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Fe_2O_3 Nanoparticle Mediated One-Pot Conversion of Aldehydes to Nitriles

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Interestingly, One pot conversion of heteroaromatic 2-chloro-3-formylquinoline into their cyano derivatives using first time Fe_2O_3 nanoparticle in aqueous ammonia has been discussed.

Keywords: One pot, oxidant, nitrile, transformation, 2-chloro-3- formyl-quinolines, Nanoparticle

In organic synthesis functional group transformations have significant importance[1] Amongst, nitriles, represent an important reagents for organic synthesis, have been attracted great attention to chemist for long time because of their transformation into variety of heterocycles such as thiazoles[2a], 2-oxazolines[2b-c], tetrazoles[2d], imidazoles[2e], triazoloannulatedpyri- midines[2f] and others[2g-h]. Formations of nitriles from the corresponding aldehydes are an important functional group transformation. Methods known in the literature either involve the initial conversion of aldehydes to aldoximes followed by dehydration[3] to give nitriles or direct conversion of aldehydes into nitriles without isolation of nitrogen containing intermediates, by treating with variety of chemicals[4]. The use of ammonia combined with different oxidants such as oxygen[5], lead tetraacetate[6], iodine[7] and hydrogen peroxide[8], is considered amongst an appropriate method for the transformation of aliphatic and aromatic aldehydes to their corresponding nitriles. These observations inspired us to investigate the transformation of 3-quinolinylformaldehyde **1a** to 3- quinolinylnitrile **2a** (ref.9f) in aqueous ammonia with easily available oxidants.

In continuation to the studies in carbo/hetero annulatedquinolines synthesis[9] from 2-chloro-3-formylquinolines **1a**. 2-chloro-3-cyanoquinolines **2a** is required to explore analogous reactions on them for synthesis of carbo/hetero annulatedquinolines. Thus, in this paper one pot synthesis of 2-chloro-3-cyanoquinolines from 2-chloro-3-formylquinolines in aqueous ammonia using cheap and easily available iodine as oxidant and Fe_2O_3 nanoparticle as catalyst is described.

The reaction of 2-chloro-3-formylquinoline **1a** with iodine in aqueous ammonia along with Fe_2O_3 nanoparticle was chosen as model and the reaction condition was optimized. It is found that reaction proceeded well and completed in a short period at RT. The better yield of product, 2-chloro-3-cyanoquinoline **2a**, was obtained by using 6 mL of aqueous ammonia (30% solution, **Table I**). Thus, the reaction of 2-chloro-3-formylquinoline **1a** in THF (5 mL) was treated with aqueous ammonia (6 mL), Fe_2O_3 nanoparticle (0.5mmole) and iodine (1.1 mmole) at RT for 75 minutes to afford the desired nitrile **2a** in good yield. The structure of compound **2a** was characterized from its NMR and IR spectra. The ^{1}H NMR spectrum of compound **2a** showed absence of formyl peak at δ 10.5 and its IR spectrum showed absence of carbonyl absorption at 1687 $cm^{-1}$and presence of weak absorption of nitrile group at 2226 cm^{-1}. After optimizing reaction conditions for transformation of **1a** into **2a**, reaction of other substrates **1b-k** were carried out. These afforded the corresponding nitriles **2b-k** in a short time (20-85 min) in good yields (**Table I**).

In summary, a general and simple method for the transformation of carbaldehydes into nitriles in a better yield in aqueous medium is described using cheap and easily available reagents.

Experimental Section

Melting points were measured in an open capillary tube with a Buchi melting point apparatus and are uncorrected. Elemental analysis was obtained using Perkin-Elmer 240C CHN-analyzer. IR spectra were recorded on a FT/IR-5300 (JASCO) spectro- photometer; ^{1}H NMR spectra in $CDCl_3$/DMSO-d_6 at

