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Friedel–Crafts Acylation Catalysed by Heteropoly Acids

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The Friedel–Crafts acylation of anisole (AN) with acetic anhydride (AA) in liquid phase catalysed by bulk and silica-supported heteropoly acids (HPA), mainly $H_3PW_{12}O_{40}$ (PW), has been studied. The PW exhibit very high activity, yielding up to 98% para and 2–4% ortho isomer of methoxyacetophenone (MOAP) at 90–110°C and an AN/AA molar ratio of 10–20. Catalyst pretreatment is essential; the activity passes a maximum at a pretreatment temperature of 150°C. The acylation of anisole appears to be heterogeneously catalysed; no contribution of homogeneous catalysis by HPA was observed. PW is almost a factor of 100 more active than the zeolite H-beta, which is in agreement with the higher acid strength of HPA. The PW catalyst is reusable, although gradual decline of activity was observed due to the coking of the catalyst. The acylation is inhibited by product because of adsorption of MOAP on the catalyst surface. The ratio of adsorption coefficients of MOAP and anisole has been found to be 37 at 90°C. Anisole acylation is first order in acetic anhydride, the order in catalyst is 0.66, and the apparent activation energy is 41 kJ/mol in the temperature range of 70–110°C. In contrast to anisole, the acylation of toluene with HPA is far less efficient than that with H-beta. Evidence is provided that the activity of HPA in toluene acylation is inhibited by preferential adsorption of acetic anhydride on the catalyst.

Key Words: **heterogeneous catalysis; Freidel–Crafts reaction; acylation; heteropoly acid.**

INTRODUCTION

The Friedel–Crafts acylation of aromatic compounds is the most important route for the synthesis of aromatic ketones that are intermediates in manufacturing fine and speciality chemicals as well as pharmaceuticals (1). The reaction occurs by interaction of the aromatic compound with a carboxylic acid derivative (e.g., acid anhydride, acyl chloride, or the acid itself) in the presence of an acid catalyst and involves acylium ion intermediates that are generated from the acylating agent by interaction with the acid catalyst. Present industrial practice requires a stoichiometric amount of soluble Lewis acids (e.g., $AlCl_3$) or strong mineral acids (e.g., HF) as catalysts, which results in a substantial amount of waste and corrosion problems (2). The overuse of catalyst is caused by product inhibition—the formation of strong complexes between the aromatic ketone and the catalyst. In view of the increasingly strict environmental legislation, the application of heterogeneous catalysis has become attractive. In the last couple of decades, considerable effort has been put into developing heterogeneously catalysed Friedel–Crafts chemistry using solid acid catalysts such as zeolites, clays, Nafion-H, and so forth (2), with zeolites being the most-studied catalysts (2–8 and references therein). The acylation of anisole with acetic anhydride using a zeolite catalyst has been commercialised by Rhodia (2).

Although relatively active catalysts, the zeolites (e.g., H-beta) are deactivated in the acylation (6–8). The main deactivation is deemed to be reversible; this is attributed to the strong adsorption of the acylation product on the catalyst, blocking access to the active sites. Another type of deactivation, which is irreversible, is caused by tar deposition on the catalyst surface (coking). The carbonaceous deposit could be removable by aerobic treatment at high temperatures (500–550°C). Deactivation may also be caused by dealumination of zeolite with by-product acid (e.g., acetic acid).

Heteropoly acids (HPAs) are another type of promising solid acid catalyst for aromatic acylation. Heteropoly acids are strong Brønsted acids composed of heteropoly anions and protons as the countercations. The Keggin-type HPAs typically represented by the formula $H_{x-8}[XM_{12}O_{40}]$, where X is the heteroatom, x is its oxidation state, and M is the addenda atom (usually Mo^{6+}or W^{6+}), are the most important for catalysis (9–12). They are stronger than many conventional solid acids such as mixed oxides, zeolites, and so forth. In the last three decades, HPAs have been widely used as acid and oxidation catalysts for organic synthesis and they are found in several industrial applications (9–11). However, only a few studies on the use of HPAs for Friedel–Crafts acylation have been published (9, 13).

The aim of the present work is to study the acylation of anisole (AN) and toluene with acetic anhydride (AA) in liquid phase catalysed by bulk and silica-supported

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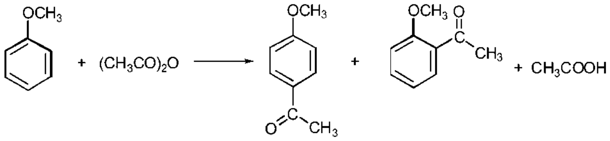
Keggin heteropoly acids such as $H_3PW_{12}O_{40}$ (PW), $H_4SiW_{12}O_{40}$ (SiW), and $H_3PMo_{12}O_{40}$ (PMo). The acylation of anisole with the strongest acid PW to yield para-methoxyacetophenone (*p*-MOAP) and ortho-methoxyacetophenone (*o*-MOAP) (Eq. [1]) has been studied in more detail.



[1]

Emphasis is put on the optimisation of catalyst performance, product yield, and selectivity, on product inhibition, on catalyst deactivation and reuse, and on reaction kinetics. The results for HPA are compared with those for H-beta zeolite (7, 8).

