

## Green Synthesis of Derivatives of Coumarin Using Potassium Dihydrogen Phosphate as an Effective Catalyst

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### Abstract

The Chemists all over the globe are motivated not only for the environmentally benign synthesis of new products but also to develop green synthesis for existing chemicals. This has been possible by the replacement of the organic solvents, which are hazardous by water or eliminate the use of solvent altogether. coumarin and its derivative are biologically active compounds and widely occur in nature. Some Coumarinderivates have been widely used as an important chemical in perfume, cosmetic as well as pharmaceutical industrial preparation. The Coumarin heterocyclic ring is a common feature of various bioactive compounds such as Calanolides, lipid lowering agents. Coumarins, the most important classes of fluorescent molecules constitute important structural features present in a number of bioactive natural products. Recent studies have been revealed that coumarin and the derivatives exhibit several other medicinal applications such as anti-coagulants, antifungal, insecticidal, hypnoticsphytoalexins, HIV protease & inhibitors. Coumarins act as in intermediate for the synthesis of various biologically active molecule such as coumarones, and fluorocoumarins . Thus the synthesis of coumarins is of continuing interest.

Potassium dihydrogen phosphate a commercially available environmentally benign catalyst non-toxic widely used for the synthesis of the substituted coumarine .The scope of this catalyst has not been fully explored, but can be used as buffer, neutralizing agent. Owing to the numerous advantages associated with cheap and non-hazardous catalyst, and also realizing g the importance of coumarin herein we would like to focus the eco – friendly method for his synthesis of derivatives of coumarin using cheaper and commercially available acid catalyst Potassium dihydrogen phosphate and also by the Knoevenagel condensation under microwave irradiation.

This paper focuses is to develop environment friendly reactions, simple, highly efficient and high yielding protocol for the synthesis of coumarin derivatives using Potassium dihydrogen phosphate as a catalyst.All the compounds are characterized by IR and NMR spectroscopy. Even though a number of modified methods have been reported, but many of them suffer from drawbacks such as unsatisfactory yields, longer reaction time, and corrosive reagents. Thus the development of an efficient and versatile method to synthesis of coumarin derivatives is an active on-going research and there is a scope further improvement towards milder reaction condition and yield. This methodology offers significant improvements for the synthesis of derivatives of coumarins with regard to yield of products, simplicity in operation and green aspects by avoiding toxic conventional catalysts and solvents. Therefore owing the importance of Potassium dihydrogen phosphate a facile catalyst used for the green synthesis of new derivatives of coumarin .

**KEYWORDS:** Potassium dihydrogenphosphate , microwave irradiation, anti-microbial activity.

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**Introduction:**The Chemists all over the globe are motivated not only for the environmentally benign synthesis of new products but also to develop green synthesis for existing chemicals. This has been possible by the replacement of the organic solvents, which are hazardous by water or eliminate the use of solvent altogether. Coumarin and its derivatives are biologically active compounds and widely occur in nature. Some Coumarin derivatives have been widely used as an important chemical in perfume, cosmetic as well as pharmaceutical industrial preparation. The Coumarin heterocyclic ring is a common feature of various bioactive compounds such as Calanolides, lipid lowering agents. Coumarins, the most important classes of fluorescent molecules constitute important structural features present in a number of bioactive natural products. Recent studies have been revealed that coumarin and the derivatives exhibit several other medicinal applications such as anti-coagulants, antifungal, insecticidal, hypnoticsphytoalexins, HIV protease & inhibitors. Coumarins act as in intermediate for the synthesis of various biologically active molecule such as coumarones, and fluorocoumarins . Thus the synthesis of coumarins is of continuing interest.

