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An efficient iodine–DMSO catalyzed synthesis of quinoxaline derivatives

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ABSTRACT

An efficient iodine–DMSO catalyzed system for the synthesis of quinoxaline derivatives was developed. The construction of this quinoxaline system went through a one-pot oxidation/cyclization process. The reaction afforded a variety of products in good to excellent yields. This methodology has potential applications in the synthesis of biologically and medicinally relevant compounds.

1. Introduction

Quinoxaline derivatives are important classes of nitrogen containing heterocycles that are found in various natural products and biologically active compounds. Their antiviral[1] and antibacterial[2] activities have been widely reported. And they are also powerful in antitumor agents.[3] In addition, compounds, whose structures consist of quinoxaline, can be used in phytohormone,[4] combination drugs,[5] antipsychotics,[6] electroluminescent materials[7] and dye.[8]

Because of these extensive functions, a lot of methods have been reported for the preparation of this type of compounds. Generally, the following strategies are mentioned: (1) The condensation of 1, 2-dicarbonyl and *o*-diaminobenzene catalyzed by iodine, PAST or Zr.[9] (2) Ruthenium-catalyzed or gold-catalyzed synthesis with *o*-diaminobenzene and vicinal-diols.[10] (3) The reaction of α-bromoketones and 1,2-diamines under $HClO_4/SiO_2$.[11] (4) The oxidation and condensation of hydroxyl ketones and 1,2-henylenediamine catalyzed by Mn.[12] (5) Copper-catalyzed synthesis with *o*-diaminobenzene and terminal alkyne in the presence of bases.[13] (6) Au/Ag-catalyzed[14] or iodine-catalyzed[15] synthesis with *o*-diaminobenzene and alkynes. Many other methods have also been reported, for example, Wu and co-workers[16] disclosed one-pot synthesis of the quinoxaline derivatives from aryl arylmethyl (or methyl) ketones and 1,2-diaminoarenes catalyzed by CuO–iodine–DMSO in good to excellent yields. However, some of these methods suffer from several disadvantages, such as unsatisfactory yields, expensive metal precursors, and excessive reactants. Moreover, most of these reports could not produce the products bearing strong electron-withdrawing groups in good yields.

Iodine has been used as catalyst in the synthesis of organic compounds for a long time due to its low cost and eco-friendliness.[17] And it has been discovered to act as an oxidant from many previous work[18,21] and we learned that the hydroxylated carbon can be oxidized to the corresponding carbonyl with iodine as the oxidant.[17b] As well as a polar aprotic solvent, DMSO is a nontoxic, inexpensive and readily available oxidant for various organic transformations.[19] A one-pot synthetic route would be a very useful improvement. We have been focusing on the development of direct synthesis of heterocyclic systems using tandem reactions.[20] Herein, we report a highly efficient and simple one-pot tandem method to synthesize quinoxaline derivatives with *o*-diaminobenzene and 2-hydroxy-2-phenylacetophenone catalyzed by iodine in DMSO (Scheme 1).

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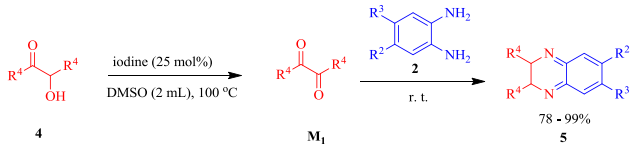
0040-4020/

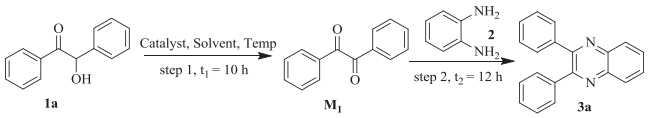


Scheme 1. Proposed procedure for the synthesis of quinoxaline derivatives.

2. Results and discussion

Our initial efforts were directed towards the best reaction conditions to synthesize quinoxaline derivatives. The reaction was initially conducted in a one-pot manner. *O*-diaminobenzene (1 mmol) and 2-hydroxy-2-phenylacetophenone (1 mmol) was heated in DMSO at 100 °C for 12 h in the presence of iodine with N_2 protection. We found that the product was obtained with a 22% yield (Table 1, entry 1). Then we attempted to do this experiment in a one-pot two-step manner. Gratifyingly, the product was obtained with a 59% yield (Table 1, entry 4). Inspired by this result, the reaction of *o*-diaminobenzene and 2-hydroxy-2-phenylacetophenone was optimized and the results are summarized in Table 1.

