



NOTE

One Pot Synthesis of Nitriles from Aldehydes and Hydroxylamine Hydrochloride Using Ferrous Sulphate in DMF Under Reflux Condition†

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(Received: 16 February 2011;

Accepted: 14 November 2011)

AJC-10671

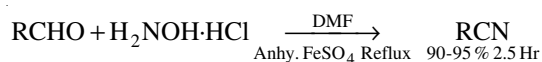
A rapid and facile one pot synthesis of nitrile has been carried out in high yields from the corresponding aldehydes and hydroxylamine hydrochloride in the presence of anhydrous ferrous sulphate and DMF under reflux condition.

Key Words: Aldehydes, Hydroxylamine hydrochloride, Anhydrous ferrous sulphate, Nitriles.

Nitriles are widely used for transformation into amides amines, esters, carboxylic acid *etc.*¹ hence they have been used as intermediates for the synthesis of fine chemicals such as agricultural chemicals, dyes and medicines². One of the most general methods for the synthesis of nitriles is the nucleophilic substitution reaction of alkylhalide with metal cyanides. The method is however inconvenient because of high toxicity of metal cyanides and their trouble in handling. Consequently other method such as dehydration of primary amide³ or aldoximes⁴⁻⁷ has attracted attention.

It is known that dehydration of aldoximes into nitriles can be achieved by using variety of reagents like triethylamine/sulphur dioxide⁴, zeolites⁵, fluoride⁶, sulfurylchloride⁷, *etc.* but many of these suffer from limitations such as high toxicity, vigorous reaction conditions, unsatisfactory yield, tedious work up and use of large excess of reagents. A rapid synthesis of nitriles in high yields from aldoximes using silica gel^{8a} and also one pot synthesis of nitrile from aldehyde and hydroxylamine hydrochloride using silica gel, Mont K.10 and KSF catalyst in dry media under microwave irradiation^{8b}. Some rapid procedure for one pot synthesis of nitriles have been described using formic acid⁹ and potassium peroxy monosulphate¹⁰ but where as the first method suffers from undesirable action of formic acid that can affect acid sensitive aldehydes, the second suffers from the undesirable oxidation of some of the functional group. So there exists a need for developing rapid and facile methods for one pot synthesis of nitriles. We report a rapid

one pot synthesis of nitriles from aldehydes and hydroxylamine hydrochloride using anhydrous ferrous sulphate and DMF under reflux condition which we thought would catalyze both the oxime formation and the consequent nitrile formation step.



Scheme-I

There has been a growing interest over the past few years to carry out organic reactions. over heterogeneous catalyst, because of simple set ups and workup, lesser chemical degradation, higher product purity and chemical yield.

Investigations were initiated with 4-methyl benzaldehyde being chosen as a model compound. It was refluxed with hydroxylamine hydrochloride in presence of anhydrous ferrous sulphate and DMF.

General procedures, melting points were determined in open capillaries. ¹H NMR (CDCl₃) spectra were recorded on a jeol F × 90 Q. Instrument using TMS as internal standard. IR spectra were recorded on a Perkin Elmer 782 spectrophotometer. TLC was carried out on silica gel G plates with benzene/ethyl acetate (4:1) system.

Typical experimental procedure: 4-Methyl benzaldehyde (120 mg, 1 mmol), hydroxylamine hydrochloride (105 mg 1.2 mmol) were mixed with ferrous sulphate (1 mmol) and taken in 25 mL round bottom flask and 5 mL DMF was added. Whole

†This work is dedicated to Late (Dr.) D.G. Desai.

