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Zwitterionic imidazolium salt of [MOEI]-BSA: An efficient solid acid catalyst-promoted green synthesis of quinoxaline derivatives

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ABSTRACT

Easily synthesized1-methyl-3-(2-oxyethyl)-1H-imidazol-3-ium-borate sulfonic acid {[MOEI]-BSA} as a novel catalyst efficiently promoted the synthesis of quinoxaline derivatives via condensation of various diamines with 1,2-dicarbonyl compounds at room temperature conditions in ethanol. This research provides a new method for the synthesis of quinoxalines in good to excellent yields with little catalyst loading. The catalyst could be recycled and reused several times without any loss of efficiency.

***Keywords**: [MOEI]-BSA, Quinoxaline synthesis, Solid acid, Green chemistry, Heterogeneous catalyst, Diamine, 1,2-Diketone.*

1. Introduction

In recent years, studies on environmentally benign chemical processes or methodologies have received much attention. The development of heterogeneous catalysts for fine chemical synthesis has become a major area of research. Optimal use of material and energy and efficient waste management can be recognized as important factors for environmental protection. In recent years, performing the reaction in a grinding mode is a significant way to realize this goal [1-3]. It is clear that green chemistry requires the use of environmentally benign reagents and solvents, and it is very crucial to recover and reuse the catalyst. Solid acids have many advantages such as simplicity in handling, decreased reactor and plant corrosion problems, and more environmentally safe disposal in different chemical processes. Also, wastes and by products can be minimized or avoided by using solid acids in developing cleaner synthesis routes. The quinoxaline derivatives are well known and possess a broad spectrum of biological activities including antiviral, antibacterial, anti-inflammatory, as kinase inhibitors, anticancer and anthelmintic properties [4-6]. Quinoxaline structure has been found in a number of antibiotics such as echinomycin, levomycin, and actinomycin, which are known as gram-positive bacteria inhibitors and anti-tumors [7-8].

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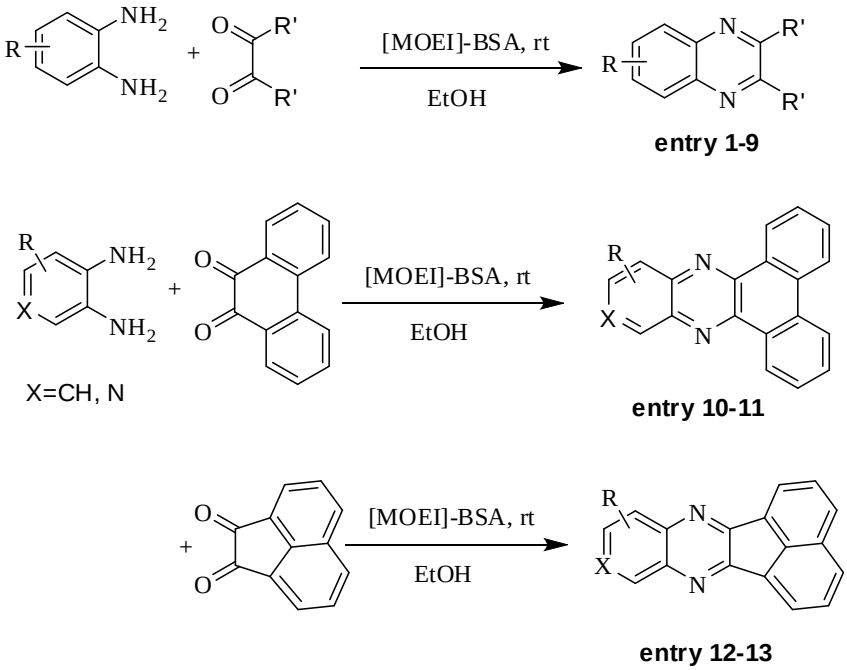
Moreover, these compounds have also been used for the preparation of various dyes [9], organic semi-conductors [10], efficient electroluminescent materials [11-12] and DNA cleaving agents [13].

