

# Facile preparation of symmetrical and unsymmetrical ethers from their corresponding alcohols catalyzed by aluminumdodecatangstophosphate (AIPW<sub>12</sub>O<sub>40</sub>), as a versatile and a highly water tolerant Lewis acid

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## Abstract

AIPW<sub>12</sub>O<sub>40</sub> as a highly water tolerant Lewis acid is a suitable catalyst for the condensations in which water molecules generated in the process of the reaction. Therefore, efficient etherification of different classes of alcohols was performed using catalytic amounts of AIPW<sub>12</sub>O<sub>40</sub>. Preparation of symmetrical dibenzyl ethers especially bis(4-nitrobenzyl)ether also proceeded well with high yields in the presence of catalytic amounts of AIPW<sub>12</sub>O<sub>40</sub>. This compound acts as a heterogeneous, efficient and a reusable catalyst when used in aprotic organic solvents. © 2004 Elsevier B.V. All rights reserved.

**Keywords:** Aluminumdodecatangstophosphate; AIPW<sub>12</sub>O<sub>40</sub>; Lewis acid; Water tolerant; Reusable catalyst; Alcohol; Ether

## 1. Introduction

The strong Brønsted acidity [1,2] of heteropolyacids (HPAs) and the softness of the heteropoly anions are responsible for their high catalytic activities in the reactions [3]. Today, because of the strict environmental legislation, heterogeneous catalysis has become attractive in view of their isolation and separation from the reaction media. In comparison with the conventional liquid acid catalysts, heteropolyacids as heterogeneous catalysts have the advantages of being non-corrosive, environmentally benign, and presenting fewer disposal problems [4]. Due to the more reactivity of these compounds than conventional inorganic and organic acids, they have found interesting applications in various solution reactions and as industrial catalysts for several liquid-phase reactions [5–9].

Salts of heteropoly acids have been used as efficient catalysts in organic reactions. For example, cesium salts of HPAs

are good samples of active and useful solid acid catalysts. They exhibit an excellent performance in several organic reactions owing to their high surface acidity and also probably to their unique basicity [10,11]. It has been demonstrated that the acidic cesium salts of HPAs are very water-tolerant catalysts for hydration of olefins [12] and hydrolysis of esters [13]. This nature was assigned to moderate hydrophobicity of the catalysts [14].

In recent years, we have reported new catalytic applications of heteropoly acids in organic reactions [15–22].

Preparation of ethers is an important reaction for which a wide variety of procedures have been developed during the last decades. The most commonly used protocol is Williamson ether synthesis [23] which requires initial transformation of alcohols into their corresponding halides or tosylates followed by their displacement with strongly basic alkoxides or phenoxides. Strong basic condition is hazardous to complex molecules carrying base sensitive functional groups. Etherification by direct condensation of alcohols has been considered as an alternative which is conducted in the presence of catalytic amounts of organic or inorganic protic acids [24]. Lewis acids have been also used for direct

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etherification condensation reactions [25]. In most cases, the reactions suffer from the use of stoichiometric amounts of the Lewis acids which is due to their decomposition by water generated in the process of etherification reactions [25a].

Reductive etherification of carbonyl compounds by  $\text{BiBr}_3/\text{Et}_3\text{Si-H}$  and  $\text{BiBr}_3/\text{ClR}_2\text{Si-H}$  are also reported [26]. However, these systems suffer from being highly water sensitive, expensive and not easily available.

We have recently reported easy etherification of different allylic and benzylic alcohols in the presence of catalytic amounts of DDQ [27a] and  $\text{Fe}(\text{ClO}_4)_3$  [27b].

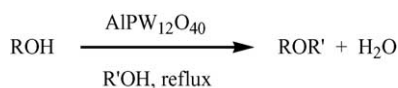
Here we wish to disclose a new catalytic application of aluminumdodecatangstophosphate ( $\text{AlPW}_{12}\text{O}_{40}$ ), as an efficient, easily available, cheap, recyclable, and water tolerant Lewis acid for the etherification of primary, secondary and tertiary benzylic alcohols.

## 2. Results and discussion

We first examined benzylation of methanol by *p*-methoxy benzyl alcohol as a model compound in the presence of a catalytic amount (5 mol%) of aluminumdodecatangstophosphate ( $\text{AlPW}_{12}\text{O}_{40}$ ). The reaction proceeded smoothly and produced *p*-methoxy benzyl methyl ether in 91% yield after 10 min under reflux conditions (Table 1, entry 3). The corresponding ether was produced in only 30% yield at room temperature after prolonged reaction time (24 h) with 5 mol% of  $\text{AlPW}_{12}\text{O}_{40}$  (Table 1, entry 2). In the absence of the catalyst, similar reaction did not proceed under reflux conditions after 24 h (Table 1, entry 1). In order to show the general application of the protocol, we have studied the etherification of primary, secondary and tertiary benzylic alcohols with methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, and *t*-butanol (Scheme 1). All the reactions proceeded well in short reaction times with the production of benzyl alkyl ethers in excellent yields (Table 1).

