

Effect of Protecting Agent Concentration, Catalyst (mol %) and Temperature on the Protection of 2-Propanol Catalyzed by Dodeca-Tungstophosphoric Acid

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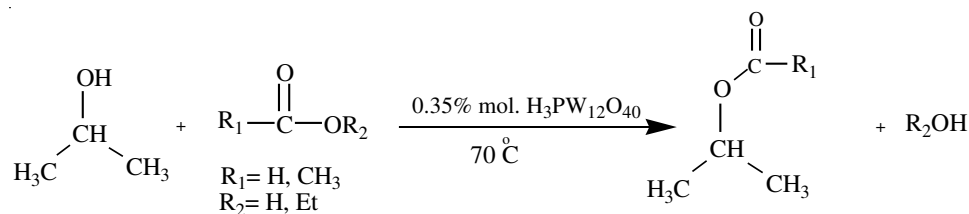
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Protection of various alcohols with carboxylic acids catalyzed by heteropolyacids is realized as an efficient method among different familiar reaction pathways. Herein, effective reaction parameters such as temperature, alcohol:protecting agent mole ratio and catalyst (mol %) were investigated on the acetylation and formylation of 2-propanol with acetic acid, formic acid and ethyl formate, as acetylating agents, in the presence of dodeca-tungstophosphoric acid, $H_3PW_{12}O_{40}$. Findings showed that efficiency of the protection system was increased by enhancing temperature, using higher amounts of catalyst and increasing concentration of the protecting agent. Obviously, enhancing concentration of the protecting agent was more effective than elevation of temperature on the reaction progress.

Key Words: Acetylation, Formylation, Dodeca-tungstophosphoric acid, Reaction parameters, 2-Propanol.

INTRODUCTION

Organic esters are important family of intermediates which are widely employed in the synthesis of industrial chemicals, drugs, cosmetics and food additives. There are a number of procedures for the protection of alcohols in organic synthesis in the presence of stoichiometric or catalytic amounts of amine bases or Lewis acids¹⁻⁶. Considering various limitations in using familiar acetylating agents such as acid anhydrides or acetyl chlorides, heteropolyacids are good choices as Lewis acids catalyzing acetylation of alcohols with mild acetylating reagents under mild and simple reaction conditions^{7,8}. Previously, we described efficiency of heteropoly-oxometalates as catalyst in the acetylation reactions of alcohols with carboxylic acids, acetates and formates⁹⁻¹¹. Herein, we wish to present our findings on the role of some effective reaction parameters such as mole ratio of the protecting agent (acetic acid, formic acid and ethyl formate), raising reaction temperature and catalyst concentration (mol %) on the protection of 2-propanol in the presence of dodeca-tungstophosphoric acid, as catalyst (**Scheme-I**).



Scheme-I

EXPERIMENTAL

2-Propanol, glacial acetic acid, formic acid, ethyl formate and other solvents were commercially available and their purity was monitored by gas chromatography or by TLC. 2-Propyl acetate and 2-propyl formate were characterized by comparing their spectral and physical data with those of known samples. Progress of the reactions was monitored by gas chromatography. GLC analyses were performed on a Shimadzu GC-17A instrument equipped with a flame ionization detector using 25 m \times 0.25 mm CPB (5-20) capillary columns packed with fused silica. $\text{H}_3\text{PW}_{12}\text{O}_{40}$ was purchased commercially.

General experimental procedure for the acetylation of 2-propanol with glacial acetic acid catalyzed by $\text{H}_3\text{PW}_{12}\text{O}_{40}$: In a round-bottom flask (10 mL) equipped with a magnetic stirrer, $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (0.035 mmol, 0.35 mol %) was dissolved in glacial acetic acid (50 mmol). Then 2-propanol (10 mmol) was added to the stirred solution and the reaction mixture was heated to 70 °C for the required time. The reaction progress was monitored by gas chromatography. After completion of the reaction, acetic acid was removed under reduced pressure and 20 mL of ether was added. The reaction mixture was washed with 5 % NaHCO_3 solution, then with H_2O and dried with MgSO_4 . Evaporation of the solvent followed by silica-gel chromatography provided the pure acetate.

Spectral data of iso-propyl acetate and iso-propyl formate

Iso-propyl acetate: A colourless liquid with a strong fruity odour.; b.p. 2 °C; IR (liquid film) cm^{-1} : 2984-2884 (C-H), 1754 (C=O), 1470-1250 (C-O); ^1H NMR (CDCl_3 , 100 MHz): δ 1.22-1.026 (d, 6H), δ 1.95-2.05 (s, 3H), δ 4.70-5.30 (m, 1H).

