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RESEARCH LETTER

Sodium dodecyl sulfate in water: greener approach for the synthesis of quinoxaline derivatives

Pranab Ghosh* and Amitava Mandal

Department of Chemistry, University of North Bengal, Darjeeling, West Bengal 734 013, India

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A mild and efficient synthetic method has been developed for the preparation of biologically important quinoxalines in excellent yield from relatively safe precursor α-bromoketones and 1,2-diamines using catalytic amount of micellar sodium dodecyl sulfate in water at ambient temperature. The method is also found effective for the introduction of quinoxaline moiety into the ring A of pentacyclic triterpenoid, friedelin. Ambient reaction conditions, renewable catalytic condition, inherently safer chemistry, excellent product yields, and water as a reaction medium display both economic and environmental advantages.

Keywords: quinoxaline; water; miceller SDS; room temperature; greener approach

Introduction

Quinoxalines are ubiquitous heterocyclic units in pharmaceuticals and bioactive natural products (*1–4*). They are used as pharmaceuticals and antibiotics such as echinomycin, levomycin, and actinoleutin which are known to inhibit the growth of Gram-positive bacteria and are also active against various transplantable tumors (*1–3*). Antitumoral properties of quinoxaline compounds have also been investigated (*4*). Beside these, they are well known for their application in dyes (*5*) as an efficient electroluminescent materials (*6*) in organic semiconductors (*7*) as building blocks for the synthesis of anion receptors (*8*) as cavitands (*9,10*), dehydroannulenes (*11*), and DNA cleaving agents (*12, 13*). Conventionally, quinoxalines are synthesized by a double condensation reaction involving a dicarbonyl precursor and *o*-phenylenediamine (*14, 15*). Due to the highly reactive nature of the dicarbonyls, alternative routes have been proposed recently (*16*). Antoniotti and Donach (*16*) have reported one of these methods to synthesize quinoxalines from epoxides and ene-1,2-diamines. Active manganese oxide and molecular sieves in combination or manganese oxides in combination with microwaves have also been used in producing quinoxalines (*17, 18*). These processes, however, require excessive amounts of corrosive manganese oxide as stoichiometric oxidants and scaling them up for industrial processes can lead to the formation of large amounts of toxic waste leading to environmental issues. In additional studies, Robinson and Taylor reported a homogeneous catalytic process utilizing $Pd(OAc)_2$, $RuCl_2$ $(PPh_3)_2$ to synthesize quinoxalines from hydroxy ketones (*19*) and recently a copper catalyzed oxidative cyclization process has been reported (*20*). An improved ruthenium catalyzed using direct approach to synthesize quinoxalines from diols and *o*-diamines have also been reported (*21*). These processes suffer from the major drawback that the catalysts are expensive, toxic, and cannot be recovered and reused. In addition to the above catalytic methods, synthesis of quinoxalines using zeolites (*22–25*) microwave (*26, 27*) and solid supports (*28–30*) has also been reported. Nevertheless, these methods suffer from unsatisfactory product yields, critical product isolation procedures, expensive, and detrimental metal precursors and harsh reaction conditions, which limit their use as environmentally friendly protocol. In addition most of the reported methods are not recommended as a clean protocol.

Although very few of the recent reports have claimed α-bromoketones as an equivalent safe chemical precursor of α-hydroxyketones, epoxides, or dicarbonyls as reaction partners of *o*-phenylenediamine to prepare quinoxalines (*31, 32*) they involved the use of either $HClO_4$-SiO_2 or TMSCl as catalyst. Although useful, $HClO_4$ has huge hazardous nature than its potential usefulness, whereas those catalyzed by TMSCl needs higher temperature, with lower yield of the desired products not satisfying the principles of green chemistry protocol in contemporary science as well as their acceptance for industrial applications.

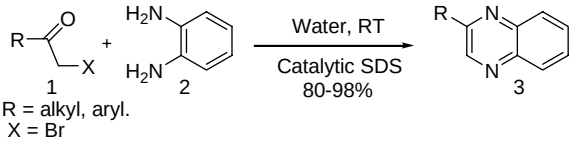
*Corresponding author. Email: pizy12@yahoo.com

In this context the development of an alternative route to quinoxaline from less reactive α-bromoketones in aqueous medium was felt necessary not only due to the increased regulatory pressure focusing on organic solvents, but also because of the emphasis given toward the development of green protocol for organic synthesis nowadays.

