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Catalytic synthesis of warfarin acetals by using different heteropolyacid catalysts

Ali Gharib[1,2*], Manouchehr Jahangir[1], Mina Roshani[1], J. (Hans) W. Scheeren[3], Sara Mohadeszadeh[2], Lida Bakhtiari[2], Shirin Lagzian[2]

[1]*Department of Chemistry, Islamic Azad University, Mashhad, IRAN*
[2]*Agricultural Researches and Services Center, Mashhad, IRAN*
[3]*Cluster for Molecular Chemistry, Department of Organic Chemistry, Radboud University Nijmegen, The Netherlands*
[*]*Corresponding author: e-mail: aligharib5@yahoo.com*

In this research, we report on the synthesis of warfarin acetals by using Preyssler's anion, $[NaP_5W_{30}O_{110}]^{-14}$ and heteropolyacids (HPAs) catalysts. This reaction was performed using methanol and ethanol at reflux temperature conditions. Under these conditions we have excellent yields and high selectivity. Preyssler heteropolyacid catalyst were easily recycled recovery and reused without the loss of its catalytic activities. The synthesis of warfarin acetals has been achieved using the catalytic amounts of green, inexpensive and eco-friendly Keggin types heteropolyacids. The products were obtained in high yields.

Keywords: Heteropolyacid; Preyssler; Catalyst; Warfarin; Cyclic acetals.

INTRODUCTION

Coumarin and its derivatives form an elite class of compounds; they represent the ring systems of several important groups of natural products. They have been used as anticoagulants[1,2], additives in food and cosmetics[3], and in the preparation of insecticides, optical brighteners[4] and dispersed fluorescent and laser dyes[5]. These compounds can also be used for the synthesis of other products as furocoumarins, chromones, coumarones and 2-acylresorcinols[6]. In continuation of our investigations in the field of the synthesis of coumarin derivatives, the synthesis of heterocyclic condensed 4-hydroxycoumarin derivatives is described herein. In the previous syntheses of a warfarin cyclic acetal, as a blood anticoagulant[7], Lewis acids were used as catalysts (zinc chloride, iron (III) chloride). There is a number of methods available for the synthesis of acetals. Usually, the synthesis of acetals is carried out with catalysis by a strong proton acid, such as sulfuric acid[8,9] phosphoric or methanesulfonic acid[10] or by Lewis acids. These methods are not entirely satisfactory, owing to drawbacks such as low yield, long reaction times, corrosive properties of catalysts and difficult work-up. There are many structural types of heteropoly compounds (polyoxometalates), which have been reviewed in detail elsewhere[11]. The majority of catalytic applications use the most stable and easily available Keggin HPAs, especially for acid catalysis. The Keggin HPAs comprise heteropoly anions of the formula $[XM_{12}O_{40}]^{n-}$ (α-isomer), where X is the heteroatom (P^{5+}, Si^{4+}, etc.) and M the addendum atom (Mo^{6+}, W^{6+}, etc.). The structure of the heteropoly anion is composed of a central tetrahedron XO_4 surrounded by 12 edge- and corner-sharing metal-oxygen octahedra MO_6. Figure. 1 shows the Keggin structure in polyhedral representation. Most typical Keggin HPAs such as $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ are commercially available.

Heteropolyacids (HPAs) are applied both in bulk or supported forms, with a homogeneous and heterogeneous catalysis being possible. Heteroplyacids (HPAs) have many advantages that make them environmentally attractive in the academic, industrial and economical signification. These are useful acids and oxidation catalysts in various reactions since their catalytic features can be varied at a molecular level[12]. Among them, the Keggin-type, HPAs have long been known to be good catalysts for oxidation reactions[13]. They exhibit great advantages: for example, their catalytic properties can be tuned by changing the identity of the charge-compensating counter cations, heteroatoms and framework metal atoms[13].

Heteropolyacids catalyze a wide variety of reactions in homogeneous or heterogeneous (liquid-solid, gas-solid or liquid-liquid biphasic) systems, offering strong options for more efficient and cleaner processing compared to conventional mineral acids[13–17]. Being stronger acids, heteropolyacids will have significantly higher catalytic activity than the conventional catalysts such as mineral

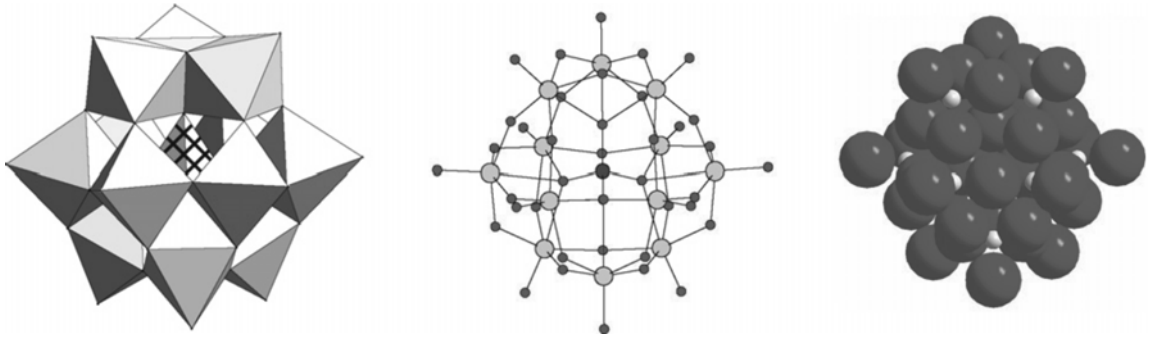


Figure 1. The structure of the Keggin heteropoly anion $[\alpha\text{-}XM_{12}O_{40}]^{n-}$ in polyhedral (left), ball-and-stick (middle) and space-filling (right) representations[6,11]

