Monatshefte für Chemie 138, 165–170 (2007)
DOI 10.1007/s00706-006-0573-2
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Short Communication

A Method for the Acetylation of Alcohols Catalyzed by Heteropolyoxometallates

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Received July 11, 2006; accepted (revised) November 5, 2006; published online January 22, 2007

Summary. Esterifications of acetic acid with some linear, secondary, tertiary, and benzylic alcohols mediated by catalytic amounts of *Keggin*, *Wells–Dawson*, and *Preyssler* type heteropolyacids were carried out under reflux at mild reaction conditions with good to excellent yields. Among the examined catalysts, $H_3PW_{12}O_{40}$ and $H_{14}NaP_5W_{30}O_{110}$ revealed better results than other heteropolyacids. This work was performed with the aim of simplifying the esterification process by omitting any solvents and mineral acid catalysts. Easy work-up, low cost, and acidic waste reduction, which are all important features from the environmental and economical points of view, are distinct aspects of this protocol. Heteropolyacid catalysts could be separated after a simple work-up and reused for several times.

Keywords. Esterification; Heteropolyoxometalate; Catalytic; Alcohol.

Introduction

Selective esterification of carboxylic acids using aliphatic alcohols is one of the most frequently used transformations in organic chemistry [1]. It provides an efficient and inexpensive route for the protection of hydroxyl/carboxyl groups in multi-step synthetic processes and for the synthesis processes of valuable industrial and pharmaceutical compounds, food preservatives, solvents, perfumes, plasticizers, and cosmetics [2–3].

Esterification and transesterification reactions are usually carried out in hydrocarbon solvents using an inorganic or organic catalyst. The catalysts employed in the esterification reactions of carboxylic acids with alcohols include mineral acids [4], anhydrous magnesium sulfate and catalytic amounts of sulfuric acid [5], tosyl chloride/pyridine [6], boron trifluoride etherate/alcohol [7], titanium and tin salts [8], hafnium salts [9], aluminum phosphate molecular sieves [10], polymer protected reagents [11], graphite bisulfite [12], diorganotin dichloride [13], Filtrol-24™, Amberlyst®-15, sulfated zirconia [14], ion exchange resins [15], and *Lewis* acid catalysts such as Sc(O*Tf*)$_3$ [16], *TMS*O*Tf* [17], Cu(O*Tf*)$_2$ [18], $TaCl_4$ [19], and $CoCl_2$ [20]. Synthesis of some of these catalysts is difficult and there is always the problem of unfavorable side reactions. Moreover, some of the conventional acetylation media using mineral acids such as H_2SO_4 or HF are very corrosive and not only pose problems for the design and construction of reactors, vessels, and piping systems, which must be made of expensive alloys, but also raise concerns because of their toxicity and environmental impact [21–24]. Consequently, replacement of corrosive liquid acid catalysts by solid acid catalysts is an important objective.

The replacement of current chemical processing methods with more environmentally benign alternatives is an increasingly attractive subject. In view of

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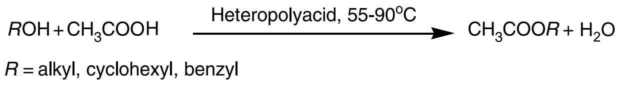

Scheme 1

changing environmental mandates, there is a global effort to replace conventional catalysts by eco-friendly ones. In this regard, heteropolyacids have attracted considerable interest due to their less toxic nature, in addition to possessing high acidity [25, 26]. Homogeneous catalysis using heteropolyoxometalates has been widely developed for a broad range of organic syntheses and environmentally benign catalysis procedures during the past few decades. Good yield, high selectivity, economy, ease of work-up, high stability, and high catalytic activity of heteropolyacids have motivated their increasing use for catalysis in organic synthesis, biomedical transformations, and environmentally benign catalysis [27, 28]. These well defined molecular clusters are commonly used for industrial catalysis of a variety of reactions such as oxidations of olefins, alkanes, alcohols, amines, esterification, and Sn-C bond-breaking [29–37].

