

## Selective Acetylation of Alcohols and Amines with Ethyl Acetate in the Presence of $H_6[PMo_9V_3O_{40}]$ as the Catalyst

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**Summary.** Acetylation of various alcohols and benzyl amine was tested in the presence of  $H_6[PMo_9V_3O_{40}]$ , a mixed addenda heteropolyacid, in ethyl acetate under reflux condition. Phenols and anilines are not affected under the reaction conditions. Selective transesterification of alcohols can be achieved in the presence of phenol and aniline derivatives using this method.

**Keywords.** Acetylation; Transesterification; Alcohols; Mixed addenda heteropolyacids; Ethyl acetate.

### Introduction

Acetylation of alcohols and amines is one of the most frequently used transformations in organic synthesis as it provides an efficient and inexpensive means for protecting hydroxy and amino groups in a multistep synthesis process [1, 2]. Esters are usually synthesized from alcohols and carboxylic acids [3, 4], or acid chloride and acid anhydride or an ester [5, 6] as the acylating agent.

Many acidic [7] or basic [8] catalysts have been used for this purpose. A variety of *Lewis* acids such as  $Sc(NTf_2)_3$  [9],  $TiCl(OTf)_3$  [10],  $TMSCl$  and  $TMSOTf$  [11],  $La(Oi-Pr)_3$  [12],  $Sn(OTf)_2$  [13],  $TiCl_4/AgClO_4$  [14], have also been applied as catalysts or reagents to mediate the reaction between alcohols and acylating agent.

Most of the acidic and basic catalysts lack the ability to differentiate between primary and second-

ary hydroxy and amino groups. Thus, acylation by transesterification with an ester or an enol ester constitutes a simple, practical, and selective alternative. A variety of procedures involving different catalysts have been developed for this transformation [15, 16] and this process is under constant study to make it more effective and selective [17, 18].

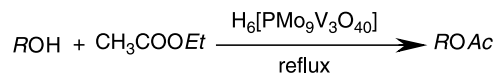
Heteropolyacids, *HPAs*, catalyze a wide variety of reactions in homogeneous or heterogeneous (liquid-solid, gas-solid, or liquid-liquid biphasic) systems, offering strong options for more efficient and cleaner processing compared to conventional mineral acids [19–22]. Catalysts based on heteropolyacids as *Brønsted* acids have many advantages over liquid acid catalysts. They are non-corrosive and environmentally benign presenting fewer disposal problems. Solid heteropolyacids have attracted much attention in organic synthesis owing to easy work-up procedures, easy filtration, and minimization of cost and waste generation due to reuse and recycling of the catalysts [23]. Being stronger acids, heteropolyacids will have significantly higher catalytic activity than conventional catalysts such as mineral 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  $H_2SO_4$  [21, 22]. This makes it possible to carry out the catalytic process at a lower catalyst concentration and/or at a lower temperature. Further, heteropolyacid catalysis

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lacks side reactions such as sulfonation, chlorination, nitration, *etc.* which occur with mineral acids [21, 22]. As stable, relatively nontoxic crystalline substances, heteropolyacids are also preferable regarding safety and ease of handling.

The *Keggin*-type *HPAs* typically represented by the formula  $H_{8-x}[XM_{12}O_{40}]$ , when *X* is the heteroatom (most frequently  $P^{+5}$  or  $Si^{+4}$ ), *x* is the oxidation state, and *M* is the addenda atom (usually  $W^{+6}$  or  $Mo^{+6}$ ), are the most important ones for catalysis [19–22]. They have been widely used as acid and oxidation catalysts for organic synthesis and found several industrial applications.

Recently, we have reported acetylation of alcohols and phenols with acetic acid and acetic anhydride in the presence of ferric perchlorate [24] or  $H_{14}[NaP_5W_{30}O_{110}]$  [25]. In continuation of our investigation on the use of heteropolyacids as catalysts for chemical preparations [26–31] we wish now to report that the mixed addenda heteropolyacid  $H_6[PMo_9V_3O_{40}]$  catalyzes the transesterification of various alcohols and benzyl amines with ethyl acetate very efficiently (Scheme 1).



**Scheme 1**

## Results and Discussion

When 2-chlorobenzyl alcohol was treated with ethyl acetate in the presence of  $H_6[PMo_9V_3O_{40}]$  under reflux condition the corresponding acetate was obtained in good yield (Table 1, Entry 6). The reaction of various benzyl alcohols with ethyl acetate under the same condition afforded the corresponding products in high yields. The results are summarized in Table 1. In all cases, the reactions proceeded efficiently and completed within 40–70 min. All of the products were characterized by comparison of their spectra and physical data with those reported in literature. This method is effective for the preparation of acetates from both electron-rich as well as electron-deficient benzyl alcohols. Allylic, propargylic, primary, and secondary alcohols were also successfully acetylated under these conditions. However, phenol and aniline derivatives failed to react with ethyl acetate to give the analogous products under these reaction conditions. Moreover, treatment of benzyl amine and ethyl acetate under the same reaction condition afforded *N*-benzylacetamide in 90% yield after 70 min (see Table 1). In order to show the selectivity of the procedure for the acetylation of different benzyl alcohols, we investigated the competitive reaction for the preparation of benzyl acetates from benzyl alcohols in the presence of phenols or anilines using a catalytic