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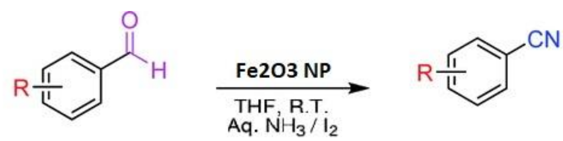
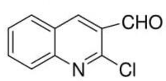
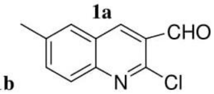
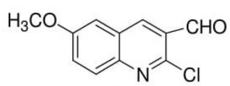
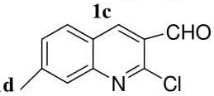
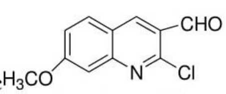
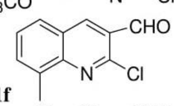
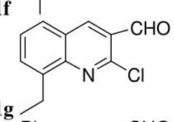
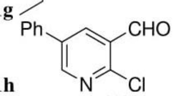
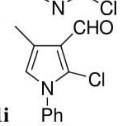
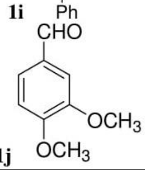
300 MHz on a Jeol AL-300 spectrometer (chemical shifts in δ ppm) relative to TMS as an internal standard. Reactions were monitored by TLC, using silica gel $PF_{254+366}$ as an adsorbent and ethyl acetate- hexane in different ratios as eluent.

General method for conversion of carbaldehyde into nitrile

To a stirred solution of formyl compound (1 mmole) in MeOH (2 mL) was added aq. NH_3 (30%, 6 mL), Cat.Fe_2O_3 Nanoparticle followed by sublimed I_2 (1 mmole) and stirred the reaction- mixture at RT for the mentioned period



R = H, Me, MeO, Et

Entry	Substrate	Product	Time (min)	Yield (%)
1	 **1a**	**2a**	75	82
2	**1b** 	**2b**	72	80
3	 **1c**	**2c**	20	78
4	**1d** 	**2d**	68	80
5	**1c** 	**2e**	85	83
6	 **1f**	**2f**	72	79
7	 **1g**	**2g**	60	80
8	 **1h**	**2h**	75	73
9	 **1i**	**2i**	68	77
10	 **1j**	**2j**	50	67

(**Table I**). The dark violet/brown solution became colourless after completion of reaction (checked by TLC).The reaction-mixture was treated with aqueous $Na_2S_2O_3$ solution (5 mL of 5% solution) and extracted with ethyl acetate. The solution was dried, filtered and evaporated under vacuum to give pure

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nitrile product.

2-Chloro-3-cyanoquinoline, 2a: Yield 82%, m.p. 144-45°C; IR (KBr): 2226 cm^{-1}; ^1H NMR ($CDCl_3$): δ
7.70 (t, *J* = 7.8 Hz, 7-H), 7.90 (d, *J* = 8.1 Hz, 5-H), 7.92
(t, *J* = 8.1 Hz, 6-H), 8.09 (d, *J* = 8.1 Hz, 8-H), 8.57 (s,
4-H); Anal. Calcd for $C_{10}H_5N_2Cl$: C, 63.82; H, 2.68; N,
14.90. Found: C, 63.75; H, 2.70; N, 14.82%.

6-Methyl-2-chloro-3-cyanoquinoline, 2b: Yield 80%, m.p. 142-45°C; IR (KBr): 2228 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.58 (s, CH_3), 7.65 (s, 5-H), 7.73 (d, *J* =
8.7 Hz. 7-H), 7.97 (d, *J* = 8.1 Hz, 8-H), 8.46 (s, 4-H). Anal. Calcd for $C_{11}H_7N_2Cl$: C, 65.34; H, 3.49; N, 13.86. Found: C, 65.21; H, 3.63; N, 13.48%.

6-**Methoxy-2-chloro-3-cyanoquinoline, 2c**: Yield 78%, m.p. 157-60°C; IR (KBr): 2231 cm^{-1}; ^1H NMR

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($CDCl_3$): δ 3.96 (s, OCH_3), 7.10 (d, *J* = 2.4 Hz, 5-H),
7.54 (dd, *J* = 2.7, 9.0 Hz, 7-H), 7.97 (d, *J* = 9.3 Hz, 8- H), 8.43 (s, 4-H); Anal. Calcd for $C_{11}H_7N_2OCl$: C, 60.54; H, 3.24; N, 12.85. Found: C, 60.35; H, 3.18; N,
12.90%.

