

Catalytic activity of Keggin heteropolycompounds in the Pechmann reaction

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Abstract

Different heteropolycompounds were used as catalysts in the synthesis of coumarins from phenols and ethyl acetoacetate. The $H_3PMo_{12}O_{40}$ and $H_3PW_{12}O_{40}$ Keggin heteropolyacids were supported on different types of silica. On the other hand, the aluminium salts of these heteropolyacids and that of the $H_4SiW_{12}O_{40}$ acid were prepared. The specific surface area (S_{BET}), and the mean pore diameter of the obtained catalysts were estimated from the adsorption isotherms of nitrogen at 77 K. Their Fourier transform infrared spectra were recorded and their acidity was determined by potentiometric titration with a solution of *n*-butylamine in acetonitrile. The catalytic activity using several phenols such as resorcinol, 3,5-dimethoxyphenol, α -naphthol and β -naphthol were determined. High yield of product was obtained in the case of 4-methyl-7-hydroxycoumarin (80–95%), 4-methyl-5,7-dimethoxycoumarin (60–92%) and 4-methyl-7,8-benzocoumarin (90%). However, the 4-methyl-5,6-benzocoumarin yield was low. The use of microwave radiation as power source increases the reaction yield and mainly decreases the reaction time. © 2008 Elsevier B.V. All rights reserved.

Keywords: Catalysts; Keggin heteropolycompounds; Pechmann reaction

1. Introduction

Coumarin is the parent organic compound (Scheme 1) of a family of naturally occurring phytochemicals found in many plant species, including lavender, sweet clover, strawberry, apricot, cherry and cinnamon. The oxygen of the heterocycle is best known for its fragrance, described as a vanilla-like odour or the aroma of freshly mowed hay. It is also used to prepare other chemicals, in particular antioxidants [1], anticoagulants and rodent poison, such as warfarin or insecticides such as hymecromone. The anti-inflammatory activity is usually associated with their capability of modulating the inflammatory cells [2].

Identified in the 1820s, coumarin has been synthesized in the laboratory since 1868 and used to make perfumes and flavours [3]. There are many synthetic routes to obtain coumarins, such

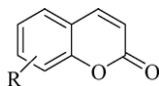
as Pechmann [4], Perkins [5], Knoevenagel [6,7], Reformasky [8] and Wittig [9–12] reactions. However, Pechmann reaction has been the most useful due to the good yields and simple starting materials by condensation of substituted phenols with β -ketonic esters in acidic medium. A probable mechanism for the Pechmann condensation is shown in Scheme 2 [4].

Several acidic reagents have been used for this reaction, e.g. different Brønsted acid such as H_2SO_4 , HCl, H_3PO_4 [4] and F_3CCO_2H [13], or Lewis acids such as $ZnCl_2$, $FeCl_3$, $TiCl_4$ and $AlCl_3$ [4–12]. These conventional acids have been extensively used, but they have unfavourable properties such as decomposition, operating corrosion problems, difficulties in workup, not to mention the production of toxic wastes that damage the environment.

The replacement of the classical homogeneous acid catalysts by acid solids is attempted, due to the advantages involved, such as their easy separation from liquid products, as well as their non-corrosive properties and the fact that they are environmentally benign. Recently, cation exchange resins [14] and solid supported catalysts [15] have also been used for this

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Scheme 1. Coumarin structure.

reaction, but they require high temperatures, long-time reactions and sometimes give low yields.

The heteropolyacids with Keggin structure (HPA) possess special characteristics that allow their use as catalysts in acid reactions, as they have a very high intrinsic acidity (e.g. [16–18]). These HPA were usually supported on different solids with the objective to achieve the heterogeneity of these catalysts in the reaction solution (e.g. [19–22]). In previous studies, it was proved that the tungstophosphoric acid (TPA) or molybdophosphoric acid (MPA) supported on silica are catalysts with suitable properties for acid reactions. In particular, they were tested in alkylation reactions [23] and in reactions that involve a cationic intermediary [24], achieving excellent results. Besides, high conversion and selectivity was obtained in an esterification reaction, using cesium or potassium partially substituted salts of TPA as catalysts [25].

The production of coumarins depends not only on the nature of the substituents, the substitution pattern and the condensing agent, but also on the catalyst used. Moreover, the position where the C-alkylation takes place also depends on the catalyst used [26].

