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Application of a sulfonated carbon material as a reusable heterogeneous catalyst for the synthesis of biscoumarins

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ABSTRACT

A novel, efficient, and simple method for the synthesis of Biscoumarins by the reaction of 4-hydroxycoumarin with aldehydes in the presence of a catalytic amount of a sulfonated carbon material in refluxing ethanol has been developed. The results showed that this heterogeneous catalyst has high catalytic activity and the desired products were obtained in good to high yields. Moreover, the catalyst was found to be reusable and a considerable catalytic activity still could be achieved after fifth run. Easy work-up, short reaction times, and simplicity of operation are other advantages of this simple procedure.

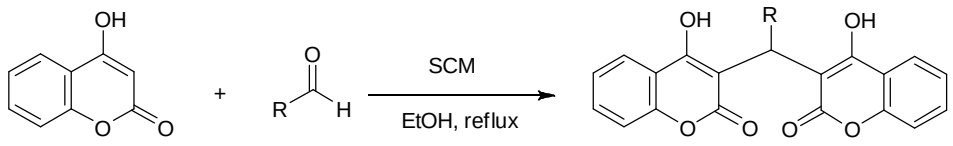
Keywords: biscoumarins, heterogeneous catalysis, sulfonated carbon material.

INTRODUCTION

Coumarins are a large group of heterocycles which known for their various biological activities such as anticoagulant, insecticidal, antihelminthic, hypnotic, antifungal, and HIV protease inhibition activities [1-3]. 3,3-(4-Aryl methylene) bis-(4-hydroxycoumarin), the bridge substituted dimers of 4-hydroxycoumarin that commonly known as biscoumarins, are also of considerable interest due to their pharmacological properties such as anticoagulant [4,5], and urease inhibitor activities [6]. In view of different biological and chemical applications of biscoumarins, the development of suitable synthetic methodologies for their generation has been a topic of great interest in recent times. The general method for synthesis of biscoumarin derivatives involves the reaction of 4-hydroxycoumarin with various aldehydes in the presence of different catalysts such as $Zn(Proline)_2$ [7], molecular iodine [8], $[TBA]_2[W_6O_{19}]$ [9], ionic liquids [10,11], $[P4VPy\text{-}BuSO_3H]HSO_4$ [12], silica-supported Preyssler nanoparticles [13], sodium dodecyl sulfate(SDS) [14], phosphotungstic acid [15], sulfonated rice husk ash [16], and piperidine [6]. Uncatalyzed synthesis of biscoumarines have been also reported in long reaction time [17]. However, many of these procedures are not entirely satisfactory and suffer from long reaction times, unsatisfactory yields, use of toxic organic solvents, or tedious work-up using homogeneous liquid catalysts. These problems prompted us towards further investigation in search of a new reusable heterogeneous catalyst, which will carry out the synthesis of biscoumarins under simpler experimental set-up, and green and eco-friendly conditions. The replacement of conventional toxic and polluting Brønsted and Lewis acid catalysts with environmentally benign and reusable solid catalysts is an active area of research.

Solid acid catalysts have the advantages of ease of product separation, recycling of the catalyst, and environmental compatibility as compared to liquid acid catalysts [18,19]. Sulfonated carbon materials (SCMs) as solid acid catalysts have many advantages. They are insoluble in common organic solvents, hardly cause corrosion, and have environmental compatibility. Also, the products can be easily separated from the reaction mixture and the catalyst is recoverable without loss in activity. They have been successfully used to replace sulfuric acid as catalysts [20-24]. As part of our research program directed towards the development of expedient methods using reusable catalysts for the synthesis of organic compounds [25-36], we report here our results from efficient solvent-free synthesis of

Biscoumarins from the reaction of 4-hydroxycoumarin and aldehydes using SCM as a novel heterogeneous organic catalyst (Scheme 1).



1 **2a-j** **3a-j**

Scheme 1. Synthesis of biscoumarins catalyzed by SCM

MATERIALS AND METHODS

All chemicals were available commercially and used without additional purification. Melting points were recorded on a Stuart SMP3 melting point apparatus. The IR spectra were obtained using a Tensor 27 Bruker spectrophotometer as KBr disks. The ^{1}H NMR (400 MHz) spectra were recorded with a Bruker 400 spectrometer.

Preparation of SCM

The SCM was prepared according to the reported procedure by Hara and co-workers [24]. Naphthalene (20 g) was heated in concentrated sulfuric acid (>96%, 200 mL) at 250 °C under a flow of N_2. After heating for 15 h, excess sulfuric acid was removed from the dark brown tar by vacuum distillation at 250 °C for 5 h, which resulted in a black solid. The solid was then ground to a powder and was washed repeatedly in boiling water until impurities such as sulfate ions were no longer detected in the wash water. The density of the SO_3H group was measured using NaOH (0.01 mol/L) as titrant by acid-base potentiometric titration. The amount of SO_3H attached to the polycyclic aromatic carbon was 2.80 mmol/g. The resulting black powder is insoluble in solvents such as water, methanol, ethanol, benzene, and hexane even at boiling temperatures**.**

General Procedure for the Synthesis of Biscoumarins 3a-j Catalyzed by SCM

A mixture of 4-hydroxycoumarin **1** (2 mmol), an aldehyde **2a-j** (1 mmol), SCM (0.05 g) as catalyst in ethanol (5 ml) was heated under reflux for the appropriate time. The reaction was monitored by TLC. At the end of reaction, catalyst was removed by filtration. The product was collected from the filtrate after cooling to room temperature and recrystallized from ethanol to give compounds **3a-j** in high yields.

