

Microwave promoted rapid dehydration of aldoximes to nitriles using melamine-formaldehyde resin supported sulphuric acid in dry media

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Abstract

A simple and convenient procedure for the synthesis of nitriles by dehydration of aldoxime using supported sulphuric acid on melamine-formaldehyde resin (MFR) under solvent-free condition has been developed. A variety of aromatic and aliphatic aldoximes were converted to the corresponding nitriles. The resin was recovered and reused for subsequent reactions.

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Nitriles are versatile synthetic intermediates for pharmaceuticals, agricultural chemicals and dyes [1]. The most common and well-known procedure for the preparation of nitriles is the nucleophilic displacement of substrates with suitable leaving groups such as halogen compounds, aryl sulfonates, alcohols, esters, ethers, nitro or amino compounds and diazonium salts with inorganic cyanide ions [2]. The other alternative procedures are dehydration of amides [3] and aldoximes [4], conversion of alcohols [5], aldehydes [6] and carboxylic acids [7] to nitriles using various reagents and direct conversion of amines [8].

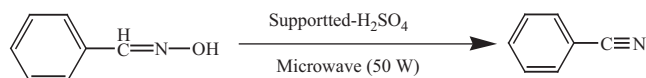
The dehydration of aldoximes which are easily prepared from the corresponding aldehydes is a candidate for clean nitrile synthesis and various procedures have been reported [9]. However, selective dehydration to the corresponding nitriles is very difficult and many reported procedures require the use of reactive reagents in stoichiometric amounts, such as the Burgess reagent [10], *N*-chlorosuccinimide/ PPh_3 [11] and thionyl chloride [12]. Such reagents present a severe drawback for scaled-up and industrial application. Therefore, efficient catalytic procedures for the dehydration of aldoximes are still in great demand. Oxorhenium(VII) complexes [13], $\text{Ga}(\text{OTf})_3$ [14], InCl_3 [15], $\text{TiCl}_3(\text{OTf})$ [15] and $\text{Cu}(\text{OAc})_2$ [16] have been reported to catalyze the dehydration homogeneously, for example. Although heterogeneous dehydration systems are environmentally and technologically the most desirable procedures, widely usable truly heterogeneous catalysts are unprecedented.

Herein we report a simple and efficient process for the dehydration of aldoximes to nitriles using supported sulphuric acid on melamine-formaldehyde resin (MFR) under microwave irradiation and solvent-free condition. Simplicity of operation, easy work-up and high yields are some advantages of this method.

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Table 1

Effect of various support-H₂SO₄ on conversion of benzaldoxime into benzonitrile under microwave irradiation.

Entry	Support	Time (min)	Yield ^a (%)
1	None	30	50
2	MFR	5	80
3	Silica gel	7	80
4	Alumina	10	75
5	Montmorillonite k-10	15	60
6	Clay	18	70
7	Kaolin	15	55
8	Zeolite	10	75

^a Isolated yield.

First, the dehydration of benzaldoxime as a model substrate was carried out with various supports, including previously reported solid supports (Table 1). Melamine-formaldehyde resin showed the highest catalytic activity for the dehydration of benzaldoxime among various supports tested (Table 1, entry 2). In the absence of support, the reaction was achieved; however, moderate yield of nitrile was attained after longer reaction time (Table 1, entry 1). Other supports such as silica gel, alumina, montmorillonite k-10, clay, kaolin and zeolite (Table 1, entries 3–8) also afford good yields of nitrile in longer reaction times.

The best ratio for H₂SO₄ and MFR was found 10 mmol H₂SO₄ per a gram of MFR.

To realize the superiority of the microwave assisted method in comparison with conventional heating method, we compared the model reaction in four different solvents with different polarity and different boiling points. In DMSO and DMF, higher power outputs provide high temperatures because solvents with high enough boiling points were used. The reactions show similar effects of temperature on the yields to those observed under thermal conditions. Similar results were observed in MeCN, because the reaction temperature was maintained by the boiling point of MeCN.

In THF solvent system the results indicate that no obvious effect of microwave irradiation on the yield was observed, because the reactants and their intermediates should locate in microscopic hot spots in the reaction system and their actual temperature is somewhat higher than solvent [17].

Several aldoximes were subjected to dehydration by this procedure using MFR-H₂SO₄ to produce the corresponding nitriles. The results are summarized in Table 2. Both electron-donating and electron-withdrawing group-substituted aromatic aldoximes provided uniformly good results (Table 2, entries 2–9). This procedure is also compatible with heteroaryl (Table 2, entry 10) and aliphatic aldoximes (Table 2, entry 11) and a variety of functionalities such as Cl, NO₂ and OH.

