

Friedel–Crafts acylation of anisole with acetic anhydride over silica-supported heteropolyphosphotungstic acid (HPW/SiO₂)

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Abstract

Methoxyacetophenones were synthesized through Friedel–Crafts acylation of anisole with acetic anhydride using a silica-supported heteropolyphosphotungstic acid (HPW) catalyst. High conversions and very high *p*-selectivity were attained in the temperature range of 61–110 °C. Nevertheless, the catalyst seemed to deactivate after half an hour at 61 and 83 °C, mainly due to strong but reversible adsorption of products. Cleaning the spent catalyst recovered the activity, indicating that it was stable under the experimental conditions and that the active HPW was not fairly leached from the silica support. In spite of this, the slower but progressive coking deactivated the catalyst.

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1. Introduction

The synthesis of aromatic ketones constitutes a very important route to the preparation of a wide variety of fine chemicals. This is usually accomplished through Friedel–Crafts acylation of aromatic substrates like phenol, anisole and many others. Traditional catalysts are inorganic acids such as sulfuric acid, polyphosphoric acid or metal halides like AlCl₃, ZnCl₂ and BF₃ [1]. Besides presenting limited selectivity, these catalysts offer the disadvantages of generating environmentally unwanted wastes and increasing costs due to premature ageing of the processing apparatus by corrosion. The acylating agents used in most of the traditional processes are the expensive and polluting acyl halides that require special cares in handling and working up. In view of that, the non-leachable ecofriendly solid

acid catalysts, as they can be regenerated and re-used many times avoiding drift accumulation, coupled with the use of cheap and promptly available non-polluting carboxylic acids and anhydrides, have been scoped as beneficial and profitable candidates.

Among the solid acid catalysts, acidic zeolites, modified clays, silica–alumina, sulphated zirconia and some others have been investigated in the production of these aromatic derivatives, some of them already in use in industrial plants. Hereupon, we have investigated the synthesis of methoxyacetophenones through the Friedel–Crafts acylation of anisole with acetic anhydride using silica-supported heteropolyphosphotungstic acid (HPW/SiO₂). The synthesis of such acylates has already been performed with some zeolite catalysts [2–4]. Heteropolyacids are very strong solid Brønsted acids [5], exhibiting high chemical and thermal stabilities and non-polluting character due to its chemical nature. Another important feature of heteropolycompounds (HPCs) is their capability for easy structural changes allowing a wide range of chemical properties with very simple synthetic procedures. These last considerations have motivated the investigation of heteropolyacids and their derivatives as catalysts for the acylation of aromatics [6–9] in the recent years.

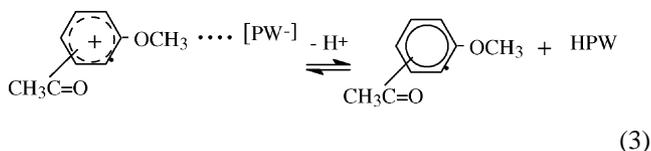
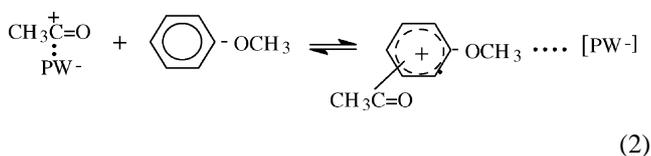
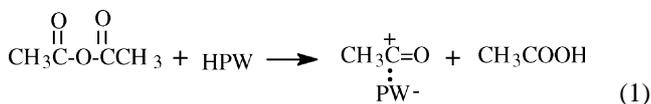
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The strong Brønsted sites on the acid HPC are able to generate acylium ions which are the active intermediates in the acylation of aromatic substrates through the electrophilic attack at the π -electron system of the substrate. A Weyland type transition state is suggested as intermediate in the formation of aromatic ketones [4,10]. The use of carboxylic acids and acid anhydrides are advantageous alternatives to halogenated agents when more efficient acid catalysts are available. On the other hand, the mobile protons in the cages of the HPCs and the homogeneous micropore structure render such catalysts high stereoselectivity and high activity in many chemical reactions, making them promising substitutes for the traditional polluting inorganic acids and metal halides.

Anisole is an *ortho/para* directing substrate for electrophilic substitution reactions, presenting a relatively high susceptibility to such reactions by means of the release of electron density from the methoxy-oxygen atom to the aromatic ring, constituting itself in a very feasible substrate for the synthesis of substituted ketones. The possible pathways for the production of methoxyacetophenones in the Friedel–Crafts acylation of anisole with acetic anhydride catalysed by heteropolyacids are shown below:



The mobile HPW proton initially protonates the anhydride molecule generating an adsorbed acylium ion which subsequently attacks the π -electrons of anisole to form methoxyacetophenones.

