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ZnO nanoparticles as an Efficient and Reusable Catalyst for Synthesis of Quinoxaline under Solvent Free Condition

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ABSTRACT

1,2-Diketones have been reacted in one-pot method with 1,2-diamines at room temperature with ZnO nanoparticles as a catalyst. ZnO nanoparticles as an available and reusable catalyst is used for the synthesis of Quinoxalinein improved yields.

***Keywords**: Quinoxaline, ZnO nanoparticles, Solvent free, Benzil, 1,2-Diamines*

1. Introduction

Among the various classes of nitrogen containing heterocyclic compounds, quinoxaline derivatives show a wide range of biological activities and play an important role as a basic skeleton for the design of a number of antibiotics such as echinomycin, actinomycin, leromycin and antifungal [1]. Quinoxalines have a variety of activities such as tranquilizing, antimycobacterial, cardiotonic, antidepressant and antitumor activities depending on the substitution pattern on the scaffold [2]. Synthesis of quinoxaline ring is still an important challenge. They have also many applications in dyes, pharmaceuticals and efficient electroluminescent materials [3]. The most common method for their synthesis relies on the condensation of an aryl 1,2-diamine with a 1,2-dicarbonyl compound in refluxing ethanol or acetic acid for 2-12h giving 34-85% yields [4].Recently, the synthesis of quinoxaline has been catalyzed by $CuSO_4.5H_2O$, microwave irradiation, $H_6P_2W_{18}O_{62}.24H_2O$, Zn[(I) proline], Acidic alumina, NH_4Cl-CH_3OH, Sulfamic acid/MeOH, Molecular iodine, Metalhydrogen sulfated, Ni-nanoparticles, Montmorillonite K-10, Task-specific ionic liquid and Oxalic acid [5-17].

In recent years, the importance of nanoparticle materials and increased investment in nanotechnology has been identified for the coming year [18]. Surface of metal oxides exhibit both Lewis acid and Lewis base character [19]. Nanomaterials are an exciting subject for both fundamental interests and their practical advanced applications [20]. ZnO nano-particles are one of the most important functional oxides with many interesting and unique electrical, catalytic and optical properties [21].

ZnO nanoparticles as a solid acid catalyst has been used in some organic reaction, such as Synthesis of β-acetamidoketones [22], removal phenol from water [23] and etc. In this article, we report a simple and efficient method for synthesis of quinoxaline derivatives using different 1,2-phenylene diamine and 1,2-dicarbonyl in the presence of ZnO nanoparticles as an efficient and reusable catalyst.

2. Experimental

Melting points were measured by using the capillary tube method with a Barnstead Electrothermal melting point apparatus. ^{1}H NMR and ^{13}C NMR spectra were recorded on a BrukerAvans 500 MHz spectrometer using TMS as an internal standard ($CDCl_3$ solution). IR spectra were recorded from KBr disk on the Shimadzu IR-470 spectrometer. Elemental analyses were performed using a Costech ECS 4010 CHNS-O analyser. All products were characterized by spectra and physical data.

2.1. Preparation of ZnO nanoparticles

The stable catalyst is easily prepared [24] and used for preparation of quinoxalines. Aqueous solutions of zinc

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nitrates and urea were added into a flask under vigorous stirring (300 rpm/min). The molar ratio of Zn^{2+} to urea was about 1:4. In order to inhibit the growth of the ZnO crystallite during the course of precipitation, a certain amount of surfactant, sodium dodecyl sulfate (SDS), was added into reaction system. Then the reaction system was heated to 95°C and maintained at that temperature. After stirring for 2 h, a semitransparent zinc hydroxide colloid was obtained. The precipitates were then filtered, washed with distilled water and alcohol for three or four times, dried in air at 80°C, and finally calcined at 350°C for 2 h to achieve samples with 30-50 nm particle size.