7-**Methyl-2-chloro-3-cyanoquinoline, 2d**: Yield 80%, m.p. 142-45°C; IR (KBr): 2222 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.62 (s, CH_3), 7.52 (d, *J* = 8.1 Hz, 5-H),
7.78 (d, *J* = 8.4 Hz, 6-H), 7.85 (s, 8-H), 8.50 (s, 4-H); Anal. Calcd for $C_{11}H_7N_2Cl$: C, 65.34; H, 3.49; N, 13.86. Found: C, 65.40; H, 3.41; N, 13.78%.

7-**Methoxy-2-chloro-3-cyanoquinoline, 2e**: Yield 83%, m.p. 147°C; IR (KBr): 2229 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.99 (s, OCH_3), 7.44 (s, 8-H), 7.46 (d, *J* =
13.5 Hz, 6-H), 7.84 (d, *J* = 9.0 Hz, 5-H), 8.67 (s, 4- H); Anal. Calcd for $C_{11}H_7N_2OCl$: C, 60.54; H, 3.24; N, 12.85. Found: C, 60.46; H, 3.21; N, 12.78%.

8-**Methyl-2-chloro-3-cyanoquinoline, 2f**: Yield 79%, m.p. 95-97°C; IR (KBr): 2228 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.77 (s, CH_3), 7.59 (t, *J* = 7.5 Hz, 6-H),
7.74 (t, *J* = 7.2 Hz, 5-H, 7-H), 8.53 (s, 4-H); Anal. Calcd for $C_{11}H_7N_2Cl$: C, 65.34; H, 3.49; N, 13.86.
Found: C, 65.41; H, 3.42; N, 13.90%.

8-Ethyl-2-chloro-3-cyanoquinoline, 2g: Yield 80%,
m.p. 124°C; IR (KBr): 2231 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.36 (t, 7.74, *J* = 7.5 Hz, CH_3), 3.25 (q, *J* = 7.5 Hz, CH_2), 7.63 (t, *J* = 7.5 Hz, 6-H), 7.75 (t, *J* = 7.2 Hz, 5-H, 7-H),
8.53 (s, 4-H); Anal. Calcd for $C_{12}H_9N_2Cl$: C, 66.65; H, 4.20; N, 12.96. Found: C, 66.48; H, 4.28; N, 13.02%.

2-Chloro-3-cyano-5-phenylpyridine, 2h: Yield 73%, m.p. 150-52°C; IR (KBr): 223 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50-7.54 (m, Ph-H), 8.15 (d, *J* = 2.7 Hz,
), 8.79 (d, *J* = 2.7 Hz, 6-H); Anal. Calcd for $C_{12}H_7N_2Cl$: C, 67.28; H, 3.30; N, 13.09. Found: C, 67.34; H, 3.22; N, 12.98%.

2-Chloro-3-cyano-4-methyl-N-phenylpyrazole, 2i: Yield 77%, m.p. 105-07°C; IR (KBr): 2227 cm^{-1};
^1H NMR ($CDCl_3$): δ 2.57 (s, CH_3), 7.50 (m, Ph-H); Anal. Calcd for $C_{12}H_9N_2Cl$: C, 66.65; H, 4.20; N,
12.96. Found: C, 66.48; H, 4.09; N, 13.04%.

3,4-Dimethoxy-benzonitrile, 2j: Yield 67%, m.p. 67-69°C; IR (KBr): 2226 cm^{-1}; ^1H NMR ($CDCl_3$): δ

3.90 (s, OCH_3), 3.94 (s, OCH_3), 6.90 (d, J = 8.4 Hz, 5-H), 7.26 (s, 2-H), 7.29 (d, J = 8.4 Hz, 6-H). Anal. Calcd for $C_9H_9NO_2$: C, 66.23; H, 5.56; N, 8.59. Found: C, 66.38; H, 5.48; N, 8.52%.

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