Indian Journal of
Advances in Chemical Science

Article

Lemon Juice Catalyzed Microwave-assisted Synthesis of Coumarin Derivatives: A Total Green Approach

Omprakash S. Chavan*

Department of Chemistry, Badrinarayan Barwale College, Jalna, Maharashtra, India

ABSTRACT

Solvent free synthesis of substituted Coumarins by Von Pechmann condensation of phenols with β-ketoesters catalyzed by lemon juice as an natural catalyst by microwave irradiation method. Our present protocol is economical and clean comprise of green reagent, solvent, and catalyst.

Key words: Pechmann condensation, Coumarins, Natural catalyst, Microwave irradiation, Green synthesis

1. INTRODUCTION

Coumarins [1] and theirs derivatives have involved considerable devotion of medicinal and organic chemist from several years, due to its great number of biological activities alike anthelmintic, anti-bacterial [2], anti-cancer [3], anti-coagulant, hypnotic, anti-inflammatory, optical brighteners [4], and anti-HIV activities [5].

The characteristic synthetic routes of Coumarin and its products include Pechmann and Duisberg [6], Knoevenagel [7], Perkin [8], Reformatsky [9], and Wittig [10] condensation responses. Among these, Pechmann condensation is unique of the most broadly used method designed for synthesis of Coumarins. Acid reagent has been used in the Pechmann reaction with use of simple starting ingredients, that is, phenol and β-ketoesters in the occurrence of variation of acidic agents, such as chlorosulfonic acid [11], sulfuric acid [12] melamine formaldehyde resin supported H+ ion catalyzed [13], ionic liquid catalyzed [14], oxalic acid catalyzed [15], alumina sulfuric acid [16] silica triflate catalyzed, dipyridine copper chloride catalyzed as heterogeneous catalyst [17], and zirconia supported catalyst.

Urgency of use of green reaction is very important as we defensing huge number of problems in era of soil, water, and air pollutions. In many transformations, there is use of large amount of hazardous reagents, solvents, and catalyst which create different biological changes or problems in ecosystems. To avoid these problems, we need to use such biodegradable, naturally occurring catalysts in the chemical transformation; hence, we use easily available fruit, that is, lemon fruit in the form of juice for this chemical reaction.

Lemon juice is chiefly consist of L-Ascorbic acid, which is very good and obviously occurring biocatalyst for diverse chemical transformation [18-21]. It has found precise vast applications in numerous reactions such as Aldol rearrangement reaction and condensation reaction, usually acts as strong Lewis acid catalyst and desiccating agent [22]. Bio-based raw materials are derived from living organisms such as different types of crops, wood, and algae have large applications in synthetic organic chemistry, they used as biocatalyst [23], bio-derived medium [24], organic waste as reagents [25], greener solvents [26], etc.

2. EXPERIMENTAL SECTION

2.1. General

The melting points of the compounds were resulted in open head capillary as well as are uncorrected. The infrared (IR) spectra of the derivatives were confirmed in the region of 4000–400 cm^{-1} by means of KBr pallet on Fourier-transform IR (FT-IR) Perkin spectrophotometer. ^1H nuclear magnetic resonance (NMR) spectra were noted on a DRX-300 Bruker FT-NMR spectrophotometer in $CDCl_3$/DMSO-d_6. The standards of chemical shift are communicated in δ ppm as a component. Totally, the compounds were checked for clarity by thin layer chromatography (TLC).

2.2. General Experimental Procedure for Preparation of Fresh Lemon Juice

First of all, take some (2–3) fresh lemon fruit, wash it with warm water to extract all juice from it, and cut it by clean and dry knife into small pieces for better extraction of juice, with the help of, by simple hand process, squeeze the complete lemon juice into a clean dry glass bowl, collected juice was filter off, then used for further process.

