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Logic design and synthesis of quinoxalines via the integration of iodination/oxidation/cyclization sequences from ketones and 1,2-diamines

Mi Lian [a], Qi Li [a], Yanping Zhu [a], Guodong Yin [b,*], Anxin Wu [a,*]

[a] Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, Central China Normal University, Wuhan 430079, China
[b] Hubei Key Laboratory of Pollutant Analysis & Reuse Technology, Hubei Normal University, Huangshi 435002, China

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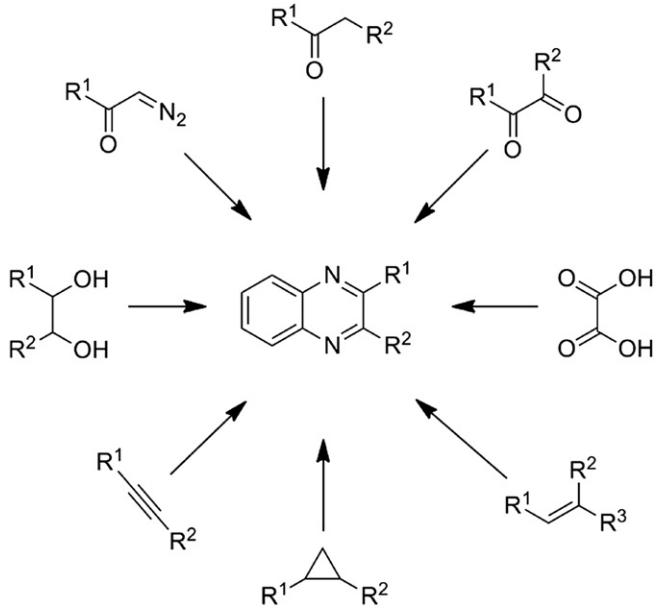
ABSTRACT

A novel protocol for the synthesis of quinoxalines has been developed from simple ketones and 1,2-diamines. This process underwent a logic approach to bis-substituted quinoxalines via a consecutive iodination/Kornblum oxidation/cyclization in the presence of I_2/CuO/DMSO and to mono-substituted quinoxalines via an iodination/cyclization/aromatization in the presence of I_2/CuO/$K_3PO_4 \cdot 3H_2O$.

1. Introduction

Quinoxaline is a common nitrogen-containing heterocyclic compound, which has wide applications in pharmaceutical chemistry, in fields, such as anticancer,[1] antiviral,[2] and antibacterial.[3] Quinoxaline and its derivatives can also act as important synthetic intermediates.[4] Due to these significant properties, a variety of methods have been reported for the synthesis of quinoxalines. The most common methods are derived by the condensation of 1,2-diamines with two-carbon synthons, such as 1,2-diketone,[5] oxalic acid,[6] aldehyde,[7] ketones,[8] diazenyl butenes,[9] epoxides,[10] alkyne,[11] vicinal diols[12] or diazoketone[13] (Scheme 1).

In previous studies, we discovered that deoxybenzoin (**1a**) could be oxidized to benzil (**B**) via an intermediate 2-iodo-1,2-diphenylethanone (**A**)[14] (Scheme 2a). In addition, it is well known that 2,3-diphenylquinoxaline (**3aa**) could be obtained when the benzil condensed with *o*-phenylenediamine (**2a**) (Scheme 2b).[5a] Here, we present a new method for the synthesis of quinoxalines via consecutive iodination/oxidation/cyclization sequences in one pot from simple ketones and 1,2-diamines based on a logic design (Scheme 2c).



Scheme 1. Methods for the synthesis of quinoxalines.

* Corresponding authors. Tel./fax: +86 27 67867773 (A.W.); tel./fax: +86 714 6515602 (G.Y.); e-mail addresses: gdyin@hbnu.edu.cn (G. Yin), chwuax@mail.ccnu.edu.cn (A. Wu).

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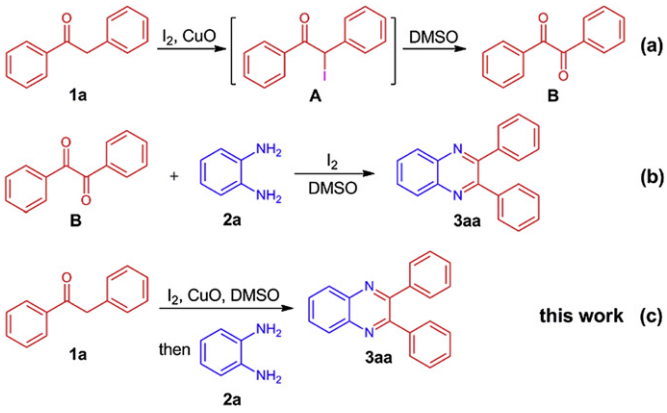


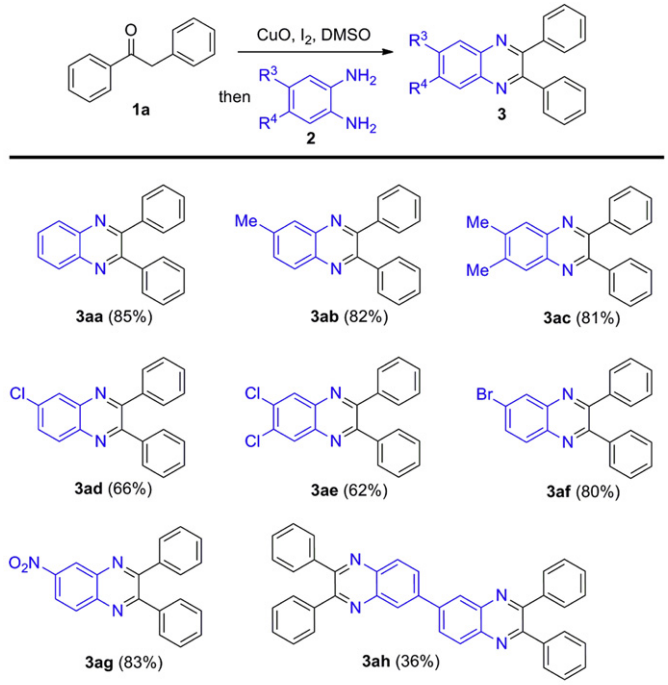
Scheme 2. Approaches to benzil and 2,3-diphenylquinoxaline.

2. Results and discussions

Firstly, deoxybenzoin (**1a**) (1.0 mmol) was treated with I_2 (1.1 mmol) and CuO (1.1 mmol) in DMSO (3 mL) at 100 °C for 4 h. After the disappearance of the starting material, *o*-phenylenediamine (**2a**) (3.0 mmol) was added and stirred for another 1 h and the desired product 2,3-diphenylquinoxaline (**3aa**) was obtained in 85% yield. Then we set out to explore the generality of this sequential process with various 1,2-diamines. The results indicated that this method was workable for 1,2-diamines with electron-withdrawing or electron-donating substituents on the aromatic backbone (Table 1). We furnished the expected quinoxalines **3aa**–**ag** in appreciable yields ranging from 62% to 85%, while the configurations of **3aa** and **3ae** were unambiguously clarified by X-ray crystallographic analysis (see Supplementary data). Methyl substituted 1,2-diamines gave the corresponding products **3ab** and **3ac** in 82% and 81% yields, respectively. The reactions between chloro-substituted 1,2-diamines and **1a** provided slightly lower yields of **3ad** and **3ae**. Notably, even electron-deficient bromo- and nitro-substituted 1,2-diamines were also shown to be excellent substrates (**3af** and **3ag**). When 3,3′,4,4′-tetraamino-1,1′-biphenyl was employed, the bis-quinoxaline product 2,2′,3,3′-tetraphenyl-6,6′-biquinoxaline (**3ah**) was isolated in 36% yield.

