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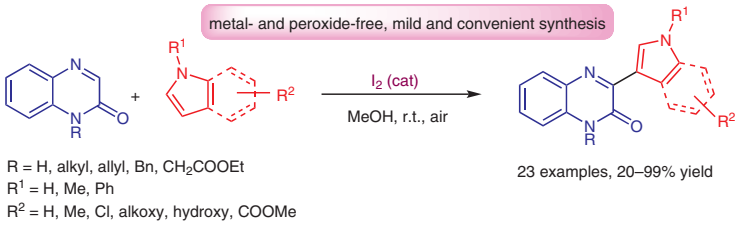
Iodine-Catalyzed Oxidative Cross-Dehydrogenative Coupling of Quinoxalinones and Indoles: Synthesis of 3-(Indol-2-yl)quinoxalin-2-one under Mild and Ambient Conditions

Medena Noikham
Tanakorn Kittikool
Sirilata Yotphan*

Center of Excellence for Innovation in Chemistry (PERCH-CIC), Department of Chemistry, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400, Thailand
sirilata.yot@mahidol.ac.th



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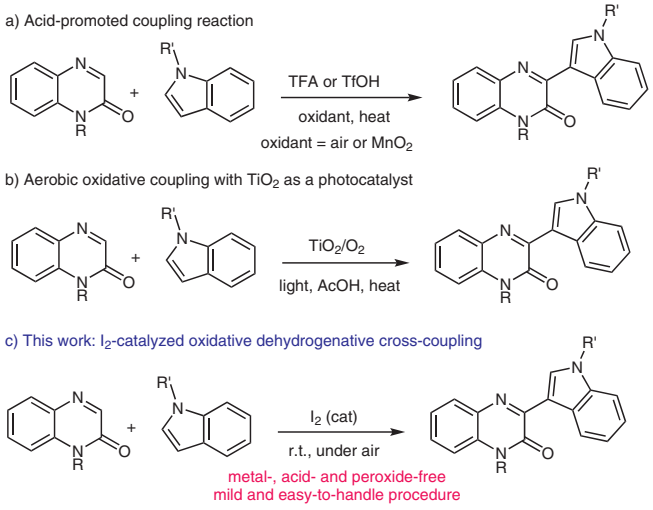
Abstract A highly efficient iodine-catalyzed oxidative cross-dehydrogenative coupling reaction of quinoxalinones and indoles has been developed. Without the requirement of peroxide and acid, this reaction utilizes a catalytic amount of molecular iodine to facilitate the C–C bond formation under ambient air. This simple and easy-to-handle protocol represents an interesting synthetic alternative with a good scope and functional group compatibility.

Key words iodine, quinoxalinone, indole, oxidative coupling, metal-free

The construction of carbon-carbon (C-C) bonds from simple non-prefunctionalized organic precursors is a state-of-art transformation that offers substantial benefits to the scientific community as it enables the direct synthesis and assembly of valuable synthetic organic building blocks, biologically active compounds, and natural product scaffolds.[1] Over the past decade, a number of synthetically useful methods featuring a direct C–C bond formation via cross-dehydrogenative coupling (CDC) reaction have been continuously reported and successfully applied to a wide variety of substrates.[2] These methods rely heavily on the use of transition-metal catalysts[3] such as palladium,[4] nickel,[5] copper,[6] or iron[7] complexes. On the other hand, a metal-free catalytic oxidative cross-dehydrogenative coupling strategy without the need of expensive and toxic heavy metal catalysts are alternatively appealing. In particular, catalysis involving molecular iodine (I_2), hypervalent iodine, and iodide salts, has recently received considerable attention in modern synthetic chemistry because of the ease of handling, commercial availability, low toxicity, mild reactivity, and versatility of the reagents.[8] During the past few years, several studies have demonstrated impressive catalytic activity of iodine in various oxidative transformations leading to the efficient formation of new C–C and carbon–heteroatom (C–X) bonds in organic compounds.[9] Further exploration into this emerging iodine-catalyzed oxidative cross-dehydrogenative coupling chemistry could result in the development of a practical synthetic tool and enhance their application in many fields.

Quinoxalin-2-ones are important classes of nitrogen-containing heterocycles found in many natural products and bioactive compounds.[10] A number of quinoxalinones and their structurally related derivatives are known to display a broad spectrum of biological activities and have been extensively utilized in several areas ranging from drug discovery and medicinal chemistry to material science and agrochemistry.[11] Among them, 3-(indol-2-yl)quinoxalin-2-ones have been identified as promising small molecules that show inhibitory activities toward the growth of human tumor cells.[12] Despite their potent pharmacological profile, only few synthetic protocols for 3-(indol-3-yl)quinoxalin-2-ones were found in literature. One of the direct route is a Brønsted acid (e.g., TFA or TfOH) promoted coupling reaction of quinoxalinones and indoles (Scheme 1, a).[13] A photocatalytic oxidation in acidic medium is the other process to construct these 3-(indol-3-yl)quinoxalin-2-ones (Scheme 1, b).[14] Nonetheless, to overcome some drawbacks and limitations of these existing methods such as harsh reaction conditions and difficulty in handling as well as to increase their structural diversity and utilization, alternative methods to access these compounds efficiently under mild conditions are highly desirable.

