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Efficient Catalytic Synthesis of Pyrazolo[3,4-*d*]pyrimidine, Pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine, Pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine, Pyrazolo[3,4-*d*]pyrimidin-4-one derivatives using Heterogeneous Preyssler Heteropolyacid, $H_{14}[NaP_5W_{30}O_{110}]/SiO_2$

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Abstract: With of reaction of 5-amino-pyrazole-4-carbonitrile derivative and using from supported Preyssler heteropolyacid catalyst in a series from reactions prepared a several new pyrazolo[3,4-*d*]pyrimidine, pyrazolo[3,4-*e*][1,4]diazepine, pyrazolo[3,4-*d*][1,2,3]triazine and pyrolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives.

Keywords: Pyrazolo, pyrimidine, Supported, Preyssler, heteropolyacid, catalyst

Introduction

Green chemistry is an approach to the synthesis, processing, and use of chemicals that reduces risks to humans and the environment. Much innovative chemistry has been developed over the past several years that are effective, efficient and more environmentally benign. These approaches include new syntheses and processes as well as new tools for instructing aspiring chemists how to do chemistry in a more environmentally benign manner. Thus the development and using of solid and green catalysts is very important in organic synthesis. Development of methods using heteropolyacids (HPAs) as solid and green catalysts for fine organic synthetic processes related to fine chemicals, such as flavors, pharmaceuticals and food industries have been under attention in the last decade [1]. HPAs are more active catalysts than conventional inorganic and organic acids for various reactions in solution [2]. They are used as industrial catalysts for several liquid-phase reactions such as esterification, etherification, hydration and dehydration, de-esterification, and condensation reactions [3-6]. Compounds containing the triazolo[1,5-*c*]pyrimidine moiety have attracted considerable attention due to their remarkable adenosine and benzodiazepine receptor affinity. Azoloazines are biologically interesting molecules and their chemistry is now

receiving considerable attention [1-3]. the 5-amino-9-chloro-2-(2-furyl)-1,2,4-triazolo[1,5-*c*]quinazoline was found to be a highly potent adenosine antagonist [8], while the 9-chloro-2-(2-fluorophenyl)-1,2,4-triazolo[1,5-*c*]quinazolin-5(6*H*)-one displayed a very significant benzodiazepine binding activity [9]. This current pharmacological interest has stimulated our interest in the synthesis of several new and biologically active derivatives with these ring systems. The considerable biological activities of pyrazole, and its annelated derivatives as antimycotics [4] antidepressants [5], fungicidal agents [6], are of increasing interest. Heteropolyacids (HPAs) have great potential as environmentally friendly alternatives to the more wasteful traditional catalysts. The problems associated with the handling and disposal of the inorganic acids, and their environmental and potential hazards have raised our interest in the development of alternative procedures using solid acid catalysts [7].

Heteropolyacids (HPAs) have many advantages finding economically and environmentally attractive in both academic and industrial significance; they are useful acids and oxidation catalysts in various reactions since their catalytic features can be varied at a molecular level [8]. Furthermore, Wells–Dawson type heteropolyacids possess super-acidity and a remarkable stability both in solution and in the solid state [9]. The application of heteropolyacids (HPAs), as catalytic materials is growing continuously in the catalytic field. These compounds possess unique properties, such as: well-defined structure, Bronsted acidity, possibility to modify their acid–base and redox properties by changing their chemical composition (substituted HPAs), ability to accept and release electrons, high proton mobility, etc [10]. In view of green chemistry, the substitution of harmful liquid acids by solid reusable HPAs as catalyst in organic synthesis is the most promising application of these acids. As part of our continued interest in the development of highly expedient methods for the synthesis of organic compounds of biological importance [11] and continuation with the application of heteropolyacids as versatile catalysts for a variety of organic transformations [11].

Instruments

GC–Mass analysis was performed on a GC–Mass model: 5973 network mass selective detector, GC 6890 Agilent. IR spectra were obtained with a Buck 500 scientific spectrometer. ¹H NMR spectra were recorded on a FT NMR Bruker 90 MHz.