The use of water as a medium for organic synthesis is one of the latest challenges in organic synthesis. Reactions in water emerged as a useful alternative route for several organic reactions owing to many of its potential advantages such as safety, economy, and friendly toward catalytic and stereoselective processes and more importantly of environmental concern (*32, 33*) and the progress has been dramatic. In addition, water facilitates ion separation through salvation which often results in altered behavior of reactants in an aqueous environment. Keeping these above facts in mind, we recently have tested water as a solvent in many of our ongoing studies toward organic syntheses and transformative reactions. Very recently we have reported (*33*) the selective synthesis of 1,2-disubstituted benzimidazole in water catalyzed by sodium dodecyl sulfate (SDS), and now reporting herein the result of another successful attempt for an efficient synthesis of quinoxaline from α-bromoketones and *o*-phenylenediamine mediated by water and catalyzed by SDS at room temperature in excellent yields. This is the first report of synthesizing quinoxaline derivatives in a very mild way in water catalyzed by nucleophilic SDS (*33*) at ambient temperature starting from the less reactive safer precursor α-bromoketones in an efficient manner.

Results and discussion

Initially, efforts were directed toward the evaluation of catalytic ability of SDS for the synthesis of quinoxalines. Preliminary studies using phenacylbromide (1 mmol) and *o*-phenylenediamine (1 mmol) without SDS in water at room temperature did not afford the desired quinoxaline. Increase of the reaction time, temperature or by changing the molar proportion of the reactants did not make any influence on the course of the reaction. Addition of some common salts like NaCl, NH_4Cl, KBr, etc. had no positive effect on the reaction. Similar molar ratios of substrates in tap water yielded the desired product (*3*) only in presence of catalytic amounts of SDS. The modified method gave excellent yield of the product within 6 hours at room temperature (Scheme 1). Thus, the catalytic role of SDS in the present transformation is well established.



Scheme 1. Sodium dodecyl sulfate catalyzed synthesis of quinoxalines in water.

This excellent catalyzing ability of SDS inspired us to investigate the above transformation in details. In order to evaluate an optimized and general reaction protocol, a couple of experiments were carried out (Table 1) using varying amounts of SDS (0.34, 0.17, 0.06, 0.03, 0.02, and 0.01 mol%) in combination with different types (both cationic and anionic) and proportions of surfactants viz. tetra-*n*-butylammonium bromide, cetyltrimethylammonium bromide, cetyl pyridinium chloride, sodium dodecylbenzenesulfonate, and tetra-*n*-butylammonium iodide, in different reaction conditions for the above model study (Table 1). It is interesting to note that, although all the surfactants can afford (*3*) as the major product but their combination with SDS showed excellent selectivity not only in forming the desired product (*3*) but also in directing the reaction to proceed in a very cleaner way (Entry 1–7, Table 1). Thus it was established that, α-bromoketone (1 mmol) and 1,2-diamine (1 mmol) in water (3 ml) gave the best result within 6 hours in presence of SDS (10 mg, 0.03 mol%) at room temperature.

It was also observed that during the reaction the substrates and reactants do not mix together in water; addition of SDS not only raised the solubility of the components in water but also catalyzed the process tremendously. Addition of catalytic amount of SDS (0.03 mol%) turned the reaction mixture into a clear yellowish colored solution that slowly transferred into reddish yellow as the reaction progressed. After completion of the reaction (checked by Thin layer chromatography (TLC)), products were purified by simple filtration (and in some cases by column chromatography, silica 60–120 mesh) followed by crystallization to get the products in good to excellent yields. Appendix.

In order to demonstrate the versatility of SDS as a catalyst for the synthesis of quinoxalines, a series of α-bromoketones and 1,2-diamines were subjected to undergo one pot condensation–aromatization in presence of SDS under the optimized reaction protocol (Table 2). All of the reactions tried showed good selectivity with excellent isolated yields. Appendix.

While investigating the influence of the substituents present either on ketone part or on 1,2-diamine on the course of the reaction, it was observed that compounds having electron donating or withdrawing

Table 1. Optimization of quinoxaline synthesis using phenacyl bromide and *o*-phenylenediamine in presence of different surfactants and their amounts.