Our research group has been interested in exploring a metal-free catalytic approach for the synthesis and modification of biologically active N-heterocycles.[15] We have previously reported an expedient iodine-catalyzed oxidative cross-coupling of indoles and azoles.[16] With our continuing efforts towards the development of alternative catalytic

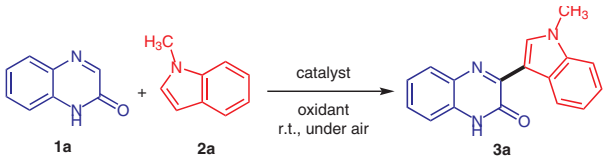


Scheme 1 Synthesis of 3-(indol-3-yl)quinoxalin-2-ones via oxidative dehydrogenative coupling reactions of quinoxalinones and indoles

methods to prepare and assemble various N-heterocyclic compounds, we envisioned that an iodine-catalyzed oxidative coupling of quinoxalinones and indoles should be feasible and provide a practical and environmentally friendly synthetic option due to the existing literature precedent on the iodine-catalyzed/mediated functionalization at the C2 or C3 positions of indole substrates.[17] In addition, Gupta and co-workers have recently reported the iodine-catalyzed C–N bond formation for the synthesis of 3-aminoquinoxalinones from quinoxalinones and amines using *tert*-butyl hydroperoxide (TBHP) as the external oxidant.[18] Herein, we disclose a convenient iodine-catalyzed oxidative cross-dehydrogenative coupling reaction between quinoxalinones and indoles in the absence of peroxide oxidant. This metal- and acid-free iodine-catalyzed protocol offers a simple approach to access 3-(indol-3-yl)quinoxalin-2-ones at room temperature under mild and ambient air conditions.

We initiated our study by examining the reaction of quinoxalinone (**1a**) and 1-methylindole (**2a**) in the presence of molecular iodine and hydrogen peroxide in methanol at room temperature for 8 hours under an air atmosphere. To our delight, the product **3a** was obtained in 78% yield (Table 1, entry 1) and the dehydrogenative cross-coupling reaction took place exclusively at the C3 position of indole. Replacing H_2O_2 by DTBP (di-*tert*-butyl peroxide) or TBHP (*tert*-butyl hydroperoxide) oxidant, excellent yield of **3a** was observed (entries 2 and 3). Surprisingly, as the oxidant was omitted from the reaction, the coupling product was successfully obtained in excellent quantity in methanol as well (entry 4, 97% isolated yield), suggesting that this reaction can be simply conducted under peroxide-free conditions. We further tested this metal-free reaction in different reaction media; however, methanol was found to be the most suitable solvent. Other solvents resulted in a decrease in yields (entries 5–11). Meanwhile, when using iodide salt such as KI, TBAI

Table 1 Optimization of Reaction Conditions[a]



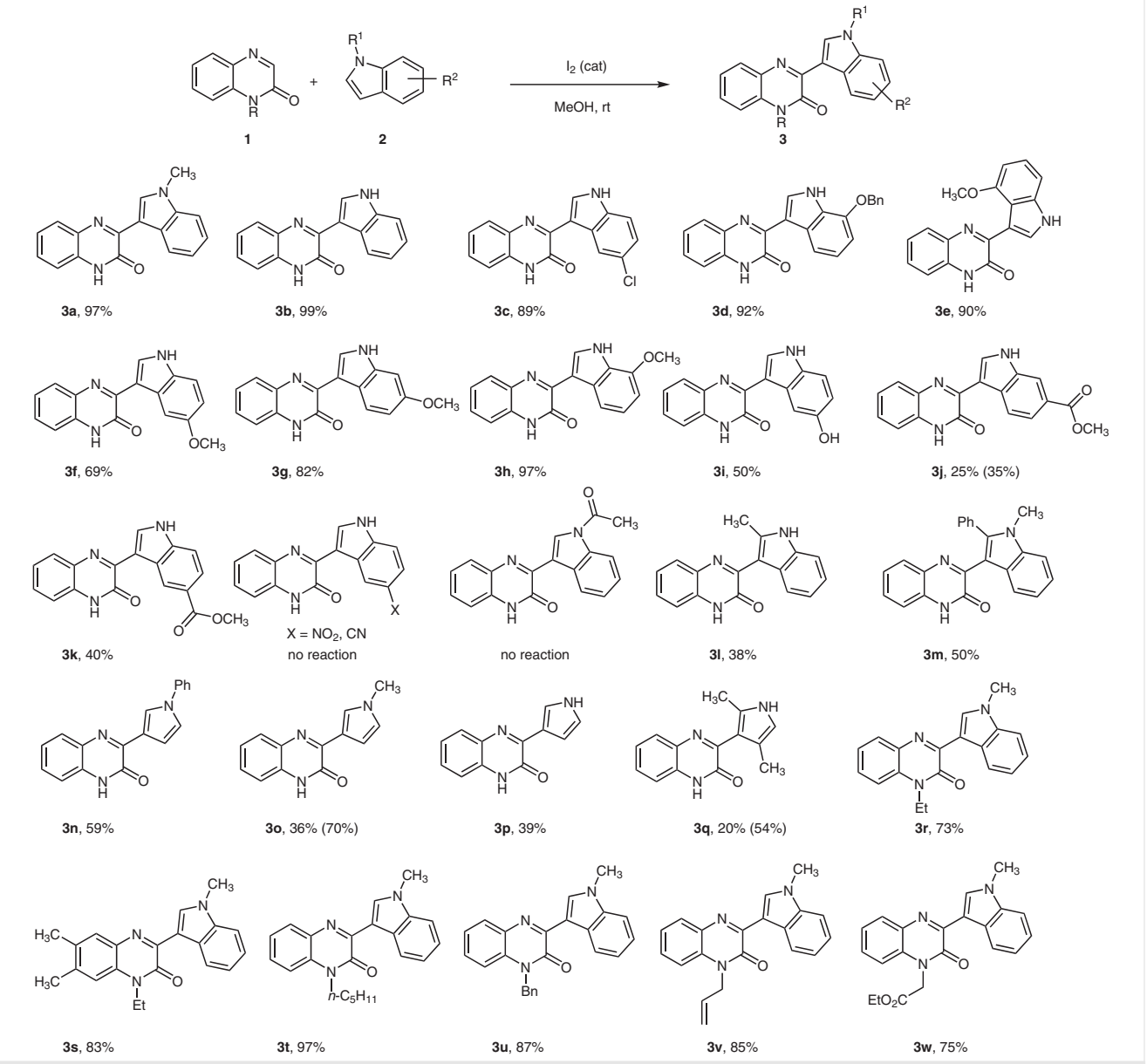
1a 2a 3a

Entry	Catalyst	Oxidant	Solvent	Yield (%)[b]
1	I_2	H_2O_2	CH_3OH	78
2	I_2	DTBP	CH_3OH	86
3	I_2	TBHP	CH_3OH	96
4	**I_2**	**–**	CH_3OH	**98** (**97**)[c]
5	I_2	–	EtOH	75
6	I_2	–	H_2O	25
7	I_2	–	MeCN	76
8	I_2	–	DMSO	69
9	I_2	–	DMF	74
10	I_2	–	THF	75
11	I_2	–	toluene	28
12	KI	–	CH_3OH	no reaction
13	TBAI	–	CH_3OH	no reaction
14	NH_4I	–	CH_3OH	no reaction
15	ICl	–	CH_3OH	73
16	NIS	–	CH_3OH	63
17	–	–	CH_3OH	no reaction