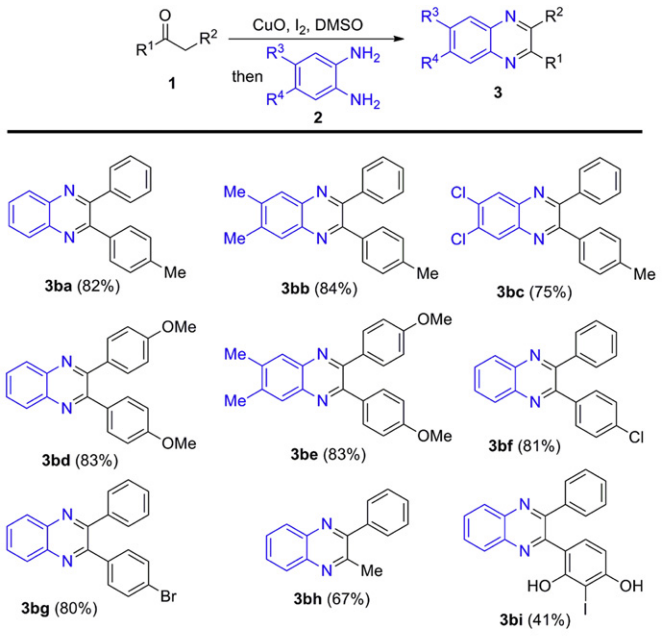
Next, the variations of substituents on the aromatic ring in the carbonyl compounds were also tested (Table 2). It was established that the conditions were mild enough to be compatible with a range of functional groups. The electron-neutral (CH_3) and electron-rich (OCH_3) substituted ketones all reacted with 1,2-diamines efficiently to give the desired products **3ba**–**be** in 75–84% yields. Substrates containing the electron-withdrawing group (Cl and Br) worked well in this transformation, and the corresponding products **3bf** and **3bg** were obtained in 81% and 80% yields, respectively. When propiophenone was subjected to standard conditions, furnishing **3bh** in 67% yield. It was found that the substrate containing hydroxyl group (OH) was also suitable for the reaction resulting in the iodinated product **3bi** in 41% yield.

Table 1
One-pot synthesis of quinoxalines from 1,2-diamines and deoxybenzoin[a,b]



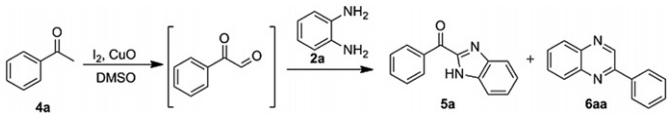
[a] Reaction conditions: **1a** (1.0 mmol), I_2 (1.1 mmol), CuO (1.1 mmol) in DMSO (3 mL) at 100 °C for 4 h, then diamine **2** (3.0 mmol) was added and the mixture was stirred for another 1 h.
[b] Isolated yield.

Table 2
Scopes of 1,2-diamines and ketones[a,b]



[a] Reaction conditions: ketone **1** (1.0 mmol), I_2 (1.1 mmol), CuO (1.1 mmol) in DMSO (3 mL) at 100°C for 4 h, then diamine **2** (3.0 mmol) was added and the mixture was stirred for another 1 h.
[b] Isolated yield.

Furthermore, the reaction substrates were extended to aryl methyl ketones for the synthesis of mono-substituted quinoxalines. However, when acetophenone (**4a**) was treated with *o*-phenylenediamine under above-mentioned standard conditions, unexpected (1*H*-benzo[*d*]imidazol-2-yl)(phenyl)methanone (**5a**) was the main product (69% yield) and 2-phenylquinoxaline (**6aa**) was only isolated in 19% yield (Scheme 3). So that, the present transformation is unsuitable for aryl methyl ketone substrates under above-mentioned standard conditions. We next explore new routes to synthesis of mono-substituted quinoxalines with high chemoselectivity.



Scheme 3. Synthesis of compounds **5a** and **6aa** acetophenone.

It was been reported that α-bromination ketones could react with 1,2-diamines to deliver quinoxaline.[8f–i] Therefore, we are attempted to a two-step one-pot synthesis of mono-substituted quinoxalines via iodinated ketones. It was found that the reaction was well performed to generate 2-iodo-1-phenylethanone in situ in the presence of I_2 and CuO at refluxing methanol in the first step.[15] Subsequently, *o*-phenylenediamine and base were added to optimize the reaction conditions in second step. The experimental results indicated that the basicity had a great effect on the yield of **6aa**. $K_3PO_4 \cdot 3H_2O$ was proved to be superior to other bases, such as K_2CO_3, Cs_2CO_3, DBU, DABCO, Et_3N, KH_2PO_4, $NaH_2PO_4 \cdot 2H_2O$, $Na_2HPO_4 \cdot 12H_2O$, $Na_3PO_4 \cdot 12H_2O$, and $Zn_3(PO_4)_2 \cdot 4H_2O$. No expected product was observed using piperidine or pyridine. Compound **6aa** was isolated in highest yield (80%) at 40 °C in the presence of $K_3PO_4 \cdot 3H_2O$. The yield of **6aa** obviously decreased with increasing or reducing the reaction temperature (see Supplementary data).

Based on the successful synthesis of **6aa**, the optimized conditions were then applied to other aryl methyl ketones (Table 3). When the substrates bearing electron-donating substituted groups on the phenyl ring, the corresponding products **6ab**–**ae** were obtained in 80–86% yields. In addition, the structure of **6ac** was confirmed by X-ray diffraction analysis (see Supplementary data). The substrates bearing electron-withdrawing substituted groups also provided the products **6af**–**ai** in good yields (63–72%). Much to our satisfaction, the substrates containing sterically hindered naphthyl ring, hydroxyl group (–OH), substituted amino group ($-NR_2$), and heterocycles (furan, thiophene, benzofuran, and 3-indole), **6aj**–**aq** were also obtained in satisfied yields (63–81%).

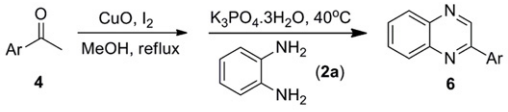
Then we explored the scopes of a series of 1,2-diamines to investigate the effect of substituents on the reactivity and regioselectivity (Table 4). 4,5-Dimethylbenzene-1,2-diamine and 4-methylbenzene-1,2-diamine gave the corresponding products **6ba**–**bd** in good yields (71–83%). Substrates containing electron-withdrawing groups (–Cl, –Br) furnished the corresponding **6be**–**bg** in moderate to good yields (50–74%). It should be notable that, unsymmetrical 1,2-diamines resulted in two isomers of **6bd**, **6bf**, **6bg** with the ratio of 1:1 to 2:3.

