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PEG-SO_3H: A mild and efficient recyclable catalyst for the synthesis of coumarin derivatives

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ABSTRACT

A simple and efficient synthesis of coumarin derivatives through condensation reaction of substituted phenols and dicarbonyl compounds using PEG-SO_3H as a recyclable catalyst under solvent-free conditions is described.

1. Introduction

The synthesis of coumarin and their derivatives has attracted considerable attention of organic and medicinal chemists, because a large number of natural products contain this heterocyclic nucleus; most of them show wide biological activities like anthelmintic, hypnotic, insecticidal and anticoagulant properties [1]. They are widely used as additives in food, cosmetics, agrochemicals, optical brightening agents, dispersed fluorescent, tunable dye lasers [2]. These compounds also act as intermediates for the synthesis of fluoro coumarins, chromenes, coumarones, 2-acyl resorcinols and others [3]. Many routes have been reported for the synthesis of coumarin derivatives including Perkin [4], Pechmann [5], Knoevenagel [6], Reformatsky [7] and Wittig [8] reactions. The Pechmann reaction involves the condensation of phenols with β-keto esters in the presence of variety of acidic condensing agents such as sulfuric acid, hydrochloric acid, trifluroacetic acid, phosphoric acids, phosphorous pentoxide and Lewis acids such as $ZnCl_2$, $FeCl_3$, $AlCl_3$ [9], ion exchange resins [10], solid acid catalysts [11], cellulose sulfuric acid [12], periodic mesoporous silica chloride (PMSCl) [13], benzylsulfonic acid functionalized mesoporous Zr-TMS [14], dipyridine copper chloride[15], indium chloride [16] have also been used. Recently, there have been also various reports on the use of microwaves [17], However, most of the reported methods suffer from one or more of the disadvantages such as long reaction time, vigorous reaction conditions, the occurrence of side reactions and unavailability of the reagents, as well as poor yields of the desired product. Thus, there is still a demand to develop new and mild methods for the synthesis of coumarin derivatives in the presence of inexpensive and bench top reagents. Hence, it is imperative to develop a convenient, efficient and user-friendly method for the synthesis of coumarins.

Development of novel synthetic methodologies to facilitate the preparation of a desired molecule is an intense area of research. Efforts have been made constantly to introduce new methodologies which are efficient and more compatible with the environment. One of the most desirable approaches to address this challenge constitutes a search of surrogates for traditionally employed organic solvents which suffer from various health and environmental concerns [18]. For many years, functionalized polymers have been employed as stoichiometric reagents and catalysts in organic synthesis.

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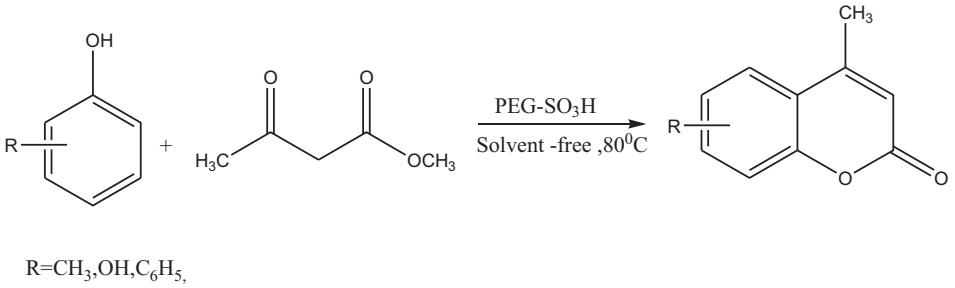


Scheme 1.

However, their development and applications in organic synthesis are undergoing a tremendous renaissance at present, which is undoubtedly being fueled by the special requirements of combinatorial and green chemistry [19,20].

