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Efficient one-pot synthesis of mono and bis-*N*-cyclohexyl-3-alkyl(aryl)-quinoxaline-2-amines using *N*-halo catalysts†

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A convenient synthetic protocol for the synthesis of mono- and bisquinoxalines involving a room temperature one-pot three-component Ugi reaction of aromatic amines, aromatic or aliphatic aldehydes and cyclohexyl isocyanide with *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide [TBBDA] or poly(*N*-bromo-*N*-ethylbenzene-1,3-disulfonamide) [PBBS] as catalysts has been developed. Thin-layer chromatography was used for purification of mono and bisquinoxalines. Mild reaction conditions, good to high yields, cheap and stable catalysts and short reaction times are some of the salient features of the protocol presented.

Introduction

Multicomponent reactions (MCRs) constitute a useful strategy for the construction in a single step of architecturally complex molecules, offering a wide range of biological activities, from readily available starting materials.[1,2] Quinoxaline and its derivatives are important nitrogen-containing heterocyclic compounds with various interesting biological properties and several pharmaceutical applications. This diversity in its biological response profile has prompted many researchers to explore the skeleton for its wide potential. Quinoxalines also play an important role as a basic skeleton for the design of a number of antibiotics, such as echinomycin and levomycin, compounds with reported inhibition of the growth of Gram-positive bacteria and activity against various transplantable tumors.[3–8] Furthermore, quinoxaline derivatives show very interesting biological properties (antibacterial, antiviral, anticancer, antifungal, antihelminthic, insecticidal).[9–13] Also, some quinoxalin-2-ones **1** and quinoxaline-2,3-diones **2** (Fig. 1) have been reported to show antimicrobial activity.[14,15] The present article reports an attempt to synthesize new mono- and bis-quinoxaline derivatives using *N*-halo catalysts. A number of synthetic strategies have been developed for the preparation of substituted quinoxalines.[16–22] Many synthetic methods for these heterocyclic compounds have been reported, which include the use of catalysts and/or some special techniques. However, many of these methods are associated with several shortcomings such as long reaction times, expensive reagents, harsh conditions, low product yields, occurrence of several side products and difficulties in recovery and reusability of the catalysts. The exploitation of catalysts to develop new synthetic methods is an art which constitutes a challenging process in organic chemistry. *N*-Halo compounds are versatile reagents and have been employed as potentially reactive intermediates widely used in organic synthesis.[23] Thus, milder, non-hazardous, inexpensive catalysts and favorable solvent system synthesis of quinoxaline derivatives are still in demand.

Results and discussion

In continuation of our interest in the application of *N*,*N*,*N*′,*N*′-tetrabromobenzene-1,3-disulfonamide [TBBDA] and poly(*N*-bromo-*N*-ethylbenzene-1,3-disulfonamide) [PBBS],[24] (Fig. 2) in organic synthesis,[25–36] we wish to report here an easy and efficient protocol for the room temperature synthesis of mono and bis-*N*-cyclohexyl-3-aryl(alkyl)-quinoxalin-2-amines in good to high yields from *o*-phenylenediamine, 3,3′-diaminobenzidine, aliphatic and aromatic aldehydes and cyclohexyl isocyanide in the presence of TBBDA and PBBS as catalysts (Scheme 1).

The advantages of TBBDA and PBBS are as follows:

(1) preparation of TBBDA and PBBS is easy.

(2) TBBDA and PBBS are stable under atmospheric conditions for at least two months.

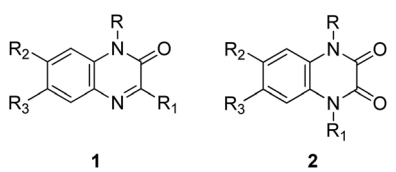

Fig. 1 Quinoxalin-2-ones **1** and quinoxaline-2,3-diones **2**.

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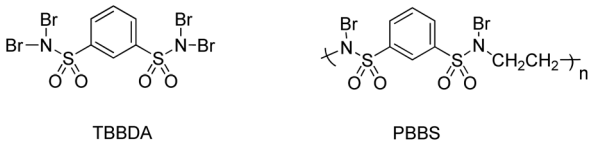
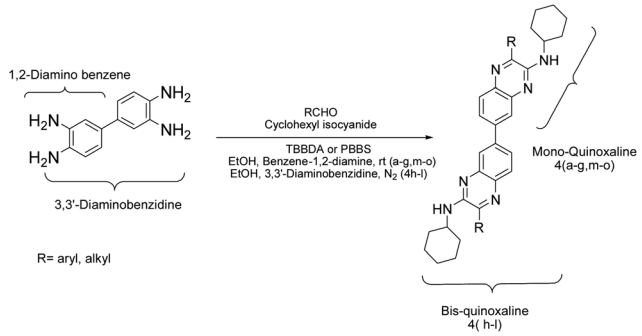


Fig. 2 Structure of *N*-halo catalysts.