Coumarins are nowadays an important group of organic compounds that are used as additives to food and cosmetics [1], optical brightening agents [2], and dispersed fluorescent and laser dyes [3]. The derivatives of coumarin usually occur as secondary metabolites present in seeds, root, and leaves of many plant species. Their function is far from clear, though suggestions include waste products, plant growth regulators, fungistats and bacteriostats [4]. It is therefore of utmost importance that the synthesis of coumarin and its derivatives should be achieved by a simple and effective method. Coumarins can be synthesised by one of such methods as the Claisen rearrangement, Perkin reaction, Pechmann reaction as well as the Knoevenagel condensation [5]. It was recently shown that the Pechman reaction could be quickly achieved using microwave irradiation of the reagents in household microwave oven [6]. Since the solvent free phase-transfer catalytic reactions under microwave irradiation has prompted us to present our results of the synthesis of coumarins by the Knoevenagel condensation under such conditions.

Potassium dihydrogen phosphate a commercially available environmentally benign catalyst non-toxic widely used for the synthesis of the substituted coumarin .The scope of this catalyst has not been fully explored, but can be used as buffer, neutralizing agent. Owing to the numerous advantages associated with cheap and non-hazardous catalyst, and also realizing g the importance of coumarin herein we would like to focus the eco – friendly method for his synthesis of derivatives of coumarin using cheaper and commercially available acid catalyst Potassium dihydrogen phosphate and also by the Knoevenagel condensation under microwave irradiation.

This paper focuses is to develop environment friendly reactions, simple, highly efficient and high yielding protocol for the synthesis of coumarin derivatives using Potassium dihydrogen phosphate as a catalyst.

**Results and Discussion:**The aim of the present paper is to show that under the microwave irradiation the Knoevenagel condensation can be successfully applied to the

synthesis of a number of coumarins, and the scope of the method is much broader. Here we report a very simple, fast and general procedure where the condensation of Condensation of 5-methoxy 2-hydroxy benzaldehyde with derivative of ethyl acetate using Potassium dihydrogen phosphate catalyst.(Figure-1)

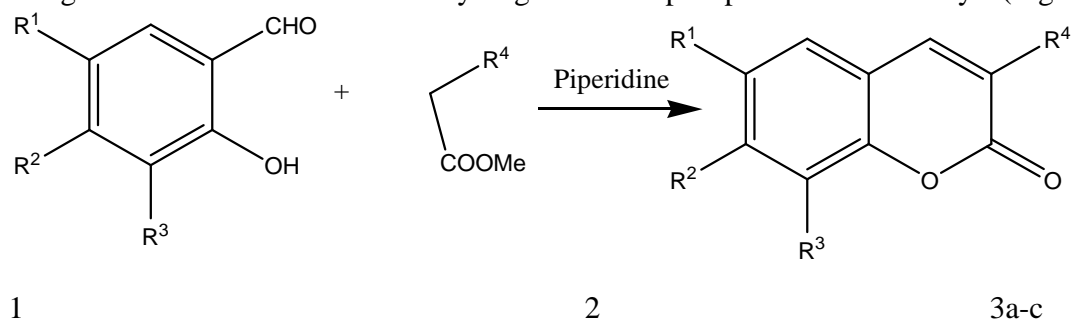


Figure 1: synthesis of derivative of coumarin using Piperidine & Potassium dihydrogen phosphate as catalyst.

Compound	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
3a	NO <sub>2</sub>	H	H	COMe
3b	NO <sub>2</sub>	H	H	COOMe
3c	NO <sub>2</sub>	H	H	CN

**Research methodology:-** A mixture of 2- hydroxyl salicylaldehyde(1) (1mmol), carbonyl compound (2) (1 mmol), and Potassium dihydrogen phosphate (20mol%) in ethanol(5ml) was stirred at room temperature for one hour .It is then neutralised with ammonium chloride solution extracted with ether. Ether layer was dried with sodium sulphate and evaporated to dryness to get the product.