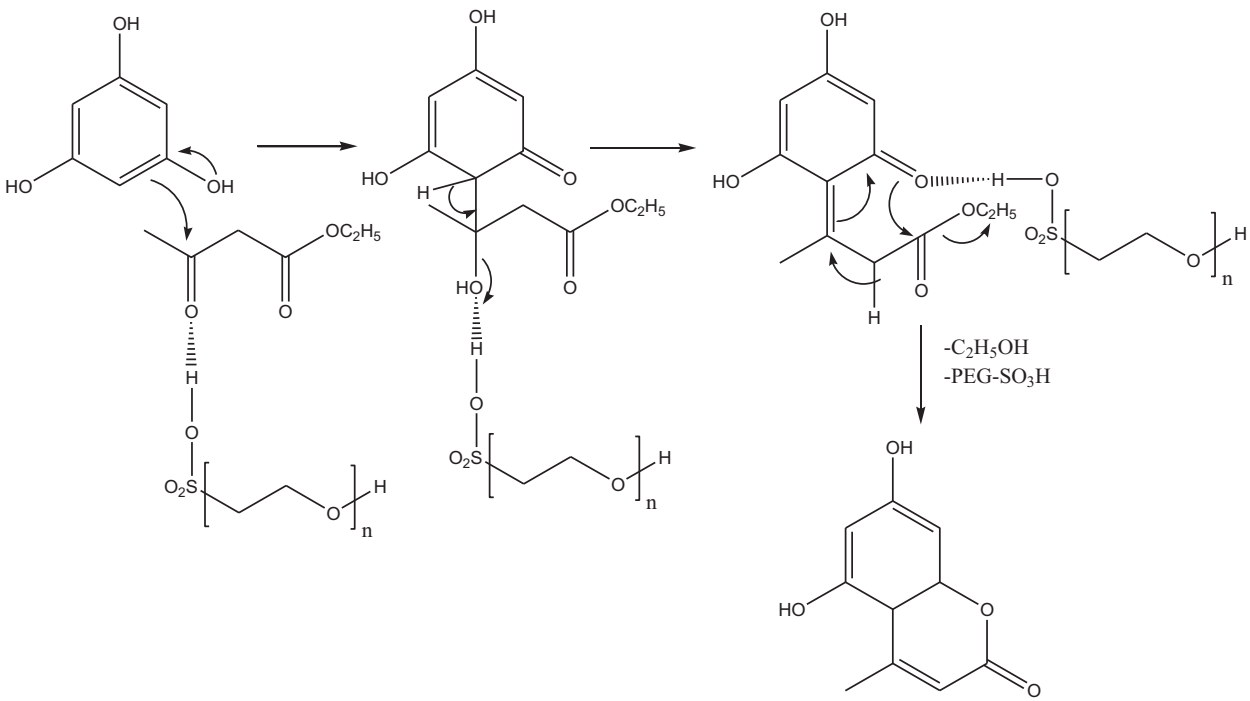
From the viewpoint of green chemistry, PEG is found to be an interesting solvent system. It is inexpensive, thermally stable, non-volatile, non-toxic and easily degradable, commercially available in different molecular weights and has broad solubility profile. According to these excellent properties, PEGs are an important group of polymers and catalysts in several branches of chemistry, particularly in organic synthesis [21]. Based on recent efforts to use eco-friendly and environmentally benign reagents in chemistry, PEGs are good candidates for these purposes [22].

In view of the emerging importance of PEGs as novel reaction media, we wish to report a mild and highly efficient method for the synthesis of coumarin derivatives. The drive towards clean synthesis has encouraged the application of solvent-free conditions [23]. A move away from the use of solvents in organic synthesis has led in some cases to improve the yields and more benign synthetic procedures. Owing to the importance of PEG-SO_3H to develop environmentally friendly reactions, herein, we report a simple, efficient and high yielding protocol for the synthesis of coumarin derivatives using PEG-SO_3H as a catalyst for the first time under solvent-free conditions (Scheme 1).