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.27 mmol, 1.1 equiv), catalyst (0.025 mmol, 10 mol%), oxidant (0.5 mmol, 2 equiv), solvent (0.5 mL), 8 h, r.t., under air.
[b] GC yield.
[c] Isolated yield.

(tetrabutylammonium iodide), or NH_4I as catalyst, no reaction was detected (entries 12–14). On the other hand, electrophilic iodine species such as ICl (iodine monochloride) or NIS (*N*-iodosuccinimide) gave the products in moderate amounts (entries 15, 16), indicating that the nature of iodine source is crucial, and molecular iodine was the most effective catalyst for this reaction. Without iodine catalyst, no reaction was observed (entry 17). This outcome also underlined the necessity of I_2 catalyst in this transformation. Overall, the optimized conditions for the iodine-catalyzed oxidative coupling reaction of quinoxalinone and indole was established as 1 equivalent of quinoxalinone, 1.1 equivalents of indole substrate, 10 mol% of I_2 in methanol at room temperature for 8 hours under air (Table 1, entry 4).

To test the generality of this reaction, the scope and limitation of this reaction was determined under the established conditions. The iodine-catalyzed dehydrogenative coupling of quinoxalinone **1a** and several indoles were tested, and the results are summarized in Scheme 2. Similar to 1-methylindole (**2a**), the NH-indole substrate underwent this catalytic transformation effectively and provided the coupling product **3b** in excellent yield. Pleasingly, the pres-



Scheme 2 Substrate scope. *Reagents and conditions*: **1** (0.5 mmol, 1 equiv), **2** (0.55 mmol, 1.1 equiv), I_2 (0.05 mmol, 10 mol%), CH_3OH (1 mL), r.t., 8 h, under ambient air. Isolated yields after chromatography are shown. Yields in parentheses are from using I_2 (0.25 mmol, 50 mol%) at 60 °C, 8 h, under ambient air.

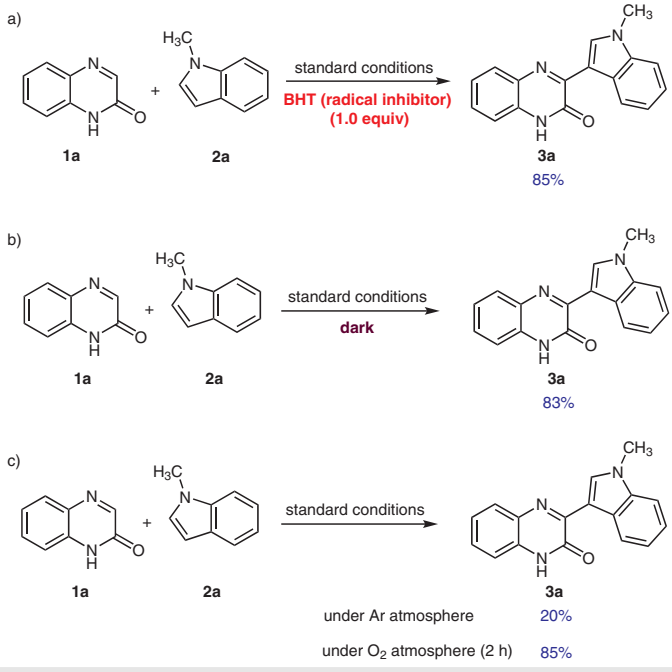
ence of a chloro group at the C5 position of NH-indole has no effect to interrupt the reaction (**3c**). Likewise, reactions of indole substrates bearing electron-rich alkoxy and hydroxyl groups proceeded smoothly and gave the desired products **3d–i** in moderate to very high yields, while the indole substrates bearing a moderate electron-deactivating ester group substituted at the C5 and C6 positions delivered products **3j** and **3k** in small to modest amounts. Nevertheless, other electron-deficient indoles such as 5-nitro- and 5-cyanoindole substrates as well as 1-acetylindole did not react under the optimal conditions. These results indicated that electronic variations from substituents have a dramatic impact on the efficiency of the reaction.

Meanwhile, in the case of C2-substituted indole substrates, slightly low to moderate yields of coupling products **3l** and **3m** were obtained, suggesting that the steric hindrance from the substituent at C2 position of indole is likely to interfere with the product formation. We next turned our attention toward the reaction of pyrrole substrates. The iodine-catalyzed dehydrogenative coupling reaction with quinoxalinone was feasible for both N-substituted pyrrole and NH-pyrrole (**3n–3q**), though low to fair quantities of products were isolated.

To improve the yields of selected compounds, a higher catalytic loading of I_2 (such as 50 mol%) was employed and the reaction was also carried out at elevated temperature (60 °C); thus the coupling products such as **3j**, **3o**, and **3q** were isolated in higher quantities (Scheme 2, yields in parentheses). Unfortunately, the electron-deficient indoles such as 5-nitroindole, 5-cyanoindole and 1-acetylindole were not converted into the expected coupling products despite increasing catalyst loading or heating at higher reaction temperature for a prolonged reaction period.