Table 1
Optimization of reaction conditions for the synthesis of quininoxaline in one pot[a]



Entry	Catalyst (mmol %)	Solvent	T_1 (°C)	T_2 (°C)	Yield (%)[b]
1[c]	I_2 (10)	DMSO	100	—	22
2	I_2 (10)	DMSO	60	rt	Trace
3	I_2 (10)	DMSO	80	rt	41
4	I_2 (10)	DMSO	100	rt	59
5	I_2 (10)	DMSO	110	rt	58
6	I_2 (20)	DMSO	100	rt	68
7	I_2 (25)	DMSO	100	rt	83
8[d]	I_2 (25)	DMSO	100	rt	65
9	I_2 (30)	DMSO	100	rt	81
10	—	DMSO	100	rt	Trace
11	I_2 (25)	Toluene	100	rt	24
12	I_2 (25)	DMF	100	rt	23
13	I_2 (25)	CH_3CN	Reflux	rt	10
14	NIS (25)	DMSO	100	rt	27
15	NBS (25)	DMSO	100	rt	45
16	TBAI (25)	DMSO	100	rt	50
17	I_2 (25)/K_2CO_3	DMSO	100	rt	61
18	I_2 (25)/AcOH	DMSO	100	rt	52
19[e]	I_2 (25)	DMSO	100	rt	92

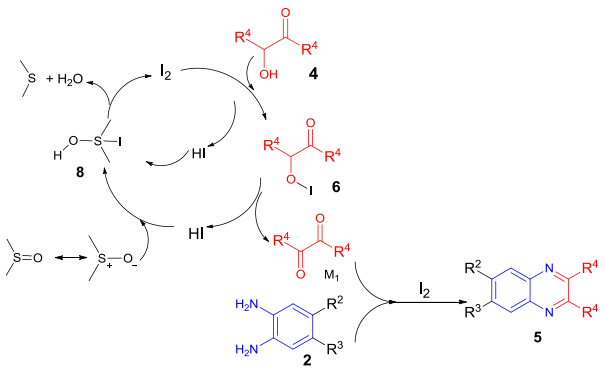
[a] Reaction conditions: **1a** (1 mmol), catalyst (25 mol %) and solvent (2 mL) were heated for 10 h in protection of nitrogen. Then **2** were added to the mixture and stirred at room temperature for 12 h.
[b] Yield of isolated product after column chromatography based on **1a**.
[c] All the reactants were added together.
[d] DMSO (4 mL) was used.
[e] The reaction proceeded under an air atmosphere.

Firstly, several temperatures were tested under N_2 atmosphere, and the highest yield (**3a**) was obtained at 100 °C (Table 1, entries 2–5). Based on this result, the dosages of I_2 were also tested and it was found that 25 mol % I_2 gave the highest yield of 83% (Table 1, entries 4 and 6–10). To get a better yield, several catalysts were then tested and we failed to get any product without iodine (Table 1, entry 10). Compared with other catalysts, the reaction catalyzed by iodine obtained a better yield (Table 1, entries 7 and 14–16). Using iodine as catalyst, several kinds of other solvents were tested and DMSO was showed to be the best one (Table 1, entries 8 and 11–13). In addition, we attempted to add some base or acid to improve this protocol, but neither of them gave better yields. Finally, we tried to investigate the possibility of direct synthesis of quinoxaline derivatives under an air atmosphere. To our delight, a higher yield of 92% was obtained. This probably owed to the oxidation of oxygen in the air. The optimized conditions were summarized as follows: 25 mol % of iodine catalyst, 2 mL DMSO as the reaction solvent, at 100 °C in the first step and room temperature in the second step without inert gas protection (Table 1, entry 19).