Entry	Ratio of aldehyde and diamine	Surfactant	Amount of surfactant (mg)	Temp (°C)	Time (hour)	% Yield of 3[a]
1	1:1	SDS	100	RT	6	96
2	1:1	SDS	50	RT	6	94
3	1:1	SDS	20	RT	6	96
4	1:1	SDS	15	RT	6	94
5	1:1	SDS	10	RT	6	95
6	1:1	SDS	7	RT	12	80
7	1:1	SDS	5	RT	15	64
8	1:1	SDS	5	50	8	68
9	1:1	SDS	100	RT	10	78
10	1:1	TBAB	100	50	10	76
11	1:1	TBAB	200	100	10	80
12	1:1	TBAB	100	RT	10	66
13	1:1	CTAB	200	100	10	68
14	1:1	CTAB	100	RT	10	78
15	1:1	CPC	200	100	10	80
16	1:1	CPC	100	RT	10	76
17	1:1	TBAH	200	100	10	78
18	1:1	TBAH	100	RT	10	68
19	1:1	TBAI	200	100	10	74
20	1:1	TBAI	100	RT	8	82
21	1:1	SDBS	50	RT	8	80
22	1:1	SDBS	30	RT	8	64
23	1:1	SDBS	30	50	10	70

CPC, cetyl pyridiniumchloride; CTAB, cetyl trimethyl ammoniumbromide; SDBS, sodium dodecylbenzenesulfonate; SDS, sodium dodecyl sulfate; TBAB, tetra-*n*-butylammonium bromide; TBAI, tetra-*n*-butylammoniumiodide[a]
% Yield refers to the isolated yield of all the compounds after chromatographic separation.

groups on the ketone (Entry 2, 3, 5–9, of Table 2) both underwent the reactions in almost similar fashion and gave good yields. Although, *p*-bromo phenacylbromide (Entry 5, of Table 2) gave better yield than its meta isomer (Entry 9, of Table 2), the corresponding *p*-nitro and *m*-nitro derivative underwent the reaction in identical fashion (Entry 10, of Table 2). Disubstituted α-bromoketones (Entry 11, 12, of Table 2) also gave excellent yields of the expected quinoxalines. Sensitive molecules like 1,2-diaminomalionitrile (Entry 15, of Table 2) was also found compatible to the reaction condition and gave 84% yield of the corresponding quinoxaline. All the observed results were summarized in Table 2.

Potential of pentacyclic triterpenoid as bioactive candidate is well described (*34*). In order to see the effect on their bioactivities by the introduction of quinoxaline ring on ring A, we applied our protocol on 2α-bromofriedelin (*5*) (prepared from friedelin) (*4*) and to our delight we have isolated the corresponding quinoxaline derivative (*6*) in 58% yield within 8 hours under identical condition (0.03 mol% of SDS). This is also the very first report of preparing quinoxaline derivative of pentacyclic triterpenoid in water at room temperature (Scheme 2).

As was mentioned earlier, a simple filtration or easy work up procedure of the reaction and reuse of the catalyst, SDS directly from the aqueous extract of the reaction mixture for a fresh run, are the great advantages of the developed process. Gratifyingly, it was tested that the recovered water layer can be reused for six consecutive runs (Table 3).

It is well known that under ambient condition surfactant molecules can aggregate in an aqueous phase to micelles with hydrophobic core and a hydrophilic corona (*35, 36*). To determine whether micellization had occurred or not we first measured the critical micellization concentration (CMC) of SDS (Figure 1) and the value was found to be 8.33 mM. In the present study, under the optimized reaction condition the concentration of SDS was 11.57 mM (10 mg of SDS in 3 ml water). Since the value was far beyond the CMC value of SDS (8.33 mM), micellization was anticipated.

It was reported in the literature (*37*) that the dimensionless packing parameter P of the molecular geometry as an index to predict the size and shape of the micelles. P was defined as $V/(a_0 l)$, where V is the hydrocarbon chain volume, a_0 is the optimum head group area per molecule, and l is the hydrocarbon

Table 2. Preperation of quinoxaline derivatives.

