
Green SDS-assisted synthesis of quinoxaline derivatives in the water

Elham Ghobadi, Marjan Peiravi and Eskandar Kolvari*

Department of Chemistry, Semnan University

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Abstract

A simple, practical and convenient procedure for the synthesis of quinoxaline derivatives has been developed by reaction of 1,2-phenylenediamines with 1,2-diketones in the presence of sodium dodecyl sulfate (SDS) in the aqueous medium at room temperature without any organic solvent.

Keywords: Quinoxaline, Surfactant, Sodium dodecyl sulfate, Water.

*. **Corresponding Author:** Assistant Professor, Department of Chemistry, Semnan University, Semnan, Iran;
E-mail address: kolvari@semnan.ac.ir

1. Introduction

Performing organic reactions in the water has attracted much attention over the past decades due to its numerous advantages such as being considerably safe, non-toxic, environmentally friendly and cheap [1-5]. In addition, using water as solvent can facilitate access to different reactivity and selectivity patterns compared with those observed in common organic solvents due to its unique physical and chemical properties.

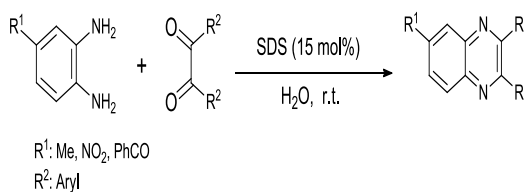
Quinoxalines and its derivatives are an important class of nitrogen-containing heterocyclic compounds and have shown a broad spectrum of biological activities such as antiviral [4], antibacterial [6], anti-inflammatory [7], and anticancer [8], which have made them privileged structures in pharmacologically active compounds. Various methods have been reported for synthesis of quinoxaline derivatives *via* a condensation process catalysed by Lewis and Bronsted acids [9-17], or using Bi, Pd(OAc)₂, and MnO₂ *via* a oxidative coupling reaction [18-20].

2. Experimental procedure

To a mixture of *o*-phenylenediamine (1.0 mmol, 282 mg) in water (3 mL) was added benzil (1.0 mmol, 210 mg) and SDS (0.15 mmol, 43 mg) at room temperature and the mixture was stirred vigorously at r.t. for 2 h. After completion of reaction (indicated by TLC), the precipitated solid which is almost a pure 2,3-diphenylquinoxaline was filtered and washed with cold water. Further purification was carried out by crystallization from hot ethanol to afford a white crystalline product (268 mg; 95%), mp 126–128 °C, which showed satisfactory analytical and spectroscopic properties.

3. Results and discussion

As a part of our continued activities surfactant-assisted reactions [21-22], we report here for the first time a simple method for the synthesis of quinoxalines through the reactions of *o*-phenylenediamine with 1,2-diketones in aqueous media, using SDS, without any catalyst (Scheme 1).



We started this synthesis by examining the reaction of *o*-phenylenediamine (1 mmol) with benzil (1 mmol) as a model reaction in different solvents using 0.1 mmol of SDS. As shown in Table 1, among the various solvents, water is obviously the best choice for this reaction. The use of SDS allowed the direct conversion of *o*-phenylenediamine into the corresponding quinoxaline in a yield of 93% in water (3 mL) at room temperature (Table 1, Entry 1).

To find the optimum amount of SDS, the yields of the model reaction using various amounts of SDS (5, 10, 15 and 20 mol%) were obtained and compared. The results were summarized in Table 2. From these results, it can be concluded that the yields of reaction in the presence small amount of SDS were good to high and the optimum amount of surfactant was 15 mol%, the desired product was obtained in 95% yield within 2 h. It is noteworthy that presence of surfactant is essential for this reaction and the reaction did not occurs in the absence of SDS even after a long time (Table 2, Entry 1).

Table 1. Comparison of various solvents for the surfactant-assisted synthesis of 2,3-diphenyl quinoxaline^a

Entry	Solvent	Time (h:min)	Yield (%) ^b
1	H ₂ O	2:00	93
2	EtOH/H ₂ O (1:3)	4:00	89
3	EtOH	4:30	82
4	THF	10:00	81
5	CH ₃ CN	10:00	81

^a Reaction conditions: Benzil (1.0 mmol), *o*-phenylenediamine (1.0 mmol), sodium dodecyl sulfate (10 mol%), solvent (3 mL) ^b Isolated yields.

Table 2. Effect amount of SDS on the yield of 2,3-diphenyl quinoxaline^a

Entry	SDS (mol %)	Time (h)	Yield (%) ^b
1	0	24	---
2	5	2	91
3	10	2	93
4	15	2	95
5	20	2	95

^a Reaction conditions: Benzil (1.0 mmol), *o*-phenylenediamine (1.0 mmol), water (3 mL) ^b Isolated yields

In addition to SDS, we screened the effect of other surfactants such as cetyl trimethylammonium bromide (CTAB), tetradecyl trimethyl ammonium bromide (TTAB), dodecyl trimethyl ammonium bromide (DTAB), and Esterquat, on the time and yield of the model reaction. As shown the best result is referred to SDS (Table 3, Entry 1).

