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Synthesis and characterization of copper and aluminum salts of $H_3PMo_{12}O_{40}$ for their use as catalysts in the eco-friendly synthesis of chromanes

Daniela S. Mansilla [b], M. Rosario Torviso [b], Elba N. Alesso [b], Patricia G. Vázquez [a], Carmen V. Cáceres [a,*]

[a] *Centro de Investigación y Desarrollo en Ciencias Aplicadas "Dr. Jorge Ronco" (CINDECA), Universidad Nacional de La Plata, Facultad de Ciencias Exactas, Calle 47 N° 257, 1900 La Plata, Argentina*

[b] *Departamento de Química Orgánica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Argentina*

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ABSTRACT

Acid catalysts based on aluminum (or copper) salts of molybdophosphoric acid ($H_3PMo_{12}O_{40}$) were prepared. They were synthesized from a heteropolyacid solution to which $Al_2(SO_4)_3$, $Al_2O(CH3COO)_4$ or $CuSO_4$ was added. The obtained salts were texturally characterized and a low specific surface area, between 1 and 9 m^2/g, was observed. The analysis of the prepared salts by ICP-AES spectrometry indicated that the molar content of Mo and P was that corresponding to the anion $[PMo_{12}O_{40}]^{3-}$. The presence of undegraded Keggin structure was confirmed by XRD, FT-IR, DRS and ^{31}P MAS-NMR. The catalyst acidity was measured by means of potentiometric titration with a solution of *n*-butylamine in acetonitrile and by temperature-programmed desorption of pyridine. The $AlPMo_{12}O_{40}$ salt (from sulfate), which at 5 h of reaction showed the highest conversion of *m*-cresol (98%) and 75% and 25% selectivity to chromane **4** and **3**, respectively, presented the highest total acidity and, simultaneously, acid sites with maximum acid strength very high. On the other hand, $Cu_{0.5}H_2PMo_{12}O_{40}$ catalysts at 5 h of reaction showed lower conversion of *m*-cresol than the former salt (90%) and also lower selectivity to chromane **4** and **3** (37% and 10%, respectively). In the latter case also 43% of open-chain compounds were observed. With the other salts, $Al_{0.5}H_{1.5}PMo_{12}O_{40}$, $Cu_3(PMo_{12}O_{40})_2$ and $AlPMo_{12}O_{40}$ (from $Al_2O(CH_3COO)_4$), only the reaction intermediaries, open-chain compounds, were obtained because these salts presented low total acidity and acid sites with maximum acid strength very low.

1. Introduction

In nature there are many compounds with recognized pharmacological activity, and most of them have been obtained by extraction from vegetables. Reactions in liquid phase have been carried out for their synthesis, and they have generally been catalyzed with the aim of optimizing their preparation. Catalysis is a key solution for the development of a new eco-friendly chemical industry [1], in particular for the pharmaceutical industry, which is one of the industries that generates greater proportion of waste according to the contamination index. The heterogeneous catalytic process as substitute for stoichiometric processes prevents the generation of environmentally harmful effluents and by-products, leading to clean technologies [2]. This calls for an innovative effort in the design of new catalysts to obtain catalytic agents more benign for the environment [3,4].

Several reviews have reported reactions catalyzed by heteropolycompounds, both in homogeneous and in heterogeneous systems [5,6]. In these papers, their properties as catalysts for acid or oxidation reactions have been highlighted. There are several industrial processes that have used heteropolycompounds with a Keggin-type structure, and the basic investigation continues [7,8]. These compounds are multielectronic oxidants and, simultaneously, they are acids with strength greater than that of the conventional acids. The reactions in which they can be used, such as cyclization, esterification, dehydration, oxidation of amines or epoxidation of alkenes, are important for a large number of industries related to fine chemicals, such as flavor, pharmaceutical and food industries, among others.

For the preparation of catalysts from the above-mentioned heteropolycompounds, their properties can be controlled by a suitable selection of the heteropolyanion and its constituent elements such as heteroatom, peripheral atom and countercation. These catalysts can be used in homogeneous processes in liquid phase, reactions in two-phase liquids (phase-transfer catalysis) or in liquid–solid or gas–solid systems.

In the preparation of supported catalysts, heteropolyacid stability in the impregnating solution is an important factor, since it influences the species present in the solid and hence, the properties of the final catalyst. Therefore in our research group, the

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* Corresponding author. Tel.: +54 221 421 1353; fax: +54 221 425 4277.
E-mail address: ccaceres@quimica.unlp.edu.ar (C.V. Cáceres).

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influence of different solvents on the species in solution and on the support has been studied [9,10].

The use of different solids as support was investigated. This study was very important due to the low specific surface area that the bulk compounds present. It was also important due to the advantage of supported catalysts of being easily separated in liquid-phase reactions. Among other systems, the impregnation on carbon, silica, titania and alumina [11,12], and on zirconia [13] has been studied.

In particular for their use in liquid-phase reactions, it is convenient to obtain insoluble or solid-supported heteropolycompounds that can be firmly immobilized. In this way additional advantages over the homogeneous catalyst were obtained, due to the facility of catalyst-product separation and their possibility of re-use. The results of studies conducted and reported by different authors and by our research group [14–20] have emphasized the importance of developing processes employing this type of catalyst to obtain products on a small scale, such as those produced for the fine chemicals industries.

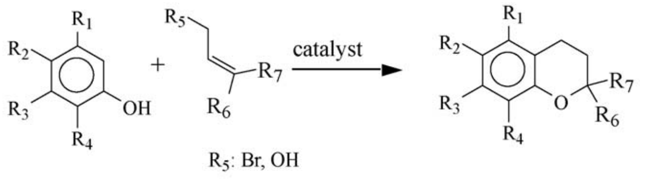
On the other hand, substances with vitamin E activity are homologues of 6-chromanol. The eight naturally occurring compounds are divided into two groups, the tocopherols, which have a saturated C16 isoprenoid side chain, and tocotrienols, which have a triply unsaturated C16 side chain (Scheme 1). This vitamin has a considerable biological role as antioxidant [21]. It is especially important to prevent the formation of hydroperoxide derivatives of the polyunsaturated fatty acid. The first synthesis of tocopherols was performed by Karrer [22], using trimethylhydroquinone and allyl bromides with aluminum trichloride as catalyst. The $ZnCl_2$ was also used as catalyst for synthesis of tocopherols [22–23]. The most important reaction of tocopherols is the oxidation to γ-hydroxyalcohylquinones, which have good activity to cure and prevent muscular dysphagia in animals.

The above-mentioned concepts show the importance of studying the substitution of aluminum trichloride by heteropolycompounds with Lewis acid characteristics in the synthesis of tocopherols. In the present work, the substitution of aluminum trichloride by aluminum (or copper) salts of molybdophosphoric acid was studied in the synthesis of chromanes.

