Short communication

Preyssler heteropolyacid $[NaP_5W_{30}O_{110}]^{14-}$, as a new, green and recyclable catalyst for the synthesis of [1,2,4]triazino[4,3-b][1,2,4,5]tetrazines

Majid M. Heravi [a,*], Fatemeh F. Bamoharram [b], Ghadir Rajabzadeh [c],
Nasim Seifi [c], Mola Khatami [c]

[a] Department of Chemistry, Faculty of Science, Azzahra University, Vanak, Tehran, Iran
[b] Department of Chemistry, Islamic Azad University, Mashhad Branch, Mashhad, Iran
[c] Department of Chemistry, Khorasan Science and Technology Park (KSTP), Iran

Abstract

Catalytic performance of Preyssler, $H_{14}[NaP_5W_{30}O_{110}]$, and Keggin, $H_3[PW_{12}O_{40}]$, heteropolyacids as pure and supported on silica, $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$, $H_3[PW_{12}O_{40}]/SiO_2$, have been studied in cyclocondensation of 4-amino-3-hydrazino-6-methyl-1,2,4-triazin-5(2H)-one (4-AHMT) with orthoesters. The catalytic activity of various forms of these catalysts in different solvents was compared with other classical catalysts, such as H_2SO_4 and HY-zeolite. In all cases the best yields were obtained, using $H_{14}[NaP_5W_{30}O_{110}]$.
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1. Introduction

Triazino-terazines are a class of heterocyclic systems, which have not received much attention. Literature survey showed only few methods for the synthesis of [1,2,4]triazino[1,2,4,5]terazine system [1,2]. In continuation of our interest in the synthesis of fused heterocyclic ring systems [3a–e], we have recently described the synthesis of [1,2,4]triazino[3,4-b][1,2,4,5] tetrazine-6-thion as a novel heterocyclic system [3f].

Various methods have been reported for the synthesis of fused heterocyclic compounds using mineral acids such as H_2SO_4 and polyphosphoric acid. These catalysts have their own disadvantages and drawbacks. They generate many problems such as pollution, care of handling, safety, corrosion and tedious workup procedures. Strong solid acids and solid acids based on supported transition metal oxides are suitable for replacement of liquid acids to decrease these disadvantages [4,5].

The catalytic function of heteropolyacids (HPAs) and related polyoxometalate compounds have attracted much attention particularly in the last two decades [6–8]. Polyoxametalates (POMs) are a class of molecularly define organic metal-oxide clusters, posses intriguing structure and diverse properties [9,10]. These compounds exhibiting high activity in acid base type of catalytic reactions, hence they are used in many catalytic areas as homogeneous and heterogeneous catalysts [11]. The application of Preyssler catalyst is mostly limited and only a few demonstrations of catalytic activity have been reported [12]. The important advantages of this heteropolyacid such as: strong Bronsted acidity with 14 acidic protons, high thermal stability, high hydrolytic stability (pH 0–12), reusability, safety, quantity of waste, separability, corrosiveness, high oxidation potential and greenness along with exclusive structure have attracted much attention on this catalyst. The structure of this catalyst is shown in Fig. 1 [13]. On the other hand Keggin structure involves 4 three-fold M_3O_{13} groups. The total assemblage contains 40 close-packed oxygen and has a tetrahedron pocket in its center for the heteroatom [14]. The structure of this polyanion is shown in Fig. 2. The Keggin anions offer a limited hydrolytic and thermal stability compared to the Preyssler structure.

Recently we have explored the application of Preyssler catalyst in various organic reactions [15,16]. In this article we wish to report an improved catalytic and general approach for the synthesis of [1,2,4]triazino[4,3-b][1,2,4,5]tetrazin-6-ones, using Pressyler's anion. The performance of this catalyst as pure

