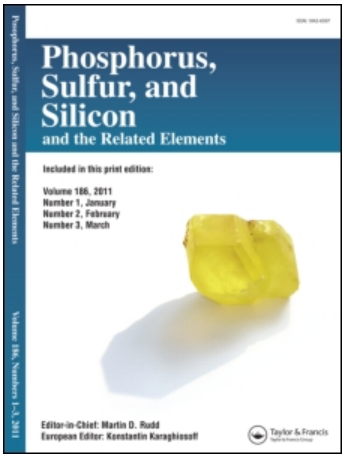

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Microwave-Assisted Efficient One-Pot Synthesis of Nitriles From Aldehydes in the Presence of P_2O_5/SiO_2 in Solvent-Free Media

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A rapid and efficient procedure is developed for a one-pot synthesis of nitriles by condensation of aldehydes with hydroxylamine hydrochloride in the presence of P_2O_5/SiO_2 in solvent-free media under microwave irradiation.

Keywords Aldehydes; aldoximes; microwave irradiation; nitriles; phosphorus pentoxide

INTRODUCTION

Nitriles, important reagents for organic synthesis have been known to chemist for a long time. In recent reports, it was shown that nitriles are very useful starting materials for the synthesis of various bioactive molecules.[1,2] Furthermore, nitriles can be converted to amides, carboxylic acids, amines, ketones, and esters.[3] For example, vanillylamine readily obtained by the reduction of vanillylonitrile,[4] could be reacted with acyl chlorides to give capsaicinoids.

Several procedures are available for the one-step conversion of aldehydes into nitriles using different chemical reagents and hydroxylamine hydrochloride.[5,6] However, most the methods suffer from serious drawbacks which include the use of hazardous and expensive or commercially unavailable reagents, long reaction times, low yields, drastic reaction conditions, and tedious workup procedure.

The efficiency of microwave irradiation (MW) in organic synthesis is currently under intensive study.[7] There are just a few publications

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describing the use of microwave irradiation for preparations of nitriles from aldehydes and hydroxylamine hydrochloride.[8] Our projects have been to develop new synthetic methods using the P_2O_5/SiO_2 in solvent-free media.[9] Having the above facts in mind, we wish to report a very simple and efficient method for one-pot synthesis of nitriles from both alkyl and aryl aldehydes using P_2O_5/SiO_2 and hydroxylamine hydrochloride in solvent-free media under microwave irradiation.

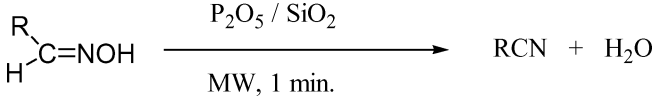
RESULTS AND DISCUSSION

In order to prepare nitriles, various types of aldehydes were mixed with hydroxylamine hydrochloride in the presence of P_2O_5/SiO_2 reagent using microwave irradiation in solvent-free media. In this approach, nitriles were obtained instead of oximes. The general reaction is illustrated in Scheme 1 and the results are reported in Table I. All reactions were performed in one minute. As shown in the Table I several structurally different aldehydes underwent cleanly and remarkably fast the one-pot reaction to the corresponding nitriles. This mild and versatile method which results in yields of 75–95% can also be applied to aldehydes containing other reactive functional groups, such as double bond and hydroxyl group. Even 2-furaldehyde gives a good yield of product in spite of the literature[10] which claims that such a reaction was not successful.

$$RCHO + NH_2OH{\cdot}HCl \xrightarrow[MW,\ 1\,min.]{P_2O_5/SiO_2} RCN + H_2O$$

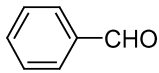
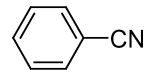
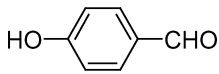
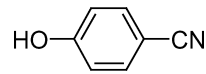
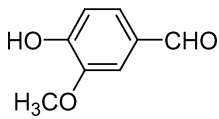
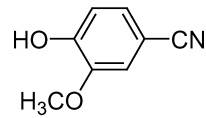
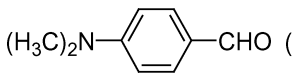
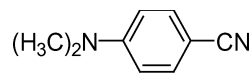
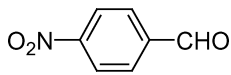
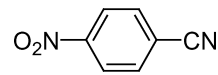
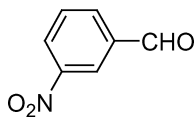
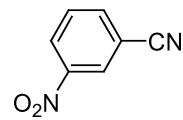
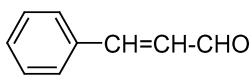
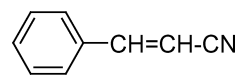
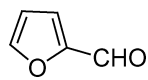
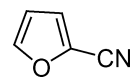
SCHEME 1 One-pot preparation of nitriles.

In the absence of microwave irradiation, after 10 min grinding of the mixture the corresponding aldoximes were exclusively formed in good yields.[9d,e] This clearly indicates that aldoxime may be an intermediate in the conversion of aldehydes to nitriles. Also, aldoximes are dehydrated to the corresponding nitriles in high yields under the same conditions. The general reaction is illustrated in Scheme 2 and the



SCHEME 2 Conversion of aldoximes to nitriles.

