Chemical Methodologies

journal homepage: http://chemmethod.com

Original Research article

# Silica Boron Sulfonic Acid as a New and Efficient Catalyst for the Green Synthesis of Quinoxaline Derivatives at Room Temperature

Sami Sajjadifar*, Issa Amini, Tayebeh Amoozadeh

*Department of Chemistry, Payame Noor University, PO BOX 19395-4697 Tehran, Iran*

ARTICLE INFORMATION

Received: 10 June 2017
Received in revised: 25 July 2017
Accepted: 10 August 2017
Available online: 24 August 2017

DOI:
10.22631/chemm.2017.88920.1000

KEYWORDS

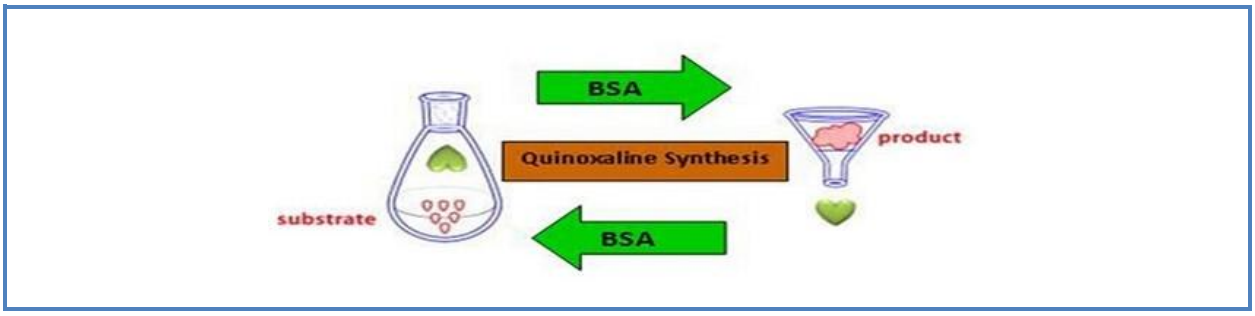
Boron sulfonic acid (BSA)
Quinoxaline synthesis
1,2-Diamine, α-diketone
Green chemistry

ABSTRACT

A simple, highly efficient and green procedure for the condensation of aryl and alkyl 1,2-diamines with α-diketones in the presence of catalytic amount of silica boron sulfonic acid (SBSA) at room temperature is described. By Using this method, quinoxaline derivatives as biologically interesting compounds are produced in high to excellent yields and short reaction times.

*Corresponding author, email: ss_sajjadifar@yahoo.com(S. Sajjadifar).
*Department of Chemistry, Payame Noor University, PO BOX 19395-4697 Tehran, Iran*
Tel.: +9884 32228316; Fax: +988432226101.

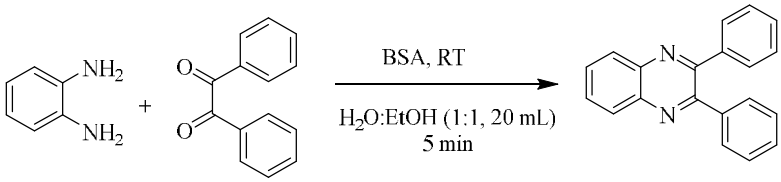
## Graphical Abstract




## Introduction

Quinoxaline derivatives have become increasingly important in the past few years because they have been proven to be extremely useful intermediates for the preparation of new biological materials [1-2]. Quinoxaline ring is a part of a number of antibiotics such as echinomycin, levomycin, and actinomycin, which are known to inhibit the growth of Gram-positive bacteria and are also active against various transplantable tumors [3].

