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Research Article

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Nano-SnO_2 as a novel and efficient catalyst for the synthesis of 3-acyl-coumarin derivatives

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ABSTRACT

3-Acyl-coumarins were obtained in high yields from ortho-hydroxybenzaldehydes and ethyl acetoacetate or ethyl benzoylacetate in acetonitrile in the presence of a catalytic amount of nano-SnO_2.

Keywords: 3-Acyl-coumarins, nano catalyst, ethyl acetoacetate, one-pot

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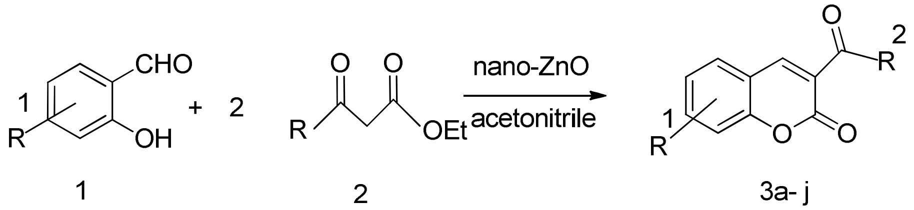
INTRODUCTION

Coumarin and its derivatives form an elite class of compounds, occupying an important position in the realm of natural products and synthetic organic chemistry.[1] 3-Acyl-coumarins are important initial compounds for the synthesis of coumarins, which has attracted considerable attention from organic and medicinal chemists for many years as a large number of natural products contain this heterocyclic nucleus. Their applications range from additives in food, perfumes, cosmetics, pharmaceuticals to the preparation of insecticides,[1] optical brighteners[2] and dispersed fluorescent and tunable laser dyes.[3] Also, coumarins have varied bioactivities, for example, inhibition of platelet aggregation,[4] anticancer[5] and inhibition of steroid 5α-reductase.[6] Their properties turn coumarins very interesting targets to organic chemists, and several strategies for their synthesis were already developed. The last decade witnessed a series of publications on the development of synthetic protocols for this important heterocyclic scaffold. Thus, it is clearly evident that the need for the development of new and flexible protocols is required.

Coumarins can be synthesized by various methods such as Pechmann,[7] Perkin,[8] Knoevenagel,[9] Reformatsky[10] and Witting[11] reactions. In 1898, Knoevenagel described the solution phase synthesis of coumarins by the condensation of malonic acid with *ortho*-hydroxyarylaldehydes.[9a] In our attempts to develop new catalyst systems, herein, we describe the use of this Knoevenagel condensation reaction to prepare 3-Acyl-coumarins in a mild and facile manner in the presence of a catalytic amount of nano-SnO_2 in high yields (Scheme 1).



Scheme 1

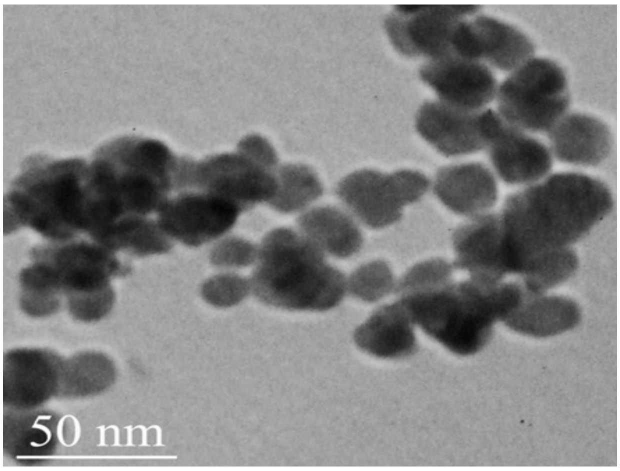
EXPERIMENTAL SECTION

Chemical and apparatus

All products are known compounds and were characterized by mp, IR, ^{1}HNMR and GC/MS. Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. ^{1}HNMR spectra were recorded on a Bruker AQS AVANCE-300 MHz spectrometer using TMS as an internal standard ($CDCl_3$ solution). IR spectra were recorded from KBr disk on the FT-IR Bruker Tensor 27. GC/MS spectra were recorded on an Agilent Technologies 6890 network GC system and an Agilent 5973 network Mass selective detector. Thin layer chromatography (TLC) on commercial aluminum-backed plates of silica gel, 60 F254 was used to monitor the progress of reactions. All products were characterized by spectra and physical data.

Preparation of catalyst

20 g $SnCl_4.5H_2O$ and 9 g NaOH were mixed in an agate mortar, and then ground at room temperature for 5~10 min. The mixture was washed with a large quantity of distilled water to remove Cl^-, dried at room temperature in vacuum for 3 h, and then calcined at 400°C. The dimensions of applied SnO_2 nanoparticles were determined with TEM (Fig.1).



TEM image of nano-SnO_2

General procedure for the synthesis of 3-acyl-coumarins

A mixture of *ortho*-hydroxybenzaldehyde (1 mmol) and Ethyl acetoacetate or Ethyl benzoylacetate (1 mmol) and nano-SnO_2 (0.02 g) in acetonitrile (5 mL) was stirred at room temperature for 1.5 h. The progress of the reaction was monitored by TLC using EtOAc: hexane (1:2) as eluent. After completion of the reaction, the catalyst was filtered and the solvent was evaporated. The residue was recrystallized from ethanol to give the pure product. mp. 123 (Lit. 121/122 [20])

3a: IR (KBr): 1712, 1657, 1623, 1567, 1455, 1240, 1220, 980, 756 cm^{-1}; ^{1}HNMR ($CDCl_3$, 500 MHz): δ=2.76 (s, 3H, CH_3), 7.35~7.39 (m, 2H, Ar-H), 7.60~7.68 (m, 2H, Ar-H), 8.43 (s, 1H, CH).