Reusability of catalyst

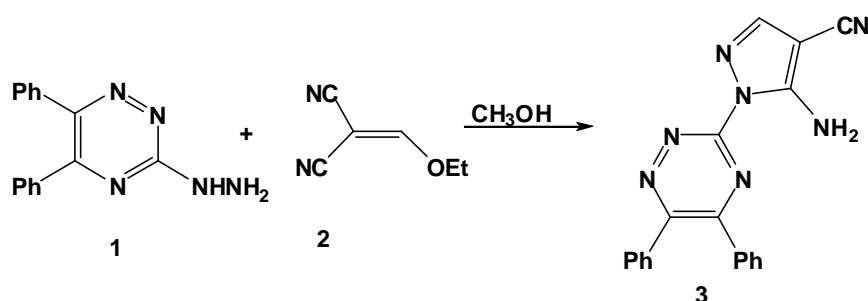
At the end of the reaction, the catalyst could be recovered by a simple filtration. The recycled catalyst could be washed with dichloromethane and subjected to a second run of the reaction process. To assure that the catalyst can not be dissolved in acetic acid the filtered catalysts were weighted before reusing. The results show that these catalysts are not soluble in acetic acid. After recovery and use of the catalyst the results of the first and subsequent experiments were almost consistent in yields. Also the catalyst has taken out of reaction system. Then, the concentrations were determined in the solution. The results showed that the concentrations are constant during the reaction time. Thus the catalyst is not leached.

Catalyst preparation

Preyssler's anion catalyst was provided in according with literature [11].

Results and Discussion

We wish to report synthesis of polycyclic azines, 5-amino-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-pyrazole-4-carbonitrile **5**, using heteropolyacid as catalyst, and with treated of 5,6-diphenyl-3-hydrazenyl-1,2,4-triazole [10] **1** with ethoxymethylenemalononitrile **2** in refluxing ethanol, (Scheme 1).

