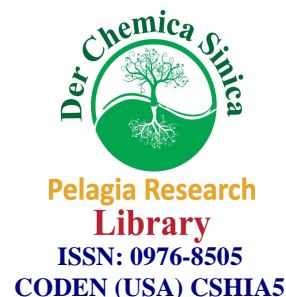




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A solvent free synthesis of coumarins via Pechmann condensation using PMA: Silica supported $\text{BF}_3\cdot\text{OEt}_2$ catalyst

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ABSTRACT

Synthesis of substituted Coumarins from phenol and β -ketoester (Ethyl Acetoacetate) via Pechmann condensation using heterogeneous catalyst Phosphomolybdic Acid (PMA):Silica supported $\text{BF}_3\cdot\text{OEt}_2$ under solvent free condition. This one required low reaction time, mild reaction condition, at room temperature and easy workup with excellent yield of the product.

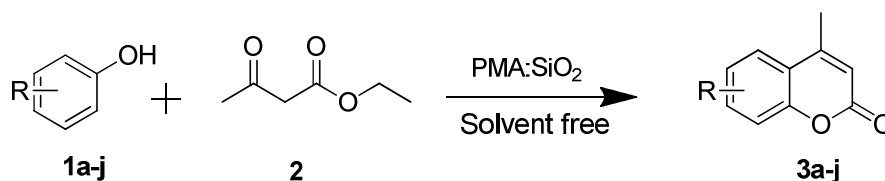
Keywords: PMA: Silica supported $\text{BF}_3\cdot\text{OEt}_2$ Catalyst, Coumarins, Pechmann condensation, Solvent free reaction.

INTRODUCTION

Coumarins and its derivatives plays an important role in medicinal chemistry, due to its vast sector of biological activities[1] like antibacterial[2], anti-cancer[3], anti-inflammatory[4], anti-pyretic, anti-biotic[5], anti-fungal [6], and also reported for exhibiting photochemical properties[7]. Coumarins can be synthesized by various methods such as Pechmann[8], Perkins[9], Knoevenagel[10], Reformatsky[11] and Wittig Reaction[12].

Pechmann condensation is one of the most common reactions for the synthesis of coumarins. This involves reaction of Phenols with β -ketoester in presences of various acid catalysts like H_2SO_4 , AlCl_3 , PPA, FeCl_3 , ZnCl_2 , POCl_3 , TFAA, P_2O_5 , etc. In recent years heterogeneous catalyst [13] are offering vast possibilities in the synthetic methods of various pharmacokinetic important molecules, due to easy workup [14], reducing reaction time, mild reaction condition, reusability of catalyst and specially enhancing product yield. In this study we prepared a heterogeneous catalyst which is useful by means of easy handling and after work done easy expelling from reaction.

Here in, we report as PMA: Silica supported $\text{BF}_3\cdot\text{OEt}_2$ catalyzed Pechmann condensation under solvent free condition at room temperature in very good yields (Scheme 1).

Scheme 1. Condensation reaction of Phenols and β -ketoester catalyzed by PMA:Silica supported $\text{BF}_3 \cdot \text{OEt}_2$

MATERIALS AND METHODS

General

All the compounds used in synthesis were of analytical grade, 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. ^1H NMR spectra were recorded on a DRX-300 Bruker FT-NMR spectrophotometer in CDCl_3 . Satisfactory elemental analysis was obtained on a Perkin Elmer CHN analyzer. 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).

Procedure for Preparation of Catalyst

An equimolar amount of PMA and silica was taken in a 100 ml of round bottom flask then $\text{BF}_3 \cdot \text{OEt}_2$ in excess amount were added, and stirred for 15 minutes at room temperature, PMA silica supported $\text{BF}_3 \cdot \text{OEt}_2$ catalyst was obtained as a free flowing powder after evaporation of $\text{BF}_3 \cdot \text{OEt}_2$ at room temperature this powder dried at 120°C for 2 hr. and stored in desiccator over CaCl_2 .

Table 1. Investigation of Effect of Catalyst on reaction of Resorcinol and Ethyl Acetoacetate^a

Entry	Catalyst	Relative mole %	Yield ^b in %
1	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	00%	00%
2	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	10%	23%
3	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	20%	56%
4	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	30%	89%
5	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	40%	89%
6	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	50%	90%
7	PMA-Silica- $\text{BF}_3 \cdot \text{OEt}_2$	60%	92%

^aReaction Condition: Resorcinol (1 mmol), EAA (1mmol), catalyst (Table 1) grind for 20 min. under solvent free condition.

