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Catalytic Synthesis of Ethyl β-arylamino Crotonates and 2-methyl-4-quinolone using Preyssler Heteropolyacid, $H_{14}[NaP_5W_{30}O_{110}]$ and its supported as Catalysts

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Abstract: A variety of aromatic anilines react with methyl acetoacetate in the presence of catalytic amount of Preyssler's and molybdenum substituted Preyssler heteropolyacid, $H_{14}[NaP_5W_{30}O_{110}]$, $H_{14}[NaP_5W_{29}MoO_{110}]$ and silica supported Preyssler, $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$, to afford the corresponding ethyl β-arylamino crotonates, in excellent yields. The catalyst can be recovered and reused. Synthesis of 4-quinolones from the cyclization of ethyl β-arylamino crotonates in the presence of diphenyl ether under reflux conditions is reported.

Keyword: ethyl β-arylamino crotonates, 4-quinolone, Preyssler, heteropolyacid, catalyst

1. Introduction

Heteropolyacids (HPAs) are good catalysts for both acid and oxidation reactions. The wide range of their uses is explained by a number of thorough reviews [1]. The HPAs can be tuned to meet the needs of a given chemistry by changing the constituent elements [2]. For example, heteropolyacids containing tungsten are good acid catalysts while those containing molybdenum are good oxidation catalysts. Heteropoly compounds are effective catalysts for various reactions and have high capability in practical uses, because their redox and acidic properties can be controlled at the atomic/molecular levels by changing the constituent elements as per the needs of the chemical process [3]. The catalytic function of heteropolyacids (HPAs) and related polyoxometallate compounds has attracted much attention particularly in the last two decades. It is a field of increasing importance in which new and promising developments are being carried out both at research and technological level [4, 5]. HPAs are widely used as model systems for fundamental research. The use of heteropolyacids, HPAs, has recently received considerable attention as nontoxic, ecofriendly and environmentally benign catalysts for various organic transformations to afford the corresponding products in good yield. Due to the numerous advantages associated with have been explored as powerful, efficient and ecofriendly catalysts in organic reactions [6-10].

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The catalysts based on heteropolyacids with keggin structure and related compounds are less corrosive and produce lower amount of wastes than conventional acid catalysts, so they can be used as replacement in eco-friendly processes. β-Arylaminocrotonates gain long-standing interests for their potential as important intermediates for the synthesis of 2, 4-disubstituted quinoline and related natural products [11]. Many efforts have been directed to improve the yield and rate of the reaction and recent modifications were mainly focused on the usage of effective catalysts, such as BF_3 [12], K-10 montomorilla [13] and lanthanide[11]. The Conrad-Limpach reaction between anilines and a β-ketoester is a general method to synthesize 4-quinolones [13]. β-arylaminocrotonates have also been synthesized through the reaction of aromatic amines with methyl acetoacetate [14]. On the other hand, 4-quinolones are important compounds and valuable synthetic intermediates for derivatives that have biological activities belonging to various types, e.g. tuberculostatic [15]. Some of 4-quinolones are used as antibacterials, e.g. ciprofloxacin and 6-fluoroquinolones [15]. Herein, we would like to report an efficient procedure for the preparation of β-arylaminocrotonates using heteropolyacids as catalyst. These compounds cyclized to 4-quinolones by heating in the solution of diphenyl ether.

2. Experimental

2.1. Instruments and chemical

^{1}H-NMR spectra were recorded on an FT-NMR Bruker 100 MHz Aspect 3000 spectrometer. IR spectra were obtained with a Bucker 500 scientific spectrometer (KBr pellets). Melting points were recorded on an Electrothermal type 9100 melting point apparatus and are uncorrected. All chemical compounds were purchased from Merck and used without further purification.

2.2. Catalyst Preparation

H_{14}-P_5 was prepared by passage of a solution of the potassium salt in water through a column (50 cm×1 cm) of Dowex50W×8 in the H^+ form and evaporation of the eluate to dryness under vacuum [16]. $H_{14}[NaP_5W_{30}O_{110}]$ and $H_{14}P_5/SiO_2$ were prepared according to earlier reports [16, 17] and $H_4[PMo_{11}VO_{40}]$ and $H_5[PMo_{10}V_2O_{40}]$, Wells-Dawson, ($H_6[P_2W_{18}O_{62}]$), $H_7[PMo_8V_4O_{40}]$ were prepared according to the literature [18-20].