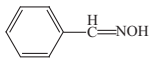
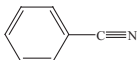
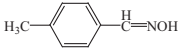
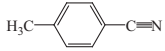
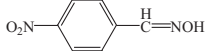
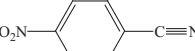
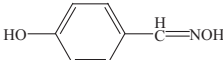
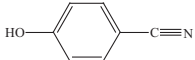
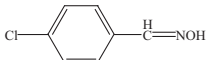
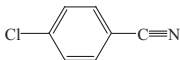
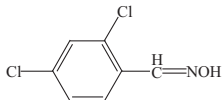
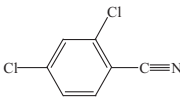
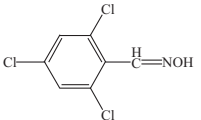
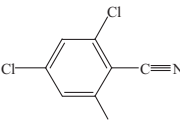
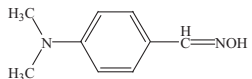
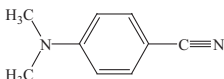
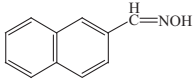
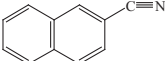
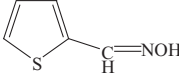
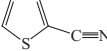
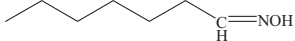

A plausible mechanism for the MFR-H₂SO₄ catalyzed reaction to form nitrile derivatives was illustrated in Scheme 1. The MFR-H₂SO₄ facilitates the dehydration process through co-ordination of its N–H with –OH of aldoxime, followed by abstraction of H⁺ by HSO₄[–].

In summary, we have developed an efficient and mild protocol for the synthesis nitriles *via* dehydration of aldoximes using supported H₂SO₄–melamine-formaldehyde resin under solvent-free condition. Furthermore, the reaction is a green process and the catalyst is recyclable for several uses. The advantages of the present method in terms of facile manipulation, fast reaction rates and formation of cleaner products under neat reaction conditions should make this protocol as a valuable alternative to the existing methods.

1. Experimental

All chemicals and analytical grade solvents were purchased from Merck or Fluka chemical company. Melting points of all nitriles were determined in open glass capillaries on Mettler FP51 melting point apparatus. ¹H NMR spectra were recorded on an Bruker AVANCE DRX 500 spectrometer. A stars SYNTH microwave oven was used at different power levels for all the experiments. The reaction was monitored by TLC using pre-coated plates (Merck).

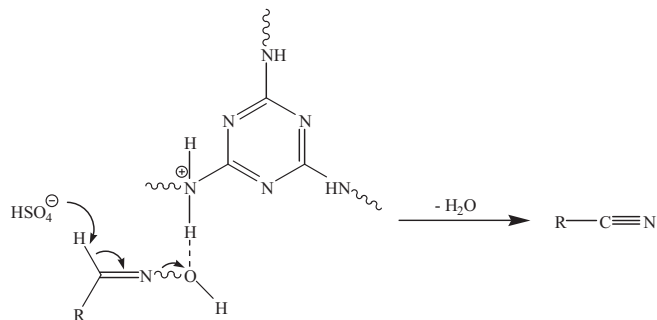
Table 2
Dehydration of aldoximes to nitriles in the presence of MFR-H₂SO₄.

Entry	Aldoxime	Nitrile ^a	MP (lit) [18]	Yield ^b (%)	Reaction time (min)
1			191 ^c	80	5
2			216 (218) ^c	85	4
3			152 (149)	90	4
4			109 (110)	75	5
5			91 (93)	70	4
6			40 (43)	65	5
7			134 (136)	80	4
8			72 (71)	82	5
9			65 (66) ^c	85	5
10			190 (192)	67	5
11			180 (183) ^c	77	3

^a All the products are known.

^b Isolated yield.

^c Boiling point.



Scheme 1.

1.1. Preparation of melamine-formaldehyde supported H_2SO_4

Commercial sulphuric acid (99%, 5 mL) was stirred with a suspension of melamine-formaldehyde resin (5 g) in acetone (50 mL) for 20 min. The catalyst obtained after filtration was dried in vacuum oven before use.

1.2. Typical experimental procedure

The aldoxime (10 mmol) was thoroughly mixed with H_2SO_4 /melamine-formaldehyde catalyst (5 g) in an agate mortar. The resulting fine powder was taken in a pyrex Erlenmeyer flask (25 mL) and irradiated in a microwave oven (conditions, see Table 2). After completion of the reaction dichloromethane 30 mL (2×15) was added to the mixture. The filtrate was dried (Na_2SO_4) and the crude product obtained after evaporation of solvent was purified by crystallisation, distillation or column chromatography.

Spectral data for selected products: **Compound 2**: 1H NMR (500 MHz, $CDCl_3$): δ 2.49 (s, 3H, Me), 7.41 (d, 2H, $J = 10$ Hz, H-Ar), 8.07 (d, 2H, $J = 5$ Hz, H-Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.56, 103.78, 114.76, 129.27 (2C), 133.94 (2C), 142.85.

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