Iso-propyl formate: IR (liquid film) cm^{-1} : 2980-2930 (C-H), 1720 (C=O), 1390-1100 (C-O); ^1H NMR (CDCl_3 , 100 MHz): δ 1.35 (d, 6H), δ 5.10-5.30 (m, 1H), δ 8.05 (s, 1H).

RESULTS AND DISCUSSION

Developing efficient and mild protocols for the protection of hydroxyl functional groups is of importance in synthetic organic chemistry. One of the most common methods for the protection of alcohols is the formation of acetyl derivatives¹². In recent years there has been a tremendous upsurge of interest in various chemical transformations performed using heteropolyacid catalysts. Moreover, by using these

inexpensive and none corrosive catalysts, chemical transformations occur with better efficiency, higher purity of products and easier work-up, with evident economic and ecological advantages especially for industrial processes.

2-Propanol was used as the selected substrate for studying acetylation reactions to produce iso-propyl acetate. This important compound with mild odour is a fast evaporating solvent and behaves as a non-hazardous air pollutant, good resin solvent and has a wide variety of manufacturing uses. This solvent is miscible with most other organic solvents and moderately soluble in water. It is used as a solvent for cellulose, plastics, oil and fats. It is a component of some printing inks and perfumes. Nowadays, over three fourths of iso-propyl acetate is used in gravure printing inks for plastic films such as bread wrap and the rest finds many uses in coatings, perfumes and adhesives.

First of all, we studied effect of increasing temperature on the acetylation of 2-propanol with glacial acetic acid catalyzed by $H_3PW_{12}O_{40}$ at 25, 40, 70 and 90 °C (Table-1, Fig. 1). Results showed that the reaction progress was improved and the ester yield % was distinctly increased with enhancing temperature from 25 to 90 °C. 2-Propanol produced only 3 % of the corresponding ester at 25 °C after 25 min (entry 1); whereas, the ester yield % was exceeded to 40 and 70 % at 70 and 90 °C, respectively, during the same time (entries 3 and 4). Comparing the obtained results at different temperatures clearly revealed that enhancing temperature, at least to 40 °C, is a necessity to obtain good conversions at short reaction times. Moreover, no important by-products were found at elevated temperatures and selectivity was *ca.* 100 % in all cases.

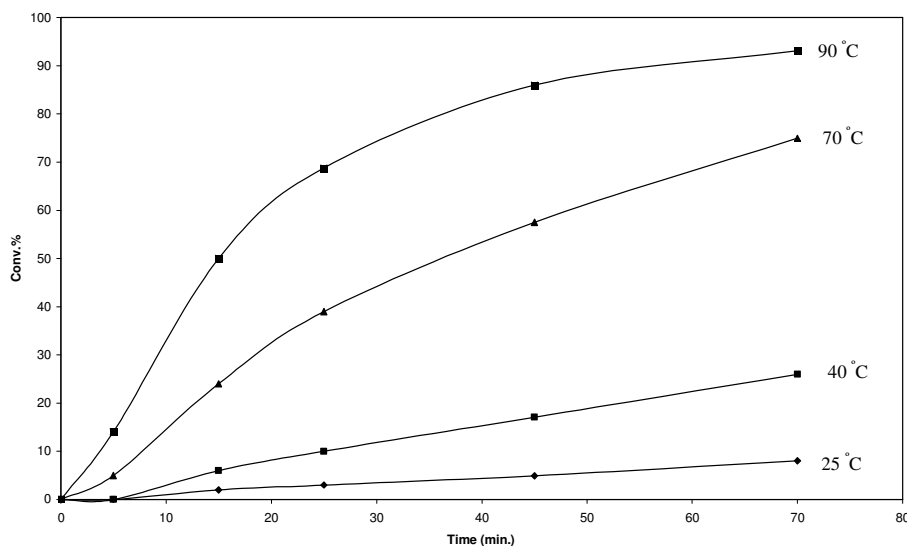


Fig. 1. Protection of 2-propanol with acetic acid at different temperatures catalyzed by $H_3PW_{12}O_{40}$

TABLE-1
EFFECT OF TEMPERATURE ON THE PROTECTION OF 2-PROPANOL WITH
ACETIC ACID CATALYZED BY $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (0.35 mol %)^a

Entry	Temp. (°C)	Yield (%) after 25 min	Yield (%) after 70 min	Selectivity (%)	TOF ^b short (long) time
1	25	3	8	100	205 (196)
2	40	10	26	100	685 (636)
3	70	39	75	98	2674 (1836)
4	90	70	93	98	4800 (2277)

^a $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (0.035 mmol) was dissolved in a solution of glacial acetic acid (50 mmol) and 2-propanol (10 mmol) and the reaction mixture was heated. iso-Propyl acetate was characterized by comparison of its IR and ¹H-NMR spectra with authentic sample.