2.2 General procedure for the synthesis of quinoxalines

A mixture of 1,2-dicarbonyl (1 mmol), orthophenylen-diamine (1 mmol) and Nano ZnO (0.0009g) were placed in a round bottom flask. The materials were mixed at room temperature for 20 min (table 3). The progress of the reaction was followed by TLC. After the completion of the reaction, dichloromethane was added to the mixture and filtered to remove the catalyst. The recovered catalyst was washed with chloroform and dried in air. Thus recovered catalyst was reused for further reactions without significant loss of activity. By evaporation of the solvent, an oily residue or an impure solid was obtained. The solid was then crystallized with ethanol and then a milky to yellow solid was obtained. All the products (except entry 7, 8, 11- 14) are known compounds, which were characterized by IR and ^{1}H NMR spectral data and their melting points compared with literature reports.

The selected spectral data

Acenaphtho [1,2-b] quinoxaline (Table 3, entry 7). IR (ν_{max}, cm^{-1}): 3040, 1622, 1571, 1480, 1297. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.73 (dd, *J*=3.4 Hz, 6.3 Hz, 2H), 7.78 (dd, *J*=7.1 Hz, 7.9 Hz, 2H), 8.03 (d, *J*=8.2 Hz, 2H), 8.17 (dd, *J*=3.4 Hz, 6.2 Hz, 2H), 8.35 (d, *J*=6.9 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 154.5, 141.7, 136.9, 132.2, 130.3, 130.0, 129.8, 129.6, 129.0, 122.2. Anal. Calcd. for $C_{18}H_{10}N_2$: C, 85.04; H, 3.94; N, 11.02 found: C, 84.8; H, 3.89; N, 11.01.

7-methylacenaphtho [1,2-b] quinoxaline (Table3, entry 8). IR (ν_{max}, cm^{-1}): 3040, 2915, 1626, 1482, 1207. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 8.36 (d, *J*=6.6 Hz, d, *J*=6.6 Hz, 2H), 8.05 (m, 3H), 7.95 (S, 1H), 7.79 (d, *J*=7.4 Hz, d, *J*=7.6 Hz, 2H), 7.55 (dd, *J*=1.3 Hz, 8.3 Hz, 1H), 2.61(S, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 154.5, 153.8, 141.7, 140.1, 140.0, 136.7, 132.4, 131.7, 130.4, 129.8, 129.6, 129.5, 129.2, 129.0, 122.1, 122.0, 22.2. Anal.calcd. for $C_{19}H_{12}N_2$: C, 85.07; H, 4.47; N, 10.44, found: C, 84.9; H, 4.43; N, 10.40.

Phenantherene [1, 2-b] quinoxaline (Table3, entry 11). IR (ν_{max}, cm^{-1}): 3020, 1614, 1490, 1356, and 1032. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 9.38 (dd, *J*=1.4 Hz, 7.9 Hz, 2H), 8.53 (d, *J*=7.9 Hz, 2H), 8.31 (dd, *J*=3.4 Hz, 6.4 Hz, 2H), 7.84 (dd, *J*=3.4 Hz, 6.5 Hz, 2H), 7.74 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 142.8, 142.6, 132.5, 130.7, 130.6, 130.1, 129.9, 128.3, 126.7, 123.3. Anal. Calcd. for $C_{20}H_{12}N_2$; C, 85.71; H, 4.28; N, 10. Found: C, 85.70; H, 3.90; N, 9.8.

7-methyl-Phenanthrene [1,2-b] quinoxaline (Table3, entry 12). IR (ν_{max}, cm^{-1}): 3010, 1622, 1499, 1354, 1206. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 9.39 (m, 2H), 8.56 (d, *J*=8.0 Hz, 2H), 8.21 (d, *J*=8.6 Hz, 1H), 8.09 (S, 1H), 7.78 (m, 4H), 7.68 (dd, *J*=1.8 Hz, 8.6 Hz, 1H), 2.68 (S, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 142.7, 142.6, 142.1, 141.2, 140.8, 132.8, 132.4, 132.2, 130.9, 130.8, 130.5, 130.4, 129.4, 128.4, 128.3, 128.2, 126.6, 126.5, 123.3, 22.5. Anal. calcd. for $C_{21}H_{14}N_2$: C, 85.71; H, 4.76; N, 9.52, found: C, 84.93; H, 4.67; N, 9.34.

