

# Zinc Triflate: A Valuable Heterogeneous Catalyst for the Synthesis of Pyrano Pyran derivatives

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**Abstract :** An efficient one-pot multi component zinc triflate as heterogeneous catalyst for the synthesis of pyrano pyran derivatives is reported. The reaction involves reaction between diversely substituted aldehydes, malononitrile and 4-hydroxy 6-methyl 2-pyrone. The cheap starting material, easy separation, high catalytic efficiency, good yield of products and simple workup are promising features of the reaction under 1:1 aqueous alcoholic media.

**Key words:** heterogeneous catalyst, pyrano pyran and zinc triflate.

## I. INTRODUCTION

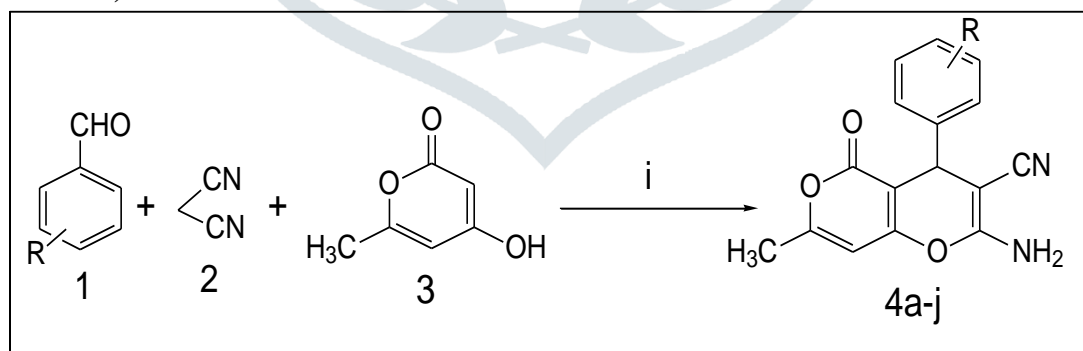
Wide range of pharmaceutical properties were exhibited by compounds containing 4*H*-Pyran skeleton. Those compounds are involved in various pharmacological activities such as antimicrobial<sup>1</sup>, antiviral<sup>2</sup>, mutagenicity<sup>3</sup>, anti-HIV<sup>4</sup>, anticancer<sup>5</sup>, antimicrobial<sup>6</sup>, antifungal<sup>7</sup>, antidiabetic<sup>8</sup>. Therefore Various methods have been reported for the synthesis of these compounds and their analogues such as Fe<sub>3-x</sub> Ti<sub>x</sub>O<sub>4</sub><sup>9</sup>, ZnO nanoparticles<sup>10</sup>, KF/Al<sub>2</sub>O<sub>3</sub><sup>11</sup>, PtCl<sub>4</sub><sup>12</sup>, thermolysis of enolizable vinyl quinones<sup>13</sup>, Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-IL-Fc<sup>14</sup>, Nanozeoliteclinoptilolite<sup>15</sup>, K<sub>2</sub>CO<sub>3</sub><sup>16</sup>, ultrasonic irradiation<sup>17</sup>, β-cyclodextrin<sup>18</sup> and ammonium acetate<sup>19,20</sup>.

Zinc trifluoro methane sulfonate (zinc triflate) known as metal organic, organo inorganic and metallo organic compound is one of the numerous organo metallic compound. Zinc trifluoromethane sulfonate is commercially available zinc salt of trifluoromethane sulfonic acid, which is commonly used as a Lewis acid catalyst as white solid. It is better catalyst amongst most of the lewis acid catalysts. For different chemical transformations zinc triflate is successfully applied<sup>21,22,23</sup>.