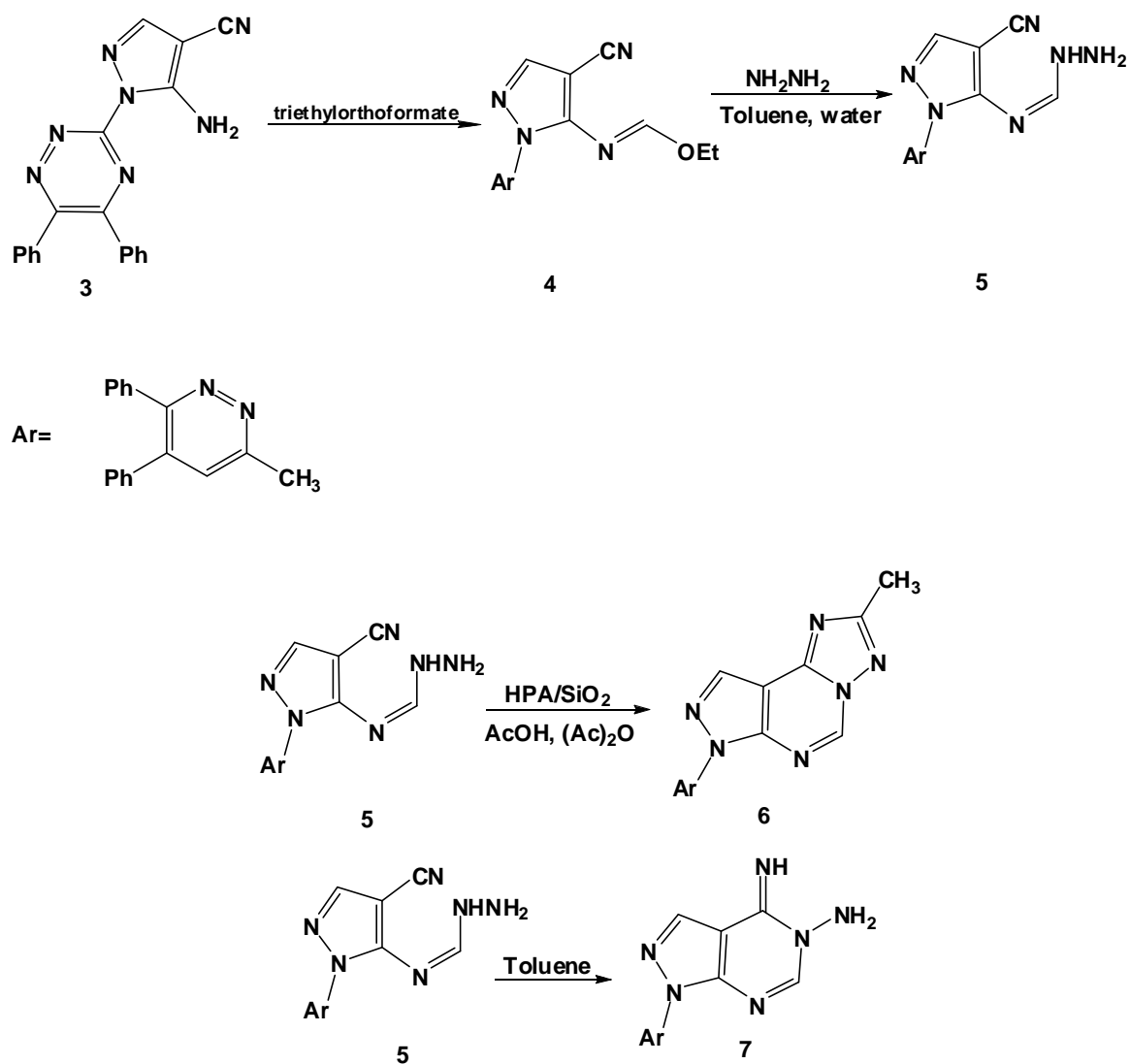


Scheme 1

Treatment of compound **3** with triethylorthoformate (T.E.O.F.), acetic anhydride and supported preyssler heteropolyacid catalyst gave the ethyl-4-cyano-1-[5,6-diphenyl-1,2,4-triazin-3-yl]-1Hpyrazol-5-ylimidoformate, **4**, with a 78% yield.

The *N*-[4-cyano-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1H-pyrazol-5-yl]imidofornic hydrazide, **5**, which transformed into the 1-(5,6-diphenyl-1,2,4-triazin-3-yl)-4-imino-1,4-dihydro-5H-pyrazolo[3,-4-*d*]pyrimidin-5-amine, **7** by refluxing toluene obtained 81% yield. Compound of **7** in acetic acid-acetic anhydride and H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) mixture, the 7-(5,6-diphenyl-1,2,4-triazin-3-yl)-2-methyl-7Hpyrazolo[

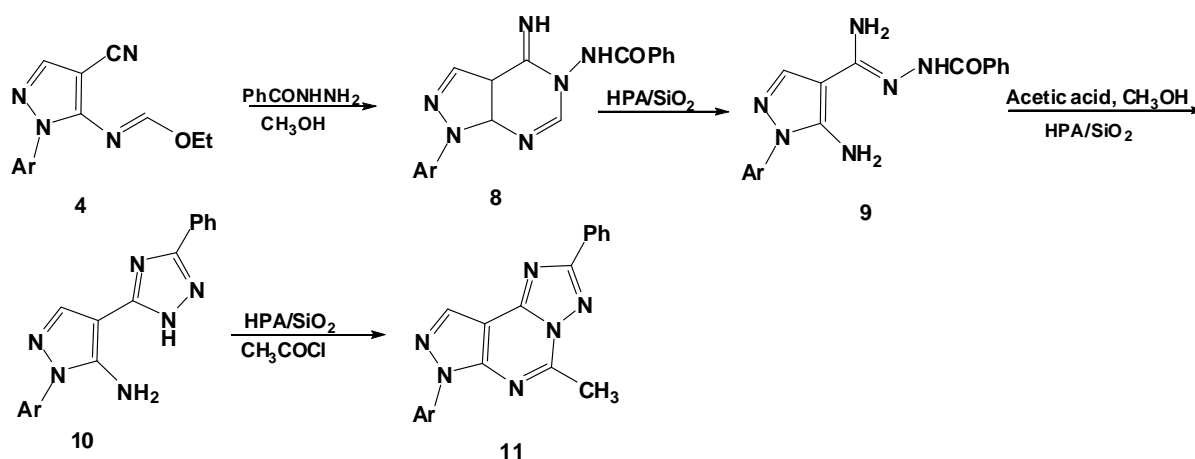
4,3-*e* [1,2,4]triazolo[1,5-*c*]pyrimidine, **6**, was obtained with a yield of 73% (Scheme 2).



