



Solvent-free Synthesis of Nitriles from Aldehydes Catalyzed by $\text{KF}/\text{Al}_2\text{O}_3$, Montmorillonite KSF and K10

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Abstract: Multistep and one-pot conversion of aldehydes to nitriles were carried out conveniently with out solvent using $\text{KF}/\text{Al}_2\text{O}_3$, montmorillonite KSF and K10 as catalyst, under microwave irradiation. The reactions are completed within 6-8 min to give satisfactory yields. $\text{KF}/\text{Al}_2\text{O}_3$ was more effective catalyst both in multistep procedure and one-pot reaction.

Keywords: aldehydes, nitriles, aldoximes, microwave irradiation

Introduction

Nitriles are very useful starting materials for the synthesis of various bioactive molecules.¹ The versatile nitriles are used for the preparation of thiazoles, 2-oxazolines, tetrazoles, imidazoles, triazoles and benzamidines possessing a broad spectrum of biological activities.² The conversion of nitriles into amides, amines, ketones, carboxylic acids and esters are of considerable interests.³

The conversion of aldehydes into the corresponding nitriles is an important organic transformation. This procedure is usually achieved by dehydration of the corresponding aldoximes using classical reagents⁴ or new milder ones such as phosphorus diiodide,⁵ trichloro-acetyl chloride,⁶ chlorosulfonyl isocyanate,⁷ or chlorosulfonyl fluoride.⁸ Bejoy

Thomas⁹ has reported conversion of aldehydes oxime into nitriles using solid acid as catalysts, but it needs high temperature and long reaction time. Recently, some one-pot transformations of aldehydes to nitriles by using various chemical reagents are also reported.¹⁰ Efficient one-pot methods were also developed using hydroxylamine hydrochloride and formic acid,¹¹ selenium dioxide,¹² pyridine in refluxing toluene,¹³ or from nitroethane in the presence of sodium acetate buffer¹⁴ or pyridine hydrochloride.¹⁵ Das¹⁶ has reported microwave assisted rapid conversion of aldehydes into nitriles using silica gel supported NaHSO₄ and NH₄OAc catalysts. However, neither of these catalysts can be recovered. The first catalyst, which could not be stored for a long time should be prepared at the time of use and the second catalyst, which decomposed under microwave irradiation should be used in a large amount.¹⁷ Most of these known methods suffer from significant drawbacks, which include toxic and non-available reagents, harsh reaction conditions, low yields and long reaction time.

We had reported that solid acids KF/Al₂O₃, Montmorillonite KSF and K10 can be used to catalyze many organic reactions.¹⁸ Here we report these three catalysts be used to convert aldehydes into the corresponding nitriles under microwave irradiation, in a simplified, rapid way, generally in excellent yield. Both the one-pot conversion and multistep procedure was studied.

Experimental

Melting points were uncorrected. Montmorillonite KSF and K-10 were purchased from Aldrich and activated at 120 °C for 3 h prior to use. KF/Al₂O₃ was prepared by literature method.¹⁹ 4-methoxybenzaldehyde oxime and 4-hydroxybenzaldehyde oxime were synthesized according to literature,²⁰ melting point data agree to the reported. Liquid aldehydes were purified by distillation prior to use. Other chemicals were commercially purchased and used as received. Microwave irradiation is performed in a Galanz WG900DSL23-K6 microwave oven with a nominal power of 900W. ¹H NMR spectra were measured on a Bruker AVANCE (400 MHz) spectrometer using TMS as internal reference and CDCl₃ or DMSO as solvent.

General Procedure

Aldoximes Dehydration Under Microwave Irradiation

p-Anisaldehyde oxime 302.3 mg (2.0 mmol, 1b) were mixed thoroughly with catalyst (100 mg) in a flask, then the mixture was placed inside microwave oven, and irradiated at designated power for 6 min. Then the reaction mixture was taken out, cooled and extracted with ethyl acetate (3 × 10 ml). After filtration, the filtrate was concentrated and purified by column chromatography over silica gel, using petroleum ether and ethyl acetate as eluent to afford *p*-methoxybenzoxime (1c). The results were summarized in Table 1.

p-Methoxybenzoxime (1c), m.p. 57-58 °C; NMR δ_H (400 MHz, CDCl₃): 3.881 (s, 3H CH₃O), 6.977 (d, 2H, ArH), 7.599 (d, 2H, ArH)

