Silicagel Supported $NaHSO_4$ Catalyzed Organic Reaction: An Efficient Synthesis of Coumarins

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Abstract: Silica gel supported $NaHSO_4$ is used as an efficient catalyst in the Pechmann condensation of phenols with ethyl acetoacetate, leading to the formation of coumarin derivatives. The reaction proceeded in acetonitrile at reflux temperature with good to excellent yields.
Keywords: Coumarins, ethyl acetoacetate, Pechmann reaction, phenols

1. Introduction

Coumarin and its derivatives occur widely in nature, particularly in plants; most of them show wide biological activities like anthelmintic, hypnotic, insecticidal, and anticoagulant properties [1] or fluorescent materials in optical devices, that is, in organic light-emitting diodes [2] and molecular photonic devices [3]. Therefore, the synthesis of coumarins and their derivatives has attracted considerable attention from chemists. Among numerous methods, the Pechmann reaction is an important approach. 4-Substituted coumarins can be synthesized simply by the condensation of substituted phenols with β-ketoesters in an acidic medium [4]. Traditional Pechmann reaction was catalyzed by acidic reagents such as H_2SO_4, HCl, CF_3COOH, and so forth [5]. It might also be catalyzed by some solid acids [6]. In these methods, long reaction times or high reaction temperatures, (above 150°C), were needed, which depended on their reactivity. In some cases, undesired side products such as chromones were also generated in addition to coumarins. Moreover, the disposal of excess acid waste might lead to environmental pollution. In recent years, Lewis acids such as $InCl_3$, $AlCl_3$-nBPC, $Yb(OTf)_3$, $ZrCl_4$, GaI_3 and $Sm(NO_3)_3$ as well as acidic ionic liquid were employed to catalyze Pechmann reactions[7]. However, some of these Lewis acids are moisture sensitive and require special care in handling and storage, and some of these methods still need a high reaction temperature or a long reaction time. Furthermore, metal triflates are highly expensive.

Recently, P. Salehi and et al have reported the preparation and application of metallic hydrogensulfates, as the source of both protic and metallic Lewis acids, in synthetic methodology [8]. They are very cheap and stable acidic reagents with, that could be used as catalyst in many important organic

reactions under heterogeneous conditions.

In the course of our recent work on heterogeneous solid acid–catalyzed organic reactions [9], Herein, we report the use of silica gel supported $NaHSO_4$ as a heterogeneous catalyst in a convenient synthesis of coumarins by the Pechmann reaction.

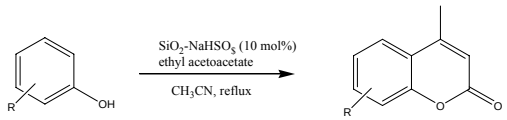
2. Experimental Section

2.1 Reagent and analysis

Sodium hydrogen sulfate were obtained from S. D. Fine Chemicals Ltd. India. Silica gel was procured from Merck grade (60, 230-400 mesh). Melting points were measured on a Micro Scientific Works apparatus and are uncorrected. IR spectra were recorded on a JASCO IR spectrophotometer. ^1H NMR spectra were recorded on Bruker 400 MHz NMR spectrometer. Reactions were monitored by thin layer chromatography on 0.2 mm silica gel F-254 plates. All the products are known compounds and are characterized by comparing their IR, ^1H NMR and melting points with those reported in literature.

2.2 Preparation of the catalyst

The catalyst was prepared by mixing silica gel (1.5 g, Merck grade 60, 230-400 mesh) with a solution of $NaHSO_4.H_2O$ (0.7 g, 5 mmol) in distilled water (10 ml). The resulting mixture was stirred for 30 minutes to absorbe $NaHSO_4$ on surface of silica gel. After removal of water in a rotary evaporator, the solid powder was dried at 120 ^oC for 2-3 h under reduced pressure. The drying temperature was maintained below the decomposition temperatures of the salts.



Scheme 1

2.2 Synthesis of 7-hydroxy-4-methyl-2H-chromen-2-one

A mixture of resorcinol (1.0 mmol), ethyl acetoacetate (1.0 mmol) in acetonitrile (10 ml) was heated under reflux condition in the presence of catalyst (10 mol%) for 1 h. the completion of the reaction was monitered by TLC. The reaction mixture was then poured on to crushed ice and the solid product was filtered and recrystallized from hot ethanol. Melting point – 185 – 187^oC [Lit [7b] m. p. 182 – 184 ^oC].