Therefore, a number of synthetic strategies have been developed for the preparation of quinoxaline derivatives [4]. One of the most common methods is the condensation of 1,2-diamines with 1,2-dicarbonyl compounds in refluxing ethanol or acetic acid for 2–12h giving 34–85% yields [5]. Later, many improved methods have been reported for the synthesis of quinoxaline derivatives in the presence of various catalysts, such as Zn/L-proline [6], bismuth(III) triflate [7], metal hydrogen sulfates [8], molecular iodine [9], silica-bonded S-sulfonic acid [10], cerium(IV) ammonium nitrate [11], stannous chloride [12], zirconium tetrakis(dodecylsulfate) [13], amidosulfonic acid [14], montmorillonite K-10 [15], polyanilinesulfate salt [16], niobium pentachloride [17], Wells- Dawson heteropolyacid [18], ionic liquid [19], citric acid [20], $ZrO_2$/MxOy (M = Al, Ga, In, and La) mixed metal oxides supported on MCM-41 mesoporous molecular sieves [21]. The condensation has also been accomplished under catalyst-free conditions, but this needs microwave heating [22] in industry. An efficient catalyst-free protocol for the synthesis of quinoxaline derivatives was reported under ultrasound irradiation [23]. In recent years, significant articles have appeared reporting solid-state reactions by grinding [24-25]. Herein, we report a green, efficient, and convenient procedure for the synthesis of quinoxaline derivatives by the condensation of 1,2-diketones and 1,2-diamines using BSA as efficient and new catalyst at room temperature (Scheme 1).




Scheme 1. Quinoxaline synthesis by using BSA

In continuation of our studies on the application of BSA in organic synthesis [26-31], we describe our successful results that led to an extremely convenient method for quinoxalines synthesis in the presence of $B(HSO_4)_3$ as a solid acid catalyst in green condition and high isolated yields.

## Materials and Methods

### General

All reagents were purchased from Merck Fine Chemicals and were used without further purification. IR spectra of the compounds were obtained on a Shimadzu IR-435 spectrometer using a KBr disk. The $^1H$ nuclear magnetic resonance ($^1H$ NMR) spectra were recorded on a Bruker AQS 300 Avance instrument at 300 MHz in $CDCl_3$ or dimethyl sulfoxide (DMSO-$d_6$) using tetramethylsilane as an internal standard. The progress of reaction was followed by a thin-layer chromatography (TLC) using silica gel SILG/UV 254 and 365 plates. New compounds and were characterized by IR, $^1H$ NMR, $^{13}C$ NMR, Mass spectroscopic data and their melting points.

### General procedure for quinoxaline synthesis

1,2-diamine (1 mmol) was added to a mixture of α-diketone (1 mmol), boron solfonic acid/$SiO_2$ (0.03 g of mix., 0.03 mmol BSA) and EtOH/$H_2O$ [1/1 (v/v), 20 mL] in a 50 mL round-bottomed flask The resulting mixture was stirred at room temperature for the times reported in Table 2. Then, $H_2O$ (20 mL) was added to the reaction mixture and was allowed to stand at room temperature for 1 h. During this time, crystals of the pure product formed and were collected by filtration and dried under air.

### Preparation of boron sulfonic acid (BSA) [26-39]

A 50 mL suction flask was equipped with a constant pressure dropping funnel. The gas outlet was connected to a vacuum system through an adsorbing solution (water) 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 in 5 ml $CH_2Cl_2$) was added dropwise over a period of 1 h at room temperature under $N_2$(g). HCl evolved immediately. After completion of the addition, the mixture was shaken for 85 min, while the residual HCl was eliminated by suction. Then the mixture was washed with diethyl ether to remove

the unreacted chlorosulfonic acid.Then, we added 14.4 g silica gel and stirred them all. Finally, dried and a grayish solid material was obtained (21.6 g, 95.66%).$^1$HNMR of BSA in Acetone-D6 show δ=12.218. After isolation of the product, the filtrate was extracted with $CHCl_3$ (2×30 mL) and collect as organic layer. The aqueous layer (including oxalic acid) was separated, and its solvent was evaporated to obtain pure boron sulfonic acid. The recycled catalyst was used for the next run under identical reaction conditions.