2. Experimental

2.1. Catalyst preparation

Heteropolyphosphotungstic acid was purchased from Merck and extracted from water solution by ethyl ether. The etherate was evaporated at room temperature and heated at 110 °C for 2 h and further on at 150 °C for 3 h. Silica was purchased from Carlo Erba Analyticals (ϕ 0.05–0.20 mm). Prior to use, the silica support was washed with nitric acid, then with water and finally calcined at 700 °C overnight.

The supported acid was prepared by incipient wetness impregnation with stoichiometrically weighed amounts of HPW and silica. After mixing thoroughly the aqueous slurry for 2 h and evaporating at 110 °C to dryness, the supported catalyst was further heated at 150 °C for 3 h.

2.2. Catalyst characterization

BET surface area by N₂ adsorption, infrared spectroscopy (FTIR), *n*-butylamine thermal desorption, *n*-butylamine titration, X-ray diffractometry and thermal analyses techniques were used to characterize the catalyst.

The primary structure (Keggin anion) of HPCs was ascertained by infrared spectroscopy [11]. The FTIR spectra were collected using a Jasco Valor III Spectrometer using KBr wafers with 1% weight of the acid.

The secondary structure was studied by X-ray diffraction on pressed samples over a flat slide and was carried out in a Shimadzu 6000 Diffractometer using a 1.54 Å (Cu K α) line, covering a 2θ range of 5–60°.

TG analyses were carried out on a Shimadzu TG-50.

In order to assess the acid strength of the catalyst, the thermal desorption of *n*-butylamine was monitored by TG. For the weight loss analysis, the catalyst was initially heated in an appropriate cell, under dry nitrogen atmosphere at 400 °C for 2 h; cooled to 95 °C and saturated with *n*-butylamine, supplied from a saturator, at this temperature. The system was kept at 95 °C for more 2 h under dry nitrogen purge. The sample was then transferred to the TG balance and analyzed at a heating rate of 10 °C/min in dry N₂ flow of 50 ml/min. A blank run was undertaken in order to follow the typical weight loss profile of the catalyst without adsorbed *n*-butylamine.

The quantitative determination of acidic sites was made by potentiometric titration with 0.05N *n*-butylamine in acetonitrile. A sample of 1 g of the catalyst was added to 50 ml of acetonitrile and the system was magnetically stirred at 25 °C. The initial potential was measured after electrode signal stabilization. Small aliquots (0.5 ml) of *n*-butylamine 0.05N in acetonitrile were added and the potential recorded after stabilization of readings [12].

2.3. Reaction procedure

The acylation reactions were carried out in a batch reactor composed of a round bottom, 100 ml Pyrex flask connected to a reflux condenser. The reactions were carried out using chloroform, dichloroethane and toluene as solvents, magnetic stirring (600 rpm) and controlled temperatures (61, 83 or 110 °C).

The reagent mixtures were heated to preset temperatures under stirring and then the catalyst was added without any previous treatment. Samples were periodically drawn from the reactor using a filtering syringe, diluted with dichloromethane and analyzed by gas chromatography (GC) Varian 3400. The products were identified by GC–MS and

^1H , ^{13}C NMR. At the end of each reaction experiment, the catalyst was filtered and washed with dichloromethane. The filtrate was analysed by GC and the catalyst was further extracted with dichloromethane using a soxhlet apparatus. Blank runs were performed using silica for 4 h and no conversion was detected under conditions similar to those used in catalytic reactions.

Conversion was defined as the percent of anisole converted into products expressed as:

$$X = (1 - x_{\text{anisole}}) \times 100 \quad (4)$$

where x_{anisole} is the mole fraction of anisole in reaction mixture.

3. Results and discussion

3.1. Catalyst characterization

The silica support exhibited a surface area of $336 \text{ m}^2/\text{g}$ and the supported HPW/ SiO_2 (40%) catalyst, $170 \text{ m}^2/\text{g}$. As pure HPW usually shows an average surface area of about $10 \text{ m}^2/\text{g}$, supporting it on silica significantly increased its surface area so that accessibility to reactants was significantly improved.

