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Starch containing ZnO nanoparticles as a highly effective heterogeneous catalyst for the synthesis of coumarins under solvent-free conditions

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ABSTRACT

Coumarins were synthesized through one-pot reactions using starch containing ZnO nanoparticles as an efficient reusable catalyst under solvent-free conditions. The catalyst is inexpensive and readily available, stableand storable, easily recycled and reused for several cycles with consistent activity. The procedure offers advantages in terms of high yields, short reaction times, and mild solvent-free reaction conditions.
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KEYWORDS

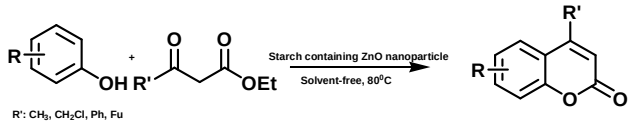
Coumarin;
Heterogeneous catalyst;
Starch;
ZnO nanoparticles;
Solvent-free.

INTRODUCTION

Coumarin and its derivatives are the important class of naturally occurring oxygen heterocyclic compounds having a distinct and important place in the realm of natural and synthetic organic chemistry as these compounds display useful and diverse biological properties, viz. antibacterial, antiviral, anticancer, anti-HIV[1-3], and also have been used as additives in food, cosmetics, optical brightening agents, and laser dyes[4-6]. Due to these applications and properties, a variety of methods have been developed to synthesize coumarins[7-11]. Despite these developments, the Pechmann reaction, a two-component (activated phenols and β-ketoesters) coupling under homogeneous acid catalysis, is a very well established method for the preparation of substituted coumarin rings[12-24]. However, this reaction usually involves the use of non-reusable homogeneous BrØnsted, Lewis, and mineral acids in an excess amount are necessary in the classicalpreparations, resulting in environmental pollution.

With the commencement of the modern era, a shift in emphasis in green chemistry is apparent with the desire to develop more environmental friendly routes to a myriad of materials. This shift has become more evident with the growth of nanotechnology[25]. Recently, mineral oxides have proved to be useful to chemists in the laboratory and industry due to the good activation of adsorbed compounds and reaction rate enhancement, selectivity, easier work-up and recyclability of the supports and the eco-friendly, green, reaction conditions[26-31].Green chemistry emphasizes the development of environmentally benign chemical processes and technology[32-33]. Recently, the direction of science and technology has been shifting toward more eco-friendly, natural product resources and reusable catalysts. Natural biopolymers are attractive candidates in the search for solid support catalysts[34-35]. It was therefore thought worthwhile to develop a new and mild method using an

inexpensive biopolymer-based catalyst that can be easily separated, reused, and is not contaminated by the products. Immobilization of catalysts on solid support improves the available active sites, stability, hygroscopic properties, handling, and reusability of catalysts, all factors that are important in industry[36]. Herein we wish to report the preparation of starch containing ZnO nanoparticles as a stable, highly active and reusable heterogeneous catalyst in the Pechmancoumarin synthesis (Scheme 1).



Scheme 1

EXPERIMENTAL

Starting materials used in the reactions were procured from Aldrich or Merck Chemical Co. Thermal gravimetric (TGA) analyses were performed using air as the oxidant at the heating rate of 2 °C/min on a Shimadzu TGA-50 system. X-ray powder diffraction (XRD) measurements were performed using an X'pert diffractometer of Philips company with monochromated Cuk_{α} radiation (λ = 1.54056 Å).The samples were characterized with a scanning electron microscope (SEM) (Philips XL 30) with gold coating.Melting points of all products were determined in open glass capillaries on a Mettler 9100 melting point apparatus. Infrared (IR) spectra were recorded by use of a 4300 Shimadzu FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Bruker 400-MHz spectrometer. Elemental analysis was performed on a Heraeus CHN Rapid analyzer. Most of the products were characterized by comparison of their melting points and IR and ^{1}H NMR spectra with those of authentic samples.

The ZnO nanoparticles were synthesized by the precipitation of zinc hydroxide in aqueous solution using

$Zn(OAc)_2{\cdot}6H_2O$ as salt and sodium hydroxide (NaOH) as the precipitating agent.First, 0.1 mol/L Zinc acetate solution was prepared by dissolving $Zn(OAc)_2{\cdot}6H_2O$ in deionized water.The pH of 100 ml deionized water was adjusted to 13.2 by the addition of sodium hydroxide (3M), After completion of the precipitation procedure, the $Zn(OH)_2$gel was transferred into the Milestone microwave oven (Micro SYNTH) operated at 350 W for 15 min. During the microwave irradiation, the temperature of the solution reached 80°C. The resulting precipitate was then cooled to room temperature, filtered, and washed with deionized water more than five times. The solid obtained was dried at 120 °C for 1 h to give the final product.In a typical procedure, starch (1 g) was added to a suspension of nanoparticles of ZnO (0.54 g) in dichloromethane (DCM) (20 mL). The mixture was stirred at room temperature overnight. Then the solvent was removed under reduced pressure and the residue was heated at 100 °C under vacuum for 5 h to furnish starch containing ZnO nanoparticles.