Benzyl alcohol and *p*-methyl benzyl alcohol produced their corresponding ethers in high yields in refluxing 1-propanol and 1-butanol (Table 1, entries 25–27, 30–32), they remained intact in methanol and ethanol under reflux conditions. The reactions proceeded smoothly in the mixture of methanol or ethanol in toluene (20/80) under reflux conditions.

Methanol and 1-butanol were reacted with 2-(4-biphenyl)-2-propanol, as a tertiary benzylic alcohol, at 65 °C to produce the corresponding ethers in excellent yields. In this study,



R: 1°, 2°, and 3° benzylic

R': Me, Et, 1-Pr, 2-Pr, 1-Bu, 2-Bu, *t*-Bu

Scheme 1.

Table 1

Etherification of benzylic alcohols with different alcohols in the presence of 5 mol% of  $\text{AlPW}_{12}\text{O}_{40}$  under reflux conditions

Entry	Alcohol	Solvent	Time (h)	Isolated yield (%)
1	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	Methanol	24	0 <sup>a</sup>
2		Methanol	24	30 <sup>b,c</sup>
3		Methanol	0.15	91
4		Ethanol	0.15	93
5		1-Propanol	0.15	93
6		2-Propanol	0.15	90
7		<i>t</i> -Butanol	0.25	92
8	PhCH(OH)CH <sub>3</sub>	Methanol	7	83
9		Ethanol	7	86
10		1-Propanol	0.5	95
11		1-Butanol	0.1	93
12		2-Butanol	0.15	90
13	PhCH:CHCH <sub>2</sub> OH <sup>d</sup>	Methanol	7	93
14		2-Propanol	2.5	85
15		1-Propanol	0.7	89
16		1-Butanol	0.5	83
17		2-Butanol	0.8	87
18	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	Methanol/toluene (20/80)	6	80
19		Ethanol/toluene (20/80)	6	78
20		1-Propanol	1	93
21		1-Butanol	0.75	95
22		2-Butanol	1.3	89
23	PhCH <sub>2</sub> OH	Methanol/toluene (20/80)	6	69
24		Ethanol/toluene (20/80)	6	72
25		1-Propanol	27	88
26		1-Butanol	5	91
27		2-Butanol	30	84
28	<i>p</i> -PhC <sub>6</sub> H <sub>4</sub> C(Me) <sub>2</sub> OH	Methanol	0.2	93
29		1-Butanol	0.25	95 <sup>e</sup>
30		2-Butanol	0.3	70 <sup>e,f</sup>

<sup>a</sup> In the absence of the catalyst.

<sup>b</sup> The reaction occurred at room temperature.

<sup>c</sup> GC yield.

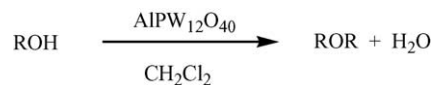
<sup>d</sup> 20 mol% of  $\text{AlPW}_{12}\text{O}_{40}$  was used.

<sup>e</sup> The reaction occurred at 65 °C.

<sup>f</sup> The alkene was also isolated in 34% yield.

no elimination reaction was observed. However, in the reaction of 2-(4-biphenyl)-2-propanol with 2-butanol under reflux conditions, the corresponding ether was produced in 66% yield, accompanied with the formation of the corresponding olefin in 34% yield (Table 1, entries 33–35).

Furthermore, we have also studied the preparation of symmetrical dibenzyl ethers from their corresponding alcohols. We found that the reactions proceeded well at room temperature in  $\text{CH}_2\text{Cl}_2$  in the presence of 7 mol% of  $\text{AlPW}_{12}\text{O}_{40}$



R: 1°, 2°, and 3° benzylic

Scheme 2.

Table 2  
Preparation of symmetrical and unsymmetrical ethers in the presence of 7 mol% of AIPW<sub>12</sub>O<sub>40</sub> as a heterogeneous catalyst

Entry	Alcohol	Product	Time (h)	Isolated yield (%)
1	PhCHOHCH <sub>3</sub>	(PhCHCH <sub>3</sub> ) <sub>2</sub> O	3	94
2	Ph <sub>2</sub> CHOH	(Ph <sub>2</sub> CH) <sub>2</sub> O	1	92
3	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	( <i>p</i> -MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> ) <sub>2</sub> O	0.33	87
4	PhCH <sub>2</sub> OH <sup>a</sup>	(PhCH <sub>2</sub> ) <sub>2</sub> O	1	86
5	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH <sup>a</sup>	( <i>p</i> -MeC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> ) <sub>2</sub> O	0.7	91
6	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH <sup>a</sup>	( <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> ) <sub>2</sub> O	1.2	96
7	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH <sup>a,b</sup>	( <i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> ) <sub>2</sub> O	10	98
8	<i>p</i> -PhC <sub>6</sub> H <sub>4</sub> C(Me) <sub>2</sub> OH	<i>p</i> -PhC <sub>6</sub> H <sub>4</sub> C(Me) <sub>2</sub> O (60%) + <i>p</i> -PhC <sub>6</sub> H <sub>4</sub> (Me)C=CH <sub>2</sub> (40%)	3.5	93

<sup>a</sup> Reaction was performed in refluxing 1,2-dichloroethane.