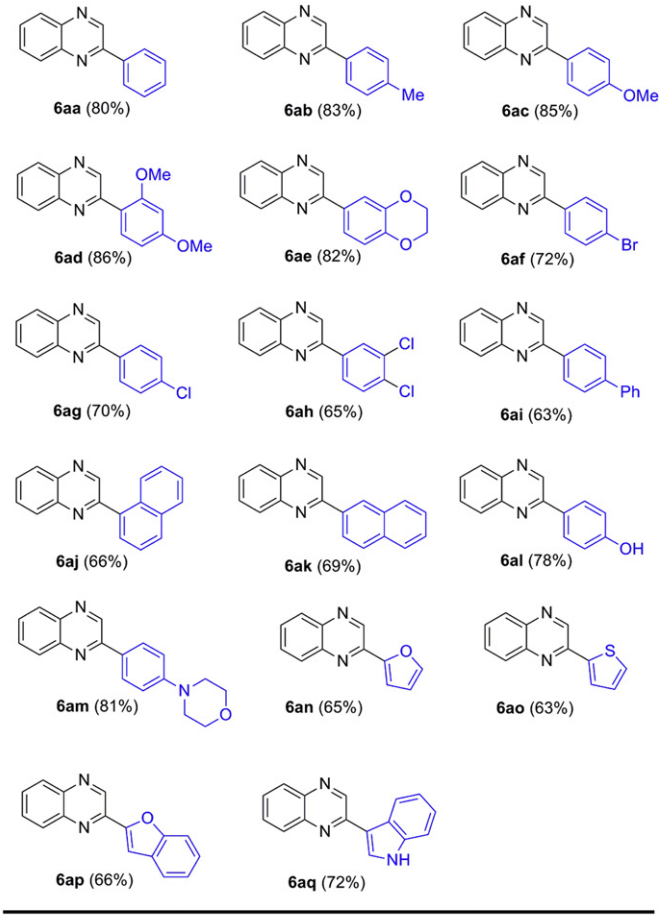
We presented a possible pathway of consecutive iodination/oxidation/cyclization sequences for the synthesis of quinoxalines (Scheme 4). The ketone was converted into the corresponding α-iodinated intermediates 2-iodo-1,2-diphenylethanone **A** (R=Ph) or 2-iodo-1-phenylethanone **C** (R=H) in the presence of I_2 and CuO. On the one hand, intermediate **A** underwent Kornblum oxidation to give benzil **B**.[14] Subsequently, I_2 catalyzed the condensation reaction of **B** and 1,2-diamine (**2a**) to afford the desired quinoxaline **3aa**.[5a] On the other hand, intermediate **C**[15] was reacted with **2a** undergoing intermolecular nucleophilic substitution and condensation reaction to form **D**,[8c,g] which underwent an oxidative aromatization step to give quinoxaline **6aa**.

To confirm the reaction process, the reactions of intermediates were carried out (Scheme 5). When iodo-phenylethanone (**A**) was stirred in DMSO and then 1,2-diamine (**2a**) was added, the target product **3aa** was obtained in 80% yield in the presence of iodine and DMSO (Scheme 5a). Benzil (**B**) was reacted with **2a** to give **3aa** in 96% yield (Scheme 5b).

Moreover, monitoring of the reaction by ^1H NMR (400 MHz) further demonstrated this plausible pathway (Fig. 1). We set up the reaction in the NMR tube that contained deoxybenzoin (**1a**) (0.10 mmol), iodine (0.11 mmol), and CuO (0.11 mmol) at 100 °C in DMSO-d_6 (0.5 mL). The reaction was monitored at different time points during the reaction course. The characteristic peak of iodophenylethanone **A** appeared after 1 h. Intermediate **A** was consumed completely after 6 h and converted to benzil **B** quantitatively. After addition of 1,2-diamine (0.30 mmol), the corresponding peaks of quinoxaline **3aa** were observed. The experimental proved that **A** and **B** were the possible intermediates.

Table 3
One-pot synthesis of **6** from methyl ketones and *o*-phenylenediamine[a,b]



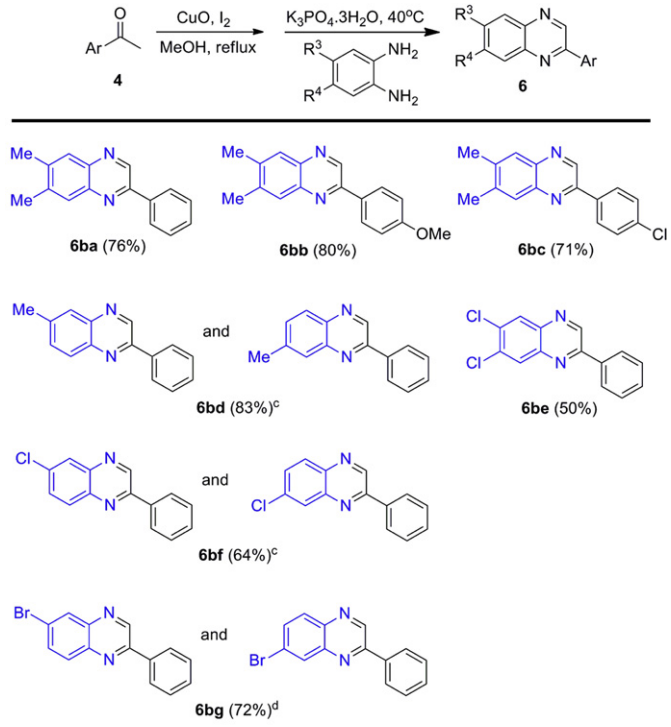


[a] Reaction conditions: aromatic ketones (1.0 mmol), diamine (1.0 mmol), I_2 (1.0 mmol), CuO (1.1 mmol), $K_3PO_4 \cdot 3H_2O$ (1.0 mmol).
[b] Isolated yield.

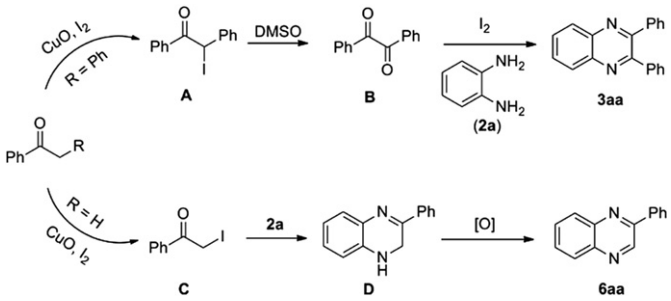
3. Conclusion

In summary, a novel and convenient one-pot protocol for the synthesis of quinoxaline derivatives has been developed from simple ketones and 1,2-diamines. This process underwent a logic approach to bis-substituted quinoxalines (**3**) via a consecutive iodination/Kornblum oxidation/cyclization in the presence of I_2/CuO/DMSO and to mono-substituted quinoxalines (**6**) via an iodination/cyclization/aromatization in the presence of I_2/CuO/$K_3PO_4 \cdot 3H_2O$. The plausible reaction mechanism was also discussed by control experimental and ^1H NMR spectroscopic monitoring.