acids, mixed-oxides, zeolites, etc. In particular, in organic media, the molar catalytic activity of heteropolyacid is often 100–1000 times higher than that of H_2SO_4 [15–16]. The acidity of HPAs is stronger than that of the conventional solid acid catalysts (e.g., acidic oxides and zeolites), decreasing in the order: $H_3PW_{12}O_{40}$ > $H_4SiW_{12}O_{40}$ > $H_3PMo_{12}O_{40}$ > $H_4SiMo_{12}O_{40}$ [14,15,16]. The acid sites in HPA are more uniform and easier to control than those in other solid acid catalysts. Being stronger acids, HPA are generally more active catalysts than the conventional solid acid catalysts, which allows efficient operating under milder conditions. However, there is a serious problem to HPA catalysts-their low thermal stability, hence limited reaction temperature and, especially, difficulty of regeneration of solid HPA catalysts (decoking)[14,16]. The thermal stability of Keggin HPAs, defined as the temperature at which all acidic protons are lost, decreases in the order: $H_3PW_{12}O_{40}$ (465°C) > $H_4SiW_{12}O_{40}$ (445°C) > $H_3PMo_{12}O_{40}$ (375°C) > $H_4SiMo_{12}O_{40}$ (350°C), the strongest acid $H_3PW_{12}O_{40}$ being the most stable[14,16], (Figure 2).

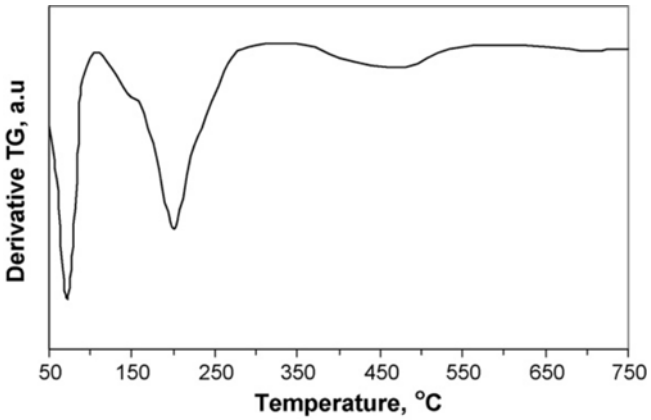


Figure 2. shows the TGA profile for $H_3PW_{12}O_{40}$ hydrate[4]

Three main peaks can be observed: (1) a peak at a temperature below 100°C corresponding to the loss of physisorbed water (a variable amount depending on the number of hydration waters in the sample); (2) a peak in the temperature range of 100–280°C centred at about 200°C accounted 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 to form the $[H_2O\cdots H^+\cdots OH_2]$ ions; and (3) a peak in the range of 370–600°C centred at 450–470°C due to the loss of 1. $5H_2O$ molecules corresponding to the loss of all acidic protons and the beginning of decomposition of the Keggin structure (Figure 2). For tungsten HPAs, the latter loss is practically irreversible, which causes the irreversible loss of catalytic activity. The decomposition is complete at about 610°C to form P_2O_5 and WO_3, which is shown by an exotherm in DTA and DSC[17,9]. Therefore, the thermal decomposition of $H_3PW_{12}O_{40}$ follows the course:

$$H_3PW_{12}O_{40}\cdot nH_2O \underset{-(n-6)H_2O}{\overset{<100^oC}{\rightleftharpoons}} H_3PW_{12}O_{40}\cdot 6H_2O \underset{-6H_2O}{\overset{200^oC}{\rightleftharpoons}} H_3PW_{12}O_{40}$$

$$\underset{-1.5H_2O}{\overset{450\text{-}470^oC}{\rightleftharpoons}} \left\{PW_{12}O_{38.5}\right\} \xrightarrow{Ca.\ 600^oC} 1/2P_2O_5 + 12WO_3$$

HPAs in solution is stronger than the usual mineral acids such as HCl, Sulfuric acid, phosphoric acid and etc[10]. 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 and HY zeolites[18] and 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[19]. 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 process 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 advantages as the catalysts which make them economically and environmentally attractive. The major disadvantage of HPAs, as the catalyst lies in their low hydrolytic stability which 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 one applies the principles proposed for green chemistry, the 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. In pharmacology, warfarin is one of the most important blood anticoagulants but the cyclic acetals **2** or **3**, are even better anticoagulants than warfarin.

MATERIALS AND METHODS

All chemicals were obtained from Merck and used as received.

Instruments

^{1}H NMR spectra were recorded on a FT NMR Bruker 250 MHz spectrometer and ^{1}H NMR, ^{31}P NMR, ^{29}Si NMR and ^{13}C NMR spectra were recorded at 298 K. Melting points were recorded on an Electrothermal type 9100 melting point apparatus andwere uncorrected. Chemical shifts were reported in ppm (δ-scale) relative to internal standard TMS (0.00 ppm); the solvent was used as a reference. The IR spectra were obtained with a Buck 500 scientific spectrometer (KBr pellets). The products were identified by comparison of their mp., IR and NMR spectra with those of authentic samples.

