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Cent. Eur. J. Chem. • 8(2) • 2010 • 320–325
DOI: 10.2478/s11532-009-0151-7

Central European Journal of **Chemistry**

ZnO-beta zeolite mediated simple and efficient method for the one-pot synthesis of quinoxaline derivatives at room temperature

Research Article

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Received 25 July 2009; Accepted 20 October 2009

Abstract: A rapid and an efficient one-pot method for the synthesis of quinoxalines catalysed by ZnO-beta zeolite at room temperature is described. This environmentally benign method provides several advantages over methods that are currently employed such as a simple work-up, mild reaction conditions, good to excellent yields, and a process to recover and reuse the catalyst for several cycles with consistent activity.

Keywords: *ZnO-beta zeolite • Quinoxaline • Room temperature • Cyclocondensation*

1.Introduction

Zeolites have been used as catalysts in the petroleum refining, chemical [1], and fine chemical industries [2]. The catalytic activity of H-beta zeolite can be adjusted by ion exchange with metal ions, acid treatment and hydrothermal treatment [3,4]. In particular, Zinc loaded zeolites are suitable catalysts for the organic transformations, such as Heck reaction [5], propane aromatization [6], dehydrogenation of small paraffins [7], hydroamination [8-10], aromatization of in situ generated ethylene [11] and hydration of acetylene [12,13].

Quinoxaline derivatives have attracted the attention of organic chemists due to their wide ranging biological activities including anticancer [14], antiviral [15] and antibacterial [16]. Also, quinoxaline moieties have found applications in dyes [17], building blocks in the synthesis of organic semiconductors [18], chemically controllable switches [19], dehydroannulenes [20], anti-inflammatory, anti-protozoal and anti-HIV [21]. In addition, they are used in the agricultural field as fungicides, herbicides, and insecticides [22].

The importance and utility of quinoxaline derivatives have led to the development of numerous synthetic routes. The most common method is the condensation of aromatic 1,2-diamines with 1,2-dicarbonyl compounds refluxing in ethanol or acetic acid [23]. Improved methods have been reported for the synthesis of quinoxaline derivatives including a bi-catalyzed oxidative coupling method [24], a microwave procedure [25] and the use of $RuCl_2$-$(PPh_3)_3$- TEMPO [26], MnO_2 [27], $POCl_3$ [28], iodine [29], cerium ammonium nitrate [30], $CuSO_4 \cdot 5H_2O$ [31], montmorillonite K-10 [32], $H_6P_2W_{18}O_{62} \cdot 24H_2O$ [33], SA/MeOH [34], polyaniline sulphate salt [35], Zn [L] Proline [36]. Some of these methods suffer from one or more drawbacks, such as long reaction times, low yields, harsh reaction conditions and tedious workup procedure. Therefore, development of an efficient and versatile method is still required.

As a part of our continued interest [37] in the development of highly expedient methods for the

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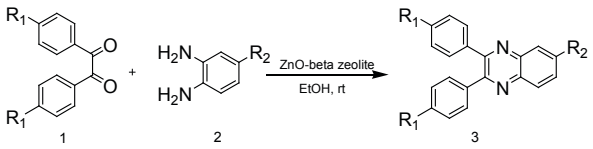

Scheme 1. Synthesis of quinoxaline derivatives catalyzed by ZnO-beta zeolite at room temperature.

synthesis of heterocyclic and biological important compounds. Herein, we report the first use of zinc modified beta zeolite as a solid acid catalyst for the synthesis of quinoxalines under benign reaction conditions. Our results demonstrate that ZnO-beta zeolite is a very effective, environmentally friendly catalyst for the one-pot condensations of *o*-phenylenediamine and benzil to form quinoxaline derivatives in excellent yields (Scheme 1).