2.3. General procedure for the synthesis of ethyl β-arylaminocrotonates (3a-g)

A mixture of aniline (1 mmol), ethyl acetoacetate (1 mmol) and toluene (2 mL)as solvent and fresh heteropolyacid catalyst (0.05 mmol) was stirred and refluxed for 2 hours. The progress of the reaction was checked by TLC. The reaction mixture was filtered and dried

with anhydrous Na_2SO_4. Evaporation of the solvent followed by flash chromatography on silica afforded the pure ethyl β-arylaminocrotonates,

3a. 80% yield, M.p.: 140-143°C, Lit(141); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.24 (t, 3H, J=7Hz) 1.95 (s, 3H) 4.10 (q, 2H, J=7Hz) 4.62 (s, 1H) 7.16 (m, 5H) 10.37 (s, 1H) ; IR (KBr): $\overline{V}$ = 3259 (NH), 2979 (aromatic), 1657(CO).

3b. 73% yield, M.p.: 54-55°C Lit(55); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.23 (t, 3H, J=7Hz) 2.05 (s, 3H) 4.16 (q, 2H, J=7Hz) 4.67 (s, 1H) 7.18 (m, 4H) 10.20 (s, 1H) ; IR (KBr): $\overline{V}$ =3367 (NH), 2980 (aromatic), 1740 (CO), 1664 (CO).

3c. 69% yield, M.p.: 146-147°C Lit(145-146); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.29 (t, 3H, J=7Hz) 2.06 (s, 3H) 4.17 (q, 2H, J=7Hz) 4.76 (s, 1H) 7.12 (m, 4H) 10.39 (s, 1H) ; IR (KBr): $\overline{V}$ =3365 (NH), 2985(aromatic), 1820(CO), 1680 (CO).

3d. 87% yield, M.p.: 44-46°C Lit(45-46); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.29 (t, 3H, J=7Hz) 1.84 (s, 3H) 3.76 (s, 3H) 4.11 (q, 2H, J=7Hz) 4.65 (s, 1H) 6.94 (m, 4H) 10.18 (s, 1H) ; IR (KBr): $\overline{V}$ =3349 (NH), 2925 (aromatic), 1790(CO), 1680 (CO).

3e. 95% yield, M.p.: 85-87°C Lit(85-86); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.24 (t, 3H, J=7Hz) 1.83 (s, 3H) 4.14 (m, 4H) 4.72 (s, 1H) 6.82 (m, 4H), 9.69 (s, 1H) ; IR (KBr): $\overline{V}$ =3256 (NH), 2974 (aromatic),1651 (CO).

3f. 90.5% yield, M.p.: 146-148°C Lit(146-147); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.28 (t, 3H, J=7Hz) 1.97 (s, 3H) 2.35 (s, 3H) 4.14 (q, 2H, J=7Hz) 4.69 (s, 1H) 7.06 (m, 4H) 10.28 (s, 1H) ; IR (KBr): $\overline{V}$ =3257 (NH), 2977 (aromatic),1652 (CO).

3g. 84% yield, M.p.: 145-146°C Lit(144-145.5); ^{1}H NMR (100 MHz, CDCl$_3$): δ=1.29 (t, 3H, J=7Hz) 1.82 (s, 3H) 2.29 (s, 3H) 4.14 (q, 2H, J=7Hz) 4.66 (s, 1H) 7.11 (m, 4H) 10.16 (s, 1H) ; IR (KBr): $\overline{V}$ =3258 (NH), 2973 (aromatic),1655 (CO).

