Acetylation of *p*-Aminophenol by Preyssler's anion $[NaP_5W_{30}O_{110}]^{14-}$, $[NaP_5W_{29}MoO_{110}]^{14-}$ with green condition at room temperature

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Synthesis of acetaminophen at green condition and room temperature in the presence of the Preyssler type heteropolyacids has been investigated in order to contribute toward clean technology, which is the most important need of the society. All of the catalysts are recyclable and reusable.

Keywords: Heteropolyacid, Preyssler, *p*-Aminophenol, Acetaminophen, Green catalyst.

INTRODUCTION

Acetaminophen is an amide, a compound that is a derivative of ammonia that has been reacted with an acidic substance, in this case, acetic acid. Acetaminophen acts as a fever as well as pain reducer and reliever. Acetaminophen is an important drug all over the world and is widely marketed as Tylenol and Datril in the United States as Panadol in Europe and Australia. The preparation of Acetaminophen with using heteropolyacid as a catalyst can be conducted in simple conditions and give reasonable yield of an isolated productand the HPA catalysts were simply filtered, dried and can be recovered with structural degradation. It can be found in several analgesic preparations, such as Tylenol, some of which may contain other ingredients, such as caffeine and buffers. Qualitatively, the purity of an acetaminophen sample can be determined from its melting point. Green chemistry has been defined as a set of principles that reduce or eliminate the use of hazardous substances or catalysts[1]. Introducing clean processes and utilizing eco-friendly and green catalysts, which can be simply recycled at the end of reactions, have been under permanent attention and demands. Recently, heteropolyacids (HPAs), which are low in toxicity and being recyclable, have attracted special attention[2]. Many reactions catalyzed by Brønsted and Lewis acids now, in the presence of HPAs, proceed more effectively under milder conditions with greater selectivity, better yields, and shorter reaction times. Among HPAs, the application of Keggin and Wells-Dawson structures has been extensively studied[3]. In comparison with the liquid mineral acids, solid acids could be easily separated from there action mixture by simple filtration with high recovery. This advantage directly leads to a decrease of equipment cauterization and environment pollution. Recently, liquid acids have been replaced by solid acid catalysts such as *p*-toluenesulfonic acid, Nafion-H, resins, silica-alumina, zeolites, niobic acid and etc [4]. HPAs in solution is stronger than the usual mineral acids such as HCl, Sulfuric acid, phosphoric acid and etc[5]. It was shown that HPAs in the solid state are pure Brønsted acids and stronger acids than the conventional solid acids such as SiO_2-Al_2O_3, H_3PO_4, HNO_3, H_2SO_4, HX, HY