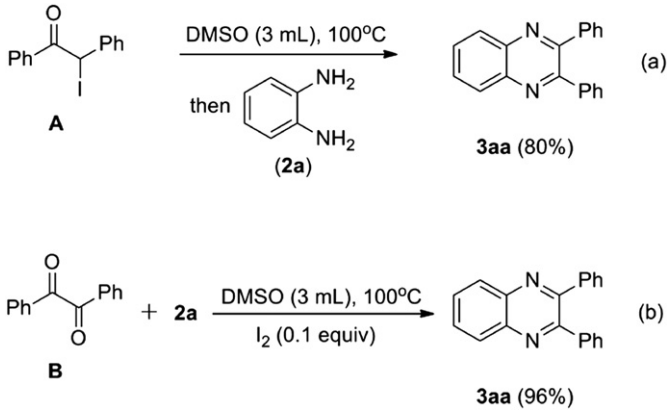
Table 4
Scopes of methyl ketones and 1,2-diamines[a,b]



[a] Reaction conditions: aromatic ketones (1.0 mmol), diamines (1.0 mmol), I_2 (1.0 mmol), CuO (1.1 mmol), $K_3PO_4{\cdot}3H_2O$ (1.0 mmol).
[b] Isolated yield.
[c] Two isomers with the ratio of 1:1 (by ^1H NMR).
[d] Two isomer with the ratio of 2:3 (by ^1H NMR).



Scheme 4. The plausible pathway of the present reaction.



Scheme 5. Control experimental.

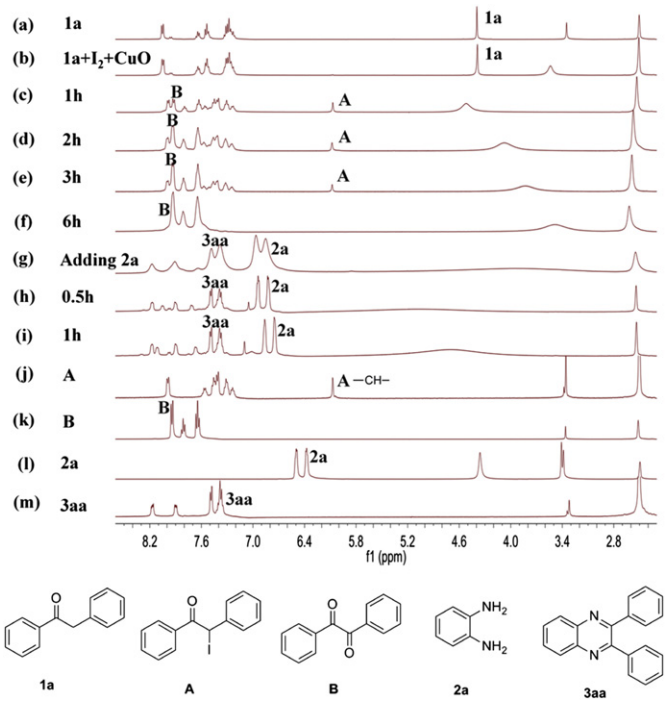


Fig. 1. ^1H NMR spectroscopic monitoring of the present reaction.

4. Experimental section

4.1. General procedure for the synthesis of compound 3 (using 2,3-diphenylquinoxaline 3aa as an example)

A stirred solution of deoxybenzoin **1a** (196 mg, 1.0 mmol), CuO (88 mg, 1.1 mmol), and iodine (279 mg, 1.1 mmol) was heated at 100 °C for 4 h in DMSO (3 mL), after the disappearance of the starting material (TLC), 1,2-diamine **2a** (324 mg, 3.0 mmol) was added and stirred for another 1 h. Then the reaction mixture was poured into 50 mL brine and the aqueous layer was extracted with EtOAc (3×50 mL). The extract was washed with $Na_2S_2O_3$ solution, dried over anhydrous Na_2SO_4 then the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the eluent to give the expected products **3aa** as the yellow solid (240 mg, 85% yield).

4.2. General procedure for the synthesis of compound 6 (using 2-phenylquinoxaline 6aa as an example)

A mixture of acetophenone **4a** (120 mg, 1.0 mmol), iodine (254 mg, 1.0 mmol), and CuO (88 mg, 1.1 mmol) in anhydrous methanol (10 mL) was heated at reflux, after disappearance of the reactant (1–12 h, monitored by TLC), 1,2-diamines **2a** (108 mg, 1.0 mmol) and $K_3PO_4{\cdot}3H_2O$ (266 mg, 1.0 mmol) was added and the mixture was stirred for 12 h at 40 °C. The solvent was removed under reduced pressure, and 50 mL water was added to mixture, extracted with EtOAc three times (3×50 mL). The extract was washed with $Na_2S_2O_3$, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as the eluent to give the expected products **6aa** as pale yellow solid, (80% yield).

4.3. Characterization data

*4.3.1. 2,3-Diphenylquinoxaline (**3aa**).*[8l] Yield 85%, yellow solid; mp 117–119 °C; IR (KBr, cm^{-1}): 3059, 1634, 1477, 1441, 1346, 1076, 1058,

770, 698; ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 8.18–8.20 (m, 2H), 7.77–7.79 (m, 2H), 7.52 (d, J=7.2 Hz, 4H), 7.33–7.38 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.4, 141.1, 138.9, 129.9, 129.8, 129.1, 128.8, 128.2; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{14}N_2$: 283.1230; found: 283.1231.

*4.3.2. 6-Methyl-2,3-diphenylquinoxaline (**3ab**).*[8l] Yield 82%, white solid; mp 110–112 °C; IR (KBr, cm^{-1}): 3056, 2940, 1618, 1486, 1444, 1200, 1057, 1022, 809, 773, 701; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.06 (d, J=8.8 Hz, 1H), 7.95 (s, 1H), 7.60 (d, J=7.6 Hz, 1H), 7.51 (d, J=6.8 Hz, 4H), 7.33 (d, J=6.4 Hz, 6H), 2.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.3, 152.5, 141.2, 140.5, 139.6, 139.1, 132.3, 129.8, 128.7, 128.6, 128.2, 128.0, 21.9; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{21}H_{16}N_2$: 297.1386; found: 297.1387.

*4.3.3. 6,7-Dimethyl-2,3-diphenylquinoxaline (**3ac**).*[8l] Yield 81%, yellow solid; mp 175–176 °C; IR (KBr, cm^{-1}): 3038, 2970, 2928, 2852, 1630, 1548, 1445, 1414, 1344, 1209, 1023, 870, 761, 700; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.93 (s, 2H), 7.50 (d, J=6.0 Hz, 4H), 7.32–7.33 (m, 6H), 2.52 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.4, 140.5, 140.1, 139.3, 129.8, 128.5, 128.2, 20.5; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}N_2$: 311.1543; found: 311.1544.

*4.3.4. 6-Chloro-2,3-diphenylquinoxaline (**3ad**).*[8l] Yield 66%, white solid; mp 117–120 °C; IR (KBr, cm^{-1}): 3053, 1605, 1550, 1468, 1444, 1341, 1069, 831, 802, 768, 695; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.16–8.16 (m, 1H), 8.08–8.10 (m, 1H), 7.67–7.70 (m, 1H), 7.51 (d, J=7.2 Hz, 4H), 7.31–7.39 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.2, 153.5, 141.4, 139.6, 138.6, 138.5, 135.6, 130.9, 130.3, 129.8, 129.7, 129.0, 128.9, 128.2, 128.0; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}ClN_2$: 317.0840; found: 317.0841.

*4.3.5. 6,7-Dichloro-2,3-diphenylquinoxaline (**3ae**).* Yield 62%, yellow solid; mp 154–156 °C; IR (KBr, cm^{-1}): 3047, 2961, 2926, 2854, 1586, 1533, 1492, 1439, 1334, 1259, 1188, 1066, 1021, 881, 768, 697; ^{1}H NMR ($CDCl_3$, 600 MHz): δ (ppm) 8.29 (s, 2H), 7.50 (d, J=7.8 Hz, 4H), 7.39 (d, J=6.6 Hz, 2H), 7.35 (t, J=7.2 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.4, 139.9, 138.3, 134.4, 129.7, 129.3, 128.3; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{12}Cl_2N_2$: 351.0450; found: 351.0451.

