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Synthesis of quinoxalines in the presence of heteropoly acids

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Efficient synthesis of quinoxaline derivatives from the reaction of *α*-diketones and *o*-phenylenediamines in the presence of Keggin-type heteropolyacids (HPA) such as $H_3PMo_{12}O_{40}$, $H_4SiW_{12}O_{40}$, $K_7PMo_2W_9O_{40}$, $H_3PW_{12}O_{40}.SiO_2$ and $H_3PW_{12}O_{40}$ in high yields and short reaction times, and at room temperature is introduced.

1. Introduction

Heteropoly acids as solid acid catalysts are green catalysts with respect to their non-corrosive nature, safety, low quantity of waste and easy separation. One of the unique features that make solid heteropoly acids economically and environmentally attractive is their stability and high acidity.

Quinoxalines are important heterocycles in medicinal chemistry[1,2] and have biological activities such as antibacterial and anti-inflammatory activities[3,4]. The best reported method for synthesis of quinoxalines is the reaction of aryl 1,2-diamines with a 1,2-dicarbonyl compounds in the presence of an acid as catalyst. Acetic acid[5], iodine[6], $CuSO_4.5H_2O$[7], Zn[(L)-proline][8], Ni-nanoparticles[9], gallium(III)triflate[10], montmorillonite K_{10}[11], task-specific ionic liquids[12], $MnCl_2$[13], and ZrO_2/Ga_2O_3/MCM-41[14] and alumina-supported heteropolyoxometalates[15] have been applied in the above mentioned method.

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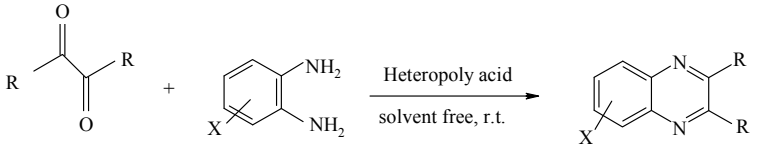
2. Result and Discussions

In continuation of our investigations on the applications of solid acids in organic synthesis, we have investigated the synthesis of quinoxalines in the presence of heteropoly acid at room temperature. Herein, we report that heteropoly acids are efficient catalysts for the synthesis of quinoxaline derivatives comparable with some other applied catalysts. The reaction of 1,2-phenylenediamine with benzil was investigated for optimization of the reaction conditions. Reaction at different temperatures and various molar ratios of substrates in the presence of heteropoly acid revealed that the best results were obtained under solvent-free conditions at room temperature and a molar ratio of 1,2-phenylenediamine: benzil: heteropoly acid equal to 1:1:0.01.

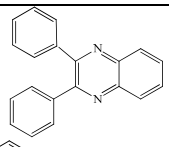
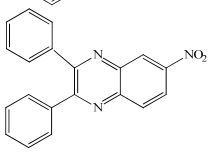
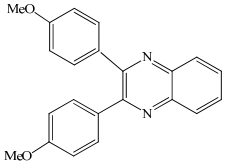
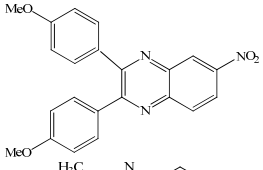
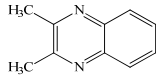
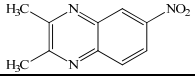
Various 1,2-phenylenediamines and 1,2-diketones were used as substrates for the synthesis of quinoxalines under solvent free at room temperature (Scheme 1 and Table 1).



R=Me, Ar X=H, 4-NO_2

Scheme 1. Preparation of quinoxaline derivatives in the presence of heteropolyacids

Table 1. The synthesis of quinoxaline from 1, 2-phenylenediamine (1 mmol) and benzil (1 mmol) using heteropoly acids (A: $H_3PMo_{12}O_{40}$, B: $H_4SiW_{12}O_{40}$, C: $K_7PMo_2W_9O_{40}$, D: $H_3PW_{12}O_{40}.SiO_2$, E: $H_3PW_{12}O_{40}$, 1 mol %) as catalyst.

Entry	R	X	Product	Time (min)/ Yield (%)					M.P. °C
				A	B	C	D	E	
1	Ph	H		3/98	3/98	2/99	2/95	10/90	127-128
2	Ph	NO_2		2/99	3/98	3/98	2/98	10/89	192-193
3	4-OCH_3Ph	H		2/99	3/98	3/98	2/99	12/88	152-153
4	4-OCH_3Ph	NO_2		3/99	3/98	2/99	2/99	10/88	193-194
5	CH_3	H		3/98	3/99	3/98	2/99	14/90	135-136
6	CH_3	NO_2		2/99	3/99	3/98	2/98	10/91	185-186

A: $H_3PMo_{12}O_{40}$, B: $H_4SiW_{12}O_{40}$, C: $K_7PMo_2W_9O_{40}$, D: $H_3PW_{12}O_{40}.SiO_2$, E: $H_3PW_{12}O_{40}$

3. Conclusions

Herein, we have reported a mild, easy applicable and efficient method for the preparation of quinoxalines from benzils and *o*-phenylenediamines using small amount of heteropolyacids as highly efficient solid catalysts. These reactions are characterized by good yields and short reaction times.