2-Methyl-3-propyl-quinoxaline (Table3, entry 13). IR (ν_{max}, cm^{-1}): 2952, 2867, 1563, 1488, 1205, 1153. ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.79 (m, 2H), 7.47 (m, 2H), 2.78 (t, *J*=8.0Hz, 3H), 2.57 (s, 3H), 1.63 (m, 2H), 0.89 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 157.03, 153.50, 141.55, 141.26, 129.11, 129.06, 128.91, 128.66, 38.19, 23.18, 21.80, 14.54. Anal. calcd. for $C_{12}H_{14}N_2$: C, 77.42; H, 15.05; N, 7.52, found: C, 77.38; H, 14.89; N, 7.49.

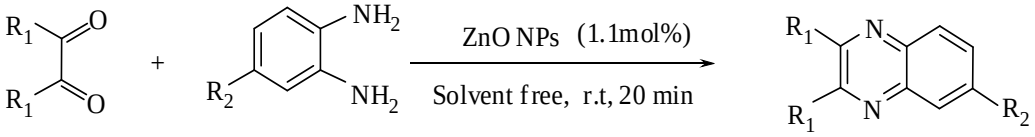
3,6-Dimethyl-2-propyl-quinoxaline (Table3, entry 14). IR (ν_{max}, cm^{-1}): 2958, 2869, 1619, 1561, 1495, 1443, 1367, 1321^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ: 7.67 (m, 1H), 7.56 (m, 1H), 7.30 (m, 1H), 2.76 (t, *J*=8.0 Hz, 3H), 2.57 (s, 3H), 2.36 (s, 3H), 1.67 (m, 2H), 0.89 (t, *J*=7.2Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 156.98, 152.55, 141.63, 139.72, 139.41, 131.39, 128.21, 127.94, 38.21, 23.12, 22.11, 21.91, 14.57. Anal. calcd. for $C_{13}H_{16}N_2$: C, 78; H, 8; N, 14, found: C, 76.08; H, 7.49; N, 13.02.

3. Results and discussion

Nanoparticles of ZnO were prepared via uniform precipitation method. The ZnO nanoparticles were characterized by scanning electron microscopy (SEM) and FT-IR spectroscopy techniques.

The SEM of ZnO nanoparticles is shown in Fig. 1. As seen, single phase primary particle is spherical in shape withthe average diameter of about 30-50 nm.

After reaction, catalyst was recycled and characterized by FT-IR spectra. The FT-IR spectrum of ZnO nanparticles in KBr matrix is shown in Fig. 2. There is a broad band at 3326 cm^{-1} corresponding to the vibration mode of water OH group indicating the



Scheme 1.

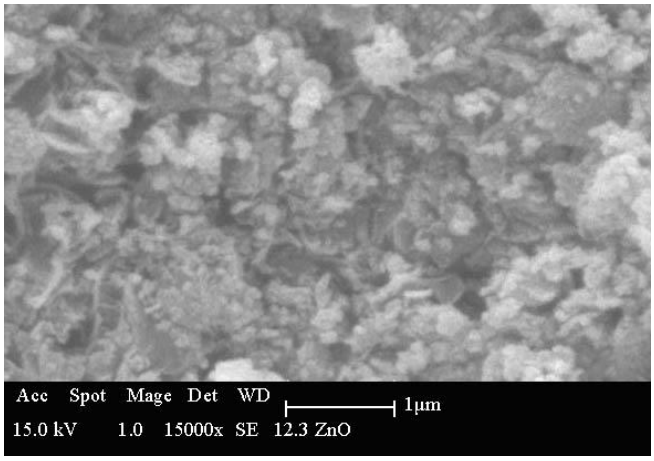


Fig. 1. The SEM of ZnO nanoparticles.

presence of small amount of water adsorbed on the ZnO nanparticles surface. The band at 1620 cm^{-1} due to the OH bending of water. A strong band at 611 cm^{-1} is attributed to the Zn-O stretching band whitch is consistent with that reported before [25].