With the optimized reaction in hand, a variety of reactants were tested to determine the generality and limitation of the method. Firstly the reactions of compounds **1** and **2** with different substituent groups were examined. As shown in Table 2, all the reactions with different *o*-diaminobenzene derivatives furnished desired products in good yields (Table 2, entries 1–5). Compounds with electron-withdrawing groups (−Cl) obtained better yields than those with electron-donating groups (Table 2, entries 2, 3 and 5). Even compounds **2** bearing a strong electron-withdrawing group ($-NO_2$) gave higher yield (Table 2, entries 4, 8 and 14), which was a major breakthrough compared with the previous work.[9] We were delighted to discover that the desired yields were obtained from the cyclization of *o*-diaminobenzene and different benzoin derivatives catalyzed by iodine in DMSO (compounds **1**). Compounds **1** with electron-donating groups gave good yields (Table 2, entries 1, 6 and 10).

Similarly, heterocyclic hydroxy ketones proceeded well for the present procedure. As shown in Table 3, the desired products in good to excellent yields could also be obtained by the reaction of **4a** and **4b**. Interestingly, both electron-donating and electron-withdrawing groups are apparently well-tolerated. Electron-withdrawing substituents in the hydroxyl ketone part led to a shorter time in the process of oxidation (Table 3, entries 1–4). On the other hand, the presence of electron-donating groups in hydroxyl ketones might retard the nucleophilic attack on the *in situ* formed dicarbonyl leading to a lower yield (Table 3, entries 5–9).

On the basis of the conventional quinoxalines syntheses,[16,21] a plausible mechanism for the generation of quinoxalines from *o*-diaminobenzenes and hydroxy ketones is depicted in Scheme 2. To start, the hydroxyl ketones **4** were oxidized to the corresponding dicarbonyl $\mathbf{M_1}$ with iodine as the oxidant. Then the iodine acted as a mild Lewis acid and promoted the cyclization of **2** and $\mathbf{M_1}$ to obtain the quinoxaline derivatives **5**. Finally, with the DMSO as oxidant, HI was oxidized into iodine, and iodine was regenerated to make the system operate in recycle.



Scheme 2. Plausible mechanism for formation of **5**.

3. Conclusion

In summary, we have presented a straight forward and efficient one-pot two-step approach for the synthesis of quinoxalines from the cyclization of *o*-diaminobenzenes with hydroxy ketones, using iodine as catalyst and DMSO as solvent and oxidant. A variety of quinoxaline derivatives were synthesized in good to excellent

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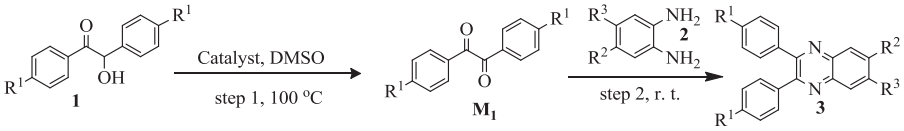
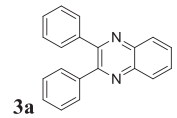
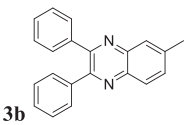
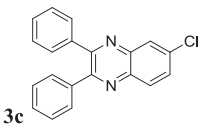
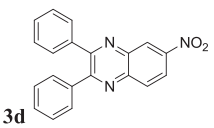
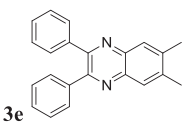
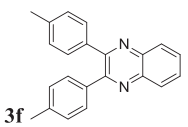
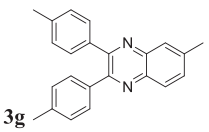
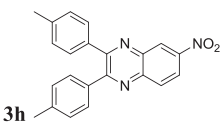
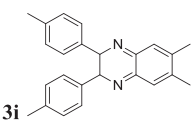
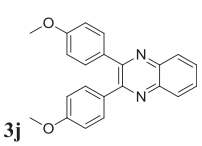
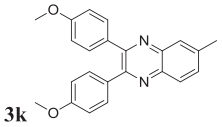
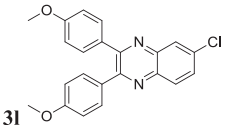
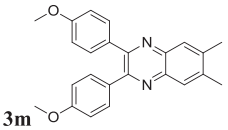
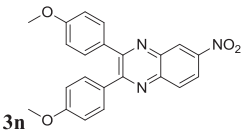
Table 2
Synthesis of quininoxalines[a]