EXPERIMENTAL

Chemicals

$H_3PW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ from Aldrich, $H_4SiW_{12}O_{40}$ from Fluka, and Aerosil 300 silica from Degussa were used. Anisole, anisole-d_8, and toluene were obtained from Aldrich and distilled over calcium hydride prior to use. Acetic anhydride and *p*-methoxyacetophenone (also from Aldrich) with greater than 99% purity were used without further purification. Other reagents and solvents were of analytical purity.

Catalysts

Supported HPA catalysts were prepared by impregnating Aerosil 300 silica (S_{BET}, 300 $m^2\,g^{-1}$) or pure-silica MCM-41 (S_{BET}, 1250 $m^2\,g^{-1}$) with a methanol solution of HPA. The mixture was stirred for 6 h at room temperature, followed by drying using a rotary evaporator, as described elsewhere (14). The acidic salt $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ was prepared by the literature method (15). Prior to the reaction, the catalysts were heated at 150°C/0.1 Torr for 1.5 h, unless stated otherwise.

Aromatic Acylation

The acylations were carried out in liquid phase in a 50-ml glass reactor equipped with a condenser and a magnetic stirrer. The reactor was charged with aromatic substrate (100 mmol) and acetic anhydride, the substrate taken in excess over the acylating agent. No solvent was used. Decane was added as a GC internal standard. The system was purged with nitrogen to expel air and moisture and heated to a required reaction temperature (70–110°C). The preactivated catalyst was added to the reactor in an appropriate amount. Initially a white powder, the catalyst turned pale orange in the colourless solution, and the colour of the reaction mixture deepened to brown-red as the reaction progressed. To monitor the reaction, 0.1-ml samples of the reaction mixture were taken periodically, diluted to 1 ml with 1,2-dichloroethane, and analysed by gas chromatography (Varian 3380 chromatograph with autosampler) using a 30 m × 0.25 mm BP1 capillary column.

Characterisation Techniques

^{31}P MAS NMR spectra were recorded on a Bruker Avance DSX 400 NMR spectrometer. FTIR spectra were recorded with KBr pellets using a Nexus FTIR spectrometer. Surface area and porosity of HPA catalysts were measured by nitrogen physisorption on a Micromeritics ASAP 2000 instrument. Thermogravimetric analyses (TGA) were performed using a Perkin–Elmer TGA 7 instrument under nitrogen flow. Thermogravimetric temperature-programmed oxidation (TGA/TPO) of coked catalysts was carried out as described elsewhere (16).

RESULTS AND DISCUSSION

Catalyst Characterisation

Bulk and silica-supported HPA catalysts, mainly those based on PW, were characterised after a standard pretreatment (150°C/0.1 Torr, 1.5 h) by ^{31}P MAS NMR, FTIR, and TGA, as well as by surface and porosity measurements. PW supported (10–50 wt%) on silica and MCM-41 showed a well-known ^{31}P NMR spectrum (a singlet line at about −15 ppm referenced to 85% H_3PO_4) characteristic of the Keggin structure (10, 11). The spectrum did not change after use of the catalysts in anisole acylation, indicating that the PW structure remained unchanged. FTIR of the bulk and supported PW contained well-known Keggin bands (1081, 985, 892, and 596 cm^{-1} for bulk PW, with the bands at 1081 and 596 cm^{-1} being obscured in supported PW catalysts by absorption of silica) (10). The BET surface area and porosity of some HPA catalysts are given in Table 1. Bulk HPAs possess very low surface areas, typically 1–10 m^2/g, as well as very low porosities (10–12). Supporting HPA on silica or MCM-41 increases the surface area of HPA. It should

TABLE 1

Surface Area and Porosity of HPA Catalysts

Catalyst	BET surface area (m^2/g)	Pore volume (cm^3/g)	Pore diameter (Å)
$H_3PW_{12}O_{40}$	7	0.01	59
$H_3PMo_{12}O_{40}$	3	0.01	68
50% PW/SiO_2	111	0.8	138
40% PW/SiO_2	130	0.4	135
20% PW/SiO_2	184	0.5	126
40% PW/MCM-41	416	0.47	23

be noted that the total surface area decreases with HPA loading (cf. 20 and 50% PW on silica).

Acylation of Anisole

Catalyst pretreatment. Control of water content in heteropoly acid catalysts proved essential for their efficient performance in aromatic acylation. This can be achieved by thermal pretreatment of the catalysts, which is typically done at 130–200°C (11). Figure 1 shows the derivative TGA for bulk PW hydrate. Three main peaks can be observed: (i) a peak at a temperature below 100°C corresponding to the loss of physisorbed water (a variable amount depending on the number of hydration water molecules in the sample); (ii) a peak in the temperature range of 100–280°C centred at about 200°C accounting for the loss of ca. $6H_2O$ molecules per Keggin unit, corresponding to the dehydration of a relatively stable hexahydrate $H_3PW_{12}O_{40} \cdot 6H_2O$ in which the waters are hydrogen bonded to the acidic protons; and (iii) a peak in the range of 370–600°C centred at about 470°C due to the loss of 1.5 H_2O molecules corresponding to the loss of all acidic protons and the beginning of decomposition of the Keggin structure (12).