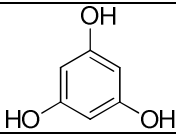
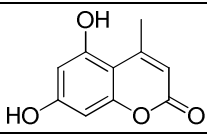
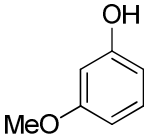
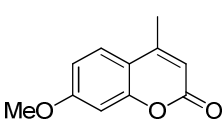
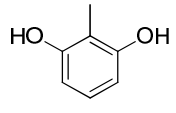
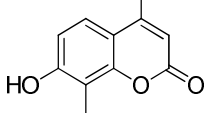
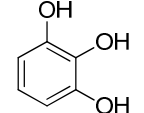
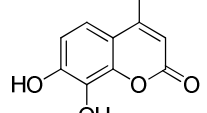
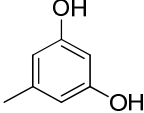
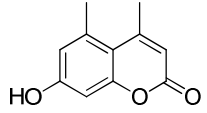
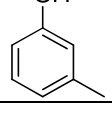
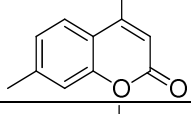
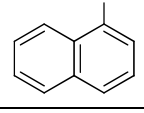
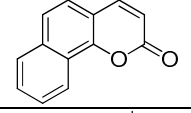
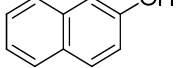
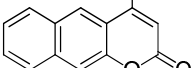
^bIsolated yield

General procedure for the synthesis of Coumarins

Substituted Phenols (1 mmol) and β - ketoester (EAA) (1 mmol), were taken with 20 mol % of PMA-Silica supported catalyst (30 mole %) grind for few minutes, in mortar and pestle at room temperature, after completion of reaction (monitored by TLC) ethyl acetate (10 ml \times 2) was added to reaction mixture and filtered to remove solid catalyst. Organic layer was wash with water (50 ml \times 2) and evaporated in reduced pressure to obtained solid products (**3a-3j**) finally recrystallized from suitable solvent.

Table 2. Synthesis of Coumarins via Pechmann condensation of phenols with Ethyl Acetoacetate catalyzed by PMA: Silica supported Catalyst

Comp.	Phenols	Coumarins	Yield	Melting point	Lit. M.P.
3a			61%	81-82°C	81°C[17]
3b			96%	183-184°C	185°C[15]

3c			82%	280-281°C	283°C[15]
3d			90%	154-155°C	156°C[16]
3e			86%	134-135°C	138°C[17]
3f			80%	240-241°C	244°C[15]
3g			79%	254-255°C	252°C[16]
3h			91%	129-130°C	132°C[15]
3i			69%	153-154°C	152°C[15]
3j			55%	172-173°C	182°C[17]

RESULTS AND DISCUSSION

In our previous study[18] ,[19],we have reported comparison of various synthesis methods of coumarin via Pechmann condensation. In this study, we focus on a heterogeneous catalyst which works efficiently at mild condition. Among various methods of synthesis of Coumarin, Pechmann is prefer due to its easy mode of operation and availability of starting materials, but very fewer study reported Synthesis of Coumarin at room temperature with supported heterogeneous catalysts. This study underlines the need and importance of search of various heterogeneous catalysts along with compatible support for useful organic transformation.

To optimized reaction condition, mixture of equimolar quantities of Resorcinol and Ethyl Acetoacetate was treated with PMA: Silica supported catalyst and grind for 20 min. to give the corresponding Coumarins (**3b**)in 96% yield, (m.p. 183-184°C; Table 2, Entry 2). By encouraging the above result, other phenolic substrate was subject to Pechmann condensation by using PMA: Silica supported catalyst and found fruitful by means of reaction time and yield (55-96%).During the course of reaction, continuous grinding is found to be necessary process for getting maximum product. After 20 min. phenolic substrate were disappeared from TLC, immediate work up reduced yield of reaction but, keeping reaction mixture left stand at room temperature for 2 hours obtained expected yield of product (Table 2).

3b: yellowish prism (yield 96%, mp 183-184 °C). ¹H NMR (CDCl₃) δ: 2.2 (s, 3H, Me), 6.1 (s, 1H), 6.83 (d, 1H, *J* 2.4 Hz), 6.97 (dd, 1H, *J* 8.7 and 2.4 Hz), 7.5 (d, 1H, *J* 8.7 Hz). IR (KBr, *v*/cm⁻¹): 2985, 1740, 1625. ES/MS, *m/z*: 175 (M-H).

CONCLUSION

In conclusion, we have achieved PMA:Silica supported BF₃:OEt₂as heterogeneous catalyst for the synthesis of Coumarin via Pechmann condensation reaction. Easy preparation, stability, simple and safe mode of handling of catalyst is the few important advantages.

Acknowledgement

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