RESULTS AND DISCUSSION

In order to evaluate the catalytic efficiency of SCM in the synthesis of biscoumarins and to determine the most appropriate reaction conditions; initially a model study was carried out on the synthesis of compound **3c** by the reaction of 4-hydroxycoumarin **1** (2 mmol) and 4-chlorobenzaldehyde **2c** (1 mmol) in different sets of reaction conditions (Table 1). To choose the most appropriate medium in this reaction, the model reaction was examined under solvent-free conditions and using EtOH, MeOH, CH_3CN, $CHCl_3$, CH_2Cl_2, and DMSO as solvents (Table 1). As shown, the reaction was more facile and proceeded to give the highest yield, using 0.05 g of the catalyst SCM in EtOH at reflux temperature (Table 1, entry 7). The efficiency of the reaction is also affected by the amount of catalyst SCM and reaction temperature. Low yield of the product **3c** was produced in the absence of the catalyst in solvent-free conditions at 110 °C and refluxing EtOH (Table 1, entries 1 and 2) or in the presence of the catalyst at room temperature even after prolonged reaction time (Table 1, entry 8), indicating that the catalyst and temperature are necessary for the reaction.

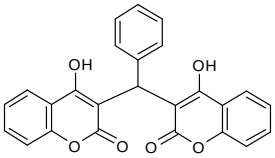
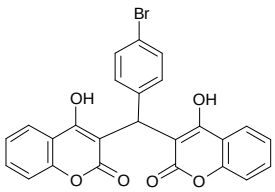
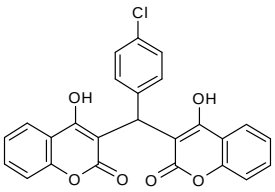
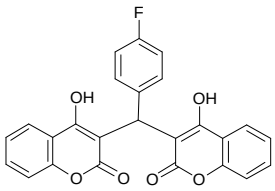
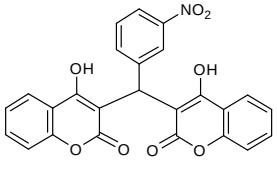
Encouraged by the remarkable results obtained with the above reaction conditions, and to show the generality and scope of this new protocol, a range of biscoumarins were prepared in the presence of SCM under optimized conditions, with the results shown in Table 2. As shown in Table 2, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the products in high yields.

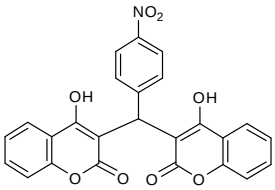
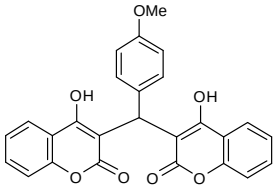
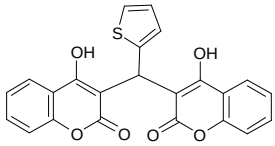
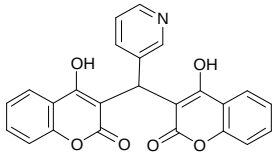
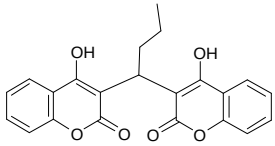
Table 1 Synthesis of compound 3c in the presence of SCM as catalyst in different reaction conditions[a]

Entry	Catalyst (g)	Solvent	T (°C)	Time (min)	Yield (%)[b]
1	-----	-----	110	80	11
2	-----	EtOH	reflux	120	23
3	0.01	EtOH	reflux	85	48
4	0.02	EtOH	reflux	45	60
5	0.03	EtOH	reflux	30	80
6	0.04	EtOH	reflux	20	83
7	0.05	EtOH	reflux	10	92
8	0.05	EtOH	r.t.	200	19
9	0.06	EtOH	reflux	10	91
10	0.05	MeOH	reflux	20	72
11	0.05	CH_3CN	reflux	20	66
12	0.05	$CHCl_3$	reflux	20	72
13	0.05	CH_2Cl_2	reflux	20	27
14	0.05	DMSO	reflux	20	69
15	0.05	-----	100	25	43
16	0.05	-----	110	25	49
17	0.05	-----	120	25	62

[a] *Reaction conditions: 4-hydroxycoumarin 1 (2 mmol) and 4-chlorobenzaldehyde 2c (1 mmol).*
[b] *Isolated yields.*