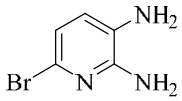
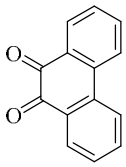
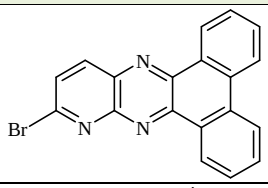
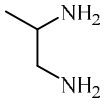
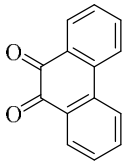
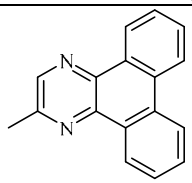
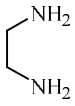
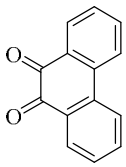
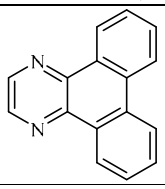
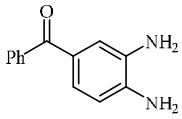
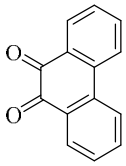
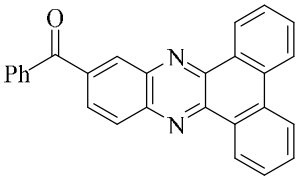
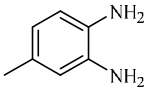
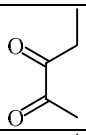
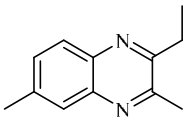
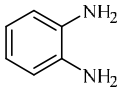
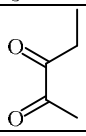
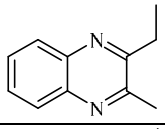
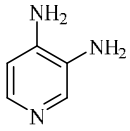
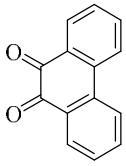
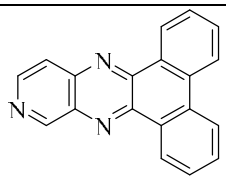
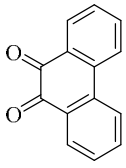
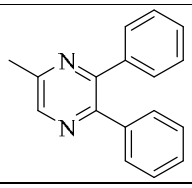
## Results and Discussion

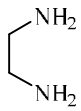
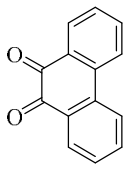
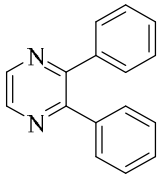
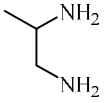
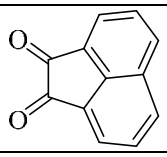
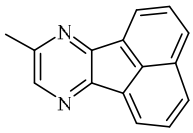
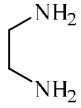
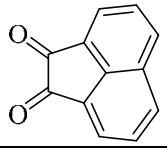
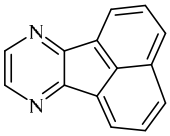
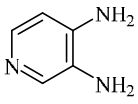
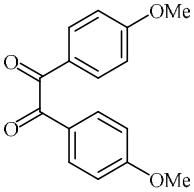
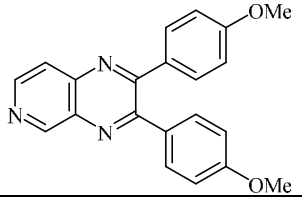
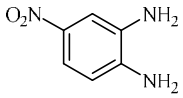
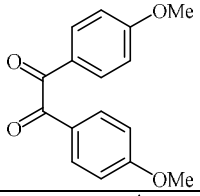
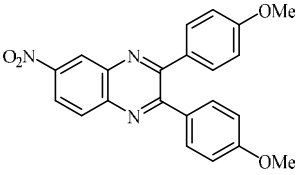
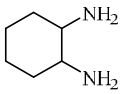
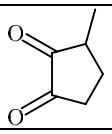
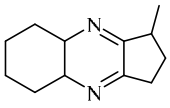
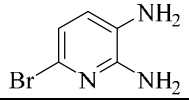
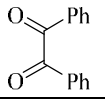
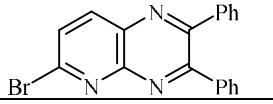
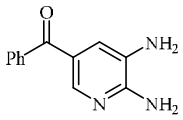
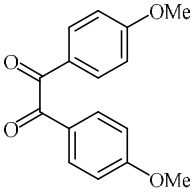
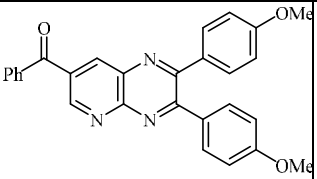
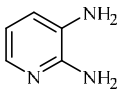
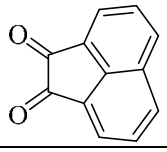
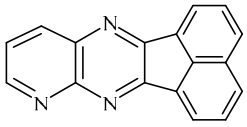
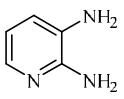
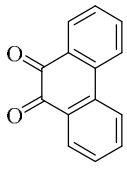
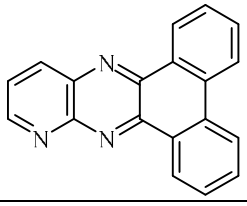
To optimize and select the best solvent for the reaction, the synthesis of quinoxaline1a was examined as a model in different solvents (Table 1). Higher yields and shorter reaction times were obtained when the reaction was carried out in EtOH:$H_2O$ (1:1). Thus, EtOH:$H_2O$ (1:1) was used as a reaction media for all reactions. Water is a desirable solvent for chemical reactions for a host of reasons such as cost, safety and environmental concerns. When 2,3- and 3,4-diaminopydrine derivatives reacted with 1,2-diketones, the yield decreased and reaction condition was harder( Table 2, Entries 1 and 7).In this research, *o*-phenylenediamines and 1,2-dicarbonyl compounds with electron-donating or electron-withdrawing groups were used. As indicated in the Table 2 both electron rich and electron deficient 1,2-dicarbonyl compounds worked pretty well, mostly leading to high yields of products.

