Advanced Synthesis & Catalysis

Accepted Article

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To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201901008

Link to VoR: http://dx.doi.org/10.1002/adsc.201901008

10.1002/adsc.201901008

FULL PAPER

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

(Thio)etherification of Quinoxalinones under Visible-Light Photoredox Catalysis

Jiadi Zhou,[a] Peng Zhou,[b] Tingting Zhao,[b] Quanlei Ren,[b] and Jianjun Li[a,b*]

[a] Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals, Zhejiang University of Technology, Hangzhou 310014, P. R. of China.
[b] College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. of China. E-mail: lijianjun@zjut.edu.cn

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. An efficient visible-light-induced (thio)etherification of quinoxalin-2(1H)-ones with divergent aliphatic alcohols and thiols (primary, secondary, and tertiary) at room temperature in air has been developed. This protocol was highlighted by its mild conditions, readily available starting materials, operational simplicity, and wide functional group tolerance.

Keywords: Quinoxalin-2(1H)-ones; (Thio)etherification; Visible-light-induced; Alcohols; Thiols

Introduction

The construction of the C−O and C-S bond has long been a fundamentally important pursuit in the synthetic community. Over the years, typical methodologies for aryl (thio)etherification have been well established, such as the Cu-based,[1] Pd-based,[2] Fe-based[3] and Ni-based[4] coupling reactions. However, the routine use of the prefunctionalized substrate precursors and often harsh reaction conditions limits their potential application. From a synthetic point of view, the (thio)etherification *via* cross-dehydrogenative coupling (CDC) represents one of the most straightforward and efficient approaches for the construction of the C−O and C-S bond due to its high atom and step economy. Nevertheless, direct C−H/O(S)−H (thio)etherification with aliphatic alcohols and thiols still remains challenging since many methods for their functionalizations lead to carbon−carbon bond formation adjacent to the oxygen atom,[5] and the thiols can be easily over-oxidized to generate sulfoxides and sulfones.[6] In the past few years, a few examples of aryl (thio)etherification of simple arenes with alcohols[7] or aryl thiols[8] were successfully demonstrated by the utilization of CDC strategy. However, in most C−H/O−H etherifications, metal catalysts and stoichiometric chemical oxidants were used, and the direct C−H/S−H thioetherifications with aliphatic thiols were rarely explored.

Quinoxalin-2(1H)-ones represent a valuable class of structural features that are extensively utilized in synthetic chemistry, materials, and pharmaceuticals (Figure 1).[9] Recently, various C3−H functionalization strategies[10] including arylation,[11] alkylation,[12] acylation,[13] phosphonation,[14] trifluoromethylation,[15] difluoroarylmethylation,[16] and amination[17] of quinoxalin-2(1H)-ones have been reported. Very recently, the oxidative C−H fluoroalkoxylation[18a] or alkoxylation[18b] of quinoxalinones with alcohols has been reported, however, the method needs stoichiometric $PhI(OTFA)_2$. For a long period of time, we have been focusing on the $C(sp^2)$−H alkylation of various *N*- Heteroarenes (quinolines, isoquinolins, pyridines, benzooxazole and benzothiazole)[19a] and the C-O bond construction by CDC.[19b,19c] Herein, we describe a O_2-mediated CDC approach for photocatalytic quinoxalinones $C(sp^2)$-H (thio)etherification by alcohols and thiols at room temperature in moderate to good yields with high regioselectivity.