The reactions of selected quinoxalinone substrates were also evaluated.[19,20] Various N-substituted quinoxalinones with alkyl groups such as *N*-ethyl-, *N*-pentyl-, and *N*-benzyl-protected derivatives are compatible and the products **3r–u** were isolated in good to excellent yields. Thus, these results implied that the amide hydrogen should not be directly involved in the iodine-catalyzed oxidative cross-dehydrogenative coupling process. In addition, *N*-allyl- and *N*-ethoxycarbonylmethylquinoxalinones are found to be viable substrates under this transformation. The reactions of these quinoxalinones proceeded readily and yielded the products **3v** and **3w** in high amounts under the optimal conditions. No side reaction at alkene or ester moieties was observed.

To gain insight into the reaction mechanism, control experiments were conducted (Scheme 3). The reaction between quinoxalinone **1a** and indole **2a** was carried out under standard conditions in the presence of BHT (butylated hydroxytoluene) as a radical scavenger; however, there was no significant change in product yield (Scheme 3, a). The reaction was also performed under dark conditions, and noticeably high yield of product **3a** was attained (Scheme 3, b). This outcome is indeed different from what was reported by Itoh using molecular iodine-catalyzed oxidative coupling reaction under visible light irradiation.[21] Therefore, based on these observations, our present transformation should proceed via a non-radical pathway and visible light

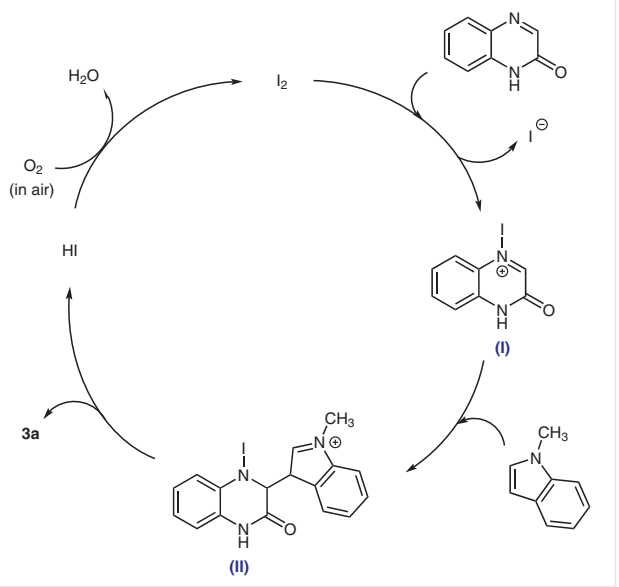


Scheme 3 Control experiments

irradiation is unlikely to involve in the reaction process. Furthermore, when conducting this present iodine-catalyzed reaction under inert atmosphere of argon, dramatically lower yield of the coupling product was observed. Thus, it is possible that oxidant is required for this iodine-catalyzed cross-dehydrogenative coupling reaction and molecular oxygen (O_2) in air is sufficient for regenerating I_2 to resume a catalytic cycle. To confirm this hypothesis, the reaction was conducted under O_2 atmosphere and 85% yield of the expected product was obtained in 2 hours (Scheme 3, c), indicating the possibility of O_2 in the air in assisting the catalytic transformation.

On the basis of our observations and relevant literature,[16,18,22] a plausible mechanism is proposed as shown in Scheme 4. An initial reaction between molecular iodine or electrophilic iodine source and quinoxalinone could lead to the formation of the intermediate **I**. Then, a nucleophilic attack of this intermediate **I** by indole will generate the intermediate **II**. Subsequent deprotonation, elimination, and oxidation by O_2 (in air)[23] would reproduce the iodine to repeat the catalytic cycle and give the corresponding 3-(indol-2-yl)quinoxalin-2-one under ambient conditions.

Lastly, the scalability of the reaction was confirmed by conducting a gram-scale reaction (10 mmol scale) between quinoxalinone **1a** and indole **2a**, and the desired product **3a** was obtained in 93% isolated yield (2.56 g) under standard conditions, suggesting a practicality of this protocol (Scheme 5).



Scheme 4 Possible reaction mechanism

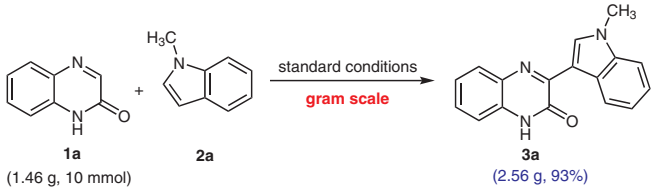
In summary, the iodine-catalyzed oxidative cross-dehydrogenative coupling of quinoxalinones and indoles was developed under ambient conditions using air as the oxidant. This reaction does not require additives and can be executed conveniently and efficiently at room temperature, furnishing the biologically useful of 3-(indol-3-yl)quinoxalin-2-ones in moderate to excellent yields. The transformation is believed to follow a non-radical pathway, and molecular iodine is likely to be directly involved in the catalytic cycle. Further expansion of the synthetic utility and evaluation of potential biological activity of these synthesized quinoxalinone derivatives are currently under exploration in our laboratory.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. All experiments were carried out under an air atmosphere, and oven-dried glassware were used in all cases. Column chromatography was performed over silica gel (SiO_2; 60 Å silica gel, Merck Grade, 70–230 mesh). GC experiments were carried out with an Agilent 6890N GC-FID on chromatograph equipped with an Agilent column ZB-1, dimethylpolysiloxane column (30 m × 0.25 mm ID × 0.25 µm). ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in DMSO-d_6 and $CDCl_3$ solutions. NMR chemical shifts are reported in ppm, and were measured relative to DMSO (2.50 ppm for ^1H and 39.52 ppm for ^{13}C) and $CHCl_3$ (7.26 ppm for ^1H and 77.16 ppm for ^{13}C). IR spectra were recorded on Bruker FT-IR spectrophotometer Model ALPHA by neat method, and only partial data are listed. Melting points were determined on Büchi Melting Point M-565 apparatus. High-resolution mass spectroscopy (HRMS) data were analyzed by a high-resolution micrOTOF instrument with electrospray ionization (ESI). The structures of known compounds were corroborated by comparing their ^1H and ^{13}C NMR data with those reported in the literature.[20]

A general procedure for the preparation of quinoxalinone substrates is provided in the Supporting Information.