^bTurnover frequency (TOF) was calculated by the expression [product]/[catalyst] × time (h⁻¹).

Since, protection of alcohols with protecting agents introduced in this report was reversible, mole ratio of protecting agent:alcohol higher than 1 was used to achieve good conversions. To study effect of increasing mole ratio of 2-propanol: glacial acetic acid on the reaction progress, the mentioned ratio was increased from 1:1 to 1:5 (Table-2, Fig. 2). It was found that conversion of alcohol grew with enhancing concentration of carboxylic acid. 42 % of ester product was obtained for 1:1 mole ratio after 70 min (entry 5); whereas, the corresponding conversion % was increased to 76 % for 1:5 mole ratio of alcohol: acid after the same time (entry 8).

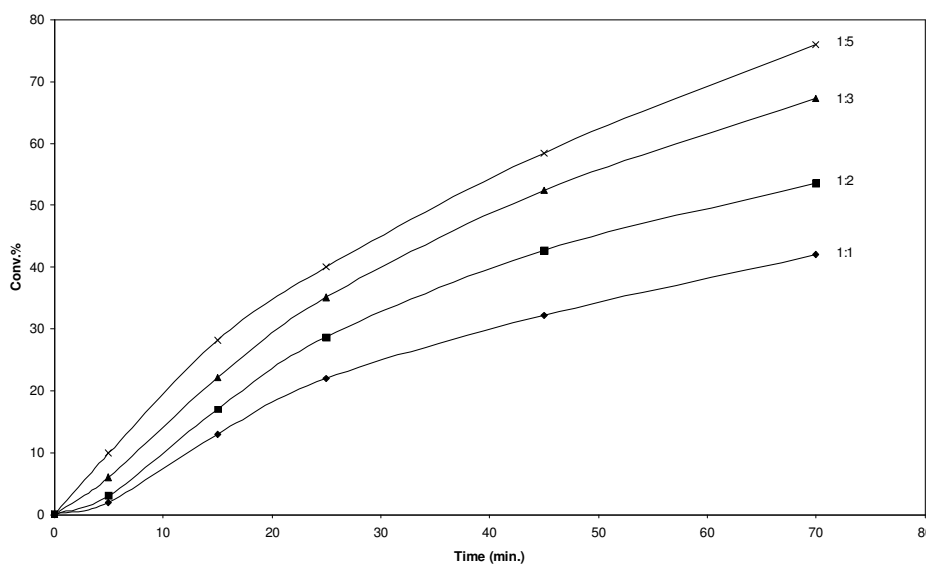


Fig. 2. Effect of 2-propanol:glacial acetic acid mole ratio on the protection reaction in the presence of 0.35 mol % $\text{H}_3\text{PW}_{12}\text{O}_{40}$

TABLE-2
EFFECT OF 2-PROPANOL:GLACIAL ACETIC ACID MOLE RATIO ON THE PROTECTION REACTION IN THE PRESENCE OF 0.35 mol % $H_3PW_{12}O_{40}$

Entry	[Alcohol]:[Acid]	Yield (%) after 25 min	Yield (%) after 70 min	TOF short (long) time
5	1:1	22	42	1508 (1028)
6	1:2	29	54	1988 (1322)
7	1:3	35	67	2400 (1640)
8	1:5	40	76	2742 (1861)

The reactions were carried out at 70 °C as described below Table-1.

As previously described⁷⁻¹⁰, different carboxylic acids, alkyl carboxylates and alkyl formates, may be used in the protection of alcohols under the reaction conditions reported here. To obtain a deeper insights on the role of concentration and kind of the protecting agents, formylation of 2-propanol (10 mmol) was carried out with 1:1 and 1:5 molar ratio of alcohol: formic acid in the presence of a catalytic amount of $H_3PW_{12}O_{40}$ (0.035 mmol) at 25 and 70 °C (Table-3, Fig. 3).

TABLE-3
PROTECTION OF 2-PROPANOL WITH FORMIC ACID (1:1 AND 1:5 MOLE RATIO OF ALCOHOL:ACID) CATALYZED BY $H_3PW_{12}O_{40}$ (0.35 mol %) AT 25 AND 70 °C

Entry	Alcohol:Formic acid (mole ratio)	Temp. (°C)	Yield (%) after 10 min	Yield (%) after 45 min	TOF short (long) time
8	1:1	25	33	53	5656 (2019)
9	1:5	25	74	90	12685 (3428)
10	1:1	70	63	85	10800 (3238)
11	1:5	70	90	95	15428 (3618)

The reactions were carried out as described below Table-1.