Herein, we report a simple and convenient method for the synthesis of 2-amino-3-cyano-4-aryl-7-methyl-5-oxo-4, 5-dihydro-pyrano [3, 2-*c*] pyran and 2-amino-3-cyano-4-aryl-6-methyl-4-hydro-pyrano [3, 2-*c*] quinoline derivatives by one pot three component condensation of aromatic aldehyde, malononitrile and 4-hydroxy 6-methyl 2-pyrone or 1-methyl 4-hydroxy 2-quinolone respectively catalyzed by zinc triflate.

## II. RESULT AND DISCUSSION:

A new reaction for the synthesis of 2-amino-3-cyano-4-aryl-7-methyl-5-oxo-4, 5-dihydro-pyrano [3, 2-*c*] pyran derivatives has been carried out by one pot three component reaction between aromatic aldehydes, malononitrile(2) and 4-hydroxy 6-methyl 2-pyrone using zinc triflate as catalyst in ethanol at 70-80°C is described (**Scheme 1**).



**Scheme1:** Reagent and conditions: (i) Zn(OTf)<sub>2</sub>, ethanol (5 MI), reflux for 28-57 min

For optimization of reaction, initially the reaction between 4-bromo benzaldehyde (1 mmol), malononitrile (1.2 mmol), 4-hydroxy 6-methyl 2-pyrone (1 mmol) is carried out in different solvents. It is found that high yield is obtained in ethanol using (**Table 1**).

**Table 1: Optimization of the reaction conditions**

Entry	Solvent	Catalyst (mol%)	Temperature (°C)	Time (min.)	Yield (%)
1	CH <sub>3</sub> CN	1	80-90	100	52
2	CH <sub>2</sub> Cl <sub>2</sub>	1	40	147	47
3	H <sub>2</sub> O	1	80-90	94	62
<b>4</b>	<b>EtOH</b>	<b>1</b>	<b>70-80</b>	<b>38</b>	<b>88</b>

Then, a series of reactions was carried out using diversely substituted aldehydes under optimized reaction conditions. All the used aldehydes undergo reaction with malononitrile and 4-hydroxy 6-methyl 2-pyrone to produce a library of 2-amino-3-cyano-4-aryl-7-methyl-5-oxo-4, 5-dihydro-pyrano [3, 2-c] pyran derivatives in good yield. (**Table 2**).

**Table 2: Synthesis of 2-amino-3-cyano-4-aryl-7-methyl-5-oxo-4, 5-dihydro-pyrano [3, 2-c] pyran derivatives.**

Entry	Aldehyde	Time (min.)	Product	Yield <sup>b</sup> (%)	MP (°C)
1	Benzaldehyde	20	4a	86	249-251 <sup>19</sup>
2	3-Bromo benzaldehyde	18	4b	88	258-260 <sup>19</sup>
3	Thiophene 2-carboxaldehyde	30	4c	84	242-243 <sup>20</sup>
4	4-Chloro benzaldehyde	21	4d	90	198-200 <sup>20</sup>
5	4-Cyano benzaldehyde	15	4e	88	230-232 <sup>19</sup>
6	2-Chloro benzaldehyde	17	4f	90	267-268 <sup>20</sup>
7	2-Fluorobenzaldehyde	20	4g	90	238-240 <sup>19</sup>
8	4-Bromo benzaldehyde	18	4h	88	214-215 <sup>19</sup>
9	3-Nitro benzaldehyde	15	4i	93	234-235 <sup>19</sup>
10	4-dimethylamino benzaldehyde	17	4j	90	217-219 <sup>19</sup>

<sup>a</sup>substituted aromatic aldehyde (1 mmol), malononitrile (1.2mmol), 4-hydroxy 6-methyl 2-pyrone (1 mmol) and C<sub>2</sub>F<sub>6</sub>O<sub>6</sub>S<sub>2</sub>Zn [Zn(OTf)<sub>2</sub>] (10 mol%), EtOH (5 ml), reflux. <sup>b</sup>isolated yield.

