Knoevenagel condensation of 4-Oxo-4\textit{H}-benzopyran-3-carbaldehyde with 3-methyl -1-phenyl -1\textit{H}-pyrazole-5-(4\textit{H})-one. using L-proline as a catalyst in aqueous media.

The 21\textsuperscript{st} century is the modern year of the green chemistry. With the increasing environmental concerns and the regulatory constraints faced in the chemical and pharmaceutical industries, development of environmentally benign organic reactions has become a crucial and demanding research area in modern organic chemical research.\textsuperscript{1} Therefore more and more chemists synthetic endeavors are devoted toward ‘green synthesis’ which means the reagents, solvent and catalyst are environmentally friendly. Recently organic reactions in water without use of harmful organic solvents have attracted much attention, because water is an inexpensive, safe and environmentally benign solvent.\textsuperscript{2}

In 1980, Breslow discovered that the Diels–Alder reaction performed in water can be subject to huge rate accelerations.\textsuperscript{3} This observation led to increased interest from synthetic organic chemists in organic reactions in water. Soon it was discovered that other organic reactions, like the Claisen rearrangement,\textsuperscript{4} the Aldol condensation,\textsuperscript{5} and the benzoin condensation\textsuperscript{6} exhibit rate enhancements in water. Many more organic transformations have been carried out in water.\textsuperscript{7}

Knoevenagel reaction\textsuperscript{8} is one of the most important C-C bond forming reactions practiced by the Synthetic chemists. It is widely used in the synthesis of important intermediates or end products for perfumes\textsuperscript{9} pharmaceuticals\textsuperscript{10} and polymers.\textsuperscript{11} Bases, acids, or catalysts containing both acid-base sites\textsuperscript{12} catalyze the reactions. Several homogeneous and heterogeneous catalysts such as CuCl\textsubscript{2},\textsuperscript{13} SmI\textsubscript{3},\textsuperscript{14} Al\textsubscript{2}O\textsubscript{3},\textsuperscript{15} anionic resins\textsuperscript{16} clays\textsuperscript{17} and calcined hydrotalcites\textsuperscript{18} have been documented in the literature for Knoevenagel condensation. Recently we
have also studied the Knoevenagel condensation reactions under different conditions.\(^{19}\)

Proline is the only natural amino acid with a secondary amine functionality, which raises the \(pK_a\) value and better nucleophilicity as compared to other amino acids. It can be regarded as a bifunctional catalyst. Proline is not the only molecule to promote catalysis, but it still seems to be one of the best in the diversity of transformations. This catalyst used in various chemical transformations, such as aldolcondensation\(^{20}\) Mannich\(^{21}\) Reactions Dielsalder\(^{22}\) Michael Reactions.\(^{23}\)

In past reports, our group described the Knoevenagel condensation reactions under several different conditions.\(^{19}\)

**Present Work:**

Literature observer that the utilizing amino acids as a new reaction media and good result have been achieved. In continuation of our work to apply amino acid to organic reaction in the context of green and economical chemistry, herein, we would like to report a facile synthesis. Herein we report a highly efficient method for the L-Proline catalyzed Knoevenagel condensation of 4-oxo-(4H)-1-benzopyran-3-carbaldehydes 3-methyl phenylpyrazolin-5(4H)-one at room temperature stirring in excellent yield using water as a solvent.

The results were summarized in Table 1 indicating that the effect of the nature of the substituents on the 4-oxo-(4H)-1-benzopyran-3-carbaldehydes showed no obvious effect on this conversion, because they were obtained in excellent yields. In conclusion, we have designed a highly efficient procedure for the Knoevenagel condensation 4-oxo-(4H)-1-benzopyran-3-carbaldehyde and 3-methyl-1-phenylpyrazolin-5-(4H)-one in water using L-Proline catalyst. In addition, this method is less expensive and less toxic than reactions carried out in organic solvents. Moreover, the procedure offers several advantages including high yields,
operational simplicity, cleaner reactions, and ecofriendly, which make it a useful and attractive process for Knoevenagel condensation.

**Scheme:**

![Scheme Image]

**Experimental Section**

The progress of reactions was monitored by TLC [silica, light petroleum-EtOAc (6:4)]. Melting points were measured in open capillaries in a paraffin bath. IR spectra were recorded as Nujol mulls on FTIR instrument. 1H NMR spectra were recorded at 300 MHz with CDCl3 as solvent and TMS as an internal standard. Elemental analysis was consistent with the structures. Spectral data matched with the authentic samples.

**General experimental procedure**

4-oxo-(4H)-1-benzopyran-3-carbaldehyde (1 mmol) and 3-methyl-1-phenylpyrazolin-5(4H)-one (1 mmol) with L-Proline (0.1 g) in water (10 mL) was stirred at room temperature for time given in Table 1. The progress of the reaction was monitored on TLC. After completion of the reaction, the reaction mixture was filtered the resultant product was filtered, washed with water and recrystallized from ethyl alcohol, to afford pure product in excellent yield. The structures of the products were confirmed by IR, 1H NMR spectroscopy. Data of compounds are shown below:
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### Spectral data:

**IR Spectra**

IR Spectra of Entry 3 showed following characteristic absorption bands in its spectrum.

- 1790 cm⁻¹ due to C=O group of pyrazolinyl
- 1685 cm⁻¹ due to C=N group of pyrazolinyl
- 1654 cm⁻¹ due to C=O group of Chromone

**¹H NMR Spectra**

¹H NMR Spectra of Entry 3

- 1.8 δ singlet 3H
7.2-7.8 δ multiplet 9H due Olefenic & Aromatic proton
10.8 δ singlet 1H due to chromone moiety

**Mass Spectral data:** Entry(2)
m/z(ES-); 285 molecular ion peak 241 Base peak
m/z(ES-); 287 Base peak and molecular ion peak 259, 207
References


