

## Three Component Reaction: An Efficient Synthesis and Reactionsof 3, 4-Dihydropyrimidin-2(1H)-Ones Using Baker's yeast in nonaqueous solvent under ultrasonication

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### Abstract

Baker yeast (BY) efficient catalyst for organic transformation. A well planned, budget Reducing, eco-friendly deals will created for the Synthesis of 3, 4-dihydropyrimidinone derivatives from aryl aldehydes, 1,3 diketone and urea in nonaqueous solvent under ultrasonication taking very cheaply, easily available biocatalyst, baker yeast. The bakers' yeast better results in organic solvent, ethanol with no any changes in catalytic power. Different derivatives of benzaldehyde used for this reaction. Synthesize product will be confirmed by using spectral analysis

**Keyword-** Baker's Yeast, 3, 4-dihydropyrimidin-2(1H)-one, 1, 3-dicarbonyl

### Introduction

Multicomponent responses (MCRs) are arising decreasingly as a synthetic plan to develop biologically active compound and natural products.<sup>1</sup> Multicomponent responses are important class in Principles of Green Chemistry and medicine discovery. Also, MCRs have the some merits including coincident creation, Clarity, facile prosecution and environmental freidnly.<sup>2-4</sup>

The Bigineli reaction is one pot reaction for synthesis of 3, 4 dihydropyrimidinones of from

1.3 diketone, urea and aryl aldehyde.<sup>5</sup> this multi component reaction for synthesis of 3,4, dihydropyrimidinones by using cheaper biocatalyst baker's yeast.

Dihydropyrimidinones (DHPMs) and their derivatives, products of the Biginelli reaction, are very important pharmacologically active molecules and they have found applications as calcium channel blockers,  $\alpha$ -adrenrgic antagonists, antihypertensive agents, inhibitors of fatty acid transporters, and in mitotic kinesin inhibition. Also, batzelladine alkaloids containing a dihydropyrimidine core have been found to show potent anti-HIV activity. The most simple and straightforward procedure for the synthesis of dihydropyrimidinones, originally reported by Bigineli in 1893, involves the acid-catalyzed one-pot condensation of  $\alpha$ ,  $\beta$ -keto ester with an aldehyde and urea derivatives. However, the product yields were very Low (20–50%).<sup>6-11</sup> The great biological importance of these heterocyclic compounds has prompted the development of new improved methodologies for the Biginelli reaction, including transition metal Lewis acid catalysis, solid phase synthesis, ionic liquids, activation with certain additives, microwave-assisted synthesis, ultrasound irradiation, solvent-free techniques, grinding techniques, and many new catalysts.<sup>12-17</sup>

Organic reactions under organic solvent by using biocatalyst we have unexperienced output of the increasing realization of chemical changes. Biocatalytic transformation are more typical reaction with many benefits such as expand selectivity, minimize energy utilization, overcome waste, harmfulness and budget value.<sup>18-20</sup>

Considering the above fact, we develop an efficiency methodology, for Synthesis of 3,4-

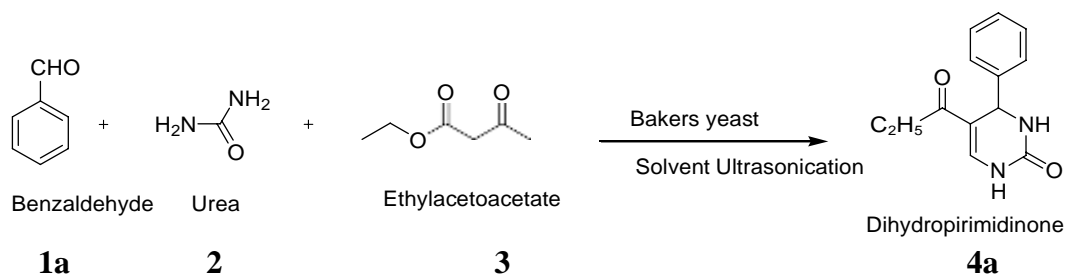
dihydropyrimidin-2(1*H*)-one derivatives from aldehydes, 1,3-dicarbonyl in nonaqueous solvent in normal condition by taking simple Baker's yeast