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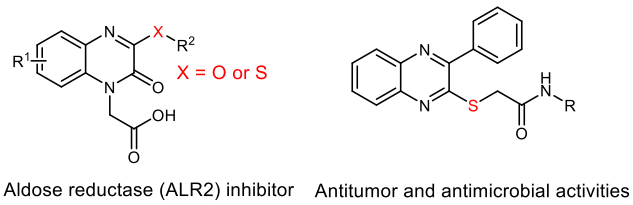
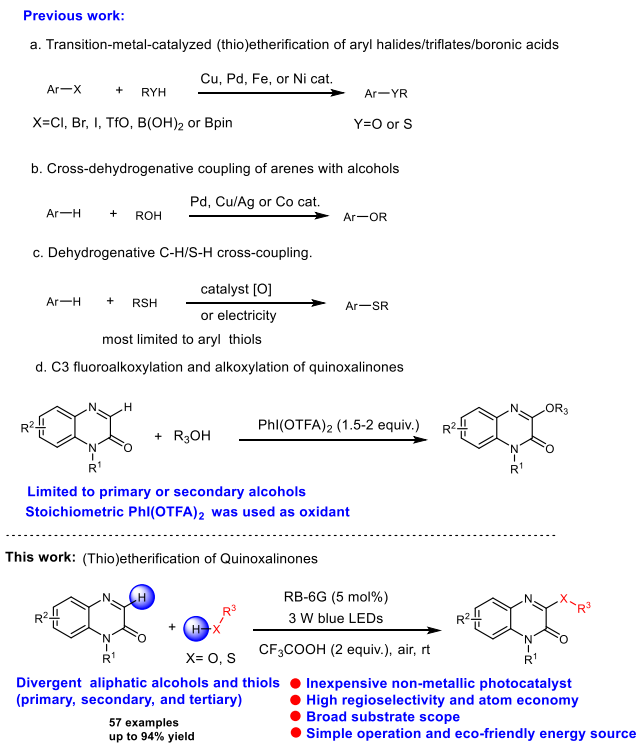


Figure 1. (Thio)ether substituted quinoxalinone derivatives

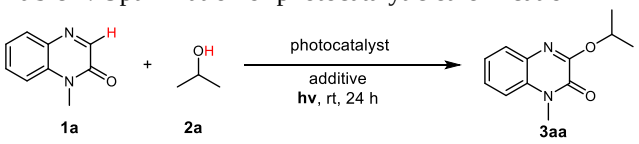


Scheme 1. The construction of the C−O and C-S bond

Results and Discussion

Initially, 1-methylquinoxalin-2(1H)-one (**1a**) was treated with isopropyl alcohol (**2a**) in the presence of $Ru(bpy)_3Cl_3$ (5 mol %) under irradiation with 3 W blue LED lamps. To our delight, the desired product **3aa** was obtained in 21% yield after 24 h (Table 1, entry 1). Furthermore, other photocatalysts such as $Ir(ppy)_3$, Rose bengal, Eosin Y, Methylene blue, and Rhodamine 6G were also examined (Table 1, entries 2-6). Rhodamine 6G was demonstrated to be the most effective one to give the desired product **3aa** in 42% yield (Table 1, entry 6). We next screened different bases and acids aiming to improve the yield, the application of CF_3COOH (2.0 equiv.) could improve the yield to 81%

Table 1. Optimization of photocatalytic etherification [a]



Entry	Photocatalyst (mol %)	Additive (equiv.)	Yield (%)[b]
1	$Ru(bpy)_3Cl_3$ (5)	—	21
2	$Ir(ppy)_3$ (5)	—	/
3	Rose bengal (5)	—	25
4	Eosin Y (5)	—	32
5	Methylene blue (5)	—	/
6	Rhodamine 6G (5)	—	42
7	Rhodamine 6G (5)	Cs_2CO_3 (2)	11
8	Rhodamine 6G (5)	NaOH (2)	/
9	Rhodamine 6G (5)	K_2CO_3 (2)	15
10	Rhodamine 6G (5)	CF_3CO_2H (2)	81
11	Rhodamine 6G (5)	CF_3SO_3H (2)	46
12	Rhodamine 6G (5)	H_2SO_4 (2)	44
13	Rhodamine 6G (1)	CF_3CO_2H (2)	69
14	Rhodamine 6G (10)	CF_3CO_2H (2)	80
15	—	CF_3CO_2H (2)	30
16	Rhodamine 6G (5)	CF_3CO_2H (3)	72
17	Rhodamine 6G (5)	CF_3CO_2H (1)	71
18[c]	Rhodamine 6G (5)	CF_3CO_2H (2)	30
19[d]	Rhodamine 6G (5)	CF_3CO_2H (2)	37
20[e]	Rhodamine 6G (5)	CF_3CO_2H (2)	/
21[f]	Rhodamine 6G (5)	CF_3CO_2H (2)	80

[a] Reaction conditions: **1a** (0.4 mmol), **2a** (1 mL), photocatalyst, additive, 3 W Blue LED, air, rt;
[b] Isolated yields based on **1a**.
[c] 3 W white LEDs.
[d] 3 W green LEDs.
[e] Without light irradiation.
[f] O_2 was used.