*4.3.6. 6-Bromo-2,3-diphenylquinoxaline (**3af**).* Yield 80%, yellow solid; mp 118–120 °C; IR (KBr, cm^{-1}): 3045, 1592, 1546, 1468, 1444, 1390, 1340, 1184, 1060, 1024, 975, 914, 829, 801, 767, 695; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.36–8.37 (m, 1H), 8.03–8.05 (m, 1H), 7.84 (q, J=7.2 Hz, 1H), 7.51 (d, J=7.2 Hz, 4H), 7.32–7.40 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.2, 153.7, 141.7, 139.9, 138.6, 138.5, 133.5, 131.4, 130.5, 129.8, 129.7, 129.1, 129.0, 128.3, 123.8; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}BrN_2$: 361.0335; found: 361.0335.

*4.3.7. 6-Nitro-2,3-diphenylquinoxaline (**3ag**).*[8l] Yield 83%, yellow solid; mp 184–186 °C; IR (KBr, cm^{-1}): 3090, 3056, 1614, 1520, 1399, 1341, 1055, 1025, 812, 769, 700; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.09–9.09 (m, 1H), 8.54 (q, J=6.8 Hz, 1H), 8.30–8.32 (m, 1H), 7.55–7.58 (m, 4H), 7.36–7.45 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 156.2, 155.5, 147.7, 143.4, 139.8, 137.9, 137.9, 130.6, 129.8, 129.7, 129.5, 128.4, 125.5, 123.2; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}N_3O_2$: 328.1081; found: 328.1082.

*4.3.8. 2,2′,3,3′-Tetraphenyl-6,6′-biquinoxaline (**3ah**).*[5d] Yield 36%, yellow solid; mp >300 °C; IR (KBr, cm^{-1}): 3056, 1613, 1553, 1476, 1444, 1390, 1344, 1190, 1058, 830, 802, 767, 697; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.60 (s, 2H), 8.33 (s, 1H), 8.31 (s, 1H), 8.25 (s, 1H), 8.23 (s, 1H), 7.57 (d, J=6.8 Hz, 8H), 7.37 (d, J=6.8 Hz, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.1, 153.7, 141.4, 141.2, 140.9, 138.9, 129.8, 129.5, 128.9, 128.3, 127.4; EI-MS: m/z 562.5 (M, 100), 355.3 (61), 280.6 (84), 228.9 (56), 215.2 (47), 178.0 (55), 150.1 (98).

*4.3.9. 2-Phenyl-3-(p-tolyl)quinoxaline (**3ba**).*[8l] Yield 82%, yellow solid; mp 112–114 °C; IR (KBr, cm^{-1}): 3053, 2923, 1613, 1554, 1512, 1476, 1442, 1394, 1345, 1055, 1019, 975, 755, 698; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.14–8.16 (m, 2H), 7.69–7.71 (m, 2H), 7.52–7.54 (m, 2H), 7.41 (d, J=8.0 Hz, 2H), 7.32 (m, 3H), 7.11 (d, J=7.6 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.4, 141.2, 141.0, 139.2, 138.8, 136.1, 129.8, 129.7, 129.1, 129.0, 128.7, 128.2, 21.3; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{21}H_{16}N_2$: 297.1386; found: 297.1387.

*4.3.10. 6,7-Dimethyl-2-phenyl-3-(p-tolyl)quinoxaline (**3bb**).* Yield 84%, white solid; mp 132–134 °C; IR (KBr, cm^{-1}): 3031, 2971, 2936, 2916, 1728, 1609, 1476, 1447, 1415, 1340, 1207, 1056, 1020, 867, 699; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.91 (s, 2H), 7.51 (d, J=6.4 Hz, 2H), 7.39 (d, J=7.6 Hz, 2H), 7.33–7.34 (m, 3H), 7.12 (d, J=7.6 Hz, 2H), 2.50 (s, 6H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.4, 140.4, 140.3, 140.2, 139.5, 138.4, 136.4, 129.7, 128.9, 128.4, 128.2, 21.3, 20.4; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{23}H_{20}N_2$: 325.1699; found: 325.1700.

*4.3.11. 6,7-Dichloro-2-phenyl-3-(p-tolyl)quinoxaline (**3bc**).* Yield 75%, yellow solid; mp 134–136 °C; IR (KBr, cm^{-1}): 3065, 3032, 2919, 2856, 1610, 1536, 1441, 1388, 1336, 1256, 1191, 1108, 1058, 1021, 960, 886, 831, 692; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.26 (s, 2H), 7.51 (d, J=6.8 Hz, 2H), 7.33–7.41 (m, 5H), 7.14 (d, J=7.6 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.4, 139.9, 139.7, 139.5, 138.5, 135.4, 134.3, 134.1, 129.7, 129.2, 129.1, 128.3, 21.4; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{21}H_{14}Cl_2N_2$: 365.0607; found: 365.0609.

*4.3.12. 2,3-Bis(4-methoxyphenyl)quinoxaline (**3bd**).*[8l] Yield 83%, yellow solid; mp 147–148 °C; IR (KBr, cm^{-1}): 3006, 2960, 2840, 1607, 1512, 1464, 1394, 1348, 1288, 1244, 1174, 1028, 830, 765; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.11–8.14 (m, 2H), 7.70–7.73 (m, 2H), 7.50 (d, J=8.4 Hz, 4H), 6.87 (d, J=8.8 Hz, 4H), 3.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 160.1, 153.0, 141.0, 131.6, 131.2, 129.5, 128.9, 113.7, 55.3; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}N_2O_2$: 343.1441; found: 343.1441.

*4.3.13. 2,3-Bis(4-methoxyphenyl)-6,7-dimethylquinoxaline (**3be**).-* Yield 83%, yellow solid; mp 123–125 °C; IR (KBr, cm^{-1}): 2931, 2835, 1605, 1512, 1457, 1419, 1342, 1296, 1248, 1174, 1027, 970, 833; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.86 (s, 2H), 7.46 (d, J=8.8 Hz, 4H), 6.85 (d, J=8.8 Hz, 4H), 3.80 (s, 6H), 2.47 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 159.8, 151.9, 138.9, 131.9, 131.1, 127.9, 113.6, 55.2, 20.3; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{24}H_{22}N_2O_2$: 371.1754; found: 371.1754.

*4.3.14. 2-(4-Chlorophenyl)-3-phenylquinoxaline (**3bf**).*[8l] Yield 81%, white solid; mp 136–138 °C; IR (KBr, cm^{-1}): 3056, 2927, 1727, 1589, 1492, 1476, 1441, 1399, 1344, 1089, 1056, 1013, 977, 843, 804, 765, 699; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.16–8.20 (m, 2H), 7.78–7.81 (m, 2H), 7.45–7.52 (m, 4H), 7.35–7.40 (m, 3H), 7.32 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.2, 152.1, 141.1, 138.7, 137.4, 135.1, 131.2, 130.2, 130.2, 129.7, 129.2, 129.1, 129.0, 128.5, 128.5; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{20}H_{13}ClN_2$: 317.0840; found: 317.0841.

