



**Synthesis of 2,2'-{[2,6-Dichloro-1-(Substituted phenyl)-1,4-Dihydropyridine-3,5-Diyl] Dimethylidene} Dipropanedinitrile Using Green Catalyst L-Proline-Fe<sub>3</sub>O<sub>4</sub> MNP**

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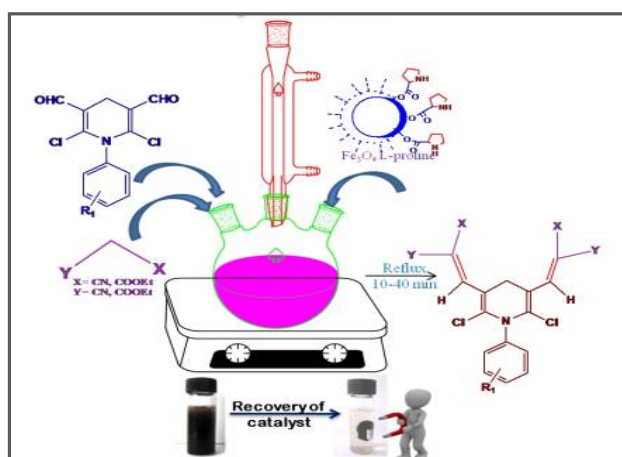
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**ABSTRACT**

The Knoevenagel reaction was mainly used in synthetic practices to achieve sigma bond formation between two carbon atoms. Hence it is need to synthesis a basic organocatalyst supported on ferrite nanoparticles. It is facile and environmentally benign L-proline-Fe<sub>3</sub>O<sub>4</sub> MNP was synthesized and was successfully used for the synthesis of 2-benzylidenemalononitrile derivatives, which were obtained in excellent yields via multicomponent reactions. Magnetic organocatalysts can be easily recovered by simple magnetic decantation and their catalytic power remains unaffected after 3 consecutive cycles, making them environmentally friendly, obeys concept of green chemistry and widely applicable in several organic transformations due to their efficiency, easy for handling, and cost effectiveness. Synthesized compounds were characterized by <sup>1</sup>H-NMR, FT-IR and Elemental analysis.

**Graphical Abstract**



**Keywords:** Vilsmeier-Haack reaction; Knoevenagel condensation; Ferrite, Magnetic Nanoparticles, Green Chemistry.

## INTRODUCTION

Today organic synthesis is based on Magnetic nanomaterials are found a major role in many fields, including industrial procedure biotechnology, biomedicine, environmental remediation, and especially catalysis. The Knoevenagel reaction was mainly used in synthetic practices to achieve sigma bond formation between two carbon atoms [1]. Hence it is need to synthesis a basic organocatalyst supported on ferrite nanoparticles [2]. Most of these reactions are generally carried out in organic solvents, with a few aqueous phase organocatalytic processes as recent exceptions [3], although water is an environmentally benign solvent [4]. The use of environmentally benign solvents like water [5] and absent of organic solvent reactions represent very effective green chemistry [6] methods from economical as well as synthetic point of view [7]. They not only reduce the load of organic solvent clearance, but also improve the speed of many organic reactions. Therefore, efforts have been made to carry out the Knoevenagel condensation in aqueous medium [8]. It was found that the Knoevenagel condensation reaction of aromatic aldehydes with malononitrile or ethyl cyanoacetate takes place in aqueous medium [9]. The separation and recycling of the catalyst is highly favorable since catalysts are often very expensive.

## MATERIALS AND METHODS

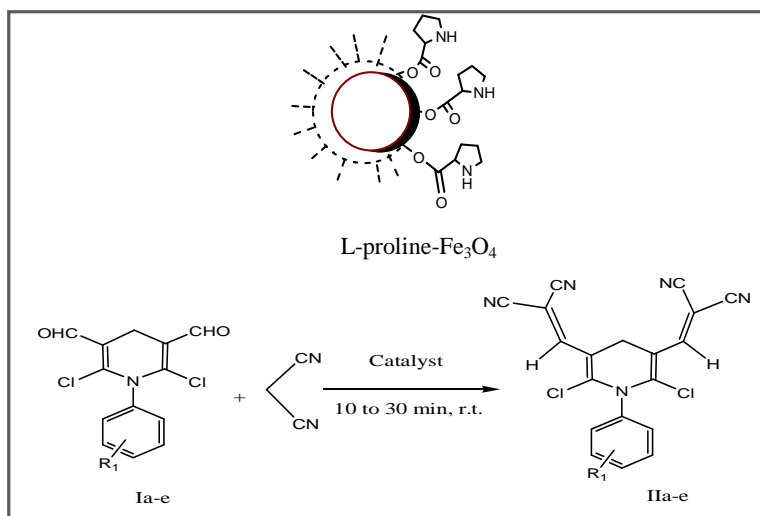
Melting Points of compounds were taken in open air capillary tube and are uncorrected.  $^1\text{H-NMR}$  spectra were recorded on 399 MHz Gemini 2000(Varian, Oxford using DMSO as solvent. IR spectra were recorded on a Perkin-Elmer spectrophotometer FT-IR 1725X. Analytical TLC, Thin-layer Chromatography (TLC) was performed on precoated on Merck silica gel 60 F254 plates. The elemental analysis was performed on the Vario EL III-C, H, N, O elemental Analyzer-GmbH, Hanau-Germany. Reagents and solvents were used without purification purchased from Loba Chem Pvt. Ltd and used as such the 'nano' word used for materials which has diameters near to <100 nm. The important facts about Nano-scale materials that they possess high specific surface areas due to large surface area, where taking a 5 nm spherical magnetite ( $\text{Fe}_3\text{O}_4$ ) particle, the coupled specific surface area ( $240 \text{ m}^2 \text{ g}^{-1}$ ) is significantly better than that ( $<10 \text{ m}^2 \text{ g}^{-1}$ ) which characterizes large mass magnetite. Moreover, as the percentage of atoms at the surface, which are more active, increases with decreasing size, particles at the nano-scale are more active than the equivalent bulk material. The most commonly used magnetic nanoparticles include magnetite ( $\text{Fe}_3\text{O}_4$ ) and L-proline  $\text{Fe}_3\text{O}_4$  has good stability, low environmental impact and high magnetic susceptibility which is used for easy and promotes separation of catalyst and also we have studied their recycling power.