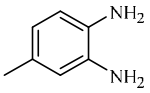
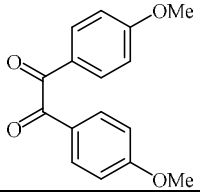
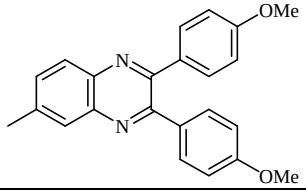
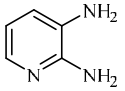
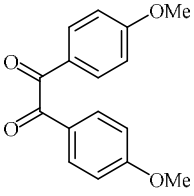
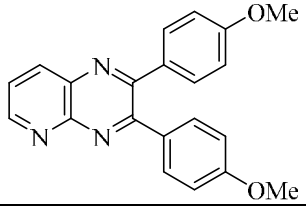
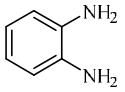
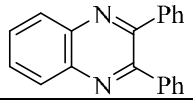
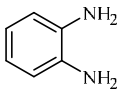
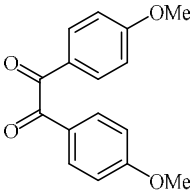
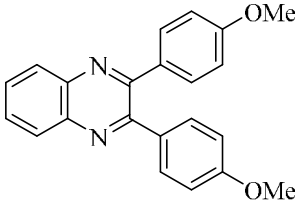
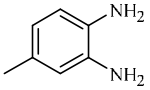
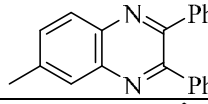
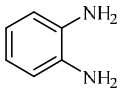
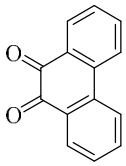
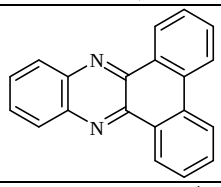
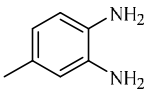
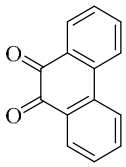
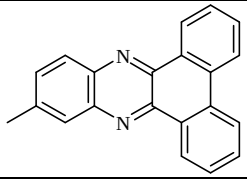
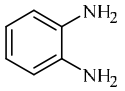
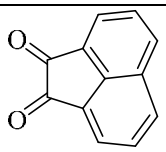
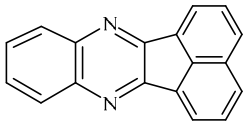
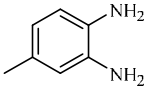
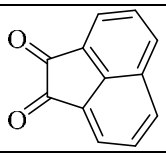
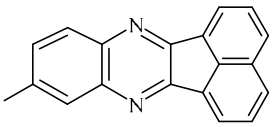
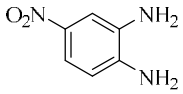
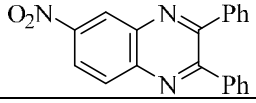
Table 1. The condensation of 1,2-diamine 1a (1 mmol) with benzyl 2b (1 mmol) in the presence of different ratios of BSA(0.03 mmol, 3 mol%) at room temperature