Entry	1	2	Time$_1$ (h)	Time$_2$ (h)	3	Yield (%)[b]
1	R^1=H	R^2=R^3=H	10	12	 **3a**	92
2	R^1=H	R^2=CH_3 R^3=H	10	12	 **3b**	84
3	R^1=H	R^2=Cl R^3=H	10	10	 **3c**	92
4	R^1=H	R^2=NO_2 R^3=H	10	12	 **3d**	94
5	R^1=H	R^2=CH_3 R^3=CH_3	10	12	 **3e**	78
6	R^1=CH_3	R^2=R^3=H	10	12	 **3f**	90
7	R^1=CH_3	R^2=CH_3 R^3=H	10	12	 **3g**	84
8	R^1=CH_3	R^2=NO_2 R^3=H	10	12	 **3h**	94
9	R^1=CH_3	R^2=R^3=CH_3	10	12	 **3i**	81
10	R^1=OCH_3	R^2=R^3=H	12	12	 **3j**	87

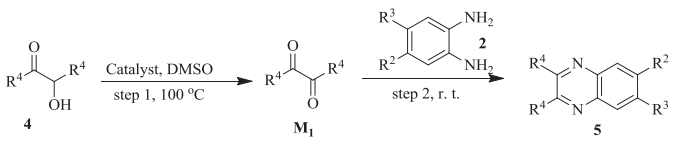
(*continued on next page*)

Table 2 (*continued*)

Entry	1	2	Time$_1$ (h)	Time$_2$ (h)	3	Yield (%)[b]
11	R^1=OCH_3	R2=CH_3 R3=H	12	12	 **3k**	82
12	R^1=OCH_3	R2=Cl R3=H	12	12	 **3l**	88
13	R_1=OCH_3	R^2=R^3=CH_3	12	12	 **3m**	80
14	R^1=OCH_3	R^2=NO_2 R^3=H	12	12	 **3n**	92

[a] Reaction conditions: **1** (1 mmol), iodine (25 mol %), DMSO (2 mL) were heated to 100 °C (TLC monitored), then **2** (1 mmol) was added.
[b] Yield of isolated product after column chromatography based on **1**.

Table 3
Synthesis of heterocyclic quininoxalines[a]



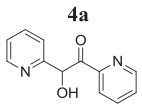
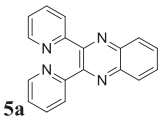
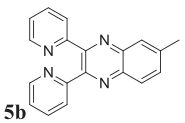
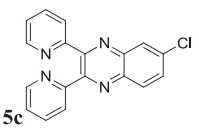
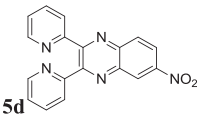
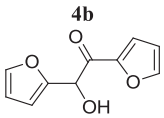
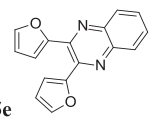
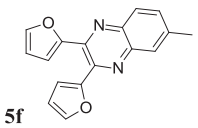
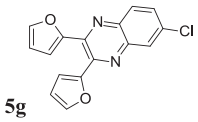
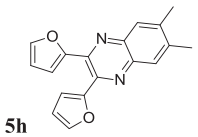
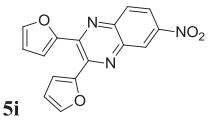
Entry	4	2	Time$_1$ (h)	Time$_2$ (h)	5	Yield (%)[b]
1	**4a** 	R^2=R^3=H	6	12	 **5a**	94
2	**4a**	R^2=H R^3=CH_3	6	12	 **5b**	92
3	**4a**	R^2=H R^3=Cl	6	12	 **5c**	99
4	**4a**	R^2=H R^3=NO_2	6	12	 **5d**	96
5	**4b** 	R^2=R^3=H	10	12	 **5e**	88

Table 3 (*continued*)