zeolites[6] and the HPAs efficient and environmentally friendly catalysts for organic reactions. HPAs will be expected as an alternative acid catalyst to improve several organic processes, which employ conventional acids[7]. Heteropolyacids (HPAs) have been extensively used as green solid acids and oxidation catalysts for many reactions and gained applications in industrial practice of both electrophilic catalysis and oxidation reactions[8]. Industrially, they have found application in several processes, such as the oxidation of methacrolein to methacrylic acid, oxidation of ethylene to acetic acid[9]. In aqueous solution HPA, such as PW, SiW, Preyssler's anion $[NaP_5W_{30}O_{110}]^{14-}$ and PMo are strong fully dissociated acids. These compounds have several adventages as catalysts, which makes them economically and environmentally attractive. The major disadvantage of HPAs, as a catalyst lies in their low hydrolytic stability that is very important in catalytic processes. Preyssler's anion has an excellent hydrolytic stability (pH 0 – 12). This stability demonstrates its functionality over a wide range of pH. If the principles proposed for green chemistry are applied, Preyssler catalyst will be introduced as a promising candidate for green catalysts. This catalyst is green with respect to corrosiveness, safety, quantity of waste, and separability. This catalyst is also unique due to its stability in pH 0 – 12. However, the catalytic applicability of Preyssler's anion with exclusive properties has been largely overlooked, with only a few demonstrations of catalytic activity[10]. This heteropolyanion with 14 acidic protons, is an efficient "supper acid" solid catalyst which can be used both in the homogeneous and heterogeneous phases[11]. Other important features of this polyanion are:(1) The anion is thermally stable, rendering high temperature reactions practical. (2) Both pure and supported catalysts can be easily recovered and recycled without degradation and loss of activity. Heteropolyacids (HPAs) are well-defined molecular clusters that are remarkable for their molecular and electronic structural diversity and their significance is quite diverse in many areas, e.g., catalysis, medicine, and materials science[12]. HPAs are complex proton acids that incorporate polyoxometalate anions (heteropolyanions) having metal-oxygen octahedra as the basic structural units and catalysis by them is a field of increasing importance[13]. $[NaP_5W_{30}O_{110}]^{14-}$, the socalled Preyssler's anion, Na^+ is encrypted inside a central cavity formed by five PW_6O_{22} units arranged in a crown[14], as shown schematically in Fig. 1,2.
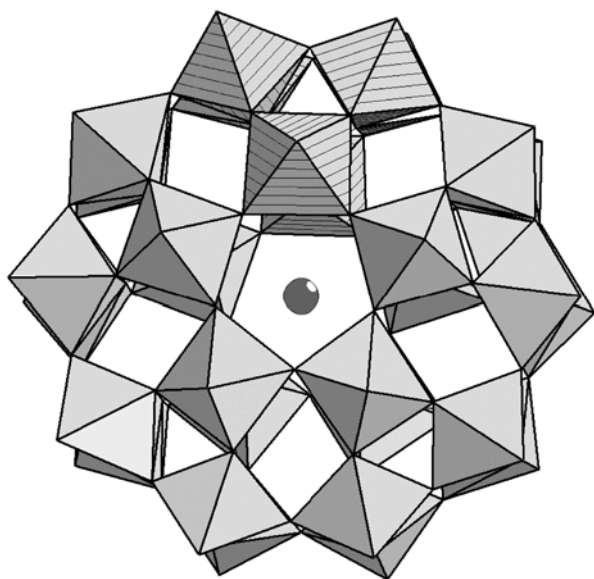
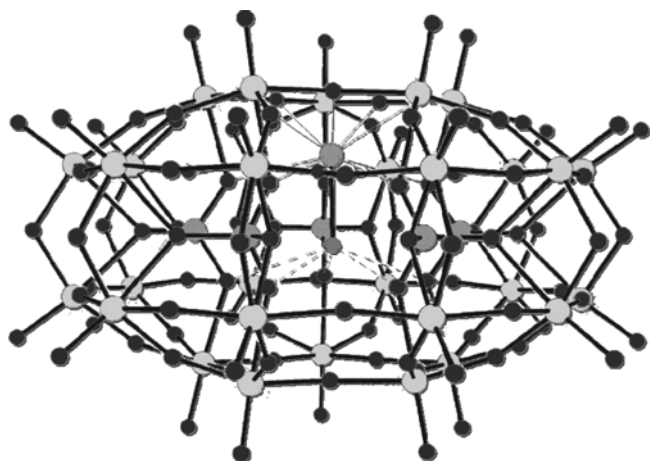**Figure 1.** The structure of $[NaP_5W_{30}O_{110}]^{14-}$ polyhedral form showing WO_6 octahedra and the central Na (open circle).