One-Pot Synthesis Under Microwave Irradiation

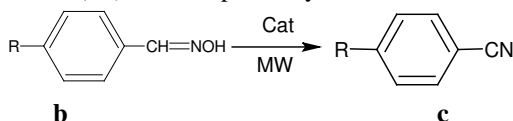
p-Hydroxybenzaldehyde 244.2 mg (2.0 mmol, 2a) and hydroxylamine hydrochloride 166.8 mg (2.4 mmol) were mixed thoroughly with catalyst (100 mg) in a flask, the mixture was placed inside a microwave oven, and irradiated for 6 min. Then the products were cooled

and extracted with ethyl acetate (3 × 10 ml). After filtration the filtrate was concentrated and the residue was purified by column chromatography over silica gel using petroleum ether and ethyl acetate as eluent to afford *p*-hydroxybenzoxime (2c). The results were summarized in Table 2.

p-Hydroxybenzoxime (2c), m.p. 110-112 °C; NMR δ_{H} (400 MHz, CDCl₃): 6.014 (s, 1H, OH), 6.954 (d, 2H, ArH), 7.558 (d, 2H, ArH)

Results and Discussion

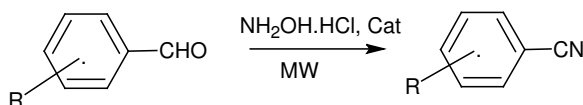
As shown in Scheme 1 and Table 1, two aromatic aldehydes, *p*-anisaldehyde (1a) and *p*-hydroxybenzaldehyde (2a), was transferred to its oximes, ²⁰ and then 1b and 2b was treated with different catalysts under irradiation of microwave to give aromatic nitriles in 28-76% yield respectively. The dehydration procedure was done with a solvent-free system and the reaction was usually completed within 8 minutes. Three kinds of catalyst, montmorillonite KSF, montmorillonite K10 and KF/Al₂O₃, were investigated in this reaction. KSF and K10 shown similar activity, gave out lower yield (20-38%), while KF/Al₂O₃ was more effective in this dehydration, gave out 76% and 36% yield in *p*-anisaldehyde oxime (1b) and *p*-hydroxybenzaldehyde oxime (2b) case, respectively.



1, R= MeO; 2, R=OH

Scheme 1.

In order to obtain higher yield of nitriles and avoid the troublesome separation of oxime, a one-pot conversion of *p*-hydroxybenzaldehyde (2a) to *p*-hydroxybenzoxime (2c) was investigated. The reaction was catalyzed by montmorillonite KSF, K10 and KF/Al₂O₃, with similar solvent-free condition in 6 minutes (Scheme 2), gave out 63%, 67% and 70% yield respectively. Compare with the same product in Table 1, it's obvious that the one-pot conversion gave out higher yield with different catalysts among the three catalysts; KF/Al₂O₃ was proved to be the most effective catalyst once again in the one-pot procedure.



Scheme 2.

Table 1. Aldoximes Dehydration Under Microwave Irradiation

Entry	R	Catalyst	t/min	MW power / %	Yield/ %
1	OMe	KSF	8	100	28
		K10	5	100	38
		KF/Al ₂ O ₃	6	60	76
2	OH	KSF	5	60	28
		K10	6	60	20
		KF/Al ₂ O ₃	5	60	36

Table 2. One-Pot Synthesis of Nitriles Catalyzed by KF / Al₂O₃

Entry	R	t/min	MW	Yield/ %	m.p. (Ref) / °C
			power / %		
1	4-MeO	6	100	80	57-58 (57-59)
2	4-OH	6	60	70	110-112
3	H	6	60	51	Liquid
4	4-CH ₃	6	100	52	76-78
5	3-MeO-4-OH	6	100	72	85 (85-87)
6	2,4-diCl	6	100	42	58-60
7	4-4-NO ₂	8	60	82	148 (149)

As shown in Table 2, the synthesis of aromatic nitriles (**1-7c**) were carried out in good yields by the one-pot reaction of aromatic aldehyde (**1-7a**) and hydroxylamine hydrochloride without solvent, catalyzed by KF/Al₂O₃ under microwave irradiation for 6-8 minutes. Benzaldehyde (**3a**), *p*-tolualdehyde (**4a**) and 2,4-dichlorobenzaldehyde (**6a**) gave out moderate yield (42-52%), while *p*-methoxybenzoxonitrile (**1c**) and *p*-nitrobenzoxonitrile (**7c**) yield 80% and 82%, in 6 and 8 minute respectively. There was no evidence for the formation of any other products. Further increasing the reaction time gave no significant improvement in yields but rather decomposition occurred. Compare with multistep method, the main advantages of the present procedure are mild conditions, higher yield, short reaction time and simple workup

Conclusion

We have developed a convenient one-pot method for conversion of aldehydes to nitriles without solvent, under microwave irradiation. Three kinds of catalyst were used for these reactions. Catalyst KF/Al₂O₃ was more effective than montmorillonite KSF and K10, both in multistep procedure and one-pot reaction

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