Entry	4	2	Time$_1$ (h)	Time$_2$ (h)	5	Yield (%)[b]
6	**4b**	R^2=H R^3=CH_3	10	12	 **5f**	85
7	**4b**	R^2=H R^3=Cl	10	12	 **5g**	95
8	**4b**	R^2=R^3=CH_3	10	12	 **5h**	81
9	**4b**	R^2=H R^3=NO_2	10	12	 **5i**	97

[a] Reaction conditions: **4** (1 mmol), iodine (25 mol %), DMSO (2 mL) were heated to 100 °C (TLC monitored), then **2** (1 mmol) was added.
[b] Yield of isolated product after column chromatography based on **4**.

yields. This one-pot metal-free approach for the construction of quinoxaline has potential applications in biological chemistry and medicinal chemistry.

4. Experimental section

4.1. General

All the reagents were commercially available and were used without further purification. All reactions were monitored by thin-layer chromatography (TLC). ^{1}H NMR spectra were recorded on a Bruker Avance 400 or 300 spectrometer 400 or 300 MHz, using $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were run in the same instrument 75 MHz. HRMS spectra were determined on a Q-TOF6510 spectrograph (Agilent).

4.2. General procedure for the synthesis of 3-diphenylquinoxaline 3a

A mixture of 2-hydroxy-1, 2-diphenylethanone (1.0 mmol) and iodine (25 mol %) in DMSO (2 mL) was stirred at 100 °C under an air atmosphere. TLC monitored the end of the reaction. Then the mixture was cooled to room temperature, and benzene-1,2-diamine (1.0 mmol) was added into the mixture and stirred for several hours. TLC monitored the end of the reaction. Then H_2O (100 mL) was added and the mixture was filtered and extracted with ethyl acetate. The combined organic layer was washed by chilled water, dried by Mg_2SO_4 for 10 min, filtered, and evaporated in vacuo. The product was purified by flash column chromatography on silica gel by petroleum ether and ethyl acetate (20:1). White solid was obtained as **3a** (0.25 g).

*4.2.1. 2,3-Diphenylquinoxaline (**3a**).* White solid. Mp 116.5–117.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.19–8.14 (2H, m), 7.95–7.81 (2H, m), 7.50–7.47 (4H, m), 7.45–7.33 (6H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 153.04, 140.43, 138.75, 130.38, 129.66, 129.55, 129.47, 128.78, 128.73, 128.01; HRMS calcd for $C_{20}H_{14}N_2$ $(M+H)^+$ 283.1230; found: 283.1232.

*4.2.2. 6-Methyl-2,3-diphenylquinoxaline (**3b**).* White solid. Mp 115.7–116.9 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.04 (1H, J=8.4 Hz, d), 7.94 (1H, s), 7.71 (2H, J=8.4, 1.8 Hz, dd), 7.48–7.45 (4H, m), 7.43–7.32 (6H, m), 2.59 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 152.82, 152.08, 140.52, 140.50, 138.92, 138.85, 132.52, 129.63, 128.64, 128.57, 128.32, 127.98, 127.47, 21.32; HRMS calcd for $C_{21}H_{16}N_2$ $(M+H)^+$ 297.1386; found: 297.1391.

*4.2.3. 6-Chloro-2,3-diphenylquinoxaline (**3c**).* White solid. Mp 122.0–122.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.25 (1H, J=2.1 Hz, d), 8.19 (1H, J=9.0 Hz), 7.92 (1H, J=2.1, 9.0 Hz, dd), 7.50–7.35 (10H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 154.04, 153.45, 140.76, 139.10, 138.39, 138.33, 134.60, 130.94, 129.68, 129.65, 129.00, 128.04, 127.48; HRMS calcd for $C_{20}H_{13}ClN_2$ $(M+H)^+$ 317.0840; found: 317.0851.

*4.2.4. 6-Nitro-2,3-diphenylquinoxaline (**3d**).* Yellow solid. Mp 184.7–185.5 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.95 (1H, J=1.8 Hz, d), 8.57 (1H, J=1.8, 9.0 Hz, dd), 8.38 (1H, J=9.3 Hz, d), 7.54–7.52 (4H, m), 7.48–7.37 (6H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.04, 155.38, 147.64, 142.98, 139.21, 137.97, 137.94, 130.94, 129.79, 129.71, 129.5, 129.36, 128.13, 124.83, 123.57; HRMS calcd for $C_{20}H_{13}N_3O_2$ $(M+H)^+$ 328.1081; found: 328.1083.