2. Result and discussion

The condensation of substituted phenol (1 mmol) and dicarbonyl compounds (1.1 mmol) in the presence of PEG-SO_3H (10 mol %) as a catalyst under solvent-free conditions at 80 °C furnished the desired product in excellent yield. Also the catalyst was successfully recovered and recycled at least for three runs without significant loss in activity.

The results are shown in Table 1 and the possible mechanism of the reaction is depicted in Scheme 2. To



Scheme 2.

Table 1
Synthesis of coumarin derivatives using PEG-SO_3H catalyst.

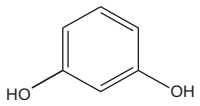
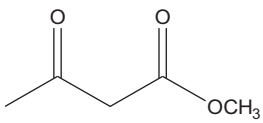
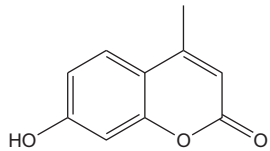
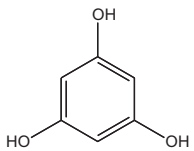
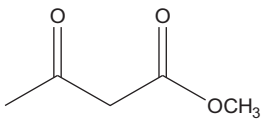
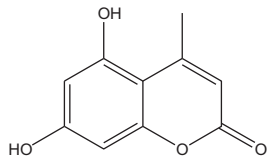
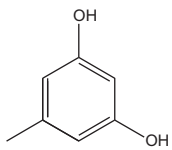
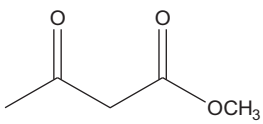
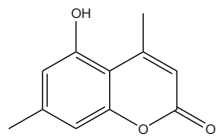
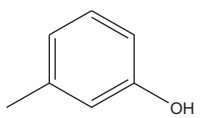
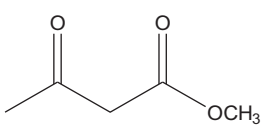
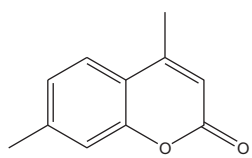
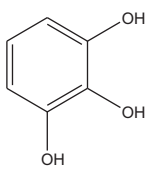
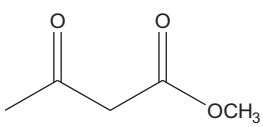
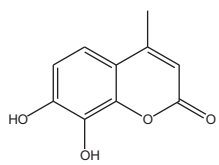
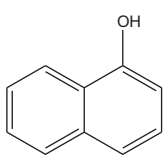
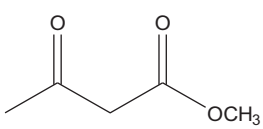
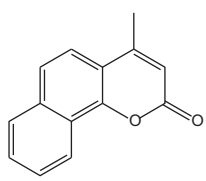
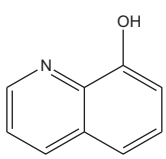
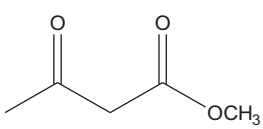
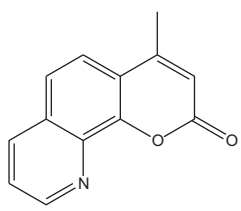
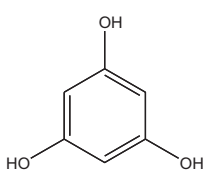
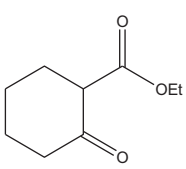
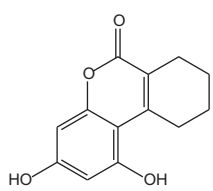
Entry	Phenol	β-keto ester	Product	Reaction time (min)	Yield (%)	Melting Point (°C)
3a				10	91	183–184 [25]
3b				15	89	283–285 [25]
3c				20	83	250–252 [25]
3d				40	78	131–132 [26]
3e				20	89	244–246 [25]
3f				40	88	154–156 [26]
3g				40	81	102–103
3h				60	80	263–265

Table 2
Optimum conditions for the preparation of coumarin derivatives using different catalyst by reaction between resorcinol and methyl acetoacetate.