Figure 2 shows the effect of catalyst pretreatment on the yield of *p*-MOAP and on the initial rate of anisole acylation with bulk PW and 50% PW/SiO_2. It can be seen that both curves pass a maximum at an optimum pretreatment temperature of 150°C. This justifies our choice of this pretreatment temperature throughout this work. From TGA, the amount of water remaining in the bulk PW after pretreatment at 150°C is about 3–4 H_2O molecules per Keggin unit. Apparently, these waters are hydrogen bonded to the acidic protons. The effect of water may be attributed to the HPA acid strength and the number of proton sites as well as to catalyst deactivation (11). The amount of acetic anhydride that may be consumed reacting with this water is negligible (ca. 1% of AA). Excess water causes a decrease in the HPA acid strength—and thus in its catalytic activity. Dehydration of the catalyst increases the acid strength but decreases the number of acid sites, which will reduce the catalytic activity unless the reaction is highly demanding for the catalyst acid strength. In addition, too strong acid sites thus created tend to deactivate (coke) faster.

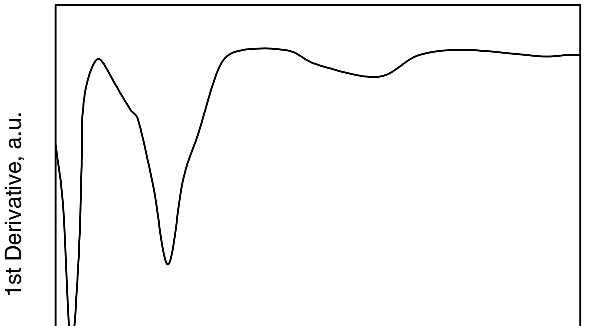


FIG. 1. TGA of $H_3PW_{12}O_{40}$ hydrate.

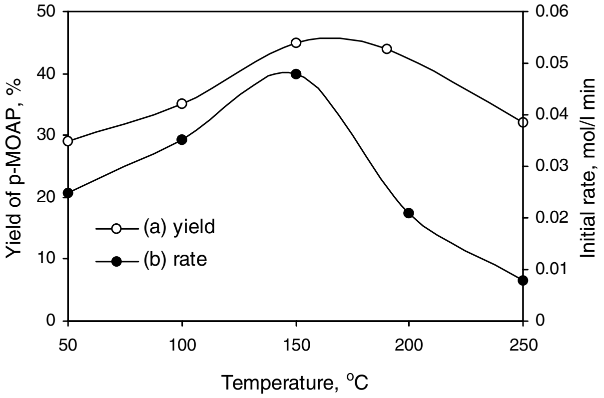


FIG. 2. Effect of catalyst pretreatment (specified temperature/0.1 Torr, 1.5 h) in the acylation of anisole: (a) yield of *p*-MOAP (50% PW/SiO_2 (0.83 wt%), AN/AA = 10 mol/mol, 50°C, 2 h); (b) initial rate (bulk PW (0.83 wt%), AN/AA = 10 mol/mol, 70°C).

Product yield and selectivity. Table 2 illustrates the performance of various bulk and supported HPAs at 70–110°C and anisole-to-acetic anhydride molar ratios, AN/AA, of 10–20. The para-acylation by far dominates, with only a few percent of the ortho-acylation product being formed, which is typical of this reaction. The selectivity towards monoacylation is practically 100%; no other aromatic products were found. The strongest acid, PW, is the most efficient catalyst, as expected, closely followed by SiW, which is a slightly weaker acid than PW (11). With PW, the yield of *p*-MOAP is up to 98%, with only 2–4% *o*-MOAP being formed. In contrast, PMo shows a very poor performance. This is probably due to reduction of this HPA by the reaction medium (11). The acylation of anisole appears to be a truly heterogeneously catalysed reaction. No contribution of homogeneous catalysis by HPA was observed when the catalyst (40% PW/SiO_2) was filtered off at the reaction temperature.

Table 3 compares our results for PW/SiO_2 with those for H-beta zeolite (8) under similar reaction conditions. Both systems give comparable yields; however, the HPA is much more active. Catalyst turnover numbers (TON) were calculated as the number of moles of *p*-MOAP obtained per mole of protons in the catalyst. For 10% PW/SiO_2, it was assumed to be three active H^+ per Keggin unit, and for H-beta the number of active protons was taken to be equivalent to the Al content (Si/Al = 12.5). For the HPA, TON is found to be 14 times greater than that for H-beta. The turnover frequency (TOF) for HPA, corresponding to the reaction

TABLE 2

Acylation of Anisole with Acetic Anhydride Catalysed by Heteropoly Acids[a]