Iodine-Catalyzed Oxidative Cross-Dehydrogenative Coupling of Quinoxalin-2(1*H*)-ones 1 and Indoles 2; General Procedure

To a 2 dram vial (8 mL) equipped with a magnetic stir bar were added quinoxalinone **1** (0.50 mmol, 1.0 equiv), indole **2** (0.55 mmol, 1.1 equiv), molecular I_2 (7.2 mg, 0.05 mmol, 0.10 equiv), and CH_3OH (1.00 mL), respectively. The reaction mixture was stirred at r.t. under atmospheric air for 8 h. Upon completion, distilled deionized H_2O (10 mL) and sat. aq $Na_2S_2O_3$ (5 mL) were added, and the mixture was extracted



Scheme 5 Gram-scale synthesis

with EtOAc (2 × 10 mL). The combined organic layers were washed with brine, dried (anhyd Na_2SO_4), and concentrated in vacuo. The crude product was purified by SiO_2 column chromatography to afford the desired indolylquinoxalin-2(1*H*)-one product **3**.

3-(1-Methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3a)

Yellow solid; yield: 133 mg (97%); mp 290.1–292.0 °C.

IR (neat): 2834, 1650, 1529, 1458, 1373, 1348, 1194, 1118, 1087, 935, 896, 735 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.45 (s, 1 H), 8.93 (s, 1 H), 8.90 (d, *J* = 6.9 Hz, 1 H), 7.86 (d, *J* = 7.9 Hz, 1 H), 7.55 (d, *J* = 7.3 Hz, 1 H), 7.42 (t, *J* = 7.5 Hz, 1 H), 7.32–7.26 (m, 4 H), 3.91 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.3, 151.6, 136.8, 136.8, 132.6, 130.1, 127.9, 127.5, 126.7, 123.2, 123.1, 122.6, 121.2, 114.9, 110.3, 110.1, 33.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}N_3O$: 276.1131; found: 276.1139.

3-(1*H*-Indol-3-yl)quinoxalin-2(1*H*)-one (3b)

Brown solid; yield: 129 mg (99%); mp 328.8–329.4 °C.

IR (neat): 2920, 2850, 1656, 1610, 1529, 1423, 1236, 1149, 1112, 936, 917, 738 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ =12.43 (s, 1 H), 11.80 (s, 1 H), 8.96 (d, *J* = 2.8 Hz, 1 H), 8.91–8.87 (m, 1 H), 7.87 (d, *J* = 7.6 Hz, 1 H), 7.54–7.50 (m, 1 H), 7.44–7.40 (m, 1 H), 7.34–7.28 (m, 2 H), 7.27–7.22 (m, 2 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.5, 152.0, 136.3, 133.1, 132.7, 130.2, 128.0, 127.6, 126.2, 123.3, 123.0, 122.6, 121.0, 114.9, 111.9, 111.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{12}N_3O$: 262.0975; found: 262.0979.

The spectroscopic data are in accordance with those reported.[13b]

3-(5-Chloro-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3c)

Yellow solid; yield: 131 mg (89%); mp 311.5–312.5 °C.

IR (neat): 3439, 2829, 1659, 1609, 1531, 1448, 1420, 1273, 1147, 1125, 1098, 887, 861, 790, 743 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.47 (s, 1 H), 11.96 (s, 1 H), 8.97 (d, *J* = 2.8 Hz, 1 H), 8.85 (d, *J* = 2.4 Hz, 1 H), 7.86 (d, *J* = 7.6 Hz, 1 H), 7.54 (d, *J* = 8.8 Hz, 1 H), 7.47–7.43 (m, 1 H), 7.33–7.30 (m, 2 H), 7.26 (dd, *J* = 8.8, 2.4 Hz, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.3, 151.6, 134.8, 134.4, 132.5, 130.3, 128.3, 127.7, 127.3, 125.7, 123.3, 122.5, 121.9, 115.0, 113.5, 110.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{10}ClN_3ONa$: 318.0405; found: 318.0412.

3-(7-Benzyloxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3d)

Yellow solid; yield: 169 mg (92%); mp 279.0–280.2 °C.

IR (neat): 3446, 2840, 1657, 1577, 1538, 1496, 1420, 1371, 1256, 1243, 1103, 1064, 980, 755, 731 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.43 (s, 1 H), 11.92 (s, 1 H), 8.86 (dd, *J* = 8.4, 2.8 Hz, 1 H), 8.48 (dd, *J* = 8.0, 4.0 Hz, 1 H), 7.86 (d, *J* = 7.6 Hz, 1 H), 7.60 (d, *J* = 7.2 Hz, 2 H), 7.44–7.41 (m, 3 H), 7.38–7.29 (m, 3 H), 7.15 (td, *J* = 8.0, 1.2 Hz, 1 H), 6.92 (d, *J* = 7.8 Hz, 1 H), 5.30 (s, 2 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.4, 152.0, 145.2, 137.2, 132.6, 132.5, 130.2, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 126.4, 123.3, 121.6, 115.9, 115.0, 111.9, 104.7, 69.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{17}N_3O_2Na$: 390.1213; found: 390.1214.

3-(4-Methoxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3e)

Brown solid; yield: 131 mg (90%); mp 264.1–265.3 °C.

IR (neat): 3368, 2921, 2849, 1650, 1527, 1410, 1197, 1149, 1107, 1026, 937, 805, 738 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.38 (s, 1 H), 11.58 (d, *J* = 1.6 Hz, 1 H), 8.83 (d, *J* = 2.4 Hz, 1 H), 8.74 (d, *J* = 8.8 Hz, 1 H), 7.85–7.83 (m, 1 H), 7.41 (td, *J* = 8.4, 1.2 Hz, 1 H), 7.33–7.27 (m, 2 H), 7.02 (d, *J* = 2.0 Hz, 1 H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1 H), 3.82 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 156.3, 154.4, 151.9, 137.2, 132.7, 132.2, 130.2, 127.9, 127.5, 123.7, 123.2, 120.3, 114.9, 111.5, 110.7, 94.9, 55.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}N_3O_2$: 292.1081; found: 292.1088.