**Table 1.** Acetylation of alcohols and amines by transesterification with *EtOAc* using  $H_6[PMo_9V_3O_{40}]$  as the catalyst

Entry	Substrate	Product	Time/min	Yield/% <sup>a</sup>
1	<i>Ph</i> CH <sub>2</sub> OH	<i>Ph</i> CH <sub>2</sub> OAc	50	96
2	2- <i>Me-Ph</i> CH <sub>2</sub> OH	2- <i>Me-Ph</i> CH <sub>2</sub> OAc	40	92
3	2-OH- <i>Ph</i> CH <sub>2</sub> OH	2-OH- <i>Ph</i> CH <sub>2</sub> OAc	50	92
4	4-NO <sub>2</sub> - <i>Ph</i> CH <sub>2</sub> OH	4-NO <sub>2</sub> - <i>Ph</i> CH <sub>2</sub> OAc	50	99
5	4-Br- <i>Ph</i> CH <sub>2</sub> OH	4-Br- <i>Ph</i> CH <sub>2</sub> OAc	50	99
6	2-Cl- <i>Ph</i> CH <sub>2</sub> OH	2-Cl- <i>Ph</i> CH <sub>2</sub> OAc	45	85
7	4- <i>OMe-Ph</i> CH <sub>2</sub> OH	4- <i>OMe-Ph</i> CH <sub>2</sub> OAc	50	94
8	Furyl-CH <sub>2</sub> OH	Furyl-CH <sub>2</sub> OAc	60	90
9	C <sub>2</sub> HCH <sub>2</sub> OH	C <sub>2</sub> HCH <sub>2</sub> OAc	60	90
10	C <sub>2</sub> H <sub>3</sub> CH <sub>2</sub> OH	C <sub>2</sub> H <sub>3</sub> CH <sub>2</sub> OAc	70	93
11	<i>Ph</i> <sub>2</sub> CHOH	<i>Ph</i> <sub>2</sub> CHOAc	60	98
12	CH <sub>3</sub> CH(OH)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	CH <sub>3</sub> CH(OAc)(CH <sub>2</sub> ) <sub>5</sub> CH <sub>3</sub>	60	99
13	CH <sub>3</sub> CH(OH)(CH <sub>2</sub> ) <sub>7</sub> CH <sub>3</sub>	CH <sub>3</sub> CH(OAc)(CH <sub>2</sub> ) <sub>7</sub> CH <sub>3</sub>	70	98
14	<i>Ph</i> CH <sub>2</sub> NH <sub>2</sub>	<i>Ph</i> CH <sub>2</sub> NHOAc	70	97
15	<i>Ph</i> NH <sub>2</sub>	No reaction	1440	–
16	4-NO <sub>2</sub> - <i>Ph</i> NH <sub>2</sub>	No reaction	1440	–
17	4-Br- <i>Ph</i> NH <sub>2</sub>	No reaction	1440	–
18	<i>Ph</i> OH	No reaction	1440	–
19	4-Br- <i>Ph</i> OH	No reaction	1440	–
20	2-NO <sub>2</sub> - <i>Ph</i> OH	No reaction	1440	–

<sup>a</sup> Yields analyzed by GC

amount of  $H_6[PMo_9V_3O_{40}]$  under reflux conditions. We found that benzyl alcohols were converted to the corresponding acetates in high selectivity in the presence of phenols or anilines. This suggested that selective preparation of acetates in the presence of phenols or anilines could be achieved with this procedure.

In conclusion,  $H_6[PMo_9V_3O_{40}]$  was employed as an effective heterogeneous catalyst for the transesterification of alcohols in high yields in solution. The catalyst is recyclable and was used in several runs without losing its catalytic activity. Relatively short reaction time, very simple performance and work-up procedure, high yields, easy recycling, and reusability are worth of mentioning for the present protocol.  $H_6[PMo_9V_3O_{40}]$  is non-corrosive and environmentally benign and presents fewer disposal problems. The use of this green, available, and inexpensive solid acid catalyst allows replacement of the usual soluble inorganic acids, contributing in this way to the reduction of wastes.

## Experimental

All chemicals were purchased from commercial suppliers and were used as received. All products were identified by their spectra and physical data. Melting points were measured by using the capillary tube method with an electrothermal 9100 apparatus. IR spectra were recorded from KBr disks on the FT-IR Bruker Tensor 27. Mass spectra were recorded on MS 5973 Network Mass Selective detector. All the yields were calculated from isolated products, and GC was used to establish their purities.

### *Acetylation of Alcohols Catalyzed by $H_6[PMo_9V_3O_{40}]$ :*

#### *Typical Procedure*

$H_6[PMo_9V_3O_{40}]$  (0.03 g, 1 mol%), 0.10 g benzyl alcohol (1 mmol), and 0.9 cm<sup>3</sup> ethyl acetate (10 mmol) were refluxed for 50 min. The progress of the reaction was monitored by TLC using petroleum ether-ethyl acetate as eluent. After completion of the reaction the catalyst was removed by filtration. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography over silica gel to furnish pure benzyl acetate for which spectra are in full agreement with data of an authentic sample. This procedure is followed for acylation of all substrates included in Table 1. All products are known compounds and were identified by comparison of their spectra with those of authentic samples.

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