Scheme 1 Synthesis of mono- and bisquinoxaline derivatives using *N*-halo catalysts.

Table 1 Optimization of reaction conditions for the synthesis of *N*-cyclohexyl-3-(biphenyl-4-yl)quinoxalin-2-amine

Entry	Solvent	Catalyst amount TBBDA (mol%)/ PBBS (g)	Time (h)	Yield[a] (%) TBBDA/PBBS
1	EtOH	—	24	0/0
2	EtOH	3.6/0.05	1	35/20
3	EtOH	7.2/0.07	1	65/40
4	EtOH	9/0.09	1	80/75
5	EtOH	10.8/0.10	1	98/85
6	EtOH	12.7/0.12	2	94/85
7	EtOH	18.1/0.13	5	94/80
8	CH_3CN	10/0.15	2	60/50
9	CH_2Cl_2	10/0.10	2	25/15
10	THF	10/0.10	2	45/40
11	DMSO	10/0.10	2	15/5
12	DMF	10/0.10	2	10/10
13	CH_3OH	10/0.10	2	45/35
14	CH_3CO_2Et	10/0.10	2	30/15
15	Neat	10/0.10	7	40/25
16	Neat	10/0.10	24	5/5

[a] Standardization of reaction conditions: biphenyl-4-carbaldehyde (1 mmol), *o*-phenylenediamine (1 mmol), cyclohexyl isocyanide (1 mmol) and solvent (5 mL) at room temperature.

(3) After completion of the reaction, the catalysts are recovered and can be used several times without substantially affecting the yields.

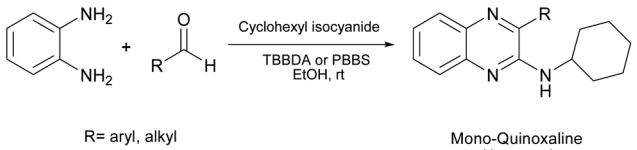
In this context, ethanol (EtOH) was chosen as the best solvent for these reactions. Reactions in EtOH are generally considered environmentally safe, devoid of any carcinogenic effects, simple to handle, cheaper to operate and especially important in industry. Initially, we decided to explore the role of our catalysts the preparation of *N*-cyclohexyl-3-([1,1′-biphenyl]-4-yl)-quinoxalin-2-amine (**4a**) as a model compound using EtOH as solvent. In the absence of a catalyst, no product was observed, even after prolonged reaction times. Since the synthesis failed in the absence of a catalyst, we then tested various solvents such as CH_3CN, CH_2Cl_2, THF, DMSO, DMF, CH_3OH, and CH_3CO_2Et for the synthesis of *N*-cyclohexyl-3-(biphenyl-4-yl)-quinoxalin-2-amine in the presence of the *N*-halo catalyst under similar conditions, but after an appropriate time, we couldn't obtain suitable yields (Table 1, entries 8–16). The best results (98% yield) were obtained when the reaction was carried out in EtOH (5 mL) at room temperature for 1 h, using *o*-phenylenediamine (1 mmol), biphenyl-4-carbaldehyde (1 mmol) and cyclohexyl isocyanide (1 mmol) in the presence of TBBDA (10 mol%) or PBBS (18 mol%), respectively (Table 1, entry 5). The results encouraged us to investigate the scope and generality of this new protocol for various aldehydes and *o*-phenylenediamine under the optimized conditions. As shown in Table 2, a series of aliphatic and aromatic aldehydes containing either electron-withdrawing or electron-donating substituents reacted successfully under room temperature conditions giving good to high yields of products in high purity. Except for a few examples, TBBDA usually afforded slightly better yields than PBBS. The structures of the products **4a–o** were deduced from their IR, ^{1}H-NMR, ^{13}C-NMR spectra and CHN elemental analysis. For example, the ^{1}H-NMR spectrum of **4a** consisted of a multiplet of signals at δ_H 1.11–2.15 for the cyclohexyl ring, a multiplet for the NH–CH at δ_H 4.20 and a doublet for the NH–CH at δ_H 5.17. A multiplet corresponding to the aromatic protons was observed centered at δ_H 7.25–7.76. The ^{1}H decoupled ^{13}C-NMR spectrum of **4a** showed 19 distinct resonances. Partial assignment of these resonances is given in the Experimental section. Our preliminary examination shows TBBDA is a reusable catalyst in these reactions. Thus, after the production of *N*-cyclohexyl-3-(biphenyl-4-yl)quinoxaline-2-amine in the first run with TBBDA, which gave the corresponding product in 98% isolated yield (Table 1, entry 5), the catalyst was subjected to a second reaction which gave the product in 90% yield; the average chemical yield for five consecutive runs was 50%. In Fig. 3, we show with repetition the yield is reduced gradually.