Typical experimental procedure for the synthesis of coumarins

A mixture of phenol (1 mmol), β-ketoester (1 mmol) and starch containing ZnO nanoparticles (0.1 g) was ground and heated to 80ºC. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and extracted with EtOAc (2×5mL).The solution was concentrated and the crude product was recrystallized from ethanol yielding each of purecoumarins.All the coumarin derivatives are well known in literature and were identified by comparison of their physical and spectral data.

4-(Chloromethyl)-5, 7-dihydroxy-2H-chromen-2-one(2)

^{1}H NMR (250 MHz, DMSO-d_6): 5.11 (s, 2H, CH_2Cl), 6.25 (d, J = 2.60, 1H, ArH), 6.29(d, J = 2.60, 1H, ArH), 6.35 (s, 1H, C=CH), OH not observed, IR (KBr): 3157, 1655 cm^{-1}. EIMS: m/z: 226 (M^+).

5, 7-Dihydroxy-4-phenyl-2H- chromen-2-one(3)

^{1}H NMR (250 MHz, DMSO-d_6): 5.74 (s, 1H, C=CH), 6.15 (d, J = 2.55, 1H, ArH), 6.26 (d, J = 2.55, 1H, ArH),7.31–7.38 (m, 5H, ArH), OH not observed, IR (KBr): 3155, 1660 cm^{-1}. EIMS: m/z:255.

5, 7-Dihydroxy-4-trifluoromethyl-2H-chromen-2-one(4)

^{1}H NMR (250 MHz, DMSO-d_6): 6.24 (d, J = 2.62, 1H, ArH), 6.34 (d, J = 2.62, 1H, ArH), 6.50 (s, 1H, C=CH), OH not observed, IR (KBr): 3158, 1665 cm^{-1}. EIMS: m/z: 246 (M^+).

7-Hydroxy-4-methyl-2H-chromen-2-one(5)

^{1}H NMR (250 MHz, DMSO-d_6): 2.65 (s, 3H, Me), 6.41 (s, 1H, C=CH), 6.91–7.72 (m, 3H, ArH), ArH 3155, 1690 cm^{-1}. EIMS: m/z: 176 (M^+)

7-Methoxy-4-methyl-2H-chromen-2-one(8)

^{1}H NMR ($CDCl_3$): 2.59(s, 3H, Me), 4.22 (s, 3H, OMe), 6.51 (s, 1H, C=CH), 7.01–7.51 (m, 3H, ArH), IR, (KBr): 1685 cm^{-1}. EIMS: m/z: 190 (M^+).

7, 8-Benzo-4-methyl-2H-chromen-2-one(12)

^{1}H NMR ($CDCl_3$): 2.71 (s, 3H, Me), 6.51 (s, 1H, C=CH), 7.50–8.91 (m, 6H, ArH), IR, (KBr): 1675 cm^{-1}. EIMS: m/z: 210 (M^+).

RESULTS AND DISCUSSION

Characterization results of the ZnO nanoparticles

TGA analysis of the zinc hydroxide were investigated by raising its temperature at the rate of 2 °C/min in air up to 720°C to analyze it's thermal decomposition behavior. Figure 1 shows the TGA curves of the as-prepared zinc hydroxide. One main stage of mass loss was observed. The strong peak observed at 415 °C in the derivative thermogram can be attributed to the decomposition of Zn(OH)2 to ZnO. The observed mass loss at 415 °C was 13%, which was in good agreement with the nominal value for the Zn(OH)2 to ZnO transformation (18%).