2. Experimental Procedure

Melting points were taken in an open capillary and are uncorrected. IR spectra were recorded on Jasco FT-IR-4100, Japan, in KBr disc. All Chemicals were purchased either from Merck or Fluka and used without further purification. ^{1}H NMR spectra were recorded on an 80 MHz and 400 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shifts values are recorded in δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard.

2.1. Preparation of catalyst

In a typical synthesis, tetraethyl orthosilicate (TEOS), was added to a mixture of tetraethyl ammonium hydroxide (TEAOH), sodium hydroxide (NaOH) and an aqueous solution of aluminium sulphate ($Al_2(SO_4)_3$) and stirred at room temperature for 24 h. Then this mixture hydrothermally treated at 120°C for 96 h in autoclavable bottle. After this mixture was cooled at room temperature solid material obtained was filtered and washed with deionised water, dried at 80°C for 6 h and calcined at 550°C for 12 h. H-form of beta zeolite was prepared through ion exchange of the above sample with 1M ammonium acetate solution at 80°C for 10 h. The ion exchange procedure was repeated twice and the resulting product was calcined at 550°C for 8 h. Beta zeolite was modified by mixing H-form of respective zeolite with aqueous solution of zinc acetate. The mixture was digested at 80°C for 8 h, dried and calcined at 550°C for 8 h.

2.2. Catalyst characterization

The X-ray diffraction (XRD) patterns were recorded on Bruker 8D advance X-ray diffractometer using monochromator Cu-Kα_1 radiation (40 Kv and 30 mv) of wavelength=1.5405 A°. Conventional scanning electron microscopy (SEM) images were obtained on JEOL; JSM-6330 LA operated at 20.0 kV and 1.0000 nA. The chemical composition of the sample was determined by energy-dispersive X-ray spectroscopy (EDS) on a JEOL, JSM-6330. BET surface area has been measured by means of N_2 adsorption at 77 K preformed on a Quantachrome CHEMBET 3000 instrument. Temperature-Programmed Desorption (TPD) measurements were carried out on a Quantachrome CHEMBET 3000 TPR/TPD instrument.

2.3. General procedure for the synthesis of quinoxaline derivatives catalyzed by ZnO-beta zeolite

A mixture of 1,2-diamine (10 mmol), benzil (10 mmol), and catalytic amount of ZnO-beta zeolite (0.1 g) was taken in ethanol (10 mL) and stirred at room temperature for the appropriate reaction time (Table 2). The progress of the reaction was monitored by thin layer chromatography using pet ether, ethyl acetate as solvent system. After completion of the reaction, the reaction mass was filtered, the filtrate was concentrated under reduced pressure, and the crude product obtained was crystallized from ethanol to afford pure products.

2.4. Spectroscopic data

2,3-diphenylquinoxaline (3a)

IR (cm^{-1}) 1596, 1514, 1448, 1346. ^{1}H NMR ($CDCl_3$, 80 MHz) δ 8.20 (m, 2H), 7.76 (m, 2H), 7.56 (m, 4H), 7.35 (m, 6H); m/z (EI) 282 (M^+)

6-Methyl-2,3-diphenylquinoxaline (3b)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.14 (d, 1H), 8.03 (s, 1H), 7.63 (d, 1H), 7.54 (m, 4H), 7.35 (m, 6H), 2.64 (s, 3H)

6-Nitro-2,3-diphenylquinoxaline (3c)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.10 (d, 1H), 8.57 (m, 1H), 8.32 (d, 1H), 7.58 (m, 4H), 7.42 (m, 6H)

2, 3 Bis (4-methoxy-phenyl) quinoxaline (3d)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (m, 2H), 7.68 (m, 2H), 7.55 (d, 4H). 6.89 (d, 4H). 3.81 (s, 6H).\

2, 3 Bis (4-methoxy-phenyl)-6-nitroquinoxaline (3e)

^{1}H NMR ($CDCl_3$, 400 MHz) 9.1 (d, 1H), 8.49 (dd, 1H). 8.24 (d, 1H), 7.56 (m, 4H), 6.98 (d, 4H), 3.9 (s, 6H).