Herein we report the esterification of acetic acid with some alcohols at relatively low temperatures and after short times in the presence of several *Keggin*, *Dawson*, and *Preyssler* heteropolyacids (Scheme 1).

Results and Discussion

Production of ethyl acetate and water from the esterification of acetic acid with ethanol is equilibrium limited in the liquid phase for both the neat form and in various non-reactive solvents. Since this reaction progresses very slowly, a strong acid catalyst, typically sulfuric or hydrochloric acid, is generally added to increase the rate of the reaction; however, too much catalyst may cause dehydration of the alcohol or isomerization. The most effective way to increase product formation is to carry out this reaction in such a manner so as to remove one of the products during the reaction process, effectively pushing the equilibrium to the right. We now present a new method involving direct isolation of products from the reaction mixture. Continuous removal of products improved the yield of ester production several-fold.

Table 1 describes acetylation of ethanol with one and two equivalents of acetic acid catalyzed by some common heteropolyacids (entries 1–2). Findings showed that the *Preyssler* acid $H_{14}NaP_5W_{30}O_{110}$ was the best catalyst in the acetylation of ethanol with one equivalent of acid affording an 84% yield of ethyl acetate after 40 min. Other catalysts led to 54–78% yields of ethyl acetate with one equivalent of acid under similar reaction conditions after the same reaction time. Notably, no acetylation of ethanol was observed in the absence of catalyst with one equivalent of acetic acid over the same or prolonged reaction times. Entry 2 in Table 1 shows the results of acetylation of ethanol with two equivalents of acetic acid. This experiment showed that the efficiency of the acetylation increased noticeably in the presence of two equivalents of acid with all the examined catalysts except for $H_{14}NaP_5W_{30}O_{110}$. The yields were also dependent on the alcohol used, as shown by entries 3–4 for methanol and 1-butanol, respectively. In both cases the best catalyst for the reactions with two equivalents of acid was unsupported $H_3PW_{12}O_{40}$.

Table 1. Esterification of acetic acid with ethanol, methanol, and 1-butanol catalyzed by some heteropolyacids

Entry	Substrate	Product	Molar ratio of alcohol/acid	Yield/%				
				$H_3PW_{12}O_{40}$ (*Keggin*)	$H_6P_2W_{18}O_{62}$ (*Wells–Dawson*)	$H_4SiW_{12}O_{40}$ (*Keggin*)	$H_{14}NaP_5W_{30}O_{110}$ (*Preyssler*)	$H_3PW_{12}O_{40}$-SiO_2
1	Ethanol	Ethyl acetate	1:1	78	65	71	84	54
2	Ethanol	Ethyl acetate	1:2	88	90	92	83	63
3	Methanol	Methyl acetate	1:2	100	90	84	68	71
4	1-Butanol	1-Butyl acetate	1:2	97	19	35	92	20

Comparison of the findings obtained for the supported and unsupported $H_3PW_{12}O_{40}$ showed that the supported heteropolyacid was less effective than the unsupported one in the presence of one and two equivalents of acetic acid. Thus, $H_3PW_{12}O_{40}$ was almost 1.4 times more reactive than the supported catalyst $H_3PW_{12}O_{40}$-SiO_2. One plausible interpretation for the lesser reactivity of the supported catalyst is that some protons of the polyacid interacted with some basic sites of the support. Therefore, different acid–base interactions between heteropolyanion and support decreased availability of $H_3PW_{12}O_{40}$ in the catalytic cycle.

To explore the influence of the ethanol/acetic acid molar ratio on yield and selectivity of ester production, esterification of acetic acid with ethanol was examined with different molar ratios of alcohol/acid acid in the presence of $H_3PW_{12}O_{40}$ and $H_4SiW_{12}O_{40}$ (Table 2). Since esterification is a straightforward reaction subject to general *Brønsted* acid catalysis, the yield of ester can be enhanced by increasing the concentration of either alcohol or acid. In the present study, acetic acid, the reactant that is usually less expensive, was used in excess. The best molar ratio of ethanol/acetic acid was found to be 1:4 for both catalysts (Fig. 1). When the acid concentration was increased, the ester yield was enhanced smoothly. Any further increase in the mole ratio of acid above 4 decreased the yield of ester. It was found that the selectivity of esterification reactions was ~100% for all the examined molar ratios of ethanol/acetic acid.