* Corresponding author. Tel.: +98 9121329147; fax: +98 218047861.
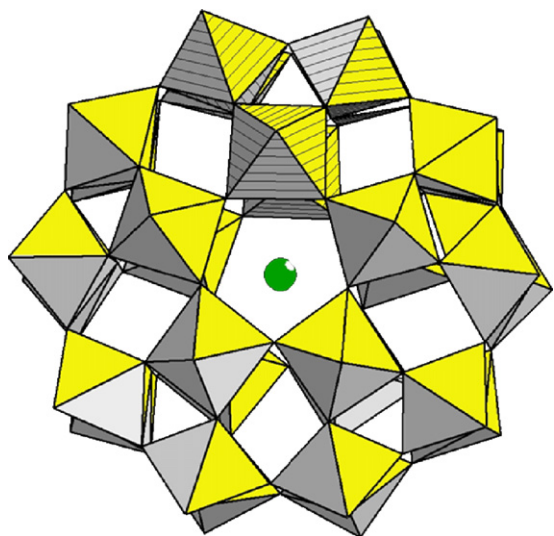E-mail address: mmh1331@yahoo.com (M.M. Heravi).
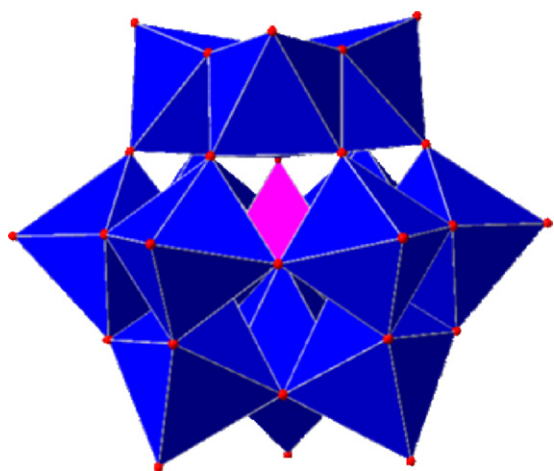
Fig. 1. Preyssler structure.

Fig. 2. Keggin structure.

acid and supported on silica was compared with Keggin type such as $H_3[PW_{12}O_{40}]$ and traditional acids in homogeneous and heterogeneous conditions.

2. Results and discussion

The environmental care is one of the world wide increasing worries. This fact encourages scientists to make efforts in finding processes working in this direction. The replacement of environmental hazardous catalysts in various processes, with green catalysts, is one of the innovative trends. For this reason, there is still a good scope for research towards finding green and eco-friendly catalysts in organic syntheses.

The synthesis of [1,2,4]triazino[4,3-b][1,2,4,5]tetrazin-6-ones from orthoesters (orthoacetate, orthoformate) and 6-methyl-3-hydrazino-1,2,4-triazin-5-one was carried out with different forms of Preyssler catalyst as a green and reusable catalyst. For the sake of comparison, this study also extended to Keggin and other classical catalysts.

The effect of various parameters such as catalyst type, solvent type, temperature, and reaction time on the yield of products were studied and compared with those obtained, using traditional acids. We have found that Preyssler catalyst in acetic acid as solvent is an eco-friendly catalyst for aforementioned cyclo-condensation reaction.

2.1. Effect of the solvent

The cyclocondensation reaction of 4-AHMT with orthoesters was carried out in various solvents, such as ethanol, acetic acid, n-butanol, and a mixture of acetonitrile/ethanol.

We have found that acetic acid is the most effective solvent. The results are shown in Tables 1–4. The yields of product increased in the following order: acetic acid > acetonitrile/ethanol > ethanol > n-butanol. It is noteworthy to mention that heating of the reactants in neat acetic acid without any catalyst did not give the products even in prolonged reaction time.

2.2. Effect of the catalyst type

The progress of reaction in cyclocondensation of 4-AHMT with orthoesters was monitored, by TLC and reported yields are based on isolated product. The results showed that, the highest yield of the products were achieved when $H_{14}[NaP_5W_{30}O_{110}]$ was used as catalyst.