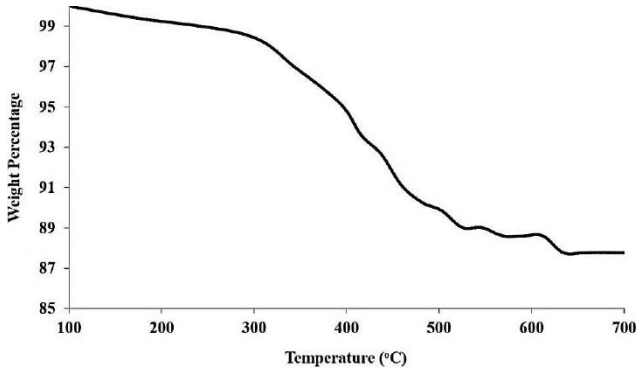


Figure 1 : TGA curves of $Zn(OH)_2$

The XRD pattern of the ZnO sample is presented in Figure 2. All the peaks in Figure 2 could be indexed to cubic ZnO crystallites. No peak arising from an impurity was observed in Figure 2. The average particle size in the ZnO nanoparticles was estimated by the Debye-Scherrer equation[37]: $D = k\lambda/\beta\cos\theta$, where D is the crystal size, k is the shape factor, which usually takes a value of about 0.9[38], λ is the wavelength of X-ray source used, β is the full width at half-maximum (FWHM), and θ is the Bragg diffraction angle. The average particle size of ZnO particles was estimated to be 28 nm (Figure 2). The SEM image of the ZnO nanoparticles is shown in Figure 3.

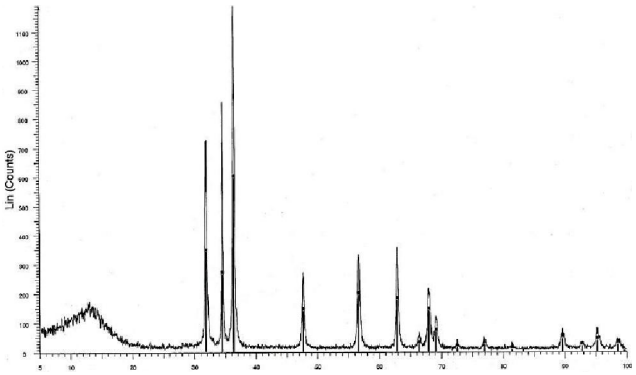


Figure 2 : XRD pattern of starch containing ZnO nanoparticles

Figure 3 : SEM image of starch containing ZnO nanoparticles.

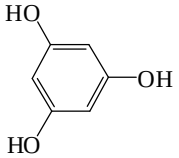
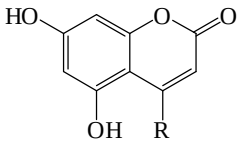
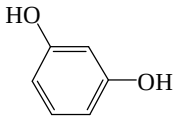
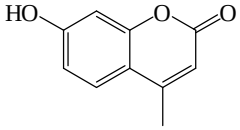
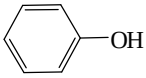
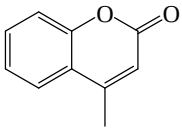
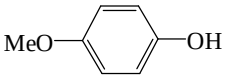
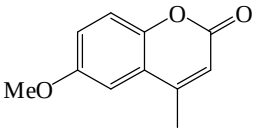
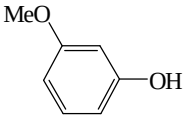
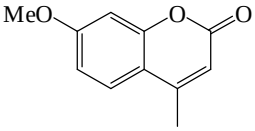
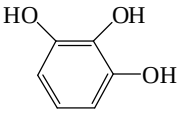
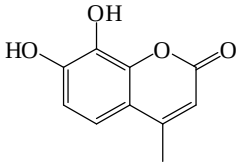
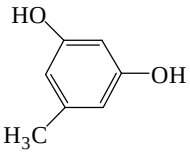
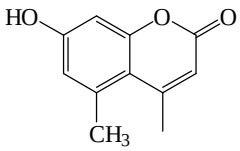
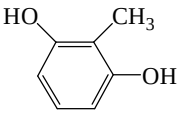
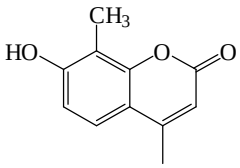
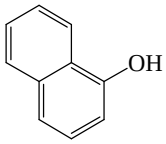
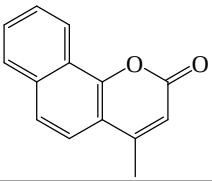
TABLE 1 : Effect of different amounts of starch containing ZnO nanoparticlesand solvents on formation of 7-hydroxy-4-methyl-2H-chromen-2-one[a]

Entry	Starch Containing ZnO (g)	Condition/solvent	Time (min)	Yield (%)[b]
1	0	80 °C/solvent free	120	30
2	0.05	80 °C/solvent free	120	65
3	0.10	80 °C/solvent free	10	90
4	0.10	Reflux/ EtOH	30	70
5	0.10	Reflux/ H_2O	30	75
6	0.10	Reflux/ $CHCl_3$	60	40
7	0.10	Reflux/ CH_3CN	120	55

[a]Reaction conditions: resorcinol (1 mmol), ethyl acetoacetate (1 mmol), 80°C, solvent-free.; [b]Isolated yield.

