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ORIGINAL PAPER

Poly(4-vinylpyridine)-supported sulfuric acid: an efficient solid acid catalyst for the synthesis of coumarin derivatives under solvent-free conditions

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Abstract Poly(4-vinylpyridine)-supported sulfuric acid is an efficient catalyst for the Pechmann condensation of acetoacetic esters with phenols, leading to the formation of coumarins in good yields within a few minutes under solvent-free microwave conditions. The catalyst used can be recovered and reused after activation.

Keywords Pechmann reaction · Solid acid · Coumarin · Polymer support · Solvent-free

Introduction

Coumarins are important naturally occurring plant constituents, many of which exhibit a broad spectrum of biological activity [1–4], e.g., antitumor, anti-HIV, antioxidation, anticoagulant, and antimicrobial activity, as well as inhibition of steroid 5α-reductase and platelet aggregation. In addition, coumarins are widely used as additives in food and cosmetics, dispersed fluorescent, optical brighteners, and tunable laser dyes [1–7]. Coumarins can also be used for the synthesis of various products such as chromenes, fluorocoumarin, coumarones, and 2-acylresorcinol [8].

Many synthetic routes have been developed for the synthesis of coumarins, including Pechmann, Perkin, Knoevenagel, Reformatsky, and Wittig reactions [9–13]. The Pechmann reaction is one of the most widely employed methods, as it involves the use of simple starting materials, that is a β-ketoester and phenol (Scheme 1), in the presence of a variety of Lewis [14–19] or Brønsted acid catalysts [20–22] such as $FeCl_3$, ZnI_2, $AlCl_3$, $TiCl_4$, $Bi(NO_3)_3$, I_2, H_2SO_4, CF_3COOH, and $HClO_4$. However, most of the methods using strong acid catalysts [20–22] involve high temperature reaction conditions, prolonged reaction times, use of excess catalyst, environmental pollution from organic solvents, non-recycling of catalysts, side product formation, and complicated product purification. For example sulfuric acid requires ten to twelve equivalents [20] and trifluoroacetic acid needs three to four equivalents [21] to complete the reaction. The disposal of toxic and corrosive acidic waste leads to environmental pollution. Many cleaner and safer methods have therefore been developed for the Pechmann reaction using ionic liquid [23, 24], microwave irradiation [25–27], and solid acid catalysts [28, 29]. However, there is scope for the development of milder reaction conditions for the Pechmann reaction using eco-friendly and reusable solid acid catalysts.

Polymer-supported catalysts have major advantages: the physical separation of the supported catalyst from the substrates and products is trivial, thereby allowing the recycling of expensive or toxic catalysts; and thus less waste material is released to the environment. The potential use of polymer-supported reusable solid catalysts in organic transformations makes reaction methods more convenient, safer, and environmentally benign [30]. Poly(4-vinylpyridine) seems an attractive support to immobilize acidic dopants because of the basic nature of the pyridyl group [31]. In continuation of our previous work on poly(4-vinylpyridine)-supported acid catalysts [32], herein, we report the successful synthesis of coumarins via Pechmann reaction under solvent-free microwave irradiation using poly(4-vinylpyridine)-supported sulfuric acid ($P4VP–H_2SO_4$) as reusable catalyst.

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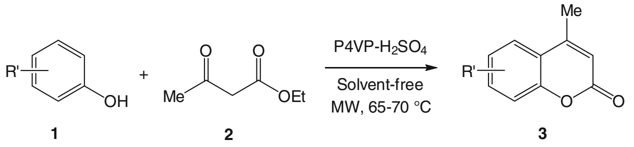


Scheme 1

Results and discussion

In contrast to conventional methods, this report describes the use of only 0.2 equivalents of P4VP–H_2SO_4 as acid catalyst for the Pechmann reaction under solvent-free microwave conditions without forming any side product. The catalyst P4VP–H_2SO_4 was prepared by a simple wet impregnation method [32]. The amount of acid groups present in the polymeric chain was calculated based on the weight of supported polymer salt obtained and the weight of poly(4-vinylpyridine) used. The amount of dopants present in the P4VP–H_2SO_4 was found to be 0.652 mol%. The characterization of the polymer-supported catalyst so formed was done by Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), thermogravimetric analysis (TGA), and energy dispersive X-ray analysis (EDX) studies [32]. P4VP–H_2SO_4 is relatively non-toxic, safe to handle, and reused after reactivation, which makes the synthetic process more economical and benign.