In a preliminary study,to optimize the reaction conditions,the reaction of benzil and orthophenilendiamin was used as a model reaction (Table 1). The efficiency of ZnO nanoparticles is comparable with other catalysts such as $CuSO_4.5H_2O$, NH_4Cl, Sulfamic acid, Iodine and Acidic alumina. According to the obtained data, NH_4Cl and sulfamic acid have more yield but NH_4Cl was applied (50 mol%) more amount. These results clearly show the advantages of our methodology over other protic or Lewis acid catalyzed quinoxaline synthesis such as low consumption of catalyst and solvent free condition.

As a result, ZnO nanoparticles was selected as an efficient solid acid catalyst, the model reaction was done with various amount of catalyst and various condition. According to the obtained data, using the Nano ZnO (1.1 mol%) under solvent free at 25 ºC is the best condition for the quinoxaline formation (Table 2, entry 3).

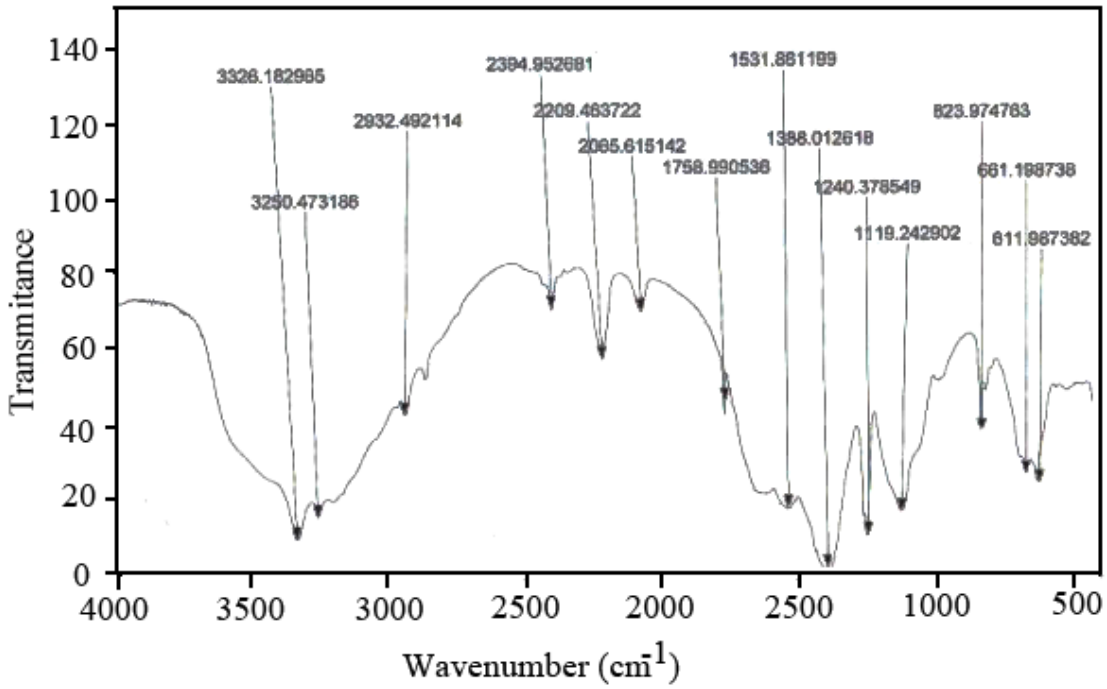


Fig. 2. FT-IR Spectrum of ZnO nanoparticles.

Table 1. Comparison of the efficiency of ZnO nanoparticles with reported catalysts.

