydes.

II.D.2.Procedure for the synthesis of nitrile from aldoxime

Aldoxime (1 mmol) and anhydrous $FeCl_3$ (1 mmol) were intimately mixed with silica gel 60–120 mesh (1 g) in mortar and pestle. The resulting solid mixture was poured into a round-bottom flask (50 mL) and allowed to stir on magnetic stirrer at 110 °C for an appropriate time (Table. III.2). The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the reaction mixture was extracted with ethyl acetate (15 mL) for 3 times and washed several times with water. The combined organic mixture was dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography on silica gel 60–120 mesh using petroleum ether/ethyl acetate as eluent to afford pure nitrile. The desired isolated products were characterized by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy.

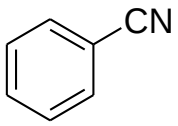
II.D.3. Spectroscopic data of synthesized nitriles

Benzonitrile (Table II.2, Entry a)

IR (cm^{-1}, KBr): 3066, 2230(-CN), 1641, 1572.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.47 (m, 2H), 7.56-7.62 (m, 3H) ppm.

^{13}C NMR (75 MHz,): δ 112, 118, 128, 132, 133 ppm.

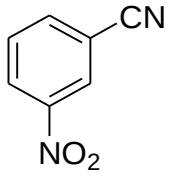


3-Nitro-benzonitrile (Table II.2, Entry b)

IR (cm^{-1}, KBr): 3080, 2238 (-CN), 1618, 1534, 1356, 1102, 735.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71-7.76 (m, 1H), 7.98-8.01 (m, 1H), 8.46-8.5 (m, 1H), 8.53-8.84 (m, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 114.2, 116.5, 127.1, 127.3, 127.6, 130.6, 137.6 ppm.

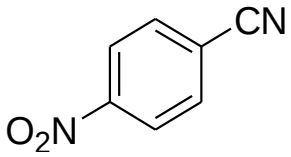


4-Nitro-benzonitrile (Table II.2, Entry c)

IR (cm^{-1}, KBr): 3107, 2233 (-CN), 1602, 1526, 1349, 1295, 1106, 860, 682.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86-7.9 (d, *J*=15 Hz, 2H), 8.33-8.38 (d, *J*=15 Hz, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 116.7, 118.3, 124.3, 133.4, 150 ppm.

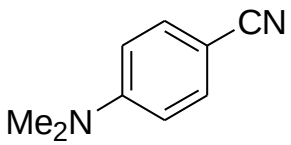


4-Dimethylamino-benzonitrile (Table II.2, Entry d)

IR (cm^{-1}, KBr): 2909, 2211 (-CN), 1608, 1527, 1371, 1173, 818.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.04 (s, 6H), 6.67-6.7 (d, *J*=15 Hz, 2H), 7.46-7.49 (d, *J*=15Hz, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 39.9, 97.4, 111.4, 120.6, 133.4, 152.5 ppm.

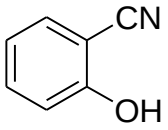


2-Hydroxy-benzonitrile (Table II.2, Entry e)

IR (cm^{-1}, KBr): 3281 (-OH), 2231 (-CN), 1605, 1505, 1361, 1236, 848, 751, 668.

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95-7.03 (m, 2H), 7.43-7.52 (m, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 99.5, 116.4, 120.9, 132.9, 133.2, 134.7, 158.5 ppm.

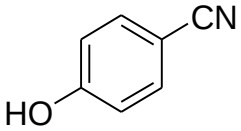


4-Hydroxy-benzonitrile (Table II.2, Entry g)

IR (cm^{-1}, KBr): 3292 (-OH), 2234 (-CN), 1613, 1586, 1509, 1285, 1167, 838,702.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.14 (s, 1H), 6.89-6.93 (d, *J*=15 Hz, 2H), 7.52-7.57 (d, *J*=15.5 Hz ,2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 103.4, 116.4, 119.2, 134.2, 159.9 ppm.

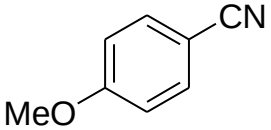


4-Methoxy-benzonitrile (Table II.2, Entry h)

IR (cm^{-1}, KBr): 2942, 2218 (-CN), 1606, 1509, 1305, 1258, 1177, 1024, 830, 683.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.93-6.95 (d, *J*=9 Hz, 2H), 7.57-7.59 (d, *J*=9 Hz, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 55.5, 103.9, 114.7, 119.2, 133.9, 162.8 ppm.

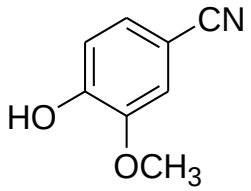


4-Hydroxy-3-methoxy-benzonitrile (Table II.2, Entry i)

IR (cm^{-1}, KBr): 3388 (-OH), 2227 (-CN), 1605, 1591, 1517, 1028, 819, 616.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H), 6.1 (s, 1H), 6.95-6.97 (d, *J*=10 Hz, 1H), 7.08 (s, 1H), 7.22-7.26 (m, 1H) ppm.