Figure 2. $[NaP_5W_{30}O_{110}]^{14-}$ viewed perpendicularly to the anion's C_5 axis. Tungsten and oxygen atoms are represented by large and small circles respectively, phosphorus atoms are represented by shaded circles and the sodium atom is represented by a broken-hatched circle, $[NaP_5W_{30}O_{110}]^{14-}$ same perspective as in part a but with nearest ring of five WO_6 octahedra removed, revealing PO_4 tetrahedra (shaded).

This polyanion consists of a cyclic assembly of five PW_6O_{22} units, each driven from the Keggin anion, $[PW_{12}O_{40}]^{3-}$, by the removal of two sets of three corner shared WO_6 octahedra.

A sodium ion is located within the polyanion on the five-fold axis and 1.25 A° above the pseudomirror plane that contains the five phosphorus atom.

EXPERIMENTAL SECTION

Materials

All chemicals were obtained from Merck and used as received. Acetic anhydride, *p*-aminophenol, sodium tungstate dihydrate, molybdotungstate dihydrate, orthophosphoric acid, phosphoric acid, ethyl acetate,

potassium chloride and silica gel, $Co(NO_3)_2 \cdot 6H_2O$, $Ni(NO_3)_2\ 6H_2O$, $Zn(NO_3)_2 \cdot 4H_2O$. The spectra were recorded on an FT-NMR Bruker 100 MHz Aspect 3000 spectrometer. The IR spectra were obtained with a Buck 500 scientific spectrometer (KBr pellets).

Catalyst Preparation

Keggin type heteropolyacids were acquired from commercial sources. $H_{14}[NaP_5W_{30}O_{110}]$ $H_4[PMo_{11}VO_{40}]$ and $H_5[PMo_{10}V_2O_{40}]$, PW_{11}, $PW_{11}NiO_{40}$, $PW_{11}ZnO_{40}$, $PW_{11}CoO_{40}$ were prepared in accordance to the literature[16 – 18].

The Wells-Dawson species $H_6[P_2W_{18}O_{62}]$ was prepared as described elsewhere[19]. Potassium salt of Preyssler's anion was prepared in accordance to the procedure developed in our laboratory[1]. The free acid was prepared by the passage of a solution of the potassium salt in water through a column of Dowex 50wx8 in the H^+ form and evaporation of the elute to dryness under vacuum 1. Molybdenum substituted Preyssler heteropolyanion, H_{14}-P_5Mo, was prepared as follows: 2.8 g (0.169 mol) $Na_2WO_4 \cdot 2H_2O$ and 2 g (0.008 mol) $Na_2MoO_4 \cdot 2H_2O$ were dissolved in 35 mL of water and mixed at 60 °C for 30 min.

Then this solution was cooled to room temperature and 25 mL of concentrated phosphoric acid was added. The resulting yellow solution was refluxed for 18 h. The solution was brought to room temperature, diluted with water and then during stirring, 10 g of KCl was added. The mixture was stirred and then heated up to dryness.

The product was dissolved in warm water and upon cooling to room temperature yellow crystals formed. The acidic form of molybdenum substituted heteropolyacid was obtained as described above, for the unsubstituted analogue. Supported heteropolyacid catalysts were prepared by impregnating a support in the form of powder (SiO_2) with an aqueous solution of the heteropolyacid with different concentrations. The samples were dried at 120 – 140 °C, and the catalysts were calcined at 300 °C in the furnace prior to use.

General Procedure

The homogeneous process was performed by adding acetic anhydride (5 mL) to a solution of H_{14}-P_5 (0.02 g) and *p*-aminophenol (2 g) at room temperature with stirring.

The heterogeneous reactions were performed by contacting *p*-aminophenol (2 g), acetic anhydride (5 mL) with 0.1 g of 10 – 50% H_{14}-P_5/SiO_2 at room temperature for the mentioned time with intense stirring. At the end of reaction, the mixture was diluted with 50 mL of water, and the crude product was precipitated in an ice bath. The crude product was removed and after the usual work up, the resulting solid was washed with cold water and recrystallized in ethyl acetate. The product was characterized by comparison of its spectroscopic (IR, ^{1}H-NMR, Mass) data and the melting point, with that of an authentic sample. The product yield was determined quantitatively.

Upon the completion of the reaction monitored by (TLC) the reaction mixture was diluted with sodium bicarbonate 10% (15 ml) and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed by evaporation to afford the acetylated compound.
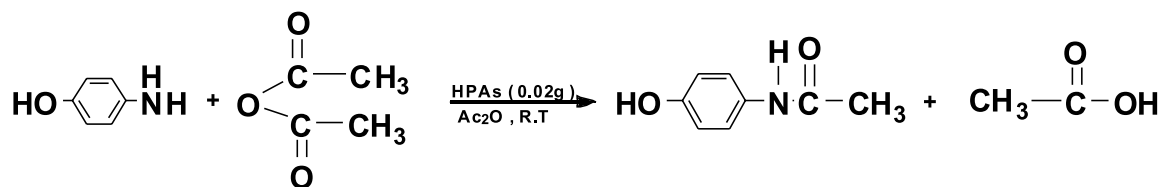
Scheme 1. The acetylation of *p*-aminophenol into acetaminophen with various heteropolyacids

Catalyst reusability

At the end of the reaction, the catalysts could be recovered by a simple filtration. The recycled catalyst could be washed with an organic solvent for the use in the next reaction process. The results of the other experiments were almost consistent in yields.