Catalyst Preparation

The Keggin type heteropolyacids ($H_3[PMo_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$, $H_4[SiW_{12}O_{40}]$, $H_4[SiMo_{12}O_{40}]$) were acquired from commercial sources. $H_{14}[NaP_5W_{30}O_{110}]$, $H_4[PMo_{11}VO_{40}]$, $H_5[PMo_{10}V_2O_{40}]$, $H_6[PMo_9V_3O_{40}]$, $H_7[PMo_8V_4O_{40}]$ and Wells-Dawson, $H_6[P_2W_{18}O_{62}]$ were prepared according to the literature[19–25,15]. The analytical results are presented in terms of the P_5W_{30} stoichiometry revealed by the crystallographic measurements. Anal. Calcd (Found) for $H_{14}[NaP_5W_{30}O_{110}]\cdot 58H_2O$:, 1.57 (1.74); Na, 0.27 (0.21); P, 1.82 (1.86); W, 64.80 (64.82).

General procedure

Warfarin (1.0 g, 0.003 mol) was dissolved in a small amount of dry methanol, or ethanol (10 ml) and heteropolyacid catalyst (0.03 mmol). Then the mixture was stirred at reflux temperature for the appropriate time (10–19 min). The progress of the reaction was monitored by TLC. After the completion of the reaction (monitored by TLC) the mixture was filtered to separate the catalyst (heterogeneous catalyst) and then the solvent was evaporated to dryness under reduced pressure. The reaction mixture (product) had to be dissolved prior to filtration and washing with dry methanol or ethanol (5–15 mL). The solvent was removed under the reduced pressure to afford the crude product. The crude product was purified by crystallization from methanol. The catalyst (homogeneous catalyst) could be recycled after the evaporation of the solvent from the residue solution and washing with diethyl ether and the obtained solid acid was filtered off and washed with diethyl ether, which could be reused in another reaction.

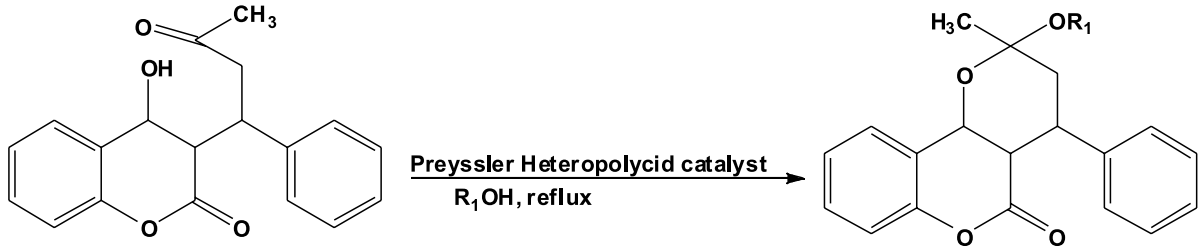
2-Methoxy-2-methyl-4-phenyl-3,4-dihydro-2*H*-pyrano[3,2-c]chromen-5-one (**2**) as white needles, yield 0.82 g (94%), mp. 165–166°C, IR (KBr)ν_{max}/cm^{-1}: 1708, 1625, 1611, 1493, 1379, 1142, 1102, 1054, 730, 690. ^{1}H-NMR($CDCl_3$): 1.47 (3H, s, CH_3) 2.25–2.32 (2H,AB*q*, C-3, *J* = 14.2 Hz, *J* = 7.3 Hz, *J* = 5.4 Hz), 3.17 (3H, *s*, OCH_3), 4.15 (H, *dd*, C-4, *J* = 7.3 Hz, *J* = 5.4 Hz), 7.13–7.17 (3H, *m*, Ar), 7.43–7.58 (5H, *m*, C-8, C-9, C-7, Ar), 7.66 (H, *dd*, C-10, *J* = 7.8, *J* = 1.6 Hz,). 13C($CDCl_3$): 23.41 (CH_3), 38,99 (C-3), 42.18 (C-4), 48.83 (CH_3O), 102.29 (C-2), 105.95 (C-4a), 161.04 (C-5), 161.99 (C-10b). MS = [M$^+$+1]323, M$^+$ 322, M$^+$-15 (CH_3, 100%) 307, M$^+$– 31 (OCH_3) 291.

2-Ethoxy-2-methyl-4-phenyl-3,4-dihydro-2***H***-pyrano[3,2-c]chromen-5-one (**3**), as white needles, yield 0.59 g (87%) mp. 174–176°C, IR (KBr) ν_{max}/cm^{-1}: 1710, 1629, 1607, 1490, 1377, 1142, 1102, 1054, 730, 690. ^{1}H-NMR ($CDCl_3$): 1.45 (3H, s, CH_3), 1.15 (3H, t, CH_3, *J* = 7.15 Hz), 2.23–2.54 (2H, AB*q*, C-3, *J* = 14.5 Hz, *J* = 7.5 Hz, *J* = 5.5 Hz, *J* = 0.85Hz), 3.37 (2H, *q*, OCH_2, *J* = 7.15Hz), 4.13 (H, *dd*, C-4, *J* = 5.5 Hz, *J* = 7.5 Hz), 7.13–7.16 (3H, *m*, Ar), 7.43/7.56 (5H, *m*, C-8, C-9, C-7, Ar) 7.61 (H, *dd*, C-10, *J* = 7,8 *J* = 1.6 Hz). 13C ($CDCl_3$): 15.61 (CH_3), 25.01 (CH_3), 38.99 (C-3), 57.41 (CH_2O), 42.38 (C-4), 102.79 (C-2), 105.55 (C-4a), 160.54 (C-5), 162.19 (C-10b). MS = [M$^+$+ 1] 337, M$^+$ 336, M$^+$– 15 (CH_3 100%) 321, M$^+$– 45 (OCH_2CH_3) 291.