Table 2. Esterification of acetic acid with ethanol catalyzed by $H_3PW_{12}O_{40}$ and $H_4SiW_{12}O_{40}$ under different molar ratios of ethanol/acetic acid

Entry	Alcohol/acid	Yield/%	
		$H_3PW_{12}O_{40}$	$H_4SiW_{12}O_{40}$
1	1:1	77	70
2	1:2	88	92
3	1:3	85	97
4	1:4	97	98
5	1:5	87	61

Table 3 presents the results of acetylation of different mole ratios of ethanol and 1-butanol with acetic acid catalyzed by $H_3PW_{12}O_{40}$ or $H_{14}NaP_5W_{30}O_{110}$. These findings proved that $H_3PW_{12}O_{40}$ is more efficient than the *Preyssler* acid $H_{14}NaP_5W_{30}O_{110}$ in the acetylation of ethanol and butanol under all the examined mole ratios. Moreover, the best molar ratio of alcohol/acid depends on the selected catalyst. For example, a 2:5 molar ratio was the best in the esterification of both alcohols with $H_3PW_{12}O_{40}$, whereas the best results were obtained at a 3:5 molar ratio of alcohol/acid in the acetylation of 1-butanol with $H_{14}NaP_5W_{30}O_{110}$. In the esterification of ethanol with $H_{14}NaP_5W_{30}O_{110}$ the results are almost similar for all molar ratios of alcohol/acid.

Esterification of two equivalents of acetic acid with one equivalent of some linear, secondary, tertiary, and benzylic alcohols catalyzed by *Preyssler* acid $H_{14}NaP_5W_{30}O_{110}$ is reported in Table 4. Results confirmed that benzylic, tertiary, and open-chain

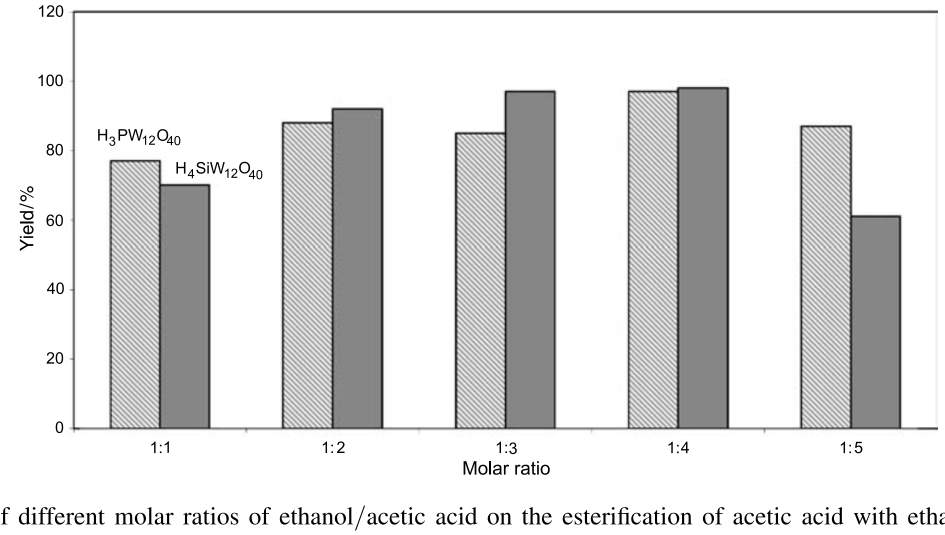

Fig. 1. Effect of different molar ratios of ethanol/acetic acid on the esterification of acetic acid with ethanol catalyzed by $H_3PW_{12}O_{40}$ and $H_4SiW_{12}O_{40}$

Table 3. Acetylation of different mole ratios of ethanol and 1-butanol with acetic acid catalyzed by $H_3PW_{12}O_{40}$ and $H_{14}NaP_5W_{30}O_{110}$ after 45 min