Entry	Catalyst (amount, wt%)[b]	AN/AA (mol/mol)	T (°C)	Yield[c] (%) p-MOAP	Yield[c] (%) o-MOAP
1	PW (0.83)	10	70	67	[d]
2	PW (0.83)	10	90	96	3.8
3	PW (0.30)	20	70	67	2.0
4	PW (0.30)	20	90	90	3.5
5	50% PW/SiO_2 (0.83)	10	90	88	4.0
6	50% PW/SiO_2 (0.60)	20	70	77	2.7
7	50% PW/SiO_2 (0.60)	20	90	89	3.3
8	40% PW/SiO_2 (0.83)	10	90	88	4.0
9	40% PW/SiO_2 (0.75)	20	70	80	2.8
10	40% PW/SiO_2 (0.75)	20	90	89	3.3
11	40% PW/SiO_2 (0.88)	20	110	98[e]	2.1
12	30% PW/SiO_2 (0.83)	10	90	82	3.7
13	30% PW/SiO_2 (1.0)	20	70	64	2.3
14	30% PW/SiO_2 (1.0)	20	90	92	3.4
15	20% PW/SiO_2 (0.83)	10	90	79	3.3
16	20% PW/SiO_2 (1.5)	20	70	71	2.5
17	20% PW/SiO_2 (1.5)	20	90	89	3.0
18	10% PW/SiO_2 (0.83)	10	90	78	3.5
19	10% PW/SiO_2 (3.0)	20	70	64	2.3
20	10% PW/SiO_2 (3.0)	20	90	85	3.7
21	SiW (0.83)	10	70	70	[d]
22	40% SiW/SiO_2 (0.83)	10	70	61	[d]
23	40% SiW/MCM-41 (0.83)	10	70	72	[d]
24	PMo (0.83)	10	70	0	0
25	40% PMo/SiO_2 (0.83)	10	70	2	0
26	40% PMo/MCM-41 (0.83)	10	70	3	0
27	$Cs_{2.5}H_{0.5}PW_{12}O_{40}$ (0.83)	10	90	44	1.5

[a] Anisole (AN), 100 mmol (10.8 g), reacted with acetic anhydride (AA) in the presence of a solid HPA catalyst without solvent in a stirred batch reactor for 2 h to yield para-methoxyacetophenone (p-MOAP) and ortho-methoxyacetophenone (o-MOAP).

[b] The amount of catalysts per total reaction mixture.

[c] Yield based on acetic anhydride.

[d] The yield of o-MOAP ca. 2–3%.

[e] Yield in 10 min.

halftime, is almost two orders of magnitude greater that for H-beta. This is not unexpected because PW is a stronger acid than zeolite (11).

Catalyst reuse. The PW catalyst was found to be reusable, although gradual decline of activity was observed. Better results were obtained when, after the first run, the catalyst was filtered off, washed with CH_2Cl_2, and rerun. Apparently, the treatment with CH_2Cl_2 removed tars more efficiently from the catalyst surface. Such procedure allowed obtainment of 82% of the initial p-MOAP yield in the second run (40% PW/SiO_2 (0.83 wt%), AN/AA = 100/10 mmol, 90°C, 2 h). Coking may cause partial deactivation of the PW catalyst, which was evident from the dark brown colour of the catalyst. After the first run, the 40% PW/SiO_2 catalyst was separated, washed with CH_2Cl_2, dried (150°C/0.1 Torr, 1.5 h), and subjected to elemental and TGA/TPO analyses. From the elemental analysis, the carbon content was found to be 3.2%. The TGA/TPO of the catalyst showed a weight loss of 2.5% at 530°C, which can be attributed to hard coke (16).

Reaction kinetics. The time course for the HPA-catalysed acylation of anisole was found to depend greatly on reaction conditions, i.e., the catalyst type (bulk or supported), the temperature, and the AN/AA molar ratio (Figs. 3 and 4). With bulk PW at higher temperatures and higher AN/AA ratios, the acylation fits quite well first-order kinetics (Fig. 3),

$$d[\mathrm{P}]/dt = k[\mathrm{AA}], \qquad [2]$$

where P is p-MOAP and k is the rate constant. Otherwise, the reaction obeys a more complex time course, with a relatively fast initial stage followed by a slower stage (Fig. 4). This complexity can be attributed to product inhibition (see below).

In general, as found from the initial rates, the acylation of anisole is almost first order in acetic anhydride, as exemplified by the results for the reaction with 40% PW/SiO_2 (0.45 wt%) at $[\mathrm{AN}] \gg [\mathrm{AA}]$, 70°C.

AN/AA, mol/mol:	10	20	50	75	100.
$10^2 k$, min^{-1}:	7.2	12	12	15	12.

The reaction order in the catalyst was found to be 0.66 (40% PW/SiO_2, AN/AA = 20, 90°C). That the order is not equal to 1 may be explained by catalyst deactivation caused by product adsorption (see below). In the temperature range of 70–110°C, the acylation has an apparent activation energy of 41 kJ/mol (40% PW/SiO_2 (0.83 wt%), AN/AA =

TABLE 3

Acylation of Anisole with Acetic Anhydride: HPA Versus Zeolite[a]

Reaction conditions	Catalyst		
	10% PW/SiO_2	10% PW/SiO_2	H-beta[b] (8)
Catalyst amount (wt%)	0.83	0.83	1.33
AN/AA (mol/mol)	10	6	6
Yield of p-MOAP [c] (%)	78	50	75
TON[d]	780	830	61
TOF[e] (min^{-1})	78		1.2

[a] 90°C, 2 h.