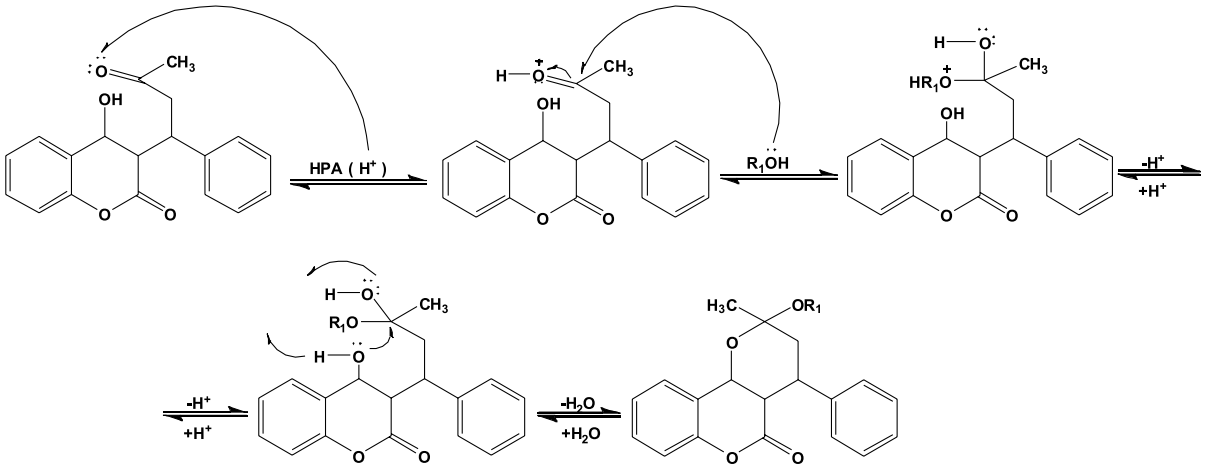
RESULTS AND DISCUSSION

We wish to report an easy and efficient procedure for the synthesis of the cyclic acetals 2-methoxy-2-methyl-4-phenyl-3,4-dihydro-2*H*-pyrano[3,2-c]chromen-5-one (**2**) and 2-ethoxy-2-methyl-4-phenyl-3,4-dihydro-2*H*-pyrano[3,2-c]chromen-5-one (**3**) in good yields from 4-hydroxy-3-(3-oxo-1-phenylbutyl)-chromen-2-one (**1**) catalyzed by Preyssler heteropolyacid (Scheme **1** and **2**).

We used Preyssler heteropolyacid (Scheme 1, Table 1) for this reaction. The yields of the synthesis of warfarin acetals with Preyssler heteropolyacid are given in Table 1. Here, there is a mechanism of the synthesis of warfarin acetals (Scheme 2). Generally, on the basis of the results obtained as shown in Scheme **1**, **2**, the reflux promoted intra-cyclodehydration reaction of warfarin with methanol and or ethanol, to the corresponding acetals **2** or **3**, in the presence of Preyssler heteropolyacid as a catalyst is a better choice than the conventional methods in term of reaction temperature, reaction time and yield. Above the synthesis reaction was created in the presence of the recycled catalysts and the results are summarized in (Table 1–3, entries 1–2). The recovered catalyst was reused successfully.



Scheme 1. Synthesis of warfarin acetals with Preyssler heteropolyacid



Scheme 2. Mechanism of the synthesis of Warfarin acetals

Table 1. Preparation of warfarin acetals using Preyssler heteropolyacid catalyst ($H_{14}[NaP_5W_{30}O_{110}]$) at reflux conditions

Entry	R	Time (min)	Temp (^{O}C)	[a]Yield (%)	M.P. (^{O}C)
1	CH_3 (2)	10	66	94 (94, 93, 91) [b] (Lit 1,7)	165
2	CH_2CH_3 (3)	14	84	87 (87, 85, 84) [b] (Lit 1,7)	175

[a]Isolated yields. [b]In parentheses, yields obtained in the first, second, third reuse of the catalyst

Table 2. Preparation of warfarin acetals using Keggin heteropolyacid catalyst ($H_3[PW_{12}O_{40}]$) at reflux conditions

Entry	R	Time (min)	Temp (^{O}C)	[a]Yield (%)	M.P. (^{O}C)
1	CH_3 (2)	15	66	65.5 (65, 64, 62.5)[b]	165
2	CH_2CH_3 (3)	19	84	87 (87, 85, 84) [b]	175

[a]Isolated yields. [b] In parentheses, yields obtained in the first, second, third reuse of the catalyst

Table 3. Preparation of warfarin acetals using Wells-Dawson heteropolyacid catalyst ($H_6[P_2W_{18}O_{62}]$) at reflux conditions

Entry	R	Time (min)	Temp (^{O}C)	[a]Yield (%)	M.P. (^{O}C)
1	CH_3 (2)	13.5	66	86 (86, 84, 83)[b]	165
2	CH_2CH_3 (3)	16	84	87 (87, 85, 84) [b]	175

[a]Isolated yields. [b] In parentheses, yields obtained in the first, second, third reuse of the catalyst

Table 4. Preparation of warfarin acetal ($R=CH_3$) using heteropolyacid catalysts types at reflux conditions