*4.3.15. 2-(4-Bromophenyl)-3-phenylquinoxaline (**3bg**).*[8l] Yield 80%, white solid; mp 146–147 °C; IR (KBr, cm^{-1}): 3055, 1584, 1535, 1478, 1441, 1396, 1343, 1220, 1071, 1054, 1009, 976, 840, 803, 765, 700; ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.19 (s, 2H), 7.80 (d, J=6.4 Hz, 2H), 7.50 (q, J=8.0 Hz, 4H), 7.39–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 153.2, 152.1, 141.2, 141.1, 138.7, 137.9, 131.5, 130.2,

130.2, 129.7, 129.2, 129.1, 129.0, 128.5, 123.5; HRMS (APCI): *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{13}BrN_2$: 361.0335; found: 361.0336.

*4.3.16. 2-Methyl-3-phenylquinoxaline (**3bh**).*[5g] Yield 67%, red oil; IR (KBr, cm^{-1}): 3059, 3031, 2923, 1561, 1482, 1444, 1396, 1374, 1343, 1249, 1220, 1191, 1129, 1005, 764, 700; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.04–8.12 (m, 2H), 7.64–7.74 (m, 4H), 7.47–7.53 (m, 3H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.7, 152.3, 141.0, 140.8, 138.8, 129.6, 129.1, 128.8, 128.8, 128.4, 128.1, 24.3; HRMS (APCI): *m*/*z* $[M+H]^+$ calcd for $C_{15}H_{12}N_2$: 221.1073; found: 211.1074.

*4.3.17. 4-(3-Phenylquinoxalin-2-yl)benzene-1,3-diol (**3bi**).* Yield 41%, yellow solid; mp 189–192 °C; IR (KBr, cm^{-1}): 3100, 3057, 1614, 1600, 1568, 1531, 1431, 1398, 1328, 1308, 1218, 1138, 1025, 874, 757, 698; ^1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 8.13 (d, *J*=7.8 Hz, 1H), 8.00 (d, *J*=7.8 Hz, 1H), 7.75–7.78 (m, 2H), 7.62–7.62 (m, 2H), 7.46 (s, 3H), 6.97 (d, *J*=9.0 Hz, 1H), 6.25 (d, *J*=9.0 Hz, 1H), 5.81 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 159.7, 157.7, 153.2, 150.4, 140.1, 139.6, 136.9, 132.9, 130.0, 130.9, 130.0, 129.3, 129.1, 128.9, 126.7; HRMS (APCI): *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{13}IN_2O_2$: 441.0094; found: 441.0094.

*4.3.18. (1H-Benzo[d]imidazol-2-yl)(phenyl)methanone (**5a**).*[16] Yield 69%, white solid; mp 212–215 °C; IR (KBr, cm^{-1}): 3443, 1656, 1429, 1316, 1260, 919; ^1H NMR (DMSO-d_6, 400 MHz): δ (ppm) 13.57 (s, 1H), 8.64 (d, *J*=7.6 Hz, 2H), 7.94 (s, 1H), 7.66–7.77 (m, 4H), 7.40–7.44 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 183.5, 147.9, 143.2, 135.6, 134.1, 133.56, 130.9, 130.8, 128.4, 125.9, 123.1, 121.3, 112.8, MS (ES, 70 eV) *m*/*z*: 222 (53), 194 (100), 105 (49), 77 (44).

*4.3.19. 2-Phenylquinoxaline (**6aa**).*[8i] Yield 80%, pale yellow solid; mp 70 °C; IR (KBr, cm^{-1}): 3061, 1544, 1487, 1445, 1313, 1029; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.34 (s, 1H), 8.12–8.21 (m, 4H), 7.74–7.81 (m, 2H), 7.51–7.60 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.8, 143.3, 141.5, 136.7, 130.3, 130.2, 129.6, 129.5, 129.2, 129.1, 127.5.

*4.3.20. 2-(p-Tolyl)quinoxaline (**6ab**).*[8i] Yield 83%, yellow solid; mp 91–93 °C; IR (KBr, cm^{-1}): 3055, 1613, 1545, 1310, 1046; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.30 (s, 1H), 8.09–8.14 (q, *J*=6.4 Hz, 4H), 7.70–7.78 (m, 2H), 7.36 (d, *J*=8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.8, 143.2, 142.3, 141.4, 140.5, 133.9, 130.2, 129.9, 129.5, 129.3, 129.0, 127.4, 21.4; HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{15}H_{12}N_2Na$: 243.0893; found: 243.0893.

*4.3.21. 2-(4-Methoxyphenyl)quinoxaline (**6ac**).*[8i] Yield 85%, pale yellow solid; mp 97–98 °C; IR (KBr, cm^{-1}): 1602, 1537, 1437, 1182, 1031; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.28 (s, 1H), 8.17 (d, *J*=8.8 Hz, 2H), 8.10 (t, *J*=8.9 Hz, 2H), 7.68–7.77 (m, 2H), 7.07 (d, *J*=8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 161.3, 151.3, 143.0, 142.2, 141.1, 130.1, 129.3, 129.1, 129.0, 128.9, 114.5, 55.3; HRMS (ESI): *m*/*z* $[M+Na]^+$ calcd for $C_{15}H_{12}N_2ONa$: 259.0841; found: 259.0842.

*4.3.22. 2-(2,4-Dimethoxyphenyl)quinoxaline (**6ad**).* Yield 86%, pale white solid; mp 54–56 °C; IR (KBr, cm^{-1}): 2954, 1616, 1509, 1276, 1207, 1160, 1128; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.35 (s, 1H), 8.11 (t, *J*=9.2 Hz, 2H), 7.91–7.94 (m, 1H), 7.73–7.74 (m, 2H), 6.67 (d, *J*=8.4 Hz, 1H), 6.61 (s, 1H), 3.90 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 162.4, 158.5, 151.7, 147.1, 142.5, 140.5, 132.4, 129.5, 129.1, 128.9, 119.1, 105.7, 98.5, 55.4, 55.3; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{15}N_2O_2$: 267.1130; found: 267.1128.

*4.3.23. 2-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)quinoxaline (**6ae**).* Yield 82%, yellow solid; mp 144–147 °C; IR (KBr, cm^{-1}): 1514, 1435, 1323, 1292, 1053; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.25 (s, 1H), 8.10 (t, *J*=8.6 Hz, 2H), 7.69–7.77 (m, 4H), 7.04 (d, *J*=8.4 Hz, 1H), 4.34 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.0, 145.6, 143.9, 142.9, 142.1, 141.1, 130.0, 129.3, 129.0, 128.9, 120.7, 117.8, 116.4, 64.5, 64.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{13}N_2O_2$: 265.0973; found: 265.0972.

*4.3.24. 2-(4-Bromophenyl)quinoxaline (**6af**).*[8i] Yield 72%, pale yellow solid; mp: 134–137 °C; IR (KBr, cm^{-1}): 1586, 1538, 1484, 1124, 1072, 1046; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.29 (s, 1H), 8.06–8.14 (m, 4H), 7.75–7.81 (m, 2H), 7.68 (d, *J*=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 150.6, 142.7, 142.15, 141.6, 135.5, 132.3, 130.5, 129.8, 129.5, 129.1, 128.9, 124.9; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{14}H_{10}BrN_2$: 285.0023; found: 285.0022.