The aim of the present study is to evaluate whether different heteropolycompounds (HPC) can be used as catalysts in the synthesis of coumarins. The yield obtained with bulk HPA, their aluminium salts as well as HPA supported on different types of silica is presented. The catalytic activity in the reaction of several phenols such as resorcinol, 3,5-dimethoxyphenol, α -naphthol and β -naphthol, and ethyl acetoacetate is studied.

2. Experimental

2.1. Catalyst preparation

2.1.1. Silica-supported Keggin heteropolyacids

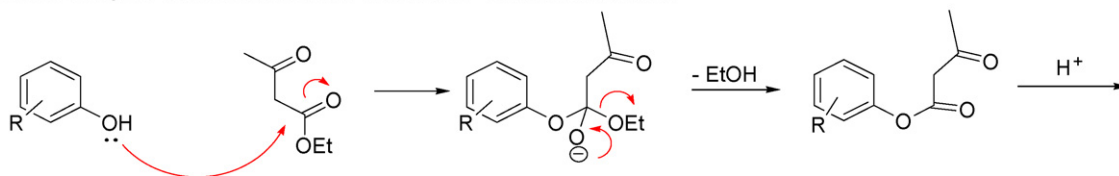
Impregnating solutions were prepared from $\text{H}_3\text{PMo}_{12}\text{O}_{40} \cdot n\text{H}_2\text{O}$ (Merck) or $\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot n\text{H}_2\text{O}$ (Fluka). The solvent was a mixture of demineralised water and 96% ethanol (Soria), in a 1:1 volumetric ratio. The supports were silica Grace (S_G) with a specific surface area of $311 \text{ m}^2/\text{g}$ and a mean pore diameter of 3.4 nm, and silica Ralt-Chemie (S_R) with a specific surface area of $253 \text{ m}^2/\text{g}$ and a mean pore diameter of 11.3 nm.

Catalysts based on MPA or TPA supported on S_G were prepared using the equilibrium impregnation technique. Experiments were performed at 20°C ; 1 g of support was placed in contact with 4 ml of solution under constant stirring. Contact time was 72 h, long enough to attain the equilibrium of adsorption–desorption processes. The solution and the solid were then separated by centrifugation and the catalysts were dried at room temperature for 24 h and calcined at 200°C for 3 h.

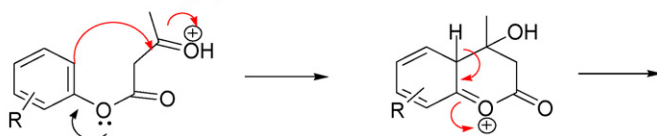
Solids thus obtained were washed with chloroform for three periods of 24 h, in a system with continuous stirring. Lastly, catalysts were thermally treated under the same conditions as before washing, and hereinafter will be named catalysts MPA/ S_G and TPA/ S_G .

The preparation of the TPA/ S_R and MPA/ S_R catalysts was carried out by impregnating spheres of S_R . The pore filling impregnation technique was utilised, with impregnating solutions of TPA or MPA prepared in the same solvent mentioned above. After the impregnation, the catalysts were dried at room temperature for 24 h, calcined at 200°C and washed with toluene for three periods of 24 h, in a device with continuous stirring. Subsequently, the catalysts were thermally treated again under the same conditions mentioned above.

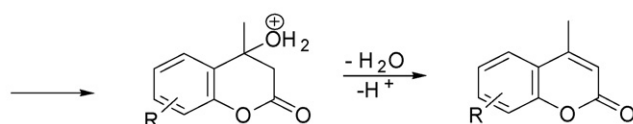
The acid catalyzes transesterification as well as keto-enol tautomerisation:



The electrophilic attack on the benzene ring by protonated ketone carbonyl leads to the formation of coumarin skeleton. This addition is following by rearomatization.



Subsequent acid-induced elimination of water gives the product:



Scheme 2. Mechanism of Pechmann reaction.

The concentration of molybdenum or tungsten, both in impregnating solutions, before and after being in contact with the support, and in washing solutions, was determined by atomic absorption spectrophotometry.

