Research Article

Easy Access to Coumarin Derivatives Using Alumina Sulfuric Acid as an Efficient and Reusable Catalyst under Solvent-Free Conditions

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A new and efficient condition for the use of alumina sulfuric acid (ASA) as a heterogeneous catalyst in the Pechmann condensation reaction in solvent-free condition for the formation of coumarins has been reported.

1. Introduction

Coumarins play an important role in the realm of natural products and synthetic organic chemistry [1]. They have been used in food and cosmetic industry [2] and also they have been used as optical brighteners [3] and dispersed fluorescent and laser dyes [4], anticoagulants [5], and in the preparation of insecticides [6]. There are several methods for their synthesis like Perkin [7–9], Knoevenagel [10–15], Reformatsky [14], Wittig [16], and Pechmann [17–21].

The Pechmann condensation reaction is one of the most popular procedures for the preparation of coumarins and their derivatives. It involves the condensation of phenols with β -ketoesters usually in the presence of different acid as catalyst to provide 4-substituted coumarins [22].

On the other hand in the recent years, the use of inorganic solids as heterogeneous catalysts has ameliorated the yields and the conditions of many organic reactions. These catalysts are easy to handle, and usually have simple separation procedure and they can be recycled and reused so they provide environmental and economic advantages [23–26]. Between inorganic solids, alumina is an interesting choice. In industry it has been used as drying agent, adsorbent, filter, and catalyst [27].

2. Results and Discussion

In continuation of our studies on developing cheap and environmentally benign methodologies for organic reactions especially solvent-free conditions and using solid acids as a heterogeneous and reusable catalyst we have decided to use alumina sulfuric acid (ASA) as catalyst in Pechmann reaction [28–31], to the best of our knowledge, ASA has not yet been used for these types of condensations in solvent-free conditions (Scheme 1).

Initially we started with Pechmann condensation of resorcinol and ethyl acetoacetate that had already been used vastly by other chemists in different conditions. In the first glance, we compared different alumina and alumina-supported acids for Pechmann condensation. The results are summarized in Table 1.

As it is indicated in Table 1, sulfuric- and perchloric-acid-supported alumina provides good yields (entries 5 and 6) but ASA is the most potent catalyst for this reaction with 85% yield (Table 1, entry 7).

To study the limitation of catalyst amounts we explored some reaction conditions in solvent-free conditions which results are summarized in Table 2.

Our results showed that by increasing the catalytic load of ASA from 0.01 g to 0.02 g it improved the yield from 70% to

SCHEME 1: ASA catalyzed synthesis of coumarins under solvent-free conditions.

TABLE 1: Pechman condensation of resorcinol with ethylacetoacetate using different types of alumina-based catalyst^a.

Entry	Catalyst	Yield (%)
1	Al ₂ O ₃ (Neuter)	5
2	Al ₂ O ₃ (Acidic)	10
3	Al ₂ O ₃ /H ₃ PO ₄	60
4	Al ₂ O ₃ /HNO ₃	50
5	Al ₂ O ₃ /H ₂ SO ₄	80
6	Al ₂ O ₃ /HClO ₄	80
7	H ₂ SO ₄	80
8	ASA	85

^aReaction conditions: resorcinol (1 mmol), ethylacetoacetate (1 mmol), ASA (0.04 g), and solvent free, 110 °C.

TABLE 2: Optimization of the amount of ASA in Pechmann condensation of resorcinol (1 mmol) with ethyl acetoacetate (1 mmol) in solvent-free conditions at 110 °C.

Entry	ASA (g)	Yield (%)
1	0.01	70
2	0.02	90
3	0.03	85
4	0.04	85

TABLE 3: Optimization of temperature in Pechmann condensation of resorcinol (1 mmol) with ethyl acetoacetate (1 mmol) and ASA (0.02 g) in solvent-free conditions.

Entry	Temperature (°C)	Yield (%)
1	80	70
2	90	80
3	100	98
4	110	90

90% (Table 2, entries 1 and 2). This showed that the catalyst concentration plays a major role in this reaction. But more increasing in the catalyst amount is not appropriate and the yield diminished (conditions for Table 2, entries 3 and 4).

To study the limitations of temperature, we explored some reaction Pechmann condensation of resorcinol and ethyl acetoacetate in presence of ASA in solvent-free conditions at 110 °C. The results are summarized in Table 3.

As indicated in Table 3, increasing the temperature until 100 °C, resulted a 98% yield (Table 3, entry 3) but by increasing the temperature up to 110 °C, the obtained yield was decreased to 85% (Table 3, entry 4). So we have followed our experiences at 100 °C.

Now, with different optimum conditions in hand, we selected the optimized reaction conditions (phenolic compound (1 mmol), β -keto ester (1 mmol), and ASA (0.02 g) in solvent-free conditions at 100 °C to determine the scope of this procedure. The results are summarized in Table 4.

As indicated in Table 4, the reaction works easily for a vast range of phenols with electron-donating groups with different β -ketoesters. As evidence we can mention resorcinol (Table 4, entry 1) that provide corresponding coumarin with 98% yield. Also the reaction works well in the case of hydroquinone 1 (Table 4, entry 2), *p*-methoxy phenol (Table 4, entry 3), α -naphthol (Table 4, entry 8), and β -naphthol (Table 4, entry 9). The reaction does not work in the case of phenols with electron withdrawing groups like *o*-nitro, *p*-chloro, and *p*-bromo phenols (Table 4, entries 4–6). This order has been justified by moderate yield of phenol (Table 4, entry 7).

