

Keggin-Type Heteropolyacids-Catalyzed One Pot Oxidation-Trimerization of Alcohols into 2,4,6-Trisubstituted-1,3,5-Trioxanes

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ABSTRACT: *The catalytic air oxidation-trimerization of alcohols was carried out with hetropolyacids. In the presence of hetropolyacid formation of cyclotrimers of alcohols and aldol condensation products was observed. The 1,3,5-trioxanes were major and aldol condensation compounds were minor products.*

KEY WORDS: *Heteropolyacids, 1,3,5-Trioxanes, Alcohols, Oxidation, Trimerization, Aldol condensation.*

INTRODUCTION

The copolymerization of trioxane and cyclic ethers, such as ethylene oxide, produced acetal resins used as engineering thermoplastics. Trioxane was commonly produced by the liquid- and vapor-phase catalytic trimerization of aqueous formaldehyde in the presence of an acid [1]. 1,3,5-Trioxanes have many applications in various fields, such as stabilizers in color photography, burning regulators in fumigants, flavoring materials, carriers for scents, repellents, deodorants, and insecticides [2].

1,3,5-Trioxanes could be formed by cyclo-trimerization of aldehydes catalyzed by protic acids [3,4], Keggin-type heteropolyacids [2], cation-exchange resins [5] or Lewis acids such as zinc chloride [2], tantalum

pentachloride [6], bismuth trichloride [2], titanium or tin tetrachlorides [7]. Other catalysts including zeolites [2], bentonitic earth [8], methylrhenium trioxide [9], or acetyltriphenylphosphonium bromide [10] were investigated. Other reactions have been also described but they required drastic conditions of pressure or gave poor yields of products [11].

The oxidation of alcohols to carbonyl compounds is an important transformation of organic synthesis, and several methods have been explored to accomplish such a conversion [12]. These methods involve the use of expensive reagents, long reaction times, strongly acidic condition and tedious work-up procedure leading to the generation of a large amount of toxic waste.

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1021-9986/09/2/131

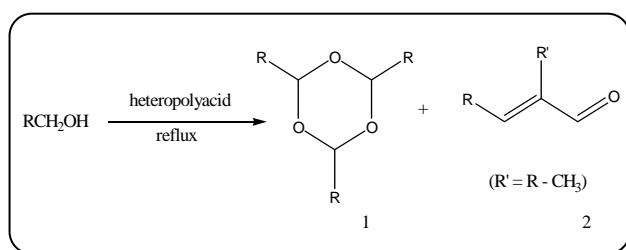
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Table 1: Oxidation-trimerization of alcohols.

Entry	Alcohols	Conversion (%) ^b	Yield 1 (%) ^b	Yield 2 (%) ^b
1	MeCH ₂ OH	98	84	14
2	MeCH ₂ CH ₂ OH	96	82	14
3	(Me) ₂ CHCH ₂ OH	93	79	14
4	Me(CH ₂) ₂ CH ₂ OH	91	72	19
5	Me(CH ₂) ₃ CH ₂ OH	83	67	16
6	(Me) ₂ CHCH ₂ CH ₂ OH	87	65	22
7	Me(CH ₂) ₄ CH ₂ OH	84	64	20
8	Me(CH ₂) ₆ CH ₂ OH	81	60	21

a) Reaction conditions: H₄[PMo₁₁VO₄₀] (0.03 mmol), alcohols (1 mmol), solvent-free system, 100 °C, 2 h.

b) Yields analyzed by GC.



Scheme 1.

Considering these facts, there is still a need to introduce new catalysts for this conversion. Instead of conventional waste-producing oxidation procedures such as the stoichiometric application of environmentally benign oxidants has gained the preference in the past years.

Heteropolyacids, HPAs, have many advantages that make them economical and environmentally attractive in both academic and industrial signification; they are useful acids and oxidation catalysts in various reactions since their catalytic features can be varied at a molecular level. Among them, the Keggin-type HPAs have long been known to be good catalysts for oxidation reactions. They exhibit great advantages: for example, their catalytic properties can be tuned by changing the identity of charge-compensating counter cations, heteroatoms and framework metal atoms [12].