The spectroscopic data are in accordance with those reported.[13c]

3-(5-Methoxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3f)

Brown solid; yield: 100 mg (69%); mp 317.5–317.9 °C.

IR (neat): 3384, 2920, 2850, 1650, 1582, 1481, 1412, 1206, 1129, 1106, 1026, 919, 749 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.39 (s, 1 H), 11.67 (s, 1 H), 8.89 (d, *J* = 3.2 Hz, 1 H), 8.46 (d, *J* = 2.4 Hz, 1 H), 7.85 (d, *J* = 7.6 Hz, 1 H), 7.43–7.39 (m, 2 H), 7.32–7.28 (m, 2 H), 6.88 (dd, *J* = 8.8, 2.4 Hz, 1 H), 3.88 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.9, 154.4, 152.0, 133.4, 132.6, 131.2, 130.1, 127.8, 127.5, 126.9, 123.2, 114.9, 112.5, 112.1, 111.1, 105.1, 55.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}N_3O_2$: 292.1081; found: 292.1079.

The spectroscopic data are in accordance with those reported.[13c]

3-(6-Methoxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3g)

Brown solid; yield: 120 mg (82%); mp 147.1–149.2 °C.

IR (neat): 3306, 2921, 2850, 1654, 1507, 1420, 1382, 1352, 1220, 1088, 739, 724 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 12.37 (s, 1 H), 11.58 (s, 1 H), 8.81 (d, *J* = 2.7 Hz, 1 H), 8.72 (d, *J* = 8.7 Hz, 1 H), 7.84 (d, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 8.2 Hz, 1 H), 7.32–7.29 (m, 2 H), 7.00 (d, *J* = 2.0 Hz, 1 H), 6.87 (dd, *J* = 8.8, 2.2 Hz, 1 H), 3.81 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 156.2, 154.4, 151.9, 137.2, 132.7, 132.2, 130.2, 127.9, 127.5, 123.6, 123.2, 120.2, 114.9, 111.4, 110.6, 95.0, 55.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}N_3O_2$: 292.1081; found: 292.1081.

3-(7-Methoxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3h)

Yellow solid; yield: 141 mg (97%); mp 322.9–323.4 °C.

IR (neat): 3426, 2922, 2848, 1651, 1577, 1538, 1422, 1371, 1253, 1241, 1207, 1066, 738 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.41 (s, 1 H), 11.92 (s, 1 H), 8.85 (s, 1 H), 8.46 (d, *J* = 7.6 Hz, 1 H), 7.85 (d, *J* = 7.6 Hz, 1 H), 7.44–7.40 (m, 1 H), 7.33–7.28 (m, 2 H), 7.16 (t, *J* = 8.0 Hz, 1 H), 6.82 (d, *J* = 7.6 Hz, 1 H), 3.96 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.4, 152.0, 146.1, 132.6, 132.4, 130.2, 128.0, 127.7, 127.6, 126.2, 123.2, 121.7, 115.7, 114.9, 111.9, 103.3, 55.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{14}N_3O_2$: 292.1081; found: 292.1088.

3-(5-Hydroxy-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3i)

Brown solid; yield: 69 mg (50%); mp 251.7–253.1 °C.

IR (neat): 3276, 2923, 1649, 1585, 1523, 1435, 1244, 1192, 1145, 925, 868, 791, 748 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.36 (s, 1 H), 11.55 (d, *J* = 2.4 Hz, 1 H), 8.95 (s, 1 H), 8.85 (d, *J* = 3.2 Hz, 1 H), 8.31 (d, *J* = 2.4 Hz, 1 H), 7.80 (d, *J* = 7.6 Hz, 1 H), 7.43–7.38 (m, 1 H), 7.33–7.29 (m, 3 H), 6.75 (dd, *J* = 8.4, 2.4 Hz, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.5, 152.5, 152.1, 133.3, 132.8, 130.5, 130.1, 127.7, 127.2, 123.2, 123.1, 115.0, 112.3, 112.2, 110.8, 107.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{12}N_3O_2$: 278.0924; found: 278.0927.

Methyl 3-(3-Oxo-3,4-dihydroquinoxalin-2-yl)-1*H*-indole-6-carboxylate (3j)

Yellow solid; yield: 40 mg (25%); mp 324.2–325.1 °C.

IR (neat): 3323, 2922, 2847, 1697, 1665, 1619, 1539, 1502, 1426, 1286, 1201, 1081, 736 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.49 (s, 3 H), 12.15 (s, 3 H), 9.11 (d, *J* = 2.8 Hz, 1 H), 8.94 (d, *J* = 8.4 Hz, 1 H), 8.16 (d, *J* = 0.8 Hz, 1 H), 7.89 (d, *J* = 7.2 Hz, 1 H), 7.84 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.46–7.42 (m, 1 H), 7.34–7.29 (m, 2 H), 3.88 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 167.0, 154.3, 151.6, 135.9, 135.7, 132.5, 130.3, 129.8, 128.4, 127.8, 123.5, 123.3, 122.7, 121.5, 115.0, 113.7, 111.6, 52.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}N_3O_3$: 320.1030; found: 320.1036.

Methyl 3-(3-Oxo-3,4-dihydroquinoxalin-2-yl)-1*H*-indole-5-carboxylate (3k)

Orange solid; yield: 64 mg (40%); mp 338.3–339.7 °C.

