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Efficient one pot synthesis of Nitriles from Aldehydes in solid state using Peroxymonosulfate on Alumina

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Abstract:

In an environmentally benign solvent-free system, aldehydes are rapidly transformed into nitriles using peroxymonosulfate-alumina under microwave irradiation.

Keywords: Microwave irradiation, potassium peroxymonosulfate, nitriles, alumina

The remarkable synthetic properties of the nitrile group have ensured long standing studies of their utilization in organic synthesis [1]. Several methods are available to accomplish the conversion of alkyl or aryl aldehydes to their corresponding nitriles under a variety of reaction conditions [2]. Because of its role in synthetic chemistry, this reaction continues to receive attention from the chemists in search for newer methods. In the majority of cases the aldoxime is prepared initially and then dehydrated by a wide variety of reagents [3]. There are only a few methods known for the conversion of aldehydes to nitriles in one-pot procedure [4]. Unfortunately, many of these one-pot conversions are limited to aromatic aldehydes which, generally, are transformed more readily to nitriles than the aliphatic aldehydes. Recent methods which have been successfully applied to both the aliphatic and aromatic compounds include the use of expensive (*o*-2,4-dinitrophenyl hydroxylamine)[5], (hydroxylamine *o*-sulfonic acid) [6], hazardous (selenium dioxide) [7] or corrosive (formic acid) [8] reagents and tedious work-up procedures. Consequently, there is a need for the development of protocols using readily available and safer reagents which lead to high yields of nitrile compounds.

In recent years, reagents impregnated on mineral solid supports [9], which are efficient in 'dry' media [10], and assisted by microwaves [11] have gained popularity in organic synthesis because of their enhanced selectivity, improved reaction rates and associated ease of manipulation. Even though Villemin et al reported [12] microwave activation for the one pot synthesis of nitriles from aldehydes, the actual application of microwave energy is limited to the preparation of intermediate oximate, which in turn was reacted with CS_2 for sufficiently long time (16-48 h) to get the corresponding nitrile.

In continuation of our ongoing programme to develop environmentally benign reactions [13], we now wish to report a facile conversion of aldehydes to their corresponding nitriles by alumina supported potassium peroxymonosulfate that proceeds in the solid state using microwaves. The reaction proceeds efficiently in high yields at ambient pressure within a few minutes. The role of peroxymonosulfate was confirmed

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$$\text{R-CHO} \xrightarrow[\text{Mw}]{\text{NH}_2\text{OH.HCl; peroxymonosulfate-alumina}} \text{R-C}\equiv\text{N}$$

by conducting a blank experiment, where the formation of nitrile was not observed. Potassium peroxymonosulfate is an inexpensive and readily accessible oxidising agent. It is commonly used as oxone® ($2KHSO_5$, $KHSO_4$, K_2SO_4) and is a, versatile oxidant for the transformation of a wide range of functional groups [14]. The results shown in Table 1 indicate that the reaction is successful for a variety of aromatic and aliphatic aldehydes[†].

Table 1 conversion of aldehydes into nitriles under microwave irradiations

Entry	Substrate **1**	Time/min.	Product[a] **2**	yield (%)[b]
1	Benzaldehyde	7.5	Benzonitrile	77
2	4-Chlorobenzaldehyde	8.0	4-Chlorobenzonitrile	88
3	3,4,5-Trimethoxybenzaldehyde	7.0	3,4,5-Trimethoxybenzonitrile	95
4	2-Nitrobenzaldehyde	9.5	2-Nitrobenzonitrile	90
5	2,4-Dichlorobenzaldehyde	9.0	2,4-Dichlorobenzonitrile	85
6	3,4-Methylenedioxybenzaldehyde	8.5	3,4-Methylenedioxybenzonitrile	87
7	Caprylaldehyde	12.0	Caprylonitrile	73[c]
8	Cyclohexane carboxaldehyde	11.5	Cyclohexane carbonitrile	70[c]
9	Phenylacetaldehyde	10.0	Phenylacetonitrile	83
10	9-Anthraldehyde	8.0	9-Anthacene carbonitrile	93

[a] All products were characterized by comparison of their m.p, IR and ^1H NMR spectra with those of the authentic samples. [b] Unoptimized yields of pure isolated products. [c] Further increasing the reaction time gave no significant improvement in yields but rather decomposition occurred.

In conclusion, we have developed a convenient method for the solid state conversion of aldehydes to nitriles using a solvent-free system, peroxymonosulfate-alumina, that is accelerated by microwave irradiation.

Footnotes: [†] In a typical procedure, trimethoxybenzaldehyde **1** (0.196 g, 1.0 mmol), hydroxylamine hydrochloride (0.077 g, 1.1 mmol) and peroxymonosulfate (0.61 g, 1.0 mmol) doped on a neutral alumina (1.0 g) were mixed thoroughly on a vortex mixer. The reaction mixture was placed in an alumina bath inside an commercial microwave oven (operating at 2450 MHz frequency) and irradiated for a period of 7 min. After completion of the reaction (monitored by TLC) and the inorganic support was separated by filtration, after eluting the product with dichloromethane (2 x 15 ml). Removal of solvent and the residue on purification by column chromatography on silica gel gave the corresponding trimethoxybenzonitrile **2** in 95% yield and there was no evidence for the formation of any side products.

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