The starting material for this synthesis 2,6-dichloro-(substitutedphenyl)-1,4-dihydropyridine-3,5-dicarbaldehyde **1a-e** were synthesized by Vilsmeier-Haack reactions on (substituted phenyl) piperidine -2,6-diones [10-14].

**Preparation of magnetic  $\text{Fe}_3\text{O}_4$  nanoparticles (MNPs):** It begins with mixture of  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  (5.838 g, 0.022 mol) and  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$  (2.147 g, 0.011 mol) were dissolved in 100 mL of deionized water in a round bottom flask (250 mL) at under room temperature. Then 2 mmol of L-proline (0.230 gm) was added after stirring thereafter, 10 mL of aqueous.  $\text{NH}_3$  solution (32%) was then added into mixture within 40 min with vigorous mechanical stirring throughout mixing. Finally, the black precipitate solid was collected by magnetic decantation, washed with distilled water until solution becomes neutral, and then washed with ethanol to remove unreacted L-proline and dried at  $80^\circ\text{C}$  in scientific oven [15, 16]. After the performing the procedure the magnetic nano material was characterized by using a Scanning Electron Microscopy (SEM). The structure of magnetic catalysts is usually determined by X-ray diffraction (XRD) and organocatalyst immobilization confirmed by FT-IR Spectra.

## RESULTS AND DISCUSSION

## Catalyst used for optimization



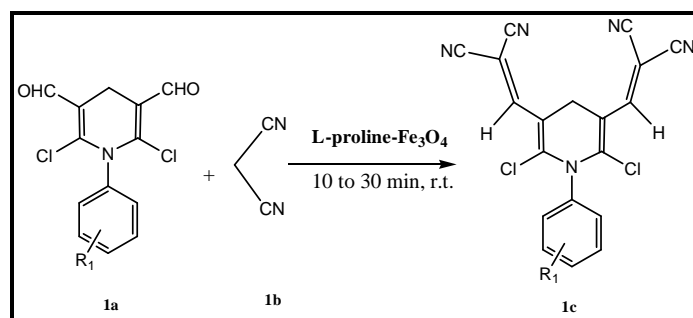
Scheme I

Table 1. Optimization of reaction parameters<sup>a</sup>

Entry	Catalyst <sup>b</sup>	Solvent	Time (min)	Yield <sup>c</sup> (%)
1	A	Ethanol	05	60
2	A	Ethanol	10	86
3	A	Ethanol	20	90
4	A	Ethanol	30	92
5	A	Solvent free	40	--
6	A	H <sub>2</sub> O	15	--

<sup>a</sup>Reaction conditions: Aldehyde (0.01 mol), <sup>b</sup>Active Methylene Compounds(a-e) (0.01 mol), <sup>c</sup>Proline-Ferrite, under R.T

**General Procedure:** A mixture of malononitrile **1b** (4.4 mmol), 2,6-dichloro-(substitutedphenyl)-1,4-dihydropyridine-3,5-dicarbaldehyde **1a** (2 mmol), malononitrile (2 mmol) and L-proline Fe<sub>3</sub>O<sub>4</sub> water/ethanol or water (10 mL) was heated at reflux for 10-30 min in order to synthesize 2, 2'-[[2,6-dichloro-1-(substitutedphenyl)-1,4-dihydropyridine-3,5-diyl]dimethylidene}dipropanedinitril derivatives. Progress of the reaction was monitored by TLC. The catalyst was recovered by simple decantation of reaction mixture by pouring content in to ice water. The product was filtered. The recovered catalyst was washed with ethanol, dried in oven. The resulting catalyst can be used for second cycle of reaction.