IR (neat): 3234, 2922, 2850, 1686, 1659, 1536, 1433, 1278, 1259, 1230, 1097, 988, 797, 739 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.50 (s, 1 H), 12.11 (s, 1 H), 9.57 (s, 1 H), 9.01 (d, *J* = 2.4 Hz, 1 H), 7.87 (d, *J* = 8.0 Hz, 1 H), 7.82 (d, *J* = 7.6 Hz, 1 H), 7.60 (d, *J* = 8.4 Hz, 1 H), 7.48–7.44 (m, 1 H), 7.37–7.33 (m, 2 H), 3.92 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 167.3, 154.3, 151.6, 138.9, 134.5, 132.4, 130.4, 128.5, 127.6, 125.8, 125.6, 123.5, 123.4, 122.4, 115.1, 112.2, 111.9, 51.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{13}N_3O_3Na$: 342.0849; found: 342.0850.

3-(2-Methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3l)

Brown solid; yield: 52 mg (38%); mp 289.3–289.9 °C.

IR (neat): 2918, 2849, 1656, 1607, 1546, 1527, 1454, 1429, 1182, 1146, 893, 748 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.28 (s, 1 H), 11.44 (s, 1 H), 7.73 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H), 7.29–7.21 (m, 3 H), 7.02 (t, *J* = 7.6 Hz, 1 H), 6.96 (t, *J* = 7.6 Hz, 1 H), 2.45 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.5, 151.6, 139.3, 135.1, 132.5, 130.8, 128.8, 128.7, 128.0, 127.9, 123.3, 123.1, 119.5, 115.7, 114.9, 110.6, 14.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{13}N_3ONa$: 298.0951; found: 298.0964.

The spectroscopic data are in accordance with those reported.[13c]

3-(1-Methyl-2-phenyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3m)

Yellow solid; yield: 88 mg (50%); mp 260.1–261.2 °C.

IR (neat): 2920, 2849, 1651, 1540, 1464, 1428, 1396, 1364, 1078, 869, 748, 733, 701 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.18 (s, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 7.59 (d, *J* = 8.1 Hz, 1 H), 7.46–7.37 (m, 6 H), 7.29–7.22 (m, 3 H), 7.19–7.14 (m, 1 H), 3.72 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.5, 153.9, 141.9, 136.8, 132.3, 131.9, 131.6, 130.2, 129.2, 128.1, 128.0, 127.0, 122.9, 122.0 120.6, 120.4, 114.9, 110.2, 110.1, 31.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{18}N_3O$: 352.1444; found: 352.1453.

3-(1-Phenyl-1*H*-pyrrol-3-yl)quinoxalin-2(1*H*)-one (3n)

Brown solid; yield: 85 mg (59%); mp 232.4–234.6 °C.

IR (neat): 2847, 1658, 1592, 1545, 1509, 1275, 1205, 1064, 812, 788, 749, 683 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.48 (s, 1 H), 8.57 (t, *J* = 1.8 Hz, 1 H), 7.76 (dd, *J* = 8.0, 1.1 Hz, 1 H), 7.65 (d, *J* = 8.0 Hz, 2 H), 7.54–7.50 (m, 3 H), 7.49–7.42 (m, 1 H), 7.35–7.29 (m, 3 H), 7.12 (dd, *J* = 3.0, 1.5 Hz, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.2, 150.4, 139.4, 132.4, 130.9, 129.9, 128.6, 128.5, 127.8, 126.2, 125.7, 123.7, 123.3, 122.5, 120.5, 119.8, 115.0, 110.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}N_3O$: 288.1131; found: 288.1138.

3-(1-Methyl-1*H*-pyrrol-3-yl)quinoxalin-2(1*H*)-one (3o)

Yellow solid; yield: 41 mg (36%); mp 220.4–221.7 °C.

IR (neat): 3106, 2919, 2849, 1660, 1538, 1484, 1415, 1313, 1217, 1062, 754, 744 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.35 (s, 1 H), 8.06 (t, *J* = 1.2 Hz, 1 H), 7.69 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.41–7.37 (m, 1 H), 7.28–7.23 (m, 2 H), 6.86 (dd, *J* = 2.8, 1.6 Hz, 1 H), 6.81 (t, *J* = 2.4 Hz, 1 H), 3.70 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.2, 151.0, 132.4, 130.7, 128.0, 127.8, 127.5, 123.1, 123.0, 120.1, 114.9, 108.5, 36.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{11}N_3ONa$: 248.0794; found: 248.0789.

3-(1*H*-Pyrrol-3-yl)quinoxalin-2(1*H*)-one (3p)

Brown solid; yield: 41 mg (39%); mp 248.7–250.5 °C.

IR (neat): 3426, 2919, 2848, 1657, 1552, 1529, 1476, 1423, 1099, 1020, 833, 727 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.45 (s, 1 H), 11.66 (s, 1 H), 7.72–7.70 (m, 1 H), 7.44–7.40 (m, 2 H), 7.31–7.26 (m, 2 H), 7.06 (td, *J* = 2.4, 1.2 Hz, 1 H), 6.24–6.22 (m, 1 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 153.7, 146.4, 132.2, 130.7, 128.2, 128.1, 127.3, 123.6, 123.3, 115.7, 115.0, 109.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{10}N_3O$: 212.0818; found: 212.0830.

3-(2,4-Dimethyl-1*H*-pyrrol-3-yl)quinoxalin-2(1*H*)-one (3q)

Yellow solid; yield: 24 mg (20%); mp 203.2–204.5 °C.

IR (neat): 3357, 2920, 2851, 1648, 1558, 1487, 1207, 1146, 894, 789, 743, 673 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 12.52 (s, 1 H), 11.37 (s, 1 H), 7.62 (d, *J* = 8.1 Hz, 1 H), 7.38–7.33 (m, 1 H), 7.27–7.23 (m, 2 H), 5.88 (d, *J* = 2.4 Hz, 1 H), 2.49 (s, 3 H), 2.28 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 155.3, 146.7, 133.0, 131.2, 129.5, 127.4, 127.2, 126.8, 123.6, 123.5, 115.0, 111.9, 15.2, 13.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{14}N_3O$: 240.1131; found: 240.1131.

1-Ethyl-3-(1-methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3r)

Yellow solid; yield: 111 mg (73%); mp 172.2–173.2 °C.