Scheme 2

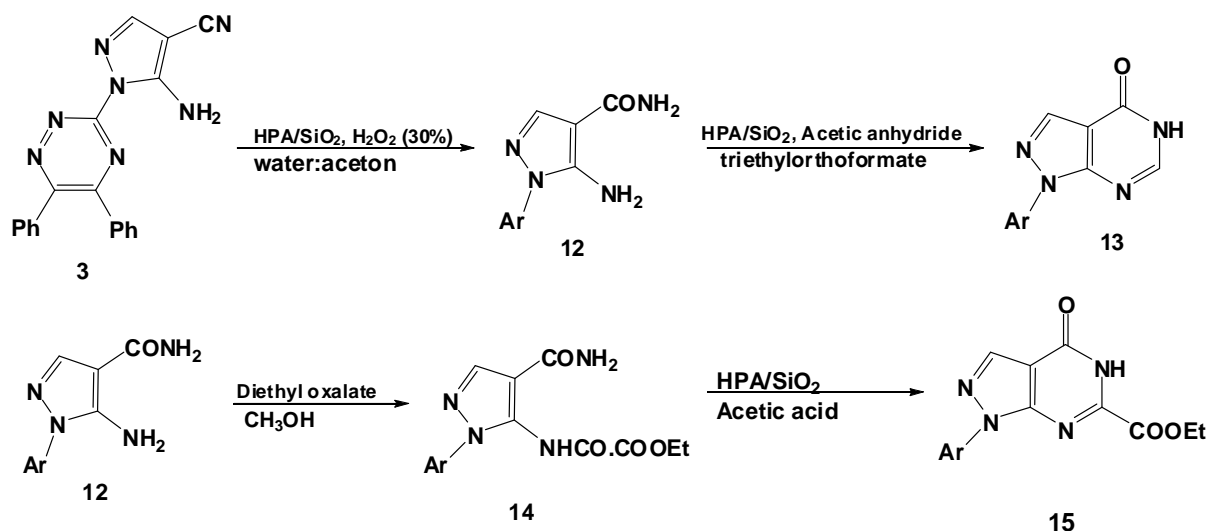
With treatment of **4** with benzohydrazide in refluxing ethanol, the *N*-[4-imino-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1,4-dihydro-5*H*-pyrazolo[3,4-*d*]pyrimidin-5-yl] benzamide **8** was formed with a 76% yield, which was converted into 5-amino-*N*1-benzoyl-1(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazole-4-carbohydrazonamide **9**, with a 61% yield, in 10% Preyssler heteropolyacid. By refluxing of compound **9** in acetic acid and H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) as catalyst gave 1-(5,6-diphenyl-1,2,4-triazin-3-yl)-4-(3-phenyl-1*H*-1,2,4-triazol-5-yl)-1*H*-pyrazol-5-amine, **10**, with a 67.8% yield. Treatment of **10** with acetyl chloride and chloroacetyl chloride in refluxing acetic acid and H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) as catalyst gave 7-(5,6-diphenyl-1,2,4-triazin-3-yl)-2-phenyl-5-methyl-7*H*-pyrazolo-[4,3-*e*] [1,2,4]triazolo[1,5-*c*] pyrimidine, **11**,