<sup>b</sup> 14 mol% of AIPW<sub>12</sub>O<sub>40</sub> was used.

(Scheme 2). The results of this study are summarized in Table 2.

Using this method, 1-phenyl ethanol produced bis(1-phenylethyl)ether in 94% yield at room temperature after 3 h in the presence of 7 mol% of AIPW<sub>12</sub>O<sub>40</sub>. It is reported that equimolar amount of zinc chloride has been required to furnish the production of this ether in 91% yield after 4 h [25a]. This conversion has also been performed in 80% yield after 48 h with methylrhenium trioxide which is an expensive catalyst [25e]. BF<sub>3</sub>Et<sub>2</sub>O has been also employed for this transformation but it suffers from producing several products along with the polymerization reaction. Similar reaction in the presence of TiCl<sub>4</sub> [25a], proceeded with the production of 1-chloro-1-phenylethane as the major product. Bis(1-phenylethyl)ether was also produced in 70% yield in the presence of BiCl<sub>3</sub> [25a] with the formation of 1-chloro-1-phenylethane as a byproduct in 30% yield. Other Lewis acids such as AlCl<sub>3</sub> and BBr<sub>3</sub> failed to catalyze this reaction [25a]. These comparisons clearly show the efficiency and suitability of the presented catalyst for such etherification reactions.

In addition, the preparation of bis(4-nitrobenzyl)ether from *p*-nitro-benzyl alcohol is a difficult task. However, *p*-nitro-benzyl alcohol in the presence of a catalytic amount of AIPW<sub>12</sub>O<sub>40</sub> (14 mol%) in refluxing ClCH<sub>2</sub>CH<sub>2</sub>Cl produced the corresponding ether in 96% yield after 10 h. The results of this study are summarized in Table 2. We also studied the reaction of 1- and 2-octanol and allyl alcohol for the preparation of their corresponding ethers in refluxing ClCH<sub>2</sub>CH<sub>2</sub>Cl in the presence of AIPW<sub>12</sub>O<sub>40</sub> (14 mol%). Our observations showed that the reaction did not proceed well and the corresponding ethers were not produced even after prolonged reaction time (10 h). Therefore, we believe, this protocol is not suitable for the preparation of aliphatic and allylic ethers.

The reactions proceeded in CH<sub>2</sub>Cl<sub>2</sub> and ClCH<sub>2</sub>CH<sub>2</sub>Cl were performed heterogeneously and the isolation of the catalyst from the reaction mixture was easy and not a time-consuming process and the ethers were isolated from high to excellent yields.

In conclusion, in this study we have introduced aluminum-dodecatungstophosphate (AIPW<sub>12</sub>O<sub>40</sub>) as a water tolerant, reusable and environmentally benign catalyst which has been

used under heterogeneous or homogeneous conditions for the efficient etherification of benzylic alcohols with different acyclic alcohols under mild traction conditions. By using this catalyst, preparation of *p*-nitrobenzyl ether which is a difficult task and the preparation of symmetrical and unsymmetrical benzyl ethers, have been achieved in excellent yields.

### 3. Experimental

#### 3.1. General

Chemicals were purchased from Merck and Fluka Chemical Companies. All the products are known and were characterized by comparison of their physical data with those reported in the literature. IR spectra were run on a Shimadzu model 8300 FT-IR spectrophotometer. NMR spectra were recorded on a Bruker Avance DPX-250. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX. The purity of the products and the progress of the reactions were accomplished by TLC on silica-gel polygram SILG/UV<sub>254</sub> plates or by a Shimadzu Gas Chromatograph GC-14A instrument with a flame ionization detector.

#### 3.2. Preparation of bis(1-phenylethyl) ether as a typical procedure

1-Phenylethanol (5 mmol, 0.615 g), and AIPW<sub>12</sub>O<sub>40</sub> (0.35 mmol, ~1 g) in CH<sub>2</sub>Cl<sub>2</sub> (30 ml) was stirred at room temperature for 3 h. After completion of the reaction (monitored by TLC), CH<sub>2</sub>Cl<sub>2</sub> (50 ml) was added to the reaction mixture in order to precipitate the catalyst which was removed by filtration. After evaporation of the solvent, the almost pure product was obtained in 94% yield, 0.213 g, bp = 143–145/10; ([25a], 144–150/10).

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