Scheme 2. 2,2'-[[2,6-dichloro-1-(substitutedphenyl)-1,4-dihydropyridine-3,5-diyl]dimethylidene}dipropanedinitrile

Table 2. Recyclizing study of Catalyst

Entry	Compounds	Cycle	Yield (%)
1	1a	1 <sup>st</sup>	92
2	1a	2 <sup>nd</sup>	82
3	1a	3 <sup>rd</sup>	65

Table 3. Substrate Study<sup>a</sup>

S. No.	V-H Aldehyde (-R) <sup>b</sup>	X	Y	Product	Yield (%) <sup>c</sup>	M.P. (°C)
1	-H	CN	CN	IIa	94	>280
2	4-Cl	CN	CN	IIb	89	260-262
3	2-Cl	CN	CN	IIc	82	270-72
4	4-NO <sub>2</sub>	CN	CN	IId	94	>280
5	3-NO <sub>2</sub>	CN	CN	IIe	90	>280
6	2-NO <sub>2</sub>	CN	CN	IIf	90	230-232
7	-H	CN	COOEt	IIg	91	192-194
8	4-Cl	CN	COOEt	IIh	85	200-202
9	2-Cl	CN	COOEt	IIi	81	212-14
10	4-NO <sub>2</sub>	CN	COOEt	IIj	93	180-82
11	3-NO <sub>2</sub>	CN	COOEt	IIk	80	176-178
12	2-NO <sub>2</sub>	CN	COOEt	III	82	>280

<sup>a</sup>Reaction conditions: Aldehyde (0.01 mol)<sup>b</sup>, Active Methylene Compounds(a-e) (0.01 mol), Proline-Ferrite, under r.t.<sup>c</sup>Isolated yield.

### Spectral Data for the Synthesized Compounds:

1). **2,2'-{[2,6-dichloro-1-(4-methylphenyl)-1,4-dihydropyridine-3,5-diyl]dimethylidene}dipropanedinitrile**: M.P.=180-184°C. IR (KBr, cm<sup>-1</sup>)=2345, 2225, 1589, 1271, 684, <sup>1</sup>H NMR (DMSO-d<sub>6</sub> 400 MHz) δ:=8.56(s,2H), 7.96(2,H) 7.93(s,2H), 2.50(s,3H), 3.33(2,H), <sup>13</sup>C NMR (DMSO-d<sub>6</sub> 100 MHz): 159, 149, 154, 128, 124, 114, 78,113,111,110 , 56., LC-MS: 392.

2). **2,2'-{[2,6-dichloro-1-(4-chlorophenyl)-1,4-dihydropyridine-3,5-diyl] dimethylidene}dipropanedinitrile**: M.P.= 260-26°C. IR (KBr, cm-1) = 621, 2239, 1641, 1236. <sup>1</sup>H NMR (DMSO-d<sub>6</sub> 400 MHz) δ:= 2.15(s,2H), 7.06(s,1H), 6.8(d,2H), 6.6(d,2H), <sup>13</sup>C NMR(DMSO-d<sub>6</sub> 100 MHz) :167,121, 159, 132,129,118, 114 , 55. LC-MS: 414.

3). **2,2'-{[2,6-dichloro-1-(4-chlorophenyl)-1,4-dihydropyridine-3,5-diyl]dimethylidene} bis(2-cyanoprop-2-enoate)**. M.P.= 200-202°C. IR (KBr, cm-1) = 609, 1265, 1625, 2224. <sup>1</sup>H NMR (DMSO-d<sub>6</sub> 400 MHz) δ:=1.26(t,3H), 4.15(q,2H), 7.41(s,1H), 3.61(s, 2H), 6.24(d,1H), 6.33(s,1H), 6.67(d,1H), 6.86(dd,1H ), <sup>13</sup>C NMR(DMSO-d<sub>6</sub> 100 MHz) :139, 133, 131, 130, 124, 123, 120, 119, 119.0,40, 38, 34. LCMS: 506.

4). **2,2'-{[2,6-dichloro-1-(4-nitrophenyl)-1,4-dihydropyridine-3,5-diyl] dimethylidene}dipropanedinitrile**. M.P.=>280 °C. IR (KBr, cm-1): 3043, 2227, 1571, 1394, 1207, 1101, 609. <sup>1</sup>H NMR (DMSO-d<sub>6</sub> 400 MHz) δ:= 4.71(s,2H), 7.5(s, 1H), 7.1(d, 2H), 7.0(d,2H). LC MS: 421.

### APPLICATION

The present method was environmentally benign. L-proline-Fe<sub>3</sub>O<sub>4</sub> MNP displaces all other methods that use various organic solvents, catalysts and that are performed at higher temperature.

## CONCLUSION

In conclusion, we have demonstrated a very simple and highly efficient method for the Knoevenagel reaction of aromatic aldehydes with various active methylene containing compounds to give 2,2'-[[2,6-dichloro-1-(substitutedphenyl)-1,4-dihydropyridine-3,5-diyl]dimethylylidene]dipropanedinitrile product in good to excellent yields at room temperature. In the above research we suggest that the present method of environmentally benign L-proline-Fe<sub>3</sub>O<sub>4</sub> MNP displaces all other methods that use various organic solvents, catalysts and that are performed at higher temperature.

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