Comparison of the catalysts in Tables 1–4 showed that $H_{14}[NaP_5W_{30}O_{110}]$ is the catalyst of choice. Comparison of supported and non-supported Preyssler catalyst showed that, in all cases, the supported polyacid is less active than the non-supported one. One plausible interpretation of this observation

Table 1

Catalytic cyclocondensation of 4-AHMT with orthoacetate and orthoformate in n-butanol as solvent

Entry	Catalyst	Percentage yield of products at 1 h		Percentage yield of products at 6 h	
		45 °C	Reflux	45 °C	Reflux
1	$H_{14}[NaP_5W_{30}O_{110}]$	39%[a] 32%[b]	61%[a] 49%[b]	52%[a] 48%[b]	72%[a] 67%[b]
2	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$	30%[a] 28%[b]	53%[a] 46%[b]	50%[a] 43%[b]	65% 51%[b]
3	$H_3PW_{12}O_{40}$	20%[a] 10%[b]	46%[a] 32%[b]	32%[a] 28%[b]	48%[a] 41%[b]
4	$H_3PW_{12}O_{40}/SiO_2$	20%[a] Trace	34%[a] 30%[b]	31%[a] 21%[b]	42%[a] 39%[b]
5	H_2SO_4	Trace Trace	21%[a] 20%[b]	Trace Trace	32%[a] 29%[b]
6	H_2SO_4/SiO_2	Trace Trace	20%[a] 14%[b]	Trace Trace	31%[a] 25%[b]
7	HY-zeolit	Trace Trace	25%[a] 29%[b]	Trace Trace	35%[a] 33%[b]
8	None catalyst	Trace Trace	23%[a] 21%[b]	Trace Trace	30%[a] 27%[b]

[a] With orthoacetate.
[b] With orthoformate

Table 2
Catalytic cyclocondensation of 4-AHMT with orthoacetate and orthoformate in ethanol as solvent

Entry	Catalyst	Percentage yields of product at 1 h		Percentage yield of product at 6 h	
		45 °C	Reflux	45 °C	Reflux
1	$H_{14}[NaP_5W_{30}O_{110}]$	48%[a] 30%[b]	78%[a] 71%[b]	61%[a] 52%[b]	82%[a] 78%[b]
2	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$	39%[a] 25%[b]	67%[a] 67%[b]	51%[a] 46%[b]	80%[a] 71%[b]
3	$H_3PW_{12}O_{40}$	25%[a] 10%[b]	57%[a] 39%[b]	39%[a] 25%[b]	68%[a] 58%[b]
4	$H_3PW_{12}O_{40}/SiO_2$	10%[a] Trace	51%[a] 31%[b]	22%[a] Trace	55%[a] 46%[b]
5	H_2SO_4	Trace Trace	45%[a] 30%[b]	Trace Trace	48%[a] 32%[b]
6	H_2SO_4/SiO_2	Trace Trace	30%[a] 21%[b]	Trace Trace	38%[a] 25%[b]
7	HY-Zeolit	Trace Trace	35%[a] 21%[b]	Trace Trace	45%[a] 25%[b]
8	None catalyst	Trace Trace	31%[a] 29%[b]	Trace Trace	42%[a] 39%[b]

[a] With orthoacetate.
[b] With orthoformate

Table 4
Catalytic cyclocondensation of 4-AHMT with orthoacetate and orthoformate in acetic acid as solvent

Entry	Catalyst	Percentage yields of product at 1 h		Percentage yield of product at 6 h	
		45 °C	Reflux	45 °C	Reflux
1	$H_{14}[NaP_5W_{30}O_{110}]$	57%[a] 38%[b]	81%[a] 79%[b]	71%[a] 53%[b]	95%[a] 88%[b]
2	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$	41%[a] 31%[b]	82%[a] 69%[b]	58%[a] 51%[b]	87%[a] 77%[b]
3	$H_3PW_{12}O_{40}$	35%[a] 22%[b]	61%[a] 53%[b]	40%[a] 22%[b]	68%[a] 60%[b]
4	$H_3PW_{12}O_{40}/SiO_2$	20%[a] 10%[b]	51%[a] 42%[b]	21%[a] 12%[b]	58%[a] 51%[b]
5	H_2SO_4	Trace Trace	41%[a] 32%[b]	Trace Trace	52%[a] 35%[b]
6	H_2SO_4/SiO_2	Trace Trace	35%[a] 27%[b]	Trace Trace	40%[a] 31%[b]
7	HY-Zeolit	Trace Trace	37%[a] 25%[b]	Trace Trace	42%[a] 36%[b]
8	None catalyst	Trace Trace	32%[a] 18%[b]	Trace Trace	41%[a] 32%[b]

[a] With orthoacetate.
[b] With orthoformate

is that, in supported type, there are polyanion-support interactions of an acid–base nature. Some protons of the polyacid and some basic sites of the support (for example hydroxyl groups) can interact. This would lead to diminished availability of hydrogens due to this extra ionic interaction [17].