*4.3.25. 2-(4-Chlorophenyl)quinoxaline (**6ag**).*[8i] Yield 70%, yellow solid; mp: 131–134 °C; IR (KBr, cm^{-1}): 3451, 3056, 1538, 1486, 1312, 1094; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.29 (s, 1H), 8.11–8.16 (m, 4H), 7.74–7.81 (m, 2H), 7.53 (d, *J*=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ (ppm) 150.4, 142.7, 142.1, 141.5, 136.4, 135.0, 130.4, 129.7, 129.5, 129.3, 129.0, 128.6; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{14}H_{10}ClN_2$: 241.0528; found: 241.0527.

*4.3.26. 2-(3,4-Dichlorophenyl)quinoxaline (**6ah**).* Yield 65%, pale green solid; mp: 187–189 °C; IR (KBr, cm^{-1}): 1537, 1477, 1312, 1145, 1028; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.29 (s, 1H), 8.35 (s, 1H), 8.14 (t, *J*=6.8 Hz, 2H), 8.04 (d, *J*=8.4 Hz, 1H), 7.77–7.84 (m, 2H), 7.64 (d, *J*=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 149.2, 142.6, 142.4, 142.1, 141.8, 136.6, 133.6, 131.1, 130.7, 130.1, 129.6, 129.3, 129.2, 126.4; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{14}H_9Cl_2N_2$: 275.0135; found: 275.0137.

*4.3.27. 2-([1,1′-Biphenyl]-4-yl)quinoxaline (**6ai**).*[8i] Yield 63%, pale yellow solid; mp: 130–133 °C; IR (KBr, cm^{-1}): 3060, 1538, 1484, 1419, 1316, 1053; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.36 (s, 1H), 8.28 (d, *J*=8.4 Hz, 2H), 8.11–8.17 (m, 2H), 7.80 (s, 1H), 7.78 (s, 1H), 7.71–7.76 (m, 2H), 7.68 (s, 1H), 7.66 (s, 1H), 7.48 (t, *J*=7.4 Hz, 2H), 7.39 (t, *J*=7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.3, 143.2, 142.9, 142.3, 141.5, 140.1, 135.5, 130.3, 129.5, 129.5, 129.1, 128.9, 127.9, 127.8, 127.1; HRMS (APCI): *m*/*z* $[M+H]^+$ calcd for $C_{20}H_{15}N_2$: 283.1231; found: 283.1230.

*4.3.28. 2-(Naphthalen-1-yl)quinoxaline (**6aj**).*[8i] Yield 69%, dark yellow solid; mp: 136 °C; IR (KBr, cm^{-1}): 3045, 1542, 1487, 1183, 1111; ^1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 9.17 (s, 1H), 8.22 (t, *J*=9.3 Hz, 2H), 8.17 (d, *J*=8.4 Hz, 1H), 8.01 (d, *J*=7.8 Hz, 1H), 7.96 (d, *J*=7.8 Hz, 1H), 7.83 (s, 2H), 7.78 (d, *J*=6.6 Hz, 1H), 7.64 (t, *J*=7.5 Hz, 1H), 7.52–7.57 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 154.2, 146.6, 142.1, 141.3, 135.0, 134.0, 130.4, 130.1, 129.9, 129.6, 129.2, 128.6, 128.5, 128.3, 127.2, 126.3, 125.4, 125.0; HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{18}H_{13}N_2$: 257.1072; found: 257.1073.

*4.3.29. 2-(Naphthalen-2-yl)quinoxaline **(6ak).*** Yield 66%, dark yellow solid; mp: 138 °C; IR (KBr, cm^{-1}): 3042, 1547, 1491, 1308, 1197; ^1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 9.45 (s, 1H), 8.63 (s, 1H), 8.34 (d, *J*=8.4 Hz, 1H) 8.18 (d, *J*=8.0 Hz, 1H), 8.13 (d, *J*=8.4 Hz, 1H), 7.99 (t, *J*=7 Hz, 2H), 7.88–7.90 (m, 1H), 7.72–7.80 (m, 2H), 7.53–7.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.6, 143.4, 142.3, 141.5, 134.0, 134.0, 133.3, 130.3, 129.5, 129.1, 129.0, 128.8, 127.7, 127.4, 127.2, 126.6, 124.4; HRMS (APCl): *m*/*z* $[M+H]^+$ calcd for $C_{18}H_{13}N_2$: 257.1075; found: 257.1073.

*4.3.30. 4-(Quinoxalin-2-yl)phenol (**6al**).*[8g] Yield 78%, white solid; mp: 208–209 °C; IR (KBr, cm^{-1}): 3070, 3013, 1608, 1589, 1492, 1442, 1272, 1168; ^1H NMR (DMSO-d_6, 400 MHz): δ (ppm) 10.14 (s, 1H), 9.53 (br s, 1H), 8.24–8.26 (m, 2H), 8.08–8.09 (m, 2H), 7.81–7.87 (m, 2H), 7.02 (d, *J*=8.0 Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm)

159.7, 150.9, 143.4, 141.4, 140.5, 130.3, 129.1, 129.0, 128.8, 128.7, 126.9, 115.9; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{14}H_{11}N_2O$: 223.0866; found: 223.0866.

*4.3.31. 4-(4-(Quinoxalin-2-yl)phenyl)morpholine (**6am**).* Yield 81%, yellow crystals; mp: 220–223 °C; IR (KBr, cm^{-1}): 2964, 2863, 2841, 1606, 1533, 1444, 1382, 1247, 1121; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.28 (s, 1H), 8.16 (d, J=8.8 Hz, 2H), 8.06–8.11 (m, 2H), 7.67–7.76 (m, 2H), 7.04 (d, J=8.4 Hz, 2H), 3.90 (d, J=4 Hz, 4H), 3.30 (d, J=4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.5, 151.4, 143.0, 142.3, 141.0, 130.1, 129.2, 129.0, 128.8, 128.5, 127.4, 115.1, 66.7, 48.2; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{18}N_3O$: 292.1446; found: 292.1444.

*4.3.32. 2-(Furan-2-yl)quinoxaline (**6an**).*[8i] Yield 65%, pale yellow solid; mp: 131–136 °C; IR (KBr, cm^{-1}): 3136, 3116, 1612, 1552, 1497, 1297, 1225, 1126, 1082; ^1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 9.24 (s, 1H), 8.09 (d, J=7.8 Hz, 1H), 8.06 (d, J=8.4 Hz, 1H), 7.75 (t, J=7.4 Hz, 1H), 7.70 (d, J=7.2 Hz, 1H), 7.68 (s, 1H), 7.31 (d, J=3 Hz, 1H), 6.62 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.4, 145.0, 143.7, 141.9, 141.1, 130.3, 129.2, 129.1, 112.4, 111.7; HRMS (APCI): m/z $[M+Na]^+$ calcd for $C_{12}H_8N_2NaO$: 219.0530; found: 219.0529.

*4.3.33. 2-(Thiophen-2-yl)quinoxaline (**6ao**).*[8i] Yield 63%, pale yellow solid; mp: 116–117 °C; IR (KBr, cm^{-1}): 3120, 3058, 1547, 1427, 1320, 1054; ^1H NMR ($CDCl_3$, 600 MHz): δ (ppm) 9.21 (s, 1H), 8.05 (d, J=3.6 Hz, 2H), 7.84 (s, 1H), 7.72 (d, J=8.4 Hz, 1H), 7.68 (d, J=8.4 Hz, 1H), 7.53 (d, J=4.2 Hz, 1H), 7.18 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 147.3, 142.0, 141.7, 141.2, 130.4, 130.2, 129.8, 129.1, 129.0, 128.4, 126.9; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{12}H_9N_2S$: 213.0483; found: 213.0481.