### Result and Discussion

We describe a systematic and eco- three component reaction using benzaldehyde, urea and ethylacetoacetate in organic solvent under mild condition by employing baker yeast as catalyst. In arrangement of experimental setup, we taking aryl aldehyde (1a) urea and ethylacetoacetate by using baker yeast as traditional standard reaction

We observed that the effect of solvent on yield and time of reaction, standard reaction was proceed in various solvent, Starting of solvent from natural solvent i.e. water (H<sub>2</sub>O), reaction stir with 20 hrs but reaction not proceed in this solvent because of insolubility of benzaldehyde then we taking organic solvent like ethanol (EtOH), Methanol, Acetonitrile, Dichloromethane, Dimethylformamide, Dimethylsulphoxide, Tetrahydrofuran (THF) (**Table-1 Entry 1-7**). Reaction proceed in all organic solvent but it was interesting observed that resulting product are high yield in ethanol, ethanol has better yield of product (**4a**) and minimum time to achieved goal of reaction (**Table 1 entry 2**). Therefore ethyl alcohol was selected for model reaction.

To analyse this reactions the derivatives of aryl aldehyde reacted urea and ethylacetoacetate by using baker's yeast in Ethyl alcohol to get final product in average yields (**Table 2, Entry 1-10**).



**Scheme -1**

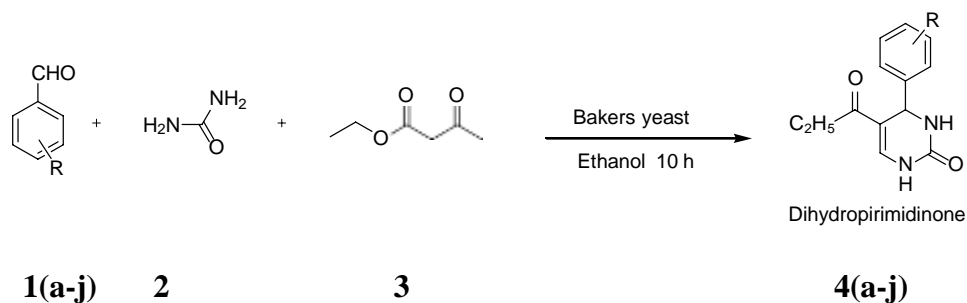
**Table 1** Screening of solvent on biginelli reaction

| SN | Solvent            | Time (h) | Yields <sup>b</sup> (%) |
|----|--------------------|----------|-------------------------|
| 1  | Methanol           | 05       | 80                      |
| 2  | Ethanol            | 05       | 85                      |
| 3  | Acetonitrile       | 07       | 70                      |
| 4  | Dichloromethane    | 07       | 65                      |
| 5  | Dimethylformamide  | 07       | 65                      |
| 6  | Dimethylsulphoxide | 08       | 65                      |
| 7  | Tetrahydrofuran    | 08       | 60                      |

<sup>a</sup>Reaction condition (benzaldehyde 5 mmol, Urea 5 mmol ethyl acetoacetate 5 mmol, 2 gm. baker's yeast and 20 ml solvent at room temperature

<sup>b</sup>isolated yield

When urea and ethylacetoacetate was added on aryl aldehyde with electron donating and withdrawing group in high percentage yield of the products (**Table 2, Entry 2-10**).