The condensation of 1,2-diamines with 1,2-diketones has been used as a useful synthetic route for quinoxalines synthesis. For this transformation, several catalysts and reagents have been reported, including *o*-iodoxybenzoic acid [14], Ceric (IV) ammonium nitrate [15], $Yb(OTf)_3$ [16], zirconium tetrakis (dodecylsulfate) [17], zeolites [18], sulfamic acid [19], $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ [20], $H_6P_2W_{18}O_{62}\cdot 24H_2O$ [21], LiBr [22], Zn (*L*-proline) [23], polyaniline-sulfate salt [24], and iodine in DMSO [25]. However, many of them suffer from drawbacks such as unsatisfactory yields, high temperatures and long reaction times. All these facts clearly demonstrate the importance of developing new, efficient and versatile procedures for the preparation of this class of compounds.

As a part of our research interest towards the development of efficient and environmentally benign synthetic methodologies using eco-friendly conditions [22,23] we report here the synthesis of quinoxalines from aryl *o*-phenylenediamines and various 1,2-diketones in the presence of catalytic amount of [MOEI]-BSA as a solid acid catalyst in EtOH at room temperature (Scheme 1).



Scheme 1. Quinoxaline synthesis using [MOEI]-BSA.

2. Experimental

2.1. General

All products are known and their structures were identified by comparison of their IR, ^{1}HNMR, ^{13}CNMR data and also melting points with those of the authentic samples. IR spectra of the compounds were obtained on a Perkin Elmer spectrometer version 10.03.06 using a KBr disk.^{1}HNMR Spectra were recorded on an 400 MHz FT-NMR Spectrometer in DMSO-d_6 as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard. Reaction progress was followed by TLC using silica gel SILG/UV 254 plates. All chemicals were purchased from Merck or Fluka Chemical Companies.

2.2. Preparation of catalyst ([MOEI]-BSA)

A 50 mL suction flask was equipped with a constant pressure dropping funnel. The gas outlet was connected to a vacuum system through water adsorbing solution and an alkali trap. Boric acid (1.55 g, 25 mmol) was charged in the flask and chlorosulfonic acid (8.74 g, ca. 5 mL, 75 mmol) was added drop wise over a period of 1 h at room temperature under N_2(g). Hydrogen chloride evolved immediately. After completion of the addition, the mixture was shaken for 85 min, while the residual HCl was eliminated by suction. Then, the liquid form of 1-methyl-3-(2-hydroxyethyl)-1H-imidazol-3-ium chloride (40 mmol) was added to the mixture within a 45-60 minute. Finally, a grayish solid material was obtained in 99% yield.

2.3. General procedure for the synthesis of quinoxalines

A mixture of various diamines (1 mmol) and 1,2-dicarbonyl compound (1 mmol) in absolute ethanol (10 ml) was stirred at room temperature in the presence of catalytic amount of Bronsted acidic ionic liquid [MOEI]-BSA (0.0086 g, 1 mol%). The progress of the reaction was monitored by TLC. After the completion of the reaction, H_2O (20 mL) was added to the reaction mixture and was allowed to stand at room temperature for 1 h. The reaction mixture was filtered to recover the catalyst and the filtrate was concentrated under vacuum. The crude product was purified by silica gel column chromatography (*n*-hexan:Ethylacetate, 20:1) to give the pure product.

Selected spectral data

*2,3-Diphenylquinoxaline(**1Q**)*:

White solid; m.p.= 125-127 °C; FT-IR (KBr): $\bar{\nu}$ = 1556; ^{1}HNMR (300 MHz, $CDCl_3$): δ= 7.34 (bs, 6H, Ar-H), 7.54 (bs, 4H, Ar-H), 7.74 (bs, 2H, Ar-H), 8.2 (bs, 2H, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$): δ= 128.3, 128.9, 129.1, 129.9, 130.1, 138.9, 141.1, 153.384; MS: *m/z* = 282 (M^+).

*6-Methyl-2,3-diphenylquinoxaline(**2Q**)*:

Brown solid; m.p.= 113-115 °C; FT-IR (KBr): $\bar{\nu}$ =1619 (stretching C=N); ^{1}HNMR (300 MHz, $CDCl_3$): δ= 2.61 (s, 3H, Ar-CH_3), 7.35 (s, 6H, Ar-H),