In order to evaluate the catalytic efficiency of the ZnO nanoparticleson the Pechmann condensationand to determine the most appropriate reaction conditions, initially a model study was carried out on the synthesis of compound 4by the cyclocondensation of resorcinol (1 mmol) and ethyl acetoacetate (1 mmol) under differ-

TABLE 2 : Starch containing ZnO nanoparticlescatalyzed synthesis of coumarins[a]

Entry	Substrate	Product	Time (min)	Yield[b] (%)	Mp(^{0}C) (found)	Mp(^{0}C) (reported)
						
1		R= CH_3	10	95	274-276	280-281
2		R= CH_2Cl	15	85	178-180	187–189
3		R= Ph	15	78	239-241	243–246
4		R= Furyl	20	70	244-246	254–255
5			5	90	180-182	185-187
6			25	80	76-78	78–80
7			15	75	160-162	164–166
8			10	92	170-172	171
9			10	90	236-238	241–243
10			10	85	248-250	256–257
11			15	82	258-260	263-265
12			20	80	150-152	154–156

[a]*Reaction conditions: phenol (1 mmol), β-ketoesters (1.1 mmol), starch, ZnO nanoparticles (0.1 g) and 80°C.;* [b]*Isolated yield.*

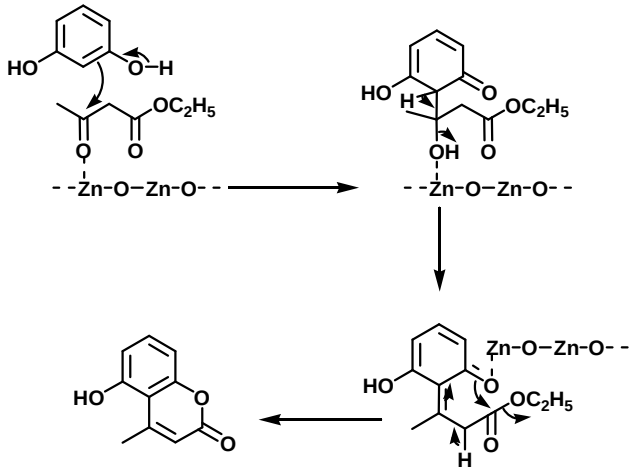
ent sets of reaction conditions (TABLE 2). With the various solvents of EtOH,H_2O, $CHCl_3$, $CH_3CN$and also under solvent-free conditions, and with various amounts of the catalyst, the reaction was faster and proceeded to give the highest yield with 0.1 g ofstarch containing ZnO nanoparticles under solvent-free conditionsin at 80°C (entry3).

To study substituent effects on the reactivity of the phenol, the reactions were performed on a variety of phenols. The reactions worked well and the results are illustrated in TABLE 2. Substrates having electron-donating groups in parato the site of electrophilic substitution gave maximum yields at 80°C in the minimum time. Methoxyphenols (entries 7, 8) showed no detectable demethylation under the given conditions. Simple phenol without any substituents (entry 6) required longer reaction duration, as no electron-donating group is present. Similarly, 1-naphthol (entry 12) requires longer reaction time, due to the presence of another phenyl ring. To generalize the protocol, we also attempted the condensation reaction using a further variety of β-ketoesters such as ethyl 4-chloroacetoacetate, ethyl benzoylacetate and ethyl furoacetate (TABLE 3). In all these cases, good yields of the corresponding coumarin derivatives were obtained.

The reusability of the catalyst was also investigated.

TABLE 3 : Recyclability ofstarch containing ZnOnanoparticles

Run	1	2	3
Time (min)	5	10	10
Yield (%)	90	88	80



Scheme 2 : Plausible mechanism for the catalytic activity of starch, ZnO nanoparticles

For this purpose, the same model reaction was again studied under the optimized conditions. After the completion of the reaction, the catalyst was recovered using the procedure described in the experimental section and reused for the reaction. The catalyst could be used at least three times with only a slight reduction in the catalytic activity (90% yield for 1st use; 88% for 2nd use; 80% for 3rd use).

A reaction mechanism is proposed in scheme 2. In ZnO nanoparticles, there are acid-base bifunctional sites where Zn and O act as a weak Lewis acidic site and relatively high strength Brönsted basic site, respectively.

CONCLUSIONS

In conclusion, we describe a mild and convenient method for the preparation of some coumarins by the Pechmann cyclocondensation reaction of phenols and β-ketoesters using cheap, non-toxic, recyclable, and easily available and support biodegradable catalyst under solvent-free conditions. Additionally, this new reaction might be a useful tool for high-throughput organic synthesis.

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