*4.2.5. 6,7-Dimethyl-2,3-diphenylquinoxalin (**3e**).* White solid. Mp 175.5–176.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (2H, s), 7.511–7.47 (4H, m), 7.35–7.26 (6H, m), 2.52 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.50, 140.53, 140.22, 139.38, 129.86, 128.53, 128.22, 128.19, 20.42; HRMS calcd for $C_{22}H_{18}N_2$ $(M+H)^+$ 311.1543; found: 311.1550.

*4.2.6. 2,3-Di-p-tolylquinoxaline (**3f**).* White solid. Mp 148.5–149.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.16–8.10 (2H, m), 7.89–7.83 (2H, m), 7.39 (4H, J=8.1 Hz, d), 7.18 (4H, J=7.8 Hz, d), 2.33 (6H, s); ^{13}C NMR (75 MHz, DMSO-d_6): δ 152.93, 140.34, 138.27,

136.04, 130.14, 129.56, 128.68, 128.64, 20.81; HRMS calcd for $C_{22}H_{18}N_2$ $(M+H)^+$ 311.1543; *found: 311.1542*.

*4.2.7. 6-Methyl-2,3-di-p-tolylquinoxaline (**3g**).* White solid. Mp 130.7–132.0 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (1H, *J*=8.4 Hz, d), 7.93 (1H, s), 7.57 (1H, *J*=8.4, 1.8 Hz, dd), 7.41 (4H, *J*=1.2, 7.8 Hz, dd), 7.13 (4H, *J*=7.8 Hz, d), 2.60 (3H, s), 2.36 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.30, 152.59, 141.14, 140.18, 139.59, 138.65, 138.57,136.47, 132.02, 129.74, 129.71, 128.94, 128.60, 127.92, 21.87, 21.83; HRMS calcd for $C_{23}H_{20}N_2$ $(M+H)^+$ 325.1699; found: 325.1699.

*4.2.8. 6-Nitro-2,3-di-p-tolylquinoxaline (**3h**).* Yellow solid. Mp 169.3–170.1 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.40 (1H, *J*=2.7 Hz, d), 8.49 (1H, *J*=2.4, 9.0 Hz, dd), 8.25 (1H, *J*=9.0 Hz, d), 7.49–7.45 (4H, m), 7.26–7.17 (4H, m), 2.39 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.32, 155.70, 147,71, 143.56, 140.02, 139.88, 139.83, 135.44, 135.38, 130.61, 129.84, 129.74, 129.18, 125.54, 123.03, 21.42; HRMS calcd for $C_{22}H_{17}N_3O_2$ $(M+H)^+$ 356.1394; found: 356.1390.

*4.2.9. 6,7-Dimethyl-2,3-di-p-tolylquinoxaline (**3i**).* White solid. Mp 130.6–131.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (2H, s), 7.40 (4H, *J*=8.1 Hz, d), 7.13 (4H, *J*=8.1 Hz, d), 2.50 (6H, s), 2.36 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.49, 140.19, 140.09, 138.43, 136.63, 129.73, 128.90, 128.13, 21.32, 20.37; HRMS calcd for $C_{24}H_{22}N_2$ $(M+H)^+$ 339.1856; found: 339.1874.

*4.2.10. 2,3-Bis(4-methoxyphenyl) quinoxaline (**3j**).* White solid. Mp 131.6–132.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17–8.12 (2H, m), 7.76–7.70 (2H, m), 7.52–7.48 (4H, m), 7.26–6.85 (4H, m), 3.84 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.24, 152.99, 140.96, 131.57, 131.28, 129.61, 128.94, 113.81, 55.31; HRMS calcd for $C_{22}H_{18}N_20_2$ $(M+H)^+$ 343.1441; found: 343.1442.