To study the feasibility of the P4VP–H_2SO_4-catalyzed Pechmann reaction, resorcinol (1 mmol) and ethyl acetoacetate (1 mmol) were irradiated using microwave energy in the presence of P4VP–H_2SO_4 catalyst under solvent-free conditions. The best result was obtained with 0.2 equivalents of catalyst at 560-W microwave power (Table 1, entry 1) at 65 °C (Catalyst System microwave reactor). An increase in the catalyst to 0.5 equivalents showed no significant improvement in yield (entry 2), though a slight improvement in reaction time was observed. We therefore selected 0.2 equivalents of acid as the standard amount to generalize this protocol, and applied these conditions to structurally diverse monohydric and polyhydric phenols to obtain the corresponding coumarins in good to moderate yields (Table 1). The results showed that this method is effective for both electron-rich and electron-poor phenols. The reaction of catechol with acetoacetic ester afforded a good yield of coumarin (entry 4), whereas most of the reported protocols failed to produce the corresponding product [14–22]. Heravi et al. [33] carried out the Pechmann reaction of catechol at 130 °C during a 1.7-h reaction period using sodium 30-tungstopentaphosphate as catalyst. Interestingly, resacetophenone reacts efficiently in the presence of the supported sulfuric acid catalyst under solvent-free conditions (entry 12), but by the conventional method using liquid sulfuric acid it did not give any coumarin product [20]. With the supported catalyst, the reaction of 4-nitrophenol with acetoacetic ester yielded only 50% product within a 20-min reaction time (entry 16).

The catalyst was separated by simple filtration, washed with organic solvent, and reactivated by treatment with sulfuric acid in diethyl ether; in this manner, the catalyst can be recycled three times without signifcant loss of catalytic activity (Table 2). The reactivation of the catalyst is necessary because it loses some amount of sulfuric acid above 80 °C [32]. The reaction temperature varied within the range of 65–70 °C at 560-W microwave power depending on the polarity of the substrate molecules.

Conclusion

We have successfully demonstrated the catalytic activity of P4VP–H_2SO_4 as a simple, eco-friendly, and efficient supported solid acid catalyst for the synthesis of a variety of coumarins under solvent-free microwave irradiation.

Experimental

All chemicals are commercially available and were used without further purification. The products were identified by comparison of their FT-IR, ^{1}H, and ^{13}C NMR spectroscopic data and CHN analysis data with those of authentic compounds (prepared by a known method) and literature data [14–22, 34–38].

Preparation of catalyst P4VP–H_2SO_4

Poly(4-vinylpyridine) (500 mg) and 0.6 cm^3 sulfuric acid were stirred in 5 cm^3 diethyl ether at room temperature for 15 min. The solid catalyst was filtered and washed with diethyl ether three times. The catalyst was dried at 70 °C for 2 h and stored in a vacuum desiccator until use.

Typical procedure for the synthesis of coumarin derivatives under microwave irradiation

Acetoacetic ester (1 mmol) and phenol (1 mmol) were mixed thoroughly and 0.2 mmol P4VP–H_2SO_4 was added. The reaction mixture was irradiated in a microwave reactor (Catalyst System) at a temperature of 65 °C and 560-W power for the specified time. After completion of the reaction, as indicated by TLC, the reaction mixture was cooled to room temperature and ethanol was added in order to recover the insoluble catalyst by filtration. The product was purified by column chromatography using ethyl acetate and hexane as solvent system. The recovered catalyst was dried and reactivated through treatment with sulfuric

Table 1 P4VP–H_2SO_4-catalyzed Pechmann reaction under solvent-free microwave irradiation