TABLE I One-Pot Preparation of Nitriles from Aldehydes by Using P_2O_5/SiO_2 and Hydroxylamine Hydrochloride in Solvent-Free Media under Microwave Irradiation

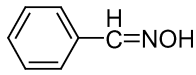
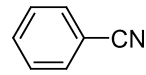
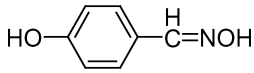
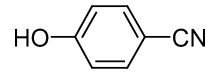
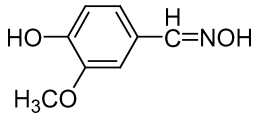
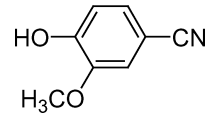
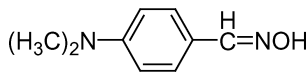
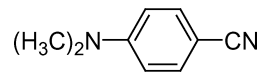
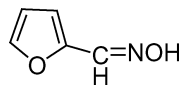
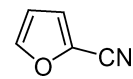
Entry	Aldehyde	Nitrile	Yield (%)[a]	Mp or bp (°C)/ mmHg(lit.)
1	CH_3CHO	CH_3CN	75	81/760 (80/760)[11]
2	C_3H_7CHO	C_3H_7CN	78	113/760 (110/760)[11]
3	$C_5H_{11}CHO$	$C_5H_{11}CN$	78	160/760 (162/760)[11]
4	$C_6H_{13}CHO$	$C_6H_{13}CN$	75	198/760 (70-71/10)[12]
5			95	190/760 (187/760)[11]
6			80	113 (112–114)[10]
7			89	82–83 (81)[13]
8			85	74–75 (74–76)[12]
9			85	146–147 (148)[11]
10			85	116–117 (117)[11]
11			85	258/760 (260/760)[11]
12			75	147 (147–148)[12]

[a]IR, ^{1}H-NMR, and mp or bp confirmed the structures.

results are reported in Table II. As shown in Table II the corresponding nitriles were obtained in 85–95% yields from both alkyl and aryl aldoximes.

In conclusion, this one-pot synthesis of nitriles from aldehydes, without isolation of aldoximes, offers significant improvements over the existing procedures and thus makes available a variety of nitriles and related compounds. Also this simple and readily available reagent affords various nitriles in a short reaction time, with excellent yields,

TABLE II Conversion of Aldoximes to Nitriles by Using P_2O_5/SiO_2 in Solvent-Free Media under Microwave Irradiation

Entry	Aldoxime	Nitrile	Yield (%)[a]	Mp or bp (°C)/ mmHg(lit.)
1	$CH_3CH{=}NOH$	CH_3CN	85	81/760 (80/760)[11]
2	$C_3H_7CH{=}NOH$	C_3H_7CN	88	113/760 (110/760)[11]
3	$C_6H_{13}CH{=}NOH$	$C_6H_{13}CN$	85	198/760 (70–71/10)[12]
4			90	190/760 (187/760)[11]
5			95	113 (112–114)[10]
6			95	82–83 (81)[13]
7			92	74–75 (74–76)[12]
8			85	147 (147–148)[12]

[a]IR, ^{1}H-NMR, and mp or bp confirmed the structures.

and good selectivity. Further applications of the P_2O_5/SiO_2reagent in organic synthesis are under investigation.

EXPERIMENTAL

All melting points recorded are uncorrected open capillary measurements. IR spectra were recorded on a Shimadzu-IR 470 spectrophotometer. ^{1}H-NMR spectra were recorded on a Bruker-80 and 500 MHz instrument using tetramethylsilane (TMS) as an internal standard. Silica gel 60(230–400 mesh) was obtained from Fluka and was dried in an oven at 120°C for 2 h. Irradiation was carried out in a domestic microwave oven (Electra, 2450 MHz, and 800 W) for an optimized time. The P_2O_5/SiO_2 reagent was obtained according to the early reported procedure.[9]

Preparation of Nitriles

General Procedure

In a typical reaction, a mixture of aldehyde (2 mmol), hydroxylamine hydrochloride (4 mmol) and the P_2O_5/SiO_2 reagent (1 g), or a mixture of aldoxime (2 mmol) and the P_2O_5/SiO_2 reagent (1 g) was ground thoroughly in the mortar. Usually an immediate colour change was observed. The mortar was covered with a watch glass and put inside the microwave oven. The mixture was irradiated for one minute and the completion of the reaction was monitored by TLC. After the completion of the reaction, the mortar was removed from the oven, the mixture was cooled to room temperature and then 10 ml of 5% aqueous HCl was added to the mixture. The resulting solution was extracted with CH_2Cl_2 (2×10 ml). The extracts were combined and dried over $CaCl_2$. Evaporation of the solvent under vacuum gave nitriles with high purity (based on TLC, ^{1}H-NMR, IR and melting point). Column chromatography or recrystalization from benzene or benzene-cyclohexane gave pure products.

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