[b] Si/Al = 12.5.

[c] Yield based on acetic anhydride.

[d] Turnover number: moles of product obtained per mole of protons in the catalyst.

[e] Turnover frequency corresponding to reaction halftime, i.e., half of the total conversion of AA.

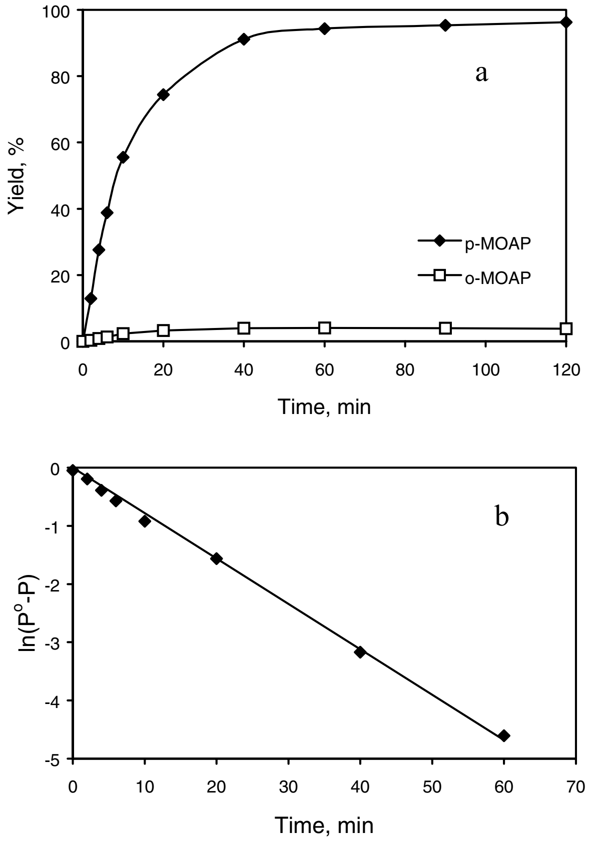
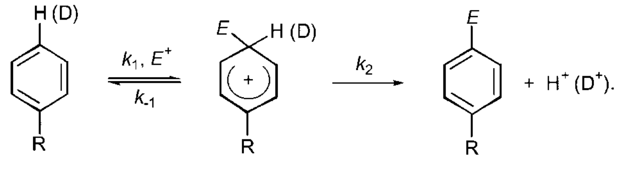


FIG. 3. Product yield versus time (a) and first-order kinetic plot (b) for the acylation of anisole (Table 2, Entry 2, bulk PW (0.83 wt%), AN/AA = 10 mol/mol, 90°C; P is the yield of *p*-MOAP, P° is the yield at an infinite time; $k = 0.078\ \mathrm{min}^{-1}$).

20). This value is close to that reported for the reaction with H-beta (46 kJ/mol) (7).

From concurrent acylation of a 50/50 mol% mixture of deuterated (d_8) and nondeuterated anisole (90°C, AN/AA = 10 mol/mol, 0.91 wt% of 40% PW/SiO$_2$, 1 h), measuring the product ratio MOAP-d_0/MOAP-d_8 by GS-MS, the kinetic isotope effect (KIE) was found to be $k_H/k_D = 1.6 \pm 0.1$. No isotope scrambling was observed under such conditions. The acylation can be represented by the general two-stage mechanism of aromatic electrophilic substitution (17):



Here E^+ is the acylium ion, and k_1, k_{-1}, and k_2 are the rate constants. Applying the steady-state approximation, one can obtain the rate and KIE equations [17]:

$$\frac{d[\mathrm{P}]}{dt} = \frac{k_1 k_2 [\mathrm{AN}][\mathrm{E}^+]}{k_{-1} + k_2},$$

$$k_\mathrm{H}/k_\mathrm{D} = \frac{\left(k_{-1} + k_2^\mathrm{D}\right) k_2^\mathrm{H}}{\left(k_{-1} + k_2^\mathrm{H}\right) k_2^\mathrm{D}}.$$

In many typical aromatic electrophilic substitutions (e.g., nitration), $k_\mathrm{H}/k_\mathrm{D} = 1$, indicating that $k_2 \gg k_{-1}$. The moderate KIE value of 1.6 found here indicates that the rate of the HPA-catalysed acylation is determined by both k_1 and k_2, i.e., $k_2 \sim k_{-1}$(17).