2.4. General procedure for the synthesis of 2-methyl-4-quinolone (4a)

A mixture of ethyl β-arylaminocrotonates (Scheme 1, **3a**) (1 mmol) and diphenyl ether (1mL) was refluxed at 250°C for 30 min, after which the flask was cooled at room temperature. The purification was obtained by column chromatography and gave pure 2-methyl-4-quinolone **4a** with 91% yield (Scheme 1, 2, **4a**). Compound of 2-methyl-4-quinolone (**4a**) is confirmed by ^{1}HNMR, IR.
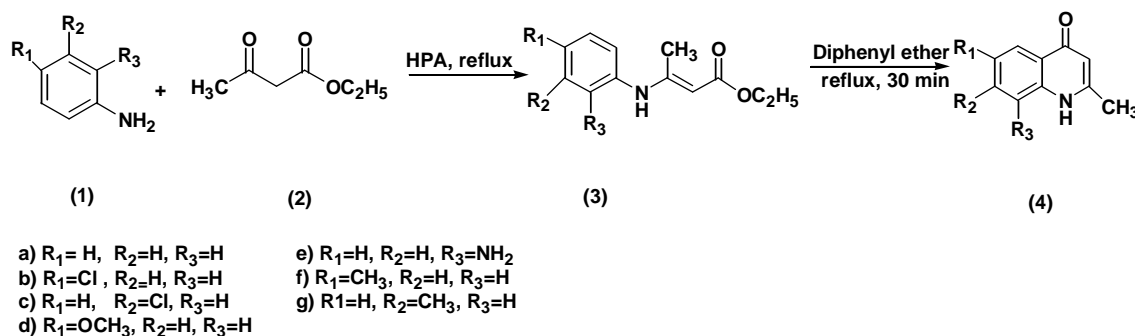
^{1}H NMR (100 MHz, CDCl$_3$): δ=9.32 (s, 1H, NH), 8.06 (d, J = 7.2 Hz, 2H, aromatic), 7.35 (t, J = 7.2 Hz, 2H, aromatic), 7.14 (t, J = 7.2 Hz, 1H, CH), 4.15 (s, 2H, CH2) ; IR (KBr): $\overline{V}$ =3305 (NH), 2983 (aromatic),1680 (CO).

2.5. Reusability of the catalyst

At the end of the reaction, the catalyst was filtered, washed with diethyl ether, dried at $130^{o}C$ for 1 h, and re-used in another reaction. The recycled catalyst was used for three reactions without observation of appreciable lost in its catalytic activities. Our studies have also shown that the Preyssler catalyst can catalyze oxidations of amines with retention of structure, which is very important in catalytic processes, specially, in industry.

This behavior is accordance to earlier works [16,21]. Several times recovery has decreased the catalytic activity only 1-2% (Table 1).

3. Results and Discussion

Synthesis of ethyl β-arylaminocrotonates was carried out using heteropolyacids (HPAs) in reflux conditions (Scheme 1).

(1)   (2)   (3)   (4)

a) R_1= H, R_2=H, R_3=H   e) R_1=H, R_2=H, R_3=NH$_2$
b) R_1=Cl , R_2=H, R_3=H   f) R_1=CH$_3$, R_2=H, R_3=H
c) R_1=H, R_2=Cl, R_3=H   g) $R1$=H, R_2=CH$_3$, R_3=H
d) R_1=OCH$_3$, R_2=H, R_3=H

In the past two decades, the broad utility of heteropolyacids, HPAs, as acid and oxidative catalysts in solution as well as in the solid state for various industrial processes has been demonstrated for a wide variety of synthetically useful transformation of organic substrates [22,23]. Due to their acidic and redox properties heteropoly compounds (heteropoly acids and their salts) are useful and versatile catalysts in a number of transformations [24]. Since they exhibit weak super acidic properties they can be used in reactions requiring electrophilic catalysts. They have also been proven to be equally good catalysts in various oxidations. These solid acids are applied in bulk or supported forms, and both homogeneous and heterogeneous catalysis are possible [26]. It has been reported that these atalysts are recyclable [25].

In the synthesis of ethyl β-arylaminocrotonates derivatives, the influence of substituent groups over the reaction yield was studied. In our studies, we investigated the activity of various Preyssler forms such as, pure Preyssler and supported Preyssler over silica with different laodings and various heteropolyacids. Representative results in Table 1 are shown.