2. Experimental

2.1. Salts of molybdophosphoric acid synthesis

The salts of $H_3PMo_{12}O_{40}$ were prepared by the technique described by Silvani and Burns [24]. In a typical preparation 5.48 mmol of $H_3PMo_{12}O_{40}$ (MPA) was dissolved in 12 ml of distilled water. The necessary mmol of $Al_2(SO4)_3 \cdot 18H_2O$, $Al_2O(CH3COO)_4$ or $CuSO_4 \cdot H_2O$, to get the desired salt, were added to the previous solution. The solution was continuously stirred and heated to 50–60 °C. Then, 8.22 mmol of $BaCO_3$ was slowly added; the reaction was continued to the complete elimination of CO_2. On cooling, the mixture was stirred for 2 h. Then, the $BaSO_4$ or $Ba(CH_3COO)_2$ solid was removed by filtration and it was washed three times with distilled water. Al or Cu salts were obtained by evaporation of remnant water after a week. These salts were $AlPMo_{12}O_{40}$, $Al_{0.5}H_{1.5}PMo_{12}O_{40}$, $Cu_{0.5}H_2PMo_{12}O_{40}$, $Cu_3(PMo_{12}O_{40})_2$ (all from $Al_2(SO_4)_3$) and $AlPMo_{12}O_{40}$ (from $Al_2O(CH_3COO)_4$). They were called AlPMo, Al0.5HPMo, Cu0.5HPMo, CuPMo, and AlPMoAct, respectively.



Vitamin E: R1: R3: H or CH3 R2: OH R4:R6: CH3
Tocopherols: R7: 4,8,12-trimethyltridecyl
Tocotrienols: R7: 4,8,12-trimethyltridecyl-3,7,11-triene

Scheme 1. Synthesis of chromanes.

2.2. Salt characterization

2.2.1. Inductively coupled plasma atomic emission spectroscopy (ICP-AES)

The analyses were performed using a Shimadzu Sequential Plasma Spectrometer 1000, model III, and conventional pneumatic nebulization (Meinhard), according to EPA 200.7 standard. The operating conditions were plasma power, 1.2 kW; torch height, 15 mm; plasma gas (Ar) at 14 l/min; cooling Ar flow, 1.4 l/min; and Ar carrier, 1 l/min.

2.2.2. Fourier transform infrared spectroscopy (FT-IR)

FT-IR spectra of solid samples were recorded using a Bruker IFS 66 FT-IR spectrometer, with pellet samples, and a measuring range of 400–4000 cm^{-1}.

2.3. X-ray diffraction (XRD)

XRD patterns of solid samples were recorded. To obtain these diagrams, a Philips PW-1390 device with built-in recorder was used. Conditions were as follows: Cu Kα radiation; Ni filter; 20 mA and 40 kV in the high voltage source; scanning angle (2θ) from 5° to 60°; and scanning rate, 1°/min.

2.4. Diffuse reflectance spectroscopy (DRS)

The solid samples were studied in the range 200–600 nm, using UV–visible Varian Super Scan 3 equipment, fitted with a diffuse reflectance chamber with $BaSO_4$ inner surface.

2.4.1. Magic-angle spinning nuclear magnetic resonance (MAS-NMR)

Solid samples were analyzed by ^{31}P MAS-NMR by means of Varian Mercury Plus 300 equipment with a sample holder 7 mm in diameter, a resonant frequency of 121.469 MHz, and a spinning rate of 5 kHz. The measurements were carried out at room temperature using 85% H_3PO_4 as external reference.

2.5. Acidity measurements

2.5.1. Potentiometric titration

The catalyst acidity was measured by means of potentiometric titration. A known mass of solid (0.05 g) suspended in 45 ml of acetonitrile was stirred for 8 min. Later the suspension was titrated with a solution of *n*-butylamine in acetonitrile (0.025 N) at a flow rate of 0.025 cm^3/min. The electrode potential (mV) variation was measured using a titrating device with a Metrohm 806 exchange unit.

2.5.2. Temperature-programmed desorption of pyridine and trimethylpyridine

Also the catalyst acidity was assessed by temperature-programmed desorption of probe molecules (pyridine and trimethylpyridine). The pyridine is a probe molecule that allows determining the total acidity of a compound, and the trimethylpyridine makes it possible to determine the sites with Brφnsted acidity. Two hundred milligrams of the catalyst was immersed in a closed vial containing pure pyridine (or trimethylpyridine) for 4 h.

Then the catalyst was taken out from the vial and excess pyridine (or trimethylpyridine) was removed by evaporation at room temperature under a fume hood. The sample was then charged to a quartz microreactor, and a constant nitrogen flow (40 ml/min) was set up. Weakly adsorbed pyridine (or trimethylpyridine) was first desorbed in a first stage of stabilization by heating the sample at 110 °C for 2 h. The temperature of the oven was then raised to 600 °C at a heating rate of 10 °C/min. The reactor outlet was directly connected to a flame ionization detector to measure the desorption rate of pyridine or trimethylpyridine.

2.6. Textural properties

Specific surface area (SBET), pore volume, and mean pore diameter of solid samples were determined by nitrogen adsorption/desorption techniques using Micromeritics Accusorb 2100E equipment.

2.7. Synthesis of chromanes

Reactions were carried out in a glass batch reactor. In all of them, the ratios 1:1:0.033 mmol of *m*-cresol:geraniol:catalyst were used. The *m*-cresol and geraniol were solubilized in the chosen solvent (chloroform, heptane, hexane and heptane/ethyl carbonate), then the catalyst was added. The mixture was stirred at reflux temperature, and the reaction was followed by thin-layer chromatography (TLC) for 5 h. The TLC test was carried out using layers of aluminum with silica gel 60 F254, the hexane:ethyl acetate mixture (ratio 2:1) as eluent, and the reagents as reference. On completion, the catalyst was separated by filtration. The crude reaction was washed with 10% NaOH, then with water and dried (Na_2SO_4 anh.). The solvent was removed in vacuum (except in the case of heptane/ethyl carbonate). In the case of the reaction with heptane/ethyl carbonate, following filtration the phases were separated in a decanting vial. The carbonate phase was extracted with heptane. Then the heptane phase was treated with 10% NaOH, and the same procedure as the above-mentioned for the rest of the solvents was applied.

The reaction products were purified by preparative thin-layer chromatography (*p*-TLC), using the same mixture as that used in TLC as elution solvent. The *p*-TLC was performed on a 20 cm × 20 cm glass plate coated with silica gel 60 F_{254} (0.50 mm).

The obtained compounds were identified by proton and carbon nuclear magnetic resonance spectroscopy (^{1}H NMR and ^{13}C NMR), using TMS as reference, and $CDCl_3$ as solvent. The spectra were recorded in Bruker AM 500 equipment.