The IR absorption bands assigned to the Keggin anion ($800\text{--}1100 \text{ cm}^{-1}$) in pure and silica-supported HPW are seen in Fig. 1. A shoulder of silica band appeared at approximately 1200 cm^{-1} , partially superseding HPW 1080 cm^{-1}

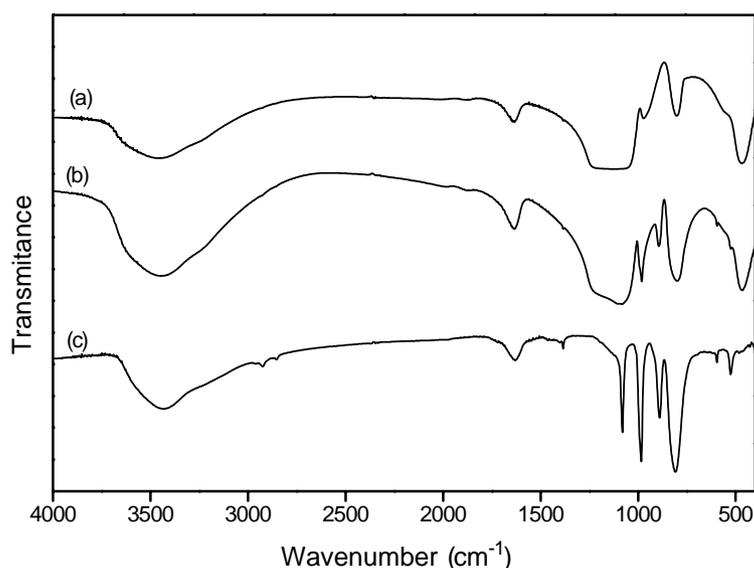


Fig. 1. IR spectra: (a) silica; (b) silica-supported HPW (40%); (c) phosphotungstic acid (HPW).

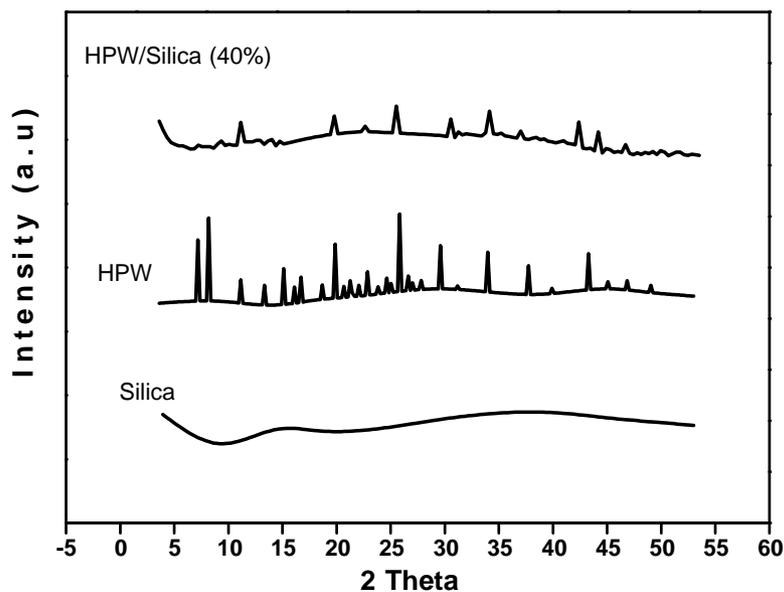


Fig. 2. X-rays diffractograms: (a) silica; (b) phosphotungstic acid (HPW); (c) silica-supported HPW (40%).

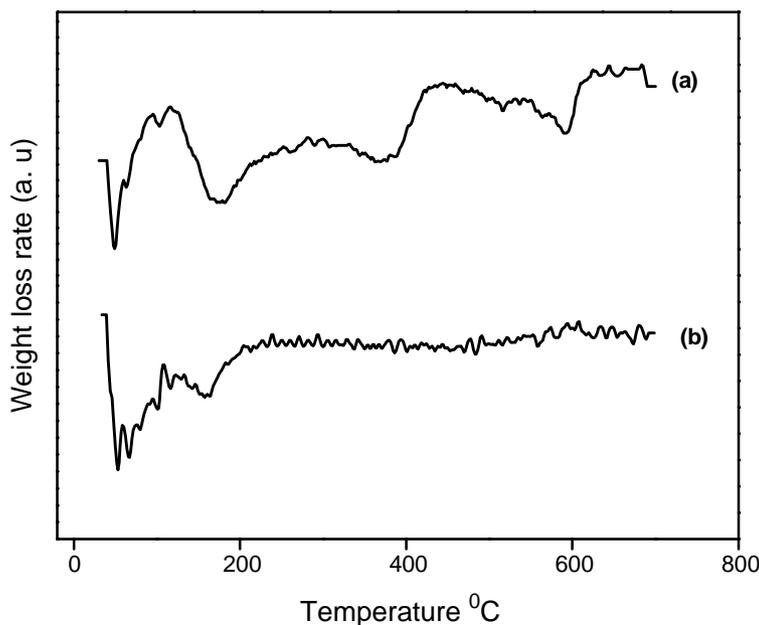


Fig. 3. Weight loss thermograms: (a) *n*-butylamine saturated (HPW/SiO₂—40%); (b) HPW/SiO₂ (40%).

stretching (Fig. 1b). Due to strong absorption of silica in the region of the Keggin anion “fingerprint”, some of its characteristic absorption bands become uncleaned, however some could still be detected for the supported catalyst, Fig. 1(b), as that band at 881 cm⁻¹, typical of the Keggin anion and not observed in the silica spectrum. The band around 1080 cm⁻¹ is attributed to the stretching vibration of P–O, that at 970 cm⁻¹ to the stretching vibration of W=O and those at 880 and 805 cm⁻¹ to the stretching vibrations of W–O_b–W and W–O_c–W where O_b and O_c are the corner sharing and edge-sharing bridge oxygen [11,12].