Table 1. Catalytic effect of various heteropolyacids for the reaction of aniline with ethyl acetoacetate under reflux temperature for 2 hr

Entry	HPAs Catalyst	[a]Yield % (4a)
1	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (50%)	70(70,70,69)[b]
2	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (40%)	65.5
3	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (30%)	59
4	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (20%)	48
5	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$ (10%)	39
6	$H_6[P_2W_{18}O_{62}]$	69(69,69,68)[b]
7	$H_7[PMo_8V_4O_{40}]$	70(70,70,69)[b]
8	$H_6[P_2W_{18}O_{62}]$	68
9	$H_5[PMo_{10}V_2O_{40}]$	64
10	$H_4[PMo_{11}V_1O_{40}]$	61.5
11	$H_3[PW_{12}O_{40}]$	67(67,66,66)[b]

[a] Yields were isolated. Solvent was toluene. [b] In parentheses, yields obtained in the first, second and third reuse of the catalyst.

The results indicate that the nature of the catalyst plays an important role on their catalytic activities. The highest yield of (80%) products has been acieved in the presence of H_{14}-P_5 as catalyst, and H_{14}-P_5/SiO_2 (10%) gave the lowest yields. The yields are shown in Table 1.
In order to obtain the best reaction time, the effect of reaction time on the % yield of major product was studied. The optimum reaction time has been found to be 2 hours in reflux conditions (Table 2). The reaction was not progressed at room temperature.
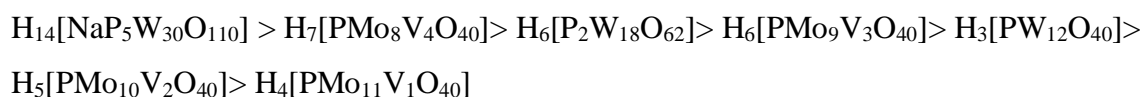
Table 2. Effect of reflux time for the reaction of aniline with ethyl acetoacetate using preyssler heteropolyacid as catalyst ($H_{14}[NaP_5W_{30}O_{110}]$)

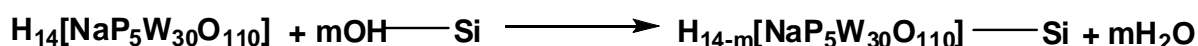| Time (h)	1	2	3	4
Yield (4a)%	37	80	80	80

[a] Yields were isolated.

We found that the substrate having either electron donating (3d, 3g) or electron-withdrawing groups on (3b, 3c) on the aromatic ring reacted (Table 1). It is noteworthy to metinon that the catalyst is recyclable and could be reused without significant loss of activity.

The effects of various substituents on the yield of the products have been examined in the presence of Preyssler catalyst. The data (3a-3g) compounds indicates that while substrates with electron-donating substituents are converted to the corresponding ethyl β-arylaminocrotonates with good yields, low yields are observed for the synthesis of ethyl β-arylaminocrotonates substituted. The results show that both the nature of the substituent is important. Electron-donating substituents result in higher yields than electron-withdrawing substituents. In order to compare heteropolyacids type catalyst with Preyssler's catalyst in the synthesis of ethyl β-arylaminocrotonates, we selected the vanadium substituted heteropolyacids including $H_{3+x}PMo_{12-x}V_xO_{40}$ ($x = 1$–4), the wells-Dawson, $H_6[P_2W_{18}O_{62}]$. The results are shown in Table 1. The yield of β-arylaminocrotonates decreases in the following order:

$H_{14}[NaP_5W_{30}O_{110}]$ > $H_7[PMo_8V_4O_{40}]$> $H_6[P_2W_{18}O_{62}]$> $H_6[PMo_9V_3O_{40}]$> $H_3[PW_{12}O_{40}]$> $H_5[PMo_{10}V_2O_{40}]$> $H_4[PMo_{11}V_1O_{40}]$

Supported Preyssler over silica with different loadings from 10% to 50% were checked, the results showed in the following order: 10%< 20%< 30< 40 <50%, and supported Preyssler with loading 10% gave low yield. Because, the silan hydroxyl groups are involved with the acidic protons of Preyssler catalyst, and acidic strong is decreased (Figure 1, Equation 1).