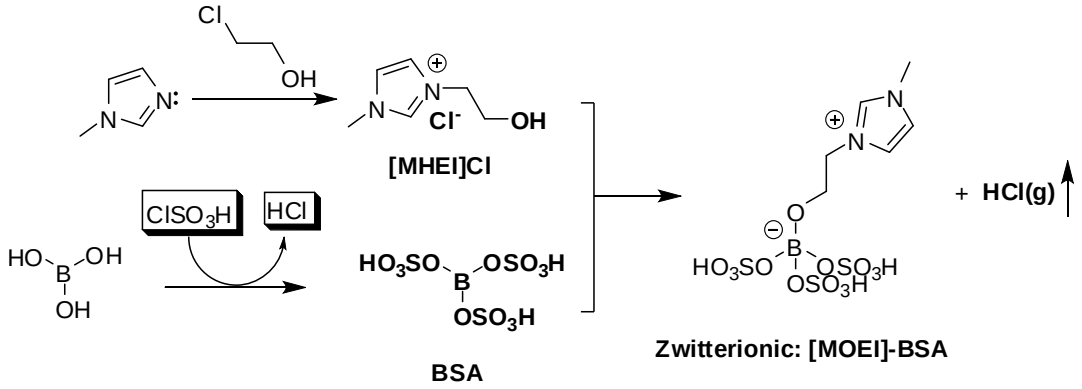
7.55 (d, *J*=6.48, 4H, Ar-H), 7.60 (s, 1H, Ar-H), 7.98 (s, 1H, Ar-H), 8.09 (d, *J*=8.4, 1H, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$): δ= 21.9, 128.0, 128.2, 128.7, 128.7, 129.9, 129.9, 132.3, 139.2, 139.728, 140.5, 141.3, 152.5, 153.3; MS: *m/z* = 296 (M^+).

*6-Nitro-2,3-diphenylquinoxaline(**4Q**)*

Red solid; m.p.= 185-187 °C, FT-IR (KBr): $\bar{\nu}$ =1656 (stretching C=N); ^{1}HNMR (300 MHz, $CDCl_3$): δ= 7.38 (bs, 6H, Ar-H), 7.56 (bs, 4H, Ar-H), 8.28 (bs, 1H, Ar-H), 8.45 (bs, 1H, Ar-H), 9.02 (bs, 1H, Ar-H); ^{13}CNMR (75 MHz, $CDCl_3$): δ=123.3, 125.5, 128.450, 129.7, 129.8, 129.9, 130.7, 137.9, 139.9, 143.4, 147.8, 155.6, 156.2; MS: *m/z* = 327 (M^+).

3. Results and Discussion

Recently, we reported the application of 1-methyl-3-(2-(sulfooxy) ethyl) -1*H*- imidazol-3-ium chloride [MSEI]Cl in preparation of 1,4-dihydropyridines [26] and Hantzsch reaction [27]. 1-Methyl-3-(2-oxyethyl)-1*H*-imidazol-3-ium-borate sulfonic acid [MOEI]-BSA was easily prepared by addition of 1-methyl-3-(2-(hydroxy)ethyl)-1*H*-imidazol-3-ium chloride [26] to boron sulfonic acid [28,29] at room temperature. This reaction was easy and clean. The HCl gas evolved from the reaction vessel immediately (Scheme 2). At the first step, the effect of catalyst amount on the condensation reaction of benzil and *o*-phenylene diamine was studied and the results were summarized in Table 1.



Scheme 2. Synthesis of [MOEI]-BSA as a catalyst.

Table 1. The Optimization of reaction conditions in the synthesis of quinxaline.

Entry	Catalyst amount (mol%)	Time (min)	Yield(%)[c]
1	-	130	88
2	SiO_2	120	83
3	0.5[a]	130	92
4	1[a]	37	99
5	1[b]	63	91
6	1.5[a]	63	86
7	2[a]	82	89
8	3[a]	120	89
9	7[a]	70	45
10	10[a]	40	81
11	15[a]	60	61

[a]Catalyst=[MOEI]-BSA
[b]BSA:SiO_2 (1:2)
[c]Yield of isolated products

The solvent effect on the model reaction was also investigated. According to the results in Table 2, ethanol was found to be the best solvent for this purpose.

Under the optimized reaction conditions, the reaction was performed using various 1,2-diamines and 1,2-dicarbonyl compounds. As shown in Table 3, various 1,2-diketones bearing electron-donating or electron-withdrawing groups reacted with different diamines to afford their corresponding quinoxalines in excellent yields.

In order to show the validity of our work, a comparison of the current catalyst with those reported in literature has been presented in Table 4.