2.1.2. Aluminium salts of tungstophosphoric and tungstosilicic acids

The aluminium salts of the TPA and tungstosilicic acid (TSA), named TPAAl and TSAAl respectively, were prepared from aqueous solutions of the corresponding acids ($\text{H}_3\text{PW}_{12}\text{O}_{40}\cdot 21\text{H}_2\text{O}$ and $\text{H}_4\text{SiW}_{12}\text{O}_{40}\cdot 23\text{H}_2\text{O}$, Fluka p.a.), to which the required stoichiometric amount of the cation was added, employing $\text{Al}_2(\text{SO}_4)_3$ as cation source. The resulting solution was stirred at room temperature for 60 min to assure a complete reaction. The salts were crystallised by evaporation till dryness in air at 70 °C, then they were washed with ethanol, and dried again at 70 °C.

2.1.3. Aluminium salt of molybdophosphoric acid

The stoichiometric aluminium salt of the molybdophosphoric acid (MPAAl) was synthesised by the technique described by Silvani and Burns [27]. In a typical preparation the MPA acid was dissolved in distilled water, followed by the addition of 2.74 mmol of $\text{Al}_2(\text{SO}_4)_3\cdot 18\text{H}_2\text{O}$. The solution was continuously stirred and heated to 50–60 °C. Then, BaCO_3 was slowly added; the reaction was continued up to the complete elimination of CO_2 . On cooling, the mixture was stirred for 2 h. The BaSO_4 solid was removed by filtration, and was washed three times with distilled water. Aluminium salt was obtained by evaporation of water after a week.

2.2. Catalyst characterisation

The specific surface area (S_{BET}) and the mean pore diameter of solids were estimated from the adsorption–desorption isotherms of nitrogen at 77 K, using ASAP 2020 Micromeritics equipment.

To obtain the Fourier transform infrared (FT-IR) spectra, IFS 66 Bruker equipment and pellets of the samples in BrK were utilised.

For the potentiometric titration, 0.05 g of solid was suspended in acetonitrile (90 ml) and stirred for 3 h. The suspension was titrated with a 0.05N solution of *n*-butylamine in acetonitrile. The potential variation was measured with a Hanna 211 pH meter and a double junction electrode.

2.3. Synthesis of coumarins

The reaction was carried out in a glass batch reactor at atmospheric pressure, under two conditions: (a) ethyl acetoacetate was used as solvent of the reaction, phenol was dissolved and then the solid catalyst was added to the solution in a phenol:HPA molar ratio of 1:0.03. The resulting mixture was heated to 110 °C; (b) toluene was used as dissolvent of the reaction, the reagents ethyl acetoacetate, phenol and HPA were used in a molar ratio of 1:1:0.03. The mixture was heated to reflux (110 °C) or a domestic microwave oven at 210 W was employed for microwave irradiation. In this case temperature approxima-

tion was obtained by using sealed capillaries containing compounds of known melting point within the reaction container [28].

In all cases, the reaction was followed by thin layer chromatography (TLC). Finally, the catalyst was separated by filtration and washed with HCCl_3 . The crude of the reaction was washed with a solution of 5% NaOH (3×5 ml) and then with water. The organic solution was dried over anhydrous Na_2SO_4 , then it was filtered and the solvent was removed. The reaction products were purified by preparative-TLC using hexane and ethyl acetate (1:0.5 ratio) as solvent, and identified by means of physical and spectroscopic data. For the product obtained from resorcinol, the purification of the solid was made under the same above-mentioned conditions, but it was not washed with a solution of 5% NaOH. The possible supported catalyst leaching was also tested, by following the reaction after the filtration of the catalyst. In the case of homogeneous catalysts, they were separated from the reaction mixture using a silica gel column.

The conversion was calculated as the ratio between mmoles of transformed reagent and 100 mmol of initial reagent, and the product yield as the ratio between mmoles of coumarin and 100 mmol of initial reagent.

3. Results and discussion

3.1. Catalyst characterisation

The textural properties of the supports (S_{G} and S_{R}) and the catalysts based on the molybdophosphoric or tungstophosphoric acids supported on them are shown in Table 1. The specific surface area of the silica-supported catalysts was 50–80 m^2/g lower than that of the supports (Table 1), due to pore blockage. The same effect led to the change of bimodal to unimodal distribution of S_{G} -supported catalyst pores. It can also be observed that all the silica-supported catalysts presented a similar mean pore size.

