

## Simple and Solvent Free Knoevenagel Condensation by Using Gadolinium Oxide Catalyst

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**ABSTRACT:** A simple solvent free reaction between aromatic aldehydes and active methylene compounds in presence of gadolinium oxide as a catalyst at room temperature has been described. The reaction was carried by simple grinding method with good yield. The catalyst was recovered by filtration and can be reused. All the synthesized compounds were characterized by spectral and analytical methods by IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR.

**Keywords:** Aromatic aldehydes; active methylene compounds; gadolinium oxide; Knoevenagel condensation; solvent free.

**INTRODUCTION:** The Knoevenagel condensation is one of the important reaction in organic synthesis. In this reaction aromatic aldehydes were reacted with numerous active methylene groups like ethyl acetoacetate, malanonitrile, diethyl malonate etc. It shows number of applications in various areas like drugs, cosmetics, perfumes<sup>1,2</sup>, insecticides, herbicides, polymers<sup>3-5</sup>. It has shown significant biological activities like ECG receptor, antiproliferative effects on keratinocytes<sup>6</sup>. It is also useful in the synthesis of fine chemicals and various biologically active heterocyclic compounds.

This reaction was carried out by using various catalyst and systems like  $\text{ZnCl}_2$ <sup>7</sup>,  $\text{CuCl}_2$ ,  $\text{LaCl}_3$ <sup>8</sup>,  $\text{GaCl}_3$ <sup>9</sup>,  $\text{SeO}_2/\text{ZrO}_2$ <sup>10</sup> with various bases like piperidine, ethylenediamine<sup>11</sup>, zeolites, ionic liquids<sup>12-14</sup>, polymer supported heterogeneous catalysts<sup>15</sup>. Recently number of groups reported solvent free green reactions by using lemon juice etc.<sup>16</sup>. But many of these type of reactions shows significant problems in carryout, disposal, regenerative and toxic nature. The green chemistry and solvent free approach reduces or eliminates the use of toxic and hazardous chemicals. In past decade numerous inorganic materials like clays<sup>17</sup>, hydrotalcites<sup>18</sup>, solid bases<sup>19</sup>, modified silica<sup>20</sup> and zeolites<sup>21,22</sup> frequently showed environmentally benign properties in the chemical conversions. Therefore ecofriendly and economic reactions were widely accepted by chemical industries.

In the present work, we have developed simple and ecofriendly, solvent free method by using Gadolinium oxide ( $\text{Gd}_2\text{O}_3$ ) as catalyst for Knoevenagel condensation.

### MATERIALS AND METHODS:

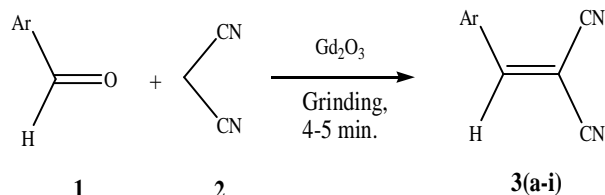
**Experimental section:** All the reagents for the reactions were purchased from Merck, SD-fine and Spectrochem chemicals. Melting points were recorded by using open capillary method and were corrected. All the synthesized compounds were characterized by IR,  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR recorded on advance Bruker II 400 NMR spectrometer using  $\text{DMSO}-d_6$  solvent while IR recorded on FTIR (Shimadzu) spectrometer.

### Synthetic procedures:

**Procedure for synthesis of gadolinium oxide ( $\text{Gd}_2\text{O}_3$ ):** Gadolinium oxide catalyst was prepared by using  $\text{Gd}(\text{NO}_3)_3$  (1mmol), ethyl cellulose (1mmol) and  $\text{NaOH}$  (1mmol) in 40 ml water at  $120^\circ\text{C}$  for 24 hours. The precursor obtained after completion of reaction was calcined at  $750^\circ\text{C}$  for 2 hours in hot air oven. The formed oxide was characterized by using IR, XRD and SEM methods.

**General Procedure for synthesis of 2-benzylidene malanonitrile:** Aromatic aldehydes (2mmol), malanonitrile (2.2 mmol) and gadolinium oxide (1 mol %) was grinded in stoneware mortar and pestle at room temperature. The progress of reaction monitored

by TLC using n-hexane and ethyl acetate (1:1). The reaction was completed within 4-5 minutes. Then ethyl acetate added to reaction mixture and catalyst was separated by filtration and reused. The reaction mixture extracted by using ethyl acetate. The extracted solvent layer was dried by using sodium sulphate and solvent was removed under pressure. Further product was purified by column chromatography by using n-hexane and ethyl acetate (7:3) as an eluent.



