

Short communication

Catalytic synthesis of 6-aryl-1H-pyrazolo[3,4-d]pyrimidin-4[5H]-ones by heteropolyacid: $H_{14}[NaP_5W_{30}O_{110}]$ and $H_3PW_{12}O_{40}$

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Abstract

Reaction of 5-amino-1-phenyl-1H-pyrazolo-4-carboxamide **1** with aromatic aldehyde in presence of heteropoly acids, $H_3PW_{12}O_{40}$ and $H_{14}[NaP_5W_{30}MoO_{110}]$ gave derivatives of 6-aryl-1H-pyrazolo[3,4-d]pyrimidin-4[5H]-ones **4**.

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1. Introduction

Pyrazolo[3,4-d]pyrimidines are of considerable chemical and pharmacological importance as purine analogues [1–3]. Various compounds with related structures also passes anti-tumor and anti-leukemia activities [4,5]. Therefore, investigation about new methods and synthesis of new derivatives of these compounds attracted considerable amount of interest.

Recently Akira Miyashita et al. have prepared some 6-alkyl-1-phenylpyrazolopyrimidine derivatives from the reaction of 5-amino-1-phenyl-1H-pyrazolo-4-carboxamide **1** with aliphatic esters in presence of sodium ethoxide and ethanol [6]. Veerangaiah et al. also have reported a versatile synthesis of 1H-pyrazolo[3,4-d]pyrimidin-4(5H)ones by the condensation of 5-amino-1H-pyrazole-4-carboxamide **1** with aromatic aldehydes and carboxylic acids by refluxing in acetic acid or methanol/HCl and poly phosphoric acid or poly phosphate ester [7].

The extensive demand for cleaner environment is forcing chemists to use less hazardous materials in this regard, heteropolyacids attracted considerable amount of interest due to the less toxic behavior in addition of possessing higher acidity [8–10]. Heteropolyacids are widely used in variety of acid-

catalyzed reactions such as esterification [11], etherification [12], hydration and dehydration [13,14], de-esterification [15], polymerization [16], condensation [17,18] in homogenous and heterogeneous systems.

Here in, we present our investigation of synthesis of some new derivatives of 1H-pyrazolo[3,4-d]pyrimidin-4(5H)ones **4** by a Keggin type heteropolyacid $H_3PW_{12}O_{40}$ and a Preyssler type, $H_{14}[NaP_5W_{30}O_{110}]$ as a acidic catalyst instead of mineral acid like HCl or polyphosphoric acid as a more eco-friendly and suitable method.

2. Experimental

2.1. General procedure for the synthesis of 6-substitued-pyrazolo[3,4-d]pyrimidin-4(5H)-ones (**4a–4n**)

A solution of **1** (0.9 mmol) and appropriate aromatic aldehyde **2** (0.9 mmol) and an appropriate heteropolyacid (0.04 mmol) in acetic acid (10 ml) was refluxed for 0.5–3 h. The catalyst was removed by filtering and washed with warmed acetic acid (the catalyst is not soluble in acetic acid). The filtrate was cooled and the solid was filtered, washed with water, dried and recrystallized from ethanol to give pure product **4** (Table 1). After removing the reaction product by filtration and washing the solid catalyst with diethyl ether, it could be reused and subjected to a second run of the reaction. The result of the first experiment and subsequent experiment were almost consistent in yields. All compounds

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Table 1
Catalytic synthesis of 6-substitued-pyrazolo[3,4-d]pyrimidin-4(5H)-ones **4**

Compound	R	R ₁	Reaction time (min)	Yield (%) using H ₃ PW ₁₂ O ₄₀	Yield (%) using H ₁₄ [NaP ₅ W ₃₀ O ₁₁₀]	m.p. (°C)
4a	CH ₃	ph	30	55	80	300–301
4b	CH ₃	4-MeC ₆ H ₄	60	65	86	275–277
4c	CH ₃	3-MeC ₆ H ₄	60	65	80	279–281
4d	CH ₃	4-NO ₂ C ₆ H ₄	15	70	85	308–310
4e	CH ₃	3-NO ₂ C ₆ H ₄	30	74	85	293–295
4f	CH ₃	4-ClC ₆ H ₄	30	73	78	316–318
4g	CH ₃	4-BrC ₆ H ₄	45	73	78	310–311
4h	H	Ph	30	60	85	288–290 [1]
4i	H	4-MeC ₆ H ₄	60	76	85	253–255 [1]
4j	H	3-MeC ₆ H ₄	60	78	85	263–264
4k	H	4-NO ₂ C ₆ H ₄	15	70	87	278–280 [1]
4l	H	3-NO ₂ C ₆ H ₄	15	74	87	285–287
4m	H	4-ClC ₆ H ₄	30	68	78	235–237 [1]
4n	H	4-BrC ₆ H ₄	30	68	80	338–340

(unknown or known) were characterized by mass, IR and ¹H NMR spectra.