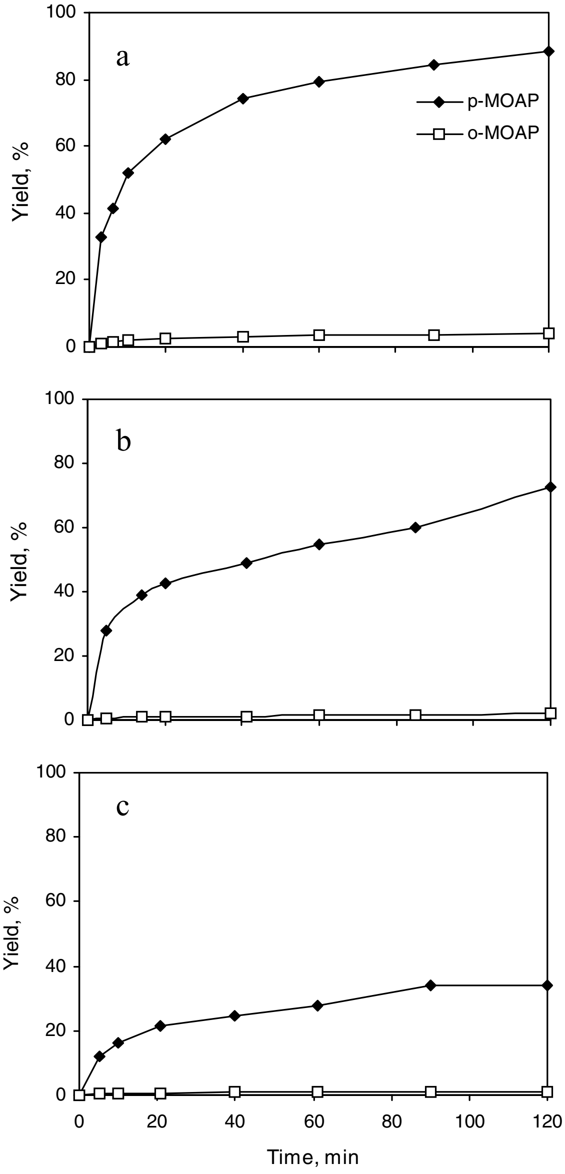


FIG. 4. Yield-time plots for the acylation of anisole with 40% PW/SiO$_2$ (0.83 wt%): (a) 90°C, AN/AA = 10 mol/mol; (b) 70°C, AN/AA = 10 mol/mol; (c) 70°C, AN/AA = 5 mol/mol. Yields are based on acetic anhydride.

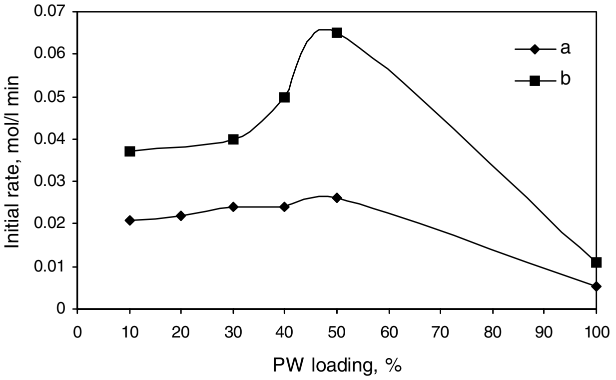


FIG. 5. Effect of PW loading in the PW/SiO_2 catalyst on the initial rate of anisole acylation at AN/AA = 20 mol/mol and a constant total amount of PW (0.010 mmol): (a) 90°C; (b) 70°C.

The effect of PW loading on silica upon the initial rate of anisole acylation at 70 and 90°C is shown in Fig. 5. In these experiments, the total amount of PW was kept constant. The activity of PW increases with the loading, passing a maximum at about 50% loading. It should be noted that the specific catalytic activity (per Keggin unit) of supported HPA is greater than that of bulk HPA. This demonstrates that the reaction occurs via the surface-type catalysis in terms of Misono's classification ("bulk vs surface type") (10). Similar dependencies have been reported for other HPA-catalysed reactions (9, 18). Such a behaviour has been explained as a result of increasing the HPA acid strength on the one hand, and as the loading increases decreasing the HPA surface area on the other (11).

Inhibition by product. The inhibition of heterogeneous aromatic acylation by the acylation product has been reported (2, 6–8). It is caused by product adsorption on the surface of the catalyst (e.g., zeolite) and is, therefore, similar to the reaction inhibition by complex formation when $AlCl_3$ is used as the catalyst. As found here, the product inhibition plays a significant role in the HPA-catalysed acylation as well.

The reaction time course shown in Fig. 4 is typical of a process gradually inhibited by the product formed. A similar course has been found for anisole acylation with zeolite catalysts (7, 8). It can be seen that the inhibition intensifies at lower temperatures and lower AN/AA ratios as the product adsorption increases. Also it grows stronger when supported PW is used as compared to bulk PW (cf. Figs. 3 and 4). Apparently, this is because the bulk PW has a much smaller surface area (Table 1). The product inhibition is further demonstrated by the addition of *p*-MOAP to the initial reaction mixture, showing that the yield decreases as the product is added (Fig. 6). Similarly, the yield sharply decreases as the AN/AA ratio decreases (Fig. 7). It should be noted that the addition of by-product acetic acid (AcOH/AA = 1 : 2 mol/mol) had no effect on the product yield. As the HPA catalyst is reusable, the product inhibition is largely reversible. Choosing higher temperatures and higher AN/AA ratios as well as bulk HPA catalysts can reduce the inhibition.