It is likely that these reagents release Br^+ *in situ*, which can act as an electrophilic species. Therefore, the mechanism shown in Scheme 2 can be suggested for the conversion of the benzene-1,2-diamine, 3,3′-diaminobenzidine, various aliphatic and aromatic aldehydes and cyclohexyl isocyanide to mono- and bis-*N*-cyclohexyl-3-alkyl(aryl)-quinoxaline-2-amines. Also, using a catalytic amount of aqueous 48% HBr instead of TBBDA gave lower yields (10%). This result indicates that the generation of the protic acid HBr may not be the only factor responsible for the catalytic activity of TBBDA. It is possible that the positive brominum moiety also has some role in facilitating the process.

Conclusions

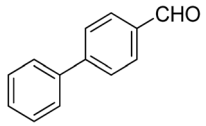
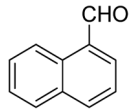
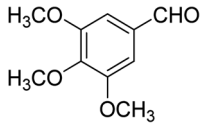
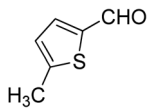
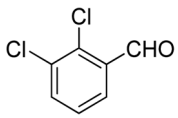
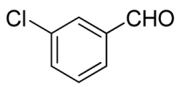
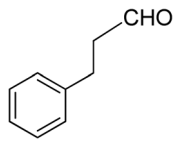
In summary, we have developed a new and facile protocol for the synthesis of polysubstituted *N*-cyclohexyl-3-aryl(alkyl)-quinoxalin-2-amines derivatives starting from simple and readily available substrates (aliphatic or aromatic aldehydes, *o*-phenylenediamine, 3,3′-diaminobenzidine and cyclohexyl

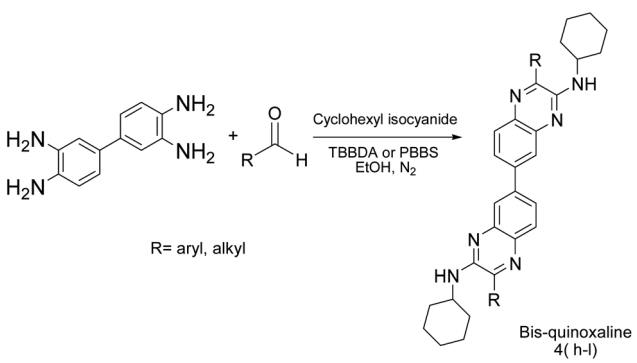
Table 2 Synthesis of mono and bis-*N*-cyclohexyl-3-aryl(alkyl)-quinoxalin-2-amines using TBBDA and PBBS



R= aryl, alkyl

Mono-Quinoxaline 4(a-g,m-o)

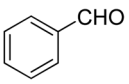
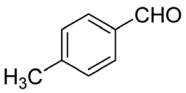
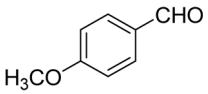
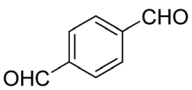
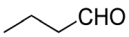
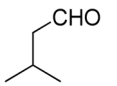
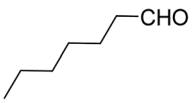
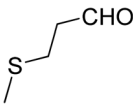
Entry	Substrate	TBBDA Time (h)/ yield (%)	PBBS Time (h)/ yield (%)
4a		1/98	1.1/85
4b		1/92	1.4/90
4c		1.2/85	1.35/60
4d		1.5/80	2/80
4e		1.15/90	1.2/80
4f		1.05/94	1.15/85
4g		1.15/90	1.05/90



R= aryl, alkyl

Bis-quinoxaline 4(h-l)

Table 2 (*Contd.*)

Entry	Substrate	TBBDA Time (h)/ yield (%)	PBBS Time (h)/ yield (%)
4h		3/65	3.4/60
4i		1.35/60	1.55/55
4j		2/55	2.3/50
4k		2.2/70	3/55
4l		3.4/60	4/55
4m		1/85	1.25/90
4n		1.1/94	1.1/80
4o		1.3/90	2/85

isocyanide), using stable and inexpensive *N*-halo catalysts (TBBDA and PBBS) at room temperature. This reaction can be regarded as a new approach for the preparation of pharmaceutically relevant, highly substituted quinoxaline derivatives.

Materials and equipment

All commercially available chemicals were obtained from Merck and Fluka and used without further purification unless otherwise stated. ^{1}H and ^{13}C-NMR spectra were recorded on Bruker Avance 200 or 500 FT NMR spectrometers. Infrared (IR) spectroscopy was performed on a Perkin Elmer GX FT-IR spectrometer. Mass spectra were recorded on a Shimadzu QP 1100 BX mass spectrometer. Elemental analyses (CHN) were performed with a Heraeus CHN-Rapid analyzer.