The aluminum tungstosilicate and tungstophosphate, synthesised employing $\text{Al}_2(\text{SO}_4)_3$ presented a specific surface area, estimated by the BET method, lower than 10 m^2/g . The aluminium salt of the molybdophosphoric acid, obtained using $\text{Al}_2(\text{SO}_4)_3$ presented a similar specific surface area (8.5 m^2/g).

The FT-IR spectra of the supported catalysts based on MPA showed bands at 1056, 958, 870 and 791 cm^{-1} and those corresponding to TPA presented bands at 1079, 983, 891 and

Table 1
Textural properties of the supports and catalysts

Support	Specific surface area (m^2/g)	Pore volume (cm^3/g)	Mean pore diameter (nm)
S_{G}	311	1.70	5–10
S_{R}	253	1.04	11.3
TPA/ S_{G}	249	0.86	10.0
MPA/ S_{G}	218	0.80	10.0
TPA/ S_{R}	190	0.49	10.4
MPA/ S_{R}	206	0.58	11.3

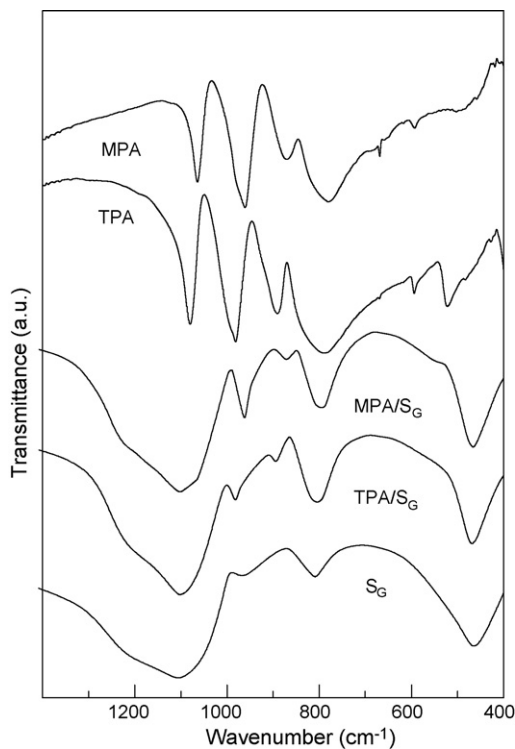


Fig. 1. FT-IR spectra of bulk MPA and TPA, S_G silica and S_G -supported MPA and TPA.

800 cm^{-1} , which are characteristic of the molybdophosphate and tungstophosphate anions, respectively [29–31]. However, some bands were overlapped with those of the supports. The FT-IR spectra of the silica supports (S_G , S_R) exhibited bands at 1100 , 800 and 470 cm^{-1} . Fig. 1 shows the spectra of the HPA supported on S_G , which are similar to those of the catalysts based on the HPA supported on S_R .

With regard to the TPAAl and MPAAl salts, the FT-IR spectra showed the above-mentioned characteristic bands of the tungstophosphate and molybdophosphate anions, respectively. On the other hand, bands at 1019 , 982 , 926 , 884 , 778 and 541 cm^{-1} were present in the FT-IR spectra of TSAAl salt; these bands correspond to the bulk tungstosilicic acid spectrum.

Thus, the characterisation by FT-IR showed that, in all the prepared catalysts, the corresponding anion is present with undegraded Keggin structure.

The acidity of the solids was characterised by potentiometric titration with *n*-butylamine. By this technique, it is possible to estimate the strength and the number of acid sites present in the solids. It is considered that the initial electrode potential (E_i) indicates the maximum strength of the acid sites, and the value from which the plateau is reached (meq amine/mmol HPA) indicates the total number of acid sites that are present in the titrated solid. The strength of the acid sites can be classified according to the following scale: $E_i > 100\text{ mV}$ (very strong sites), $0 < E_i < 100\text{ mV}$ (strong sites), $-100 < E_i < 0\text{ mV}$ (weak sites) and $E_i < -100\text{ mV}$ (very weak sites) [32].