3. Result and discussion

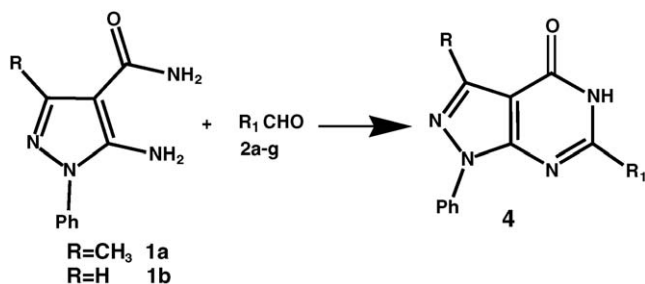
Due to the ever-mounting environmental concern in the field of chemistry, it is advisable to use easily recovered and recycled catalyst especially expensive or toxic metallic ones for the next use [19]. In this respect, only few of the aforementioned, catalysts meet this criterion of green chemistry. As mentioned, the synthesis of 6-substitued-pyrazolo[3,4-d]pyrimidin-4(5H)-ones systems from related aldehyde were done in basic or acidic con-

ditions. The use of typical acid-catalysts like hydrochloride or acid phosphoric leads the environmental pollution and corrosion problems which can be avoided by using catalysts based on HPAs [20]. In connection with our program of using heteropoly acid in organic reactions [21] we wish to report the result of a study on the use of a Keggin type heteropolyacid, H₃PW₁₂O₄₀ and a Preyssler type, H₁₄[NaP₅W₃₀O₁₁₀] in the synthesis of 6-substitued-pyrazolo[3,4-d]pyrimidin-4(5H)-ones.

When the mixtures of 5-amino-1-phenyl-1H-pyrazolo-4-carboxamide **1** [22] and aromatic aldehyde **2** in acetic acid in presence of catalytic amounts of heteropolyacids were refluxed in specific times, 6-Aryl-1H-Pyrazolo[3,4-d]pyrimidin-