TABLE-1
ONE POT SYNTHESIS OF NITRILES FROM ALDEHYDES AND HYDROXYLAMINE HYDROCHLORIDE
USING ANHY. FERROUS SULPHATE IN DMF AT REFLUX CONDITION

Entry	Reactant	Product	Isolated yield (%)	Time (h)
1	Benzaldehyde	Benzonitrile	90	3 h 30 min
2	4-Methyl benzaldehyde	4-Methyl benzonitrile	95	3 h 20 min
3	4-Methoxy benzaldehyde	4-Methoxybenzonitrile	88	4 h
4	2-Hydroxy benzaldehyde	2-Hydroxy benzonitrile	85	4 h
5	4-Hydroxy benzaldehyde	4-Hydroxy benzonitrile	80	4 h
6	2-Chloro benzaldehyde	2-Chloro benzonitrile	90	2 h 30 min
7	4-Hydroxy-3-methoxy benzaldehyde	4-Hydroxy-3-methoxy benzonitrile	91	5 h
8	2,3-dimethoxy benzaldehyde	2,3-dimethoxy benzonitrile	90	5 h
9	2,3,4-trimethoxy benzaldehyde	2,3,4-trimethoxy benzonitrile	85	6 h
10	3-N,N-Dimethyl benzaldehyde	3-N,N-Dimethyl benzonitrile	93	4 h 30 min
11	2-Nitro benzaldehyde	2-Nitro benzonitrile	85	2 h 20 min
12	4-Methyl-3-nitro benzaldehyde	4-Methyl-3-nitro benzonitrile	90	3 h 3 min
13	3-Nitro benzaldehyde	3-Nitro benzonitrile	83	2 h 20 min
14	Pentanal	Pentanitrile	90	4 h 30 min
15	Hexanal	Hexanitrile	92	4 h 15 min
16	Heptanal	Heptanitrile	95	4 h

mixture was refluxed for 3-6 h. The catalyst was filtered off and the resultant solution extracted and evaporated to give residue which was purified by chromatography using benzene/ethyl acetate (4:1) as eluent to afford the desired nitrile (95 % yield).

Spectral data

p-Tolunitrile (2): b.p. 215-217 °C [lit. 220 °C]; IR (KBr, ν_{\max} , cm^{-1}): 3039, 2229; $^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ_{H} 7.23 (2H, d, $J = 7.4$ Hz, H-Ar), 7.47 (2H, d, $J = 7.4$ Hz, H-Ar).

Pentanenitrile (14): b.p. 139-141 °C [lit. 142 °C]; IR (KBr, ν_{\max} , cm^{-1}): 2742, 2683, 2247; $^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ_{H} 0.96 (3H, t, $J = 2.8$ Hz, H-aliph), 1.68 (2H, m, H-aliph), 1.50 (2H, m, H-aliph), 2.34 (2H, t, $J = 2.8$ Hz, H-aliph).

4-Methoxybenzonitrile (3h): m.p. 57-59 °C [lit. 62-63 °C]; IR (KBr, ν_{\max} , cm^{-1}): 3068, 2219; $^1\text{H NMR}$ (CDCl_3 , 500 MHz): δ_{H} 3.73 (3H, s, Me), 6.95 (2H, d, $J = 9.1$ Hz, H-Ar), 7.40 (2H, d, $J = 9.1$ Hz, H-Ar).

The best yield of 92 % was obtained after 3.2 h. Hence, all the subsequent reactions were carried out under this reaction conditions a verity of substituted aromatic aldehydes (1-13) and aliphatic aldehydes (14-16) including. The reactions were monitored by TLC. The products yields and reaction times are collected and presented in Table-1. All the products are known compounds and were identified on the basis of their spectroscopic analysis and by direct comparison of their m.p. with those of authentic samples¹¹. The products were obtained in more than 90 % purity as determined by $^1\text{H NMR}$ and were further purified by chromatography.

As we have observed, the nitriles were formed in high yield of 90-95 % within 3-6 h. It should be noted that the nitriles were formed with 1-2 % yield under identical reaction conditions in the absence of catalyst thereby confirming the role of the catalyst in the reaction.

In summary, we have demonstrated the use of inexpensive, easy to handle and environmental friendly anhydrous ferrous sulphate as catalyst in rapid one pot synthesis of nitriles from aldehyde and hydroxylamine hydrochloride in high yield.

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