### 2-benzylidene malanitrile(3a):

IR (KBr,  $\nu_{\max}$ (cm<sup>-1</sup>): 2222, 1581, 1450, 1377, 1303, 1215, 960, 756, 679; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz,  $\delta$  ppm): 7.612 (d, 2H, Ar-H), 7.659 (d, 1H, Ar-H), 7.964 (d, 2H, Ar-H), 8.478 (s, 1H, =CH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 100 MHz,  $\delta$  ppm): 78.50, 78.95, 81.45, 112.84, 113.83, 129.26, 130.45, 131.13, 134.17, 161.31

### 2-(4-fluorobenzylidene) malanitrile(3b):

IR (KBr,  $\nu_{\max}$  (cm<sup>-1</sup>): 2226, 1585, 1496, 1373, 1304, 1234, 1157, 837, 617; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz,  $\delta$  ppm): 7.367 (d, 2H, Ar-H), 8.065 (d, 2H, Ar-H), 8.436 (s, 1H, =CH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 100 MHz,  $\delta$  ppm): 78.76, 112.72, 113.71, 116.64, 127.71, 133.43, 159.79, 163.98, 166.53

### 2-(2-chlorobenzylidene) malanitrile(3h):

IR (KBr,  $\nu_{\max}$  (cm<sup>-1</sup>): 2225, 1583, 1499, 1371, 1305, 1232, 1153, 835, 613; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 400 MHz,  $\delta$  ppm): 7.8757 (d, 2H, Ar-H), 7.9575 (d, 1H, Ar-H), 8.3243 (d, 1H, Ar-H), 8.9208 (s, 1H, =CH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 100 MHz,  $\delta$  ppm): 78.76, 112.72, 113.71, 116.64, 127.71, 133.43, 159.79, 163.98, 166.53

**RESULTS AND DISCUSSION:** Knoevenagel condensation is base catalyzed reaction of aromatic aldehydes and active methylene groups. Various methods were reported as shown in table-1. But these methods have some draw backs like long reaction time, harmful solvents, poor yield, recovery conditions etc. Therefore herein report a Knoevenagel condensation of different aromatic aldehydes with active methylene group compounds with a gadolinium oxide in a catalytic amount under solvent free conditions. Initially reaction of benzaldehyde (2mmol) was carried out with malanitrile (2mmol) in presence of 5 mol% of gadolinium oxide in mortar and pestle by simply grinding. The reaction was completed within 5

minutes. After optimizing reaction at various amount of catalyst under similar conditions, 1mol% was found better to accelerate the 95% reaction in 4-5minutes.

**Table 1: Comparison of Different catalyst used for synthesis of 2-benzylidene malanitrile.**

Entry	Catalyst	Condition	Solvent	Time	Yield (%)
1	ZnCl <sub>2</sub>	100°C	Free	20 min.	90
2	NbCl <sub>5</sub>	Reflux	Ethyl acetate	4 h	88
3	LaCl <sub>3</sub> .7H <sub>2</sub> O	80°C	Free	1hr	95
4	I <sub>2</sub> /K <sub>2</sub> CO <sub>3</sub>	RT	EtOH/DMF	12 min	90
5	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub>	Reflux	Water	15 min	91
6	NaF&LiCl	MW	Free	1 min.	96
7	GaCl <sub>3</sub>	Grinding	Free	2 min	98
8	Lemon juice	RT	Free	2hr.	91
9	Gd <sub>2</sub> O <sub>3</sub>	Grinding	Free	5 min	95

**Table 2: Knoevenagel condensation of aromatic aldehydes with malanitrile catalyzed by Gd<sub>2</sub>O<sub>3</sub> at room temperature.**

Entry	Compound No.	Ar	Yield	Melting point	
				Obtained	Reported
1	3a	C <sub>6</sub> H <sub>5</sub>	95	82-83	83-84
2	3b	4-F-C <sub>6</sub> H <sub>4</sub>	94	127-128	127
3	3c	4-Cl-C <sub>6</sub> H <sub>4</sub>	95	161-162	161-162
4	3d	2-Cl-C <sub>6</sub> H <sub>4</sub>	96	94-95	95-96
5	3e	4-MeO-C <sub>6</sub> H <sub>4</sub>	94	114-115	114-115
6	3f	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	95	159-160	160-161
7	3g	2-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	93	104-105	-
8	3h	2,4,6-(MeO) <sub>3</sub> -C <sub>6</sub> H <sub>2</sub>	94	138-140	-
9	3i	4-NMe <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	96	178-179	179-180
10	3j	Furfural	94	68-69	68-69

A wide range of substituted aromatic aldehydes were reacted with malanonitrile in presence of similar conditions to give different 2-benzylidene malanonitrile derivatives. There is no effect of various electron donating and withdrawing groups on activity of catalyst and yield of resultant products. All the resultant compounds (3a-j) were characterized by IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR methods and compared with literature reports.

**CONCLUSION:** We have synthesized various 2-benzylidene malanonitrile derivatives by using gadolinium oxide as a catalyst under solvent free conditions. The reaction is simple, workable with good product yield in less time and the catalyst can be reused several times.

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