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Eco-Friendly One Pot Synthesis of Coumarin Derivatives by Pechmann Condensation using Tamarind Juice as a Biocatalyst

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Abstract:- An efficient and eco-friendly synthetic method has been established for synthesis of 7-hydroxy-4-methyl coumarin and its derivatives using tamarind juice as a biocatalyst. The condensation reaction of Substituted phenol with ethyl acetoacetate (EAA) successfully carried out using tamarind juice as a green and efficient catalyst at 90°C in aqueous condition. This green biocatalyst has been utilised effectively for pechmann reaction with good yield of product, easy workup and eco-friendly reaction conditions.

Keywords:- *Pechmann Reaction, Tamarind Juice, Resorcinol, Ethyl Acetoacetate, Green Synthesis.*

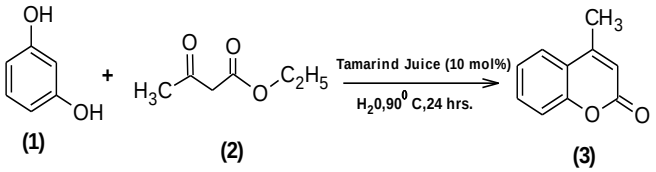
I. INTRODUCTION

In Recent years, scientists have been fascinated with biologically active and medicinal significant heterocyclic compounds [1]. This remarkable scope of heterocyclic compounds many researchers were engaged in synthesis of novel bioactive heterocyclic moieties as well as attempt to invent the alternative synthetic methodology for the various name reactions. Many organic and medicinal chemistry research groups have been focused their research in the field of heterocyclic chemistry and applications of heterocycles[2]. Among the various heterocyclic compounds, Coumarin and their derivatives have been proven itself as a biologically potent heterocycles with wide range of applications such as anti-inflammatory, anti-bacterial anti-cancer, and anti-HIV agent etc. [3-5]. Besides the biological applications and activities, coumarin derivatives utilised in manufacture of range of insecticides, pesticides, cosmetics, and dye lasers etc.[6-8].Thus, multiple applications of the coumarin ring enclosing compounds attributed keen attention of chemist and they produced it by using Knoevenagel, Reformatsky, Witting, Pechmann and Perkin reactions etc.[9-11] In the synthesis of coumarin, mostly Pechmann condensation widely used as it comprises the acid catalysed condensation of a substituted phenol with a β-ketoester. The wide range of acidic reagents, such as sulphuric acid, phosphoric acid, hydrochloric acid, trifluoroacetic acid were used for preparation of the same. Along with these common acidic agents, synthesis of coumarin derivatives were reported with use of ionic liquid as well as heterogeneous catalyst such as silica supported, zirconium supported, alumina supported catalysts [12-14].The reported catalytic synthetic strategies involved excessive catalyst loading which may cause environmental concerns.

In recent years, many researchers adopted green chemistry approach for the synthesis of various heterocyclic compounds which involves utilization of environmentally friendly biocatalyst [15]. Thus, with the deep interest in the area of green chemistry, we have reported synthesis of coumarin derivatives by Pechmann condensation between substituted phenol and ethyl acetoacetate using tamarind juice as a biocatalyst.

II. RESULT AND DISCUSSION

To explore green synthesis of Coumarin derivatives by Pechamann condensation reaction using environmentally friendly catalyst tamarind juice. Initially, tamarind juice was synthesised using reported literature procedure [16]. We decide to monitor model reaction between resorcinol (1) as a substituted phenol and ethyl acetoacetate (2) as a β-ketoester using biocatalyst tamarind juice (10 mol %) at 90° C for 24 hrs. as shown in scheme-1.



(1) (2) (3)

Scheme-1: Reaction of Resorcinol and ethyl acetoacetate using Tamarind juice.

We observed that, the green tamarind juice catalysed model pechmann condensation reaction gave product 7-hydroxy-4-methyl coumarin (3) with moderate yield 48%. The compound melting point was compare with reported value

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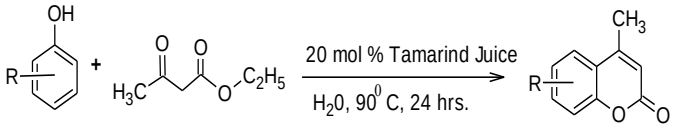
[17] and also confirmed with all possible spectroscopic techniques such as IR, NMR, mass which found to be same with reported literature. The yield and spectroscopic confirmations, demonstrate feasibility of tamarind juice as a biocatalyst for pechmann reaction. Based on this result, we were eager to screen biocatalyst tamarind juice for the optimization of reaction conditions with respect to catalyst loading (mol %) and it's substrate study.

Sr. No.	Catalyst	Mol %	Yield (%)
1	Tamarind Juice	0	No reaction
2	Tamarind Juice	5	20
3	Tamarind Juice	10	48
4	Tamarind Juice	15	62
5	Tamarind Juice	20	83
6	Tamarind Juice	25	81

Table-1: Optimisation study of mol % of tamarind juice Catalysted Pechmann reaction