Entry	Catalyst	[a] Yield (%)
1	$H_{14}[NaP_5W_{30}O_{110}]$	94
2	$H_{14}[NaP_5W_{29}MoO_{110}]$	90
3	$H_3[PMo_{12}O_{40}]$	61
4	$H_3[PW_{12}O_{40}]$	65.5
5	$H_4[SiW_{12}O_{40}]$	63
6	$H_4[SiMo_{12}O_{40}]$	51
7	$H_4[PMo_{11}V_1O_{40}]$	69
8	$H_5[P\ Mo_{10}V_2O_{40}]$	73
9	$H_6[PMo_9V_3O_{40}]$	77
10	$H_7[PMo_8V_4O_{40}]$	82
11	$H_6[P_2W_{18}O_{62}]$	86
12	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$(10%)	30
13	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$(20%)	45
14	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$(30%)	61
15	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$(40%)	72
16	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$(50%)	81

[a] Isolated yields and were analyzed by GC

In all the cases, the heteropolyacids with Preyssler structures show higher activity in these reactions compared with Keggin type heteropolyacids. The catalytic activity of Keggin heteropolyacids such as $H_4[SiMo_{12}O_{40}]$, $H_4[SiW_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$, $H_3[PMo_{12}O_{40}]$ and Wells-Dawson, $H_6[P_2W_{18}O_{62}]$ was less than Preyssler's anion. They lead to 51, 63, 65.5 and 61%, 86% respectively, with 90–95% selectivity (Table 4, entries 3–6 and entry 11). The yields in the presence of silica-supported Preyssler increased from 30% to 81% with an increase in catalyst loading from 10% to 50% (entries 12–16). It is clear that Warfarin acetals yield depends on the nature of the acid. The hetropolyacids of the series $H_{3+x}PMo_{12-x}V_xO_{40}$ (x = 1–4) showed good to excellent catalytic behaviors in methanol or ethanol. The results are shown in Table 4. $H_7[PMo_8V_4O_{40}]$ catalyzes efficiently the formation of Warfarin acetals giving a total yield of 82% in methanol or ethanol. The yield with this catalyst was found to be decreased from 69% to 82% (Table 4, entries 7–10). In other words, the activities of the $H_{3+x}PMo_{12-x}V_xO_{40}$ (x = 1–4) catalysts in the synthesis of Warfarin acetals in methanol or ethanol were found to decrease in the following order: $H_7[PMo_8V_4O_{40}]$ > $H_6[PMo_9V_3O_{40}]$ > $H_5[PMo_{10}V_2O_{40}]$ > $H_4[PMo_{11}VO_{40}]$. The Keggin anion have an assembly of 12 corner-shared octahedral MoO_6 from trimetallic groups $[Mo_3O_{13}]$ around a heteroatom tetrahedron PO_4 [11]. The introduction of vanadium(V) into the Keggin framework of $[PMo_{12}O_{40}]^{3-}$ is beneficial for catalysis reactions[23]. Usually positional isomers are possible and coexist when two or more vanadium atoms are incorporated into the Keggin structure (for example 5 and 13 isomers for x=2 and 4, respectively)[24,25]. Studies on these isomers in catalytic reactions indicate that different isomers cause to show different reactivities[26,27].

The structural characteristics of the catalysts are as follow:

Preyssler's anion, $[NaP_5W_{30}O_{110}]^{14-}$, has an approximate D_5h symmetry and consists of a cyclic assembly of five PW_6O_{22} units. A sodium ion is located within the polyanion on the fivefold axis and 1.25 above the pseudo mirror plane that contains the five phosphorus atoms[26,27]. Preyssler polyanion as a large anion can provide many "sites" on the oval-shaped molecule that are likely to render the catalyst effective. The Keggin anions have an assembly of 12 corner-shared octahedral MoO_6 from trimetallic groups $[Mo_3O_{13}]$ around a heteroatom tetrahedron PO_4. The introduction of vanadium (V) into the Keggin framework of $[PMo_{12}O_{40}]^{3-}$ is beneficial for catalysis reactions. Usually positional isomers are possible and coexist when two or more vanadium atoms are incorporated into the Keggin structure. Studies on these isomers in catalytic reactions indicate that different isomers cause to show different reactivities. The performance of this polyanion in different forms was compared with Keggin types: $H_4[SiMo_{12}O_{40}]$, $H_4[SiW_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$ and $H_3[PMo_{12}O_{40}]$.

Structure and Chemistry of $H_4[SiW_{12}O_{40}]$, $H_3[PW_{12}O_{40}]$: Analyses:

These characteristic IR absorption data are very useful to identify the structures of POMs. It can be seen that the PW_{11}/SiO_2 films have vibration bands similar to those of the corresponding starting XW_{11} (X = P), suggesting that the primary PW_{11} structures remained intact regardless of the functionality of the polyanions. The shifts of the bands may be due to chemical interaction between the surface of the XW_{11} and the silica matrix, as described earlier. In the case of SiW_{11}/SiO_2 film, the intense and broad Si-O-Si vibration band of the silica framework at 1080 cm^{-1} covered that of Si-O from the central SiO_4 unit of SiW_{11}. Therefore, based on the peaks appearing at mid-

IR region, we cannot confirm that the structural integrity of the SiW_{11} remained intact after the formation of the SiW_{11}/SiO_2 film. Evidence for the presence of the Si-O bond from the central SiO_4 of SiW_{11} in the films was obtained from ^{28}Si MAS NMR (Fig. 3). That is, the resonance at δ–94.31 ppm originated from the central SiO_4 unit of SiW_{11} cluster, which is nearly the same as that of the parent SiW_{11} (δ–93.0 ppm), suggesting that the Si-O bond from the central SiO_4 existed in the hybrid materials. The other signals in Fig. 3 indicate the existence of silanol groups such as $Si^*(OSi)_4$ (–122.31); $Si^*(OSi)_3(OH)$ (–112.17) and $Si^*(OSi)_2(OH)_2$ (–101.51), which come from the incomplete condensation of the silica network. Therefore, we confirm retention of the structural integrity of SiW_{11} after the formation of the composite film. In the case of pure PW_{11}, two IR vibration bands of P-O in the central PO_4 were at 1095 and 1043 cm^{-1}, respectively. However, only one vibration band at 1079 cm^{-1} was observed for the PW_{11}/SiO_2 film. At the same time, ^{31}P MAS NMR showed that one resonance at δ–13.5 ppm appeared (Fig. 3).