IR (neat): 2920, 2850, 1643, 1577, 1530, 1454, 1370, 1198, 1153, 1120, 1082, 739 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.93 (s, 1 H), 8.92–8.89 (m, 1 H), 7.93 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.61–7.51(m, 3 H), 7.39 (t, *J* = 7.6 Hz, 1 H), 7.33–7.26 (m, 2 H), 4.38 (q, *J* = 7.2 Hz, 2 H), 3.92 (s, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 153.1, 150.3, 137.0, 136.9, 133.3, 130.2, 128.7, 128.5, 126.8, 123.4, 123.1, 122.7, 121.3, 114.1, 110.3, 110.2, 36.9, 33.1, 12.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{17}N_3ONa$: 326.1264; found: 326.1269.

1-Ethyl-6,7-dimethyl-3-(1-methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3s)

Yellow solid; yield: 137 mg (83%); mp 278.1–278.8 °C.

IR (neat): 2966, 2914, 1693, 1640, 1567, 1454, 1365, 1311, 1116, 1082, 874, 850, 747 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.02 (d, *J* = 5.2 Hz, 1 H), 8.83 (s, 1 H), 7.77 (s, 1 H), 7.39–7.33 (m, 3 H), 7.09 (s, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 3.87 (s, 3 H), 2.42 (s, 3 H), 2.39 (s, 3 H), 1.43 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 154.2, 150.0, 137.8, 137.2, 136.2, 132.7, 132.3, 129.9, 128.5, 127.6, 123.8, 122.7, 121.5, 113.9, 111.6, 109.4, 37.3, 33.4, 20.7, 19.3, 12.6.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}N_3O$: 332.1757; found: 332.1764.

3-(1-Methyl-1*H*-indol-3-yl)-1-pentylquinoxalin-2(1*H*)-one (3t)

Orange solid; yield: 168 mg (97%); mp 131.7–132.5 °C.

IR (neat): 3040, 2922, 2851, 1645, 1578, 1533, 1455, 1373, 1119, 1085, 1009, 734 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.93 (s, 1 H), 8.92–8.89 (m, 1 H), 7.91 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.57–7.50 (m, 3 H), 7.40–7.35(m, 1 H), 7.33–7.25 (m, 2 H), 4.31 (t, *J* = 7.6 Hz, 2 H), 3.91 (s, 3 H), 1.73–1.65 (m, 2 H), 1.43–1.35 (m, 4 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 153.3, 150.3, 137.1, 136.8, 133.2, 130.4, 128.7, 128.3, 126.8, 123.3, 123.1, 122.6, 121.3, 114.2, 110.3, 110.2, 41.6, 33.0, 28.5, 26.6, 21.9, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}N_3O$: 346.1914; found: 346.1910.

1-Benzyl-3-(1-methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3u)

Yellow solid; yield: 159 mg (87%); mp 195.8–196.1 °C.

IR (neat): 3029, 2920, 2850, 1636, 1576, 1528, 1528, 1454, 1367, 1088, 723, 666 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.96 (s, 1 H), 8.95–8.93 (m, 1 H), 7.94 (d, *J* = 7.5 Hz, 1 H), 7.58–7.56 (m, 1 H), 7.46–7.41 (m, 2 H), 7.38–7.20 (m, 8 H), 5.62 (s, 2 H), 3.92 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 153.7, 150.4, 137.1, 136.9, 136.2, 133.3, 130.6, 128.7, 128.6, 128.2, 127.2, 126.8, 123.6, 123.1, 122.7, 121.4, 114.7, 110.3, 110.2, 45.0, 33.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{20}N_3O$: 366.1601; found: 366.1605.

1-Allyl-3-(1-methyl-1*H*-indol-3-yl)quinoxalin-2(1*H*)-one (3v)

Brown solid; yield: 134 mg (85%); mp 147.2–154.7 °C.

IR (neat): 2919, 2850, 1642, 1533, 1454, 1370, 1308, 1188, 1120, 1082, 735, 679 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 8.93–8.91 (m, 2 H), 7.92 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.56–7.54 (m, 1 H), 7.52–7.45 (m, 2 H), 7.39–7.35 (m, 1 H), 7.34–7.27 (m, 2 H), 6.05–5.96 (m, 1 H), 5.20 (dd, *J* = 10.4, 1.2 Hz, 1 H), 5.10 (dd, *J* = 17.2, 1.2 Hz, 1 H), 4.99 (dd, *J* = 3.2, 1.2 Hz, 2 H), 3.91 (s, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 153.2, 150.3, 137.1, 136.9, 133.2, 131.8, 130.5, 128.5, 128.2, 126.8, 123.5, 123.1, 122.6, 121.3, 117.0, 114.7, 110.3, 110.2, 43.9, 33.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{18}N_3O$: 316.1444; found: 316.1453.

Ethyl 2-[3-(1-Methyl-1*H*-indol-3-yl)-2-oxoquinoxalin-1(2*H*)-yl]acetate (3w)

Yellow solid; yield: 135 mg (75%); mp 223.5–224.1 °C.

IR (neat): 2922, 2851, 1737, 1639, 1536, 1457, 1370, 1214, 1187, 1090, 750, 732 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 9.02 (dd, *J* = 5.4, 2.6 Hz, 1 H), 8.80 (d, *J* = 2.1 Hz, 1 H), 8.00 (d, *J* = 7.8 Hz, 1 H), 7.44–7.35 (m, 5 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 5.10 (d, *J* = 2.0 Hz, 2 H), 4.29–4.23 (m, 2 H), 3.86 (d, *J* = 2.1 Hz, 3 H), 1.27 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (DMSO-d_6, 100 MHz): δ = 167.6, 154.4, 150.7, 137.3, 136.9, 134.1, 130.8, 129.7, 128.3, 127.5, 123.9, 123.7, 123.0, 121.8, 112.9, 111.3, 109.50, 62.1, 43.7, 33.5, 14.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{10}N_3O_3$: 362.1499; found: 362.1504.

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