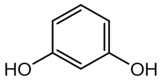
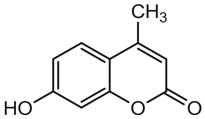
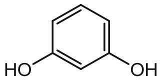
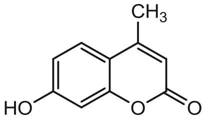
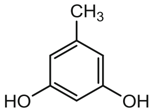
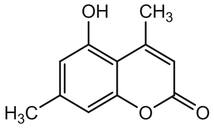
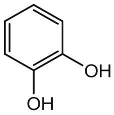
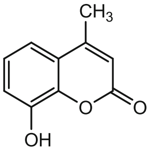
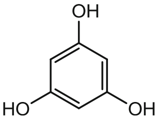
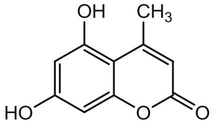
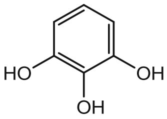
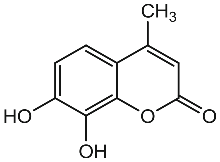
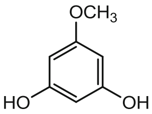
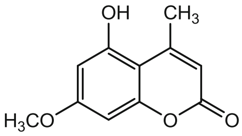
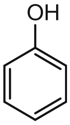
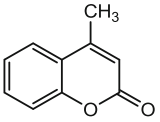
Entry	Phenol	Product		Time/min	Yield/%	M.p. (lit. m.p.)/°C
1			**3a**	7	85	182–184 (183–184 [19])
2			**3a**	5	86	182–184
3			**3b**	10	86	257 (257–258 [34])
4			**3c**	12	77	Semi-solid [33]
5			**3d**	9	85	284–285 (282–284 [34])
6			**3e**	10	84	241–243 (242–244 [35])
7			**3f**	12	83	117–120 (118–120 [19])
8			**3g**	15	71	82–83 (83–84 [19])

Table 1 continued

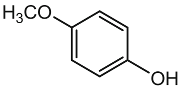
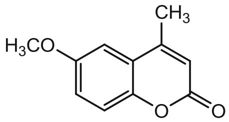
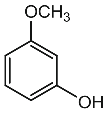
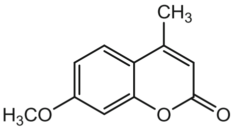
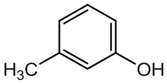
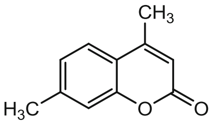
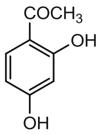
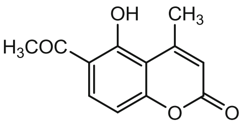
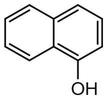
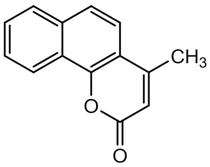
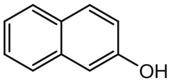
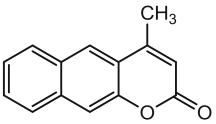
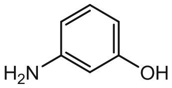
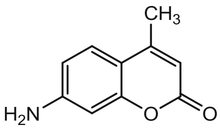
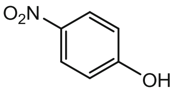
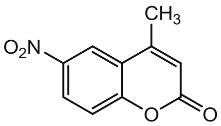
Entry	Phenol	Product		Time/min	Yield/%	M.p. (lit. m.p.)/°C
9			**3h**	10	77	164–166 (163–165 [35])
10			**3i**	12	75	160–161 (160–162 [36])
11			**3j**	12	78	130–132 (133–134 [37])
12			**3k**	15	73	163–165 (164–165 [19])
13			**3l**	15	71	152–154 (155 [24])
14			**3m**	15	70	182–183 (183–184 [19])
15			**3n**	14	75	222–223 (221–224 [19])
16			**3o**	20	50	152–154 (151–154 [34])

Table 2 Recycling of P4VP–H_2SO_4-catalyzed reaction of resorcinol with acetoacetic ester under solvent-free microwave irradiation

Entry	Time/min	Number of cycles	Yield of **3a**/%[a]
1	7	1	85
2	7	2	85
3	7	3	84

[a] The reaction was carried out on a 1-mmol scale with a 1:1:0.2 molar ratio of resorcinol/acetoacetic ester/catalyst

acid in diethyl ether solution. The catalyst was filtered, washed with ether, and reused after drying at 70 °C in an oven.

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