Typical experimental procedure for the synthesis of mono-quinoxaline compounds 4a–g and 4m–o derivatives using TBBDA and PBBS catalysts, preparation of *N*-cyclohexyl-3-(biphenyl-4-yl)quinoxaline-2-amine (4a)

A catalytic amount of TBBDA (0.109 mmol, 0.06 g) or PBBS (0.10 g) was added to a mixture of *o*-phenylenediamine (1 mmol, 0.108 g), biphenyl-4-carbaldehyde (1 mmol, 0.182 g) and cyclohexyl isocyanide (1 mmol, 0.109 g) and dry ethanol (EtOH, 5 mL), and the mixture was stirred for the appropriate time

(Table 2, entry 1). The progress of the reaction was monitored by TLC (*n*-hexane–ethyl acetate, 3 : 2). After completion of the reaction, CH_2Cl_2 (10 mL) was added (TBBDA was precipitated) and the catalyst was removed by filtration. Evaporation of the solvent under reduced pressure gave the crude product, which was purified by thin-layer chromatography using *n*-hexane–ethyl acetate (70 : 50) as the eluent system to afford the title compound in 98% yield (Table 2, entry **4a**).

Typical experimental procedure for the synthesis of bis-quinoxaline compounds 4h–l derivatives using TBBDA and PBBS catalysts, preparation of *N*3,*N*3′-dicyclohexyl-2,2′-diphenyl-6,6′-biquinoxaline-3,3′-diamine (4h)

A catalytic amount of TBBDA (0.217 mmol, 0.12 g) or PBBS (0.20 g) was added to a mixture of 3,3′-diaminobenzidine (1 mmol, 0.214 g), benzaldehyde (2 mmol, 0.216 g), cyclohexyl isocyanide (2 mmol, 0.218 g), and dry ethanol (EtOH, 5 mL), and the mixture was stirred for an appropriate time under inert atmosphere (Table 2, entry **4h**). The progress of the reaction was monitored by TLC (*n*-hexane–ethyl acetate, 3 : 2). After completion of the reaction, CH_2Cl_2 (2 × 15 mL) was added and the catalyst was removed by filtration. Evaporation of the solvent under reduced pressure gave the crude product that was purified by thin layer chromatography using *n*-hexane–ethyl acetate (70 : 65) as the eluent system to afford the title compound in 65% yield (Table 2, entry **4h**).

***N*-Cyclohexyl-3-(biphenyl-4-yl)quinoxaline-2-amine 4a.** Yield: 98%; m.p. 195–197 °C; elem. anal.: found: C, 82.51; H, 6.68; N, 11.16; calc. for $C_{26}H_{25}N_3$: C, 82.29; H, 6.64; N, 11.07%. IR (KBr, ν_{max}/cm^{-1}): 3300, 1645, 1625; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.11–2.15 (m, 10H, cyclohexyl), 4.20 (m, 1H, CH–NH), 5.17 (s br, 1H, CH–NH), 7.30–7.36 (m, 3H, Ar), 7.43–7.68 (m, 6H, Ar), 7.72–7.76 (d, *J* 7.5, 2H), 7.85–7.89 (d, *J* 8.0, 2H); ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 24.77, 25.81, 49.34, 124.16, 125.69, 128.19, 128.82, 129.55, 130.03, 131.12, 133.88, 135.84, 136.82, 139.78, 140.80, 141.20, 146.91, 149.26; MS *m*/*z*: 379 (M+, 19%), 283 (20), 254 (93), 201 (63), 149 (52), 55 (28), 41 (30).

***N*-Cyclohexyl-3-(naphthalen-1-yl)-quinoxaline-2-amine 4b.** Yield: 92%; m.p. 180–182 °C; elem. anal.: found: C, 81.84; H, 6.60; N, 11.91; calc. for $C_{24}H_{23}N_3$: C, 81.55; H, 6.56; N, 11.89%. IR (KBr, ν_{max}/cm^{-1}): 3240, 1645, 1640; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 0.86–2.16 (m, 10H, cyclohexyl), 4.19 (m, 1H, CH–NH), 4.59 (s br, 1H, CH–NH), 7.40–7.65 (m, 7H, Ar), 7.92–8.03 (m, 4H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 23.66, 23.79, 32.82, 50.41, 123.27, 123.59, 125.72, 126.63, 126.87, 128.78, 128.86, 136.82, 141.05, 141.30, 146.19, 148.15; MS *m*/*z*: 353 (M^+, 25%), 296 (17), 270 (98), 201 (95), 149 (80), 127 (42), 55 (32), 41 (35).