(Table 1, entries 7-12). The CF_3CO_2H may protonate **1a**, thus facilitating the subsequent nucleophilic substitution. Further optimization of the reaction was carried out by screening of the loading amounts of Rhodamine 6G and CF_3CO_2H. However, the yield has no significant improvement (Table 1, entries 13-17). Unexpectedly, when the reaction was carried out in the absence of Rhodamine 6G, **3aa** was obtained in 30% yield. In addition, when the reaction was conducted under irradiation with 3 W white and green LED lamps, **3aa** was also obtained in 30% and 37% yield, respectively (Table 1, entries 18 and 19). No transformation was observed when the reaction was carried out in the dark (Table 1, entry 20). Moreover, when the reaction was carried out under O_2, the yield has no significant improvement (Table 1, entry 21).

With the optimized reaction conditions in hand, the scope of the present transformation was further investigated by employing various quinoxalin-2-one derivatives and alcohols (Scheme 2). Firstly, a series

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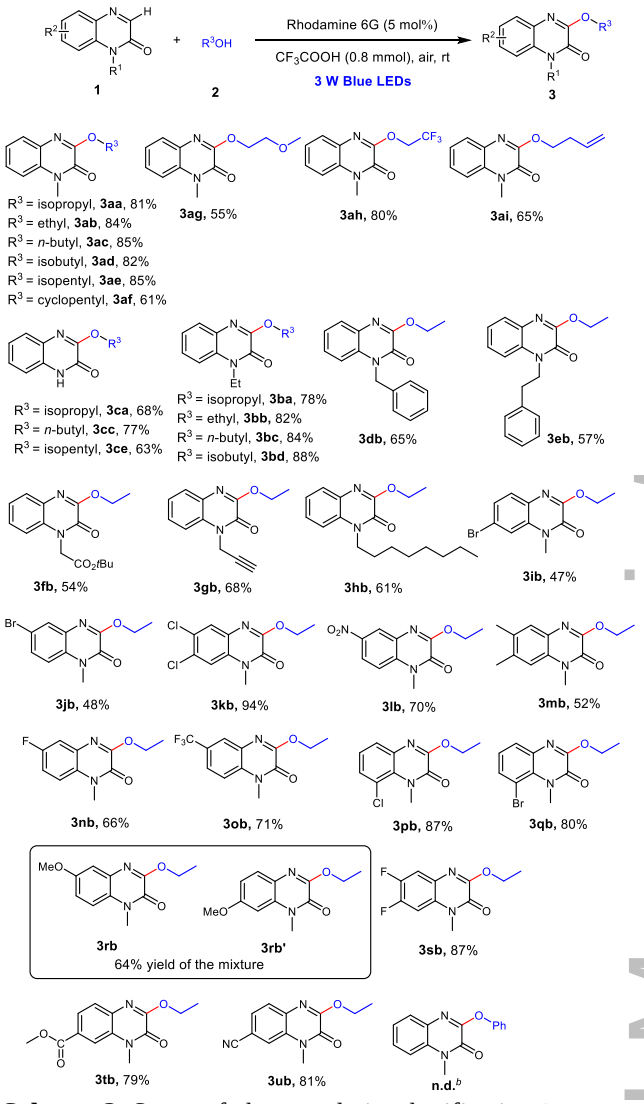
of alcohols were attempted under the standard conditions. Simple aliphatic alcohols, such as isopropyl alcohol, ethanol, butyl alcohol, 2-methylpropan-1-ol, 3-methylbutan-1-ol, and cyclopentanol were all compatible with the reaction to give the desired products in 61-85% yields (**3aa, 3ab, 3ac, 3ad, 3ae,** and **3af**). Importantly, the use of glycol ethers as starting materials did not compromise the efficiency of the cross-coupling (**3ag**). Moreover, 2,2,2-trifluoroethan-1-ol were also found to participate efficiently in the reactions (**3ah**). Enyl group was also tolerated, the corresponding product **3ai** was obtained. Nevertheless, none of desired product was detected when phenol were employed in the present reaction system. Notably, *N*-free protected quinoxalin-2(1H)-ones also worked well (**3ca**, **3cc**, and **3ce**). The compatibility with *N*-substituted quinoxalinones was then examined. Various *N*-protected groups such as *N*-ethyl, *N*-benzyl, *N*-phenyl, *N*-esteryl, *N*-propynyl, and *N*-octyl groups were all well tolerated in this reaction system to give the desired products in 54-88% yields (**3ba**, **3bb**, **3bc**, **3bd**, **3db**, **3eb**, **3fb**, **3gb**, and **3hb**). Furthermore, a broad tolerance of substituted quinoxalin-2(1H)-ones with an electron-withdrawing or electron-donating group, such as F, Cl, Br, NO_2, CO_2Me, CF_3, CN, and Me at 6 or 7-position of the aromatic rings, reacted with ethanol smoothly to generate the anticipated products (**3ib**, **3jb**, **3kb**, **3lb**, **3mb**, **3nb**, **3ob**, **3sb**, **3tb**, **3ub**) in moderate to good yields. A mixture of 6-MeO and 7-MeO substituted quinoxalin-2(1H)-ones reacted with ethanol gave the products (**3rb** and **3rb'**) in 64 % yields. A substituted quinoxalin-2(1H)-one with Cl or Br on the 8-position was also the suitable substrate, giving the desired product (**3pb** and **3qb)** in 87% and 80% yield, respectively.