Acknowledgements

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Experimental

Chemicals and apparatus

All chemicals were purchased from commercial suppliers and were used as received. All products were identified by their spectra and physical data. Melting points were measured by using the capillary tube method with an electrothermal 9100 apparatus. Polyoxometalates were prepared according to literature procedures[16]. The IR spectra were recorded on a Shimadzu DT-40 model 883 IR Spectrophotometer (KBr pellets, Nujol mulls, 4000–400 cm^{-1}). ^1H NMR spectra were recorded on a Bruker- Avance DRX 400 spectrometer using TMS as an internal standard. Elemental analyses were done by Costech ECS 4010 CHNS-O analyzer.

Preparation of quinoxalines catalyzed using heteropoly acids:

A mixture of *o*-phenylenediamine (1 mmol), 1,2-dicarbonyl (1 mmol) and catalyst (1 mol %) was grounded in a mortar for 2-4 minute. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was dissolved in CH_2Cl_2, filtered and washed with diethyl ether (5 mL) to isolate the catalyst. The solvent was evaporated under reduced pressure and the pure product was obtained.

Selected spectroscopic data

2,3-Diphenylquinoxaline (Table 1, entry 1), FT- IR: $\bar{\upsilon}$ (KBr) = 3055, 1541, 1348, 1053, 771, 697 cm^{-1}, ^1H-NMR (400 MHz, $CDCl_3$) δ = 8.01 (dd, *J*=6.3 and 3.6 Hz, 2H), 7.79 (dd, *J*= 6.3 and 3.4 Hz, 2H), 7.5 (m, 4H), 7.39 (m, 6H) ppm. Elemental analysis, Found, %: C 85.03; H 5.11; N 9.86. $C_{20}H_{14}N_2$. Calculated, %: C 85.08; H 5.00; N 9.92,

2,3-Bis(4-methoxyphenyl)quinoxaline (Table 1, entry 3), FT- IR: $\bar{\upsilon}$ (KBr) = 2958, 2838, 1606, 1511, 1461, 1393, 1347, 1287, 1243, 1172, 1027, 829, 764, 596 cm^{-1}, ^1H-NMR (400 MHz, $CDCl_3$) δ=3.65 (s, 6H), 6.69 (d, *J*=8.8 Hz, 4H), 7.30 (d, *J*=8.8 Hz, 4H), 7.54 (dd, *J*=6.2 and 3.2 Hz, 2H), 7.95 (dd, *J*=6.2 and 3.2 Hz, 2H) ppm. Elemental analysis. Found, %: C 77.07; H 5.15;.N 8.26; O 9.52. $C_{22}H_{18}N_2O_2$. Calculated, %: C 77.17; H 5.30; N 8.18; O 9.35.

2,3-Dimethylquinoxaline (Table 1, entry 5), FT-IR: $\bar{\upsilon}$ (KBr)=2923, 1568, 1489, 1437, 1363, 1317, 1164, 762 cm^{-1}, ^1H-NMR (400 MHz, $CDCl_3$) δ = 2.55 (s, 6H), 7.77 (dd, *J*=8.8 and 2.5 Hz, 1H), 7.79 (dd, *J*=8.8 and 2.4 Hz, 1H) ppm.^{13}C-NMR (100 MHz, $CDCl_3$) δ = 23.54, 30.09, 128.69, 129.21, 141.45, 153.85 ppm. Elemental analysis, Found, %: C 75.97; H 6.27; N 17.76. $C_{10}H_{10}N_2$. Calculated, %: C 75.92; H 6.37; N 17.71.

2,3-Dimethyl-6-nitro-quinoxaline (Table 1, entry 6), FT- IR: $\bar{\upsilon}$ (KBr) = 3057, 2923, 1616, 1579, 1525, 1342, 1164, 743 cm^{-1}, ^1H-NMR (500 MHz, $CDCl_3$) δ=2.57 (s, 3H), 2.60 (s, 3H), 7.92 (d, *J*=9.2 Hz, 1H), 8.25 (d, *J*= 8.8 Hz, 1H), 8.70 (s, 1H) ppm, ^{13}C-NMR (125 MHz, $CDCl_3$) δ=23.72, 23.93,

122.75, 125.29, 130.34, 140.34, 144.13, 147.58, 156.69, 157.62 ppm. Elemental analysis, Found, %: C 59.15; H 4.41; N 20.71; O 15.73. $C_{10}H_9N_3O_2$. Calculated, %: C 59.11; H 4.46; N 20.68; O 15.75.

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