Continuing our research into the development of new synthetic methodologies and the utilization of heteropolyacids, we studied the behavior of aliphatic alcohols against this reagent, and report a new one pot

reaction that includes oxidation-trimerization of alcohols (scheme 1).

EXPERIMENTAL

Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. ¹HNMR spectra were recorded on a Bruker AC-80 MHz spectrometer using TMS as an internal standard (CDCl₃ solvent). IR spectra were recorded from a KBr disk on the FT-IR Bruker Tensor 27. GC spectra were carried out on a Network GC System-Agilent 5973 spectrometer.

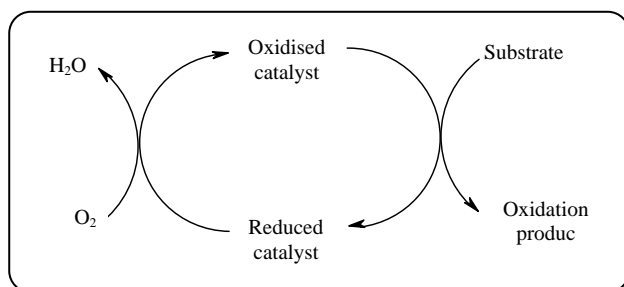
Oxidation-trimerization of alcohols using Keggin-type heteropolyacids

A mixture of alcohols (1 mmol) and catalyst (0.03 mmol) was refluxed at 100 °C for 2 h. The progress of the reaction was monitored by TLC. As evident by both HPLC and TLC, the crude product was found to be a mixture of two components with a major spot ~85% and minor <10 %. The two spots were separated by column chromatography using 10-30 % EtOAc-hexane as mobile phase and characterized by Mass and NMR. One of the components was found to be the cyclotrimer and the second component was the aldol condensation product. In all cases, the title compounds were obtained in excellent yields (75-82 %) (table 1).

At the end of the reaction, the catalyst was filtered, washed with dichloromethane, dried at 130 °C for 1 h, and re-used in another reaction. The recycled catalyst was

Table 2: Oxidation-trimerization of propanol with various molar ratios of alcohol and hetropolyacid.

Entry	Molar ratio of alcohol: hetropolyacid	Percentage yield of 2,4,6-triethyl-[1,3,5]trioxane with			
		H ₃ [PW ₁₂ O ₄₀]	H ₄ [SiW ₁₂ O ₄₀]	H ₅ [PMo ₁₂ O ₄₀]	H ₅ [PMo ₁₁ VO ₄₀]
1	1:0.01	36	50	58	62
2	1:0.02	43	56	65	76
3	1:0.03	58	62	78	82
4	1:0.04	58	62	78	82

**Scheme 2.**

used for five reactions without observation of an appreciable loss in its catalytic activities.

RESULTS AND DISCUSSION

The liquid-phase oxidation of organic substances catalysed by heteropolyacids is usually carried out in homogenous or biphasic systems. Heterogeneous liquid-solid systems are also used but less frequently. Amongst various oxidants that can be used in these reactions, oxygen (air) and hydrogen peroxide are the most important [13]. In our previous papers, we reported the oxidation of tertiary amines and primary aromatic amines with aqueous hydrogen peroxide under the influence of Preyssler catalyst [14], N-oxidation of pyridine carboxylic acids using hydrogen peroxide catalyzed by Preyssler's anion [15], and oxidation of benzylic, allylic and aliphatic alcohols to carbonyl compounds [12].

Herein we wish to report the catalytic ability of this catalyst in air oxidation-trimerization of alcohols. The 1,3,5-trioxanes were major and the aldol condensation compounds were minor products. Our study has been focused on 1,3,5-trioxanes compounds as the major product. The effects of various parameters such as solvent, catalyst type, temperature and times of reactions were studied.