Entry	Catalyst	Reaction time	Yield (%)
1	37% $BF_3.SiO_2$	1.5 h	65
2	PEG-6000	8 h	35
3	PEG-SO_3H	10 min	86
4	Silica sulfuric acid	5 min	80 [20]
5	$SnCl_2$	2.5 h	52 [21]

Table 3
Optimum temperature for the preparation of coumarin derivatives using PEG-SO_3H by reaction between resorcinol and methyl acetoacetate.

Entry	Temperature in °C	Reaction time in min	Yield (%)
1	50	45	60
2	60	30	78
3	80	10	91

compare the activity of various catalysts such as silica sulfuric acid, $SnCl_2$, BF_3SiO_2, PEG itself with PEG-SO_3H, Pechmann condensation of resorcinol and methyl acetoacetate in ratio (1:1.1) was carried out in the presence of different catalyst (10 mol%) at 80 °C under solvent-free conditions (Table 2). Excellent yield of desired product was obtained when PEG-SO_3H was used as a catalyst. But when the temperature was less than 80 °C, low yield of the product was obtained, as shown in Table 3.

3. Experimental

All reagents were purchased from Merck and Loba and used without further purification. Melting points were measured in open capillary and are uncorrected. The products were characterized by IR spectra, ^1H NMR, and elemental analyses. IR spectra were recorded on Perkin-Elmer FT-IR-1710 instrument. ^1H NMR was recorded on BrukerAC-200 MHz and BrukerMSL-300 instrument using TMS as an internal standard. Elemental analyses were determined by an elemental analyser (CHNS-O, EA 1108-elemental analyser, Carlo Erba instruments).

4. Preparation of PEG-SO_3H catalyst

A catalyst was prepared according to reported procedure [24] at 0 °C, chlorosulfonic acid (1.16 g, 10 mmol) was added to a solution of PEG-6000 (6.0 g, 1 mmol) in 10 mL of CH_2Cl_2. Then the resulting solution was stirred at room temperature for overnight and concentrated under vacuum. Followed by addition of 60 mL of ether and precipitate obtained by filtration was washed with 30 mL of ether three times to afford the PEG-SO_3H.

5. General procedure for synthesis of coumarin derivatives

To a mixture of the phenolic compound (1 mmol) and dicarbonyl compound (1.1 mmol), PEG-SO_3H (10 mol%) was added and the resulting mixture was heated at 80 °C (Table 1). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and poured into crushed ice and stirred for 5 min. The crude product was collected by filtration under suction, washed with ice cold water and recrystallized from hot ethanol to afford pure coumarin derivatives. In order to recover the catalyst totally, the filtrate was dried under vacuum and washed with diethyl ether and reused after drying under vacuum.

6. Conclusion

We have developed an efficient and environmentally benign strategy for the synthesis of coumarin derivatives using PEG-SO_3H as a catalyst. This method offers several advantages including high yield of products, short reaction time, low cost, cleaner reaction profile and ease of preparation of catalyst and ease of product isolation. Also the catalyst was successfully recovered and recycled at least for three runs without significant loss in activity.

7. The spectral data

3a: ^1H NMR ($CDCl_3$ + DMSO, 200 MHz); 2.4 (s, 3H, CH3); 6.06 (s, 1H, CH); 6.80 (d, J = 8.3 Hz, Ar-2H), 7.48 (d, J = 8.3 Hz, Ar-1H), 10.0 (s, OH); IR (KBr) 3198, 1679, 1600, 1451, 1390, 1330, 1273, 1239, 1133, 1068, 845; Anal. Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58; Found C, 68.30; H, 4.51.