RESULTS AND DISCUSSION

We used Keggin HPAs (scheme 1, Table 1) for these reactions. The catalytic activity of Keggin heteropolyacids such as $H_4[SiMo_{12}O_{40}]$, $H_4[SiW_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$, PW_{11} and $H_3[PMo_{12}O_{40}]$, was less than Preyssler's anion. The yields of the acetylation of *p*-aminophenol into acetaminophen with various heteropolyacids are given in Table 1.

The formula for the reaction.

The yield of acetaminophen in the presence of silica-supported Preyssler increased from 22% to 69%, with an increase in catalyst loading from 10% to 50% (entries 11 – 15).

In the presence of $H_{14}-P_5$, *p*-aminophenol was converted to acetaminophen with acetic anhydride in 91% yield with 100% selectivity at room temperature in 15 minutes (entry 1). $H_{14}P_5$-Mo has lower activity than $H_{14}-P_5$. It leads to 83% acetaminophen with 100% selectivity after 15 minutes (entry 2).

It is clear that acetylation yield depends on the nature of the acid. Heteropolyacid with tungsten atom shows

Table 1. The acetylation of *p*-aminophenol by various heteropolyacids in acetic anhydride at room temperature

Entry	Catalyst	Time(min)	Yield%
1	$H_{14}[NaP_5W_{30}O_{110}]$	15	91
2	$H_{14}[NaP_5W_{29}MoO_{110}]$	15	83
3	$H_3[PMo_{12}O_{40}]$	20	51
4	$H_3[PW_{12}O_{40}]$	20	60
5	$H_4[SiW_{12}O_{40}]$	20	62
6	$H_4[SiMo_{12}O_{40}]$	20	59
7	$H_4[PMo_{11}V_1O_{40}]$	20	65
8	$H_5[PMo_{10}V_2O_{40}]$	20	70
9	$HNa_2[PW_{12}O_{40}]$	20	45
10	$H_6[P_2W_{18}O_{62}]$	20	78
11	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2(\%10)$	15	22
12	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2(\%20)$	15	38
13	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2(\%30)$	15	46
14	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2(\%40)$	15	54
15	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2(\%50)$	15	69
16	PW_{11}	30	41
17	$PW_{11}ZnO_{40}$	30	32
18	$PW_{11}NiO_{40}$	30	30
19	$PW_{11}CoO_{40}$	30	33
20	None Catalyst	70	9

higher acidity than a molybdenum analogue[15]. When tungsten is replaced by molybdenum, the negative charge on the oxygen atoms increases, which leads to a decrease in acidity[15, 16]. In homogeneous conditions higher activity of Preyssler is attributed to the higher number of acidic protons.

The results point out that the catalytic effectiveness may be enhanced as the number of tungsten atoms (or the number of protons) is increased. Both possibilities are logical.

The large anion with the larger number of tungsten atoms also provides many "sites" on the oval-shaped molecule that are likely to render the catalyst effective.

It is also interesting to consider that, like the Keggin types, by replacing one of the tungsten atoms of $H_{14}-P_5$ with molybdenum in $H_{14}-P_5Mo$, the yield of acetaminophen decreases.

By replacing tungsten with molybdenum, symmetry is also decreased, and this distortion may affect the nature of polyacid and acidity of a heteropolyacid. However, the results show that among all of the heteropolyacid catalysts, $H_{14}-P_5$ shows the highest yield.

In order to achieve heterogeneous catalysis, the acetylation was carried out by $H_{14}-P_5/SiO_2$ with different loadings. Catalyst loading was varied from 10% to 50%.