In the first stage, many oxidation reactions in various solvents have been performed. Solvent free system was

found to be the best choice for the reaction. The influence of the mole ratio of catalyst to substrate on the yields in the solvent free system with Keggin was investigated. The molar ratio of substrate: hetropolyacid was varied as 1:0.01 to 1:0.04. Our studies showed that, the reaction yield was affected by changing the molar ratio of alcohol: hetropolyacid. The yield increases with that of the molar ratio up to 1:0.03 and any further increasing of the molar ratio does not have any appreciable effect on the yield. (table 2).

On the basis of these results, reactions were performed with hetropolyacid with a molar ratio of 1:0.03 in the solvent free system.

OXIDATION REACTION

A mixture of alcohols and catalyst was refluxed at 100 °C. The progress of the reaction was monitored by TLC. Aliquots of the reaction were collected over different time intervals and analyzed by gas chromatography. The results indicate that oxidation of alcohols to corresponding aldehydes were in most cases completed within 15-30 minutes, and the structures of these products were easily assigned on the basis of their IR and Mass spectra.

Selective oxidation with mixed oxides and oxide-like catalysts such as heteropolyacids involves the activation of C-H or C-C bonds as well as of the oxidant on the catalyst surface and frequently occurs by a Mars-van Krevelen redox mechanism [13], which may be represented by (scheme 2). The catalyst oxidized the substrate and then, in another step, is re-oxidised by O₂. Heteropolyacid maintained their Keggin structure in the course of the reactions, which were confirmed by examining their IR spectra. Previous study, indicated the re-oxidation of the catalyst without losing the Keggin structure [15].

Table 3: Time dependence degree of the conversion (in mol %) of the reaction of EtCH₂OH yielding (EtCHO)₃ (1) and Et CH C(Me) C(O/H) (2) catalyzed by H₄[PMo₁₁VO₄₀] (0.03 mmol), propanol (1 mmol), solvent-free system.

Time (h)	Conversion (%)	Yield 1 (%)	Yield 2 (%)
2	98	84	14
5	100	75	25
12	100	62	38
24	100	50	50

The results indicate that with an increase in reaction time, formation of cyclotrimers of aldehydes has been catalyzed in the presence of heteropolyacids.

Since heteropolyacids were also used as a catalyst in the reaction with aldehydes, in the presence of heteropolyacids formation of cyclotrimers of aldehydes (1) and aldol condensation products (2) was catalyzed (scheme 1). Most likely due to the reversibility of cyclotrimerization reactions of aldehydes, the ratio 1/2 is shifted in favor of 2 with longer reaction times (table 3). Thus, heteropolyacid was found to catalyze cyclotrimerization of aldehydes selectively as well as the reverse reaction.

The effect of solvent on the model reaction was studied by carrying out the reaction in a solvent-free system and in a variety of solvents including chloroform, dichloromethane, and acetonitrile at different temperatures. As shown in (table 4) the best results in terms of yield and time have been achieved in solvent-free systems.

In our studies, we investigated the activity of various Keggin-type heteropolyacids. Representative results in (table 5) are shown. The results indicate that the nature of the catalyst plays an important role on their catalytic activities. The highest yield of products has been achieved in the presence of H₅[PMo₁₁VO₄₀] as catalyst, and H₃[PW₁₂O₄₀] gave the lowest yields.

Due to the complicated nature of the reaction, obtaining the variety of products, it seemed rather difficult to make an exact assessment of the catalyst role. However, we may make some assumptions that agree with the experimental data and literature.

The Keggin anion has an assembly of 12 corner-shared octahedral MoO₆ from trimetallic groups [Mo₃O₁₃] around a heteroatom tetrahedron PO₄. The introduction of vanadium (V) into the Keggin framework of [PMo₁₂O₄₀]³⁻

Table 4: Oxidation-trimerization of propanol: effect of the temperature and the type of solvent. a) Reaction conditions: H₄[PMo₁₁VO₄₀] (0.03 mmol), propanol (1 mmol), 2 h. b) Yields analyzed by GC.

Entry	Solvent	T (°C)	Percentage yield of 2,4,6-triethyl-1-[1,3,5]trioxane with
1	Dichloromethane	40	40
2	Chloroform	61	60
3	Acetonitrile	82	75
4	Solvent free	100	84

is beneficial for catalysis reactions [16]. 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 3, respectively) [17]. Studies on these isomers in catalytic reactions indicate that different isomers cause to show different reactivities [18].

