

RESEARCH LETTER

Solvent-free and atom efficient conversion of aldehydes into nitriles

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Nitriles are readily prepared from aliphatic and aromatic aldehydes upon heating with hydroxylamine hydrochloride at 100°C in a solvent-free, one-pot process.

Keywords: solvent-free; aldehyde; nitrile; one-pot; tandem reaction

Methods for preparing nitriles are highly desirable as the carbon–nitrogen triple bond can be readily converted into a variety of other functional groups (1,2). A widely used method for preparing nitriles involves the dehydration of aldoximes. Although a number of dehydration reagents have been described,¹ we recently reported that simply heating a mixture of an aldehyde with hydroxylamine hydrochloride in dimethylsulfoxide to 100°C readily affords the corresponding nitrile in good yield (3). In an effort to minimize waste and to make this reaction more environmentally acceptable we have now determined that this reaction can be performed in the absence of solvent and we present our results herein.

The experimental procedure for the one-pot, solvent-free conversion of aldehydes into nitriles is simple and straightforward and affords nitriles in good yields.² As seen in Table 1, both aliphatic and aromatic nitriles can be prepared from their corresponding aldehydes. As an illustrative example, decanal, **1d**, (2.0 mmol) was heated with hydroxylamine hydrochloride (2.2 mmol) for 60 min in a sand bath maintained at 100°C. After cooling to room temperature, the reaction mixture was dissolved in ethyl acetate (50 mL) and this organic layer was washed with water (1 × 20 mL) and saturated aqueous sodium bicarbonate (1 × 20 mL). The organic layer was dried (anhydrous potassium carbonate) and the solvent removed by rotary evaporation and high vacuum to yield 3-phenylpropanenitrile, **2d**, as a light oil (1.7 mmol, 87%) which was shown by ¹H-NMR and gas chromatography (gc) to have a purity greater than 95%. All the nitriles prepared in this study were confirmed by comparison of ¹H- and ¹³C-NMR spectra and mass spectra with authentic nitrile samples.

Reaction times to reach complete conversion varied from 15 min to 4 h. As determined by monitoring the reactions by gc/mass spectrometry (ms), all the reactions were greater than 90% complete after 15–60 min. Reaction times could be shortened by increasing the amount of hydroxylamine hydrochloride used; however, a 10 mol% excess of the hydroxylamine hydrochloride was considered optimal to maintain atom efficiency. As seen in reaction scheme found in Table 1, the products of the reaction are one equivalent of nitrile and HCl and two equivalent of water.

In conclusion, we have demonstrated that aldehydes can be readily converted into nitriles in a one-pot, solvent-free manner by heating the aldehydes with hydroxylamine hydrochloride at 100°C. Furthermore, the reaction only produces HCl (aq) as a waste product and the atom efficiency of the reaction is good.

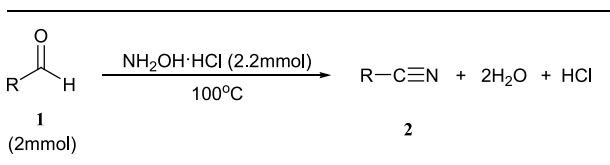
Experimental

All reagents and solvents were obtained from commercial sources and were used without purification. ¹H-NMR and ¹³C-NMR spectra were recorded on a JEOL ECX 400 MHz NMR spectrometer using CDCl₃ as solvent and reference. The progress of the reactions was monitored by gc/ms obtained on a Perkin-Elmer TurboMass gas chromatograph/mass spectrometer system. The NMR spectra and mass spectra of the nitriles obtained in this work were identical to authentic spectra.

As an illustrative example, decanal, **1d**, (0.312 g, 2.00 mmol) was heated in a sand bath maintained at 100°C with hydroxylamine hydrochloride (0.153 g, 2.20 mmol) for 60 min. After cooling to room

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Table 1. Solvent-free and atom efficient conversion of aldehydes into nitriles.



Entry	1	R	2^a	Time, min ^b	Yield (%) ^{c,d}
1	1a	n-hexyl	2a	20	85
2	1b	n-heptyl	2b	15	68
3	1c	n-octyl	2c	240	93
4	1d	n-nonyl	2d	60	87
5	1e	1-methylbutyl	2e	60	36
6	1f	benzyl	2f	60	60
7	1g	4-methylbenzyl	2g	240	75
8	1h	4-isopropylbenzyl	2h	240	82
9	1i	4-chlorobenzyl	2i	240	80
10	1j	4-nitrobenzyl	2j	240	97
11	1k	2-phenylethenyl	2k	60	71
12	1l	2-phenylethyl	2l	60	96
13	1m	1-naphthyl	2m	240	96
14	1n	2-naphthyl	2n	240	91

^a¹H-NMR, ¹³C-NMR and mass spectra of nitrile products were identical to authentic samples; ^btime to reach complete conversion to nitrile as determined by gc/ms; ^cisolated yields; ^dNitrile purities > 95% as determined by ¹H-NMR.

temperature ethyl acetate (50 mL) was added to reaction flask and this organic layer was washed with water (1 × 20 mL) and saturated aqueous sodium bicarbonate (1 × 20 mL). The organic layer was dried (anhydrous potassium carbonate) and the solvent removed by rotary evaporation and high vacuum to yield decanenitrile, **2d**, as a light oil (0.266 g, 1.74 mmol, 87%) which was shown by ¹H-NMR and ¹³C-NMR to have a purity greater

than 95% and was identical to the spectra of an authentic sample (**4**). ¹³C NMR: δ 119.7, 31.7, 29.1, 29.0, 28.6, 28.5, 25.2, 22.5, 16.9, 13.9.

Heptanenitrile (entry 1). ¹³C NMR: δ 119.6, 30.7, 28.1, 25.1, 22.1, 16.9, 13.8.

4-Methylbenzonitrile (entry 7). ¹³C NMR: δ 143.6, 131.9, 129.7, 119.0, 109.1, 21.7.

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Notes

- For a review of dehydration methods see references in ref. 4 below.
- The reaction does not have to be worked up immediately. For example, nonanal, **1c**, was reacted with hydroxylamine hydrochloride for 4 h and the reaction mixture was allowed to sit at room temperature and open to the atmosphere for 6 week. After the usual workup, nonanenitrile, **2c**, was obtained with an isolated yield of 93% and >95% purity as determined by ¹H-NMR.

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