The curves of the electrode potential as a function of meq amine/mmol HPA of the supported catalysts showed

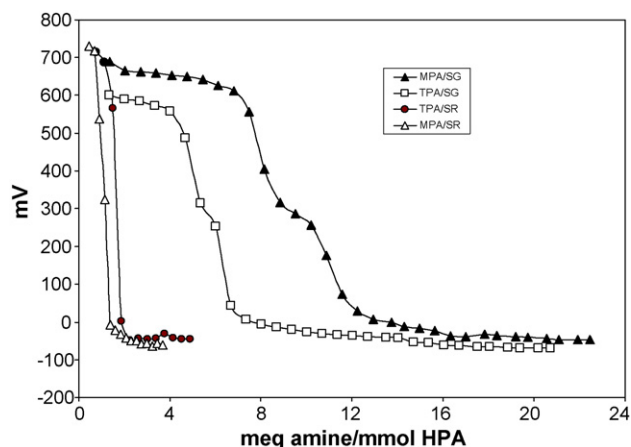


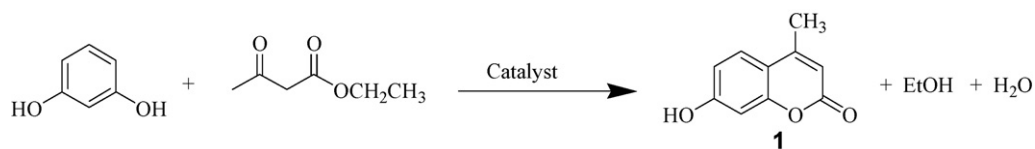
Fig. 2. Potentiometric titration curves of MPA and TPA supported on S_G and S_R silicas.

that, according to the previous scale, all the catalysts present very strong acid sites. The solids obtained by supporting the heteropolyacids on S_R have slightly stronger acid sites, with $E_i = 730$ and 714 mV for MPA/ S_R and TPA/ S_R , respectively, than those of the HPA supported on S_G , which presented $E_i = 690$ and 601 mV for MPA/ S_G and TPA/ S_G , respectively (Fig. 2). Besides, both HPA supported on S_R showed a similar number of sites between each other, though lower than that of the S_G -supported heteropolyacids. The fact that MPA presents a stronger acidity than TPA when supported on S_G , apparently contrary to the literature, is mainly due to the catalyst preparation conditions. These catalysts were obtained by the equilibrium impregnation technique and their content after leaching with chloroform was $0.217\text{ mmol MPA/g cat}$ and $0.133\text{ mmol TPA/g cat}$. In previous reports [33,21] equilibrium adsorption isotherms of both HPA from solutions in water–ethanol were determined on the S_G support. It was found that the amount adsorbed on the support surface is $0.067\text{ mmol MPA/g cat}$ and $0.025\text{ mmol TPA/g cat}$. So the washed catalysts keep a considerable amount of both HPA occluded in the pores of the support, which is higher for MPA/ S_G . This HPA amount occluded in the pores should be interacting more weakly on the surface of the support than the adsorbed fraction, leading to a higher amount of protons less engaged to the surface groups of the support. As a consequence, the S_G -supported molybdophosphoric acid presented a higher acidity than the catalyst based on tungstophosphoric acid.

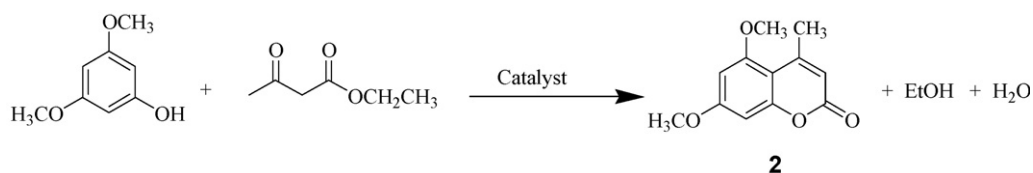
The potentiometric titration curves of the HPA salts showed that the TPAAl, MPAAl and TSAAl samples present very strong acid sites, with similar acid strength, with $E_i = 640$, 560 and 590 mV , respectively.

3.2. Synthesis of 4-methyl-7-hydroxycoumarin

β -Methylumbelliferone (**1**) is used as building block in the synthesis of the insecticide hycromone. Resorcinol and ethyl acetoacetate were used to obtain (**1**), with MPA/ S_G or TPA/ S_G as catalysts.



When the reaction is carried out using a 1:8 resorcinol:ethyl acetoacetate molar ratio, that is with ester in excess, compound **1** is obtained in 40 min with a yield of 95% (Table 2, entries 1 and 2). The ester is acting both as reagent and solvent due to the excess used. If the reaction is carried out employing toluene as solvent (Table 3), using a 1:1 molar ratio of reagents and MPA/S_G as catalyst (entry 1), the yield is 80% in the same reaction time. This behaviour shows that by using ester in excess, the probability of contact with the catalyst surface and between both reagents increases, and this helps the reaction of coumarin synthesis.