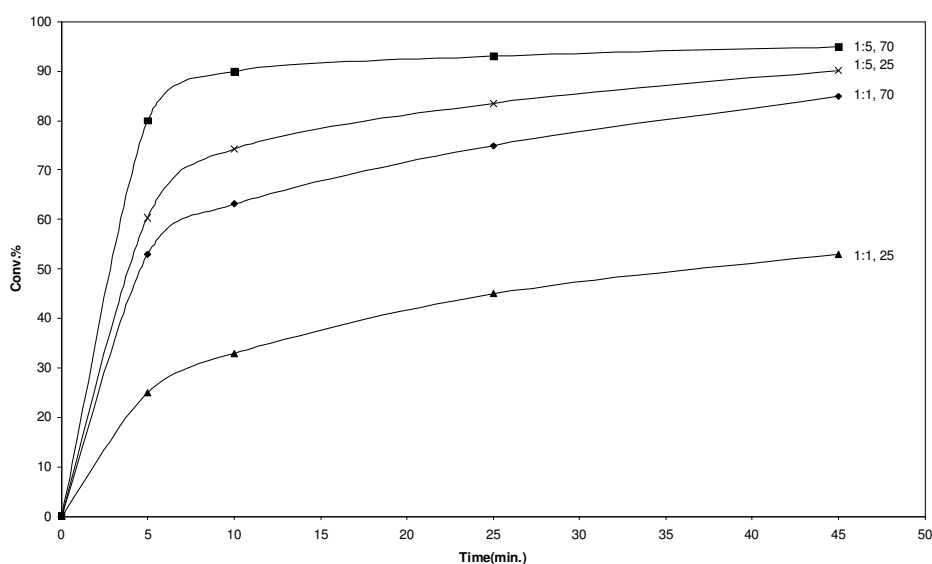


Fig. 3. Protection of 2-propanol with formic acid (1:1 and 1:5 mole ratio of alcohol:acid) catalyzed by $H_3PW_{12}O_{40}$ (0.35 mol %) at 25 and 70 °C

It is observed that the conversions were increased sharply by increase of temperature from 25 to 70 °C and/or by five-fold enhancing concentration of acid. 2-Propanol led to a maximum of 53 % conversion under 1:1 mole ratio of alcohol: acid at 25 °C after 45 min (entry 8); whereas, five-fold increase in acid concentration led to 90 % of conversion under similar reaction conditions (entry 9). Moreover, increasing reaction temperature from 25 to 70 °C affected the reaction progress for both mole ratios. 2-Propanol produced 85 % of conversion with 1:1 mole ratio of alcohol:acid at 70 °C after 45 min (entry 10). The best results were achieved at 1:5 mole ratio at 70 °C and 2-propanol produced > 90 % of conversion after 10 min. Results obtained for 2-propanol clearly showed that formylation of OH group was developed by increasing concentration of formic acid or by accretion of the reaction temperature¹². As an interesting result based on Fig. 3, it seems that enhancing acid concentration was clearly more effective than increase of temperature on the reaction progress.

Formylation of 10 mmol of 2-propanol with 10 and 50 mmols of ethyl formate was also studied in the presence of 0.035 mmol of H₃PW₁₂O₄₀ at 25 and 70 °C (Table-4, Fig. 4). According to the obtained results and our previous findings⁹⁻¹¹, formic acid was more pronounced formylating agent than ethyl formate. 1:1 mole ratio of 2-propanol:formylating agent led to 53 % of conversion for formic acid at room temperature after 45 min (entry 8); whereas, ethyl formate resulted in 38 % of product under similar reaction conditions (entry 12). As mentioned for formic acid, product yield was increased with enhancing concentration of ethyl formate and with elevation of temperature. 1:1 mole ratio of alcohol: formate led to 38 % of conversion after 45 min at room temperature; whereas, 80 % of product achieved at 70 °C at the same time (entry 14). Increasing concentration of formate along with elevation of temperature (1:5 mole ratio at 70 °C) led to the best results. 2-Propanol led to 68 % of conversion at 25 °C with 1:5 mole ratio after 45 min (entry 13); whereas, 95 % of conversion was achieved with this ratio at 70 °C at the same time (entry 15). Analogous to formic acid, it seems that elevation of temperature was more effective than increasing concentration of ethyl formate on the reaction progress. Five-fold increase in concentration of formate led to an increase in the product yield from 38 % to *ca.* 70 % at 25 °C after 45 min; whereas, elevation of temperature (25 to 70 °C) for 1:1 mole ratio, led to > 40 % increase in the conversion % at the same time.