^{13}C NMR (75 MHz,): δ 56.4, 103.3, 113.7, 115.2, 119.2, 127, 146.6, 149.9 ppm.

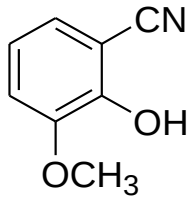


2-Hydroxy-3-methoxy-benzonitrile (Table II.2, Entry j)

IR (cm^{-1}, neat): 3351 (-OH), 2231 (-CN), 1611, 1591, 1492, 1070, 730.

^{1}H NMR (500 MHz, $CDCl_3$): δ 3.92 (s, 3H), 6.32 (s, 1H), 6.87-6.9 (m, 1H), 7.02-7.04 (m, 1H), 7.08-7.1 (d, 1H, J=7 Hz) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 56.3, 98.6, 114.6, 115.9, 120.4, 123.9, 146.7, 148.9 ppm.

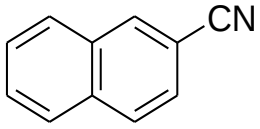


Napthalene-2-carbonitrile (Table II.2, Entry k)

IR (cm^{-1}, KBr): 2226 (-CN), 1594, 1500, 1273, 966, 826, 755, 643.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58-7.67 (m, 3H), 7.88-7.93 (m, 3H), 8.23 (s, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ 109.3, 119.2, 126.3, 127.6, 128, 128.4, 129, 129.1, 132.2, 134.1, 134.6, ppm.

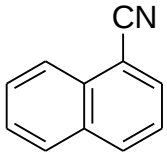


Napthalene-1-carbonitrile (Table II.2, Entry l)

IR (cm^{-1}, neat): 3061, 2222 (-CN), 1590, 1512, 1375, 1213, 801, 771.

^{1}H NMR (300 MHz, $CDCl_3$): δ, 7.48-7.7 (m, 3H), 7.88-7.92 (m, 2H), 8.06 (d, *J*=8.1 Hz, 1H), 8.22 (d, *J*=8.4 Hz, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ, 110.1, 117.8, 124.9, 125.1, 127.5, 128.5, 128.6, 132.3, 132.6, 132.9, 133.2 ppm.