The major diffraction peaks of crystalline HPW ({110} and {222}) are seen in Fig. 2. The broadening of the peaks of the supported acid as compared to those of the pure acid suggests that solid HPW has been finely deposited onto the silica surface, as also observed by Blasco et al. [13].

In the TG profile collected for *n*-butylamine desorption from the saturated catalyst, one peak in the range of 350–450 °C is assigned to desorption of *n*-butylamine from strong Brønsted sites. The weight loss between 550 and 630 °C can be attributed to *n*-butylamine desorption or decomposition from the remaining very strong acid sites of the active HPW (Fig. 3(a)). In the temperature range

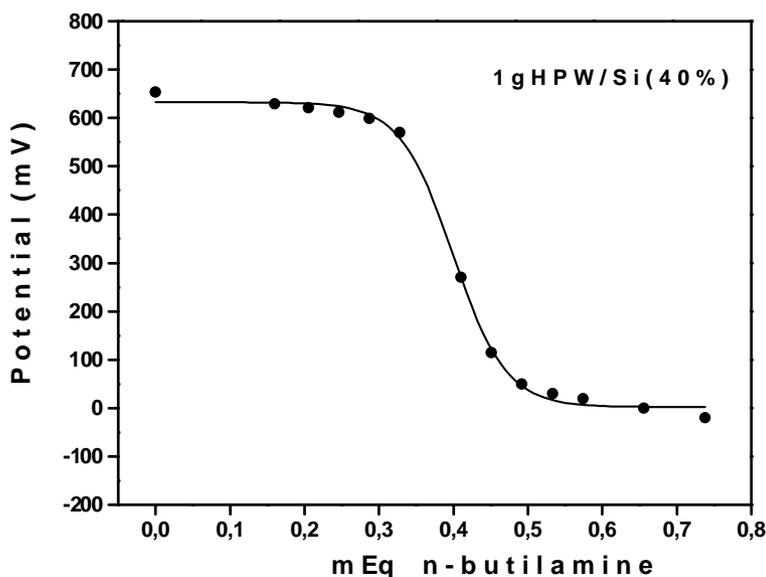


Fig. 4. Potentiometric titration of 1 g HPW/SiO₂ (40%) in acetonitrile with 0.05N *n*-butylamine in acetonitrile.

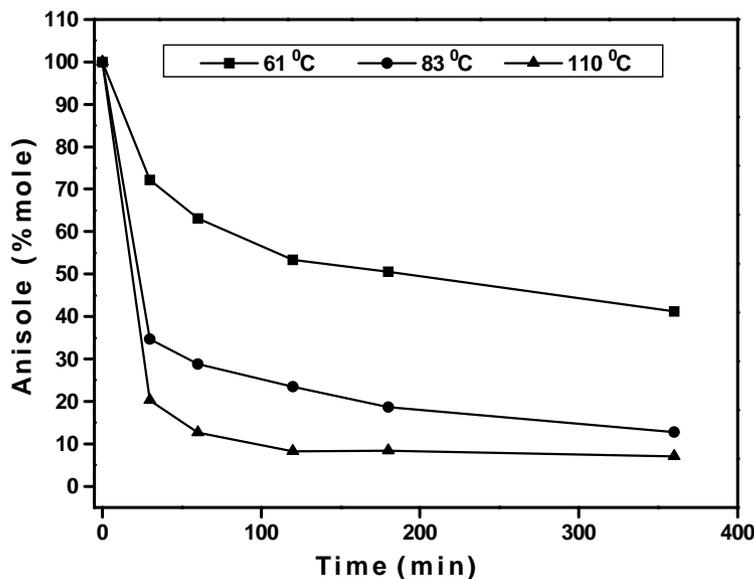


Fig. 5. Effect of temperature on the conversion of anisole: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol. 61 °C, chloroform; 83 °C, dichloroethane; 110 °C, toluene.

below 200 °C, the usual weight loss peaks due to water desorption are also seen. For comparison, the weight loss profile of a clean HPW/SiO₂ (40%) sample is shown in Fig. 3(b). The peaks below 200 °C are due to physisorbed and crystallization water in HPW. No weight loss was detected above 200 °C on the profile of silica-supported HPW (Fig. 3(b)). This should corroborate the interpretation that the two peaks above 350 °C on the weight loss profile of the saturated catalyst (Fig. 3(a)) are either due to desorption or decomposition of *n*-butylamine adsorbed on highly acidic sites and not to decomposition of HPW.