*4.2.11. 2,3-Bis(4-methoxyphenyl)-6-methylquinoxaline (**3k**).* White solid. Mp 99.5–100.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (1H, *J*=8.4 Hz, d), 7.92 (1H, s), 7.56 (1H, *J*=1.8, 8.7 Hz, dd), 7.51–7.45 (4H, m), 6.89–6.85 (4H, m), 3.83 (6H, s), 2.60 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.16, 160.09, 152.81, 152.12, 140.99, 140.11, 139.46, 131.93, 131.75, 131.70, 131.27, 131.22, 128.47, 127.78, 113.76, 55.30; HRMS calcd for $C_{23}H_{20}N_2O_2$ $(M+H)^+$ 357.1598; found: 357.1587.

*4.2.12. 6-Chloro-2,3-bis(4-methoxyphenyl)quinoxaline (**3l**).* White solid. Mp 148.6–149.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (1H, *J*=2.1 Hz, d), 8.07 (1H, *J*=9.0 Hz, d), 7.66 (1H, *J*=2.4, 9.0 Hz, dd), 7.51–7.47 (4H, m), 6.90–6.85 (4H, m), 3.84 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.49, 160.42, 153.79,153.11,141.24, 139.42, 135.24, 131.32, 131.25, 131.20,131.13, 130.55, 130.13, 127.82, 113.86,55.33; HRMS calcd for $C_{22}H_{17}ClN_2O_2$ $(M+H)^+$ 377.1051; found: 377.1050.

*4.2.13. 2,3-Bis(4-methoxyphenyl)-6,7-dimethylquinoxaline (**3m**).* White solid. Mp 123.6–124.7 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (2H, s), 7.49–7.44 (4H, m), 6.89–6.84 (4H, m), 3.83 (6H, s), 2.50 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.98, 152.08, 140.06, 140.00, 132.09, 131.22, 128.10, 113.72, 55.31; HRMS calcd for $C_{24}H_{22}N_2O_2$ $(M+H)^+$ 371.1754; found: 371.1756.

*4.2.14. 2,3-Bis(4-methoxyphenyl)-6-nitroquinoxaline (**3n**).* Yellow solid. Mp 190.5–191.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.02 (1H, *J*=2.4 Hz, d), 8.48 (1H, *J*=2.4, 9.0 Hz, dd), 8.24 (1H, *J*=9.0 Hz, d), 7.59–7.52 (4H, m), 6.92–6.89 (4H, t), 3.86 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.02, 160.87, 155.75, 155.17, 147.58, 143.46, 139.75, 131.50, 131.34, 130.64, 130.39, 125.39, 122.87, 113.98, 55.37; HRMS calcd for $C_{22}H_{17}N_3O_4$ $(M+H)^+$ 388.1292; found: 388.1393.

*4.2.15. 2,3-Di(pyridin-2-yl)quinoxaline (**5a**).* Yellow solid. Mp 179.4–181.1 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.29–8.20 (4H, m), 8.03–7.93 (6H, m), 7.38–7.34 (2H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 158.09, 153.54, 149.20, 141.37, 137.94, 132.14, 130.08, 125.01, 124.39; HRMS calcd for $C_{18}H_{12}N_4$ $(M+H)^+$ 285.1135; found: 285.1135.

*4.2.16. 6-Methyl-2,3-di (pyridin-2-yl)quinoxaline (**5b**).* Yellow solid. Mp 136.8–137.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.39–8.37 (2H, m), 8.12 (1H, *J*=8.7 Hz, d), 8.00–7.94 (3H, m), 7.85–7.78 (2H, m), 7.66 (1H, *J*=8.7, 2.1 Hz, dd), 7.26–7.22 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.46, 152.18, 148.43, 141.27, 142.19, 139.69, 136.73, 132.90, 128.90, 124.32, 124.30, 122.95, 122.89, 21.95; HRMS calcd for $C_{19}H_{14}N_4$ $(M+H)^+$ 299.1291; found: 299.1294.