Fortunately, our protocol is efficient for the Pechmann condensation of phenols with electron-donating groups and different β -ketoesters even with electron withdrawing groups (Table 4, entries 13–16). As one additional interesting result we can report that in the case of different β -ketoesters with electron withdrawing groups, the reaction is slower than corresponding β -ketoester without electron withdrawing groups (Table 4, entries 1 and 14) and (Table 4, entries 8 and 15). All the products were characterized by IR, ¹H NMR, and ¹³C NMR, and were identified by the comparison of the spectral data with those reported in literature.

As testing the recyclability of the catalyst, it was separated from the reaction mixture and washed with EtOH and dried at air to give recycled catalyst. The Pechmann condensation of resorcinol and ethyl acetoacetate was repeated with recycled catalyst and the yields were found to remain in the range of 90% for three recycles (Table 5).

A proposed mechanism for this reaction is illustrated in Scheme 2.

3. Experimental Section

3.1. General. The IR spectrum was taken on a Perkin-Elmer, model 783 spectrophotometer. The NMR spectrum has been recorded by a Bruker AMX-300 (300 MHz) spectrometer. The solvent was DMSO-*d*₆. The chemical shifts are expressed in parts per million (ppm), and tetramethylsilane (TMS) was used as internal reference. Elemental analyses were performed by Perkin Elmer CHN analyzer, 2400 series II.

3.2. Preparation of Catalysts

3.2.1. Preparation of Alumina Sulfuric Acid (ASA). Chlorosulfonic acid (0.3 mmol.) was added drop wise to alumina

TABLE 4: Preparation of different coumarins catalyzed by ASA (0.02 g) in solvent-free conditions at 100°C.

Entry	R ¹	R ²	Phenol	Time (min)	Product	Yield (%)	M.P. (°C)	
							Found	Reported
1	Me	Et		30		98	187-188	182-190 [32]
2	Me	Et		75		85	239-240	240 [32]
3	Me	Et		35		89	165	165 [32]
4	Me	Et		180		25	183-184	183-185 [1]
5	Me	Et		180		N.R	—	
6	Me	Et		180		N.R	—	
7	Me	Et		110		60	79-80	79-81 [33]
8	Me	Et		60		91	154-156	153-155 [33]
9	Me	Et		90		85	180-182	180-181 [32]
10	Me	Et		20		55	261-263 [22]	263-265

TABLE 4: Continued.

Entry	R ¹	R ²	Phenol	Time (min)	Product	Yield (%)	M.P. (°C)	
							Found	Reported
11	Me	Me		25		99	185-186	185-190 [22]
12	Me	Me		30		80	261-263	263-265 [22]
13	CH ₂ Cl	Et		100		96	180	180-181 [22]
14	CH ₂ Cl	Et		35		97	283-285	284-285 [22]
15	CH ₂ Cl	Et		500		88	165-166	165-167 [22]
17	Ph	Et		140		91	256	256 [22]

^aIsolated yield.

SCHEME 2: A plausible mechanism for the Pechmann condensation of resorcinol and ethyl acetoacetate.

TABLE 5: The recycling experiment ASA in Pechmann condensation of resorcinol (1 mmol) with ethyl acetoacetate (1 mmol) using ASA (0.02 g) at 100°C in solvent-free conditions.

Run	1	2	3
Yield (%)	98	96	90

(1 g, 200–400 mesh) at room temperature and mixed until no HCl evolved. The residue was dried by heating at 130°C for three hours. The obtained alumina sulfuric acid has been used for experiences [29].

3.2.2. Preparation of Other Acidic Alumina. To a suspension of alumina (1.7 g, 200–400 mesh) in dry diethyl ether (5 mL) was added corresponding acid (2 mL) and the slurry shaken for 5 minutes. The solvent was evaporated in reduced pressure and the residue was dried at 110°C for 3 h and used for the reactions [34].

3.2.3. Typical Procedure for Preparation of Coumarin in Presence of ASA. A mixture of resorcinol (110 mg, 1 mmol) and ethyl acetoacetate (130 mg, 1 mmol) and ASA (0.02 g) was heated at 100°C for 30 minutes. After compilation the reaction (monitored by TLC), the residue was dissolved in hot ethanol (2 mL) and filtered to separate the catalyst. The mother liquid was concentrated to 1 mL and cooled in ice bath. The crystalline product was collected by filtration under suction. The pure 7-hydroxy-4-methylcoumarin as colorless prisms was obtained (1.73 g, 98%). This procedure was followed for the preparation of all the substituted coumarins listed in Table 4.

Spectral Data of Selected Compounds. 7-hydroxy-4-methylcoumarin (Table 4, entry 1), $^1\text{H NMR}$ ($\text{DMSO}-d_6$): 2.65 (s, 3H, Me), 6.41 (s, 1H), 6.91–7.72 (m, 3H, ArH), IR, (KBr): 3260–3080, 1690 cm^{-1} .

4-methyl-coumarin (Table 4, entry 1): $^1\text{H NMR}$ ($\text{DMSO}-d_6$): 2.62 (s, 3H, Me), 6.48 (s, 1H), 7.30–7.65 (m, 4H, ArH), IR (KBr): 1665, 1610, 1450, 1400 cm^{-1} .

4-methyl-2H-benzo[h]chromen-2-one (Table 4, entry 8): $^1\text{H NMR}$ ($\text{DMSO}-d_6$): 2.71 (s, 3H, Me), 6.51 (s, 1H), 7.50–8.91 (m, 6H, ArH), IR (KBr): 1675 cm^{-1} .

4. Conclusions

In conclusion, the efficient use of alumina sulfuric acid (ASA) as a heterogeneous catalyst in the Pechmann condensation reaction in solvent-free media has been reported. This reaction leads to the formation of coumarin derivatives in excellent yields with good purity. The catalyst has been recycled and reused three times for the reaction without losing its activity. This new condition has several advantages such as good yields, mild conditions, simple workup, and has no environmental hazards. A proposed mechanism has been reported.

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