As illustrated in Table 1, the yield of acetaminophen increased with an increase in catalyst loading from 10% to 50%. It is attributed to the increase in the total number of available active catalytic sites for the reaction. For heterogeneous catalyzed reactions, it is not very good to use more than 50% (w/w) catalyst loading, and hence it can be concluded that the optimal catalyst loading based on the current findings was 50%(w/w). In all cases, the supported heteropolyacid is less active than that of the non-supported. Oxide supports such as SiO_2 have a large surface area and a peculiar pore structure. In the process of adsorption, surface hydroxyl groups play a very important role in adsorbing different ions from solution.

Then the sequence in activity is drawn as follows:
10% <20% <30% < 40% <50%.

The effect of catalyst loading was varied from 10 to 50%.

The effect of catalyst loading on the yield of acetaminophen was studied at room temperature over silica as support. On the other hand, although SiO_2-supported HPAs are acidity and redox property of HPAs[17].

On the basis of the obtained results, we can suggest that there is a direct interaction between Preyssler and the surface of the support. So it is reasonable to assume that the adsorption of Preyssler on support could be ascribed to an acid-base reaction.

It is well known that heteropolyacid is an acid with higher acid strength. Heteropolyanion (HPAs), analogous to the anions such as SO^{2-}_4, PO^{3-}_4, and ASO^{3-}_4, also belongs to the inorganic Oxygen-containing anion . In

view of the difference in softness or hardness of hydroxyl of various supports and HPAs, the reaction between heteropolyanion and hydroxyl on the support may proceed in accordance to a two-step ligand exchange mechanism as follows (hard-hard reaction), (equation.1) or coordination of protonated surface hydroxyl with heteropolyanion in solution to form an outer sphere surface complex instead of exchange reaction (hard-soft reaction), (equation.2) , Fig 3 and 4.

$$M- OH + H^+ \rightarrow MOH^+_2 \qquad (1)$$

$$MOH^+_2 \text{ (support) } + HPA^{-1}_{(aq)} \rightarrow MOH^+_2 (HPA)^{-1} \quad (2)$$
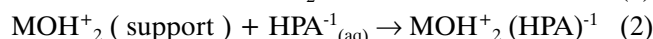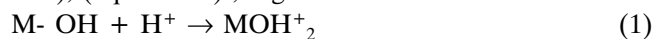
Where M and MOH are Si ion and surface hydroxyl, respectively.

Owing to the difference in acid-Base strength of the surface hydroxyl as well as HPA, the result of their interaction would lead to the formation of active intermediates with different acid strength and immobilized firmness,
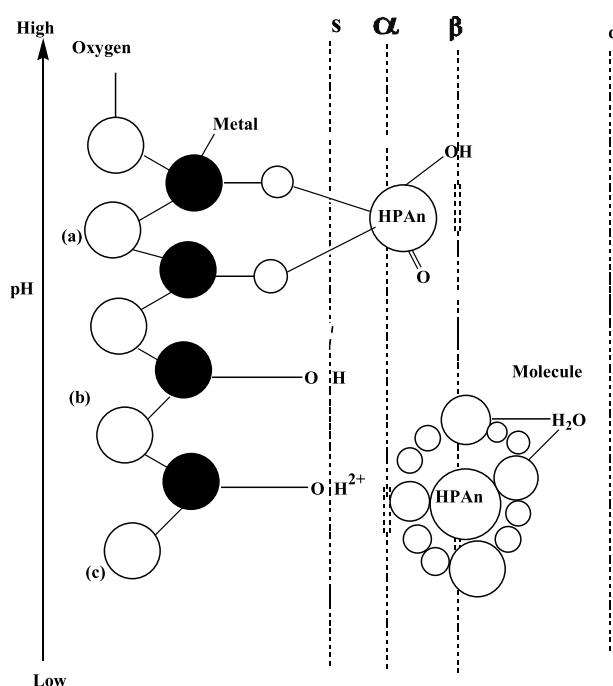
such an active intermediate has acidity like HPA. The pH value of the medium and the acidity of HPA itself have an effect on its immobilized firmness. The models of the two mechanisms can be described as shown in Fig 3, 4.

In addition, because of the higher surface density of most anions it is likely that the reason is related to the interaction between the surface and the dissolved anion as well as the interaction among adsorbed molecules in the horizontal direction. In ideal conditions, it is reasonable to assume that the first step of the dissociation of HPA in solvent should be considered as HPA.