Entry	Substrate	Product	Molar ratio of alcohol/acid	Yield/%	
				$H_3PW_{12}O_{40}$	$H_{14}NaP_5W_{30}O_{110}$
1	Ethanol	Ethyl acetate	1:5	87	70
2	1-Butanol	1-Butyl acetate	1:5	61	55
3	Ethanol	Ethyl acetate	2:5	97	65
4	1-Butanol	1-Butyl acetate	2:5	96	72
5	Ethanol	Ethyl acetate	3:5	92	65
6	1-Butanol	1-Butyl acetate	3:5	95	90

Table 4. Acetylation of different alcohols with acetic acid catalyzed by $H_{14}NaP_5W_{30}O_{110}$ under 1:2 molar ratio of alcohol:acid

Entry	Substrate	Product	Yield/%
			$H_{14}NaP_5W_{30}O_{110}$ (*Preyssler*)
1	$C_6H_5CH_2OH$	$C_6H_5CH_2OAc$	85
2	$(CH_3)_3COH$	$(CH_3)_3COAc$	75
3	$CH_3CH(OH)CH_2CH_3$	$CH_3CH(OAc)CH_2CH_3$	72
4	$CH_3(CH_2)_3CH_2OH$	$CH_3(CH_2)_3CH_2OAc$	45
5	$CH_3(CH_2)_4CH_2OH$	$CH_3(CH_2)_4CH_2OAc$	40
6	Cyclohexanol	Cyclohexyl acetate	15

secondary alcohols were more effective in the acetylation reactions than primary alcohols. Benzyl alcohol, *t*-butanol, and 2-butanol led to >72% conversion, whereas the linear alcohols and cyclohexanol produced <45% of the corresponding acetylated products under the same reaction conditions and at the same time.

In order to know whether the catalysts would lose their catalytic activity during the reaction, they were recovered after the reaction and were reused in the esterification reactions. It was found that the catalysts could be reused several times without any appreciable loss of activity.

In conclusion, this protocol introduces a simple route for efficient acetylation of alcohols in the absence of any solvents and mineral acid catalysts. Important aspects of this cheap methodology are easy work-up and reduction of acidic waste which are crucial from the economical and environmental points of view.

Experimental

Acetic acid, alkyl acetates, alcohols, and other solvents were commercially available, and their purities were monitored by gas chromatography. All products were characterized by comparing their spectral and physical data with those of known samples. Purity of the substances and reaction progress were monitored by TLC on silica gel or by GLC analyses performed on a PU-4500 Perkin Elmer instrument equipped with a flame ionization detector. $H_3PW_{12}O_{40}$, $H_6P_2W_{18}O_{62}$, $H_4SiW_{12}O_{40}$, $H_{14}NaP_5W_{30}O_{110}$, and $H_3PW_{12}O_{40}$-SiO_2 were prepared according to literature [38–41] or were purchased.

Preparation of Preyssler's Anion $K_{12.5}Na_{1.5}[NaP_5W_{30}O_{110}]$ and its Acidic Form $H_{14}[NaP_5W_{30}O_{110}]$

The potassium salt was prepared following the method of *Alizadeh et al.* [38] or a slight variation thereof. Orthophosphoric acid (75 cm^3, 90%, 1.2 mol) was slowly added to a solution of 99 g $Na_2WO_4 \cdot 2H_2O$ (0.3 mol) in 50 cm^3 H_2O at 45°C and the resulting mixture was refluxed for 5 h, then cooled to room temperature, and diluted with 15 cm^3 H_2O. Powdered KCl (22.5 g, 0.32 mol) was then slowly added to the vigorously stirred solution during 35 min at room temperature. The pale green impure precipitate was filtered off and washed with 0.1 *M* CH_3COOK. The white needle-like crystals of the potassium salt of *Preyssler*'s anion were recrystallized from hot water. The free acid was prepared by passage of a solution of 11.4 g of the potassium salt in 20 cm^3 H_2O through a column (50 × 1 cm) of Dowex®-50W-X8 in the H^+ form. Evaporation of the elute to dryness under vacuum afforded $H_{14}[NaP_5W_{30}O_{110}]$.