Table 3. Effect of different surfactants on the reaction time and yield of 2,3-diphenylquinoxaline^a

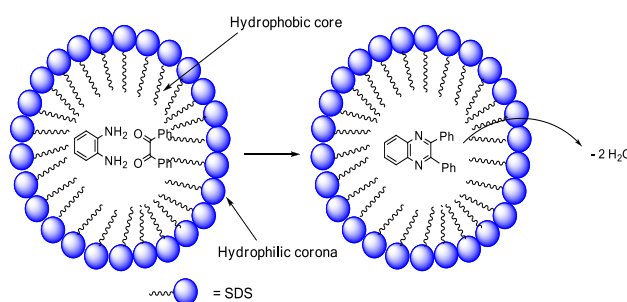
Entry	Surfactant	Time (h)	Yield (%) ^b
1	SDS	2:00	93
2	CTAB	3:30	85
3	TTAB	5:00	85
4	DTAB	4:00	86
5	Esterquat	3:00	76
6	DBSA[22]	2:00	96

^a Reaction conditions: Benzil (1.0 mmol), *o*-phenylenediamine (1.0 mmol) in the presence of 0.1 of various surfactants ^b Isolated yield

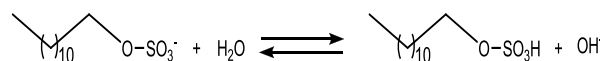
The scope and the generality of the present method was then demonstrated by the condensation of various substituted *o*-phenylenediamine with 1,2-diketones using catalytic amount of SDS in water and the results are presented in Table 4. Using water as solvent at room temperature, quinoxaline derivatives with various functional groups were obtained in 1.25–14 h with excellent yields 92–97%. Among the reactions of different *o*-phenylenediamines and 1,2-diketones, no significant distinction on the yields of target products was observed. Even the sensitive substrate α -furyl (Table 4, entries 9–11) produced the corresponding quinoxalines without any difficulty. All substrates gave their corresponding quinoxaline exclusively as a single product. *o*-phenylenediamines with electron-donating and electron withdrawing groups both participated in this reaction equally well, apparently, the nature and position of substitution on the aryl ring does not make much difference in reactivity.

Two different mechanisms can be suggested for the synthesis of quinoxalines using SDS: (i) the micelle-promoted mechanism in which the SDS micelles promotes formation of the quinoxalines in the micellar

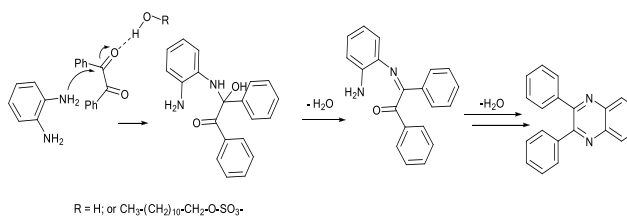
solution. *o*-Phenylenediamine and 1,2-diketone, which are both hydrophobic, are forced inside the hydrophobic core of the micelles, thus allowing the reaction to take place more easily (Scheme 2) [23], or (ii) the acid-catalyzed mechanism which water or dodecyl hydrogen sulfate, which is formed in-situ by hydrolysis of SDS in water (Scheme 3) [24], can act as protic acids and facilitate nucleophilic attack of 1,2-diamines to 1,2-diketones (Scheme 4) [25]



Scheme 2



Scheme 3



Scheme 4

Table 4. SDS assisted synthesis of quinoxaline derivatives in water^a

Entry	1,2-Diketone	1,2-Diamine	Product	Time (h:min.)	Yield (%) ^b
1	Benzil	<i>o</i> -Phenylenediamine	Quinoxaline	2:00	95
2	Benzil	4-Methylbenzene-1,2-diamine	6-Methyl-2,3-diphenylquinoxaline	1:40	96
3	Benzil	4-Nitrobenzene-1,2-diamine	6-Nitro-2,3-diphenylquinoxaline	3:00	90
4	Benzil	3,4-Diaminobenzophenone	6-Benzoyl-2,3-diphenylquinoxaline	5:00	94
5	4,4'-Dimethoxybenzil	4-Methylbenzene-1,2-diamine	2,3-Bis(4-methoxyphenyl)-6-methylquinoxaline	2:00	95
6	4,4'-Dimethoxybenzil	4-Methylbenzene-1,2-diamine	2,3-Bis(4-methoxyphenyl)-6-methylquinoxaline	1:30	97
7	Phenanthrenequinone	4-Methylbenzene-1,2-diamine	11-Methyldibenzo[a,c]phenazine	1:40	97
8	Phenanthrenequinone	3,4-Diaminobenzophenone	11-Benzoyldibenzo[a,c]phenazine	14:00	92
9	Phenanthrenequinone	<i>o</i> -Phenylenediamine	Dibenzo[a,c]phenazine	2:00	96
10	α -Furil	<i>o</i> -Phenylenediamine	2,3-Di(furan-2-yl)quinoxaline	1:35	95
11	α -Furil	4-Methylbenzene-1,2-diamine	2,3-Di(furan-2-yl)-6-methylquinoxaline	1:20	96
12	α -Furil	3,4-Diaminobenzophenone	6-Benzoyl-2,3-bis(furan-2-yl)quinoxaline	14:00	93