Spectral data for reaction products are as follows:

(**3**) ^{1}H NMR ($CDCl_3$): $\delta = 7.03$ (t, $J = 7.7$ Hz, 1H), 6.74 (d, $J = 7.7$ Hz, 1H), 6.66 (d, $J = 7.7$ Hz, 1H), 5.27 (bs, 1H), 2.63 (dd, $J = 5.0$, $J = 16.4$, 1H), 2.36 (dd, $J = 16.4$, $J = 13.2$ Hz, 1H), 2.26 (s, 3H), 2.00 (m, 2H), 1.73 (dd, $J = 5$, $J = 13.2$ Hz, 2H), 1.36 (m, 2H), 1.22 (s, 3H), 1.05 (s, 3H), 0.95 (s, 3H) ppm.

(**4**) ^{1}H NMR (^{13}C NMR) ($CDCl_3$): $\delta = 7.04$ (d, $J = 8.2$ Hz, 1H) (130.3), 6.65 (d, $J = 2.3$ Hz, 1H) (116.5), 6.62 (dd, $J = 2.5$ Hz, $J = 8.2$ Hz, 1H) (112.2), 5.30 (bs, 1H) (120.3), 2.90 (dd, $J = 5.0$, $J = 13.8$, 1H), 2.40 (dd, $J = 9.4$ Hz, $J = 13.8$ Hz, 1H) (34.2), 2.32 (s, 3H) (19), 1.90 (m, 2H) (49.50), 1.40 (m, 2H, 2H) (28), 1.00 (s, 3H) (28.4), 0.93 (s, 3H) (27) ppm. Chemical shifts for ^{13}C were determined by means of HMQC ($CDCl_3$).

(**5** and **6**) ^{1}H NMR ($CDCl_3$): $\delta = 7.00$ (t, $J = 8.0$ Hz, 1H), 6.98 (d, $J = 8.0$ Hz, 1H), 6.76 (d, $J = 8.0$ Hz, 1H), 6.69 (d, $J = 8.0$ Hz, 1H), 6.64 (s, 1H), 5.32 (bt, 1H), 5.17 (bt, 1H), 5.05 (m, 2H), 3.38 (d, $J = 7.0$ Hz, 2H), 3.33 (d, $J = 7.0$, 2H), 2.30 (s, 3H), 2.28 (s, 3H), 2.08 (m, 8H), 1.79 (s, 3H), 1.76 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H), 1.58 (s, 3H), 1.56 (s, 3H). (^{13}C NMR) ($CDCl_3$): $\delta = 154.5$, 138.5, 137.7, 132, 130, 127, 124, 123.8, 123, 12, 121.5, 121.3, 116.5, 113.6, 39.5, 32, 29.7, 29.5, 26.5, 25.5, 21, 20, 17.6, 16 ppm.

(**7**) ^{1}H NMR (^{13}C NMR) ($CDCl_3$): $\delta = 7.00$ (d, $J = 8.0$ Hz, 1H) (129.8), 6.65 (d, $J = 2.5$ Hz, 1H) (117), 6.60 (dd, $J = 2.5$ Hz, $J = 8.0$ Hz, 1H) (112.5), 5.20 (bt, 1H) (123), 5.10 (bt, 1H) (124), 3.30 (d, $J = 6.9$ Hz, 2H) (31), 2.25 (s, 3H) (19.5), 2.10 (m, 2H) (39.5), 2.07 (m, 2H) (26.7), 1.72 (s, 3H) (16), 1.70 (s, 3H) (25.7), 1.62 (s, 3H) (17.6) ppm. Chemical shifts for ^{13}C were determined by means of HMQC ($CDCl_3$).

The product yield was calculated as the mass ratio between the obtained purified amount of product and the theoretical mass expected for the total conversion of *m*-cresol.

When the best reaction conditions were determined, the traditional catalysts $ZnCl_2$ and $AlCl_3$ were tested.

Also under these optimal conditions, all the synthesized salts were tested following the reaction by high performance liquid chromatography (HPLC) for 5 h, with a Konik 500-A device, fitted with a UV detector (204 nm), C-18 column and acetonitrile as solvent at 0.5 cm^3/min flow rate.

The conversion by HPLC was calculated as the ratio between mmol of transformed *m*-cresol and 100 mmol of initial reagent, and the product selectivity as the ratio between mmol obtained of each product and 100 mmol of final reaction solution.

AlPMo catalyst leaching was evaluated. The reaction was carried out under the optimal conditions during 10 min, the catalyst was filtered, and then the solution was stirred at reflux temperature, and it was evaluated if the reaction was completed. On the other hand, experiences about re-use were realised.

3. Results and discussion

The analysis of the prepared salts by ICP-AES spectroscopy indicated that the molar content of Mo and P is that corresponding to the anion $[PMo_{12}O_{40}]^{3-}$.

In Fig. 1 the FT-IR spectrum of molybdophosphoric acid is shown. Its characteristic bands at 1064 cm^{-1} due to stretching POa, 962 cm^{-1} to stretching Mo = Od, 870 cm^{-1} to stretching Mo–Ob–Mo, and 775 cm^{-1} to stretching Mo–Oc–Mo are observed. The subindexes indicate oxygen bridging Mo and the heteroatom (a), at corners (b) and edges (c) belonging to MoO_6, and terminal oxygen (d) [25].

The FT-IR spectra of prepared Al and Cu salts show the characteristic bands of molybdophosphoric anion, which demonstrates that the Keggin structure is intact. In Fig. 1 the spectra (in the range 600–1300 cm^{-1}) of salts AlPMo, Al0.5HPMo, Cu0.5HPMo, CuPMo, and AlPMoAct are shown.

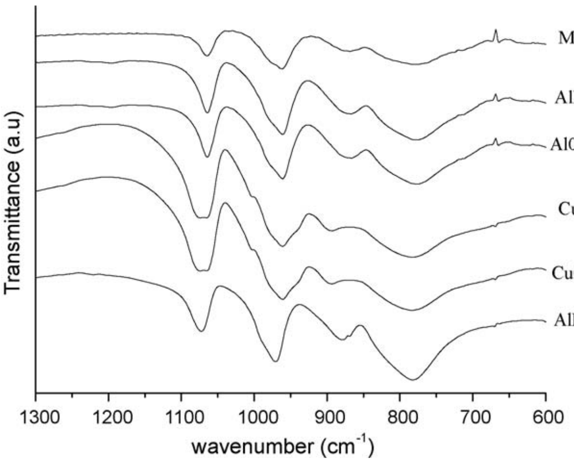


Fig. 1. FT-IR spectra of MPA and its Al or Cu salts.