Scheme 2. Scope of photocatalytic etherification [a]

[a] Reaction conditions: **1** (0.4 mmol), **2** (1 mL), Rhodamine 6G (5 mol %), CF_3COOH (0.8 mmol), 3 W Blue LEDs, air, rt, 24 h; isolated yields based on **1**.

[b] Phenol (3 equiv.) and CH_3CN (1 mL) was used.

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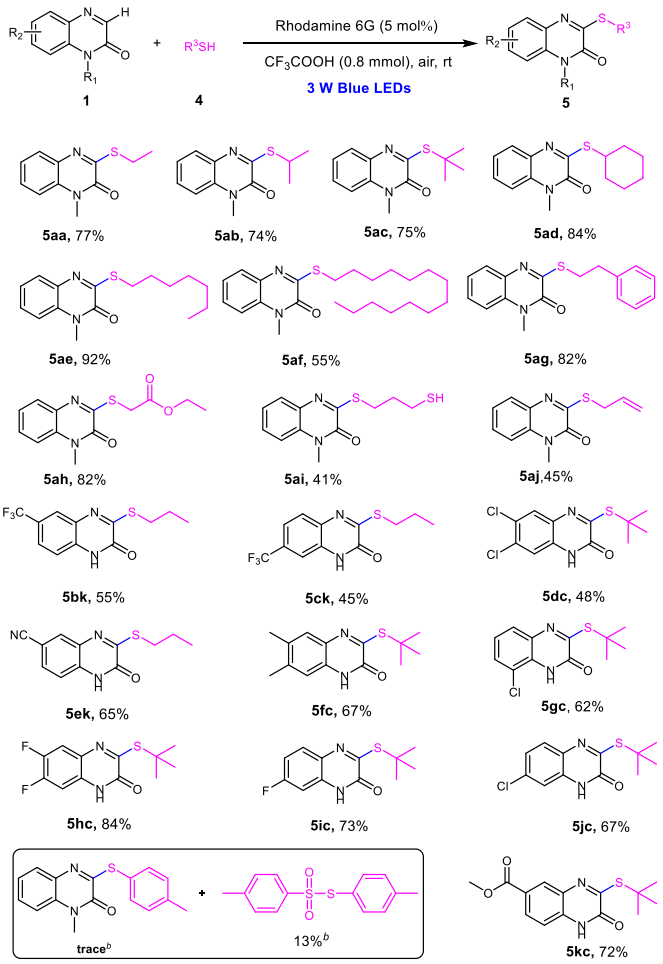
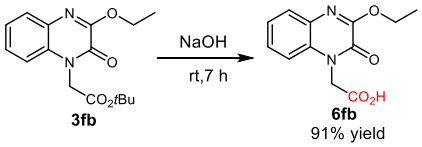


