

# International Journal of Chemistry and Pharmaceutical Sciences

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## **Research Article**

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## Multi-component, Catalyst free Synthesis of Aminonitrile by Using of Glycerol as Recyclable and Green Solvent

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## ABSTRACT

We describe the use of glycerol as an efficient, safe and recyclable solvent in the one-pot reaction of aldehydes, amines, and trimethyl silylcyanide to afford corresponding -aminonitriles in excellent yields under mild conditions. Catalyst-free, high yields, and simple product isolation method without use of column chromatography are the noteworthy aspects of the synthetic route. Mechanistic route of the reaction proves the promoting nature of the glycerol.

Keywords: Glycerol, -Aminonitriles, Hydrogen bonding, Strecker reaction, Multi-component reactions

## ARTICLE INFO

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Article History: Received 15 July 2015, Accepted 31 August 2015, Available Online 27 September 2015

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**Citation:** Amir Hossein Zamani, et al. Multi-component, Catalyst free Synthesis of -Aminonitrile by Using of Glycerol as Recyclable and Green Solvent. *Int. J. Chem, Pharm, Sci.*, 2015, 3(9): 1970-1974.

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## **1. Introduction**

The majority of pollution and waste generated by the chemical processes is directly related to traditional organic solvents [1-3]. Taking into account the impact of chemical processes on the environment, the search for innovative concepts for the substitution of volatile organic solvents has become a tremendous challenge in academia and industry

[4]. In the past decade, water [5], ionic liquids [6], polyethylene glycol [7], supercritical fluids [8] (particularly supercritical carbon dioxide ( $scCO_2$ ) [9] and perfluorinated solvents [10] appeared as the most promising approaches for current solvent innovation. Although fascinating results have been reported, use of these solvents is still subject to

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strict limitations such as high cost equipment for scCO<sub>2</sub>,[11] or high prices and lack of data about the toxicity and bio-compatibility for ionic liquids [12] or product separation for aqueous-based processes [13]. In other words, a universal green solvent doesn't exist and for this reason, the scientific community is continuously searching for new sustainable media in order to widen their use in catalytic and organic processes. Biomass-based solvents such as glycerol exhibit many advantages such as biodegradability, low vapor pressure and high boiling point. In fact, as suggested by Jerome and co-workers, glycerol can be considered as "organic water". It combines the advantages of water(low toxicity, low price, wide availability) and ionic liquids (highly boiling point, low vapor pressure, ability to form hydrogen bonds) [14]. These advantages make it ideal for use as a sustainable solvent in organic synthesis.

Herein, we would like to communicate that glycerol can be used as a green solvent and hydrogen bond forming in the Strecker reaction to synthesize -aminonitriles through onepot three-component condensation of aldehydes (not ketones), amines, and trimethylsilyl cyanide under mild and catalysis free conditions. The classical Strecker reaction is generally carried out with alkaline cyanides in aqueous solution.A variety of cvanating agents [15-18] have been reported under hazardous and special caution. It has been observed that the use of Me<sub>3</sub>SiCN could overcome all these problems as it is safe to handle and is an effective cyanide source [19-29]. However, most of these methods require expensive reagents, long reaction times, harsh reaction conditions and tedious work-up procedure and give unsatisfactory yields.

## 2. Materials and Methods

All chemicals were purchased from Merck and Sigma-Aldrich companies and used without any further purification. Melting points were recorded on a Buchi B-540 apparatus. Infrared (IR) spectra were recorded on an ABB Bomem model FTLA200-100 instrument.<sup>1</sup>H and <sup>13</sup>C NMR spectra were measured with a Bruker DRX-300 Avance spectrometer at 300 and 75MHz using tetramethyl

#### ISSN: 2321-3132 | CODEN (USA): IJCPNH

silane (TMS) as an internal standard. Chemical shifts () are reported relative to TMS, and coupling constants (J) are reported in hertz (Hz).

2.1 General procedure for the preparation of -amino nitriles: A mixture f amine (1 mmol), aldehyde (1 mmol), in glycerol (3 mL) was stirred at 50°C for the appropriate amount of time (Table 1). After completion of imine formation as indicated by TLC, trimethyl silyl cyanide (1 mmol) was added and stirred at room temperature (Table 1). Oncompletion the product was extracted with 10 ml of ethyl acetatetwice, followed by washing with brine and dried over anhydrous sodium sulphate. The ethyl acetate was removed under reduced pressure to obtain the desired product. The physical data (mp, IR, NMR) of known compounds were found to be identical with those reported in the literature.

## **3. Results and Discussion**

To optimize the reaction conditions to afford the desired amino nitriles, the reaction of benzaldehyde and aniline with TMSCN was chosen as a model reaction. The same reaction was conducted at different temperature and it was observed that as slightly increasing temperature, the rate of reaction increases and good amount of yield was obtained at 50°C within 3.5 h. The reaction was unsuccessful when carried out at room temperature, even after 24 h. Next, we studied the effect of aromatic aldehyde substituent's on the reaction rate and the overall yield (Table 1).

## 4. Conclusion

In summary, we have described an efficient protocol for preparing -aminonitriles using glycerol as a solvent. The advantages of the present method lie in using economic and environmentally benign glycerol as solvent, no use of catalyst, mild reaction conditions, and good yields. This methodis suitable for large-scale synthesis, providing a valuable synthetic tool for industrial applications.

## 5. Acknowledgment

The authors are thankful to MalekAshtar University for providing financial assistance.

	Table 1: Synthesis of	-amino nitriles in	the presence of glycrol as a	solvent and catalyst	
Entry	Aldehyde/Ketone	Amine	Time (min) Formation of imine at 50 °C	Time (hr) Formation of the product at RT	Yield <sup>a</sup> (%)
1	ОН	NH <sub>2</sub>	15	3.15	98[30]
2	O-N H	NH <sub>2</sub>	10	2.10	75[31]

3	O H Cl	NH <sub>2</sub>	80	5	80[32]
4		NH <sub>2</sub>	20	2.15	80[25]
5	Н3СО Н	NH <sub>2</sub>	90	7	70[30]
6	O H	NH <sub>2</sub>	140		70[28]
7	Н	NH <sub>2</sub>	10	2.30	85[33]
8	ОН	Br NH <sub>2</sub>	15	2	88[34]
9	ОН	CI NH2	20	2.30	75[25]
10	CH <sub>3</sub>	NH <sub>2</sub>	N.R	N.R <sup>b</sup>	
11	°	NH <sub>2</sub>	N.R	N.R	
12		NH <sub>2</sub>	N.R	N.R	

<sup>a</sup>Isolated yield

<sup>b</sup>This reaction was done again at 120 °C and any product was not observed.

With both electron withdrawing and electron donating groups, the reaction proceeds smoothly, with an increase in the yield when the arylsubstituent bore an electron withdrawing group. Furthermore as shown in Scheme 1, benzaldehyde was selectively converted to its corresponding -amino nitrile and the starting ketone was intact.



Scheme 1: Selective preparation of -amino nitrile from benzaldehyde in the presence of ketone

Methyl group to hydrogen is donor. Thus a negative charge on the carbonyl in ketones is greater and to form hydrogen bonds should be higher and stronger. But steric hindrance or steric resistance occurs between ketones and glycerol prevents any interactions for formation of hydrogen bond between glycerol and ketone.



Scheme 2: Ketones cannot be formed any interaction with glycerol

Although until now the reasons behind the promoting effect of glycerol are still unclear, amechanism to account for the formation of -aminonitrilesis postulated in Scheme 3.



Scheme 3: A proposed mechanism for the formation of -aminonitriles

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