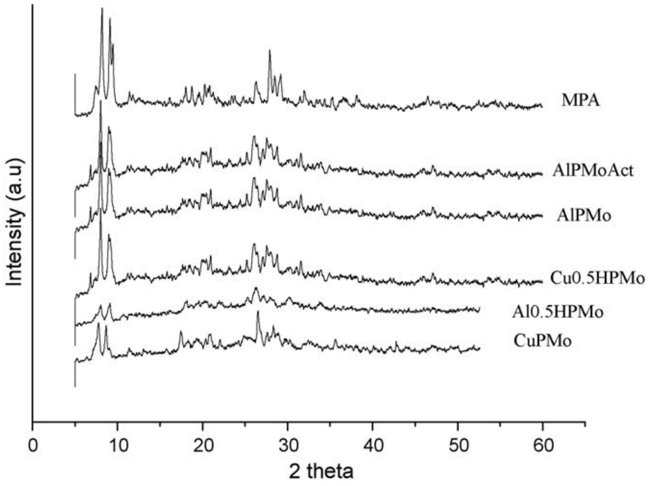


Fig. 2. X-ray diffraction patterns of MPA and its Al or Cu salts.

The FT-IR spectrum corresponding to the copper salt presents the following characteristics:

- Splitting of the band corresponding to stretching POa (1075 and 1065 cm^{-1}).
- Shift of the band corresponding to stretching Mo-Ob-Mo (870 cm^{-1}).

These differences with the aluminum salt (although both cations are in the secondary structure) are because the cation Cu^{2+} has a greater ionic radius, and it is generally found as $Cu(OH)_6$. This hydration degree can be conserved when it is incorporated to the secondary structure.

The bands corresponding to the protonic sites υ(OH) and $\delta(H_2O)$ were observed in the zone 4000–1500 cm^{-1}. The spectrum shows a broad band near 3400 cm^{-1} corresponding to υ(OH), and that corresponding to $\delta(H_2O)$ near 1600 cm^{-1}. In the copper salts, Cu0.5HPMo and CuPMo, this band allows corroborating the above-mentioned with respect to the presence of OH.

In the X-ray diffraction patterns of aluminum and copper salts, well-defined diffraction lines of the heteropolyacid bulk were observed (Fig. 2), which indicates that the salts present a crystalline structure. According to bibliographic data, the crystalline structure corresponds to $H_3PMo_{12}O_{40}\cdot 13H_2O$ and it presents triclinic symmetry [26]. Then it is possible to assure that the Keggin-type heteropolyanion is undegraded.

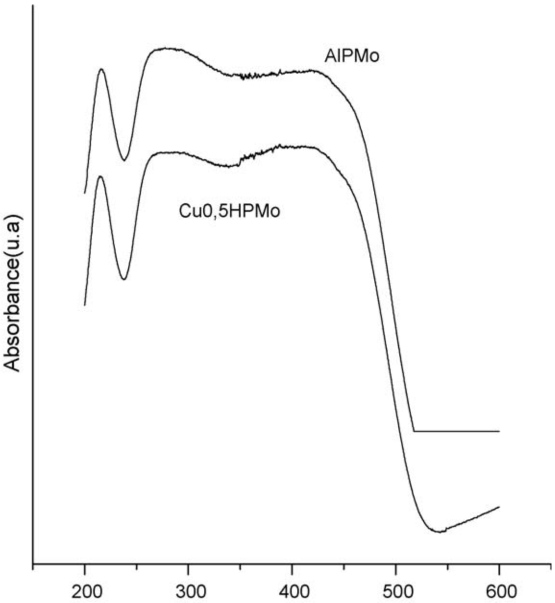


Fig. 3. DRS spectra of AlPMo and Cu0.5HPMo salts.

Table 1
^{31}P MAS-NMR results.

Solid	Chemical shifts (ppm)
MPA	−3.77
AlPMo	−3.19
Al0.5HPMo	−3.31
AlPMoAct	−3.60
CuPMo	−3.38
Cu0.5HPMo	−3.51

By diffuse reflectance spectroscopy it is possible to verify the presence of the $[PMo_{12}O_{40}]^{3-}$ species for the Al and Cu salts of the MPA. The characteristic absorption bands, according to bibliographic data [27], at 220 and 260 nm of the tetrahedral Mo, and bands attributed to oxygen-metal transfers at 210–230 nm and another one that extends from 240 up to 545 nm indicating Mo in octahedral position, can be observed in Fig. 3 for AlPMo and Cu0.5HPMo salts of the MPA. Analogous spectra were obtained for the other salts prepared.

The results obtained by ^{31}P MAS-NMR are shown in Table 1. All the chemical shifts appear at higher magnetic fields than that of the external reference used (H_3PO_4). The spectrum of the commercial sample MPA has only one sharp line at −3.77 ppm (Fig. 4d). For the Al and Cu salts of the MPA, a small chemical shift displacement to lower fields was observed (Fig. 4). This may be due to the interaction of Cu^{2+} and Al^{3+}, instead of H^+, with the hydration water molecules that the HPAs have in their

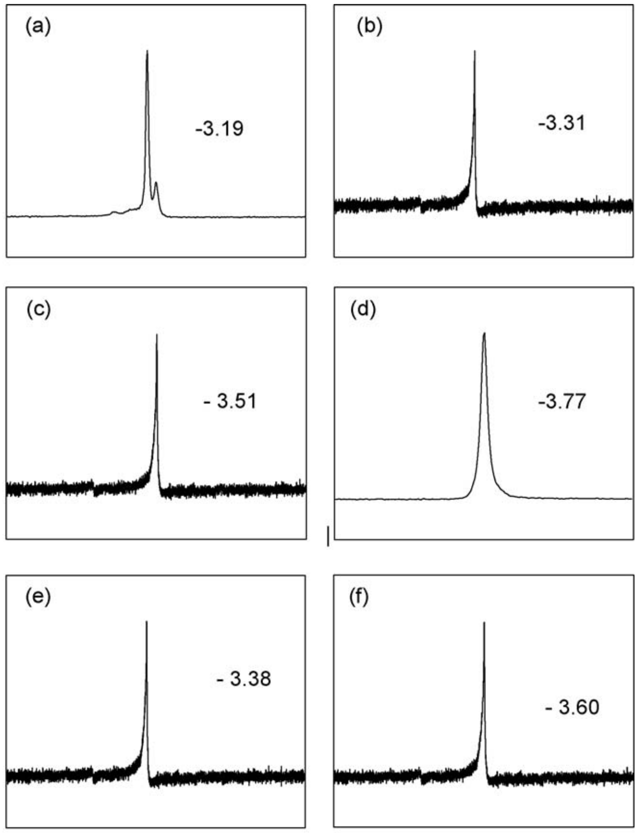


Fig. 4. ^{31}P NMR-MAS spectra (a) AlPMo, (b) Al0.5HPMo, (c) Cu0.5HPMo, (d) MPA, (e) CuPMo and (f) AlPMoAct.

