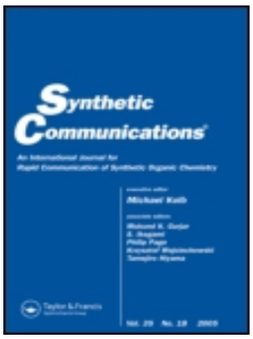

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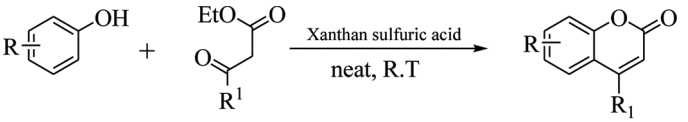
XANTHAN SULFURIC ACID: AN EFFICIENT AND RECYCLABLE SOLID ACID CATALYST FOR PECHMANN CONDENSATION

B. Suresh Kuarm, J. Venu Madhav, and B. Rajitha
Department of Chemistry, National Institute of Technology, Warangal, India

GRAPHICAL ABSTRACT



1 2 3

Abstract *In this report, substituted coumarins are formed via Pechmann condensation using various substituted phenols and ethyl acetoacetates in the presence of xanthan sulfuric acid as a solid acid catalyst under solvent-free conditions. This method is very simple, cost-effective, and has shorter reaction times, and the catalyst could be reused.*

Keywords Biodegradable xanthan sulfuric acid (XSA); coumarins; Pechmann condensation; solvent-free conditions

INTRODUCTION

The synthesis of coumarins and their derivatives has received much attention from organic and medicinal chemists because of their wide range of biological and pharmaceutical properties. This heterocyclic system has been employed in the preparation of important drugs required for treatment of platelet aggregation,[1] bacteria,[2] and cancer.[3] Some of the coumarin analogs are used to inhibit steroid 5α-reductase[4] and HIV-1 protease.[5] Moreover, these derivatives are used as anticoagulants,[6] additives in food and cosmetics,[7] and in the preparation of insecticides, optical brighteners,[8] and dispersed fluorescent and laser dyes.[9] To synthesize coumarins and their derivatives, several methods are reported, including Pechmann,[10a] Perkin,[10b] Knoevenagel,[10c] Reformatsky,[10e] and Wittig[11] reactions. Among them, the Pechmann reaction is the most widely applied method for synthesis of coumarins as it involves the condensation of phenols with β-ketoesters in the presence of a variety of acidic condensing agents to afford good yields of coumarins.[12,13] To prepare this important moiety, various condensing agents are

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reported in literature such as polyphosphoric acid (PPA),[14] $InCl_3$,[15] $ZrCl_4$,[16] $Yb(OTf)_3$,[17] *p*-TsOH,[18] $BiCl_3$,[19] I_2 or AgOTf,[20] and $Sm(NO_3)_3$,[21] as well as chloroaluminate ionic liquids.[22,23] The main disadvantages of these methods are longer reaction times, loading of large amount of the catalyst, and tedious workup procedures. Some of the catalysts are highly expensive and after work up cannot be recovered or reused. These shortcomings surely show the need for a safe, eco-friendly, and efficient method to synthesize these important compounds.

Recently, the direction of science and technology has been shifting more toward ecofriendly, natural product resources and reusable catalysts. Thus, natural biopolymers are attractive candidates in the search for such solid support catalysts.[24,25] Among different biopolymers, xanthan is one of the most common biopolymers and has some unique properties that make it an attractive alternative to conventional organic or inorganic supports for catalytic applications.[26] Recently, sulfonated xanthan has been utilized as a biopolymeric solid support acid catalyst for the synthesis of α-amino nitriles.[27] This polymer has unlimited availability as a renewable agro-resource and is biodegradable.

RESULTS AND DISCUSSION

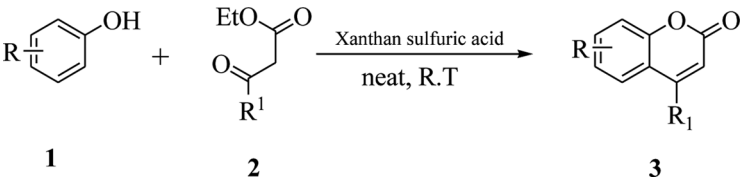
For the aforementioned reasons and in light of our general interest in synthesizing coumarins,[28] in this article, we report a simple procedure for the synthesis of coumarins by the condensation of phenols with ethylacetoacetates under solvent-free conditions using xanthan sulfuric acid (XSA) (Scheme 1). The reactions were carried out at room temperature for 20–30 min using phenol **1** (1 mmol) and β-ketoester **2** (1 mmol) and in the presence of XSA (0.08 g). The results are summarized in Table 1.

We then investigated the efficiency of the XSA compared to various sulfur analog acidic catalysts. The results are summarized in Table 2. XSA was found to be the most effective catalyst based on the product yield. The reaction did not proceed in the absence of catalyst (yield less than 10%).