### III. EXPERIMENTAL

#### General details

Chemicals were Sigma Aldrich, Alpha Aiser and Spectrochem made and used as such without further purification. <sup>1</sup>H NMR spectra was recorded on a Bruker (400 MHz) spectrophotometer using DMSO-d<sub>6</sub> as deuterated solvent with tetramethyl silane (TMS) as the internal standard. Reactions were monitored by TLC using Merk silica gel plates. Products were characterized by <sup>1</sup>H NMR and Mass spectra.

#### General procedure for the synthesis of spiroxindole derivatives:

A mixture of isatin (1 mmol), malononitrile (1.2 mmol) and 4-hydroxy 6-methyl 2-pyrone or 1-methyl 4-hydroxy 2-quinolone (1 mmol) were refluxed with stirring in the presence of Zn(OTf)<sub>2</sub> (10 mol%) in solvent system in 1:1 aqueous ethanol on oil bath. The progress of reaction was monitored by TLC. After completion of reaction, the mixture was filtered. The residue was washed with warm ethanol to separate the Zn(OTf)<sub>2</sub> catalyst. After cooling the ethanolic reaction phase, the precipitate was filtered. The crude products were purified by recrystallization from 95% ethanol.

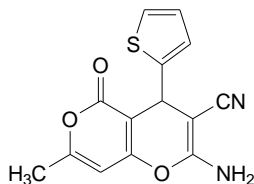
### III. CONCLUSION:

An efficient and simple method for the synthesis of 2-amino-3-cyano-4-aryl-7-methyl-5-oxo-4, 5-dihydro-pyrano [3, 2-c] pyran derivatives was developed via one pot three component reaction of aromatic aldehyde, malononitrile and 4-hydroxy 6-methyl 2-pyrone under reflux in ethanol using Zn(OTf)<sub>2</sub> as a heterogeneous catalyst. This procedure offers several advantages like higher yields, quick reactions, convenient and simple procedure and eco-friendly reaction conditions.

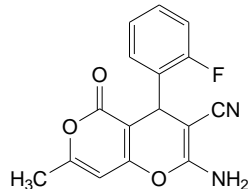
### IV. ACKNOWLEDGEMENTS:

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## Characterization Data:



**2-Amino-3-cyano-4-(thiophen-2-yl)-7-methyl-5-oxo-4, 5-dihydro 5-oxo pyrano [3, 2-c] pyran, entry 3, (3c):** Mp: 242–243°C;  $^1\text{H NMR}$ (400MHz,  $\text{DMSO-d}_6$ ):  $\delta\text{H}$  (ppm) 2.213 (s, 3H,  $\text{CH}_3$ ), 4.635 (s, 1H, CH, chiral), 6.263 (s, 1H, =CH), 6.913–6.930 (m, 2H, Ar-H), 7.1 (s, 2H,  $\text{NH}_2$ ), 7.351–7.369 (d, 1H, Ar-H); **HRMS** ( $\text{ES}^+$ ) for  $\text{C}_{14}\text{H}_{10}\text{N}_2\text{O}_3\text{S}$  ( $\text{M}+\text{H}$ ) $^+$  287.



**2-Amino-3-cyano-4-(2-fluoro phenyl)-7-methyl-5-oxo-4, 5-dihydro 5-oxo pyrano [3, 2-c] pyran, entry 7, (3g):** Mp: 238–240°C;  $^1\text{H NMR}$ (400MHz,  $\text{DMSO-d}_6$ ):  $\delta\text{H}$  (ppm) 2.226 (s, 3H,  $\text{CH}_3$ ), 4.536 (s, 1H, CH, chiral), 6.285 (s, 1H, =CH), 7.107–7.140 (m, 1H, Ar-H), 7.156–7.219 (m, 1H, ArH), 7.230 (s, 2H,  $\text{NH}_2$ ), 7.260–7.292 (m, 2H, Ar-H); **HRMS** ( $\text{ES}^+$ ) for  $\text{C}_{16}\text{H}_{11}\text{FN}_2\text{O}_3$  ( $\text{M}+\text{H}$ ) $^+$  299.

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