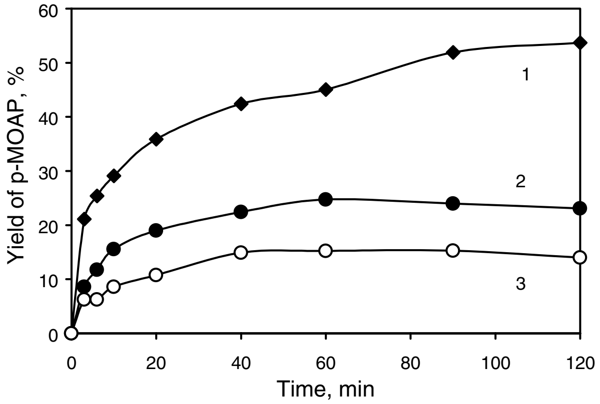


FIG. 6. Inhibition by product in the acylation of anisole (40% PW/SiO_2 (0.83 wt%), AN/AA = 10 mol/mol, 70°C, 2 h): (1) no *p*-MOAP added; (2) *p*-MOAP added initially, AA/p-MOAP = 2 mol/mol; (3) *p*-MOAP added initially, AA/p-MOAP = 1 mol/mol. Yields are based on acetic anhydride.

Langmuir–Hinshelwood model. This model has been proved useful for the acylation of anisole over zeolites (7), although another mechanism may be possible. It may include the reaction of nonchemically adsorbed anisole with chemisorbed AA molecules, with anisole, however, competing with AA for adsorption on the acid sites. It is imperative that with HPA, in contrast to zeolites, there be no diffusion limitations related to the motions of reactants or products in micropores. Following the line of reasoning given elsewhere (7), the acylation of anisole catalysed by HPA may be assumed to occur via a bimolecular Langmuir–Hinshelwood mechanism with product inhibition. The reaction rate is given by Eq. [3], where *k* is the rate constant,

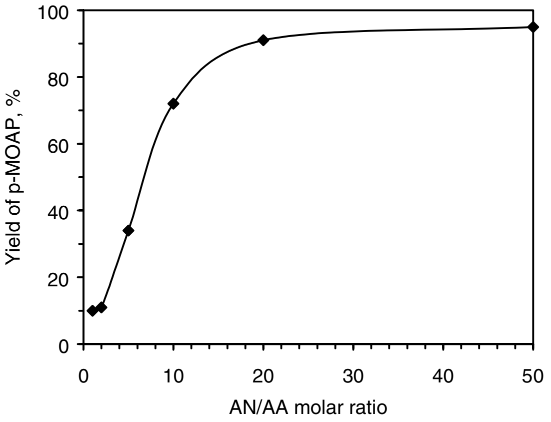


FIG. 7. Effect of the AN/AA molar ratio on the yield of *p*-MOAP (40% PW/SiO_2 (0.75 wt%), 70°C, 2 h).

and K_1, K_2, and K_p are the adsorption coefficients for acetic anhydride, anisole, and p-MOAP, respectively.

$$r = \frac{d[\mathrm{P}]}{dt} = \frac{kK_1K_2[\mathrm{AA}][\mathrm{AN}]}{(1 + K_1[\mathrm{AA}] + K_2[\mathrm{AN}] + K_p[\mathrm{P}])^2}. \quad [3]$$

As there is no solvent and anisole is present in large excess, its concentration remaining practically constant during the reaction, Eq. [3] can be rearranged to [4]. Here a is an effective first-order rate constant and $b = K_p/K_2[\mathrm{AN}]$.

$$r = \frac{kK_1K_2[\mathrm{AA}][\mathrm{AN}]}{(K_2[\mathrm{AN}] + K_p[\mathrm{P}])^2} \approx \frac{a[\mathrm{AA}]}{(1 + b[\mathrm{P}])^2}. \quad [4]$$

Now consider two limiting cases: $t \to 0$ and $t \to \infty$.

$$t \to 0; \quad r = a[\mathrm{AA}]_o. \quad [5]$$

$$t \to \infty; \quad r = \frac{a[\mathrm{AA}]}{(b[\mathrm{P}])^2}. \quad [6]$$

Applying Eq. [5] to the data shown in Fig. 4a (Table 2, Entry 8) gives $a = 0.11\ \mathrm{min}^{-1}$. The same data for the time range from 10–120 min give a very good linear plot (regression coefficient, 0.999) in accordance with Eq. [6] (Fig. 8), yielding $b = 4.3$ L/mol. As $[\mathrm{AN}] = 8.5$ mol/L, $K_p/K_2 = 37$ at 90°C. Thus the product adsorbs 37 times stronger than anisole, inhibiting the reaction.

Acylation of Toluene

Toluene is less reactive than anisole towards electrophilic substitution. The acylation of toluene over zeolite catalysts, although feasible, is more difficult to achieve than that of anisole (8).

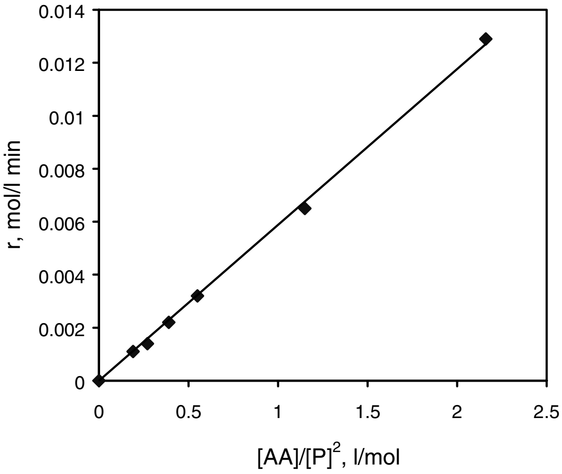


FIG. 8. Plot of the reaction rate versus $[\mathrm{AA}]/[\mathrm{P}]^2$ (40% PW/SiO_2 (0.83 wt%), AN/AA = 10 mol/mol, 90°C).