Table 2
H¹ NMR, mass and IR spectral data for **4**

Compound	m/z	IR V ^{max} cm ⁻¹ (KBr)	H ¹ NMR δ (ppm)
4a	302(M ⁺)	2900–3200 (NH), 1689 (C=O)	(CDCl ₃), 3.05 (3H, s, CH ₃), 7.2–7.6 (5H, m, Ph), 7.6–7.8 (5H, m, Ph), 10.6 (1H, bs, NH)
4b	316(M ⁺)	2700–3100 (NH), 1680 (C=O)	(DMSO), 3.06 (3H, s, CH ₃), 2.45 (3H, s, CH ₃), 7.25 (2H, d, J = 11.7, Ar), 7.36 (2H, d, J = 11.7, Ar), 7.5–7.7 (5H, m, Ph), 10.2 (1H, s, NH)
4c	316(M ⁺)	2700–3100 (NH), 1675 (C=O)	(DMSO), 3.06 (3H, s, CH ₃), 2.47 (3H, s, CH ₃), 7.4–7.8 (9H, m, Ph), 10.83 (1H, s, NH)
4d	348(M ⁺ + H ⁺)	2700–3100 (NH), 1680 (C=O)	(DMSO), 3.1 (3H, s, CH ₃), 7.3–7.67 (5H, m, Ph), 8.25 (2H, d, J = 10.2, Ph), 8.35 (2H, d, J = 10.2, Ph), 11.02 (1H, bs, NH)
4e	347(M ⁺)	2800–3100 (NH), 1689 (C=O)	(DMSO), 3.12 (3H, s, CH ₃), 7.3–7.69 (5H, m, Ph), 8.01–8.21 (4H, m, Ph), 11.04 (1H, bs, NH)
4f	336(M ⁺), 338(M ⁺ + 2)	2800–3100 (NH), 1680 (C=O)	(DMSO), 3.08 (3H, s, CH ₃), 7.3–7.7 (5H, m, Ph), 7.89 (2H, d, J = 8.5, Ph), 8.06 (2H, d, J = 8.5, Ph), 11.9 (1H, bs, NH)
4g	380(M ⁺), 382(M ⁺ + 2)	2900–3100 (NH), 1689 (C=O)	(DMSO), 3.06 (3H, s, CH ₃), 7.34–7.68 (5H, m, Ph), 7.80 (2H, d, J = 7.5, Ph), 7.9 (2H, d, J = 7.5, Ph), 11.5 (1H, s, NH)
4h	228(M ⁺)	2700–3100 (NH), 1660 (C=O)	(DMSO), 7.4–7.6 (5H, m, Ph), 7.65–7.83 (5H, m, Ph), 8.23(1H, s, C ₃ H), 12.5 (1H, bs, NH)
4i	302(M ⁺)	2900–3200 (NH), 1680 (C=O)	(DMSO), 2.45 (3H, s, CH ₃), 7.30 (2H, d, J = 11.9, Ar), 7.48 (2H, d, J = 11.9, Ar), 7.6–7.8 (5H, m, Ph), 8.02 (1H, s, C ₃ H), 11.8 (1H, s, NH)
4j	302(M ⁺)	2900–3100 (NH), 1665 (C=O)	(DMSO), 2.48 (3H, s, CH ₃), 7.5–7.8 (9H, m, Ph), 8.0 (1H, s, C ₃ H), 11.2 (1H, s, NH)
4k	333(M ⁺)	2800–3200 (NH), 1660 (C=O)	(DMSO), 7.3–7.7 (5H, m, Ph), 8.3 (1H, s, C ₃ H), 8.35 (2H, d, J = 10.2, Ph), 8.4 (2H, d, J = 10.2, Ph), 11.1 (1H, bs, NH)
4l	333(M ⁺)	2700–3200 (NH), 1690 (C=O)	(CDCl ₃), 7.3–7.8 (5H, m, Ph), 8.1–8.3 (5H, m, Ph, C ₃ H), 11.02 (1H, bs, NH)
4m	322(M ⁺), 324(M ⁺ + 2)	2700–3200 (NH), 1660 (C=O)	(DMSO), 7.3–7.6 (5H, m, Ph), 8.1 (2H, d, J = 8.6, Ar), 8.2 (2H, d, J = 8.6, Ar), 8.23 (1H, s, C ₃ H), 11.8 (1H, s, NH)
4n	366(M ⁺), 368(M ⁺ + 2)	2800–3200 (NH), 1665 (C=O)	(DMSO), 7.35–7.7 (5H, m, Ph), 7.85 (2H, d, J = 7.6, Ar), 7.96 (2H, d, J = 7.6, Ar), 8.20 (1H, s, C ₃ H), 11.7 (1H, s, NH)



Scheme 1.

4[5H]-ones **4** were obtained (Scheme 1). Comparison of yields of the reaction in previous reported method [7] with $\text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$ show a little better yields. The same reactions which have been reported by Veeranagaiah et al. (**4h–4i–4k–4m**) were done in acetic acid by 2–4 h refluxing in presence of hydrochloric acid and 5 h refluxing without any catalysts [7]. However the rates of reactions increased 2–10 times faster in presence of Preyssler type heteropolyacid. Between two heteropolyacids with Keggin and Preyssler structures used in present study, $\text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$ shows higher activity and yields due to the higher number of acidic protons which in a good agreement with the previously reported acidity order $\text{H}_3\text{PW}_{12}\text{O}_{40} > \text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$ [23]. Furthermore the catalyst is not soluble in acetic acid and enabled an easy separation and recovery by filtering for its immediate reuse without any important decrease of the catalyst reactivity. The spectral data for the products were reported in Table 2.

4. Conclusions

Among the typical acids, heteropolyacids such as $\text{H}_{14}[\text{NaP}_5\text{W}_{30}\text{O}_{110}]$ have exhibited high activities for the synthesis of 6-substituted-pyrazolo[3,4-d]pyrimidin-4(5H)-ones **4** and as an efficient, reusable and ecofriendly heterogeneous catalyst. Furthermore it was confirmed that heteropolyacid with Preyssler structure shows higher activity and yields due to the higher number of acidic protons.

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