According to Vásquez et al. [12], the potentiometric titration with 0.05N *n*-butylamine enables the quantitative determination of Brönsted acid sites. As suggested by the author, sites at potential >100 mV are very strong, sites at mV 0 < *E* < 100 are strong and those at -100 < *E* < 0 are weak.

From the plot shown in Fig. 4, an equivalent mass of 0.4 mg *n*-butylamine was determined at potentials above 250 mV, corresponding to the total number of HPW acidic protons and indicating that all those acidic sites were very strong. The silica support was titrated at lower potentials (*E* < 0 mV) in the range of very weak acid sites.

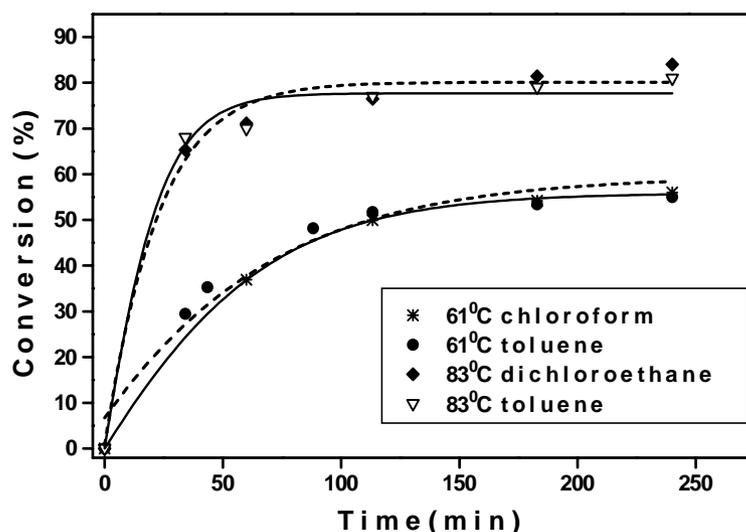


Fig. 6. Anisole conversion in toluene at 61 and 83 °C, in chloroform at 61 °C and in dichloroethane at 83 °C: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 97.5 mmol.

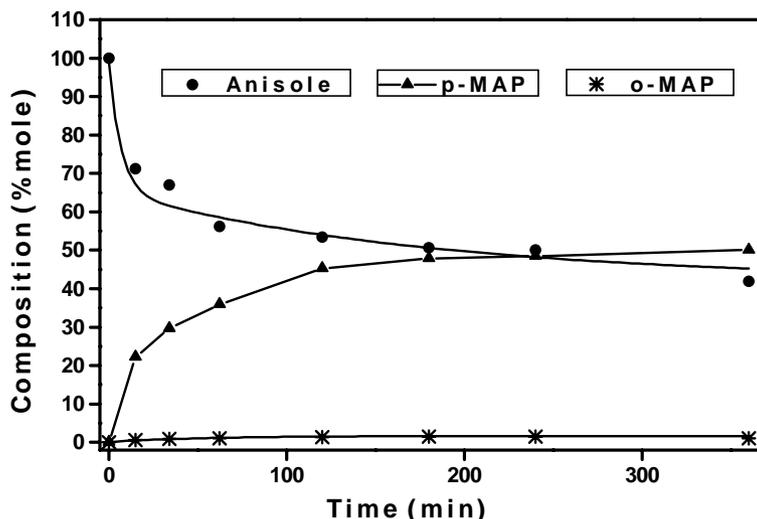


Fig. 7. Composition (% mole)—reaction time plot, using: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol; temperature 61 °C. chloroform, solvent.

3.2. Acylation results

Anisole conversion is shown in Fig. 5 as a function of reaction temperature. Using toluene as solvent, at 110 °C, the reaction almost completely ended soon after an hour, reaching 90% of conversion. At lower temperatures, using dichloroethane (83 °C) and chloroform (61 °C) as solvents, lower conversions were attained, 80 and 55%, respectively, after 1 h. The initial conversion at 83 °C was very close to that at 110 °C but that at 61 °C was fairly lower, showing a progressive deceleration after 30 min, over the investigated temperature range. Fig. 6 shows the conversion plots for the reaction conducted at 83 °C, in toluene and in dichloroethane and at 61 °C, in toluene and in chloroform. The fair coincidence of the conversion plots allows one to conclude that

solvent effects were minor and thermal effects were responsible for the kinetic behavior of the reaction.