3b: ^1H NMR ($CDCl_3$, 200 MHz); 2.52 (s, 3H, CH3); 5.89 (s, 1H, CH); 6.20 (d, J = 8.0 Hz, Ar-1H), 6.28 (d, J = 8.0 Hz, Ar-1H); 10.39 (s, OH); 10.61 (s, OH); IR (KBr) 3430, 3142, 1700, 1553, 1474, 1385, 1363, 1237, 1301, 1160, 1098, 1077, 930, 1077, 930, 832, 760; Anal. Calcd for $C_{10}H_8O_4$: C, 62.50; H, 4.20; Found C, 62.67; H, 4.32.

3c: ^1H NMR (DMSO, 200 MHz); 2.26 (s, 3H, CH3); 2.52 (s, 3H, CH3); 6.04 (s, 1H, CH), 6.56 (s, 1H, Ar-H), 6.61 (s, 1H, Ar-H); 10.56 (s, OH); IR (KBr) 3392, 3052, 1656, 1613, 1512, 1404, 1380, 1339, 1251, 1150, 1098, 1074, 920, 851, 828, 594; Anal. Calcd for $C_{11}H_{10}O_3$; C, 69.46; H, 5.30; Found C, 69.58, H, 5.43.

3d: ^1H NMR ($CDCl_3$, 300 MHz) δ2.42 (s, 3H, CH3), 2.45 (s, 3H, CH3), 6.22 (s, 1H, CH), 7.09 (d, J = 6.2 Hz, Ar-1H), 7.46 (d, J = 6.2 Hz, Ar-1H); IR (KBr) 2900, 2724, 2360, 1720, 1638, 1459, 1377, 1307, 1215, 1154, 1077, 964, 894, 722; Anal. Calcd for; $C_{11}H_{10}O_2$; C, 75.84; H, 5.79; Found C, 75.98; H, 5.64.

3e: ^1H NMR (DMSO,200 MHz) δ2.38 (s.3H, CH3), 6.14 (s, 1H, CH), 6.81 (d, J = 8.0 Hz, Ar-1H), 6.85 (d, 1H, 8.0 Hz, Ar-H), 7.4 (s, OH), 7.6 (s, OH); IR (KBr) 2942, 2727, 2361, 1455, 1377, 1303, 1154, 1063, 964, 722; Anal. Calcd for; $C_{10}H_8O_4$ C, 62.50; H, 4.20; Found C, 62.61; H, 4.29.

3f: ^1H NMR (DMSO, 300 MHz) δ2.42 (s, 3H, CH3), 6.72 (s, 1H, CH), 7.43–8.47 (m, 6H, Ar-H); IR (KBr) 3403, 3054, 2916, 1786, 1713, 1639, 1612, 1473, 1375, 1238, 1173, 1082, 943, 842, 809, 748, 890, 500; Anal. Calcd for; $C_{14}H_{10}O_2$; C, 79.98; H, 4.79; Found C, 79.85, H, 4.84.

3g: ^1H NMR (DMSO, 200 MHz)δ2.38 (s, 3H, CH3), 7.30–9.01 (m, 6H, Ar-H); IR (KBr) 3434, 3184, 2700, 2093, 1602, 1521, 1428, 1379, 1332, 1273, 1194, 1096, 883, 820, 773, 619, 559; Anal. Calcd for; $C_{13}H_9NO_2$; C, 73.92; H, 4.29; N, 6.63; Found C, 74.05; H, 4.41; N, 6.71.

3h: ^{1}H NMR (DMSO, 200 MHz) δ1.65 (m, 4H, CH2), 2.35 (m, 2H, CH2), 3.04 (m, 2H, CH2), 6.15 (s, 1H, Ar-H), 6.24 (s, 1H, Ar-H), 10.13 (s, OH), 10.38 (s, OH); IR (KBr) 2924, 2727, 2360, 1636, 1460, 1377, 1301, 1161, 820, 722; Anal. Calcd for; $C_{13}H_{12}O_4$; C, 67.23; H, 5.21; Found C, 67.34; H, 5.15.

Acknowledgement

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