Scheme -2

Table 2 Synthesis of 3, 4-Dihydropyrimidinone in Ethyl alcohol

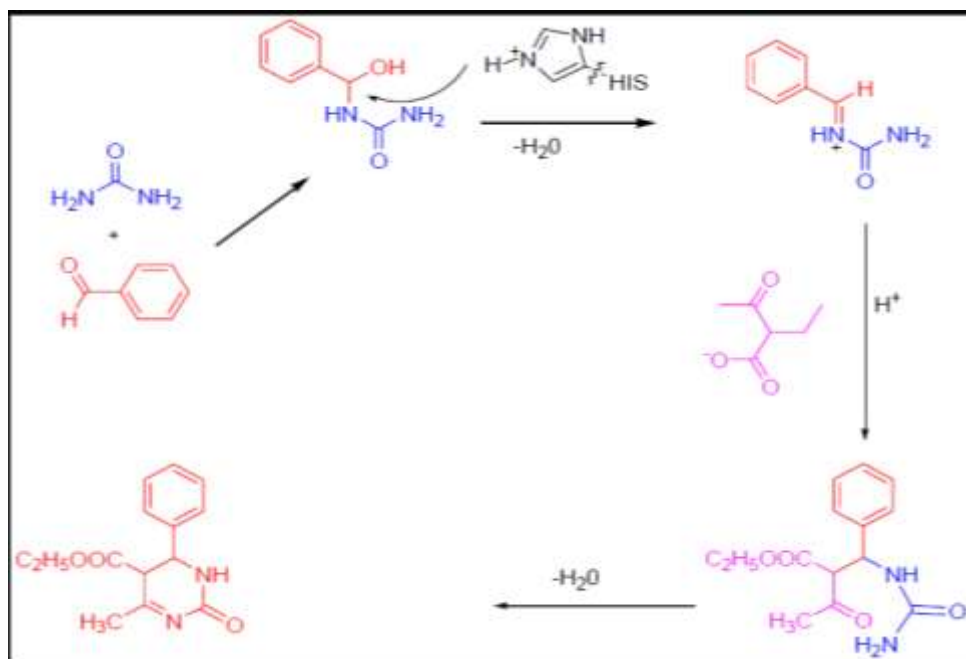
| Entry | R                                  | Product | Yields (%) | M.P. (°C)    |
|-------|------------------------------------|---------|------------|--------------|
| 1     | H                                  | 4a      | 85         | 210          |
| 2     | 4-Cl                               | 4b      | 80         | 225          |
| 3     | 3-Cl                               | 4c      | 80         | 210          |
| 4     | 4-NO <sub>2</sub>                  | 4d      | 75         | 215          |
| 5     | 3-NO <sub>2</sub>                  | 4e      | 78         | 230          |
| 6     | 4-OH                               | 4f      | 75         | 245          |
| 7     | 2-OH                               | 4g      | 65         | Not isolated |
| 8     | 2-Cl                               | 4h      | 70         | 200          |
| 9     | 4-N(CH <sub>3</sub> ) <sub>3</sub> | 4i      | 85         | 251          |
| 10    | 4-OMe                              | 4j      | 80         | 170          |

<sup>a</sup>Reaction condition benzaldehyde (0.5 g), Urea 5 (0.4 g ethyl acetoacetate (0.9 g), 2 gm. Baker yeast and 20 ml solvent at room temperature

<sup>b</sup>-Isolated yield

<sup>c</sup>Product were characterised by Melting point , <sup>1</sup>H NMR, <sup>13</sup>C NMR

Bakers' yeast is biocatalyst and it contains many enzymes. A base is required to catalyse this reaction and in every enzyme histidine is present which contains imidazole as a basic site. The histidine present might be acting as a base in this transformation. We are proposing herewith a plausible mechanism of this reaction.



## Conclusion

Final conclusion that for the first time baker's yeast is used to carry out the Biginelli reaction in ethyl alcohol. The overall synthetic process is green and high yielding. Thus, further studies on the preparation of heterocyclic compounds are being carried out.

## 4.1 General

Most of the chemicals we used are from Alfa Aesar and some are from Sigma-Aldrich. Baker's yeast was purchased from a native provider. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were characterized in a sophisticated analytical instrumentation facility (SAIF), University of Punjab at room temperature in CDCl<sub>3</sub> solvent.

### General experimental procedure for Knoevenagel condensation of malononitrile and aldehydes

A mixture of aryl aldehyde (0.5 g), urea (0.4 g) and ethyl acetoacetate (0.9 g) was stirred under ultrasonication in ethyl alcohol (20 ml). Once a homogeneous solution is created, baker's yeast (2 g) is added in a round-bottom flask. The reaction proceeds at 30 °C under ultrasonication. The reaction is monitored by TLC. After a few hours, the reaction mixture is filtered to remove the catalyst and the final product is purified by column chromatography.

### Spectral characterisation of synthesized compound

#### 3,4-dihydro-4-phenyl-5-propionylpyrimidin-2(1H)-one [4a]

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm): 7.14 (d, 1H), 7.21 (dd, 1H), 7.30 (dd, 1H), 7.93 (s, 1H)

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm): 69.3, 113.7, 126.41, 128.0, and 128.7, 135, 155

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