Scheme 3. Scope of photocatalytic thioetherification [a]

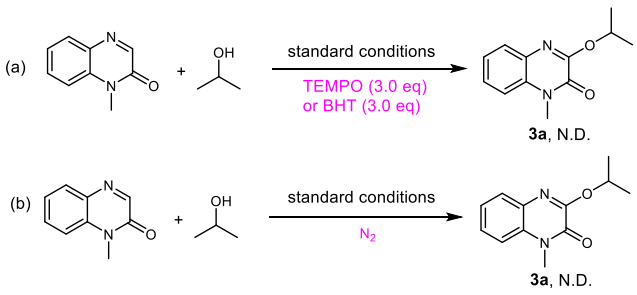
[a] Reaction conditions: **1a** (0.4 mmol), **4** (1 mL), Rhodamine 6G (5 mol %), CF_3COOH (0.8 mmol), 3 W Blue LEDs, air, rt, 24 h; isolated yields based on **1a**.
[b] *p*-Toluenethiol (3 equiv.) and CH_3CN (1 mL) was used, the yield based on *p*-toluenethiol.

We further examined the scope of this quinoxalinones thioetherification by employing various thiols (Scheme 3). Simple aliphatic thiols (primary, secondary, and tertiary) such as ethanethiol, propane-2-thiol, 2-methylpropane-2-thiol, and cyclopentanethiol were suitable substrates, and the corresponding products were obtained in 74-84 yields (**5aa**, **5ab**, **5ac**, and **5ad**). In addition, various primary aliphatic thiols containing a long aliphatic chains or aromatic ring group were also suitable substrates, and the corresponding products (**5ae**, **5af**, and **5ag**) were obtained in 55-92% yields. Ethyl 2-mercaptoacetate bearing an ester group was also an efficient substrate in this transformation, giving **5ah** in 82% yield. Notably, when ethane-1,2-dithiol bearing two hydrosulfuryl groups was used, only one of them could be coupled to **1a**, giving **5ai** in 41% yield. Enyl group was also tolerated, the corresponding product **5aj** was obtained. However, when *p*-toluenethiol was employed, only trace product was detected, along with 13% yield of S-(*p*-tolyl) 4-methylbenzenesulfonothioate. Moreover, quinoxalin-2(1H)-ones bearing CF_3, Me, F, Cl, CN, and CO_2Me groups on the benzene ring were also investigated under the optimal reaction conditions, and the corresponding products (**5bk**, **5fc, 5ck**, **5ek**, **5gc**, **5ic**, **5jc**, and **5kc**) were isolated in moderate to good yields. The reaction also processed smoothly with disubstituted quinoxalin-2(1H)-ones as the substrates, giving the corresponding products **5dc** and **5hc** in 48% and 84% yield, respectively.

Further application for such synthetic methodology was carried out. For example, a simple ester hydrolysis of **3fb** delivered the corresponding aldose reductase (ALR2) inhibitor (**6fb**) in good yield (Scheme 4).