Table 3
Catalytic cyclocondensation of 4-AHMT with orthoacetate and orthoformate in ethanol/acetonitrile as solvent

Entry	Catalyst	Percentage yields of product at 1 h		Percentage yields of product at 6 h	
		45 °C	Reflux	45 °C	Reflux
1	$H_{14}[NaP_5W_{30}O_{110}]$	52%[a] 33%[b]	71%[a] 75%[b]	79%[a] 55%[b]	88%[a] 81%[b]
2	$H_{14}[NaP_5W_{30}O_{110}]/SiO_2$	45%[a] 32%[b]	73%[a] 57%[b]	51%[a] 46%[b]	83%[a] 79%[b]
3	$H_3PW_{12}O_{40}$	25%[a] 20%[b]	59%[a] 45%[b]	44%[a] 29%[b]	78%[a] 65%[b]
4	$H_3PW_{12}O_{40}/SiO_2$	10%[a] Trace	53%[a] 29%[b]	26%[a] Trace	61%[a] 51%[b]
5	H_2SO_4	Trace Trace	33%[a] 29%[b]	Trace Trace	49%[a] 34%[b]
6	H_2SO_4/SiO_2	Trace Trace	33%[a] 21%[b]	Trace Trace	38%[a] 31%[b]
7	HY-Zeolit	Trace Trace	31%[a] 20%[b]	Trace Trace	48%[a] 28%[b]
8	None catalyst	Trace Trace	32%[a] 22%[b]	Trace Trace	41%[a] 35%[b]

[a] With orthoacetate.
[b] With orthoformate

Interestingly, this behavior is similar to that of Keggin heteropolyacids. However, when $H_3[PW_{12}O_{40}]$ was used instead of $H_{14}[NaP_5W_{30}O_{110}]$ the yield of product was decreased. The results, point out that the catalytic effectiveness may be enhanced as the number of tungsten atoms (or the number of protons) is increased. Both possibilities stand to reason. The larger number of protons may lower the activation barrier for cyclocondensation reaction. In addition, the large anion also provides many "sites" on the oval-shaped molecule that are likely to render the catalyst effectiveness. Interestingly, the comparison of, Preyssler's anion, with its exclusive properties, with Keggin heteropolyacid, HY-zeolite, H_2SO_4 and supported silica sulfuric acid showed that the activity is the most for $H_{14}[NaP_5W_{30}O_{110}]$. The catalytic activity is increased in the following order: $H_{14}[NaP_5W_{30}O_{110}] > H_{14}[NaP_5W_{30}O_{110}]/SiO_2 > H_3[PW_{12}O_{40}] > H_3[PW_{12}O_{40}]/SiO_2 > H_2SO_4 > H_2SO_4/SiO_2 > HY$-Zeolit.

2.3. Effect of the reaction time

For all substrates and catalysts, the effect of reaction time on the % yield of product in cyclocondensation of 4-AHMT with orthoesters was studied. The results in Tables 1–4 show the reaction times for the formation of products. The TLC analysis showed that the formation of product is starting after 1 h. The results indicate that there is an increase in the amount of product with increase in reaction time in the presence of heteropolyacids.