Preparation of Wells–Dawson Heteropolyacid $H_6P_2W_{18}O_{62}$

The potassium salt of the *Wells–Dawson* type heteropolyacid $K_6P_2W_{18}O_{62}$ was prepared and then converted to the corresponding acid $H_6P_2W_{18}O_{62}$ by passing it through a Dowex®-50W-X8 ion exchange column. In the final step water was removed under reduced pressure and the remaining solid was collected and dried overnight at 120°C [30].

Preparation of Silica-included 12-Tungstophosphoricacid $H_3PW_{12}O_{40}$-SiO_2

A mixture of 36.2 cm^3 H_2O (2.0 mol), 18.3 cm^3, 1-butanol (0.2 mol), and 0.967 g $H_3PW_{12}O_{40} \cdot 6.7H_2O$ (0.5 mmol) was added to 41.6 g tetraethyl orthosilicate (0.2 mol), and stirred at 80°C for 3 h. The hydrogel obtained was dehydrated slowly at 80°C for 1.5 h *in vacuo* (25 Torr). The dried gel obtained was extracted with water at 80°C for 3 h, and dried at 60°C for 12 h to give 13.5 g silica-included heteropolyacid ($H_3PW_{12}O_{40}$, 11.1 *wt%* estimated by ICP analysis). The silica-included $H_3PW_{12}O_{40}$ was vacuum dried (25 Torr) at 150°C for 3 h prior to use for catalytic reactions.

Preparation of $H_4\,[SiW_{12}O_{40}] \cdot 15H_2O$

To 300 cm^3 2 *M* aqueous solution of Na_2WO_4 was added 240 cm^3 3 *M* aqueous HCl by fraction with vigorous stirring in order to redissolve the local precipitate of tungstic acid. Then 100 cm^3 0.5 *M* aqueous solution of sodium metasilicate was quickly added. A 6 *M* aqueous HCl ($\sim$20 cm^3) solution was added to reach $pH = 5.5$. After standing for 0.5 h, the solution was mixed quickly with another fraction of 6 *M* HCl (totally 60 cm^3 6 *M* HCl added; final $pH \sim 1$). After concentration to about 400 cm^3, the solution was filtered to remove unreacted silica. The *pH* was adjusted to about 2 with aqueous 1 *M* KOH. Addition of 50 g solid KCl induced the precipitation of α-$K_4SiW_{12}O_{40} \cdot 15H_2O$, which was filtered off from warm water and dried in air without preliminary washing (yield: 60% based on W). The obtained precipitate from the saturated aqueous solution of the above compound was acidified to produce crystals of the title compound.

General Procedure for Esterification of Acetic Acid with Ethanol Catalyzed by Heteropolyacids

To a stirred solution of heteropolyacid (0.037 mmol) in 11.4 cm^3 acetic acid (200 mmol), was added 5.9 cm^3 ethanol (100 mmol) and the reaction mixture was allowed to stir at 65–70°C [42] for 40 min. An open container system was used to separate products from the reaction mixture. The produced ester, under reflux, was allowed to pass through a condenser to be liquefied. Continuous isolation of products from the reaction mixture increased efficiency of the esterification method 10-fold. Progress of the reaction was followed by analysis of aliquots withdrawn directly from the resolved products. At the end of the reaction, the reaction mixture was slowly evaporated at 50°C, then the recycled catalyst was washed with CH_2Cl_2, dried at 130°C for 1 h, and re-used in another reaction. The infrared spectrum of the catalyst did not show any significant structural changes and the recycled catalyst could be used several times without any appreciable loss of catalytic activity.