Scheme 4. Synthesis of **6fb**



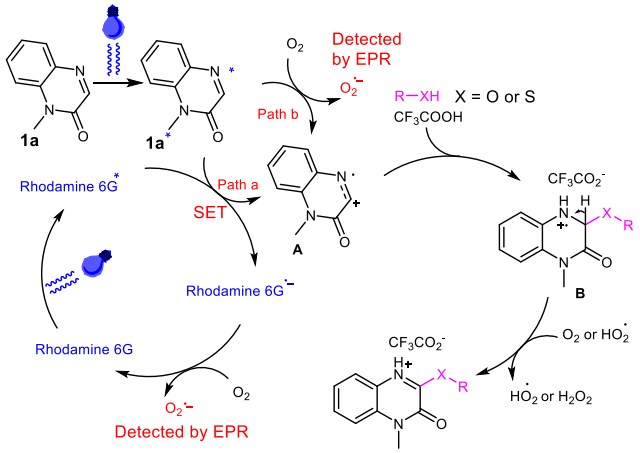
Scheme 5. Control experiment

Some preliminary mechanistic studies were conducted. When radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4methylphenol (BHT) was added into the reaction system under the standard conditions, the present transformation was completely inhibited, suggesting that this transformation might involve a radical process (Scheme 5a). Moreover, when the reaction was carried out under N_2, no product was detected. This result indicates that dioxygen is essential for the present transformation (Scheme 5b). In order to verify the formation of $O_2^{\bullet-}$ radical under photoredox catalysis, 5,5-dimethyl-pyrroline-*N*-oxide (DMPO) was employed as a capture reagent to trap the possible radical in this reaction by electron paramagnetic resonance (EPR), which was presented in Figures 6 and 7 of ESI†. When DMPO was added into a solution of **1a**, TFA, and Rhodamine 6G in air saturated ethanol or 1-propanethiol, the strong characteristic signal of an $O_2^{\bullet-}$ adduct with DMPO emerged after the reaction mixture was irradiated by 3 W blue LED lamps after 15 min. To our delight, when in the absence of Rhodamine 6G, the characteristic signal of an $O_2^{\bullet-}$ adduct with DMPO was also observed. These experimental results clearly revealed that two radical routes were involved in the reaction.

Cyclic voltammetry measurements were also performed to understand the possible mechanism. As shown in Figure 8 of ESI†, the oxidation semi-peak potential of **1a** ($E_{p/2}$= 1.83 V vs SCE in CH_3CN) and 1-propanethiol ($E_{p/2}$= 1.54 V vs SCE in CH_3CN) were both higher than that of Rhodamine 6G* (E_{red}= 0.95 V vs SCE).[23] Meanwhile, high-energy alkoxy radicals from simple alkanols ($E_{p/2}$ > 2.0 V vs SCE in CH_3CN) is very difficult.[20] We infer that **1a** might be irradiated by light to produce the excited-state **1a*** ($E_{p/2}$= −1.36 V vs SCE in CH_3CN based on the electrochemical and spectroscopic measurements, see ESI† for details),[24] which would be oxidized by Rhodamine 6G* or O_2 (E_{Red} = −0.44 V vs. SCE).[21]

The Stern−Volmer plot reveals the effective quenching of Rhodamine 6G* by 1-methylquinoxalin-2(1H)-one (**1a***) which indicates the single electron transfer (SET) step and reductive quenching cycle of the cross-coupling process (Figures 1 and 3 in ESI†). On the other hand, **1a*** also can be quenched by Rhodamine 6G* effectively (Figures 4 and 5 in ESI†). In contrast, the emission intensity of Rhodamine 6G* has no dramatically change along with the increasing of the amount of 1-propanethiol (Figures 2 and 3 in ESI†).

On the basis of these results and relevant reports,[18, 22] a possible mechanism was proposed in Scheme 6. Initially, **1a** is irradiated by light to produce the excited-state **1a***, which would be oxidized by Rhodamine 6G* (path a) or O_2 (path b) to produce reactive radical cation **A**. Subsequently, the oxidation of Rhodamine $6G^{\bullet-}$ (E_{ox}= −1.14 V vs Ag/AgCl)[23] by O_2 generates the ground state Rhodamine 6G and $O_2^{\bullet-}$. Then, **A** is trapped by alcohols or thiols to form nitrogen radical intermediate **B**. Finally, **B** is oxidized by O_2 or HO_2• to give the CDC product after deprotonation. In addition, the formation of H_2O_2 was also examined by a starch potassium iodide test paper and the paper was changed into blue.



Scheme 6. Possible reaction pathway

Conclusion

In summary, we have illustrated the visible-light-promoted quinoxalinones C(sp^2)-H (thio)etherification with diverse alcohols and thiols in air.[25] The present protocol provides a facile and practical approach to access diverse 3-alkyloxyl and 3-alkylthiol substituted quinoxalin-2(1H)-ones in moderate to good yields, which is of great value from organic synthesis perspectives due to its desirable features including a cheap catalyst, eco-friendly energy source, high atom economy, operation simplicity, and mild conditions. A detailed investigation of the mechanism and further application of this protocol is underway in our laboratory.