We examined the amount of catalyst in this reaction. The best results were obtained using 0.08 g of catalyst (96%). Using lower amounts of catalyst resulted in lower yields, and in the absence of catalyst the product yield was found to be very poor (Table 3).

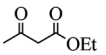
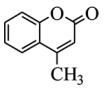
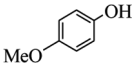
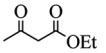
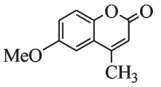
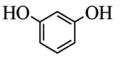
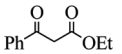
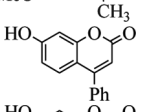
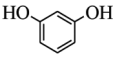
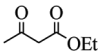
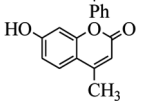
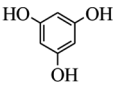
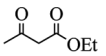
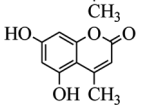
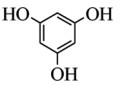
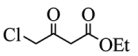
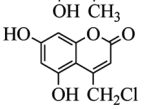
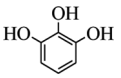
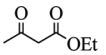
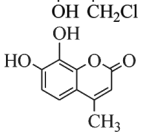
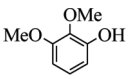
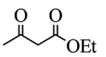
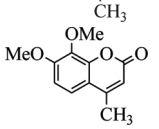
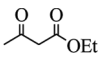
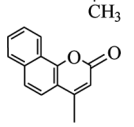
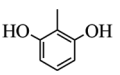
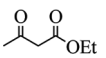
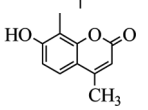
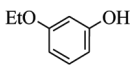
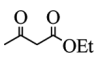
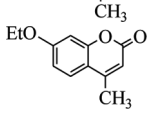
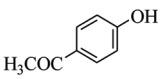
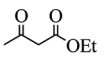
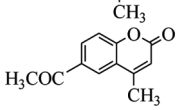
EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. The reactions were monitored by thin-layer chromatography (TLC) and visualized with



Scheme 1. Synthesis of coumarin by xanthan sulfuric acid as a solid acid catalyst.

Table 1. Xanthan sulfuric acid–catalyzed sunthesis of coumarins

Entry	Phenol	Ester	Coumarin	Time (min)	Yield[a] (%)	Mp (°C)
1				30	88	81[28b]
2				25	90	164–165[29]
3				20	96	257[30]
4				30	91	185[31]
5				25	92	280[31]
6				30	92	187[32]
7				20	94	242[31]
8				25	95	174[33]
9				20	91	153[30]
10				20	95	137[28b]
11				25	91	115–116[29]
12				30	88	260–262

[a]Yields refer to pure products and all products were characterized by comparison of their physical data, ^{1}H NMR ^{13}C NMR, IR, and mass.

ultraviolet light. Infrared (IR) spectra (KBr) were recorded on a Shimadzu FTIR model 8010 spectrometer, and the ^{1}H NMR spectra were measured on a Varian Gemini 200-MHz spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a Jeol JMS D-300 spectrometer. CHN analysis was done by Carlo Erba EA 1108 automatic elemental analyzer. All solvents and reagents were purchased from Aldrich and Fluka.

Table 2. Effect of catalysts on yield[a]

Entry	Catalyst	Quantity	Yield[b] (%)
1	Xanthan sulfuric acid	0.08 g	96
2	Silica sulfuric acid	0.08 g	92
3	Methane sulfonic acid	0.1 mmol	86
4	Sulfuric acid in acetic acid	0.1 mmol	56
5	No catalyst	None	10

[a]Mixture of phenol **1** (1 mmol) and β-ketoester **2** (1 mmol) was stirred at room temperature.
[b]Isolated yield.

Catalyst Preparation

Chlorosulfonic acid (1.00 g) was added dropwise to a magnetically stirred mixture of xanthan (5.00 g) in $CHCl_3$ (15 mL) at 0 °C during 2 h. After completion of the addition, the mixture was stirred for 3 h. Then, the mixture was filtered, washed with methanol (25 mL), and dried at room temperature to obtain XSA as white powder (5.30 g). Sulfur content of the samples by conventional elemental analysis was 0.62 mmol/g for XSA. The number of H^+ site of xanthan–SO_3H determined by acid–base titration was 0.6 meq/g. This value corresponds to about 92% of the sulfur content, indicating that most of the sulfur species on the sample are in the form of the sulfonic acid groups.

FT-IR Spectrum of Xanthan Sulfuric Acid

The FT-IR spectrum of the catalyst showed a strong absorption band at around 1200 cm^{-1} that was attributable to stretching vibrations of the SO_2 group. Two strong absorption bands at around 1400 and 1200 cm^{-1} were observed and attributed to asymmetric and symmetric stretching vibration of SO_2 group, respectively. For S–O functional group, the stretching absorption as at around 600–700 cm^{-1}. The spectrum also showed a strong broad band for OH stretching absorption at around 3400–3700 cm^{-1}. This result indicates that reaction of xanthan with chlorosulfonic acid succeeded in incorporating sulfated groups in XSA.