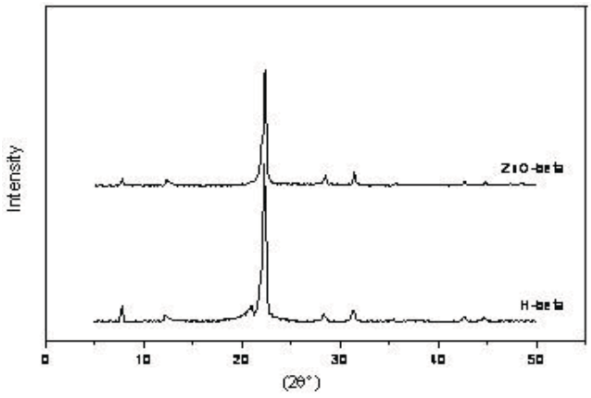

Figure 1. XRD patterns of H-beta zeolite and ZnO-beta zeolite.

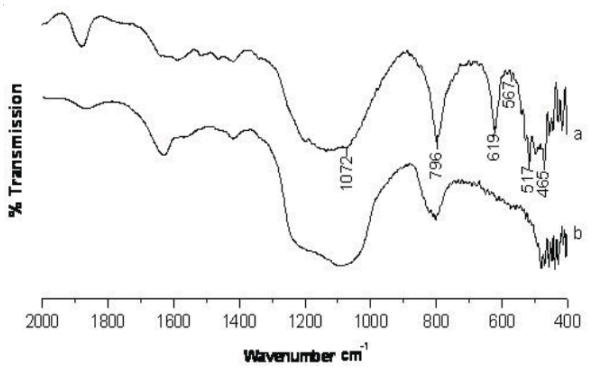

Figure 2. FT-IR spectra of H-beta zeolite (a) and ZnO-beta zeolite (b).

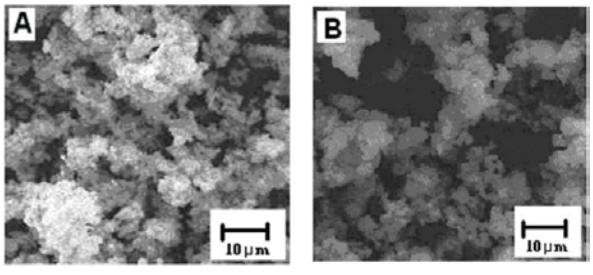

Figure 3. SEM micrograph of (A) H-beta zeolite, (B) ZnO-beta zeolite.

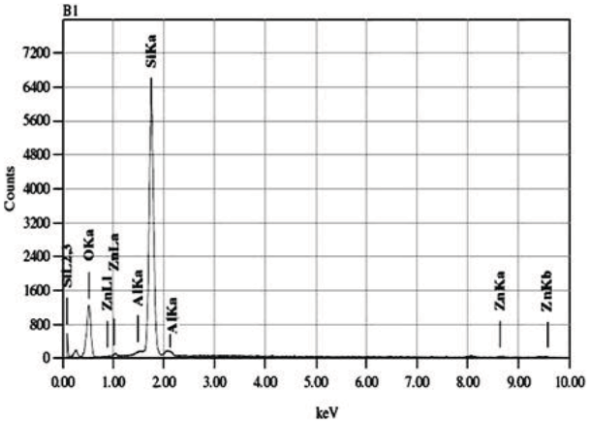

Figure 4. EDS spectrum of ZnO-beta zeolite.