Entry	Catalyst (amount)	Temp. (^{o}C)/ Solvent	Time (min)/ Yield (%)[a]	Ref.
1	$CuSO_4.5H_2O$ (10mol%)	25/H_2O	15/96	5
2	$CuSO_4.5H_2O$ (10mol%)	25/EtOH	8/97	5
3	NH_4Cl (50mol%)	25/CH_3OH	7/100	10
4	Sulfamic acid (5 mol%)	25/CH_3OH	5/100	11
5	Acidic alumina	Microwave	5/85	9
6	Glycerol	Reflux/H_2O	240/90	27
7	I_2 (10mol%)	25/DMSO	35/95	28
8	Polyaniline-sulfate salt (5wt%)	25/CH_2Cl_2	20/95	29
9	TiO_2-P_2O_5-SO_4^{2-} (0.1g)	25/EtOH	5/98	30
10	ZnOnanoparticles(1.1 mol%)	25/-	20/93	-

[a]Isolated yield.

The catalyst was reused in subsequent runs without further purification. These results clearly show the advantages of our method over protic or lewis acid catalyzed quinoxalines synthesis.

We have also found that ZnO nanoparticles can be effectively recovered from the reaction mixture during the work-up procedure. After completion ofreaction the mixture was filtered off to separate the catalyst and then dry the solid residue. When model reaction carried out by recovered ZnO nanoparticles, the corresponding quinoxaline formation was obtained in good yield (Table 2, entries 8, 9). As can be seen from Table 2, reactivity of the above protocol environmentally acceptable.

Therefore, some 1,2-diketones and 1,2-diamino-benzenes were subjected to quinoxalines (Scheme 1 and Table3).

A mechanistic route is suggested for the generation of quinoxalines from the reaction of 1,2-dicarbonyl and orthophenylendiamines in the presence of ZnO nanoparticlesand role of ZnO shown as the catalyst in this proposed mechanism (Scheme 2).

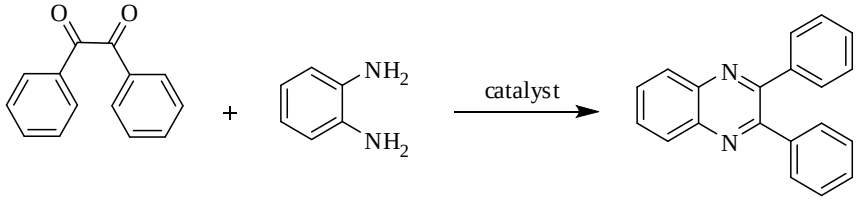


Table 2. Optimization of the reaction condition.

Entry	Catalyst (mol%)	Temp. (^{o}C)/ Solvent	Time(min)/ Yield(%)[a]
1	ZnO bulk(1.1)	25/-	20/45
2	ZnOnano (5)	25/-	20/95
3	ZnOnano (1.1)	25/-	20/93
4	ZnOnano (2)	25/-	20/95
5	ZnOnano (1.1)	25/CH_2Cl_2	20/93
6	ZnOnano (1.1)	Reflux/EtOH	20/94
7	ZnOnano (1.1)	Reflux/H_2O	20/93
8	ZnOnano (5)2nd run	25/-	20/91
9	ZnOnano (5)3rd run	25/-	20/87

[a]Isolated yield.

Table 3. A recyclable and highly effective ZnO nanoparticles catalytic system for the synthesis of quinoxalines at room temperature[a].