Table 2. Solvent effect on the synthesis of quinoxalines[a].

Entry	Solvent (10 ml)	Time (min)	Yield[b] (%)
1	H_2O	540	60
2	EtOH:H_2O (1:1)	15	60
3	EtOH:H_2O (7:3)	25	81
4	EtOH:H_2O (9:1)	35	86
5	EtOH	35	100

[a]*o*-phenylenediamine (1mmol), benzil (1.0 mmol) at room temperature.
[b]Isolated yields.

Table 3. [MOEI]-BSA catalyzed quinoxalines synthesis[a].

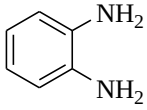
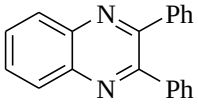
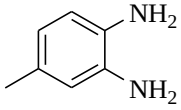
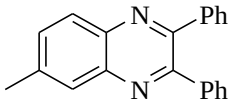
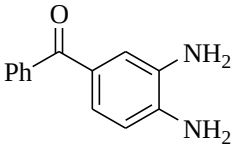
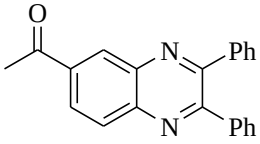
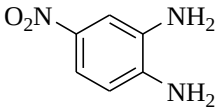
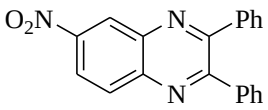
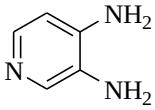
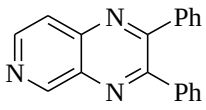
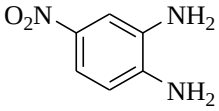
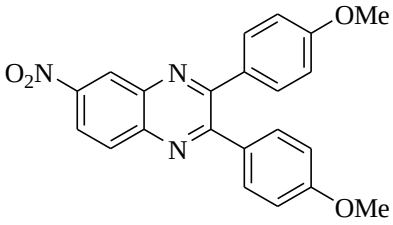
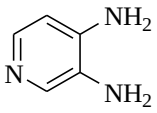
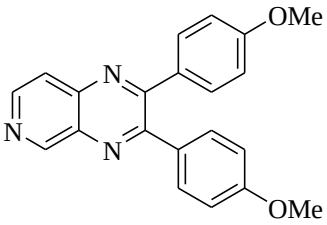
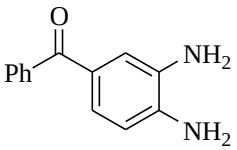
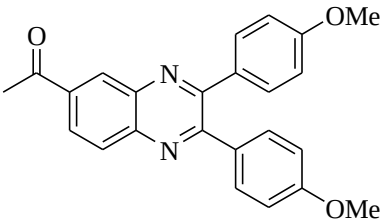
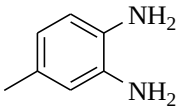
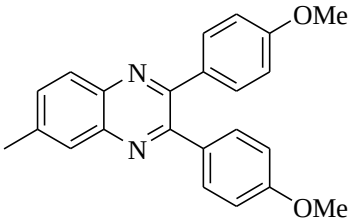
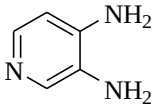
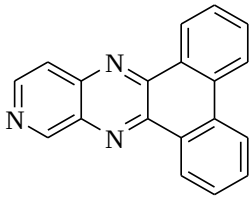
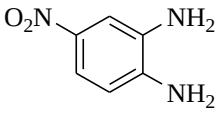
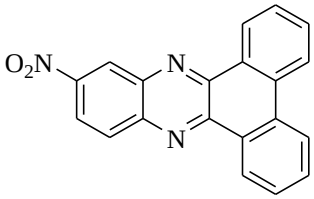
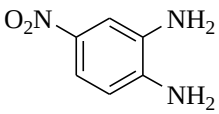
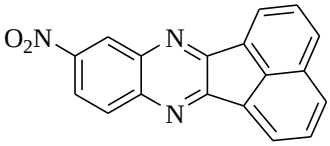
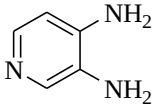
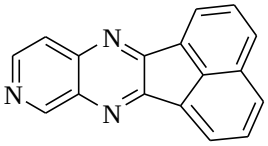
Entry	Diamine	Product (Q)	Time (min)	Yield[b] (%)	Found m.p. (°C)	Reported m.p. (°C)	Ref.
1			30	99	124-126	128-129	[31]
2			480	96	112-113	116-117	[32]
3			300	100	137-139	139-140	[33]
4			292	92	187-189	185-187	[31]
5			25	90		127-128	[27]
6			27	90	188-189	192-194	[34]