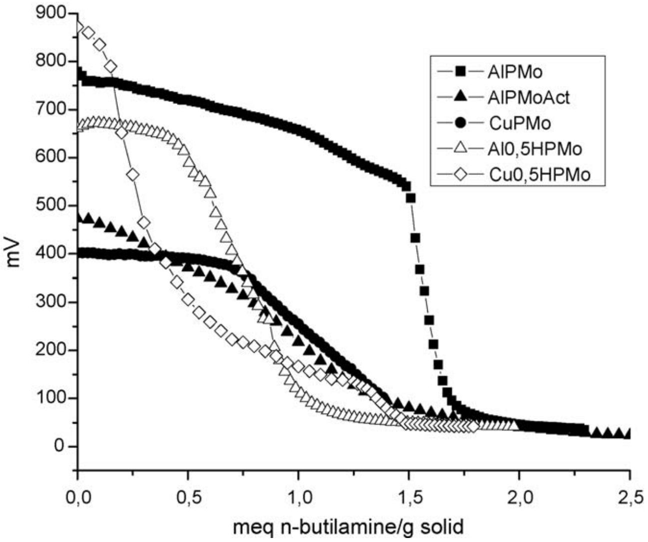


Fig. 5. Potentiometric titration curves for Al or Cu salts of MPA.

secondary structure. That is to say that by this technique it is also possible to verify the presence of the $[PMo_{12}O_{40}]^{3-}$ species in the Al and Cu salts.

The acidity of the salts determined by potentiometric titration, with a solution of *n*-butylamine in acetonitrile, is shown in Fig. 5. As a criterion for interpreting the results obtained, it is suggested that the initial electrode potential (*E*) indicates the maximum acid strength of the acid sites and the value (meq amine/g solid) where the plateau is reached indicates the total number of acid sites. The acid strength of these sites may be classified according to the following scale: $E > 100$ mV (very strong sites), $0 < E < 100$ mV (strong sites), $-100 < E < 0$ (weak sites), and $E < -100$ mV (very weak sites) [28]. The area under the curves of Fig. 5 was calculated to know the total acidity.

In Table 2, the maximum acid strength of the acid sites and total acidity of the different catalysts are shown. It is possible to observe that the Cu0.5HPMo salt presented a maximum acid strength slightly higher than that of the AlPMo salt. However, the AlPMo salt had the highest total acidity. On the other hand, Al0.5HPMo, AlPMoAct and CuPMo salts showed values of maximum acid strength lower than that corresponding to the first two salts. These catalysts presented total acidity lower than that of the AlPMo salt. The values of maximum acid strength of the acid sites observed for all salts were in the range 402–879 mV, therefore all prepared catalysts have very strong sites.

Programmed thermal desorption of the pyridine probe molecule allows determining the total acidity of the samples. The areas under the thermal desorption curves of pyridine, for the different catalysts, are shown in Fig. 6, where the area values with respect to the highest one are plotted. The AlPMo salt has the highest total acidity, whereas the other salts have a much lower total acidity. The total acidity arrangement of the different salts obtained by this technique is similar to that obtained by the potentiometric titration technique (Table 2).

Table 2
Acidity measurements by potentiometric titration with of *n*-butylamine.

Solid	Maximum acid strength (mV)	Total acidity (mV meq *n*-butylamine/g solid)
AlPMo	779	1100
Al0.5HPMo	661	562
AlPMoAct	473	490
CuPMo	402	438
Cu0.5HPMo	879	478

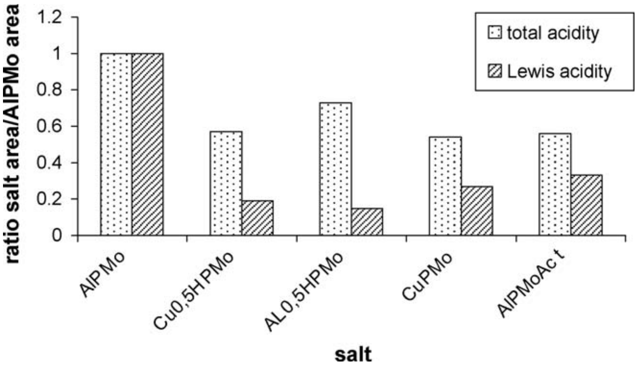


Fig. 6. Total acidity and Lewis acidity by temperature-programmed desorption of pyridine and trimethylpyridine respectively.

The fact that the acidic properties of heteropolycompounds in the solid state are sensitive to countercations explains the results obtained (Table 2, Figs. 5 and 6). The total acidity of aluminum salts were higher than that corresponding to copper salts due to the acidity increases with an increase in the calculated charge on the peripheral oxygen atom of the polyanion. This also explains the lower total acidity of Al0.5HPMo salt with respect to AlPMo salt because part of Al is substituted for H. However, this effect is not very important when Cu is replaced by H. On the other hand, the total acidity of AlPMoAct salt is lower than that of AlPMo salt due to the use of a different precursor for the salt preparation, from $Al_2O(CH_3COO)_4$) and $Al_2(SO_4)_3$), respectively. This preparation condition is also important in governing the acidic properties.

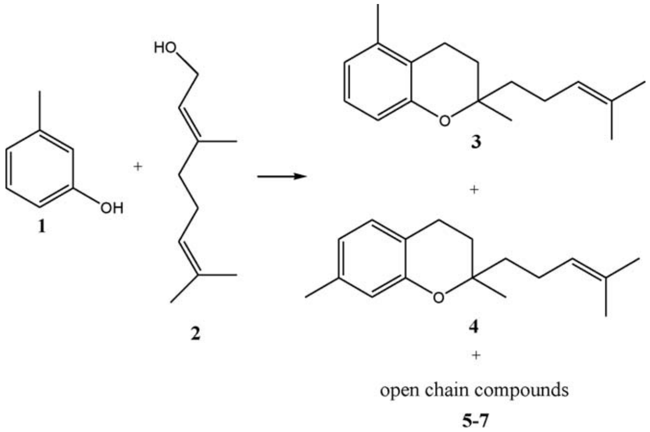
Also programmed thermal desorption tests of trimethylpyridine for the prepared salts were performed to determine Brφnsted acidity sites. The Lewis acid sites are thus obtained through the difference between the areas under the thermal desorption curves of pyridine (total acidity) and the corresponding areas under the thermal desorption curves of trimethylpyridine (Brφnsted acidity). These area values relative to the highest one are plotted for the different catalysts in Fig. 6. In this figure it is possible to observe that the AlPMo salt has a larger number of sites with Lewis acidity than the other catalysts.

With respect to the textural properties of the synthesized aluminum and copper salts, the specific surface area of the AlPMo salt (8.5 m^2/g) is generally eight times higher than that of the other catalysts, even for the similar salt obtained from aluminum acetate. On the other hand, the rest of the salts present a lower surface area than that of MPA (close to 3.0 m^2/g). Since these surface areas are small, 1.1–8.5 m^2/g, it would be advisable to support the catalysts on a porous solid.