The plots of anisole consumption and yield of products are shown in Figs. 7–9. *p*-Methoxyacetophenone (*p*-MAP) was almost the only product, attaining selectivity above 90%, all over the temperature range. The premature conversion decline in the temperature range 61–83 °C, as compared to that at 110 °C, should be attributed to catalyst deactivation, either due to coking or to reversible adsorption of products on the acidic catalyst sites. The spent catalyst was cleaned by quenching the reaction with dichloromethane, filtering the catalyst and refluxing it in dichloromethane. The dry catalyst was then reused for the acylation reaction with fresh reactants, in cycles of 6 h, comprising a total reaction time of 44 h. The analyses of the extracts revealed the removed

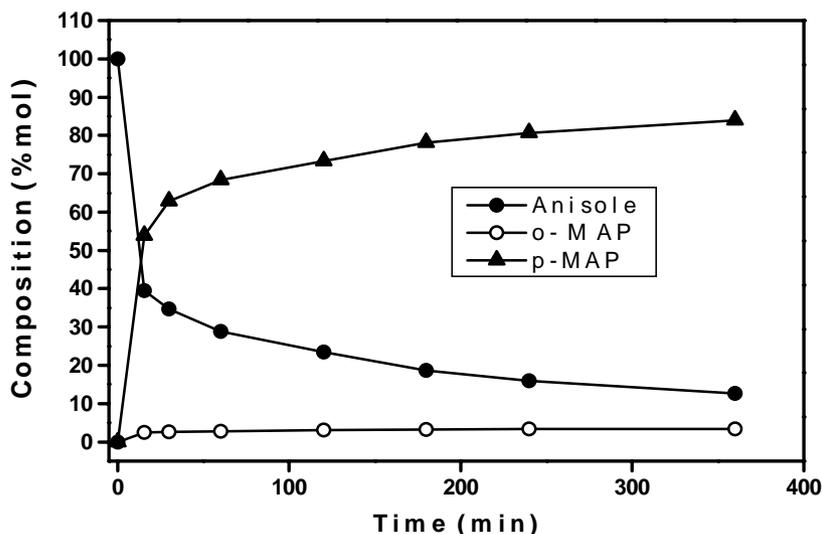


Fig. 8. Composition (% mole)—reaction time plot, using: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol; temperature: 83 °C. Dichloroethane, solvent.

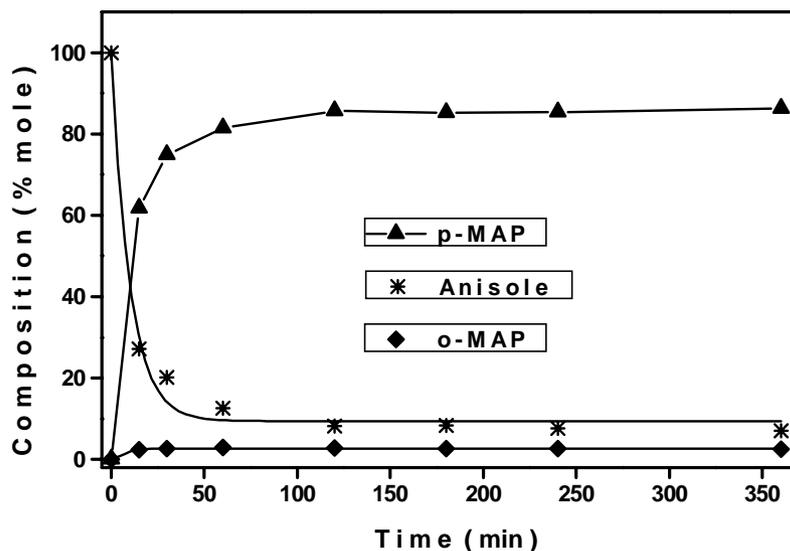


Fig. 9. Composition (% mole)—reaction time plot, using: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol; temperature, 110 °C. Toluene, solvent.

deposits contained *p*-MAP (most) and minor traces of anisole. The activity of the catalyst was completely restored up to the fourth cycle but, thereafter, a slight and progressive conversion decrease was found, as shown in Fig. 10. Either small losses of active phase due to the intensive cleaning procedure or slow coking could account for that. No significant composition change was found for the spent catalyst by chemical analyses. TG analysis in flowing air showed a weight loss of 7.6%, at 500 °C, for the catalyst used during 44 h in the acylation reaction (Fig. 11). Moreover, the resistant dark deposits on this spent catalyst were removed after burning it at 500 °C in air but the catalytic activity was no longer restored. These last findings thus suggest that both a fast but reversible and a slower but irre-

versible deactivation of the HPW catalyst may occur during the acylation reaction, respectively due to preferential adsorption of products and reagents and to catalyst coking or decomposition during the burning of the coke.