***N*-Cyclohexyl-3-(3,4,5-trimethoxyphenyl)-quinoxaline-2-amine 4c.** Yield: 85%; m.p. 228–230 °C; elem. anal.: found: C, 70.42; H, 7.04; N, 10.72; calc. for $C_{23}H_{27}N_3O_3$: C, 70.21; H, 6.92; N, 10.68%; IR (KBr, ν_{max}/cm^{-1}): 3210, 1655, 1625; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.13–2.14 (m, 10H, cyclohexyl), 3.90 (s, 9H, OCH_3), 4.18 (m, 1H, CH–NH), 5.15 (s br, 1H, CH–NH), 6.92 (s, 2H, Ar–H), 7.30–7.33 (t, *J* 8.2, 1H, Ar), 7.49–7.54 (t, *J* 8.2, 1H, Ar), 7.70–7.71 (d, *J* 2.0, 1H, Ar), 7.84–7.85 (d, *J* 3.3, 1H, Ar); ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 24.71, 25.75, 32.81, 49.24, 56.25, 60.94, 105.44, 124.25, 125.79, 128.74, 129.68, 132.07, 136.61, 139.15, 141.48, 146.35, 149.10, 153.94; MS *m*/*z*: 393 (M+, 22%), 311 (18), 280 (12), 149 (98), 55 (53), 41 (46).

***N*-Cyclohexyl-3-(5-methylthiophen-2-yl)-quinoxaline-2-amine 4d.** Yield: 80%; m.p. 190–192 °C; elem. anal.: found: C, 70.89; H, 6.64; N, 13.09; calc. for $C_{19}H_{21}N_3S$: C, 70.55; H, 6.54; N, 12.99%; IR (KBr, ν_{max}/cm^{-1}): 3230, 1638, 1624; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.10–2.12 (m, 10H, cyclohexyl), 2.42 (s, 3H, CH_3), 4.24 (m, 1H, CH–NH), 5.14 (s br, 1H, CH–NH), 6.90–6.91 (d, *J* 2.6, 2H, Ar), 7.37–7.39 (t, *J* 4.2, 1H, Ar), 7.48–7.51 (t, *J* 7.0, 1H, Ar), 7.84–7.85 (d, *J* 1.5, 1H, Ar), 7.88–7.89 (d, *J* 1.3, 1H, Ar); ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 18.24, 24.71, 25.75, 33.75, 51.14, 127.42, 128.86, 128.91, 132.64, 133.38, 134.51, 138.78, 141.23, 142.67, 148.89, 160.05; MS *m*/*z*: 323 (M+, 40%), 283 (36), 241 (96), 201 (95), 149 (42), 55 (25), 41 (31).

***N*-Cyclohexyl-3-(2,3-dichlorophenyl)-quinoxaline-2-amine 4e.** Yield: 90%; m.p. 245–247 °C; elem. anal.: found: C, 64.84; H, 5.18; N, 11.31; calc. for $C_{20}H_{19}Cl_2N_3$: C, 64.52; H, 5.14; N, 11.29%; IR (KBr, ν_{max}/cm^{-1}): 3360, 1641, 1625; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.09–2.09 (m, 10H, cyclohexyl), 4.21 (m, 1H, CH–NH) 4.41 (s br, 1H, CH–NH), 7.38–7.45 (m, 3H, Ar), 7.56–7.60 (m, 2H, Ar), 7.74 (d, *J* 1.1, 1H, Ar), 7.80 (d, *J* 1.2, 1H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 24.83, 24.88, 32.69, 33.01, 49.48, 124.51, 125.69, 128.19, 128.28, 130.03, 132.13, 133.87, 134.04, 136.32, 144.11, 149.04; MS *m*/*z*: 371 (M+, 10%), 283 (22), 254 (93), 201 (63), 149 (52), 55 (26), 41 (30).

***N*-Cyclohexyl-3-(3-chlorophenyl)-quinoxaline-2-amine 4f.** Yield: 94%; m.p. 190–192 °C; elem. anal.: found: C, 71.42; H, 6.04; N, 12.52; calc. for $C_{20}H_{20}ClN_3$: C, 71.10; H, 5.97; N, 12.44%; IR (KBr, ν_{max}/cm^{-1}): 3255, 1635, 1630; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.12–2.24 (m, 10H, cyclohexyl), 4.15 (m, 1H, CH–NH), 4.54 (s br, 1H, CH–NH), 7.45–7.47 (m, 2H, Ar), 7.67–7.70 (m, 3H, Ar), 7.80–7.83 (dd, *J* 4.5, 2H, Ar), 8.1 (s, 1H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 23.34, 26.25, 33.75, 52.14, 127.42, 128.86, 128.91, 129.70, 130.12, 131.21, 132.64, 133.38, 134.51, 138.78, 141.23, 142.67, 148.89, 160.05; MS *m*/*z*: 337 (M+, 8%), 254 (85), 149 (55), 55 (35), 41 (40).