Experimental Section

General Considerations

All purchased chemicals were used as received without further purification. All reactions were monitored by TLC with silica gel-coated plates. ^{1}H (400, 500, or 600 MHz) NMR and ^{13}C (101, 126, or 151 MHz) NMR spectra were recorded on a Varian spectrometer in $CDCl_3$ or DMSO-d_6 using tetramethylsilane (TMS) as internal standards. Data are reported as follows: Chemical shift (number of protons, multiplicity, coupling constants). Coupling constants were quoted to the nearest 0.1 Hz and multiplicity reported according to the following convention: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, hept = heptet, br = broad. Mass spectra were measured with a HRMS APCI instrument using ESI ionization. Fourier transform infrared spectroscopy (FTIR) spectra were recorded on a Nicolet iS50 in attenuated total reflectance (ATR) mode and reported with wave number (cm^{-1}). The cyclic voltammetry measurements were detected by using a CHI 600E electrochemical workstation. Fluorescence quenching experiments were performed on a Hitachi F-7000 FL Spectrophotometer. The EPR experiments were performed on Bruker A300 EPR Spectrometer. UV-visable absorption experiments were performed on UV-2250 spectrophotometer.

General procedure for the synthesis of compounds in Scheme 2

To a 25 mL dried Schlenk tube equipped with magnetic stir bar was added **1** (0.4 mmol), Rhodamine 6G (0.02 mmol, 5 mol%), alcohols (1 mL), CF_3COOH (0.8 mmol, 2 equiv.). The mixture was stirred at room temperature and irradiated by 3 W blue LEDs for 24 h, the reaction mixture was quenched with satd. aq. $NaHCO_3$ (10 mL) and extracted with EtOAc. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified on a silica gel column using hexane/EtOAc.

General procedure for the synthesis of compounds in Scheme 3

To a 25 mL dried Schlenk tube equipped with magnetic stir bar was added **1** (0.4 mmol), Rhodamine 6G (0.02 mmol, 5 mol%), thiols (1 mL), CF_3COOH (0.8 mmol, 2 equiv.). The mixture was stirred at room temperature and

irradiated by 3W blue LEDs for 24 h, the reaction mixture was quenched with satd. aq. $NaHCO_3$ (10 mL) and extracted with EtOAc. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude products were purified on a silica gel column using hexane/EtOAc.

Characterization data for the products

(3aa) 3-isopropoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.44-7.38 (m, 1H), 7.30 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.25 (dd, *J* = 8.3, 1.0 Hz, 1H), 5.49 (hept, *J* = 6.2 Hz, 1H), 3.72 (s, 3H), 1.46 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 151.4, 131.4, 131.3, 127.4, 126.7, 123.8, 113.5, 70.5, 29.5, 21.6 (2C); HRMS (ESI): $C_{12}H_{15}N_2O_2$ $[M+H]^+$ calculated: 219.1128, found: 219.1153.

(3ab) 3-ethoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.33 – 7.29 (m, 1H), 7.26 (d, *J* = 8.1 Hz,1H), 4.56 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.9, 151.2, 131.5, 131.2, 127.5, 126.9, 123.9, 113.6, 63.5, 29.5, 14.2; HRMS (ESI): $C_{11}H_{12}N_2NaO_2$ $[M+Na]^+$ calculated: 227.0791, found: 227.0813.

(3ac) 3-butoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.32 – 7.28 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 4.48 (t, *J* = 6.8 Hz, 2H), 3.72 (s, 3H), 1.91 – 1.85 (m, 2H), 1.56 – 1.48 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.1, 151.2, 131.6, 131.3, 127.5, 126.9, 123.9, 113.6, 67.4, 30.5, 29.5, 19.2, 13.8; HRMS (ESI): $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ calculated: 255.1104, found: 255.1121.

(3ad) 3-Isobutoxy-1-methylquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.32 – 7.27 (m, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 4.24 (d, *J* = 6.9 Hz, 2H), 3.72 (s, 3H), 3.32 – 2.22 (m, 1H), 1.06 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 151.1, 131.5, 131.2, 127.4, 126.9, 123.9, 113.6, 73.7, 29.4, 27.6, 19.3; HRMS (ESI): $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ calculated: 255.1104, found: 255.1128.