Yields obtained with HPA-based catalysts, under both conditions, were better than those obtained with other solid catalysts reported in the literature (Tables 2 and 3). It can be observed that, even when using toluene as solvent, the yield obtained was equal to that reported with another solid catalyst, Amberlyst-15 (Table 3, entry 2), but the reaction time was lower.

Table 2
Synthesis of 4-methyl-7-hydroxycoumarin (**1**)

Entry	Catalyst	Reaction time	Yield (%)
1	MPA/S _G (a)	40 min	95
2	TPA/S _G (a)	40 min	95
3	Amberlyst-15(b) ⁷	2 h	72
4	H-Beta (b) ⁷	2 h	78
5	Filtrol (b) ⁷	2 h	55

(a) Resorcinol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol, temperature = 110 °C; (b) resorcinol:ethyl acetoacetate:catalyst = 1:1:0.1 g, temperature = 150 °C.

Table 3
Synthesis of 4-methyl-7-hydroxycoumarin (**1**) in toluene as solvent

Entry	Catalyst	Reaction time	Solvent	Yield (%)
1	MPA/S _G (a)	40 min	Toluene	80
2	Amberlyst-15 (b) ⁷	4 h	Toluene	81
3	H-Beta (b) ⁷	4 h	Toluene	71
4	Filtrol (b) ⁷	4 h	Toluene	5

(a) Resorcinol:ethyl acetoacetate:catalyst = 1:1:0.03 mmol, temperature = 110 °C; (b) resorcinol:ethyl acetoacetate:catalyst = 1:1:0.1 g, temperature = 110 °C.

3.3. Synthesis of 4-methyl-5,7-dimethoxycoumarin

The best reaction conditions were used to synthesise 4-methyl-5,7-dimethoxycoumarin (**2**). Ethyl acetoacetate was used as reagent and solvent of the reaction, the phenol was solubilised and then, the solid catalyst was added to the solution in a phenol:HPA molar ratio of 1:0.03. The resulting mixture was heated to 110 °C. The product yield was determined using TPA/S_G and MPA/S_G catalysts, and the catalysts based on the same HPA supported on another silica, Ralt Chemie (TPA/S_R and MPA/S_R) (Table 4).

From the obtained results it may be concluded that, when the catalysts based on TPA and MPA supported on S_G (Table 4, entries 2 and 3) are compared, the best result was found using supported TPA as catalyst. TPA/S_G presents lower acidity than MPA/S_G due to the catalyst preparation conditions. However the TPA-based catalyst contains the lowest amount of occluded HPA and may be the best dispersed as mentioned in Section 3.1, so the reagent will have the highest accessibility to the active sites. So that when the performance of diverse catalysts is compared, other characteristics different to acidity can explain their catalytic behaviour.

In addition, it may be stated that S_R behaves as a better support than S_G (Table 4, entries 2 and 4) because the acid strength of TPA/S_R is higher than that corresponding to TPA/S_G (Section 3.1). It was also observed that the yield was not modified when the particle size of TPA/S_R was decreased by grinding, sample TPA/S_R ground, see Table 4, entries 4 and 5.

Table 4
Synthesis of 4-methyl-5,7-dimethoxycoumarin (**2**) using supported HPA as catalysts

Entry	Catalyst	Time (h)	Yield (%)
1	TPA ^a	1	93
2	TPA/S _G	1	78
3	MPA/S _G	1	60
4	TPA/S _R	1	91
5	TPA/S _R ground	1	92
6	H ₂ SO ₄ (con) ^a	2	20

3,5-Dimethoxyphenol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol.

^a Homogeneous catalyst.

Table 5
Synthesis of 4-methyl-5,7-dimethoxycoumarin (**2**) using HPA salts as catalysts

Entry	Catalyst	Time (h)	Yield (%)
1	TPAAI	1	85
2	TSAAI	1	84

3,5-Dimethoxyphenol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol.

This indicates that the reaction is not controlled by diffusion, which may be related to the high mean pore diameter (10.4 nm) of the catalyst (Table 1).

Also it is possible to point out that the yield using the TPA/S_R as catalyst was equal to that obtained with bulk TPA, a homogeneous catalyst.