**Table1**

Compound	colour	Melting point °C	Yield %	IR(KBr)	NMR: δ (ppm)
3a	dark brown	180	90	3082,3040,2923,1680,1552,1465,1260, 1100,1152,999.41,793,655 cm <sup>-1</sup>	2.5(s,3H),7.42(s,1H), 7.76(d,1H)7.78(d,1H) 8.34(s,1H)
3b	yellow	210	96	3345,3040,2880,1750,1556,1465,1680, 655 cm <sup>-1</sup>	1.45(t,3H)7.30(s,1H),7.68(d,1H) 7.7d,1H)8.42(s,1H)
3c	Light brown	192	88	3433,3062,2209,1735,1680,1566,1465, 817,743 cm <sup>-1</sup>	7.8(s,1H),7.67(d,1H)7.76(d,1H),8.47 (s,1H)

To study efficiency of two catalysts Potassium dihydrogenphosphate for Knoevenagel condensation, the reaction of nitro substituted, hydroxybenzaldehyde with diethylmalonate and series of ethyl acetate derivatives were selected as model. The results were summarised in Table-1. First experiments focused on carry out these reaction in piperidine in microwave under normal condition. In the second stage all the reaction were carried out in presence of potassium dihydrogenphosphate catalyst with conventional heating and in modified microwave and compared their yield with first part. Under modified microwave heating offers a convenient environmentally friendly alternative to conventional reactions. Clearly, the reaction time by microwave heating has been reduced with higher yield than conventional heating (86% versus 65 %).

Monitoring of the reactions and analysis can be accomplished by using standard methods (thin layer chromatography, column chromatography <sup>1</sup>HNMR, FT-IR spectroscopy.). Finally, the products are isolated by crystallization/column chromatography,

It is found that a 10 mol% amount catalyst Potassium dihydrogen phosphate could effectively catalyse the reaction. With inclusion of 5 mol % of catalysts the reaction took longer time. Using more amount catalysts (20 mol %) has less effect on the yield and time of the reaction (89 % versus 75 %).

In all the above mentioned methods, the reaction is not hundred percentage completed as shown by TLC. Therefore the product is purified by column chromatographic method to remove the impurity by using petroleum ether as eluent. After the impurity has been removed polarity of the eluent was increased, Petroleum ether – ethyl acetate solvent mixture is used to elute the desired product. Certain cases only crystallisation has given the purified compounds. All the derivatives of the Coumarin obtained were characterized by Infra-red spectroscopy (FTIR) and Nuclear Magnetic spectroscopy (NMR) and further screened for anti bacterial, anti-fungal and anti-inflammatory activities. IUPAC nomenclature of the synthesized compounds have mentioned earlier in the Table-2.

The formation of coumarins was evidenced by the absence of two peaks at  $2880\text{cm}^{-1}$  (Ar-CHO) and  $3550\text{cm}^{-1}$  (Ar-OH) but the appearance of two prominent peaks due to C-O-C at  $1275\text{-}1220\text{cm}^{-1}$  and lactone C=O at  $1720\text{-}1700\text{cm}^{-1}$ , rest all the substituents peaks are shown as per literature. The detailed data is as shown in the Table -3

The proton nuclear magnetic spectral analysis (<sup>1</sup>HNMR) of all the compounds showed signals corresponding to the multiplicity for different types of protons were consistent with assigned structure.

## CONCLUSION:

- ❖ Highly practical procedure has been developed, using green chemistry principles for the synthesis of coumarin derivatives.
- ❖ A practical method for an efficient synthesis of product (3a-c) using an inexpensive catalyst at ambient temperature has been described. High yields along with simple reaction condition auger well for the application of this strategy for the synthesis of derivative of coumarin.

- ❖ Mild reaction conditions, short reaction time, simple experimental work up cheapness of the reagents are the noteworthy advantages of this environment friendly protocol.
- ❖ This methodology offers significant improvements for the synthesis of derivatives of coumarins with regard to yield of products, simplicity in operation and green aspects by avoiding toxic conventional catalysts and solvents. Therefore owing the importance of Potassium dihydrogen phosphate a facile catalyst used for the green synthesis of new derivatives of coumarin .
- ❖ Thus the development of an efficient and versatile method to synthesis of coumarin derivatives is an active ongoing research and there is a scope further improvement towards milder reaction condition and yield.

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