***N*-Cyclohexyl-3-(phenethyl)-quinoxaline-2-amine 4g.** Yield: 75%; m.p. 180–182 °C; elem. anal.: found: C, 80.03; H, 7.65; N, 12.72; calc. for $C_{22}H_{25}N_3$: C, 79.72; H, 7.60; N, 12.68%; IR (KBr, ν_{max}/cm^{-1}): 3350, 1635, 1625; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.12–2.11 (m, 10H, cyclohexyl), 3.02–3.06 (t, *J* 8.2, 2H, CH_2–CH_2–Ar), 3.24–3.28 (t, *J* 7.7, 2H, –CH_2–CH_2–Ar), 4.18 (m, 1H, CH–NH), 4.60 (s, 1H, CH–NH), 7.21–7.40 (m, 6H, Ar), 7.52–7.53 (t, *J* 1.3, 1H, Ar), 7.83–7.84 (d, *J* 1.5, 2H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 24.71, 24.90, 25.38, 32.69, 35.72, 49.46, 124.21, 126.22, 126.42, 128.20, 128.32, 128.45, 128.76, 136.33, 141.47, 147.02, 158.02; MS *m*/*z*: 331 (M+, 49%), 288 (8), 249 (96), 145 (15), 91 (40), 57 (17), 41 (13).

***N*3,*N*3′-Dicyclohexyl-2,2′-diphenyl-6,6′-biquinoxaline-3,3′-diamine 4h.** Yield: 65%; m.p. >290 °C (dec); elem. anal.: found: C, 79.85; H, 6.85; N, 14.06; calc. for $C_{40}H_{40}N_6$: C, 79.44; H, 6.67; N, 13.90%; IR (KBr, ν_{max}/cm^{-1}): 3300, 1645, 1625; ^{1}H-NMR (500 MHz; DMSO-d_6) δ_H (ppm): 1.22–2.10 (m, 20H, cyclohexyl), 4.20 (m, 2H, CH–NH), 5.17 (2H, s br, CH–NH), 7.30–7.75 (m, 10H, Ar), 7.89–7.90 (d, *J* 7.7, 2H, Ar), 8.18–8.19 (d, *J* 7.8, 2H, Ar), 8.36 (s, 2H, Ar). ^{13}C-NMR (50 MHz; DMSO-d_6)

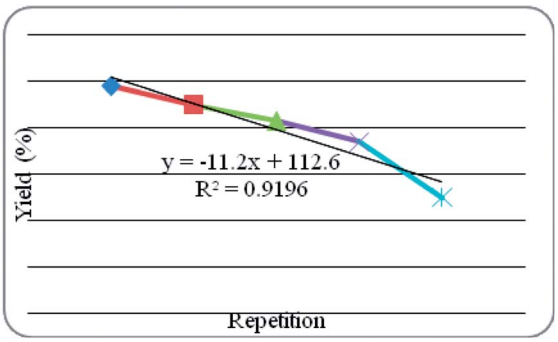
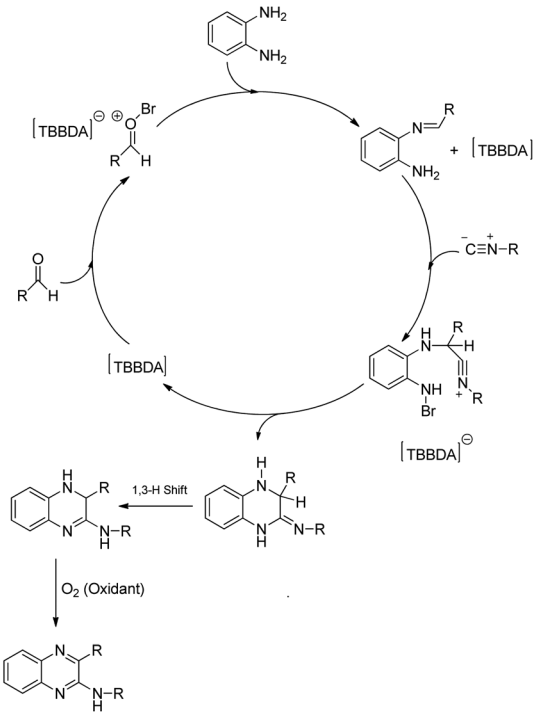


Fig. 3 Reusability of the catalyst.



Scheme 2 Suggested mechanism for the formation of quinoxaline.

δ_C (ppm): 24.77, 25.81, 49.34, 124.16, 125.69, 128.19, 128.82, 129.55, 130.03, 131.12, 133.88, 135.84, 136.82, 139.78, 140.80, 141.20, 146.91, 149.26; MS *m*/*z*: 379 (M+, 19%), 283 (20), 254 (93), 201 (63), 149 (52), 55 (28), 41 (30).