Because the metal substitution may modify the energy and composition of the LUMO and redox properties, for mentioned heteropolyacids with different charges, the energy and composition of the LUMOs have significant effects on the catalytic activity [19]. Substitution of vanadium ions into the molybdenum framework stabilize the LUMOs because these orbitals derive, in part from vanadium d-orbitals which have been assumed to be more stable than those of molybdenum and tungsten [20]. The abundance of different isomers may also play an important role in catalytic performance. In addition, different positional Mo atom(s) substituted by the V atom(s) in [PMo₁₂O₄₀]³⁻ may create different vanadium chemical environments, thus causing these catalysts to exhibit varying catalytic performances.

By variation of the addenda atoms, the electrochemical character of them can be widely changed. The addenda atoms can be ordered by decreasing oxidizing ability in the following way: V(V) > Mo(VI) > W(VI)[21].

In order to confirm the utility of HPAs, as effective catalysts, this reaction was repeated in the absence of the HPAs. The results show that in the absence of the HPAs, oxidation-trimerization reaction did not proceed.

In order to know whether the catalysts would succumb to poisoning and lose of catalytic activity during the reaction, we investigate the reusability of the catalyst. For this purpose, we first carried out the reaction in the presence of the catalyst. After completion of the reaction,

Table 5: Oxidation-trimerization of propanol; effect of the type of heteropolyacids catalysts^a

Entry	Hetropolyacid	Conversion (%) ^b	Percentage yield of 2,4,6-triethyl-[1,3,5]trioxane with
1	H ₃ [PW ₁₂ O ₄₀]	87	65
2	H ₃ [PMo ₁₂ O ₄₀]	93	79
3	H ₅ [PMo ₁₁ VO ₄₀]	96	82
4	H ₄ [SiW ₁₂ O ₄₀]	98	84

a) Reaction conditions: Keggin-type heteropolyacids (0.03 mmol), propanol (1 mmol), solvent-free system, 100 °C, 2 h.

b) Yields analyzed by GC.

Table 6: The comparison of efficiency of catalysts after five times.

Entry	Hetropolyacid	Yield % ^a (after different round of reactions)				
		First	Second	Third	Forth	Fifth
1	H ₃ [PW ₁₂ O ₄₀]	98.2	97.5	96	95.5	93.2
2	H ₃ [PMo ₁₂ O ₄₀]	97	96.3	94.9	93.5	90.8
3	H ₅ [PMo ₁₁ VO ₄₀]	97	95.6	94.2	92.7	91.2
4	H ₄ [SiW ₁₂ O ₄₀]	95.7	94.2	92.5	91.2	89.3

the catalyst was removed and washed with diethyl ether, dried at 80 °C for 1 h, and subjected to a second run of the reaction process with the same substrate. The results of the first experiment and subsequent experiments were almost consistent in yields. We have found that Keggin catalyst can be reused several times without any appreciable loss of activity. The several time recoveries had only slightly decreased the catalytic activity, pointing to the stability and retention capability of this useful polyanion. In table 6 the comparison of efficiency of the catalyst after five times reuse is reported.

CONCLUSIONS

In conclusion, we have developed a new one pot process that involves oxidation-trimerization reactions of alcohols. In our studies, we investigated the activity of various Keggin-type heteropolyacids. The highest yield of products has been achieved in the presence of H₅[PMo₁₁VO₄₀] as catalyst, and H₃[PW₁₂O₄₀] gave the lowest yields. The catalytic air oxidation-trimerization of alcohols was carried out with hetropolyacid. Because heteropolyacids, was also used as catalyst in the reaction with aldehydes. In the presence of heteropolyacids formation of cyclotrimers of aldehydes and aldol condensation products was catalyzed. The 1,3,5-trioxanes were major and aldol condensation compounds were minor products.

Received : 8th December 2007 ; Accepted : 15th July 2008

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