| Entry | solvent | % BSA | Time (min) | Yield (%) |
|---|---|---|---|---|
| 1 | EtOH | 5 | 30 | 78 |
| 2 | EtOH | 10 | 30 | 78 |
| 3 | $CH_3CN$ | 5 | 60 | 72 |
| 4 | $CH_3COOEt$ | 5 | 45 | 80 |
| 5 | EtOH:$H_2O$ ( 1:1) | 15 | 10 | 81 |
| 6 | EtOH:$H_2O$ ( 1:1) | 10 | 10 | 85 |
| 7 | EtOH:$H_2O$ ( 1:1) | 5 | 10 | 85 |
| 8 | EtOH:$H_2O$ ( 1:1) | 3 | 5 | 98 |
| 9 | EtOH:$H_2O$ ( 1:1) | 2 | 25 | 87 |
| 10 | EtOH:$H_2O$ ( 1:2) | 10 | 20 | 85 |
| 11 | EtOH:$H_2O$ ( 1:2) | 5 | 20 | 85 |
| 12 | EtOH:$H_2O$ ( 1:2) | 3 | 30 | 87 |
| 13 | EtOH:$H_2O$ ( 2:1) | 3 | 25 | 84 |
| 14 | $H_2O$ | 10 | 30 | 78 |
| 15 | $H_2O$ | 5 | 30 | 78 |
| 16 | $CH_2Cl_2$ | 5 | 80 | 45 |
| 17 | $CHCl_3$ | 5 | 80 | 50 |

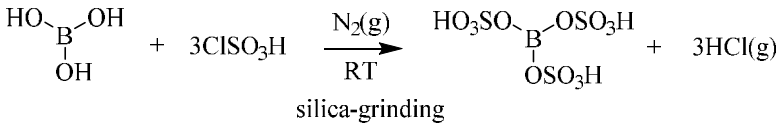
Table 2. Quinoxaline synthesis by using BSA (3 mol %) at room temperature

| Entry | Diamine (DA) | Diketone (DK) | Product (Q) | Time (min) | Yield % | M.p°C |
|---|---|---|---|---|---|---|
| 1 |  |  |  | 12 h | 96 | 216-218 |
| 2 |  |  |  | 5 | 94 | 124-126 |
| 3 |  |  |  | 10 | 95 | 184-186 |
| 4 |  |  |  | 40 | 96 | 245-247 |
| 5 |  |  |  | 10 | 90 | Liquid |
| 6 |  |  |  | 5 | 98 | 58-61 |
| 7 |  |  |  | 24h | 89 | 212-215 |
| 8 |  |  |  | 5 | 98 | 121-123 |

