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Der Chemica Sinica, 2014, 5(5):67-70



Comparative study of various synthetic methods of 7-hydroxy-4-methyl coumarins via Pechmann reaction

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ABSTRACT

Resorcinol condensed with Ethyl acetoacetate (EAA) via Pechmann condensation to form 7-hydroxy-4 -Methyl Coumarin in various reaction conditions. Present paper is comparative study of synthesis of 7-hydroxy-4 –Methyl Coumarinwith respect toyield, reaction time and reaction conditions. All products (3a- j) are characterized by spectral data and elemental analysis.

Keywords: Coumarin, Pechmann Condensation, Comparative study.

INTRODUCTION

Coumarins are naturally occurring compound and found in various plants in large quantities.Coumarins are biologically active compound used in various aspects like cosmetics, medicines and pharmaceutical industries[1]. Coumarin molecules are recently used in anti- tuberculosis and anti- AIDS[2]as active drugs. So it is interesting to study the molecule and its derivatives. It is well known that the Coumarin derivatives represent an important class of oxygen containing heterocyclic compounds. They are widely used as additives in foods, perfumes and in the preparation of optical Brighteners[3]as well as laser dyes[4].

Coumarins have been synthesized by several routes including Pechmann[5], Perkins[6], Knovengeals[7], Reformatskys[8], and Witting[9]reaction. Among the methods applied, Pechmann reaction is the most widely applied methods for synthesizing Coumarins. Pechmann involves the condensation of phenols with β - keto esters in the presence of variety of acids. Various acid types like Lewis[10], Protic[11], Solid acids[12], acid anhydrides[13], and in different ionic liquids[14], as well as solvent free condition[15].

In continuation of our interest, the current work represents the comparative study of synthesis of 7-hydroxy-4 - Methyl Coumarin by Pechmann condensation using different procedures and its influence with various aspects like yield, reaction time and conditions.

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MATERIALS AND METHODS

The melting points of the compounds were determined in open head capillary and are uncorrected. The IR spectra of the compounds were recorded in the region of 4000-400 cm⁻¹ by using KBr pallet on FT-IR Perkin spectrophotometer.H¹ NMR spectra were recorded on a DRX-300 Bruker FT-NMR spectrophotometer in CDCl₃. The values of chemical shift are expressed in δ ppm as a unit. All the compounds were checked for purity by thin layer chromatography (TLC). The sonicator was used with 100 wattspower of 230 V AC suppliers.

Synthesis of 7-hydroxy- 4-methyl Coumarin (3a) by conventional method [16]with Conc. Sulfuric acid as Catalyst:

A solution of 1.1 gm of resorcinol and 1.3 gm of EAA was added drop wise with stirring to 10 ml of conc. H_2SO_4 . So that the temperature of reaction mixture did not raise above the 10^oCthe reaction on complete addition mixture was kept at ambient temperature for 18 hr.and then poured with vigorous stirring to the mixture of ice and water. The precipitated was filter off and washed with cold water thendried under reduced pressure to afford the crude solid mass.On recrystallised from aqueous alcoholgivesfinal compound. (3a)

Synthesis of 7-hydroxy- 4-methyl Coumarin (3b) by Microwave Irradiation method [17]:

Equimolar amount of solution of Resorcinol and EAA was mixed well with the help of glass rod for fiveminutes with 1 ml of conc. H_2SO_4 and placed in an open conical flask in domestic microwave oven containing 2mg magnesium sulfate and irradiated for 5 min at 350 watts (TLC monitor) and pour to ice water mixture ,obtained precipitate filter off and recrystallized by using aqueous alcohol.

Synthesis of 7-hydroxy-4-Methyl Coumarin (3c) by Infra-Red lamp heating method[18]:

Equimolar amount of solution of Resorcinol and EAA was mixed with a glass rod for few minute containing 1 ml of Conc. H_2SO_4 and heated with medicinal Infra Red lamp (250watts) for 8-10 hours, the temperature of the reaction mixture did not exceed above 75 $^{\circ}C$. After completion of reaction (TLC)poured to ice- water mixture then filter it off and recrystallised from aqueous alcohol.

Synthesis of 7-hydroxy-4-Methyl Coumarin (3d) by Sonicator method[19]:

Equimolar amount of solution of Resorcinol and EAA was mixed in 50 ml of round bottom flask followed by addition of water (5ml). The mixture was irradiated in the water bath of an ultra sound cleaner (100 watts) for 30 min, after completion of reaction, monitor by TLC, the solid product was filtered, washed by cold water and dried under vacuum. The crude product was recrystallised in ethanol (20%) The yield of the product was listed in table 1.

Synthesis of 7-hydroxy-4-Methyl Coumarin (3e) by conventionalmethod [20]without any catalyst:

Equimolar amount of solution of Resorcinol and ethyl β - amino crotonate (Enamine derivatives of EAA) heated at 180 0 C without any catalyst, after completion of reaction, monitor by TLC, the reaction mixture was cooled and poured to cold water, obtained solid was washed with cold water and finally solid mass was recrystalised from aqueous alcohol to afford a pure product. The yield of the product was listed in table 1.