TABLE 4

Acylation of Toluene with Acetic Anhydride Catalysed by HPA[a]

Catalyst (amount, wt%)[b]	PhMe/AA (mol/mol)	T (°C)	Time (h)	Yield[c] (%)	
				p-MAP	o-MAP
PW (5.5)	20	110	6	3.0	
$Cs_{2.5}H_{0.5}PW_{12}O_{40}$ (1.1)	10	90	2	0.3	
$Cs_{2.5}H_{0.5}PW_{12}O_{40}$ (1.1)	20	150[d]	2	1.1	
40% PW/SiO_2 (1.1)	20	110	2	2.0	
40% PW/SiO_2 (1.1)	20	110	20	3.5	
40% PW/SiO_2 (1.1)	20	150[d]	2	5.2	
40% PW/SiO_2 (1.1)	200	110	22	23	4.0
40% PW/SiO_2 (1.1)	100[e]	110	24	37	4.8
H-beta (1.9)[f]	20	110	24	40	

[a] Toluene, 100 mmol (9.21 g), reacted with acetic anhydride (AA) in the presence of a solid HPA catalyst without solvent in a stirred batch reactor to yield para-methylacetophenone (p-MAP) and ortho-methylacetophenone (o-MAP).

[b] The amount of catalyst per total reaction mixture.

[c] Yield based on acetic anhydride.

[d] Reaction was carried out in a stainless steel autoclave.

[e] Acetic anhydride added dropwise.

[f] From Ref. (8).

Our results on the HPA-catalysed acylation of toluene with acetic anhydride to yield para- and ortho-methylacetophenone (p-MAP and o-MAP) are given in Table 4. Surprisingly, the reaction with HPA catalysts was found to be much less efficient than that with zeolite (e.g., H-beta) despite the stronger acidity of HPA. Bulk and silica-supported PW yielded only 3–5% p-MAP and traces of o-MAP at 90–150°C, PhMe/AA = 5–20 mol/mol, 2–20 h. The acidic salt $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ performed even more poorly. Similar results were obtained for the acylation of p-xylene with acetic anhydride. In contrast, H-beta zeolite under similar conditions gives a 40% p-MAP yield (8) (Table 4). These results could be explained by the well-known strong affinity of bulk HPA towards polar oxygenates (10, 11), which would lead to the preferential adsorption of acetic anhydride on HPA, blocking access for toluene to the catalyst surface. To overcome this, the acylation should be carried out at higher PhMe/AA molar ratios. Indeed, at PhMe/AA = 100–200 and with dropwise addition of acetic anhydride, a total acylation yield of 42% was obtained (Table 4). This proves that the preferential adsorption of the more polar acylating agent plays an important role in the acylation of toluene over HPA. It should be noted that this is not the case in the acylation of anisole over HPA because both the aromatic substrate and the acylating agent have comparable polarities. It appears that the hydrophobic acid zeolites with high Si/Al ratios less strongly differentiate the adsorption than the hydrophilic HPA and, therefore, are more suitable catalysts for the acylation of nonpolar aromatics like toluene.

CONCLUSION

Keggin-type heteropoly acid $H_3PW_{12}O_{40}$, bulk or silica supported, is a highly efficient solid acid catalyst for the liquid-phase acylation of anisole with acetic anhydride to yield up to 98% *p*-MOAP and 4% *o*-MOAP (90–110°C, AN/AA = 10–20 mol/mol). The catalyst can be reused after a simple workup, with a gradual decline of its activity being observed, however. The acylation of anisole appears to be heterogeneously catalysed; no contribution of homogeneous catalysis by HPA is observed when the catalyst is filtered off at the reaction temperature. HPA is nearly a factor of 100 more active than zeolite H-beta for this reaction—that is in line with the stronger acidity of HPA. Similarly to the reaction with zeolite catalysts, the HPA-catalysed acylation is inhibited by product because of strong adsorption of MOAP on the catalyst surface. The ratio of adsorption coefficients of *p*-MOAP and anisole is found to be 37 at 90°C. The inhibition is reduced at higher temperatures and higher AN/AA ratios as well as when using bulk instead of supported HPA. In contrast to anisole, the HPA-catalysed acylation of toluene with acetic anhydride is far less efficient than that with H-beta. Evidence is provided that the activity of HPA in toluene acylation is inhibited by preferential adsorption of acetic anhydride on the catalyst. Apparently, the hydrophobic acid zeolites (e.g., H-beta) less strongly differentiate the adsorption of aromatic substrate and acylating agent than the hydrophilic HPA and, therefore, are more suitable catalysts for the acylation of nonpolar aromatics like toluene.

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