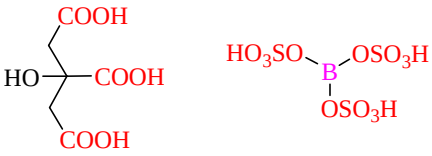
| | | | | | | |
|---|---|---|---|---|---|---|
| 9 |  |  |  | 10 | 97 | 161-164 |
| 10 |  |  |  | 5 | 98 | 68-70 |
| 11 |  |  |  | 5 | 98 | 114-116 |
| 12 |  |  |  | 7h | 93 | 120-122 |
| 13 |  |  |  | 3h | 80 | 188-189 |
| 14 |  |  |  | 45 | 87 | Oil |
| 15 |  |  |  | 4.45h | 90 | 143-145 |
| 16 |  |  |  | 41 | 86 | 145-147 |
| 17 |  |  |  | 5.5h | 90 | 225-227 |
| 18 |  |  |  | 20 | 93 | 259-260 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 19 |  |  |  | 5 | 90 | 109-111 |
| 20 |  |  |  | 2.45h | 90 | 109-111 |
| 21 |  |  |  | 3 | 98 | 125-127 |
| 22 |  |  |  | 30 | 89 | 134-136 |
| 23 |  |  |  | 15 | 97 | 113-11 |
| 24 |  |  |  | 3 | 96 | 224-226 |
| 25 |  |  |  | 5 | 97 | 219-221 |
| 26 |  |  |  | 10 | 99 | 241-242 |
| 27 |  |  |  | 10 | 99 | 231-233 |
| 28 |  |  |  | 12h | 93 | 185-187 |

Boron sulfonic acid was easily prepared by adding chlorosulfonic acid to boric acid under $N_2$ atmosphere at room temperature. This reaction was easy and clean, because HCl gas was evolved from the reaction vessel immediately (Scheme 2) [32].



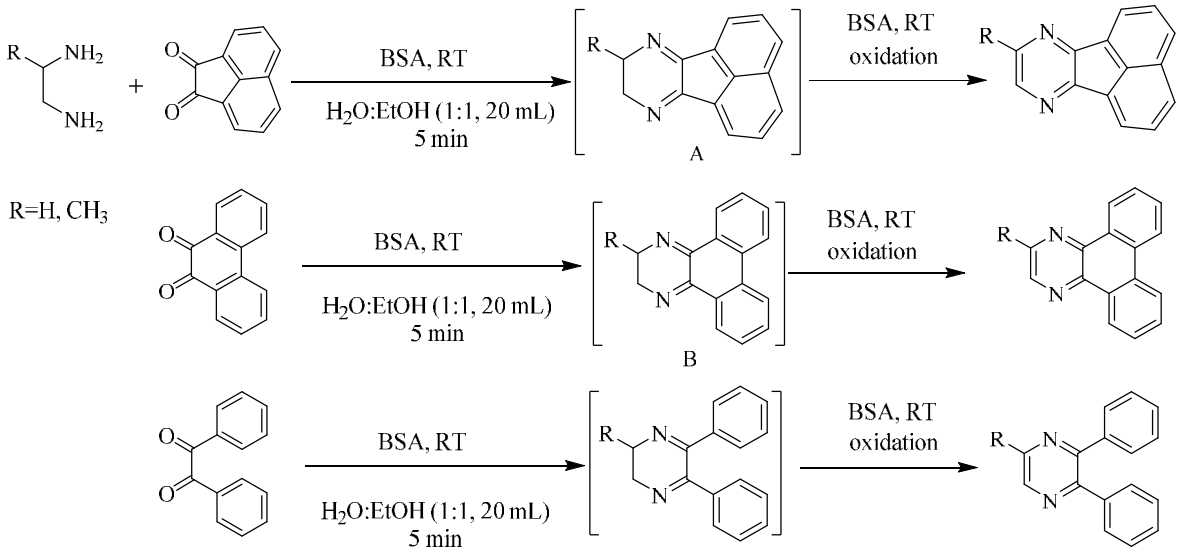

Scheme 2. Silica supported BSA production under $N_2$ atmosphere at room temperature




(A) (B)

Scheme 3 A: Citric acid Structure and B: BSA Structure

Oxidation of A, B and C were accrued in presence of BSA catalyst (Scheme 3-B) but when citric acid (Scheme 3-A) was used as aweaker organo catalyst in similar condition, only A, B and C were obtained (Scheme 4). We think that the BSA acts as an acidic catalyst and oxidant agent (-$SO_3H$ group). Similarly, when BSA was used as a catalyst for the synthesis of benzimidazole derivatives, oxidation of 2,3-dihydro-2-phenyl-1H-benzo[d]imidazole was occurred to corresponding product 2-phenyl-1H-benzo[d]imidazole.