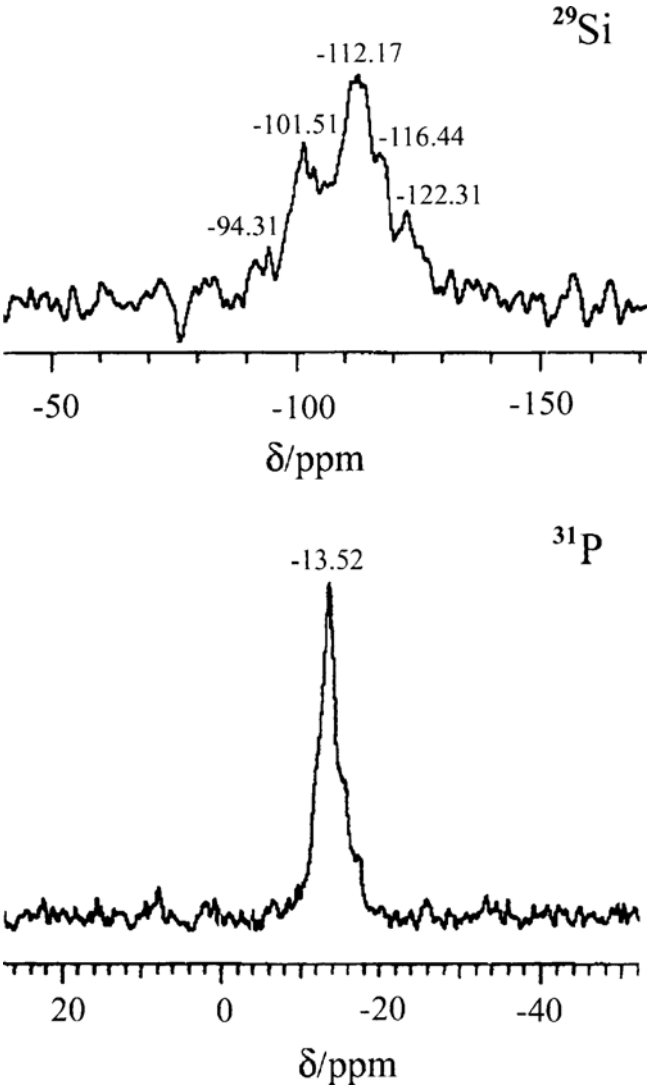


Figure 3. ^{29}Si and ^{31}P MAS NMR spectrum of SiW_{11}/SiO_2 and PW_{11}/SiO_2 films, respectively

Some of the solid Heteropolyacids are obtained by slow evaporation at room temperature. Upon combining "$H_6[PMo_9V_3O_{40}]$.aq" with $H_3[PW_{12}O_{40}]$.aq in an aqueous solution, similar changes in the ^{31}P NMR spectra occur (Fig. 4).

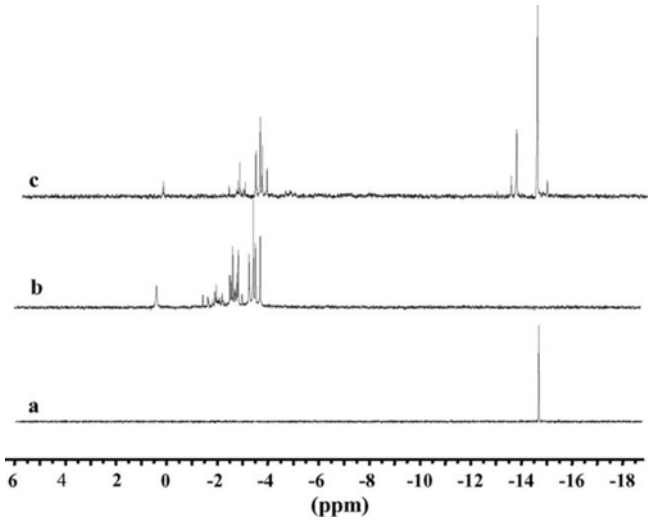


Figure 4. ^{31}P NMR spectrum of: (a) $H_3[PW_{12}O_{40}]$·aq, ca. 0.1 M; (b) $H_3[PMo_9V_3O_{40}]$·aq, ca. 0.1 M; (c) mixture of the two solutions; the spectrum was recorded 20 nm after preparation of the solution (solvent D_2O/H_2O 1/1, T = 297 K)

CATALYST REUSABILITY

At the end of the reaction, the catalysts could be recovered by a simple filtration. It is noteworthy that the catalyst may be reused without a significant loss of activity. In order to know whether the catalyst would succumb to poisoning and lose its catalytic activity during the reaction, we investigated the reusability of the catalyst. For this purpose we first carried out the reaction in the presence of the catalyst. After the completion of the reaction, the catalyst was removed and washed with diethyl ether (10 ml) and subjected to the second, third and fourth runs of the reaction process with the same substrates. The results of the first experiment and subsequent experiments were almost consistent in the yields (after three runs) (94, 93 and 91%) and the catalytic activity of $H_{14}[NaP_5W_{30}O_{110}]$ and the heteropolyacids (HPAs) was almost the same as that of fresh catalyst. We have thus found that the Preyssler catalyst can be reused several times, without any appreciable loss of activity and after recovery the catalytic activity was decreased only 2–4%, pointing to the stability and retention of catalytic capability of this useful polyanion. The IR spectra of the resulting solids indicate that the catalyst can be recovered without structural degradation (Figure 5).