References

[1] Greene TW, Wuts PGM (1999) Protective Groups in Organic Synthesis, 3rd edn, Wiley, New York

[2] Chakraborti AK, Nayak MK, Sharma L (2002) J Org Chem **67**: 1776

[3] Chakraborti AK, Sharma L, Sharma U (2001) Tetrahedron **57**: 9343

[4] Vogel A (1996) Textbook of Practical Organic Chemistry, 5th edn, Longman Group Ltd, London

[5] Wright SW, Hageman DL, Wright AS, Mc Clure LD (1997) Tetrahedron Lett **38**: 7345

[6] Brewster JH, Ciotti CJ (1955) J Am Chem Soc **77**: 6214

[7] Marshall JL, Erickson KC, Folsom TK (1970) Tetrahedron Lett **11**: 4011

[8] Otera J, Danoh N, Nozaki H (1991) J Org Chem **56**: 5307

[9] Ishihara K, Ohara S, Yamamoto H (1990) Science **290**: 1140

[10] Zhao ZH (2000) J Mol Catal A Chem **154**: 131

[11] Blossey EC, Turuer LM, Neckers DC (1973) Tetrahedron Lett **14**: 1823

[12] Bertin J, Kagan HB, Luche JL (1974) J Am Chem Soc **96**: 8113

[13] Kumar AK (1987) Tetrahedron Lett **28**: 3713

[14] Yadav GD, Mehta PH (1994) Ind Eng Chem Res **33**: 2198

[15] Saha B, Chopade SP, Mahajani SM (2000) Catal Today **60**: 147

[16] Ishihara K, Kuboto M, Kurihara H, Yamamoto H (1995) J Am Chem Soc **117**: 4413

[17] Procopiou PA, Baugh SPD, Flask SS, Ingliss GGA (1998) J Org Chem **63**: 2342

[18] Sarvanan P, Singh VK (1999) Tetrahedron Lett **40**: 2611

[19] Chandrasekhar S, Ramchander T, Takhi M (1998) Tetrahedron Lett **39**: 3263

[20] Iqbal J, Srivastava RR (1992) J Org Chem **57**: 2001

[21] Ringold HJ, Loeken B, Rosenkranz G (1956) J Am Chem Soc **78**: 816

[22] Maki-Arfela M, Salmi T, Sundell M, Ekman K, Peltonen R, Lehtonen J (1999) Appl Catal A Gen **184**: 25

[23] Arata K, Hino M (1998) Appl Catal A Gen **173**: 121

[24] Heidekum A, Harmer MA, Hoelderich WF (1999) J Catal **181**: 217

[25] Tiofeeva MN, Dimidov AV, Kozhevnikov IV (1979) J Mol Catal **179**: 21

[26] Drago RS, Dias JA, Maier T (1997) J Am Chem Soc **119**: 7702

[27] Mizuno N, Misono M (1998) Chem Rev **98**: 199

[28] Hill CL, Prosser-McCartha GM (1995) Coordn Chem Rev **143**: 407

[29] Arabi M, Mohammadpour Amini M, Abedini M, Nemati A, Alizadeh M (2003) J Mol Catal A Chem **200**: 105
[30] Hu C, Hashimoto M, Okuhara T, Misono M (1993) J Catal **143**: 437
[31] Zhao ZH (2001) J Mol Catal A Chem **168**: 147
[32] Izumi Y, Urabe K, Onaka M (1992) Zeolite, Clay and Heteropoly Acids in Organic Reactions, Kodansha/VCH, Tokyo
[33] Nishimura T, Okuhara T, Misono M (1991) Appl Catal **73**: L7–L11
[34] Alizadeh MH, Tayebee R (2005) J Braz Chem Soc **16**: 108
[35] Alizadeh MH, Holman KT, Mirzaei M, Razavi H (2006) Polyhedron **25**: 1567
[36] Alizadeh MH, Razavi H, Bamoharram FF, Hassanzadeh MK, Khoshnavazi R, Zonoz FM (2003) Kinet Catal **44**: 524
[37] Alizadeh MH, Razavi H, Zonoz FM, Mohammadi MR (2003) Polyhedron **22**: 933
[38] Alizadeh MH, Harmalker SP, Jeanin Y, Pope MT (1985) J Am Chem Soc **107**: 2662
[39] North EO (1993) Inorg Synth **1**: 129
[40] Wu HJ (1920) Biol Chem **43**: 189
[41] Brevard C, Schimpf R, Tourne G, Tourne CM (1983) J Am Chem Soc **105**: 7059
[42] Methanol and 1-butanol were refluxed at 55–60 and 85–90°C