II.D.4. Scanned copies of ^{1}H NMR, ^{13}C NMR and FT-IR of compound

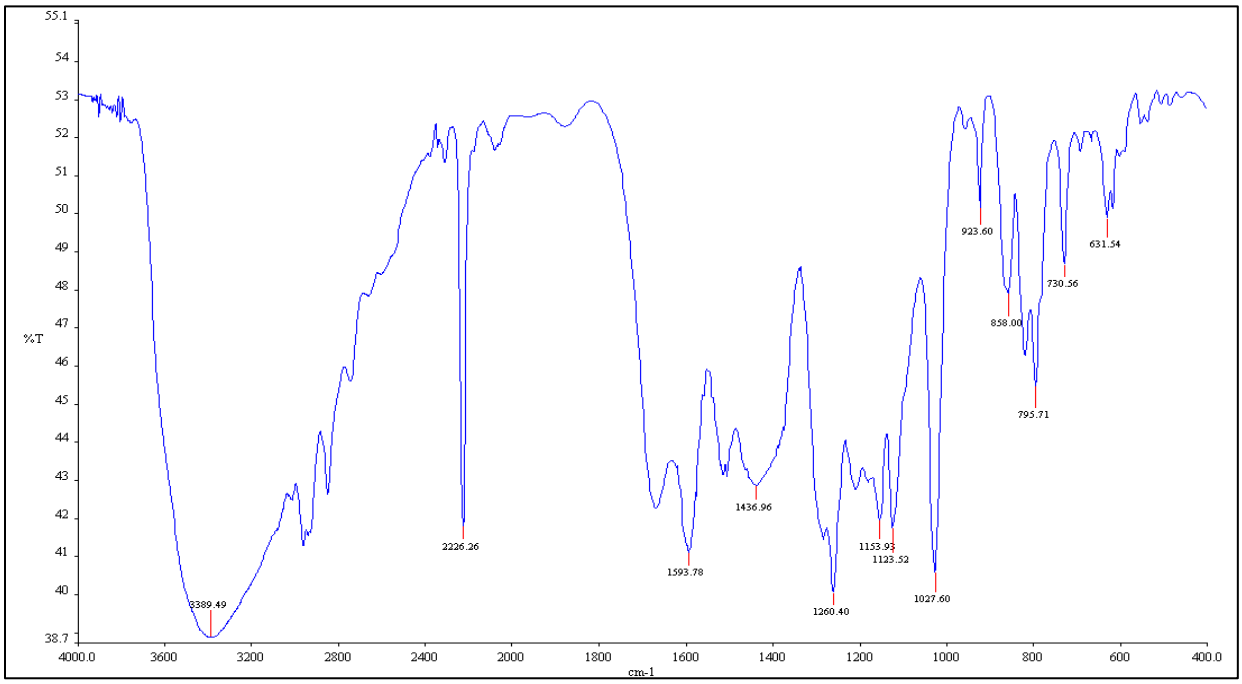


Figure II.4. Scan copy of the FT-IR spectra of 2-Hydroxy-benzonitrile

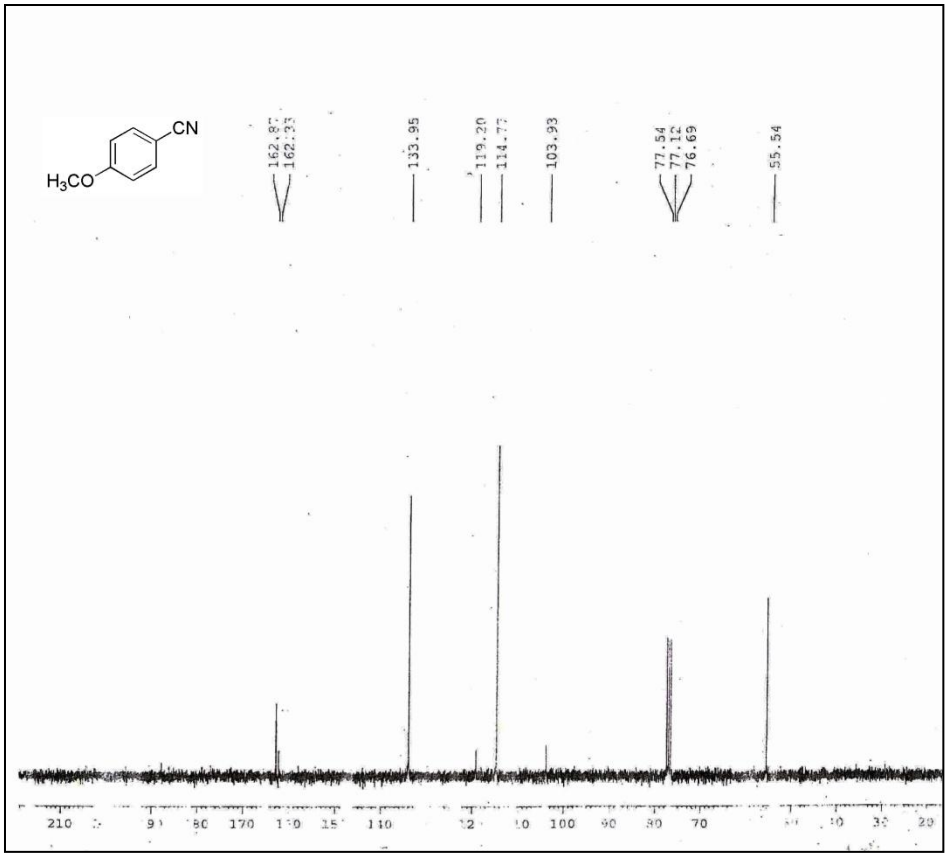


Figure II.5. Scan copy of ^{13}C NMR spectra of 4-Methoxy-benzonitrile

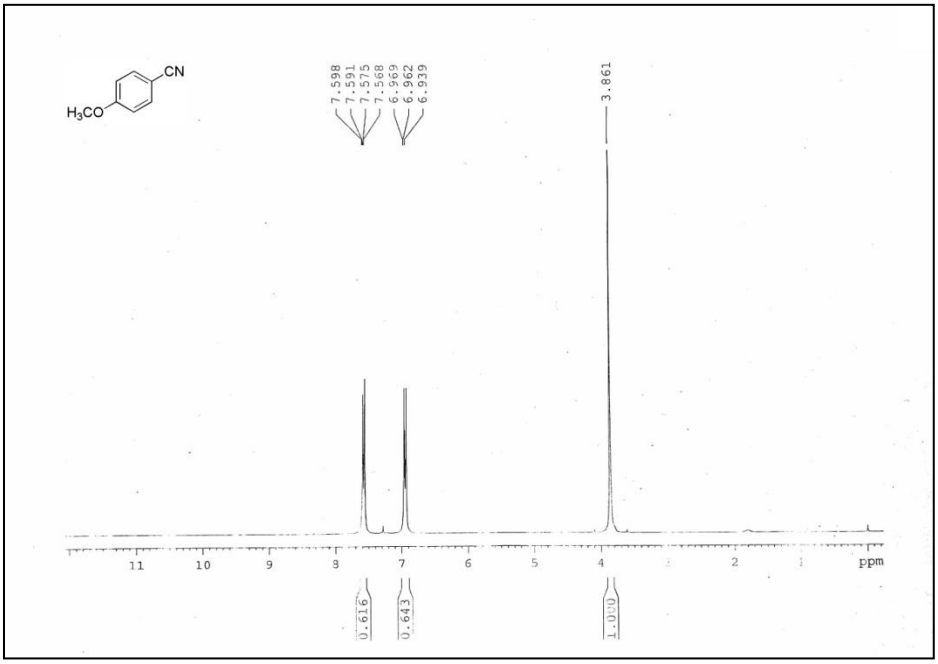


Figure II.6. Scan copy of ^{1}H NMR spectra of 4-Methoxy-benzonitrile

II.E. References

References are given in BIBLIOGRAPHY under Chapter II.