Scheme 4. Oxidation in presence of BSA

In order to further validate our work, the current protocol was compared tothe data in the literature based on the, temperature, reaction time, percentage yield, and loading catalyst.

The efficiency of various catalysts in synthesis of quinoxaline derivatives has been compared in Table 3. BSA as a catalyst afforded good results in comparison to the other catalysts.

Table 3.Comparison of catalytic ability of catalysts

| Catalyst | Time | Catalyst loading | Yield[c] (%) | [Ref.] |
|---|---|---|---|---|
| Citric acid | 1 min | 10 mol% | 94 | [20] |
| SBSSA[b] | 5 min | 3.4 mol% | 96 | [10] |
| DMSO, $I_2$ | 35 min | 10 mol%) | 95 | [9] |
| Bentonite Clay K-10 | 20 min | 2.5 g | 95 | [40] |
| BSA | 3 min | 3 mol% | 98 | This work |

[a]Modelreation is entry 21.
[b]Silica Bonded S-Sulfonic Acid
[c]Isolated yield.

To sum up our discussion, we have developed the use of BSA supported by silica gel as an inexpensive, easy to handle, non-corrosive and environmentally benign catalyst for the synthesis of quinoxalines from aromatic *o*-diamines and 1,2-dicarbonyl compounds. The advantages of the present procedure are simplicity of operation, short reaction times as compared to the other procedures for the preparation of quinoxaline derivatives, and the high yields of products. Moreover, in this reaction the catalyst can be recovered by filtration.

## Acknowledgements

The authors gratefully acknowledge partial support of this work by Payame Noor University (PNU) of Iran.

## References

[1] Sakata G., and Makino K., Kuraswa Y. *Heterocycles*, 1988, 27:2481

[2] Kim Y.B., Kim Y.H., Park J.Y., Kim S.K. *Bioorg. Med. Chem. Lett.*, 2004, 14:541

[3] Dell A., William D.H., Morris H.R., Smith G.A., Feeney J. *J. Am. Chem . Soc.*, 1975, 97:2497

[4] Brown D.J. *In The Chemistry of Heterocyclic Compounds*; AQ2 Taylor, E. C., Wipf, P., Eds.; Wiley: New Jersey, 2004

[5] Porter AEA. *In Comprehensive Heterocyclic Chemistry*; Katritsky AR, Rees CW, Eds.; Pergamon: Oxford, 1984, p 157

[6] Heravi M.M., Tehrani M.H., Bakhtiari K., Oskooie H.A. *Catal. Commun.*, 2007, 8:1341

[7] Yadav J.S., Reddy B.V.S., Premalatha K., Shankar K.S. *Synthesis*, 2008, 23:3787

[8] Niknam K., Zolfigol M.A., Tavakoli Z., Heydari Z. *J. Chin. Chem. Soc.*, 2008, 55:1373

[9] Bhosale R.S., Sarda S.R., Ardhapure S.S., Jadhav W.N., Bhusare S.R., Pawar R.P. *Tetrahedron Lett.*, 2005, 46:7183

[10] Niknam K., Saberi D., Mohagheghnejad M. *Molecules.*,2009, 14:1915

[11] More S.V., Sastry M.N.V., Yao C.F. *Green. Chem.*, 2006, 8:91

[12] Shi D.Q., Dou G.L., Ni S.N., Shi J.W., Li X.Y. *J. Heterocycl. Chem.*, 2008, 45:1797

[13] Hasaninejad A., Zare A., Zolfigol M.A., Shekouhy M. *Synth. Commun.*, 2009, 39:569

[14] Li Z.J., Li W.S., Sun Y.J., Huang H., Ouyang P.K. *J. Heterocyc l. Chem.*, 2008, 45:285

[15] Huang T.K., Wang R., Shi L., Lu X.X. *Catal. Commun.*, 2008, 9:1143

[16] Srinivas C., Kumar C., Rao V.J., Palaniappan S. *J. Mol. Catal A: Chem.*, 2007, 265:227