The work-up procedure of this reaction is very simple. After the completion of the reaction the mixture was filtered off to separate the catalyst and then the solvent was evaporated to dryness under reduced pressure. The reaction of Warfarin acetals synthesis was created in the presence of recycled catalysts and the results are summarized in (Table 1–3). The recovered catalyst was reused successfully (Figure 5).

CONCLUSIONS

In summary, we have developed an alternative and simple procedure for the intracyclodehydration of 4-hydroxy-

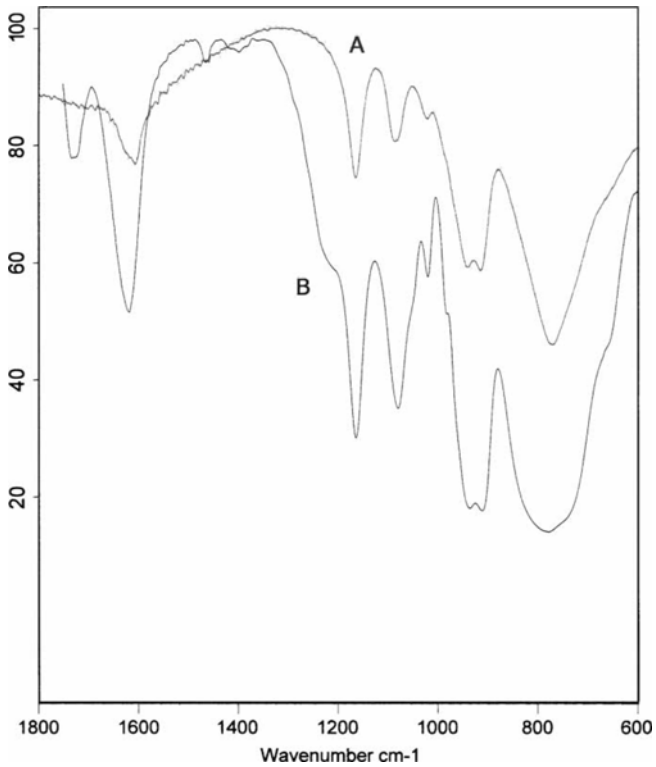


Figure 5. IR spectrum of Preyssler catalyst before (a) and after (b) the catalytic reaction

3-(3-oxo-1-phenylbutyl)-chromen-2-one (**1**) to the corresponding acetals 2-methoxy-2-methyl-4-phenyl-3,4-dihydro-2*H*-pyrano[3,2-c]chromen-5-one (**2**) or 2-ethoxy-2-methyl-4-phenyl-3,4-dihydro-2*H*-pyrano[3,2-c]chromen-5-one (**3**) on a Preyssler heteropolyacid surface using reflux has been demonstrated. With using $H_{14}[NaP_5W_{30}O_{110}]$, Preyssler type heteropolyacid, as an eco-friendly, inexpensive and efficient catalyst. The high yields, relatively short reaction times, the simplicity of the operation and an easy work-up procedure are some advantages of this protocol. $H_{14}[NaP_5W_{30}O_{110}]$ offers the advantages of a higher hydrolytic and thermal stability. The salient features of the Preyssler's anion are availability, non-toxicity and reusability. We believe this methodology will be found useful in the organic synthesis.

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LITERATURE CITED

1. Robinson, A., Li, H.Y. & Feaster, J. (1996). The first practical asymmetric synthesis of R and S-Warfarin. *Tetrahedron Lett*., 37, 8321–8324. DOI:10.1016/0040-4039(96)01796-0.

2. Cravotto, G., Nano, G.M., Palmisano, G. & Tagliapietra, S. (2001). An asymmetric approach to coumarin anticoagulants via hetero-Diels-Alder cycloaddition. *Tetrahedron: Asymmetry*., 12, 707–709. DOI:10.1016/S0957-4166(01)00124-0.

3. Kennedy, R.O. & Thornes, R.D. (2003). Coumarins: Biology, *Applications and Mode of Action*, John Wiley and Sons, Chichester.

4. Zabradnik, M. (1992). *The Production and Application of Fluorescent Brightening Agents*, John Wiley and Sons, New York.

5. Maeda, M. (1994). *Laser Dyes*, Academic, New York.

6. Tsuchiya, Y., Hamashima, Y. & Sodeoka, M. (2006). A New Entry to Pd-H Chemistry: Catalytic Asymmetric Conjugate Reduction of Enones with EtOH and a Highly Enantioselective Synthesis of Warfarin. *Org. Lett*., 8, 4851–4854. DOI: 10.1021/ol0619157.

7. Wawzoek, S. (1951). in *Heterocyclic Compounds*, R. C. Eldrfield Ed.,Wiley, NewYork, 2, 173–175.

8. Heravi, M., Zadsirjan, V., Bakhtiari, K., Oskooie, H.A. & Bamoharram, F.F. (2007). Green and reusable heteropolyacid catalyzed oxidation of benzylic, allylic and aliphatic alcohols to carbonyl compounds. *Catalysis Communications*. 8, 315–318. DOI:10.1016/j.catcom.2006.05.044.