Synthesis of 7-hydroxy- 4-methyl Coumarin (3f) by conventional method [13] with solid state Catalyst:

To a mixture of resorcinol (1 mmol) and β -keto ester (EAA) (1.2mmol) in a RBF was added silica supported Boric trisulfuric acid anhydride as a solid catalyst (40 mol%) then the flask was immersed in an oil bath adjusted at 85^oC, equipped with a condenser and the mixture was stirred for suitable period of time, monitored by TLC. After completion of reaction, the oil bath was removed and the flask was allowed to attained room temperature. Afterwards CHCl₃ was added and the suspension was filtered to remove the catalyst. The obtained solution was then washed with water and evaporated. Finally, the residue was recrystallised from aq. Ethanol to obtain the pure compounds.

Synthesis of 7-hydroxy-4-Methyl Coumarin (3g) by ionic liquid Catalyzed method [21]:

A mixture of Resorcinol (1 mmol), β -keto Ester (EAA) (1 mmol) and ionic liquid [(4-sulfo-butyl) tris (4-sulfophenyl) phosphonium hydrogen sulphate] (10 mol %) as a catalyst were mixed without any solvent and stirred at room temperature for an appropriate time (20 min). After completion of reaction, indicated by TLC, 2 ml of water was added and the mixture was stirred for an additional 5 min. the precipitated product was filtered, washed with cold water, dried and crystallized from ethanol. The aqueous layer containing ionic liquid was recovered under reduced pressure, washed with acetone, dried and reused for subsequent reactions. The yield of the product was listed in table 1.

Synthesis of 7-hydroxy-4-Methyl Coumarin (3h) by solvent free (Neat Reaction) method [22]:

A mixture of Resorcinol (1 mmol), β - keto Ester (EAA) (1 mmol) and poly vinyl sulfuric acid (10 mol %) as a catalyst was stirred at room temperature under solvent free condition for period of 20min. Completion of reaction is compared by TLC. After completion of reaction, water (5ml) was added to reaction mixture and stirred for another 2 min, filtered and recrystallised from ethanol to afford desire product in good yield. The yield of the product was listed in table 1.

Synthesis of 7-hydroxy- 4-methyl Coumarin (3i) by using Phase transfer catalyzed method [23]:

A solution of Resorcinol (5mmole), EAA (5mmole) in benzene (20 ml) with saturated aqueous potassium carbonate solution (20 ml) and tetra n butyl ammonium hydrogen sulphate (1.2 mmol) were stirred magnetically at room temperature for 30 min. The completion of reaction is checked by TLC. The benzene layer separated washed with water, and benzene removed by distillation under reduced pressure. The residue thus obtained was crystallized from methanol,to give good yield of 7-hydroxy- 4-methyl Coumarin (3i)

Synthesis of 7-hydroxy- 4-Methyl Coumarin (3j) by simple grinding technical method [15]:

To an equimolar mixture of resorcinol and Ethyl aceto acetate was added TsOH in a mortar and ground it well with a pestle at room temperature. The Mixture was heated at 60 $^{\circ}$ C for 10 min., after cooling, water was added to the reaction mixture and obtained solid products were collected by filtration to give 7-hydroxy- 4-Methyl Coumarin in very good yield. The crude crystals thus obtained were recrystallized by ethanol to afford pure colorless prisms. The yield of the product was listed in table 1.

Sr. No.	Compounds	Time with temp.	Yield	Reaction Conditions
1	3a	Overnight at RT	85%	Conc. H ₂ SO ₄ , addition at 0 ⁰ C, Overnight at RT.
2	3b	5 min at 350 Watts	95%	MW Irradiation.
3	3c	8-10 Hrs. at 250 Watts	50%	IR lamp heating.
4	3d	30 min at 100 Watts	65%	Ultra sound Irradiation.
5	3e	20 min at 180 °C	85%	Without any solvent and Without any Catalyst (Neat Reaction).
6	3f	25 min at 85 °C	93%	BTSA $-SiO_2$ catalyst.
7	3g	20 min at RT	97%	Ionic Liquid catalyzed, without any solvent.
8	3h	20 min at RT	95%	PVS Acid Catalyzed, without any solvent.
9	3i	30 min at RT	80%	PTC catalyzed.
10	3j	10 min at 60 °C	98%	Simple grinding Technique at RT, then 60 °C for 10 min.

Table No. 1. Table showing Reaction condition, Time, Temperature and Yield of Compounds 3

CONCLUSION

In conclusion, here we reported comparative study of preparation of Coumarin by various methods. Among which this study prove that green synthetic method (3j) is most efficient via by simple grinding Technique obtain product within few minutes.

Acknowledgement

Authors are thankful to the Principal, Yeshwant Mahavidhyalaya, Nanded for constant encouragement and providing necessary facilities for this work and one of the author (Chavan O.S.) is thankful to UGC, New Delhi, for providing financial Assessment.

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