TABLE-4
PROTECTION OF 2-PROPANOL WITH ETHYL FORMATE (1:1 AND 1:5 MOLE RATIO OF ALCOHOL:FORMATE) CATALYZED BY H₃PW₁₂O₄₀ (0.35 mol %) AT 25 AND 70 °C

Entry	Alcohol:Ethyl formate (mole ratio)	Temp. (°C)	Yield (%) after 10 min	Yield (%) after 45 min	TOF short (long) time
12	1:1	25	12	38	2057 (1447)
13	1:5	25	23	68	3942 (2590)
14	1:1	70	49	80	8400 (3047)
15	1:5	70	74	95	12685 (3618)

The reactions were carried out as described below Table-1.

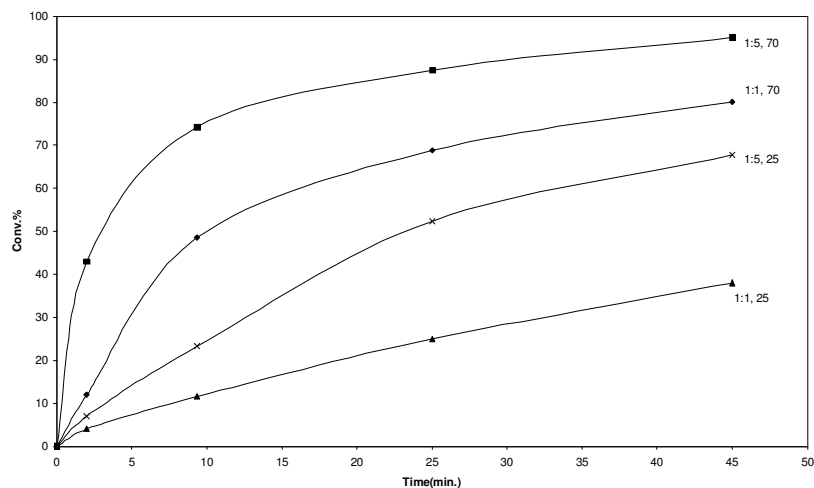


Fig. 4. Protection of 2-propanol with ethyl formate (1:1 and 1:5 mole ratio of alcohol: formate) catalyzed by $H_3PW_{12}O_{40}$ (0.35 mol %) at 25 and 70 °C

Effect of $H_3PW_{12}O_{40}$ (mol %) was investigated on the protection of 2-propanol with glacial acetic acid under 5:1 mole ratio of acid : alcohol at 70 °C. < 15 % of conversion was obtained in the absence of catalyst after prolonged reaction time; whereas, conversions % were increased with enhancing catalyst concentration (Fig. 5). Addition of 0.17 mol % catalyst led to 47 % of ester product after 70 min. Acceptable results were obtained at 0.35 mol % of catalyst and 2-propanol produced 75 % of conversion after 70 min. More increase in catalyst concentration (0.7 mol %) resulted in the best results and produced 90 % of conversion after 70 min. However, Fig. 5 shows that higher concentration of catalyst (1 mol %) led to similar conversions obtained for 0.7 mol % catalyst.

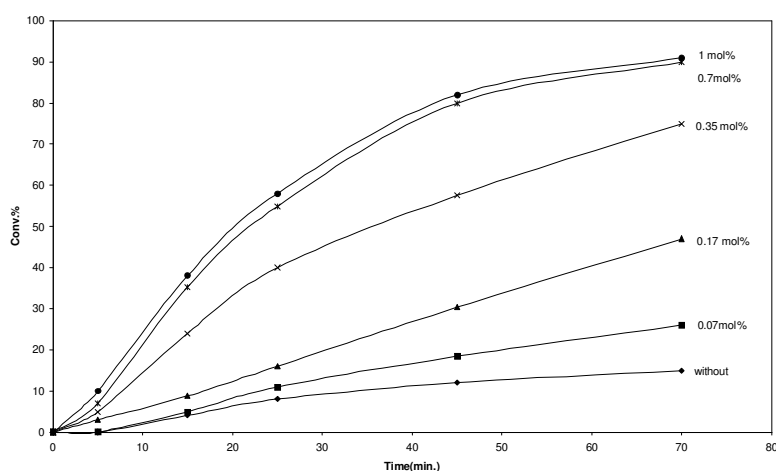


Fig. 5. Effect of catalyst ($H_3PW_{12}O_{40}$, mol %) on the protection of 2-propanol with glacial acetic acid

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