3e: IR (KBr): 1746, 1670, 1611, 1500, 1357, 1200, 980, 831, 765 cm^{-1}; ^{1}HNMR ($CDCl_3$, 500 MHz): δ=2.77 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 6.76 (d, J=2.30 Hz, 1H, Ar-H), 6.88 (q, J=3.70 Hz, 1H, Ar-H), 7.46 (d, J=8.70 Hz, 1H, Ar-H), 8.41 (s,1H, CH).

Reusability of nano- SnO_2

Next, we investigated the reusability and recycling of nano-SnO_2. At the end of the reaction, the catalyst could be recovered by a simple filtration. The recycled catalyst could be washed with methanol and subjected to a second run of the reaction process. To assure that catalysts were not dissolved in acetonitrile, the catalysts were weighted after filteration and before using and reusing for the next reaction. The results show that these catalysts are not soluble in acetonitrile. In Table 3, the comparison of efficiency of nano- SnO_2 in synthesis of 3a after five times is reported. As it is shown in Table 1 the first reaction using recovered nano- SnO_2 afforded similar yield to those obtained in the first run. In the second, third, fourth and fifth runs, the yield were gradually decreased.

Table 3. Reuse of the nano-SnO_2 for synthesis of 3-acetyl counarin (3a)

Entry	Time(h)	Yield/%[a]
1	1.5	98
2	2	95
3	3	92
4	4	83
5	4.5	80

(a) Isolated yields

RESULTS AND DISCUSSION

In this paper, we decided to investigate the Knoevenagel condensation reaction to prepare 3-acyl-coumarins, then we set out for the synthesis of coumarins via condensation of *ortho*-hydroxybenzaldehydes with ethyl acetoacetate or ethyl benzoylacetate using nano- SnO_2 as an efficient catalyst at room temperature (Scheme 1). To investigate the generality of this process, various salicylic aldehydes were reacted under similar conditions, allowing the easy synthesis of 3-acyl-coumarins in good yields (Table 1). This one-pot procedure is convenient and straightforward with simple product isolation. From Table 1, it can be observed that the reactions proceeded faster than the conventional methods and the yields were comparable.

It is known that, the specific surface area and surface-to-volume ratio increase dramatically as the size of a material decreases. The high surface area brought about by nanoparticle size is beneficial to many SnO_2-based devices, as it facilitates reaction/interaction between the devices and the interacting media. The previous research works on SnO_2 were reported by Seiyama[12] in 1962 as semiconductor materials for gas sensor materials and alternative energy. Its outstanding electrical, optical an delectro-chemical properties of SnO_2 enable applications in solar cells, catalytic support materials, transparent electrodes, and solid state chemical sensors. They were successfully synthesized by different methods. Various methods, including molten-salt synthesis[13] sol–gel[14], microwave technique[15], carbothermal reduction[16], chemical precipitation[17], laser-ablation synthesis[18], hydrothermal method[20], and sonochemical[21]have been developed to synthesize SnO_2 nanostructures. The investigation on nano-SnO_2 catalytic activity for the synthesis of many organic molecules is current work in our laboratory.

Table 1 Synthesis of 3-acyl-coumarins in the presence of nano- SnO_2 as a catalyst

Entry	R^1	R^2	Product	Yield(%)[a]
1	H	CH_3	3a	98
2	3-hydroxy	CH_3	3b	98
3	4-hydroxy	CH_3	3c	98
4	5-bromo	CH_3	3d	96
5	4-methoxy	CH_3	3e	98
6	H	Ph	3f	95
7	3-hydroxy	Ph	3g	96
8	4-hydroxy	Ph	3h	96
9	5-bromo	Ph	3i	93
10	4-methoxy	Ph	3j	95

To show the merits and advantages of using nano-SnO_2 as a catalyst, our method is compared with reported reactions (Table 2). The reaction results without catalyst decrease and the reaction time increases. This method is suitable for *ortho*-hydroxy benzaldehydes but the *ortho*-hydroxyaryl ketones were recovered and unchanged after the reaction.

We performed the effect of various solvents on the synthesis of 3a. This reaction was carried out in various solvents and the best results in terms of yield and time obtained in acetonitrile (Table 2). The effect of temperature was studied by carrying out the reactions at different temperatures. The yields of reactions increased as the reaction temperature was raised. From these results, it was decided that refluxing temperature would be the best temperature for all reactions.

Table 2 Comparison of various catalysts for the synthesis of 3-acetyl-coumarin (3a)

Entry	Catalyst	Time	Yield(%)	Reference
1	nano- SnO_2	1.5h	98	This article
2	$H_{14}[NaP_5W_{30}O_{110}]$	2h	98	22
3	Piperidinium acetate	2h	89	23
4	none	10h	90	24
5	Piperidine	2h	50	25
6	[bmIm]OH	15min	88	26

Table 2. Synthesis of 3a in the presence of different solvents using nano- SnO_2 as a catalyst

Entry	Solvent	Time(h)	Yield(%)^a
1	THF	2	68
2	CH_3OH	2	93
3	CH_3CN	2	98
4	$CHCl_3$	2	75
5	Solvent-free	2	90
6	C_2H_5OH	2	90

^{a}*Yields were analyzed by GC*

CONCLUSION

In conclusion, we have developed a simple and efficient synthesis of 3-acyl-coumarins via Knoevenagel condensations in high yields and selectivity's from *ortho*-hydroxy benzaldehydes using nano- SnO_2 as a catalyst under mild conditions at room temperature. Moreover the fast reaction time, simple experimental procedure, recyclability of the catalyst and high yields of the products are the advantages. We believe our procedure will find important applications to the synthesis of coumarins.

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