9. Kozhevnikov, I.V. (2002). *Heteropoly acids and related compounds as catalysts for fine chemical synthesis*. Wiley & Sons, Chichester, England, 216.

10. Heravi, M.M., Derikvand, F. & Bamoharram, F.F. (2005). A catalytic method for synthesis of Biginelli-type 3,4-dihydropyrimidin-2 (1H)-one using 12-tungstophosphoric acid. *J. Molecular Catalysis A: chemical*. 242, 173–175. DOI:10.1016/j.molcata.2005.08.009.

11. Pope, M.T. (1983). Heteropoly and Isopoly Oxometalates, Springer, Berlin.

12. Okuhara, T., Mizuno, N. & Misono, M. (1996). Advances in Catalysis. Catalytic Chemistry of Heteropoly compounds. 41, 113–252.

13. Kozhevnikov, I.V.(1987). Advances in catalysis by heteropoly acids. Advances in catalysis by heteropoly acids. *Russ. Chem. Rev*. 56(9), 811–825. DOI: 10.1070/RC1987v056n09ABEH003304.

14. Izumi, Y., Urabe, K. & Onaka, M. (1992). Zeolite, Clay and Heteropoly Acid in Organic Reactions, Kodansha/VCH, Tokyo.

15. Kozhevnikov, I.V. (1998). Catalysis by Heteropoly Acids and Multicomponent Polyoxometalates in Liquid-Phase Reactions. *Chem. Rev*. 98, 171–198. DOI: 10.1021/cr960400y.

16. Kozhevnikov, I.V. (2002). Catalysts for fine chemicals, in: Catalysis by Polyoxometalates, vol. 2, Wiley, Chichester.

17. Moffat, J.B. (2001). Metal-Oxygen Clusters: The Surface and Catalytic Properties of Heteropoly Oxometalates, Kluwer, New York.

18. Kozhevnikov, I.V. (2003). Friedel-Crafts acylation and related reactions catalysed by heteropoly acids. *Applied Catalysis A: General*. 256, 3–18. DOI:10.1016/S0926-860X(03)00406-X.

19. Bamoharram, F.F., Heravi, M.M., Roshani, M., Jahangir, M. & Gharib, A. (2007). Effective direct esterification of butanol by eco-friendly Preyssler catalyst, $[NaP_5W_{30}O_{110}]^{14-}$. *J. Mol. Catal.* 271, 126–130. DOI:10.1016/ j.molcata.2007.02.034.

20. Bamoharram, F.F., Heravi, M.M., Roshani, M., Gharib, A. & Jahangir M. (2006). A catalytic method for synthesis of γ-butyrolactone, ε-caprolactone and 2-cumaranone in the presence of Preyssler's anion, $[NaP_5W_{30}O_{110}]^{14-}$, as a green and reusable catalyst. *J. Mol. Catal*. 252, 90–95. DOI:10.1016/j.molcata.2006.01.067.

21. Tsigdinos, G.A. & Hallada, C.J. (1968). Molybdovanadophosphoric acids and their salts. I. Investigation of methods of preparation and characterization. *Inorg. Chem*., 7, 437–441. DOI: 10.1021/ic50061a009.

22. Mahha, Y., Atlamsani, A., Blais, J.C., Tessier, M., Brégeault, J.M. & Salles, L. (2005). Oligomerization of ε-caprolactone and δ-valerolactone using heteropolyacid initiators and vanadium or molybdenum complexes. *J. Mol. Catal. A: Chemical*., 234, 63–73. DOI:10.1016/j.molcata.2005.02.023.

23. Heravi, M.M., Bakhtiari, K., Benmorad, T., Bamoharram, F.F., Heravi, M.M., Oskooie, H.A., & Tehrani, H.M (2007).

Nitration of Aromatic Compounds Catalyzed by Divanadium-Substituted Molybdophosphoric Acid, $H_5[PMo_{10}V_2O_{40}]$. Monatshefte für Chemie. 138, 5, 449–452. DOI: 10.1007/s00706-007-0593-6.

24. Pope, M.T. (1991). *Molybdenum Oxygen Chemistry: Oxides, Oxo Complexes, and Polyoxoanions*. In: Progress in Inorganic Chemistry. Ed: S.J. Lippard, John Wiley & Sons, New York, 181–255.

25. Romanelli, G., Autino, J.C., Baronetti, G. & Thomas, H. (2001). H. Efficient Deprotection of Phenol Methoxymethyl Ethers Using a Solid Acid Catalyst with Wells-Dawson Structure. *Molecules*. 6, 1006–1010. DOI:10.3390/61201006.

26. Alizadeh, M.H., Harmalker, S.P., Jeannin, Y., Martin-Frere, J. & Pope, M.T. (1985). A Heteropolyanion with Five-fold Molecular Symmetry That Contains a Nonlabile Encapsulated Sodium Ion. The Structure and Chemistry of $[NaP_5W_{30}O_{110}]^{14-}$. *J. Am. Chem. Soc*. 107, 2662–2669. DOI: 10.1021/ja00295a019.

27. Shanshan, Wu., Weihong, Zhang., Jum, Wang., Xiaoqian, Ren. (2008). Preyssler-Structured Tungstophosphoric Acid Catalyst on Functionalized Silica for Esterification of n-Butanol with Acetic Acid. *Catal. Lett*. 123, 276–281. DOI 10.1007/s10562-008-9419-3.