Table 3. Influence of the catalytic amounts of xanthan sulfuric acid[a]

Entry	Catalyst (g)	Time (min)	Yield[b] (%)
1	None	60	Trace
2	0.01	20	28
3	0.03	20	51
4	0.05	20	79
5	0.08	40	96
6	0.08	20	96

[a]Mixture of phenol **1** (1 mmol), β-ketoester **2** (1 mmol), and xanthan sulfuric acid was stirred at room temperature.
[b]Isolated yield.

General Procedure for Synthesis of Coumarins

A mixture of the phenol **1** (1 mmol), β-ketoester **2** (1 mmol), and XSA (0.08 g) was stirred at room temperature for the appropriate time according to Table 1. Completion of the reaction was confirmed by thin-layer chromatography (TLC). After completion of the reaction, $CHCl_3$ (10 ml) was added to the reaction mixture. The reaction mixture was filtered and washed with $CHCl_3$ (5 ml), combined organic layers were concentrated in vacuum to afford the crude compound, and it was recrystallized from ethanol to afford the pure product. The reusability of the catalyst was checked by separating the XSA from the reaction mixture by simple filtration and drying it in an oven (50 mm Hg pressure) at 60 °C for 3 h prior to use in the other reaction. The recovered catalyst can be reused at least three additional times in subsequent reactions without significant decrease in product yield (Table 4).

Spectral Data

Table 1, Entry 2. IR (KBr, cm^{-1}): 2935, 1683, 1626, 1485; ^1H NMR ($CDCl_3$): δ 2.41 (3H, s), 3.89 (3H, s), 6.36 (1H, s), 7.15 (1H, d), 7.26 (1H, s), 7.35 (1H, d). ^{13}C NMR ($CDCl_3$): δ 160.1, 155.4, 153.2, 146.9, 120.2, 119.7, 117.4, 115.3, 108.3, 56.1, 18.4; EIMS (m/z) 190 (M^+). Anal. calcd. for $C_{11}H_{10}O_3$: C, 69.43; H, 5.30. Found: C, 69.45; H 5.27.

Table 1, Entry 4. IR (KBr, cm^{-1}): 3400, 1725, 1530; ^1H NMR ($CDCl_3$) δ 2.39 (3H, s), 3.28 (br s, 1H), 6.06 (s, 1H), 6.8 (s, 1H), 6.82 (d, 1H), 7.44 (d, 1H). ^{13}C NMR ($CDCl_3$): δ = 161.7, 159.6, 152.6, 151.80, 128.9, 113.9, 112.5, 111.5, 109.7, 22.0; EIMS (m/z) 176 (M^+). Anal. calcd. for $C_{10}H_8O_3$: C, 68.10; H, 4.71. Found: C, 68.18; H, 4.55.

Table 1, Entry 7. IR (KBr, cm^{-1}): 3417, 1676, 1620, 1585; ^1H NMR ($CDCl_3$): δ 2.37 (3H, s), 6.12 (1H, s), 6.86 (1H, d), 7.11 (1H, d); ^{13}C NMR ($CDCl_3$): δ 161.6, 155.5, 153.3, 149.6, 145.21, 122.3, 114.2, 112.5, 110.3, 22.5; EIMS (m/z) 192 (M^+). Anal. calcd. for $C_{10}H_8O_4$: C, 62.50; H, 4.20. Found: C, 62.54; H, 4.15.

Table 1, Entry 12. IR (KBr, cm^{-1}): 1745, 1648, 1619; ^1H NMR ($CDCl_3$): δ 7.32 (d, 1H), 7.24 (s, 1H), 6.91 (d, 1H), 6.14 (s, 1H), 2.95 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$): 189.9, 161.0, 158.4, 151.3, 149.9, 127.2, 115.7, 113.2, 110.8, 108.5,

Table 4. Effect of reusability of catalyst on yield

Run	Cycle	Yield[a] (%)
1	0	96
2	1	95
3	2	91
4	3	86

Note. Reaction conditions: phenol **1** (1 mmol), β-ketoester **2** (1 mmol), and xanthan sulfuric acid (0.08 g) were stirred at room temperature.

[a]Yields refer to the pure isolated recovered catalyst.

29.4, 22.1. EIMS (m/z) 202 (M^+). Anal. calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.98. Found: C, 71.11; H, 4.86.

CONCLUSION

In conclusion, we have developed an efficient synthesis of substituted coumarins via Pechmann condensations using XSA catalyst under solvent-free conditions. Moreover, inexpensive catalyst, solvent-free condition, low toxicity of the catalyst, fast reaction times, simple experimental procedure, recyclablity of the catalyst, and good yields of the products are the advantages. We believe this procedure will find important applications in the synthesis of coumarins.

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