In all the cases, the yields were higher than those obtained when concentrated sulphuric acid (con) was used as catalyst.

On the other hand, the Al salts of TPA (TPAAI), TSA (TSAAI) and MPA (MPAAI) were used as catalysts in the same reaction. The results shown in Table 5 indicate that, using the Al salts of TPA and TSA acids as catalysts, high yields were also obtained (85%). However, the Al salt of MPA acid was not a good catalyst for the synthesis of this coumarin under the conditions used, since it behave as a homogeneous catalyst and our purpose was obtain heterogenous system.

In addition, microwave radiation (MW) as power source was used with the main purpose of decreasing the reaction times. In the first reactions with MW, the TPA/S_R sample and the TPAAI salt were used as catalysts. The results are summarised in Table 6, and it was found that the heating with microwave radiation leads not only to an important decrease in the reaction time, as expected, but also to an increase in the reaction yield. Then the use of microwave irradiation as power source is a beneficial tool for enhancing the reaction rate and selectivity, in according to the bibliography comments. This behaviour is consequence that in this case the energy transfer occurs by dielectric loss, in comparison to the conventional heating which is by convection and conduction. On the other hand microwave heating is rapid because energy is absorbed directly by the material.

3.4. Synthesis of 4-methyl-7,8-benzocoumarin

α -Naphthol, ethyl acetoacetate and MPA/S_G catalyst were used to synthesise 4-methyl-7,8-benzocoumarin (**3**). Also the selected reaction conditions mentioned above were used and the result is reported in Table 7. In this table the yield is compared with those of other catalysts reported in literature [34,35].

Table 6
Synthesis of 4-methyl-5,7-dimethoxycoumarin (**2**) using microwave heating

Entry	Catalyst	Time (min)	Temperature	Yield (%)
1	TPA/S _R ground	60	110	92
2	TPA/S _R ground	4	MW (a)	95
3	TPAAI	60	110	85
4	TPAAI	10	MW (b)	>99

3,5-Dimethoxyphenol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol. (a) Temperature approximation 63 \pm 5 $^{\circ}$ C; (b) temperature approximation 70 \pm 5 $^{\circ}$ C.

Table 7
Synthesis of 4-methyl-7,8-benzocoumarin (**3**)

Entry	Catalyst	Time (h)	Yield (%)
1	MPA/S _G (a)	15	90
2	K10 (b) ²⁹	8	80
3	H ₂ SO ₄ (c) ²⁸	24	69

(a) 1-Naphthol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol, temperature = 110 $^{\circ}$ C; (b) 1-naphthol:ethyl acetoacetate:catalyst = 1:1:0.1 g, temperature = 150 $^{\circ}$ C; (c) sulphuric acid 90%, temperature = 20 $^{\circ}$ C. Homogeneous catalyst.

Table 8
Synthesis of 4-methyl-5,6-benzocoumarin (**4**)

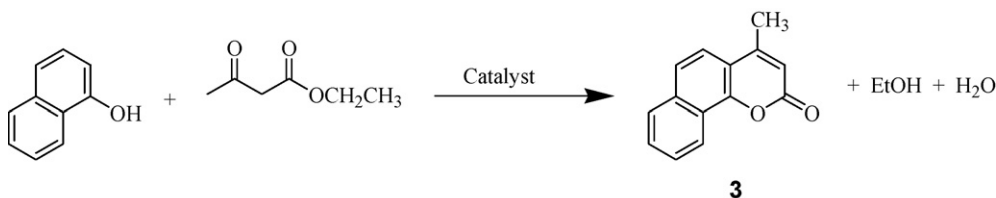
Entry	Catalysts	Time (h)	Temperature ($^{\circ}$ C)	Yield (%)
1	MPA/S _G (a)	4	110	15
2	MPA/S _R ground (a)	15	110	11
3	MPA/S _R ground (a)	1	MW	NR
4	K10 (b) ²⁹	12	150	3.4

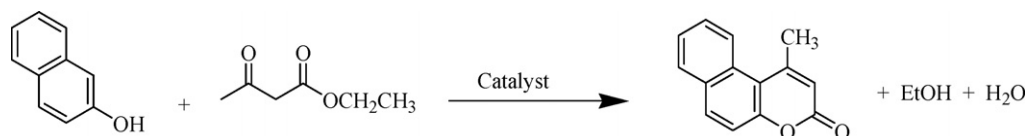
(a) 2-Naphthol:ethyl acetoacetate:catalyst = 1:8:0.03 mmol; (b) 2-naphthol:ethyl acetoacetate:catalyst = 1:1:0.1 g.