A fast deactivation is generally observed in aromatic acylation reactions when acidic porous solids such as zeolites are used [3,14] as catalysts. Rohan et al. [15] proposed that, at least in part, the deactivation of HBEA zeolite was due to the retention of *p*-MAP inside the pores of the catalyst. Smith et al. [16] suggested that acetic acid formed in reaction should reversibly interfere in the activity of the zeolitic catalyst. On the other hand, according to Kozhevnikov [9], coke formation causes the irreversible deactivation of the HPA catalysts in Friedel–Crafts reactions.

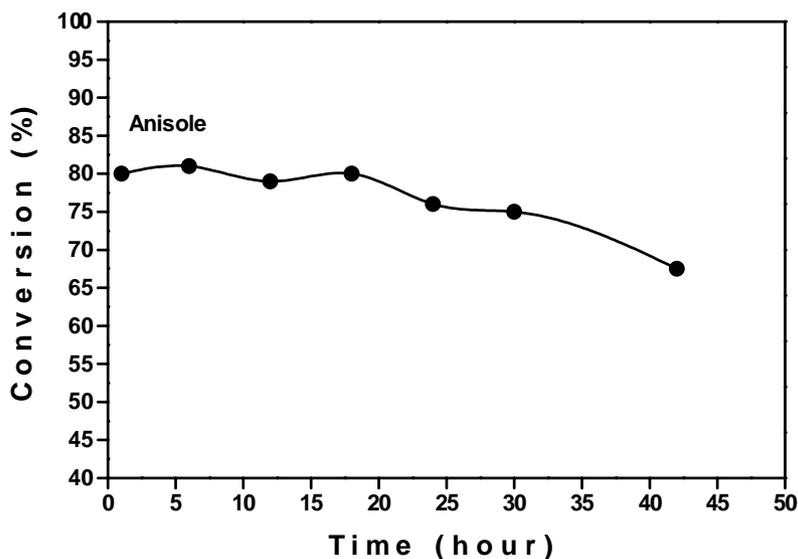


Fig. 10. Conversion of anisole as a function of time: anisole, 2.3 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol; temperature, 83 °C. Dichloroethane, solvent.

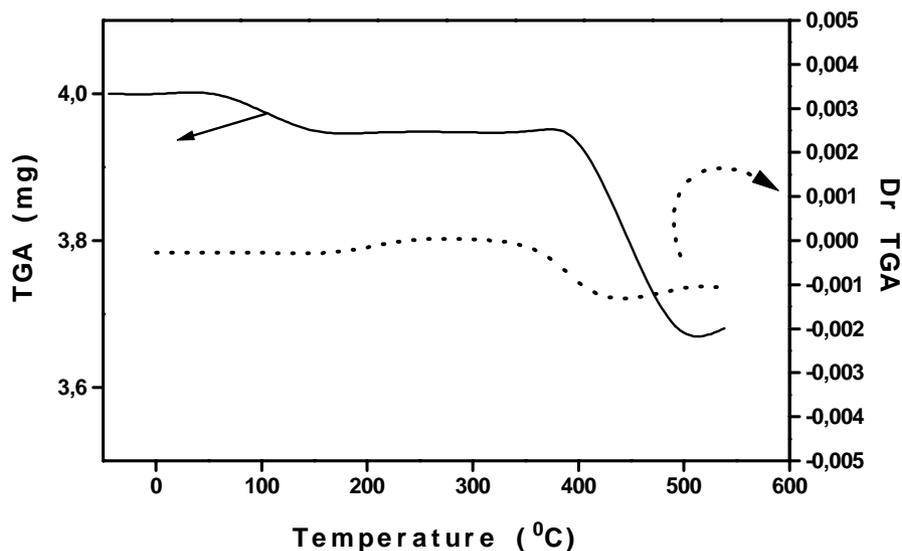


Fig. 11. Weight loss of spent catalyst used for 44 h in reaction, at 83 °C: anisole, 2.31 mmol; 0.5 g of HPW/SiO₂ 40%, 0.066 mmol HPW; acetic anhydride, 7.5 mmol. Dichloroethane, solvent.

Derouane et al. [3] used the Langmuir–Hinshelwood kinetic model in order to find out the reason of the early deactivation of zeolites in such reaction. Taking into consideration that all the catalytic active sites are equivalent and that reactants and products, except acetic acid, compete for those sites, the authors found relative adsorption equilibrium constants of 1 for acetic anhydride, 1.53 for anisole and 9.65 for *p*-MAP. These figures thereby suggested that very strong *p*-MAP adsorption on the active sites of the catalyst was responsible for the observed deactivation.