The optimum reaction time has been found to be 6 h in reflux temperature. At any reaction time, $H_{14}[NaP_5W_{30}O_{110}]$ was found to be most active catalyst, among H_2SO_4, silca

Table 5
^{1}H NMR, mass and IR spectral data for (**2a-b**)

Compound	R	mp (°C)	m/z	IR V^{max} cm^{-1} (KBr disk)	^{1}H NMR δ (ppm)
2a	H	301–302	164 (M^+)	3160 (NH, stretch) 1670 (C=O stretch)	(DMSO), 10.3 (1H, s, NH), 8.1 (1H, s, NH), 6.2 (1H, S, CH) 1.5 (3H, s, CH$_3$)
2b	CH$_3$	240–241	180 (M^+)	3349 (NH, stretch) 1710 (C=O stretch)	(DMSO), 10.64 (1H, s, NH), 8.9 (1H, s, NH), 2.4 (3H,s, CH$_3$), 2.1 (3H, s, CH$_3$).

gel supported sulfuric acid and HY-zeolite. However, when we studied the effect of reaction time for the conventional acids such as H$_2$SO$_4$ and HY-zeolite, no improvement was observed in the term of yields with increase of reaction time.

2.4. Effect of the temperature

The cyclocondensation reaction was carried out at two different temperatures including lowest temperature (45 °C, start of formation of the product) and reflux temperature. Interestingly, in cyclocondensation with orthoesters in the presence of classical acids such as H$_2$SO$_4$ and zeolite, only trace of product was observed at 45 °C. When these reactions were carried out at reflux temperature, the products were obtained in low yields. In the presence of heteropolyacids as pure acid and supported form, with increasing of the temperature, the yields of product are increased. The highest yields of products were obtained at reflux temperature.

3. Conclusion

The obtained results in cyclocondensation of 4-AHMT with orthoesters in the presence of H$_{14}$[NaP$_5$W$_{30}$O$_{110}$] is outstanding and promising. Since tetrazines are pharmacologically active, their fused ring maybe of interest from biological as well as chemical point of view. Pryessler's anion is an inexpensive, eco-friendly, and recyclable catalyst, which can be used for the synthesis of this fused tetrazine.

The results also indicate that the reaction times, temperature, and solvent types, are important factors. H$_{14}$[NaP$_5$W$_{30}$O$_{110}$], H$_3$[PW$_{12}$O$_{40}$] catalyst both in, homogenous and heterogonous phase can be recovered and reused without loss of structures and appreciable activity.

4. Experimental

4.1. Chemicals and apparatus

Ethanol, acetic acid, acetonitrile, *n*-butanol, H$_3$[PW$_{12}$O$_{40}$], H$_2$SO$_4$, orthoacetate, orthoformate, and HY-zeolite were obtained from Merck company and used as received. H$_{14}$[NaP$_5$W$_{30}$O$_{110}$] was prepared according to earlier works [15,16]. Supported heteropolyacid catalyst synthesized according to our previous reports [15,16]. Silica supported sulfuric acid was prepared according to previous report [18]. 4-AHMT derivatives were prepared by the known procedures [3f].

4.2. Instruments

The melting points were obtained using an Electro thermal IA 9100 Digital Melting Point apparatus. The IR spectra were recorded on a Bruker (4000–400 cm^{-1}) spectrometer. ^{1}H NMR spectra were recorded on a 100 MHz spectrometer using TMS as internal standard. Mass spectra were obtained from Varian CH-7 instrument at 70 eV.

4.3. General procedure

4.3.1. Synthesis of [1,2,4]triazino[4,3-b][1,2,4,5] tetrazines (2a-b)

4-Amino-3-hydrazino-6-methyl-1,2,4-triazin-5(2H)-one (**1**) (312 mg, 2 mmol) was dissolved in an appropriate solvent (5–7 mL). Orthoester (1 mL, excess) was added to the solution and catalyst (0.1 mmol) was subsequently added to the reaction mixture. The reaction mixture was stirred at reflux temperature for 1–6 h. After removal of solvent in reduced pressure, the residue was recrystallized from ethanol to afford the corresponding product (**2a-b**). Yields, melting points, and spectral data are shown in Tables 1–5.

To recover the heteropolyacids in case of using other solvents than acetic acid, acetic acid was added to the mother liquor to precipitate the catalyst out of solution. The obtained solid acid was filtered off and washed with diethyl ether, which could be reused in another reaction. When acetic acid is a solvent the catalyst was filtered directly and washed with diethyl ether to make it ready for next use. ^{1}H NMR, Mass and IR Spectral data for the products are shown in Table 5.

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