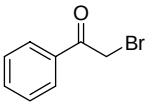
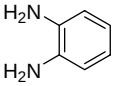
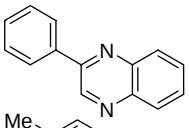
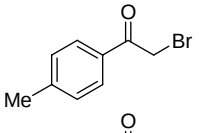
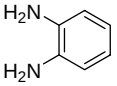
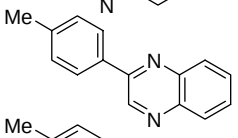
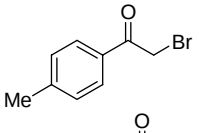
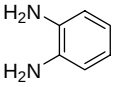
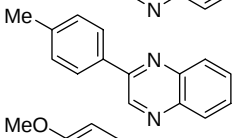
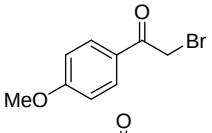
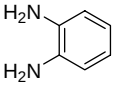
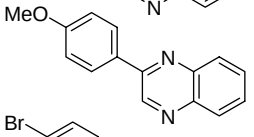
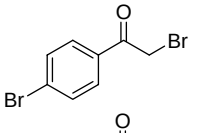
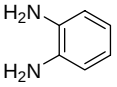
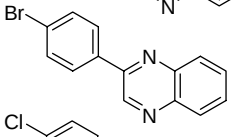
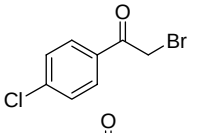
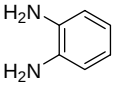
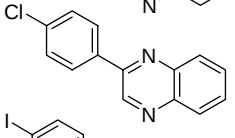
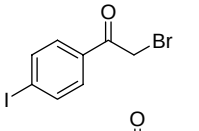
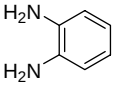
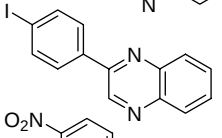
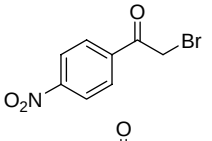
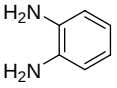
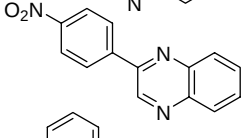
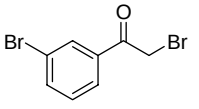
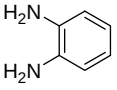
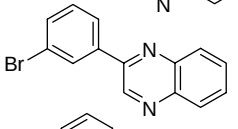
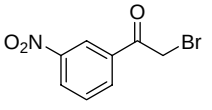
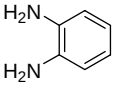
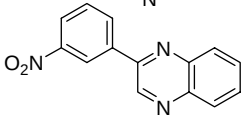
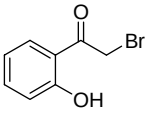
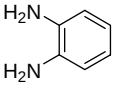
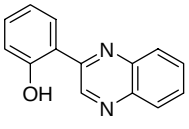
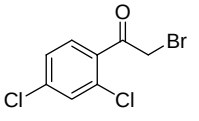
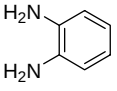
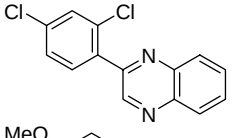
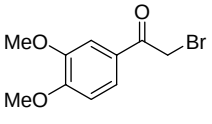
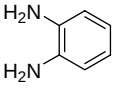
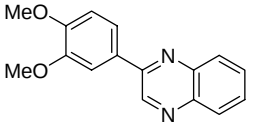
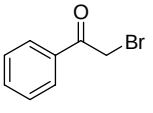
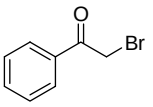
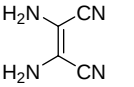
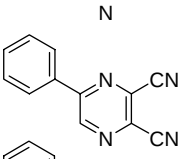
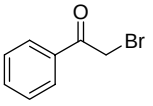
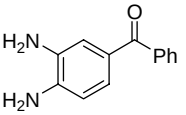
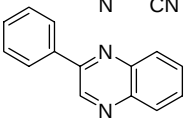
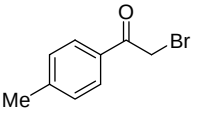
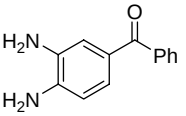
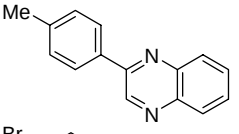
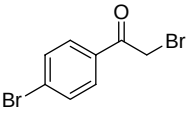
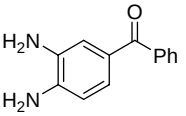
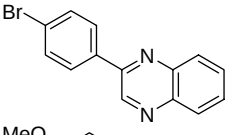
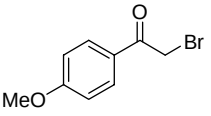
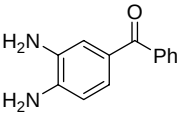
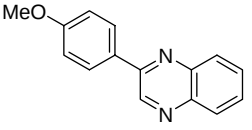
Entry	α-Bromo carbonyl compound	Diamine	Time (hour)	Product	% Yield[a]
1			6		94
2			6		92
3			6		92
4			6		86
5			6		92
6			6		89
7			6		87
8			7		84
9			6		87
10			6		85
11			7		83
12			6.5		98
13			7		82
14			6		92

Table 2 (*Continued*)

Entry	α-Bromo carbonyl compound	Diamine	Time (hour)	Product	% Yield[a]
15			5		84
16			6.5		88
17			6		86
18			6		86
19			6		86

[a]% Yield refers to the isolated yield of all the compounds.

