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RESEARCH ARTICLE

An Efficient Solvent Free Synthesis of Coumarins via Solid Phase Pechmann Reaction

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Abstract: An efficient solvent free synthesis of coumarins has been developed via sold phase Pechmann condensation reaction by making use of grindstone chemistry at room temperature. When different substituted phenols were ground with ethylacetoacetate in presence of P_2O_5 at room temperature in china pestle mortar under solvent free conditions, coumarins were obtained in good yield in a very small period of time.

Keywords: Coumarin, Ethylacetoacetate, P_2O_5, Grinding, Phenols

Introduction

Coumarins constitute an important class of oxygen containing heterocyclic compounds of natural origin[1]. Natural coumarins and their synthetic derivatives possess potent and diverse biological activities[2]. These are also used as food additives, in cosmetics, as optical brightening agents[3]. Coumarins also act as intermediates for the synthesis of other biologically active compounds such as furocoumarins, chromenes, coumarones and 2-acylresorcinols[4].

Synthesis of coumarins can be affected from different routes such as Pechmann[5], Perkin[6], Knoevengel[7] and Reformatsky[8] reaction. Among these Pechmann reaction is widely used because of simple starting materials. This reaction involves condensation of phenols with β-ketoesters. Various condensing reagents such as strong acids like H_2SO_4, HCl, H_3PO_4, F_3CCOOH, super acids[9-10], lewis acids[11-12] such as $ZnCl_2$, $FeCl_3$, $AlCl_3$, $BF_3.2H_2O$ have been used for affecting this condensation reaction. Use of ion exchange resin, ionic liquid and microwaves[13-14] have also been reported for this reaction. Many of these routes have shortcoming of using hazardous condition in terms of use of chemicals or in terms of heating at elevated temperature.

Traditional way of carrying out organic reaction require the use of organic solvents but owing to their volatile and toxic nature now a day's efforts are being made by the scientific community to make reaction solvent free[12,15]. Here in we are reporting a low energy solvent free efficient synthesis of coumarin via pechmann route using grindstone chemistry (Figure 1).

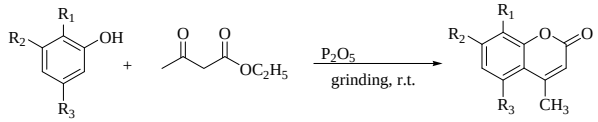


Figure 1. Synthesis of coumarin

Experimental

All the reactions were carried out in pestle mortar made up of porcelain. In all the reaction substituted phenol and ethylacetoacetate were first ground for one minute to homogenise the reaction mixture and then after adding anhydrous P_2O_5it was again ground for another five minute and then left at room temperature for the period till completion of reaction. Melting points were determined in open capillary tubes and are incorrect. Final product were analysed by melting point, comparison with authentic sample, IR (C=O) and ^{1}H NMR spectral data.

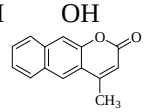
General procedure for the synthesis of coumarin

A mixture of substituted phenol (1 mmol) and ethylacetoacetate (1 mmol) was ground at room temperature for one minute by pestle in a mortar to homogenise it. To the reaction mixture was added anhydrous P_2O_5 (2 mmol) and again ground for another five minute when it turned yellow. It was then left at room temperature for 10-40 minutes till the completion of reaction. The progress of the reaction was checked by TLC. After completion of reaction ice cold water (20 mL) was added to the reaction mixture. Solid product that separated out was filtered at vacuum, washed with water and recrystallised from ethanol to give pure coumarin in good yield.

Results and Discussion

In a view to obtain coumarin via Pechmann route under solvent free condition a mixture of resorcinol, ethylacetoacetae was taken in the mortar and homogenised by grinding with pestle for one minute. To this reaction mixture was added solid anhydrous P_2O_5 and the reaction was again ground for 5 minutes when the reaction mixture turned yellow. The reaction was monitored over TLC when product was found to be formed which produced fluorescent spot over TLC in UV lamp but reaction was incomplete. It was then left at room temperature for ten minutes and again monitored over TLC when reaction was found to be completed. The reaction mixture was work up and product obtained was analysed by spectral data (IR, NMR) and melting point when it was found to be 7-hydroxy-4-methylcoumarin. To optimise the reaction condition different amount of anhydrous $P_2O_5$was used and the yield was maximum with the two equivalents of anhydrous P_2O_5. The validity of the above reaction was further confirmed by reacting differently substituted phenols with ethylacetoacetate to give coumarins in good yield under solvent free condition (Table 1). In conclusion it can be stated that this is an efficient and low energy path for Pechmann reaction where reaction under solvent free conditions producedcoumarin in good yield.

Table 1. Solvent free synthesis of coumarin by Pechmann reaction

Entry	R_1	R_2	R_3	Time of grinding	%Yield	M.Pt.	M.Pt. [Lit.]
1	H	OH	H	5+10	89	185-86	184-86[12]
2	H	OCH_3	H	5+10	90	156-58	156-58[12]
3	H	CH_3	H	5+20	85	130-32	131-32[12]
4	H	OH	OH	5+10	86	283-85	283-285[12]
5	OH	OH	H	5+30	80	240-42	240[15]
6				5+40	82	180-81	183-84[15]

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