Table 2 Synthesis of biscoumarins using SCM as catalyst[a]

Entry	R	Product[b]	Time (min)	Yield (%)[c]	mp °C		Ref.
					Found	Reported	
1	C_6H_5	 **3a**	13	90	228-229	229–231	10
2	4-BrC_6H_4	 **3b**	15	91	272-274	269–271	16
3	4-ClC_6H_4	 **3c**	10	92	258-260	261-263	10
4	4-FC_6H_4	 **3d**	14	90	213-215	214.5	17
5	3-$O_2NC_6H_4$		15	89	215-216	214-216	9

		3e					
6	4-$O_2NC_6H_4$		14	91	235-237	232-233	9
		3f					
7	4-$MeOC_6H_4$		8	95	248-250	251-253	9
		3g					
8	2-Thienyl		10	96	205-207	206–209	12
		3h					
9	3-Pyridyl		15	91	274-275	271–273	16
		3i					
10	n-Pr		15	89	121-123	123	6
		3j					

[a] *4-Hydroxycoumarin (2 mmol), aldehyde (1 mmol), SCM (0.05 g) in ethanol under reflux.*
[b] *All the products were characterized by IR spectral data and comparision of their melting points with those of authentic samples. Also, the structures of some products were confirmed by ^1H NMR spectral data.*
[c] *Isolated yields.*

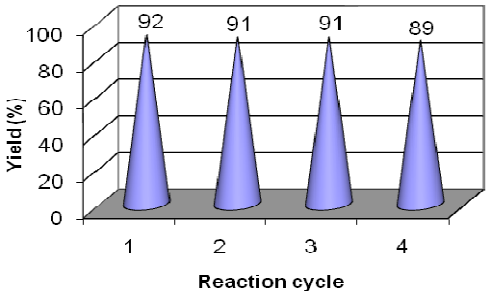
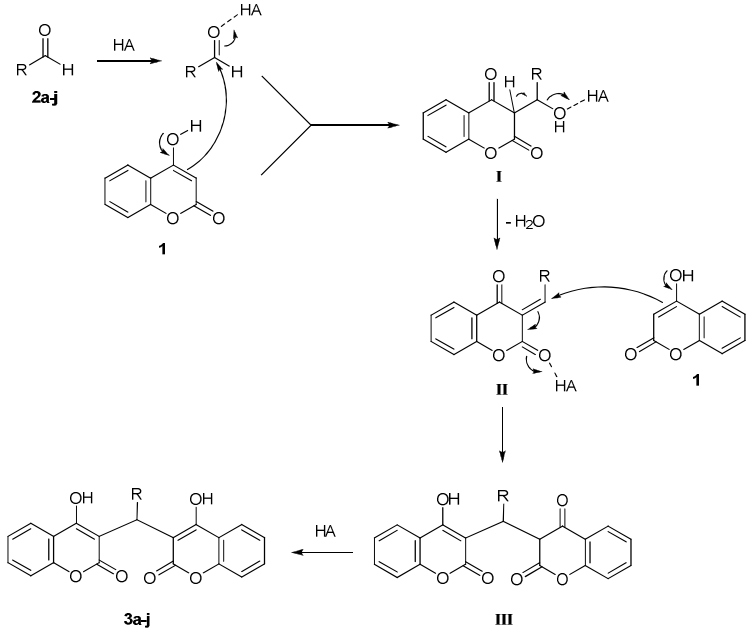


Fig. 1. Effect of recycling on catalytic performance SCM in the synthesis of 3c in model reaction

In the interests of green chemistry and developing an environmentally benign process, the reusability of the catalyst was explored using the model reaction system under the optimized conditions. After the completion of the reaction, the catalyst was readily recovered from the reaction mixture by a simple filtration. In this catalyst, SO_3H groups have been covalently bound to the polycyclic aromatic carbon sheets. Thus, the catalyst has high stability and could behave as a recyclable solid catalyst without the danger of leaching that is observed in most supported catalysts. The separated catalyst was washed with cold ethanol and subsequently dried at 60 °C under vacuum for 1 h before being

reused in a similar reaction. We found that the catalyst could be used at least four times without significant reduction in its activity (Fig. 1).

A plausible mechanism for the formation of the biscoumarins using SCM as a catalyst has been depicted in Scheme 2. It is proposed that the SCM ≡ HA facilitates the formation of the intermediates **I**, **II**, **and III**. Under the reaction conditions, attempts to isolate these intermediates failed even after careful monitoring of the reactions.



Scheme 2. Plausible mechanism for the formation of biscoumarins in the presence of SCM ≡ HA as catalyst

CONCLUSION

In conclusion, we have developed a mild and simple method for the synthesis of biscoumarins using SCM as an efficient heterogeneous organic catalyst. The catalyst can be reused after a simple work-up, with a gradual decline of its activity being observed. Good to high yields, short reaction times, simplicity of operation and easy work-up are some advantages of this protocol.

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