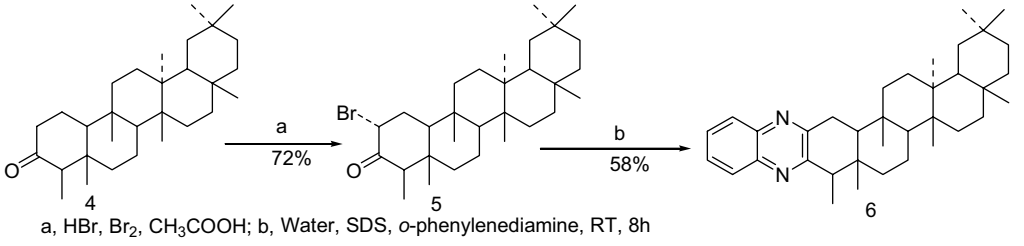
chain length that is taken to be ca. 80–90% of the fully extended chain length (*37*). The overall prediction was concluded as follows:

Spherical micelles $P < 1/3$
Cylindrical micelles $1/3 < P < 1/2$
Bilayers (or vesicles) $1/2 < P < 1$
Inverted structures $P > 1$

The value of packing parameter *P*, an index to predict the size and shape of the micelles (*37*), of SDS was found to be 0.235 (taking *l* as 90% of the fully extended chain length) indicating the spherical nature of the developed micelles.

For further confirmation dynamic light scattering (DLS) measurement was carried out of a 11.57 mM aqueous solution of SDS that indicated the presence of micelles (Figure 2) of radius 161 nm (diameter of 322 nm) with the Polydispersity index of 0.348.

The role of SDS as a nucleophile is well investigated in our previous communication (*33*). Considering the above characteristics of SDS, the most probable mechanism of the miceller SDS in effecting the present transformation may be depicted as shown in Scheme 3. In the miceller solution, 1,2-phenylenediamine and phenacyl bromide, both of which are hydrophobic in nature, are entered into the hydrophobic core of the micelles and thus assist the condensation between the phenacyl bromide and *o*-phenylenediamine to form dihydroquinoxaline derivative (**A**) (Scheme 3). Nucleophilic nature of



Scheme 2. Preparation of quinoxaline derivative of friedelin.

Table 3. Recycling experiment using sodium dodecyl sulfate.

Entry	No. of cycle	% Yield[a]
1	0	92
2	1	87
3	2	82
4	3	78
5	4	72
6	5	68

[a]% Yield refers to the isolated yield of the compound after chromatography.

SDS may have assisted the *in situ* aromatization of the dihydro derivative (**A**) to afford quinoxalines (Scheme 4).

Experimental

General

All the chemicals used were reagent grade and purified prior to their use. SDS was purchased from Sigma-Aldrich, India. The NMR chemical shift was reported in ppm relative to 7.20–77.0 ppm of $CDCl_3$ solvent as the standards. ^1H spectra were recorded in 300 MHz frequencies and ^{13}C NMR spectra were recorded in 75.4 MHz frequencies. Coupling constant "J" was calculated in Hertz. Conductance was measured in Systronics conductivity meter 304 at 25°C (298 K). DLS measurement was performed in Nano ZS90 (Malvern, UK).

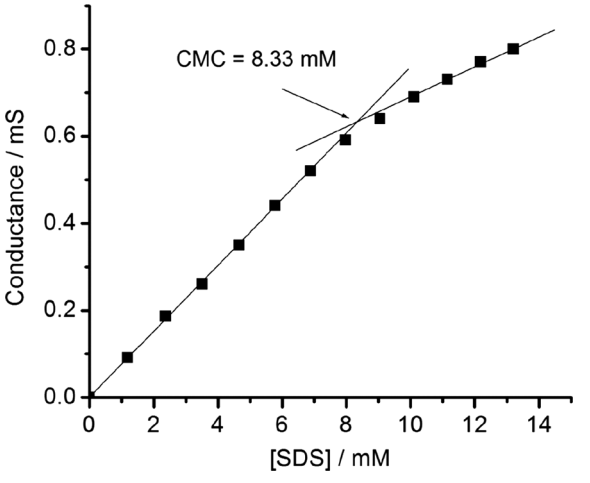


Figure 1. Plot of conductance vs. concentration of sodium dodecyl sulfate (SDS) for the calculation of critical micellization concentration value of SDS.