Following the above reasoning, the relative values $K_A = 1$ (acetic anhydride equilibrium adsorption constant), $K_B = 1.5$ (anisole equilibrium adsorption constant) and $K_P = 1.5$,

5.0 and 9.6 (*p*-MAP relative equilibrium adsorption constant) were used in Eq. (5) [3] and the obtained plots are shown in Fig. 12.

$$\text{rate} = k \frac{K_A K_B [A][B]}{(1 + K_A [A] + K_B [B] + K_P [P])^2} \quad (5)$$

The experimental data (83 °C, in dichloroethane) fitted well the plot for $K_P = 9.6$, suggesting that the kinetic model found for zeolites [3] also holds for the silica-supported HPW catalyst and that the strong adsorption of *p*-MAP onto the acidic sites accounted for the major fast decrease in anisole conversion, in the temperature range of 61–83 °C.

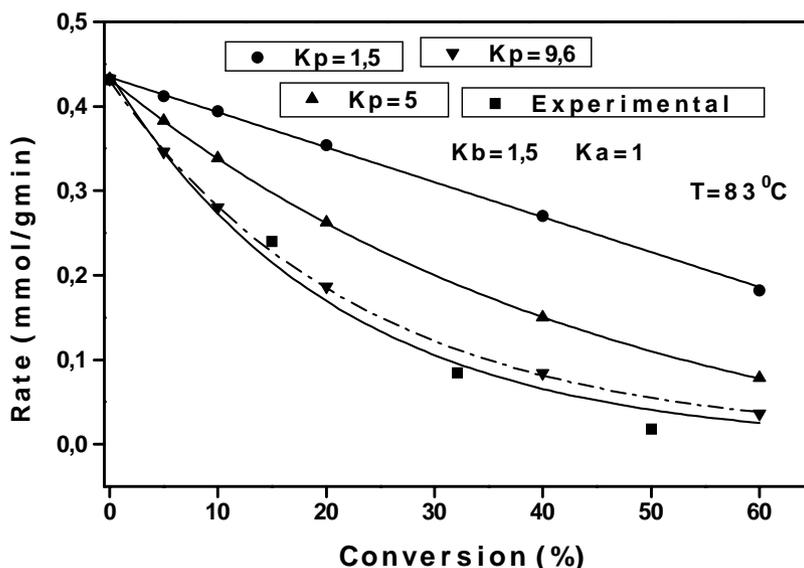
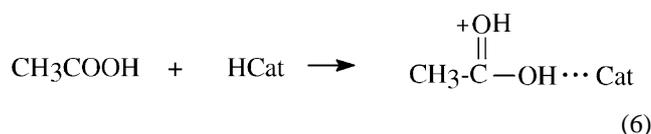


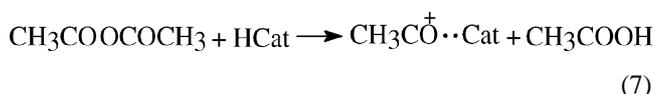
Fig. 12. Model rate plots and experimental data (dashed line), according to Eq. (5): anisole, 2.31 mmol; acetic anhydride, 7.5 mmol; 0.5 g of catalyst, 0.066 mmol HPW at 83 °C. Dichloroethane, solvent.

Kaur et al. [17] recently studied the solvent free acylation of anisole by heteropolyacids, finding a relative adsorption constant of *p*-MAP 37 times higher than that of anisole. However, the use of solvents should modify the adsorption characteristics of the produced ketones.

Ma et al. [18] have pointed out the influence of the nature of the acylating agents, the character of the aromatic substrate and the nature of the active sites of the catalyst on the reaction mechanism. Accordingly, two types of charged electrophiles are responsible for the attack at the aromatic substrate: (1) a protonated carboxylic acid (Eq. (6)):



and (2) an acylium ion (Eq. (7)):



A low conversion of nearly 5% was found when acetic acid was used as acylating agent, corroborating the assumptions that acylium ions are hardly formed from acetic acid and that *p*-MAP is formed by direct C-acylation of anisole with acylium ions. In our studies, no O-acylated product was found and the high selectivity toward *p*-MAP was ascribed to the structural and acidic properties of the catalyst.

4. Conclusion

High conversion and *p*-selectivity in the acylation of anisole with acetic anhydride were achieved in the presence of HPW/SiO₂ catalyst and solvents, under relatively mild conditions. In spite of the relatively fast reversible deacti-

vation of the catalyst, the substrate is rapidly and almost quantitatively transformed into *p*-methoxyacetophenone, at 110 °C. Flow conditions should minimize the fast deactivation by *p*-MAP adsorption but the slower coking still might limit the catalyst lifetime.

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