2,3-Bis(4-methoxy-phenyl)-6-methylquinoxaline (3f)
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, 1H), 7.92 (s, 1H), 7.58 (d, 1H), 7.48 (d, 4H), 6.9 (d, 4H) 3.9 (s, 6H), 1.58 (s, 3H)

2,3-Bis(4-chlorophenyl) quinoxaline (3g)
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39 (d, 4H), 7.51 (d, 4H), 7.83 (dd, 2H), 8.20 (dd, 2H)

2,3-Bis(4- chlorophenyl)-6-methylquinoxaline (3h)
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.95 (d, 1H), 7.85 (s,1H), 7.65 (d, 1H), 7.51 (d, 4H), 7.05 (d, 4H), 1.50 (s, 3H).

2.5. XRD analysis

Fig. 1 shows the XRD pattern of H-beta and ZnO-beta zeolite. The powder XRD pattern is the typical type for H-beta zeolite by comparing it with the reference beta zeolite [38]. There is no visible difference observed between synthetic H-beta zeolite and zinc modified beta zeolite, only the intensity of the peaks decreases than the parent zeolite. It is clear that samples contain typical diffraction peaks of H-beta zeolite (2θ =7.8° and 22.3°).

2.6. FT-IR analysis

The FT-IR spectra of H-beta zeolite and ZnO-beta zeolite are shown in Fig. 2. Synthesized material shows IR bands in the range 550-650 cm^{-1} usually indicating the presence of zeolite like material. Peaks around 575, 525 cm^{-1} (567 and 517 cm^{-1} in present work) correspond to H-beta zeolite [39] and peak at 619 cm^{-1} for the structure-sensitive double five-ring vibration. The characteristic vibrations of H-beta zeolite around 465, 427 cm^{1} also observed. In zinc modified beta zeolite, the disappearance of the peak at 619 cm^{-1} is the only change observed.

2.7. SEM-EDS analysis

SEM images of H-beta zeolite and ZnO-beta zeolite are shown in Fig. 3. It shows that interconnected porous structures by agglomerating of tiny particles of ZnO on H-beta zeolite with an average particle size less than 10 µm (Fig. 3b). From EDS analysis zinc content in modified beta zeolite is 2.75 mass % (Fig. 4).

2.8. NH_3-TPD and BET analysis

TPD measurements were carried out by (i) pre-treating of samples from room temperature to 200°C and gas flow of nitrogen; (ii) adsorption of ammonia at room temperature; (iii) Desorption of adsorbed ammonia with an heating rate 10°C min^{-1} starting from the adsorption temperature to 700°C.

Table 1. The acid strength and surface area of catalyst.

Catalyst	Total acidity (mmol g^{-1})	Acidity (mmol g^{-1})[a]		Surface area (m^2 g^{-1})[b]
		Weak (T_1)	Strong (T_2)	
ZnO-beta zeolite	0.703	0.549	0.154	137.13

[a] *Desorption temperature: T_1= 100-300°C, T_2 = 300-700°C.*
[b] *Calculated from BET.*

Table 2. Optimization of reaction conditions in the synthesis of 2, 3-diphenylquinoxaline.[a]

Entry	Solvent	Catalyst amount (g)	Time (min)	Yield (%)[b]
1	MeOH	0.05	75	48
		0.1	50	56
		0.2	50	56
2	MeCN	0.05	40	69
		0.1	20	76
		0.2	20	76
3	C_6H_6	0.05	120	29
		0.1	90	35
		0.2	90	35
4	CH_2Cl_2	0.05	155	29
		0.1	120	40
		0.2	120	40
5	EtOH	0.05	60	40
		0.1	8	98
		0.2	8	95

[a] *Reaction was carried out in presence of ZnO-beta zeolite at RT*
[b] *Isolated yields.*

The acidity of ZnO-beta zeolite detected by temperature programmed desorption of ammonia (NH_3-TPD). Total acidity and calculated BET surface area of ZnO-beta zeolite is summarized in Table 1.