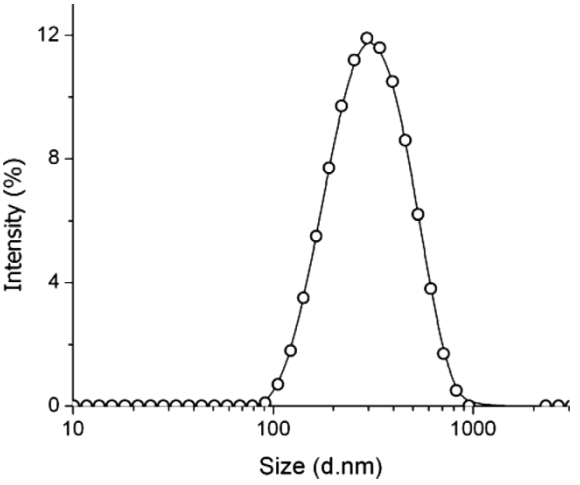


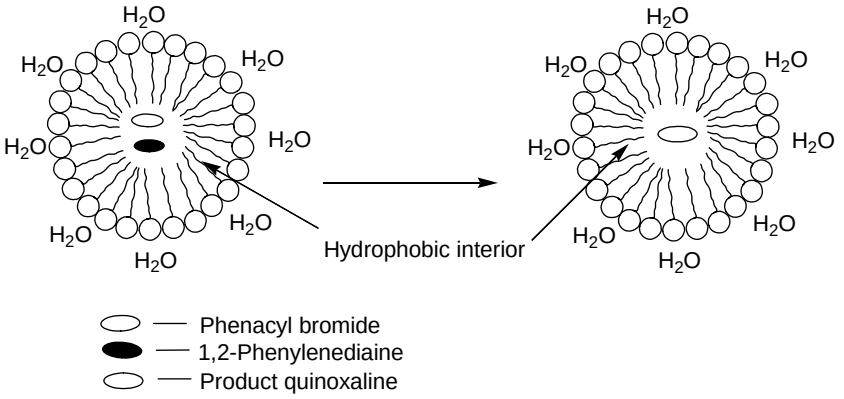
Figure 2. Graph of intensity vs. size (nm) of the micelles based on dynamic light scattering measurement.

General procedure for quinoxalines

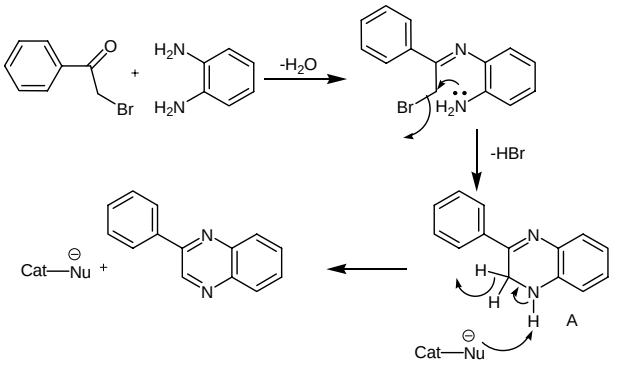
In a typical experimental procedure, *o*-phenylenediamine (1 mmol) and α-bromoketone (1 mmol) in 1:1 molar ratios was taken in a 50 ml round bottom flask. To this water (3 ml) and 10 mg (0.03 mol%) SDS was admixed. The reaction mixture was then allowed to stir with magnetic spinning bar at room temperature. After the completion of the reaction (checked by TLC), the residue was filtered, washed with water, dried and finally recrystallized from methanol. The desired pure product was characterized by spectral (IR, ^1H- and ^{13}C-NMR) data and compared to those reported in literature.