***N*3,*N*3′-Dicyclohexyl-2,2′-dip-tolyl-6,6′-biquinoxaline-3,3′-diamine 4i.** Yield: 60%; m.p. >270 °C (dec); elem. anal.: found: C, 80.01; H, 7.22; N, 13.50; calc. for $C_{42}H_{44}N_6$: C, 79.71; H, 7.01; N, 13.28%; IR (KBr, ν_{max}/cm^{-1}): 3220, 1635, 1620; ^{1}H-NMR (500 MHz; DMSO-d_6) δ_H (ppm): 1.21–2.12 (m, 20H, cyclohexyl), 2.17 (s, 6H, CH_3), 4.20 (m, 2H, CH–NH), 4.86 (s br, 2H, CH–NH), 7.04–7.40 (d, *J* 4.3, 4H, Ar–CH_3), 7.39–7.40 (d, *J* 3.8, 4H, Ar–CH_3), 8.10–8.11 (d, *J* 5.2, 2H, Ar), 8.21–8.22 (d, *J* 5.1, 2H, Ar), 8.33 (d, 2H, Ar). ^{13}C-NMR (50 MHz; DMSO-d_6) δ_C (ppm): 24.71, 25.75, 32.81, 49.25, 120.05, 124.25, 125.79, 126.84, 128.74, 129.68, 132.07, 136.61, 139.15, 141.48, 146.35, 149.10; MS *m*/*z*: 632 (M+, 31%), 590 (18), 522 (85), 490 (36), 449 (31), 409 (45), 300 (50), 214 (90), 106 (40), 75 (81).

***N*3,*N*3′-Dicyclohexyl-2,2′-bis(4-methoxyphenyl)-6,6′-biquinoxaline-3,3′-diamine 4j.** Yield: 55%; m.p. >285 °C (dec); elem. anal.: found: C, 76.20; H, 6.91; N, 12.68; calc. for $C_{42}H_{44}N_6O_2$: C, 75.88; H, 6.67; N, 12.64%; IR (KBr, ν_{max}/cm^{-1}): 3220, 1635, 1620; ^{1}H-NMR (200 MHz; DMSO-d_6) δ_H (ppm): 1.13–2.14 (m, 20H, cyclohexyl), 3.90 (s, 6H, OCH_3), 4.20 (m, 2H, CH–NH), 5.19 (s br, 2H, CH–NH), 6.80–6.81 (d, *J* 2.9, 4H, Ar), 7.31–7.32 (d, *J* 3.3, 4H, Ar), 7.52 (d, *J* 1.5, 2H, Ar), 7.9–8.0 (d, *J* 1.9, 2H, Ar), 8.23 (s, 2H, Ar). ^{13}C-NMR (50 MHz; DMSO-d_6) δ_C (ppm): 24.66, 25.79, 32.82, 54.86, 55.79, 117.58, 125.72, 126.63, 126.87, 128.78, 129.66, 133.11, 136.82, 141.05, 141.30, 146.19; MS *m*/*z*: 644 (M+, 15%), 600 (10), 582 (39), 501 (20), 486 (21), 420 (26), 319 (26), 214 (75), 108 (26), 79 (10).

***N*-Cyclohexyl-3,3′-(1,4-phenylene)bis(quinoxalin-2-amine) 4k.** Yield: 70%; m.p. >250 °C (dec); elem. anal.: found: C, 77.63; H, 6.63; N, 16.02; calc. for $C_{34}H_{36}N_6$: C, 77.24; H, 6.86; N, 15.90%; IR (KBr, ν_{max}/cm^{-1}): 3220, 1635, 1620; ^{1}H-NMR (200 MHz; DMSO-d_6) δ_H (ppm): 1.16–2.15 (m, 20H, cyclohexyl), 4.13 (m, 2H, CH–NH), 5.07 (s br, 2H, CH–NH), 7.34–7.38 (m, 4H, Ar), 7.39–7.40 (d, *J* 1.9, 4H, Ar), 7.53–7.54 (t, *J* 1.4, 2H, Ar), 7.60–7.61 (d, *J* 1.9, 2H, Ar), 7.66–7.88 (d, *J* 1.9, 2H, Ar). ^{13}C-NMR (50 MHz; DMSO-d_6) δ_C (ppm): 24.66, 25.79, 32.82, 49.41, 124.27, 125.72, 128.78, 129.66, 136.82, 141.05, 141.30, 146.19, 149.15; MS *m*/*z*: 528 (M+, 5%), 446 (7), 364 (13), 175 (51), 149 (98), 69 (72), 43 (97).