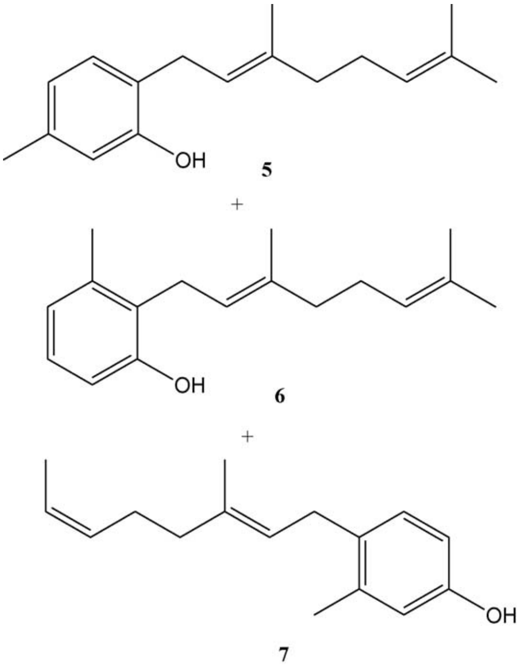
With the objective of proving the catalytic activity of these MPA salts in the synthesis of chromanes, the reaction between *m*-cresol (**1**) and geraniol (**2**) was selected, Scheme 2. In such reaction, the pyranosic ring is formed in only one stage by alkylation of the aromatic ring and a subsequent addition of phenolic OH to the double bond. In this particular case, as the aromatic ring was substituted by a methyl group, the closed ring can be in *ortho* or *para* position with respect to such group. Then it is possible that two chromane isomers be formed. These are 2-(4-methylpent-3-enil)-2,5-dimethylchromane (**3**) and 2-(4-methylpent-3-enil)-2,7-dimethylchromane (**4**) (Scheme 2).

Open-chain reaction intermediaries can also be formed (Scheme 3, **5**–**7**). Their structure was confirmed by nuclear magnetic resonance spectroscopy (^{1}H NMR, HMQC and HMBC).

A reaction time of 5 h and the *m*-cresol:geraniol:catalyst ratio of 1:1:0.033 mmol were used to find the optimum operating conditions and to compare the activity of the different catalysts. The solvent and the reaction temperature were changed.



Scheme 2. Reaction of *m*-cresol (**1**) and geraniol (**2**).



Scheme 3. Open-chain compounds.

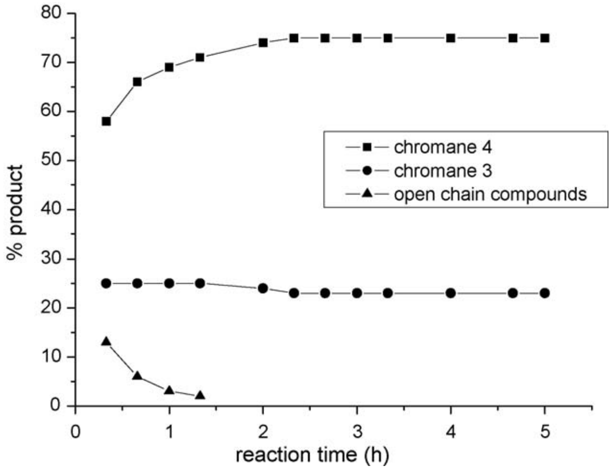


Fig. 7. Conversion of *m*-cresol using AlPMo as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, *T* = 69 °C.

Table 3 summarizes the experimental results when the AlPMo salt was used as catalyst. The yields obtained via purification by *p*-TLC are the sum of the two chromanes. The best yield (45%) resulted when hexane (boiling point: 69 °C) was used as solvent. This is why it is the solvent of choice to test the rest of the salts. In the reaction carried out in hexane when the Cu0.5HPMo salt was used as catalyst, the yield determined by preparative layer of isolated products was 29% (sum of chromanes). It can be seen that it is lower than that obtained when the AlPMo salt was used as catalyst. The following variable to be determined was the amount of geraniol. Using AlPMo as catalyst, the increase of geraniol ratio did not influence the yield.

Table 3
Yields of isolate chromane **3** and **4** determined by preparative thin layer using AlPMo as catalyst.

Solvent	Temperature (°C)	Yield (%)
Chloroform	61	26
Heptane	98	37
Heptane/diethyl carbonate	126	18
Hexane	69	45

Once the best reaction conditions had been set, the catalytic activity of the other salts was evaluated. To follow the evolution of reagents and products, reaction samples were taken at different times and analyzed by HPLC. Retention times of the different compounds are 5.45 min (*m*-cresol); 6.40 min (geraniol); 7.60 min (open-chain compounds); 8.31 min (chromane **4**); 9.40 min (chromane **3**). The three open-chain compounds had the same retention time when they were analyzed by HPLC, so they are grouped together to determine their selectivity.

The results for each catalyst are shown below.

1. AlPMo

In this case the two isomers **3** and **4**, as well as the open-chain compounds **5**–**7**, were obtained.

The conversion and product distribution as a function of reaction time obtained by HPLC are shown in Figs. 7 and 8, respectively.

In the first 20 min of reaction, a 96% conversion of *m*-cresol is achieved, reaching 98% at 1 h 20 min (Fig. 7).

As regards the products obtained (Fig. 8), selectivity at 20 min is 58% of chromane **4**, 25% of chromane **3**, and 13% of open-chain compounds (**5**–**7**). Up to 2 h 40 min the percentage of chromane **4** increases up to 75%, thereafter it keeps constant.

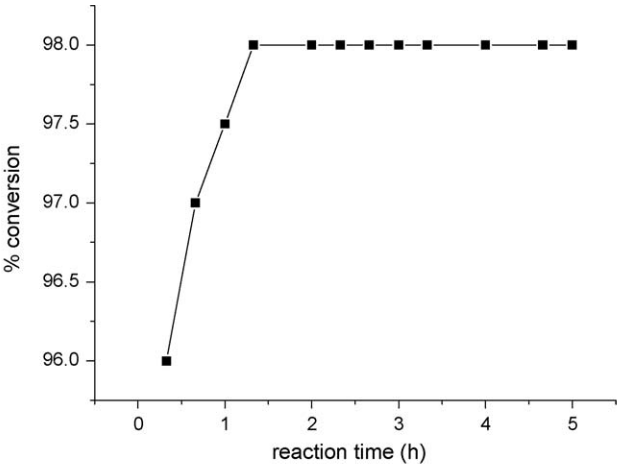


Fig. 8. Selectivity of products using AlPMo as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, *T* = 69 °C.