with a 89% yield. Heating of compound **4** with hydrazine hydrate in benzene-water mixture resulted in a 61% yield. The *N*''-[4-cyano-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazol-5-yl]imidoformic hydrazide, **5**, which transformed into the 1-(5,6-diphenyl-1,2,4-triazin-3-yl)-4-imino-1,4-dihydro-5*H*-pyrazolo[3,-4-*d*]pyrimidin-5-amine, **7** by heating in refluxing dry benzene resulted in an 83% yield. On refluxing of **7** in acetic acid-acetic anhydride and H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) as catalyst mixture, the 7-(5,6-diphenyl-1,2,4-triazin-3-yl)-2-methyl-7*H*pyrazolo[4,3-*e*] [1,2,4]triazolo[1,5-*c*]pyrimidine, **6**, was obtained with a yield of 73% (Scheme 3).



Scheme 3

The compound **3** was converted into 5-amino-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazole-4-carboxamide, **12**, at room temperature with a 93.6% yield, using an excess of hydrogen peroxide 30% in the presence of H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) as catalyst and amount of potassium carbonate in an acetone-water mixture as a solvent. Refluxing of **12** with triethylorthoformate in refluxing acetic anhydride and H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) as catalyst resulted 1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1,5-dihydro-4*H*-pyrazolo [3, 4-*d*]pyrimidin-4-one, **13**, with a 74% yield. the refluxing of **12** with diethyloxalate in refluxing ethanol yielded the ethyl {[4-(aminocarbonyl)-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazol-5-yl]amino}(oxo)acetate, **14**, which was converted into the ethyl 1-(5,6-diphenyl-1,2,4-triazin-3-yl)-4-oxo-4,5-dihydro-1*H*-pyrazolo[[3,4-*d*]pyrimidine-6-carboxylate, **15**, by refluxing in acetic acid obtaining with 73% yield (Scheme 4).



Scheme 4

We continued our researches about this project, and treated synthesis of 5-Amino-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazole-4-carboxamide (**12**) using some of various heteropolyacids and other catalysts, and obtained interesting results, also $H_3[PW_{12}O_{40}]$ has good yield in this reaction and in comparison of using other heteropolyacids with mineral acids and other catalysts, good and suitable yields are concerned in heteropolyacids (Table 1).

Table 1. Yields of various catalysts for synthesis of 5-Amino-1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1*H*-pyrazole-4-carboxamide (**12**)

Entry	Catalyst	Time Reaction (min)	^a Yield (%)
1	H ₂ SO ₄	73.6	65
2	H ₃ PO ₄	69	58.5
3	HY-Zeolite	74.7	67.5
4	H ₂ SO ₄ /SiO ₂	71.4	60
5	H ₃ [PW ₁₂ O ₄₀]	90.5	79.5
6	H ₄ [SiW ₁₂ O ₄₀]	84.4	70.5
7	H ₃ [PMo ₁₂ O ₄₀]	80.1	73
8	H ₄ [SiMo ₁₂ O ₄₀]	75.5	66.5

^aisolated yields.

Conclusion

The obtained results in Synthesis of Pyrazolo [3,4-*d*]pyrimidine, Pyrazolo[3,4-*e*][1,4]diazepine, Pyrazolo [3,4-*d*][1,2,3]triazine and Pyrolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine Derivatives in the presence of $H_{14}[NaP_5W_{30}O_{110}]/SiO_2(50\%)$ or $H_{14}-P_5/SiO_2(50\%)$ is outstanding and promising. Pryessler's anion is an inexpensive, eco-friendly, and recyclable catalyst, which can be used for the synthesis of pyrazoles derivatives.

H₁₄[NaP₅W₃₀O₁₁₀]/SiO₂(50%) or H₁₄-P₅/SiO₂(50%) heterogonous phase can be recovered and reused without loss of structures and appreciable activity.

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