[17] Hou J.T., Liu Y.H., Zhang Z.H. *J. Heterocycl Chem.*, 2010, 47:703

[18] Heravi M.M., Bakhtiari K., Bamoharram F.F., Tehrani M.H. *Monatsh. Chem.*,2007, 138:465

[19] Potewar T.M., Ingale S.A., Srinivasan K.V. *Synth.Commun.*,2008, 38:3601

[20] Mahesh R., Dhar A.K., Tara Sasank T.V.N.V., Thirunavukkarasu S., Devadoss T. *Chin . Chem. Lett.*, 2011, 22:389

[21] Ajaikumar S, Pandurangan A. *Appl. Catal. A: Gen.*, 2009, 357:184

[22] Zhao Z., Wisnoski D.D., Wolkenberg S.E., Leister W.H., Wang Y., Lindsley C.W. *Tetrahedron Lett.*,2004, 45:4873

[23] Guo W.X., Jin H.L., Chen J.X., Chen F., Ding J.C., Wu H.Y. *J. Braz. Chem. Soc.*, 2009, 8:1647

[24] Tanaka K., Kishigami S., Toda, F. *J. Org. Chem.*,1991, 56:4333

[25] Kumar S., Sharma P., Kapoor K.K., Hundal M.S. *Tetrahedron*, 2008, 64:536

[26] Sajjadifar S. *Int. J. Chem. Tech. Res.*, 2013, 5:385

[27] Sajjadifar S., Khosravani E., Shiri S. *Int. J. Chem. Tech. Res.*,2013, 5:1969

[28] Sajjadifar S., Rezayati S. *Int. J. Chem.Tech. Res.*, 2013, 5:1964

[29] Sajjadifar S., Mirshokraie S.A., Javaherneshan N., Louie O. *Am. J. Org. Chem.*, 2012, 2:1

[30] Sajjadifar S. *Am. J. Org. Chem.*, 2012, 2:116

[31] Sajjadifar S., Louie O. *J. Chem.*, 2013, 2003:No. 674946 (2013). (http://www.hindawi.com/journals/chem/2013/674946/).

[32] Kiasat A.R., Fallah-Mehrjardi M. *J. Braz. Chem. Soc.*, 2008, 19:1595

[33] Khazaeia A., Zolfigol M.A., Mokhlesi M., DerakhshanPanah F., Sajjadifar S. *Helvetica Chimica Acta*,,2012, 95:106

[34] Madje B.R., Ubale M.B., Bharad J.V., Shingare M.S. *Bull. Cataly. Soci. Ind.*,2011, 9:19

[35] Mosslemin M.H., EshaghiMovahed A. *E-Journal of Chemistry*,2012, 9:301

[36] Parhami A., Khalafi-Nezhad A., Mowlazadeh Haghighi S., Bargebid R., Zare A., Moosavi-Zare A.R., Nikrooz M. *ARKIVOC*, 2012, ix:111

[37] Sedighinia E., ZahedSargoli M. *Asian J. Chem*., 2012, 23:1456

[38] Zolfigol M.A., Vahedi H., Massoudi A.H., Sajjadifar S., Loui O., Javaherneshan, N. *Clinical Biochemistry*, 2011, 44:S219

[39] Zolfigol M.A., Khazaei A., Vahedi H., Mokhlesi M., Sajadifar S., Pirveysian M. *Sulfur, and Silicon and the Related Elements*,2012, 187:295

[40] Hasaninejad A., Zare A., Shoekouhy M., Moosavi-Zare A.R. *E-Journal of Chemistry*, 2009, 6:S247

How to cite this manuscript: Sami Sajjadifar*, Issa Amini, Tayebeh Amoozadeh. Silica Boron Sulfonic Acid as a New and Efficient Catalyst for the Green Synthesis of Quinoxaline Derivatives at Room Temperature. Chemical Methodologies 1(1), 2011, 1-11. DOI: 10.22631/chemm.2017.88920.1000.