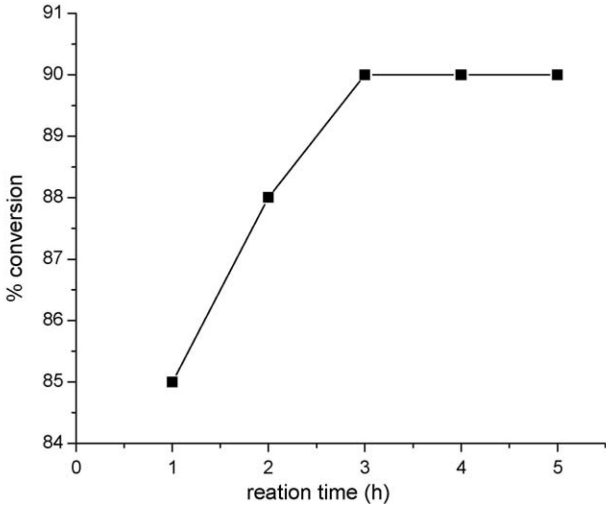


Fig. 9. Conversion of *m*-cresol using Cu0.5HPMo as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, *T* = 69 °C.

The percentage of chromane **3** reaches 25% at 20 min, and then it keeps constant in time. The maximum percentage of open-chain compounds would be formed in the first 20 min of reaction. Then such compounds would transform into the corresponding chromanes since at 2 h they can no longer be detected.

With this catalyst it was tested whether geraniol reacted with itself under the reaction conditions mentioned above (catalyst, temperature, solvent and time reaction). It could be seen that geraniol reacted completely giving autocondensation products that were detected by HPLC and ^{1}H NMR. This is why the absence of these products in the reaction under study indicates that the rate of reaction of geraniol with *m*-cresol is higher than the rate of reaction of geraniol autocondensation

2. Cu0.5HPMo

The conversion of *m*-cresol is 85% in 1 h. It increases up to 90% at 3 h, and then it keeps constant (Fig. 9).

Fig. 10 shows that during the first 3 h of reaction, open-chain compounds rather than chromanes are formed. At 4 h there is 27% of chromane **4**, 5% of chromane **3**, and 58% of open-chain compounds. At 5 h the following percentages are reached: 37% chromane **4**, 10% chromane **3**, and 43% of the rest of the compounds.

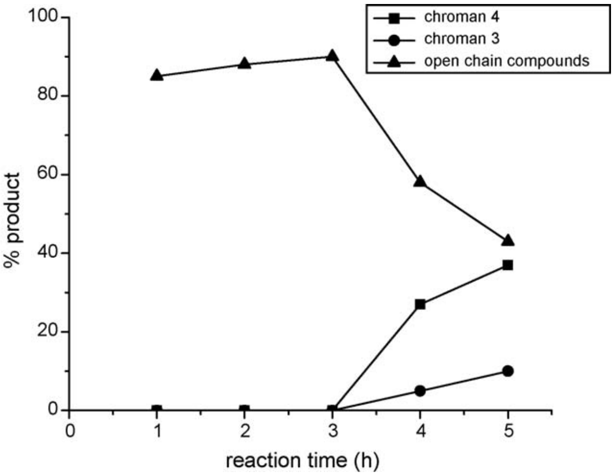


Fig. 10. Selectivity of products using Cu0.5HPMo as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, *T* = 69 °C.

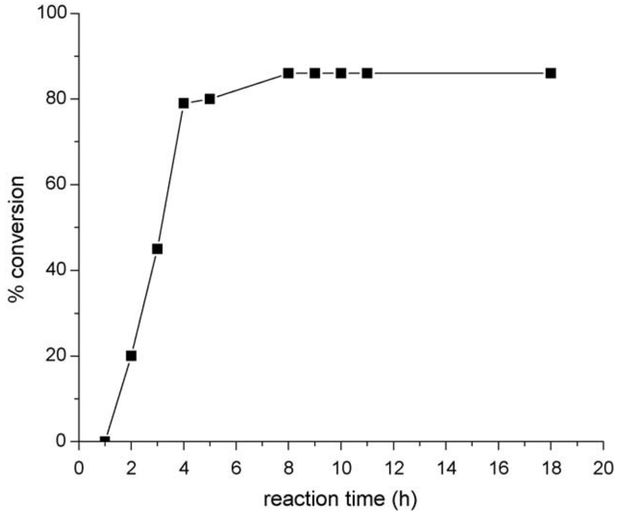


Fig. 11. Conversion of *m*-cresol using Al0.5HPMo as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, *T* = 69 °C.

3. Al0.5HPMo

In this case, only open-chain products are obtained (Fig. 11).

There is no considerable formation of products up to 2 h of reaction. Then there is an exponential increase of open-chain products up to 4 h. At 5 h the conversion is 80%, which is the yield of open-chain compounds. This value keeps constant in time.

The difference between the aluminum salt with partial substitution of protons and the one with total substitution of protons is that in the former case the reaction starts more slowly, and at 5 h *m*-cresol conversion is lower (80% *versus* 98%). Besides, it can only produce the alkylation reaction but not the subsequent ring closure for chromane formation, as occurs in the AlPMo catalyst, which basically gives chromane **3** and **4**.

4. CuPMo

At 1 h of reaction, there is 81% conversion of *m*-cresol into open-chain products, the maximum being reached at 4 h (84%) (Fig. 12).

5. AlPMoAct

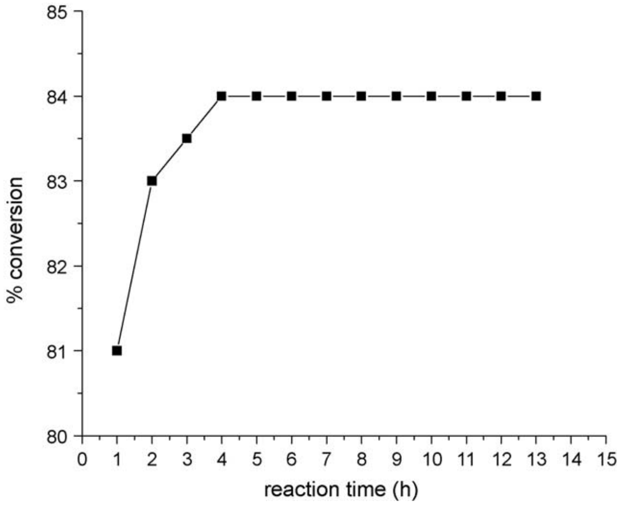


Fig. 12. Conversion of *m*-cresol using CuPMo as catalyst. Reaction condtions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, T = 69 °C.