2.3. General Experimental Procedure for Synthesis of 7-hydroxy-4-methylcoumarins

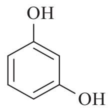
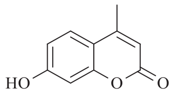
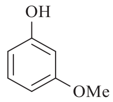
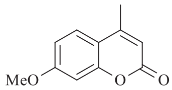
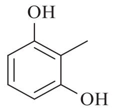
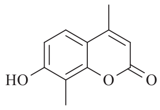
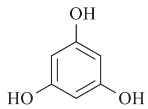
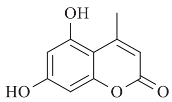
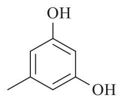
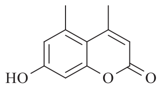
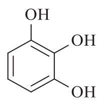
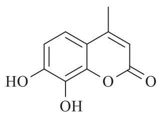
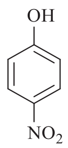
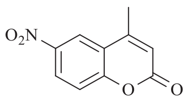
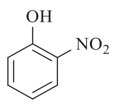
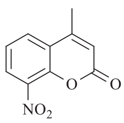
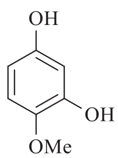
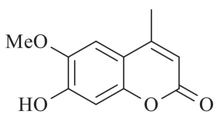
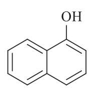
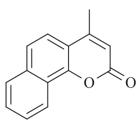
A combination of resorcinol (10 mmol), ethyl acetoacetate (10 mmol), and Lemon juice (20 mol%) remained and exposed to microwave irradiation (MWI) at 300W for suitable time (Table 1). Afterward completion of reaction, as display by TLC, the reaction combination was cooled to room temperature, water was added then

***Corresponding author:**
Omprakash S. Chavan,
Email: omprakashschavan@gmail.com

ISSN NO: 2320-0898 (p); 2320-0928 (e)
DOI: 10.22607/IJACS.2022.1002001

Received: 29th September 2021;
Revised: 18th February 2022;
Accepted: 20th March 2022

Table 1: Solvent free synthesis of Coumarins catalyzed by lemon juice microwave irradiation method (300W).

Substrate	Product	Time in Sec.	M. P. in °C		Yield[a] (%)
			Obs.	Ref [14]	
		60	184–86	185	98
		60	158–60	161	95
		60	138–39	138	90
		60	285–86	285	90
		60	257–58	258	92
		80	235–36	237	89
		110	147–49	150	72
		100	183–184	185	79
		90	164–165	165	91
		120	156–158	155	87

AQ6 **Figure 1:** Photography of Fruit and Lemon Juice of Citrus Limon.

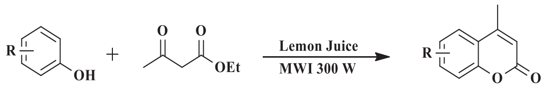
stirred for additional 2 min, in addition to precipitation, was clean off, and recrystallized from methanol to give pure 7-hydroxy-4-methylcoumarins as yellowish prism.

2.4. 7-hydroxy-4-methylcoumarins derivatives

Yield 98%, mp 185–186°C. ^{1}H NMR ($CDCl_3$) 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, 1625. ES/MS, m/z: 175.1 (M-H).

3. RESULTS AND DISCUSSION

In precipitate, it can be definite that the current practice for production of Coumarins by Pechmann condensation is extremely efficient as it



Scheme 1: Preparation of 7-hydroxy-4-methylcoumarins derivatives by Pechmann reaction.

Table 2: Optimization of reaction situation for production of Coumarins microwave irradiation method at low power (300W) using lemon juice as catalyst

Entry	Catalyst	Mol %	Yielda
1	Lemon Juice	0	--
2	Lemon Juice	5	Stress
3	Lemon Juice	10	40%
4	Lemon Juice	15	59%
5	Lemon Juice	20	98%
6	Lemon Juice	25	93%
7	Lemon Juice	30	88%

[a]Isolated Yield

avoids use of organic diluents at any step of reaction, in MWI method at very little power (300W) and existence of naturally occurring biodecomposable lemon juice as a biocatalyst.

A combination of substituted phenols and ethyl acetoacetate was exposed to MWI method for very low power (300W) in presence of lemon juice without solvent or free condition (Scheme 1). The development of reaction was tested by chromatography (TLC). Optimization of reaction condition was accomplished using variable amounts of lemon juice catalyst and best results of yields could be got using 20 mol % of lemon juice catalyst (Table 2).

4. CONCLUSION

Here, we report the Pechmann condensation reaction of phenols and β-ketoesters by lemon juice as a modest, effective, green, conservational, and biocatalyst under solvent free state (Scheme 1). We approved out a series of substituted phenols with ethyl acetoacetate to achieve corresponding Coumarin derivatives in very good to best yield (Table 1).

5. ACKNOWLEDGMENTS

The author is thankful to the Principal, Badrinarayan Barwale College, Jalna-431213 for constant encouragement and providing necessary facilities for this work.

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****Bibliographical Sketch***

Dr. Chavan Omprakash S. has completed M.Sc. Organic Chemistry from Dept. of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad, Maharashtra, India. He qualified SLET, CSIR-NET-LS, CSIR-NET-JRF and awarded Ph.D. degree from S. R. T. M. University, Nanded, Maharashtra, India. Now, Dr. Chavan O.S. is working as an Associate Prof., Dept. of Chemistry, Badrinarayan Barwale College, Jalna, Maharashtra, India.

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