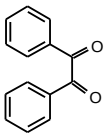
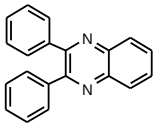
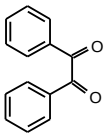
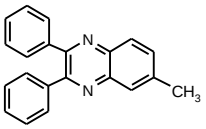
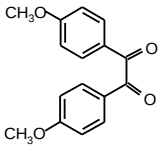
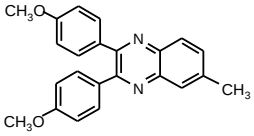
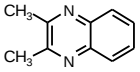
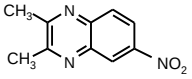
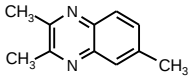
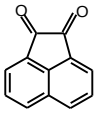
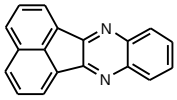
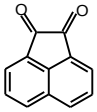
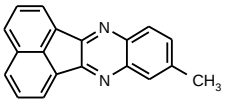
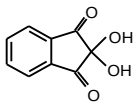
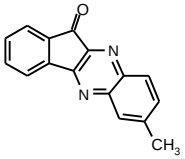
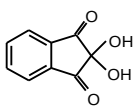
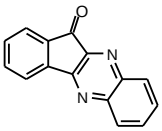
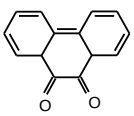
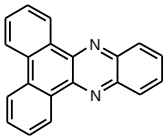
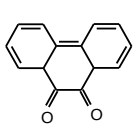
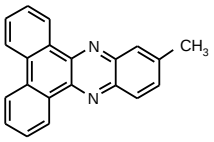
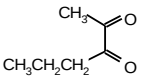
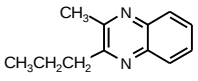
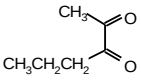
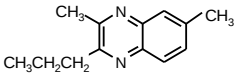
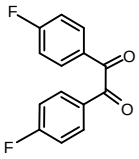
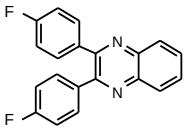
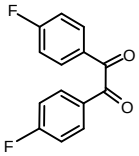
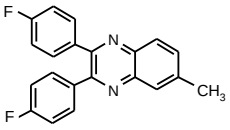
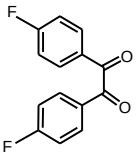
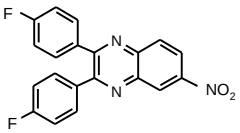
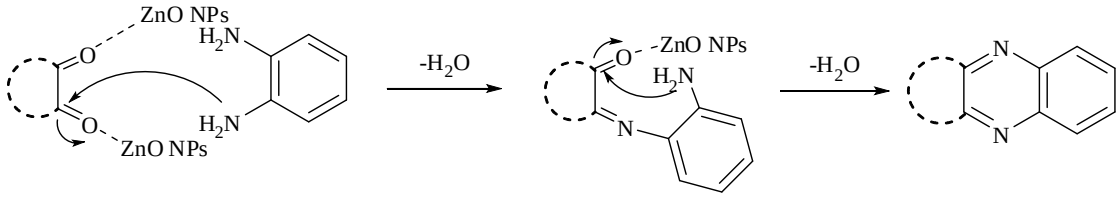
Entry	1,2-diketone	R^2	Product[b]	Yield(%)[c]	Ref	M.P(^{o}C)
1		H		92	12	126-128
2		CH_3		96	5	114-116
3		CH_3		96	5	125-127
4		H		92	11	102-104
5		NO_2		90	10	128-131
6		CH_3		94	10	76-78
7		H		93	-	242-244
8		CH_3		94	-	236-237
9		CH_3		93	26	177-179
10		H		92	26	221-225
11		H		93	-	226-228

Table 3. *(Continued).*

12		CH_3		95	-	219-232
13		H		91	-	103-104
14		CH_3		94	-	110-111
15		H		96	14	134-135
16		CH_3		93	14	164-165
17		NO_2		92	14	175-176

[a]Molar ratio of benzil, 1,2-diaminobenzene and ZnO nanoparticles(g) was 1:1:0.0009.
[b]All products were identified by their melting points, IR, ^{1}H NMR, ^{13}C NMR spectra and CHN.
[c]Isolated yield.



Scheme 2. Proposed mechanism for quinoxaline synthesis.

In the first step, Lewis acid sites of ZnO (Zn^{2+}) coordinates to the oxygen of the carbonyl group, hence reactivity of carbonyl group increases. Then a nucleophilic attack to the activated carbonyl groups proceeds the reaction forward.

4. Conclusion

ZnO nanoparticlesas a solid acid has a high efficiency as catalyst of the quinoxaline synthesis under solvent-free conditions. This simple methodology offers several advantages includinga mild reaction condition, a simple work-up, opportunities for scale-up and improved yields

Acknowledgments

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