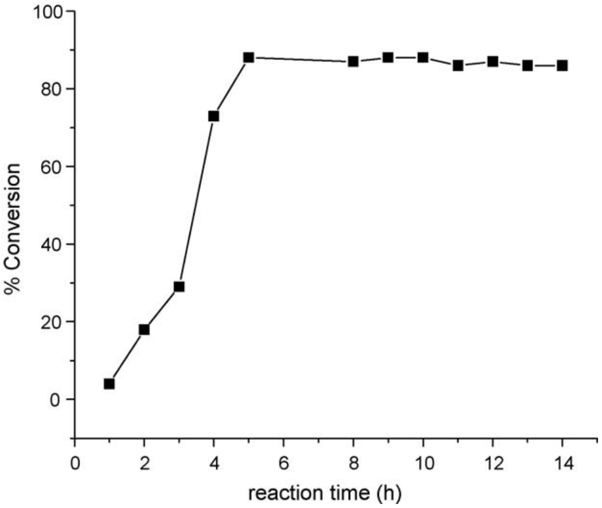


Fig. 13. Conversion of *m*-cresol using AlPMoAct as catalyst. Reaction conditions: *m*-cresol:geraniol:catalyst 1:1:0.033 mmol, hexane, $T = 69\,^{\circ}\mathrm{C}$.

In this case there is 87% conversion of *m*-cresol to open-chain compounds at 5 h of reaction, which keeps constant in time (Fig. 13).

It is worth pointing out how different these products are from those obtained with the same salt prepared from sulfate. Here there is nothing but formation of open-chain compounds. The different behavior between the two salts is due to their very different acidity, as was explained previously.

Summing up we can say that under the conditions set, the only catalysts that gave the above-mentioned chromane **3** and **4** are $AlPMo_{12}O_{40}$, prepared from sulfate, and $Cu_{0.5}H_2PMo_{12}O_{40}$.

With the rest of the salts only the reaction intermediaries **5**–**7** were obtained, where alkylation occurred but the ring was not closed (Scheme 3). The three open-chain compounds have the same retention time when they are analyzed by HPLC; that is why only total selectivity can be determined. By preparative layer, using the mixture hexane:ethyl acetate (10:1) one of them (compound 7) and a mixture of the other two (compounds **5** and **6**) could be isolated. Taking advantage of the higher efficiency of AlPMo to close the ring, both fractions were treated with this catalyst. No reaction was observed with compound **7**, whereas the mixture of compounds **5** and **6** yielded chromane **3** and **4**. These results, together with those from spectroscopic methods, allowed us to determine the structures unequivocally (Scheme 3). Moreover, these results confirm the different behavior of the catalysts.

The results from these experiences can be explained from the standpoint of the catalyst acidity. The catalysts showed different acid behavior, as can be seen in potentiometric titration and programmed thermal desorption tests (Table 2, Figs. 5 and 6).

The $AlPMo_{12}O_{40}$ salt (prepared from sulfate), which at 5 h showed the highest conversion of *m*-cresol (98%), and 75% and 25% selectivity to chromane **4** and **3**, respectively, presented the highest total acidity, as well as acid sites with maximum acid strength very high.

As for the $Cu_{0.5}H_2PMo_{12}O_{40}$ catalyst, at 5 h it showed a conversion of *m*-cresol lower than the former (90%) and lower selectivity to chromane **4** and **3** (37% and 10%, respectively). Moreover, in this case there were 43% of open-chain compounds. This catalytic behavior is on account of the fact that although this catalyst has acid sites with a maximum acid strength slightly higher than that of the catalyst $AlPMo_{12}O_{40}$ (prepared from sulfate), it has lower total acidity.

As for the Al0.5HPMo, AlPMoAct and CuPMo salts, at 5 h they showed conversions of *m*-cresol 80%, 87% and 84%, respectively, lower than corresponding to $AlPMo_{12}O_{40}$ (prepared from sulfate) and $Cu_{0.5}H_2PMo_{12}O_{40}$ catalysts. The products obtained with these catalysts were only the reaction intermediaries (open-chain compounds). The different catalytic behavior is because they showed values of maximum acid strength lower than that corresponding to the $AlPMo_{12}O_{40}$ (prepared from sulfate) and $Cu_{0.5}H_2PMo_{12}O_{40}$ catalysts, and they presented total acidity lower than that of the AlPMo salt.

On the other hand, the values of Lewis acidity determined by programmed thermal desorption tests (Fig. 6) showed that the AlPMo salt has a greater number of sites with Lewis acidity than the other catalysts. Also it is important to bear in mind the fact that copper has lower Lewis acidity than aluminum [29,30].

Under the same test conditions used with the above salts, $ZnCl_2$ and $AlCl_3$ catalysts, which are traditionally used in the synthesis reactions described, were tested. There was no reaction in either of the two cases. This can be because these salts are used in stoichiometric amounts in these studies, and in this case a 3.3% with respect to the reactants was used.

The results of the catalyst leaching experiences showed that the values of reactive conversion and products yields remained constant when the catalyst was filtered. Then, it is possible to assure that the reaction in these conditions is heterogeneous.

On the other hand, the values of reactive conversion and products yields remained nearly constant after the re-use of the catalyst, 97–99% and 80–90%, respectively.

4. Conclusions

Acid catalysts based on the aluminum (or copper) salts of molybdophosphoric acid were synthesized. Using different characterization techniques it was possible to determine that these salts present a crystalline structure and the Keggin-type heteropolyanion is undegraded. The salts prepared presented different acid characteristics. The $AlPMo_{12}O_{40}$ salt (from sulfate), presented the highest total acidity and, simultaneously, acid sites with maximum acid strength very high. The $Cu_{0.5}H_2PMo_{12}O_{40}$ catalyst showed acid sites with the highest maximum acid strength but its total acidity was low. On the other hand, the rest of the salts presented low total acidity and acid sites with maximum acid strength very low.

The prepared catalysts were used in the reaction between *m*-cresol and geraniol for the synthesis of chromanes. The conversion of *m*-cresol and product selectivity is a function of the acid characteristics of each salt.

The $AlPMo_{12}O_{40}$ salt (from sulfate), at 5 h of reaction showed the highest conversion of *m*-cresol (98%) and 75% and 25% selectivity to chromane **4** and to chromane **3**, respectively, because it presented the highest total acidity and, simultaneously, acid sites with maximum acid strength very high. On the other hand, the $Cu_{0.5}H_2PMo_{12}O_{40}$ catalyst at 5 h of reaction showed lower conversion of *m*-cresol than the former salt (90%) and also lower selectivity to chromane **4** and to chromane **3** (37% and 10%, respectively). In the latter case also 43% of open-chain compounds were observed. With the other salts, only the reaction intermediaries, open-chain compounds, were obtained.

On the other hand, a better behavior of the Keggin heteropolycompounds with respect to $ZnCl_2$ was obtained. In the latter case, under the same operating conditions, no reaction was observed.

In short, eco-friendly catalysts, insoluble in the reaction solution, were obtained for the synthesis of chromanes. With the aim of increasing the yield, due to their low specific surface area, it is planned to support these catalysts on mesoporous materials.

Acknowledgments

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