3. Results and Discussion

In order to get best experimental results, we have considered the model reaction of *o*-phenylenediamine (10 mmol) and benzil (10 mmol) in different solvents as well as different catalyst amount (Table 2). The choice of solvent proved critical. Reactions in C_6H_6, CH_2Cl_2 gave low yield of products in 90 min and 120 min respectively (Table 2 entries 3 and 4) while MeOH and MeCN gave moderate yield of products within 50 min and 20 min respectively (Table 2, entries 1 and 2). Reactions in EtOH with 0.1 g of ZnO-beta zeolite proved to be the optimized reaction condition, affording 98% yield of product (Table 2, entry 5). To investigate the role of catalyst, the same reaction was carried out in the absence of catalyst but the reaction did not yield of product even after 8 h, which indicates that catalyst is obviously necessary for the reaction. Same model reaction is carried out by using of 0.1 g of H-beta zeolite in EtOH gave 73% yield of product within 25 min.

Using the optimized reaction conditions, a range of substituted quinoxalines were synthesized 3a-h (Table 3). It can be seen that in all cases the difference in yield of products were very little and both substituted aromatic diamines such as 4-nitro and 4-methyl gave the excellent yields of products with different substituted diketones in short reaction times.

Based upon these experiments, we examined the recycling performance of ZnO-beta zeolite using the same model reaction. After the separation of products, the catalyst was washed with n-hexane, dried at 80°C and reused for next run. The data listed in Table 4 shows that the ZnO-beta zeolite could be reused at least four times without significant loss in catalytic activity. The ability to easily recycle the catalyst without loss of activity is also an attractive property for the environmental and economic reasons.

Table 3. Synthesis of quinoxaline derivatives in presence of ZnO-beta zeolite[a].

Entry	R_1	R_2	Time(min)	Yield (%)	M. P. (°C)	
					Found	Reported
3a	H	H	08	98	127-128	126-127 [31]
3b	H	Me	09	96	118-119	116-117 [31]
3c	H	NO_2	18	92	192-193	193-194 [31]
3d	OMe	H	09	98	151-152	151-152 [31]
3e	OMe	NO_2	20	90	194-195	192-194 [31]
3f	OMe	Me	12	95	126-127	125-127 [31]
3g	Cl	H	08	98	194-195	195-196 [32]
3h	Cl	Me	11	92	180-181	180 [32]

[a] *Yield refer to isolated products, which were characterized by comparing IR , ^{1}H-NMR , mass spectral data and melting points with those reported in literature.*

Table 4. Reusability of ZnO-beta zeolite catalyst for the synthesis of 2, 3-diphenylquinoxaline (Table 3, Entry 1).[a]

Entry	1	2	3	4
Cycle	Fresh	First	Second	Third
Yield (%)	98	98	97	96

[a] *All reactions carried out at RT in EtOH*
[b] *Isolated yields.*

A comparison of the catalytic efficiency of ZnO-beta zeolite with selected previously known catalysts is collected in Table 5 to demonstrate that the present protocol is indeed superior to several of the other protocols. Most of the protocols listed take either longer reaction times or use high temperatures.

4. Conclusion

In summary, the present study confirms the applicability of modified beta zeolite as an effective and reusable catalyst for one-pot synthesis of quinoxalines. The proposed method has several benefits, such as short reaction time, mild reaction condition, easy work-up procedure and minimum amount of catalyst loading.

Table 5. Comparison of ZnO-beta zeolite with other catalyst for the synthesis of 2,3 diphenylquinoxaline (Table 3, Entry 3a)[a].

Entry	Catalyst/Solvent	Time (min)	Yield (%)	Refer-ence
1	ZnO-beta/EtOH	8	98	Present
2	Polyaniline sulphate salt/CH_2Cl_2	20	95	[35]
3	$CuSO_4 \cdot 5H_2O/CH_3COOH$	10	95	[31]
4	I_2/DMSO	35	95	[29]
5	Mont. K-10/water	150	100	[32]

[a] *All reaction was carried out at RT*
[b] *Isolated yields.*

Acknowledgements

The authors are thankful to the Head, Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431 004 (MS), India for providing the laboratory facility.

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