Table 3. *(Continued).*

7			24	95		120-122	[30]
8			210	100		145-147	[30]
9			300	100	122-123	129-131	[32]
10			360	80		159-162	[27]
11			290	75		259-260	[30]
12			150	80		318-319	[30]
13			210	70		225-227	[27]

[a]Reaction conditions: 1,2-diamine (1 mmol), 1,2-diketone (1 mmol), catalyst (1 mol%), in ethanol at room temperature.
[b]Isolated yield.

The catalyst is a powder that can be stored at room temperature for several months without losing its catalytic potential. It is a low-cost solid acid catalyst that can be used instead of commercial expensive samples. Also, the catalyst can be recycled from the reaction mixture by simple filtration and reused several times as a green catalyst. Proposed mechanism of catalyst is indicated in Scheme 3.

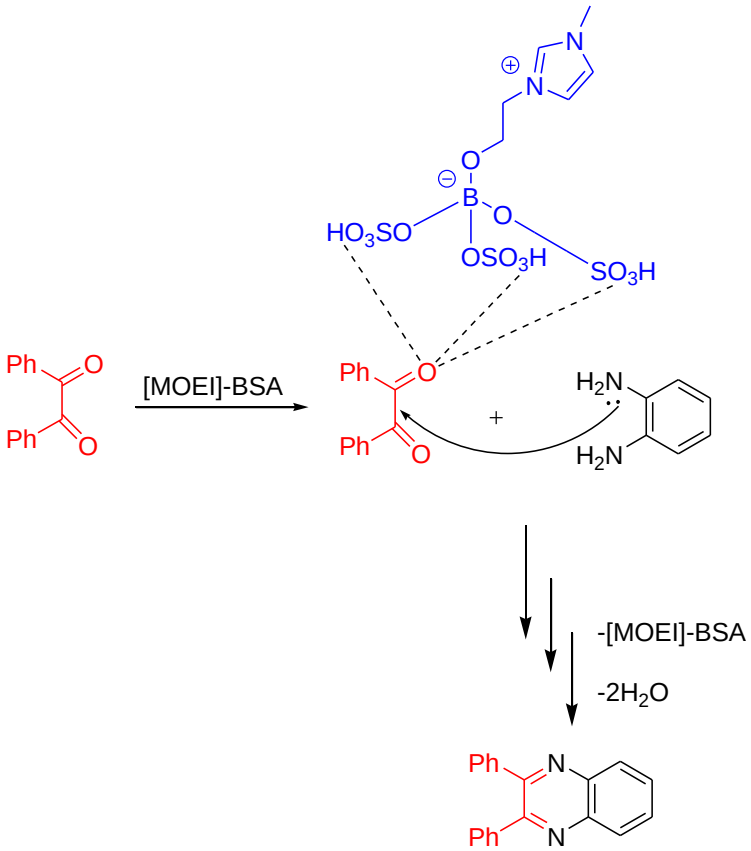
4. Conclusions

In conclusion, a novel, heterogeneous, strong and highly effective acid catalyst for the synthesis of quinoxalines has been reported. The advantages of this method are efficiency, generality, excellent yield, short reaction time, simplicity, easy work-up and reusability.

Table 4. Synthesis of 2,3-diphenyl quinoxaline in the presence of different catalysts.

Entry	Catalyst (mol %)	Time (min)	Solvent	Yield[a] (%)	Ref.
1	Sulfamic acid	5	CH_3OH	100	[19]
2	$H_4SiW_{12}O_{40}$ (1)	60	H_2O	96	[35]
3	SBA-Pr-SO_3H	5	CH_2Cl_2	98	[36]
4	Montmorillonite K-10	150	H_2O	100	[37]
5	Silica Bonded *S*-Sulfonic Acid	5	EtOH/H_2O	96	[38]
6	Iodine	50	DMSO	90	[31]
7	PEG-400	60	Solvent Free	93	[39]
8	This Work	30	EtOH	100	-

[a]Isolated yield.



Scheme 3. Proposed mechanism of catalyst.

Acknowledgment

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