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Heteropoly acid as a novel efficient catalyst for Fries rearrangement

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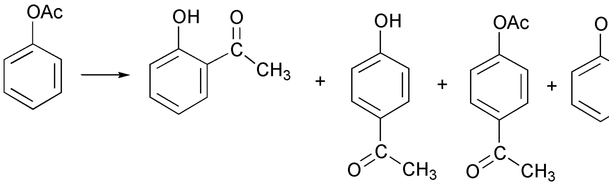
Heteropoly acid $H_3PW_{12}O_{40}$ is a very efficient and environmentally benign catalyst for the Fries rearrangement of phenyl acetate in homogeneous or heterogeneous liquid-phase systems at 100–150 °C.

The Friedel–Crafts aromatic acylation and related Fries rearrangement are the most important routes for the synthesis of aromatic ketones that are intermediates in manufacturing fine and speciality chemicals as well as pharmaceuticals.[1] The Fries rearrangement of aryl esters, *e.g.* phenyl acetate (eqn. (1) to yield hydroxyacetophenones involves acylium ion intermediates that are generated from the ester by interaction with an acid catalyst. Present industrial practice requires a stoichiometric amount of soluble Lewis acids (*e.g.* $AlCl_3$) or mineral acids (*e.g.* HF) as catalysts, which results in substantial amount of waste and corrosion problems.[2] 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, *etc.*,[2] zeolites being the most studied catalysts for both the acylation[2,3] and Fries rearrangement.[2,4]



(1)

Heteropoly acids (HPAs) are another type of promising solid acid catalysts for aromatic acylation. HPAs are Brønsted acids composed of heteropoly anions and protons as the countercations. They are stronger than many conventional solid acids such as mixed oxides, zeolites, *etc.* The Keggin-type HPAs typically represented by the formula $H_{8-x}[XM_{12}O_{40}]$, where X is the heteroatom (*e.g.* P or Si), x is its oxidation state, and M is the addenda atom (usually Mo^{6+} or W^{6+}), are the most important for catalysis.[5–7] They have been widely used as acid and oxidation catalysts for organic synthesis and found several industrial applications.[5–7] A few studies on the use of HPAs for Friedel–Crafts acylation have been published,[5,8] and only one recent communication on the Fries reaction[9] reporting that silica-supported HPAs catalyse the rearrangement of phenyl acetate in the gas phase at 200 °C with 11% conversion to 2- and 4-hydroxyacetophenone (2HAP and 4HAP).

Here we report on a very efficient and environmentally benign catalysis by the strongest heteropoly acid $H_3PW_{12}O_{40}$ (PW) for the Fries rearrangement of phenyl acetate (PhOAc) [eqn. (1)] in liquid phase. The reaction occurs at 100–150 °C to yield 2HAP, 4HAP, 4-acetoxyacetophenone (4AAP), and phenol (Table 1). One of important advantages of HPA, as compared to zeolites or mineral acids (*e.g.* H_2SO_4), is that the reaction can be carried out both homogeneously and heterogeneously. The homogeneous process occurs in polar media, for example, in neat PhOAc or polar organic solvents like nitrobenzene ($PhNO_2$) or *o*-dichlorobenzene (entries 1–5) that are commonly used for Fries reaction. All these media will easily dissolve PW at elevated temperatures (*ca.* 100 °C). On the other hand, when using nonpolar solvents, such as higher alkanes (*e.g.* dodecane) that will not dissolve HPA, the reaction proceeds heterogeneously over solid HPA catalysts (entries 7–13). In the latter case, supported HPA, preferably on silica, is the catalyst of choice, as bulk HPA possesses a low surface area (1–5 $m^2\ g^{-1}$).[5–7] The HPA catalysts are easily separated from

Table 1 Fries rearrangement of phenyl acetate catalysed by $H_3PW_{12}O_{40}$ (2 h)[a]

	Catalyst (wt%)	Solvent (PhOAc, wt%)	T °C	Conversion (%)	TOF ($\tau_{1/2}$, min)[b] min^{-1}	Selectivity, %			
						PhOH	2HAP	4HAP	4AAP
1	PW (0.60)	PhOAc (100)	150	5.5	31 (2)	49	5.2	5.6	40
2	PW (3.0)	PhOAc (100)	150	19.2	22 (2)	52	5.7	15	28
3	PW (3.0)	$PhNO_2$ (25)	150	45.8	13 (2)	52	12	24	12
4	PW (0.60)	$PhNO_2$ (25)	130	21.0	19 (3)	46	7.8	18	27
5	PW (0.60)	$PhNO_2$ (50)	100	10.5	6 (10)	55	5.1	10	29
6	H_2SO_4 (1.4)	$PhNO_2$ (25)	130	12.8	0.1 (8)	67	9.4	7.6	16
7	PW (0.60)	Dodecane (25)	130	3.1	~ 30[c] (8)	69	8.0	0	2.3
8	40% PW/SiO_2 (1.5)	Dodecane (25)	130	8.3	5[d] (5)	62	10	6.0	22
9	40% PW/SiO_2 (1.5)[e]	Dodecane (25)	130	6.7	3[d] (6)	51	11	5.0	32
10	40% PW/SiO_2 (7.5)	Dodecane (25)	130	18.0	5[d] (5)	77	12	5.0	6.0
11	10% PW/SiO_2 (6.0)	Dodecane (25)	130	11.8	17[d] (2)	66	8.0	9.6	16
12	10% PW/SiO_2 (6.0)[f]	Dodecane (25)	130	8.5	5[d] (5)	41	14	4.4	41
13	40% PW/SiO_2 (3.3)[g]	Dodecane (36)	160	18.0	12[d] (3)	66	11	8.2	14
14	H-Beta (1.3)[gh]	Dodecane (36)	160	9.3	0.1 (120)	38	32	6.4	24
15	$Cs_{2.5}H_{0.5}PWO_{40}$ (0.67)	$PhNO_2$ (25)	130	8.7	30[d] (5)	49	6.1	4.4	41