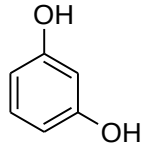
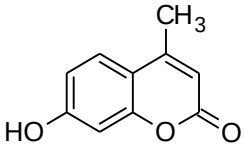
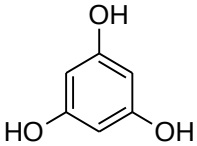
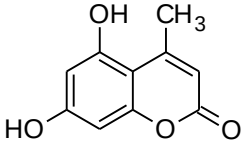
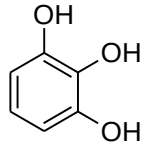
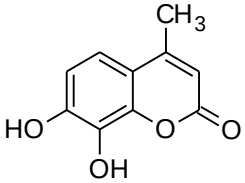
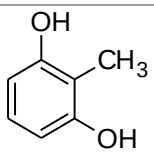
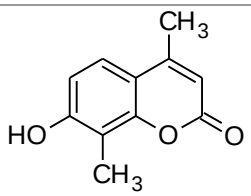
In optimal study of catalyst loading, we conduct reaction between resercinol and ethyl acetoacetate using tamarind juice biocatalyst with addition of 0 to 30 mol % at 90°C for 24 hrs. In that screening of biocatalyst, it has been seen that yield of product increases with increase in the amount of catalyst. When 5 mol% of biocatalyst was added then yield of product was 20% and for 10 mol% of catalyst addition, moderate yield of 48% was observed (Entry 2-3, Table-1).On increased mol% of biocatalyst to 15%, reaction yield also increased to 62% (Entry-4, Table-1). Whereas, for 20 mol% of catalyst loading, product enhanced to good yield of 83% (Entry-5, Table-1). Also for 25 mol% of catalyst added then yield of product slightly decreased to 81% (Entry-6, Table-1).Remarkably, in absence of catalyst, reaction does not took place on extension of reaction time (Entry-1, Table-1).Thus, on optimal study of catalyst loading, we confirmed that, 20 mol% of tamarind juice showed to be ideal catalyst loading percentage for pechmann reaction. With these success, we conclude the generality of reaction conditions as biocatalyst of 20 mol% at 90°C for 24 hrs. and conducted pechmann reaction of ethyl acetoacetate (2) with different substituents of phenol (4) containing different groups on ring shown in Scheme-2.



(4) (2) (5)

Scheme-2: Tamarind juice catalysed optimisation substrate study of coumarin derivatives.

In this optimal study of substate, it has been demonstrated that tamarind juice catalysed pechmann reaction with use of various substituted phenols produced respective substituted coumarin products with good yield in range of 79 to 85 % (Entry-1-6, Table-2).The synthesised products were purified and confirmed by their melting point which compare with literature values[13].

Sr. No.	Substrate	Product	Melting Point in °C		Yield (%)
			Observed	Reference[13]	
1			184-186	185	83
2			285-286	285	80
3			237-238	237	78
4			138-139	138	85

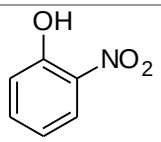
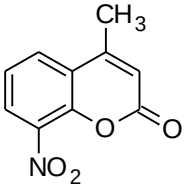
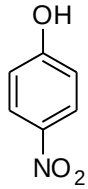
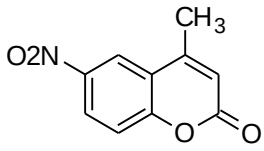
5			184-185	185	79
6			150-152	150	82

Table-2:- Optimasation study of Substrate for synthesis of coumarin derivatives using Tamarind Juice

III. EXPERIMENTAL

All reagents were purchased from SDFC Ltd. and Sigma-Aldrich and used as received. Melting points of compounds were determined using open head capillary as well as uncorrected. The progression of reaction monitored by using Thin Layer Chromatography (TLC) of silica gel of SDFC Ltd. ^{1}H NMR spectrum was recorded in $CDCl_3$ on Bruker AV-300 (300 MHz) using TMS as an internal standard. IR spectra were acquired using Perkin-Elmer Frontier model, USA.

➢ *General procedure for Preparation of Tamarind juice-*

From the local market the green tamarind fruits were purchased. Initially, upper shell of the tamarind fruit was removed Also removal of the inner grains from tamarind fruit carried out. After the removal of unnecessary material from tamarind, the green material of 100 gm. was boiled with 200 ml of water then it cooled the extract followed by centrifugation using micro centrifuge. On centrifugation resultant clear fragment of the aqueous material of the tamarind used as 'Tamarind Juice' which has *p*H=3.0. This freshly synthesied tamarind juice was utilised as bio-catalyst for a reaction.

➢ *Experimental Procedure for synthesis of 7-hydroxy-4-methyl coumarin-*

Take a 50 ml round bottom flask, add resorcinol (1 mmol) and ethyl acetoacetate (1 mmol) in 20 ml tamarind juice-water mixture (pH=3). The mixture was stirred in oil bath and heated at 90 °C for 24 hrs. The progress of reaction was monitored by thin layer chromatography (TLC). On completion of the reaction, reaction mixture was filtered. The filtrate was cooled poured in ice result into a solid (crude product) that it was filtered and then was recrystallized with ethanol to obtain pure product.

➢ *7-hydroxy-4-methylcoumarins derivatives:-*

Yield 83%, mp 184–186°C. 1H NMR (CDCl3) δ: 2.21 (s, 3H, Me), 6.10 (s, 1H), 6.83 (d, 1H, *J* 2.4 Hz), 6.98 (dd, 1H, *J* 8.7 and 2.4 Hz), 7.50 (d, 1H, *J* 8.7 Hz). IR (KBr, ν/cm-1): 2986, 1741 and 1625. ES/MS, m/z: 175.1 (M-H).

IV. CONCLUSION

Here, we report that we have established an efficient and environment friendly synthetic protocol for development of of 7-hydroxy-4-methyl coumarin and their derivatives through pechmann reaction between substituted phenol with ethyl aceto actetate using tamarind juice as a biocatalyst in aqueous condition. We have been successfully screened a biocatalyst tamarind juice for development of coumarin derivatives with moderate to good yield of products green condition. Thus, tamarind juice confirmed itself as green, eco-friendly, economical and efficient biocatalyst for the development of coumarin derivatives.

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