The spectral data of selected compound are below :

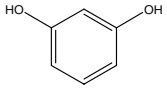
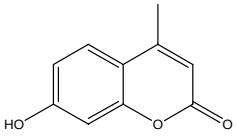
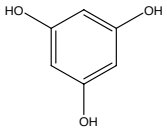
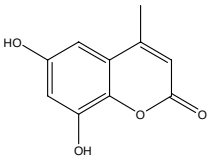
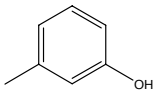
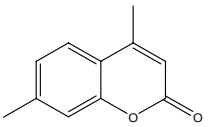
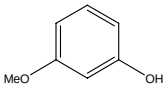
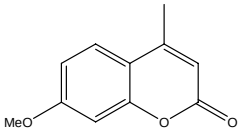
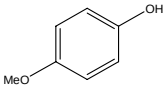
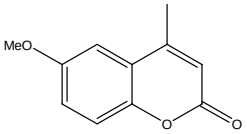
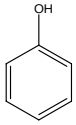
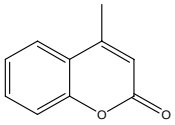
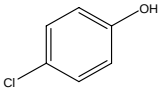
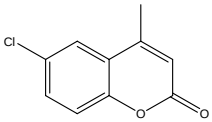
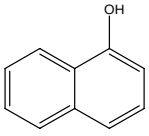
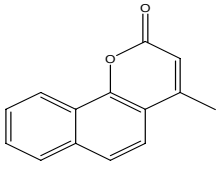
7-hydroxy-4-methyl-2H-chromen-2-one

2a[7b]: mp: 184–185^oC (lit.[7b] 182–184^oC); 1H NMR (300MHz, $CDCl_3$): d 7.51 (d, J ¼ 8.7 Hz, 1H), 6.93 (s, 1H), 6.85 (d, J ¼ 8.7 Hz, 1H), 6.17 (s, 1H), 2.43 (s, 3H); IR (KBr): 3445, 3034, 1686, 1587, 1260, 1075 cm^{-1}.

3. Result and Discussion

To optimize the reaction conditions the condensation of resorcinol with ethyl acetoacetate heated under reflux condition in the presence of silicagel supported $NaHSO_4$ to afforded 7-hydroxy-4methylcoumarin in 1 hour, similarly several phenols underwent the condensation reactions to give 4-substituted Coumarins (Scheme 1) in excellent yields (Table 1). It showed that SiO_2-$NaHSO_4$ exhibited a powerful catalytic activity in an amount as low as 10 mol%, which was enough to complete the reaction at room

Table 1 SiO_2-$NaHSO_4$-Catalyzed Synthesis of Coumarins via Pechmann Condensation of Phenols with Ethyl Acetocaetate

Entry	Substrate	Time (h)	Product	Yield (%)[a]	Melting point ^oC[b]
1		1		95	184-185 [7b]
2		1		92	282-284 [7b]
3		1.2		90	221-223 [7e]
4		1.2		94	162-164 [7e]
5		1.3		88	240-242 [5d]
6		5		92	78-80 [7e]
7		12		10	232-234
8		2		94	152-154 [5d]

[a]Isolated yields, [b]The literature references are given for known products.

temperature within a few hours for most of the substrates we used, and a larger amount of catalyst could not enhance the rates or increase the yields evidently. Acetonitrile was found to be the effective solvent for this conversion. The method was adaptive to the substrates with electron-donating groups, and the reaction gave good to excellent yields. in a short time. To the substrates with electron-withdrawing groups such as p-chlorophenol, the reaction was very sluggish and only a trace product was generated after it reacted for 12 h.

4. Conclusion

In summary, we have developed a new and efficient procedure for a Pechmann reaction catalyzed by silica gel supported $NaHSO_4$. The method offers several advantages such as mild reaction conditions, short reaction times, high yields, and a simple experimental operation, leading to a useful and attractive process for the preparation of coumarins.

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