Conclusion

A simple, energy efficient, one step SDS catalyzed (0.03 mol%) greener method for the synthesis of quinoxaline derivatives underwater mediating condition has been developed. Structurally diversified α-bromoketones, commonly regarded as safer chemicals, were used as reaction partners of 1,2-diamines in water at ambient temperature. Effect of the nature and position of the substituents on both the reactants in consideration to the reaction condition was also studied. Disubstituted α-bromoketones and 2α-bromofriedelin (a representative of pentacyclic triterpenoids) also formed the corresponding quinoxalines that may serve as lead compound in near future. Except water, no other organic solvents were used. The ambient reaction conditions, comparatively lower reaction time, excellent product yields, and simple work up procedure not only make this methodology an alternative platform to the conventional acid/base catalyzed thermal processes, but also found to be significant under the umbrella of environmentally



Scheme 3. Proposed model for the synthesis of quinoxaline in water-sodium dodecyl sulfate.



Scheme 4. Plausible mechanism of the sodium dodecyl sulfate catalyzed quinoxaline formation.

greener and safer processes that may find its place in industry. Moreover, water as a solvent used with miceller SDS has both economic and environmental advantages. As micelles of diameter of 322 nm were formed, it was anticipated that the entitled reactions were occurring inside the hydrophilic core of the micelles. Scaling up the reaction up to 5 mol scale gave good results. We believe our developed process not only satisfied the principles of green chemistry, but also can open a new way of synthesizing bioactive molecules by catalyzing SDS in water. Further explorative studies of this efficient combination to various organic syntheses is undergoing in our laboratory.

Acknowledgements

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Appendix

Characterization of some representative compounds

(1) 2-phenyl quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.91–6.96 (m, 3*H*), 7.08–7.17 (m, 2*H*), 7.48–7.58 (m, 4*H*), 8.75 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 127.5, 129.1, 129.5, 129.6, 130.1, 136.7, 141.5, 142.2, 143.3, 151.8.

(2) 2-*p*-tolylquinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (s, 2*H*), 7.35 (d, 2*H*, J = 7.8 Hz), 7.71–7.77 (m, 2*H*), 8.08–8.15 (m, 4*H*), 9.31 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.43, 126.0, 127.4, 128.9, 129.3, 129.5, 129.9, 130.5, 131.3, 133.8, 140.2, 140.5, 141.2, 143.1, 151.84.

(3) 2-(4-ethylphenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26–1.33 (m, 3*H*), 2.74 (q, 2*H*, J = 7.5 Hz), 7.35 (d, 2*H*, J = 8.1 Hz), 7.74 (q, 2*H* J = 7.5 Hz) 8.09–8.15 (m, 4*H*), 9.30 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.4, 28.8, 127.5, 128.7, 129.0, 129.3, 129.5, 130.2, 134.1, 141.3, 142.3, 143.2, 146.8, 151.8.

(4) 2-(4-bromophenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68–7.71 (m, 2*H*), 7.75–7.78 (m, 2*H*), 8.07–8.16 (m, 4*H*), 9.29 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 125.0, 129.0, 129.6, 129.9, 130.5, 132.3, 135.6, 141.6, 142.2, 142.7, 150.6.

(5) 2-(4-methoxyphenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.89 (s, 3*H*), 7.08 (s, 2*H*), 7.70–7.76 (m, 2*H*), 8.08–8.18 (m, 4*H*), 9.29 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.5, 114.6, 129.00, 129.05, 129.2, 130.3, 141.1, 142.2, 143.1, 151.4, 161.5.

(6) 2-(4-chlorophenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.54 (d, 2*H*, J = 8.4 Hz), 7.78–7.94 (m, 2*H*), 8.15 (d, 4*H*, J = 8.4 Hz), 9.32 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 128.8, 129.0, 129.4, 129.6, 130.6, 135.1, 136.7, 141.4, 142.3, 142.7, 150.7.

(7) 2-(3-nitrophenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76–7.86 (m, 3*H*), 8.15–8.21 (m, 2*H*), 8.38 (d, 1*H*, J = 6.3 Hz), 8.55 (d, 1*H*, J = 7.5 Hz), 9.11 (s, 1*H*), 9.39 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 122.5, 124.7, 129.2, 129.8, 130.2, 130.6, 130.9, 133.0, 138.4, 142.0, 142.2, 149.0, 149.1.

(8) 2-(3, 4-dimethoxyphenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.91 (s, 3*H*), 4.05 (s, 3*H*), 7.01 (d, 1*H*, J = 8.1 Hz), 7.27–7.74 (m, 3*H*), 7.86 (d, 1*H*, J = 2.1 Hz), 8.07–8.15 (m, 2*H*), 9.29 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 56.02, 56.08, 110.1, 111.1, 120.4, 129.0, 129.1, 129.3, 129.5, 130.2, 141.2, 142.2, 143.1, 149.7, 151.1, 151.3.