It can observed that the yield to this coumarin synthesised from α -naphthol and using MPA/S_G reached 90% at 15 h of reaction (Table 7, entry 1). It is higher than those obtained with other solid catalysts reported in the literature (Table 7, entries 2 and 3).

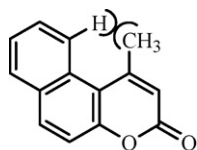
3.5. Synthesis of 4-methyl-5,6-benzocoumarin

The reaction between β -naphthol and ethyl acetoacetate only yields one of the two isomers, the 4-methyl-5,6-benzocoumarin (**4**), using the selected reaction conditions. Its structure was determined by ¹H-NMR. According to a report in the literature [29], the other isomer (4-methyl-6,7-benzocoumarin) is obtained when K10 is used as catalyst.





It can be concluded of the results presented in Table 8 that the synthesis of 4-methyl-5,6-benzocoumarin using MPA/S_G ground and MPA/S_R as catalysts, at different reaction conditions, has a very low yield (Table 8, entries 1, 2 and 3). The same result was reported in the literature for other catalyst (Table 8, entry 4). Probably the low yield of compound 4 is due to steric effects more than electronic effects.



On the other hand, phenol, thymol and cresol did not react when these catalysts and the same reaction conditions are used. From this and the previous results, it can be said that the reaction needs electron donor groups (OCH₃, OH) in the phenolic ring for the aromatic electrophilic substitution. These groups must be at *ortho*- or *para*-position to induce the closure. In the case of resorcinol, the OH group at *para*-position gives great activation for the closure. Alkyl groups in thymol and cresol are not adequate electron donor to aid in the closure of the ring.

When α -naphthol is used as starting material, 4-methyl-7,8-benzocoumarin is obtained in a very good yield (90%). In the literature it was reported that β -naphthol is not a good reagent for Pechmann reaction [28]. This was confirmed in this work since the yield was 11–15% with MPA/S_R and MPA/S_G (Table 8). To raise the yields of these reactions, MW was used and there were not higher yields under these conditions, using MPA/S_G.

4. Conclusions

In the synthesis of coumarins from phenols and ethyl acetoacetate, different heteropolycompounds were used as catalysts. The H₃PMo₁₂O₄₀ and H₃PW₁₂O₄₀ Keggin heteropolyacids were supported on different types of silica. On the other hand, the aluminium salts of these heteropolyacids and that of the H₄SiW₁₂O₄₀ acid were prepared.

The aluminium salts of tungstophosphoric, tungstosilicic or molybdophosphoric acids have a specific surface area lower than 10 m²/g. The characterisation by FT-IR indicated that, in all the prepared catalysts, the corresponding Keggin anion is present with undegraded structure. The potentiometric titration curves of the prepared catalysts showed that all of them present very strong acid sites. The solids obtained by supporting the heteropolyacids on S_R have slightly stronger acid sites than those of the HPA supported on S_G. The acid measurements of HPA salts showed that the TPAAl, MPAAl and TSAAl samples present very strong acid sites with similar acid strength.

When β -methylumbelliferone synthesis was carried out with ester excess, the obtained yield was higher than that when the reaction was performed using a reactive molar ratio of 1:1 in toluene.

The catalytic activity using several phenols such as resorcinol, 3,5-dimethoxyphenol, α -naphthol and β -naphthol was determined. High product yields were obtained in the case of 4-methyl-7-hydroxycoumarin (80–95%), 4-methyl-5,7-dimethoxycoumarin (60–92%) and 4-methyl-7,8-benzocoumarin (90%). However, the yield to 4-methyl-5,6-benzocoumarin was low. The use of microwave radiation as power supply increase the reaction yield and fundamentally decreases the reaction time.

The yields observed using the catalysts based on supported Keggin heteropolyacids or their aluminium salts were higher than those obtained when other acid solids and sulphuric acid were used as catalysts.

In short, eco-friendly catalysts, insoluble in the reaction solution and with high activity and selectivity were obtained for the synthesis of coumarins.

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