^a The products were characterized by spectroscopic (¹HNMR and ¹³CNMR) comparison of their spectroscopic and physical data with authentic samples synthesized by reported procedures. ^b Yields refer to pure isolated product

4. Conclusion

In conclusion, we have presented a green procedure for the synthesis of quinoxalines from *o*-phenylenediamine and 1,2-diketones in the presence of SDS in water as green solvent. The present procedure has many advantages such as mild conditions, easy operation procedures and environment friendly.

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References

- [1] R. Breslow, *Acc. Chem. Res* 1991; 24: 159
- [2] J.B.F.N. Engberts, M.J. Blandamer, *Chem. Commun.* 2001;1701
- [3] K. Manabe, Y. Mori, T. Wakabayashi, S. Nagayama, S. Kobayashi, *J. Am. Chem. Soc.* 2000; 122: 7202
- [4] M. Loriga, P. Moro, P. Sanna, G. Paglietti, S. Zanetti, *Farmaco.* 1997;52: 531.
- [5] U.M. Lindström, *Chem. Rev.* 2002;102: 2751.
- [6] P. Kumar, A. Kuamr, L.J. Mohan, J.K. Makrandi, *Bull. Korean Chem. Soc.* 2010; 31: 3304.
- [7] A. Kumar, A. Verma, G. Chawla, Vaishali, *Int. J. Chem. Tech Res.* 2009; 1: 1177.
- [8] M.N. Noolvi, H.M. Patel, V. Bhardwaj, A. Chauhan, *Eur. J. Med. Chem.* 2011; 46: 2327.
- [9] A. Hasaninejad, A. Zare, M. Shekouhy, A.R. Moosavi-Zare, *E-J. Chem.* 2009; 6: S247.
- [10] R. Mahesh, A.K. Dhar, T. Sasank, S. Thirunavukkarasu, T. Devadoss, *Chin. Chem. Lett.* 2011;22: 389.
- [11] A. Hasaninejad, A. Zare, M.A. Zolfigol, M. Shekouhy, *Synth. Commun.* 2009; 39:569.
- [12] A. Shaabani, A.H. Rezayan, M. Behnam, M. Heidary, *C. R. Chim.* 2009; 12:1249.
- [13] A. Hasaninejad, A. Zare, M.R. Mohammadzadeh, M. Shekouhy, *Green Chem. Lett. Rev.* 2010; 3:143.
- [14] J.T. Hou, Y.H. Liu, Z.H. Zhang, *J. Heterocycl. Chem.* 2010; 47: 703.
- [15] S.S. Katkar, P.H. Mohite, L.S. Gadekar, B.R. Arbad, M.K. Lande, *Cent. Eur. J. Chem* 2010; 8: 320
- [16] M.M. Heravi, S. Taheri, K. Bakhtiari, H.A. Oskooie, *Catal. Commun.* 2007; 8:211.
- [17] S.V. More, M.N.V. Sastry, C.-F. Yao, *Green Chem.* 2006;8: 91.
- [18] S. Antoniotti, E. Duñach, *Tetrahedron Lett.* 2002; 43: 3971.
- [19] R.S. Robinson, R.J.K. Taylor, *Synlett.* 2005; 6: 1003
- [20] S.A. Raw, C.D. Wilfred, R.J.K. Taylor, *Org. Biomol. Chem.* 2004;2: 788
- [21] E. Kolvari, M.A. Zolfigol, H. Banary, *Chin. Chem. Lett.* 2011; 22: 1305
- [22] E. Kolvari, M.A. Zolfigol, M. Peiravi, *Green Chem. Lett. Rev.* 2011; 1
- [23] K. Bahrami, M.M. Khodaei, A. Nejati, *Green Chem.* 2010; 12: 1237
- [24] G.R. Jadhav, M.U. Shaikh, R.P. Kale, C.H. Gill, *Chin. Chem. Lett.* 2009; 20: 535.
- [25] M.L. Deb, P.J. Bhuyan, *Tetrahedron Lett.* 2006; 47:1441.