At the same time, the surface hydroxyl could also form several kinds of adsorption sites in the solvent. When HPA is adsorbed, the adsorbtion states, in general, would be represented as follows (eq. 3):

$$MOH + HPA \rightarrow M\text{-}OH^+_2 \qquad (3)$$
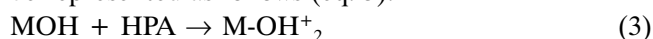
The major problem, limiting the utility of homogeneously catalyzed processes, is the well-known difficulty in catalyst recovery and recycling. The recycling of HPA catalysts is the key issue to their application.

In Keggin HPAs, the amount of proton is effective in the increase rate of reactions. We used $H_6[P_2W_{18}O_{62}]$ as a Wells-Dowsen HPA in this reaction and had a suitable yield with this catalyst because this type has some of the acidity protons, more from other keggin heteropolyacids types. Besides these HPAs, we considered other HPAs (Lacunary groups) including (PW_{11}, $PW_{11}NiO_{40}$, $PW_{11}CoO_{40}$, $PW_{11}ZnO_{40}$) for acetylation of *p*-aminophenol in acetic anhydride. These HPAs were not efficient; they are very weak for this reaction because they have not any acidity protons in their structures. When this reaction was carried out at room temperature without the catalyst, the product was obtained in low yield (9%) and long time, as it was shown in (table 1, entry 20).

Figure 3. A schematic proposal of a hydroxyl surface showing association with surface hydroxyl (S): (a) Exchange mechanism, (b) surface hydroxyl, (c) coordination mechanism, (b) (α) inner-sphere complexes, (ß)outer-sphere complexes, (d) the diffuse ion swarm

CONCLUSIONS

Inexpensive, eco-friendly, recyclable and available heteropolyacids as efficient solid acid catalysts for the acetylation of *p*-aminophenol in acetic anhydride, were used. The H_{14}-P_5 shows higher activity than the other forms of Preyssler, as well as Keggin types and phosphoric acid. One of important features of these solid acids is high thermal and hydrolytic stability throughout a wide pH range. Thus, a wide range of catalytic reactions can be affected without a loss of structure and activity. The re-
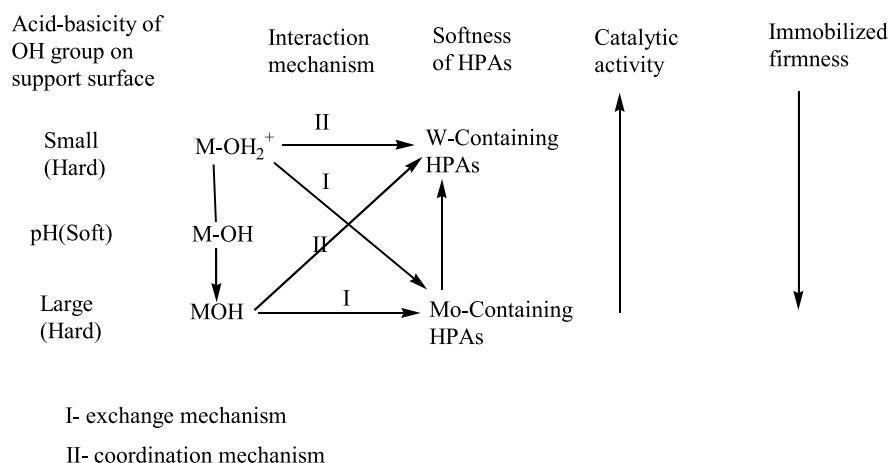

I- exchange mechanism

II- coordination mechanism

Figure 4. The mechanism of the interaction between Preyssler (HPAs) and the surface of support

sults also suggest that at the same conditions including: the molar ratio, reaction time, temperature and Preyssler catalyst is the most efficient HPA for this purpose. Finally, the simple experimental set up and procedure makes this method a useful addition to the methodologies that require solid catalysts with strong acidic strength, highly thermal stability and functionality over a wide range of pH, especially for the synthesis of acetaminophen.

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