$$H_{14}[NaP_5W_{30}O_{110}]\ +\ mOH\text{—}Si\ \longrightarrow\ H_{14-m}[NaP_5W_{30}O_{110}]\text{——}Si\ +\ mH_2O$$

Equation1. Interaction between of the acidic protons and HPAs with hydroxyl silanol groups

a)   **b)**   **c)**
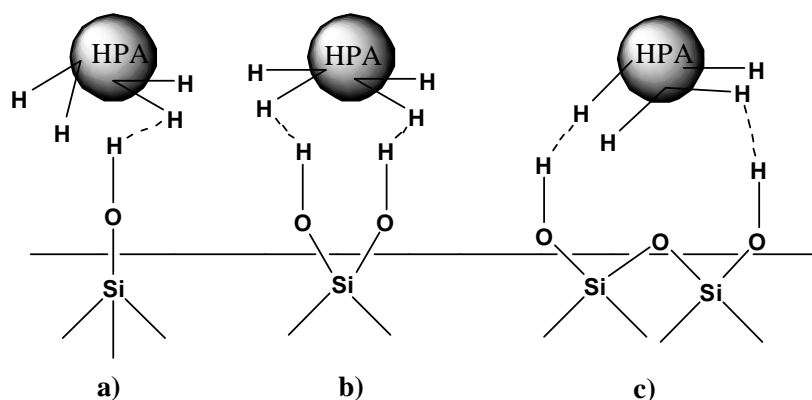
Surface active sites at the silica surface; a) isolated silanol group, b) geminal silanol groups, and c) siloxane bridge and interaction of OH groups SiO$_2$ with heteropolyacids acidic Proton

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Figure 1. Model form Keggin anion interaction acidic protons of HPAs with hydroxyl silanol groups

A mechanism was proposed in the synthesis of ethyl β-arylaminocrotonates (Scheme 2).
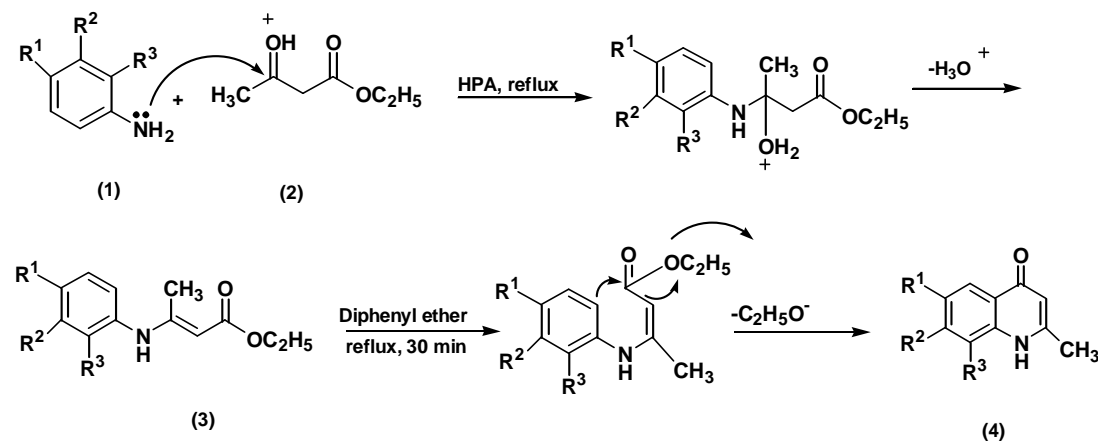
Scheme 2. Mechanism of in the synthesis of ethyl β-arylaminocrotonates and quinolones

4. Conclusion

In conclusion, heteropolyacids are effective solid acid catalysts for the synthesis of ethyl β-arylaminocrotonates. Among various heteropolyacids used for the synthesis of ethyl β-arylaminocrotonates, the Preyssler type heteropolyacid showed higher activity than heteropolyacid with Keggin and Wells-Dawson structure due to the higher number of the acidic protons. This solid catalysts are non corrosive, ecofriendly, environmentally friendly, eco-friendly, inexpensive, simple recovery, recyclable and reusable without loss of the catalytic activity and the properties in the next reactions.

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