(9) 2-(3, 4-dichloroyphenyl)quinoxaline

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26 (s, 1*H*), 7.43–7.46 (m, 1*H*), 7.57 (d, 1*H*, J = 1.8 Hz), 7.70 (d, 1*H*, J = 8.1 Hz), 7.80–7.83 (m, 2*H*), 8.14–8.19 (m, 2*H*), 9.20 (s, 1*H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 127.9, 129.2, 129.6, 130.0, 130.4, 130.5, 132.9, 133.3, 135.0, 136.3, 141.3, 142.3, 145.8, 151.3.

Isolation of friedelin

Friedelin was isolated in petroleum ether by a soxhlet apparatus for 72 hours. Solvent was removed in reduced pressure. The brown gummy residue obtained was then purified over a column of silica gel (60–120 mesh). Mixtures of petroleum ether and ethyl acetate were used to run the column. Friedelin was found as white powdered material of melting point 260–262°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.72 (s, 3*H*, $-CH_3$), 0.76(s, 3*H*, $-CH_3$), 0.86(s, 3*H*, $-CH_3$), 0.88(s, 3*H*, $-CH_3$), 0.92(s, 3*H*, $-CH_3$), 1.00(s, 3*H*, $-CH_3$), 1.05(s, 3*H*, $-CH_3$), 1.18(s, 3*H*, $-CH_3$). All other peaks are in good agreement with that reported for friedelin. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 213.1 (C-3), 7.2 (C-23), 14.6 (C-24), 18.5 (C-25), 15.7 (C-26), 18.7 (C-27), 32.1 (C-28), 31.8 (C-29), 32.8 (C-30). All other peaks are in good agreement with that reported for friedelin.

Preperation of 2α-bromofriedelin

2α-bromofriedelin was prepared from friedelin following the process of Corey and Ursprung (*38*).

A solution of 1.28 g of friedelin in 50 ml of chloroform was treated with 1 ml of saturated solution of HBr in chloroform followed by a solution of 0.55 g of bromine in 5 ml chloroform. The depolarization was instantaneous. Chloroform was evaporated in reduced pressure and the residue was purified by column chromatography Silica 60–120 mesh). Mixtures of petroleum ether and ethyl acetate were used to run the column.

Melting point was 208–210°C (210° C as reported). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.72 (s, 3*H*, $-CH_3$), 0.76(s, 3*H*, $-CH_3$), 0.86(s, 3*H*, $-CH_3$), 0.88(s, 3*H*, $-CH_3$), 0.92(s, 3*H*, $-CH_3$), 1.00(s, 3*H*, $-CH_3$), 1.05(s, 3*H*, $-CH_3$), 1.18(s, 3*H*, $-CH_3$), 3.13 (dd, 2*H*, J = 6.6 and 13.2 Hz, 2*H* −C-1), 4.40 (m, 1*H*, 1*H* −C-2). All other peaks are in good agreement with that reported for friedelin. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 213.1 (C-3), 7.2 (C-23), 14.6 (C-24), 18.5 (C-25), 15.7 (C-26), 18.7 (C-27), 32.1 (C-28), 31.8

(C-29), 32.8 (C-30), 53.0 (C-2). All other peaks are in good agreement with that reported for friedelin.

Analytical calculation:

	%C	%H	%Br
Calculated	71.26	9.65	15.81
Found	71.07	9.65	15.38

All the data was in good agreement with that reported in that reference paper.

Friedelin quinoxaline

Melting point 248–250°C (248–151°C as reported), ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (t, 1*H*, J = 7.8 Hz); 7.58 (dq, 1*H*, J = 2.4 and 8.1 Hz); 8.00 (dt, 1*H*, J = 2.7 and 7.8 Hz); 8.09 (m, 1*H*). 0.72 (s, 3*H*, $-CH_3$), 0.76(s, 3*H*, $-CH_3$), 0.86(s, 3*H*, $-CH_3$), 0.88(s, 3*H*, $-CH_3$), 0.92(s, 3*H*, $-CH_3$), 1.00(s, 3*H*, $-CH_3$), 1.05(s, 3*H*, $-CH_3$), 1.15(s, 3*H*, $-CH_3$).

Analytical calculation:

	%C	%H
Literature report	84.32	10.22
Found	83.92	10.27

The compound was found identical with that reported in literature (*39*).