*4.2.17. 6-Chloro-2,3-di(pyridin-2-yl)quinoxaline (**5c**).* Yellow solid. Mp 109.9–110.3 °C. Mp 116.5–117.7 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.32–8.24 (4H, m), 8.03–7.93 (5H, m), 7.40–7.34 (2H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.94, 156.90, 153.63, 153.04, 148.46, 140.95, 139.28, 137.22, 135.65, 131.94, 128.04, 124.29, 124.24, 123.82, 123.76; HRMS calcd for $C_{18}H_{11}ClN_4$ $(M+H)^+$ 319.0745; found: 319.0745.

*4.2.18. 6-Nitro-2,3-di(pyridin-2-yl)quinoxaline (**5d**).* Yellow solid. Mp 184.4–185.6 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.04 (1H, *J*=2.7 Hz, d), 8.49 (1H, *J*=2.4, 9.0 Hz, dd), 8.25 (1H, *J*=9.0 Hz, d), 7.49–7.45 (4H, m), 7.26–7.17 (4H, t); ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.08, 154.93, 154.34, 148.18, 148.10, 142.75, 139.10, 137.01, 130.89, 124.95, 124.19, 124.08, 123.96, 123.81, 123.71; HRMS calcd for $C_{18}H_{11}N_5O_2$ $(M+H)^+$ 330.0986; found: 330.0981.

*4.2.19. 2,3-Di(furan-2-yl)quinoxaline (**5e**).* Grey solid. Mp 131.3–131.6 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.14–8.08 (1H, m), 7.92–7.86 (4H, m), 6.74–6.72 (4H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 150.31, 144.91, 142.07, 139.92, 130.90, 128.68, 112.85, 112.15; HRMS calcd for $C_{16}H_{10}N_2O_2$ $(M+H)^+$ 263.0815; found: 263.0827.

*4.2.20. 2,3-Di(furan-2-yl)-6-methylquinoxaline (**5f**).* Grey solid. Mp 113.2–114.9 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (2H, *J*=8.4 Hz, d), 7.95 (1H, s), 7.62–7.57 (3H, t), 6.67–6.55 (4H, m), 2.60 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.89, 144.18, 144.04, 142.56, 141.85, 141.20, 140.68, 139.10, 132.84, 128.62, 127.94, 112.92, 112.64, 111.90, 111.87, 21.94; HRMS calcd for $C_{17}H_{12}N_2O_2$ $(M+H)^+$ 277.0972; found: 277.0970.

*4.2.21. 6-Chloro-2,3-di(furan-2-yl)quinoxaline (**5g**).* Grey solid. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.19 (1H, *J*=2.1 Hz, d), 8.16 (1H, *J*=9.0 Hz, d), 7.94–7.87(3H, m), 6.78–6.72 (4H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 150.03, 149.95, 145.32, 145.15, 142.83, 140.28, 138.59, 135.12, 131.37, 130.50, 127.36, 113.58, 113.28, 112.29, 112.25; HRMS calcd for $C_{16}H_9ClN_2O_2$ $(M+H)^+$ 297.0425; found: 297.0427.

*4.2.22. 2,3-Di(furan-2-yl)-6,7-dimethylquinoxaline (**5h**).* Yellow solid. Mp 115.6–116.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (2H, s), 7.61–7.60 (2H, t), 6.61–6.54 (4H, m), 2.50 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.08, 143.88, 141.85, 141.16, 139.64, 128.17, 112.38, 111.79, 20.41; HRMS calcd for $C_{18}H_{14}N_2O_2$ $(M+H)^+$ 291.1128; found: 291.1129.

*4.2.23. 2,3-Di(furan-2-yl)-6-nitroquinoxaline (**5i**).* Yellow solid. Mp 166.2–167.5 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.83 (1H, *J*=2.7 Hz, d), 8.51 (1H, *J*=2.4, 9.3 Hz, dd), 8.27 (1H, *J*=9.0 Hz, d), 8.00–7.98 (2H,

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m), 6.93–6.76 (4H, m); ^{13}C NMR (75 MHz, DMSO-d_6): δ 149.74, 149.64, 147.70, 146.10, 145.66, 144.20, 143.67, 143.48, 138.58, 130.43, 124.55, 123.86, 115.10, 114.26, 112.62, 112.43; HRMS calcd for $C_{16}H_9N_3O_4$ $(M+H)^+$ 308.0666; found: 308.0677.

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Supplementary data

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