[a] The reaction with PW is homogeneous in PhOAc and $PhNO_2$ and heterogeneous in dodecane. [b] Turnover frequency corresponding to reaction halftime ($\tau_{1/2}$). [c] Assuming PW surface area of 5 m^2g^{-1}, Keggin heteropoly anion cross section of 100 Å^2 and three accessible H^+ per Keggin anion. [d] Assuming that all H^+ in PW are accessible; the true TOF may be higher. [e] Reuse of the run given in entry 8. [f] Acetic anhydride (1.5 wt %) added. [g] 5 h. [h] Si/Al = 11; 1.4 mmol g^{-1} H^+; from Ref. 4a.

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the heterogeneous system by filtration and could be reused (entries 8 and 9). From the homogeneous systems, HPA can be effectively separated without its neutralisation by extraction with water and reused or utilised otherwise.

The heterogeneous catalysis in the PhOAc–dodecane media was clearly proved by filtering off the catalyst from the reacting system which completely terminated the reaction. In contrast, filtration did not affect the reaction course in homogeneous systems, *e.g.* PhOAc–$PhNO_2$.

Strong inhibition of HPA-catalysed process with reaction products was observed both in homogeneous and heterogeneous systems—which is not unexpected, as the same takes place with other catalysts ($AlCl_3$, zeolites, *etc.*). Addition of more HPA catalyst allowed reaching a higher PhOAc conversion (*cf.* entries 1 and 2, 8 and 10). Some catalyst deactivation was also observed. For example, the 40% PW/SiO_2 catalyst separated after the reaction in PhOAc–dodecane 25:75 wt% system showed in the second run *ca.* 80% of its initial activity (entry 9). The catalyst after the first run was significantly coked (C content *ca.* 13%) which probably caused catalyst deactivation.

The total selectivity of reaction (1) towards the sum of PhOH, 2HAP, 4HAP and 4AAP was found to be over 98%. Some acetic anhydride was also formed. The homogeneous reaction is more efficient than the heterogeneous one because it makes less phenol and more acetophenones, the selectivity to the more valuable para acetophenones, 4AAP and 4HAP, being also higher. Addition of acetic anhydride (entry 12) improves the selectivity towards acetophenones, as expected, although slightly decreases the catalytic activity. The turnover frequencies (TOF) corresponding to the reaction halftime were calculated as the number of moles of PhOAc converted per mole of total protons in the catalyst. Being a much stronger acid,[5–7] HPA is almost 200 times more active than H_2SO_4 in homogeneous reaction, as well as more selective to acetophenones (*cf.* entries 4 and 6). In heterogeneous systems, HPA is also two orders of magnitude more active than H-Beta zeolite which is one of the best zeolite catalysts for this reaction (*cf.* entries 13 and 14). (Note that in solid HPA catalysts only a small part of H^+ is accessible, thus the true TOF may be much higher.) However, H-Beta shows a higher total selectivity to acetophenones than HPA. It should be pointed out that HPA in homogeneous systems gives a higher selectivity to para acetophenones 4AAP and 4HAP than H-Beta. The efficiency of solid HPA (at constant loading) increases in the order PW < 40% PW/SiO_2 < 10% PW/SiO_2 in which the number of accessible proton sites increases (*cf.* entries 7, 8 and 11). Insoluble salt $Cs_{2.5}H_{0.5}PWO_{40}$[6] is an efficient solid catalyst for the reaction in polar media such as $PhNO_2$ (entry 15). Although less active per unit weight than the homogeneous PW or PW/SiO_2, it shows high TOF and is more selective to acetophenones than HPA. The explanation of this may be that the less hydrophilic Cs salt[6] possesses stronger proton sites than the solid PW or PW/SiO_2 which, from TGA, retain 4–6 H_2O molecules per Keggin unit after pretreatment at 150 °C (see Experimental†).

In conclusion, heteropoly acid $H_3PW_{12}O_{40}$ is a very efficient and environmentally friendly catalyst for the Fries rearrangement of phenyl acetate in homogeneous or heterogeneous liquid-phase systems.

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Notes and references

† *Experimental.* Silica-supported PW catalysts were prepared by impregnating Aerosil 300 silica (S_{BET} = 300 m^2g^{-1}) with a methanol solution of PW.[10] $Cs_{2.5}H_{0.5}PW$ was prepared as described in Ref. 11. The catalysts PW, 40% PW/SiO_2 and $Cs_{2.5}H_{0.5}PW$ had BET surface areas of 5, 130 and 112 m^2g^{-1}, respectively. Prior to the reaction, the catalysts were calcined at 150°C/0.1 torr for 1.5 h. The rearrangement of PhOAc was carried out in the liquid phase (7.0 g of PhOAc + solvent) at 100–160 °C under nitrogen atmosphere in a 25 ml glass reactor equipped with a condenser and a magnetic stirrer. Decane (1 wt%) was added as a GC internal standard. 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) using 30 m × 0.25 mm BP1 capillary column.

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