***N*3,*N*3′-Dicyclohexyl-2,2′-dipropyl-6,6′-biquinoxaline-3,3′-diamine 4l.** Yield: 60%; m.p. >260 °C (dec); elem. anal.: found: C, 76.41; H, 8.36; N, 15.68; calc. for $C_{34}H_{44}N_6$: C, 76.08; H, 8.26; N, 15.66%; ^{1}H-NMR (200 MHz; DMSO-d_6) δ_H (ppm): 1.03 (t, 6H, CH_3), 1.22–2.34 (m, 22H, cyclohexyl), 2.66 (t, 2H, Ar–CH_2), 4.21 (m, 2H, CH–NH), 4.73 (s br, 2H, CH–NH), 7.95–7.97 (d, *J* 4.2, 2H, Ar), 8.05–8.07 (d, *J* 4.6, 2H, Ar), 8.31 (s, 2H, Ar). ^{13}C-NMR (50 MHz; DMSO-d_6) δ_C (ppm): 17.54, 23.54, 24.85, 25.80, 31.75, 33.05, 49.39, 124.07, 125.36, 125.98, 128.11, 130.22, 132.63, 136.30, 148.17, 149.10; MS *m*/*z*: 536 (M+, 10%), 373 (45), 323 (62), 267 (42), 214 (77), 198 (50), 107 (22), 72 (10), 55 (5).

***N*-Cyclohexyl-3-isobutylquinoxaline-2-amine 4m.** Yield: 85%; m.p. 175–177 °C; elem. anal.: found: C, 76.48; H, 8.92; N, 14.94; calc. for $C_{18}H_{25}N_3$: C, 76.28; H, 8.89; N, 14.835%; IR (KBr, ν_{max}/cm^{-1}): 3300, 1642, 1630; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.02–1.04 (d, *J* 6.6, 6H, $2CH_3$), 1.22–2.15 (m, 10H, cyclohexyl), 2.30 (m, 1H, $CH(CH_3)_2$), 4.21 (m, 1H, CH–NH), 4.73 (s br, 1H, CH–NH), 7.31–7.32 (t, *J* 2.4, 1H, Ar), 7.45–7.49 (t, *J* 8.09, 1H, Ar), 7.73–7.74 (d, *J* 2.1, 1H, Ar), 7.80–7.81 (d, *J* 1.4, 1H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 21.53, 24.34, 24.54, 24.72, 26.54, 34.63, 49.39, 124.21, 126.22, 128.40, 128.55, 129.30, 136.3, 147.02; MS *m*/*z*: 283 (M+, 5%), 255 (79), 226 (18), 198 (48), 173 (80), 145 (26), 55 (5), 41 (4).

***N*-Cyclohexyl-3-hexylquinoxaline-2-amine 4n.** Yield: 94%; m.p. 190–192 °C; elem. anal.: found: C, 77.46; H, 9.42; N, 13.60; calc. for $C_{20}H_{29}N_3$: C, 77.12; H, 9.38; N, 13.49%; IR (KBr, ν_{max}/cm^{-1}): 3150, 1635, 1645; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 0.92 (t, 3H, CH_3), 1.24–2.16 (m, 16H, CH_2–hexyl and CH_2–cyclohexyl), 2.75 (t, 2H, CH_2), 4.25 (m, 1H, CH–NH), 4.76 (s br, 1H, CH–NH), 7.33–7.37 (t, *J* 8.2, 1H, Ar), 7.46–7.50 (t, *J* 8.2, 1H, Ar), 7.79–7.82 (d, *J* 6.7, 2H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C

(ppm): 14.03, 22.54, 24.40, 24.72, 25.60, 31.75, 32.63, 33.05, 33.60, 38.04, 49.39, 124.07, 125.36, 128.11, 128.88, 132.63, 136.30, 149.1. MS *m/z*: (M+, 311), 254 (25%), 241 (57), 229 (98), 185, 159 (60), 51 (11), 41 (6).

***N*-Cyclohexyl-3-(2-(methylthio)ethyl)quinoxaline-2-amine 4o.** Yield: 80%; m.p. 180–182 °C; elem. anal.: found: C, 68.04; H, 7.65; N, 14.10; calc. for $C_{17}H_{23}N_3S$: C, 67.73; H, 7.69; N, 13.94%; IR (KBr, ν_{max}/cm^{-1}): 3150, 1628, 1615; ^{1}H-NMR (200 MHz; $CDCl_3$) δ_H (ppm): 1.12–1.82 (m, 10H, cyclohexyl), 2.16 (s, 3H, SCH_3), 2.57 (t, *J* 2.4, 2H, Ar–CH_2–CH_2–S), 3.04 (t, *J* 2.5, 2H, Ar–CH_2–CH_2–S), 4.08 (m, 1H, CH–NH), 4.45 (s br, 1H, CH–NH), 7.53–7.56 (t, *J* 5.9, 2H, Ar), 7.75–7.78 (d, *J* 6.2, 2H, Ar). ^{13}C-NMR (50 MHz; $CDCl_3$) δ_C (ppm): 18.21, 24.42, 24.82, 32.23, 32.48, 32.70, 55.10, 124.10, 124.24, 124.65, 124.75, 135.10, 144.15, 154.10.

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