*4.3.34. 2-(Benzofuran-2-yl)quinoxaline (**6ap**).* Yield 66%, yellow solid; mp: 173–175 °C; IR (KBr, cm^{-1}): 3058, 1583, 1545, 1310, 1259, 1173, 1128, 1047; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.41 (s, 1H), 8.17 (d, J=8 Hz, 1H), 8.11 (d, J=7.9 Hz, 1H), 7.75–7.81 (m, 2H), 7.66–7.73 (m, 3H), 7.41 (t, J=7.6 Hz, 1H), 7.30 (t, J=7.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 155.8, 152.8, 143.9, 142.5, 142.1, 141.7, 130.6, 129.9, 129.4, 129.2, 128.2, 126.3, 123.6, 122.0, 111.9, 107.9; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{16}H_{11}N_2O$: 247.0868; found: 247.0866.

*4.3.35. 2-(1H-Indol-3-yl)quinoxaline (**6aq**).*[17] Yield 72%, brown solid; mp: 206–208 °C; IR (KBr, cm^{-1}): 3255, 1553, 1446, 1170, 1133; ^1H NMR (DMSO-d_6, 400 MHz): δ (ppm) 11.97 (s, 1H), 9.55 (s, 1H), 8.84–8.87 (1H, m), 8.67 (s, 1H), 8.12 (d, J=8.4 Hz, 1H), 8.05 (d, J=8.0 Hz, 1H), 7.82 (q, J=7.2 Hz, 1H), 7.69–7.74 (m, 1H), 7.56–7.58 (1H, m), 7.29–7.31 (m, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ (ppm) 151.0, 144.4, 142.0, 139.5, 137.2, 137.0, 130.0, 128.8, 128.5, 127.7, 125.6, 122.8, 122.5, 121.0, 113.0, 112.0; HRMS (ESI): m/z $[M+Na]^+$ calcd for $C_{16}H_{11}N_3Na$: 268.0846; found: 268.0845.

*4.3.36. 6,7-Dimethyl-2-phenylquinoxaline (**6ba**).* Yield 76%, pale yellow crystals; mp: 130–131 °C; IR (KBr, cm^{-1}): 3059, 3035, 2967, 1538, 1485, 1450, 1312, 1212, 1024, 1001; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.16 (s, 1H), 8.12 (d, J=7.2 Hz, 2H), 7.83 (s, 1H), 7.78 (s, 1H), 7.43–7.52 (m, 3H), 2.42 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 150.5, 142.0, 140.8, 140.4, 140.2, 139.7, 136.7, 129.5, 128.8, 128.3, 127.8, 127.0, 20.11; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{16}H_{15}N_2$: 235.1231; found: 235.1230.

*4.3.37. 2-(4-Methoxyphenyl)-6,7-dimethylquinoxaline (**6bb**).* Yield 80%, yellow solid; mp: 127–129 °C; IR (KBr, cm^{-1}): 2974, 1605, 1487, 1437, 1292, 1252, 1183, 1029; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.19 (s, 1H), 8.14 (d, J=7.6 Hz, 2H), 7.87 (s, 1H), 7.83 (s, 1H), 7.08 (d, J=8.0 Hz, 2H), 3.9 (s, 3H), 2.5 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 161.1, 150.6, 142.1, 141.1, 140.6, 140.1, 139.5, 129.6, 128.7, 128.4, 128.0, 114.4, 55.4, 20.4, 20.3; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{17}H_{17}N_2O$: 265.1337; found: 265.1335.

*4.3.38. 2-(4-Chlorophenyl)-6,7-dimethylquinoxaline (**6bc**).* Yield 71%, pale yellow solid; mp: 157–160 °C; IR (KBr, cm^{-1}): 2972, 2914, 1485, 1440, 1212, 1088, 1010; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.19 (s, 1H), 8.11 (d, J=7.6 Hz, 2H), 7.88 (s, 1H), 7.85 (s, 1H), 7.52 (d, J=7.6 Hz, 2H), 2.51 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 149.7, 141.9, 141.1, 140.5, 136.1, 135.5, 129.3, 128.6, 128.1, 20.43; HRMS (APCI): m/z $[M+H]^+$ calcd for $C_{16}H_{14}ClN_2$: 269.0842; found: 269.0840.

*4.3.39. 7-Methyl-2-phenylquinoxaline and 6-methyl-2-phenylquinoxaline (**6bd**).* Yield 83%, white solid; mp: 106–109 °C; IR (KBr, cm^{-1}): 3055, 2916, 1541, 1492, 1307, 1027; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.25–9.27 (m, 1H), 8.17 (d, J=6.8 Hz, 2H), 8.00–8.05 (m, 1H), 7.87–7.92 (m, 1H), 7.51–7.61 (m, 4H), 2.6 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 151.7, 150.9, 143.2, 142.4, 142.3, 141.5, 140.7, 140.6, 140.1, 140.0, 140.0, 136.8, 132.6, 131.8, 130.0, 129.9, 129.1, 128.5, 128.4, 127.9, 127.4, 127.3, 21.8.

*4.3.40. 6,7-Dichloro-2-phenylquinoxaline (**6be**).*[17] Yield 50%, pale yellow crystals; mp: 155–157 °C. IR (KBr, cm^{-1}): 3050, 1463, 1444, 1315, 1178, 1108; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.29 (s, 1H), 8.23 (s, 1H), 8.20 (s, 1H), 8.15–8.17 (m, 2H), 7.56 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.5, 144.2, 141.0, 140.2, 135.9, 133.9, 130.7, 130.1, 129.7, 129.2, 127.5.

*4.3.41. 7-Chloro-2-phenylquinoxaline and 6-chloro-2-phenyl-quinoxaline (**6bf**).* Yield 64%, pale yellow solid; mp: 100–102 °C; IR (KBr, cm^{-1}): 3049, 1482, 1450, 1317, 1074; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.29–9.30 (m, 1H), 8.17 (d, J=7.2 Hz, 2H), 8.02–8.13 (m, 2H), 7.66–7.72 (m, 2H), 7.55–7.58 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.4, 151.8, 144.1, 143.3, 142.6, 141.7, 140.8, 140.0, 136.3, 136.2, 136.0, 135.2, 131.3, 130.8, 130.5, 130.4, 130.4, 130.3, 129.2, 128.4, 128.0, 127.5, 127.4.

*4.3.42. 7-Bromo-2-phenylquinoxaline and 6-bromo-2-phenyl-quinoxaline (**6bg**).* Yield 72%, pale yellow solid; white solid; mp: 96–97 °C; IR (KBr, cm^{-1}): 3045, 1597, 1478, 1135; ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 9.30 (s, 1H), 8.27–8.32 (m, 1H), 8.17 (d, J=6.5 Hz, 2H), 7.94–8.00 (m, 1H), 7.78–7.84 (m, 1H), 7.55 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 152.4, 144.0, 143.5, 140.3, 136.2, 133.8, 133.0, 131.8, 131.4, 130.9, 130.5, 130.4, 130.4, 129.4, 129.2, 127.6, 127.5, 124.3.

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Supplementary data

^1H NMR, ^{13}C NMR, and HRMS spectra for all compounds, X-ray crystal structures of compounds **3aa**, **3ae** and **6ac** are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.09.056. These data include MOL files and InChiKeys of the most important compounds described in this article.

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