(3ae) 3-(isopentyloxy)-1-methylquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.32 – 7.27 (m, 1H), 7.25 (dd, *J* = 8.3, 1.1 Hz, 1H), 4.51 (t, *J* = 6.8 Hz, 2H), 3.72 (s, 3H), 1.90 – 1.83 (m, 1H), 1.78 (q, *J* = 6.9 Hz, 2H), 0.99 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 151.2, 131.5, 131.2, 127.5, 126.9, 123.9, 113.6, 66.2, 37.2, 29.5, 25.1, 22.6 (2C); ATR-FTIR (cm^{-1}):2958, 1671, 1473, 1387, 1258, 1122, 751; HRMS (ESI): $C_{14}H_{18}N_2NaO_2$ $[M+Na]^+$ calculated: 269.1260, found: 269.1278.

(3af) 3-(cyclopentyloxy)-1-methylquinoxalin-2(1H)-one

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.30 – 7.27 (m, 1H), 7.24 (dd, *J* = 8.3, 1.0 Hz, 1H), 5.58 – 5.53 (m, 1H), 3.70 (s, 3H), 2.11 – 2.03 (m, 2H), 1.98 –1.92 (m, 2H), 1.88 –1.85 (m, 2H), 1.66 –1.63 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.8, 151.3, 131.5, 131.4, 127.5, 126.7, 123.8, 113.5, 79.9, 38.8, 32.6, 29.4, 25.0, 24.0; HRMS (ESI): $C_{14}H_{18}N_2NaO_2$ $[M+Na]^+$ calculated: 267.1104, found: 267.1118.

(3ag) 3-(2-methoxyethoxy)-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.73 7.25 (m, 2H), 4.64 (t, *J* = 9.6 Hz, 2H), 3.85 (t, *J* = 10 Hz, 2H), 3.72 (s, 3H), 3.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 151.1, 131.8, 131.1, 127.7, 127.3, 124.1, 113.8, 70.3, 66.4, 59.3, 29.6; ATR-FTIR (cm^{-1}):2925, 1644, 1456, 1313, 1279, 1173, 1077, 732; HRMS (ESI): $C_{12}H_{14}N_2NaO_3$ $[M+Na]^+$ calculated: 257.0897, found: 257.0894.

(3ah) 1-methyl-3-(2,2,2-trifluoroethoxy)quinoxalin-2(1H)-one

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.36 – 7.32 (m, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 4.90 (q, *J* = 8.3 Hz, 2H), 3.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 150.2, 132.1, 130.0, 128.2, 127.9, 124.2, 123.1 (q, J_F = 276 Hz), 113.8, 62.8 (q, J_F = 37 Hz), 29.6; HRMS (ESI): $C_{11}H_9F_3N_2NaO_2$ $[M+Na]^+$ calculated: 281.0508, found: 281.0537.

(3ai) 3-(but-3-en-1-yloxy)-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 1H), 7.32 – 7.24 (m, 2H), 5.97 (ddt, *J* = 17.1, 10.3, 6.8 Hz, 1H), 5.19 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.11 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.53 (t, *J* = 7.1 Hz, 2H), 3.72 (s, 3H), 2.66 (q, *J* = 7.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 151.1, 134.0, 131.6, 131.1, 127.6, 127.0, 123.9, 117.3, 113.6, 66.6, 32.9, 29.5; HRMS (ESI): $C_{13}H_{14}N_2NaO_2$ $[M+Na]^+$ calculated: 253.0947, found: 253.0948.

(3ba) 1-Ethyl-3-isopropoxyquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.42 – 7.36 (m, 1H), 7.31 – 7.27 (m, 2H), 5.48 (hept, *J* = 6.2 Hz, 1H), 4.34 (q, *J* = 7.2 Hz, 2H), 1.47 (d, *J* = 6.2 Hz, 6H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 150.8, 131.7, 130.3, 127.7, 126.7, 123.6, 113.4, 70.4, 37.6, 21.6 (2C), 12.4; ATR-FTIR (cm^{-1}):2979, 1670, 1489, 1470, 1314, 1262, 1125; HRMS (ESI): $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ calculated: 255.1104, found: 255.1126.

(3bb) 3-Ethoxy-1-ethylquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 1H), 7.44 – 7.37 (m, 1H), 7.32 – 7.25 (m, 2H), 4.55 (q, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.51 (t, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 150.7, 131.6, 130.4, 127.8, 126.9, 123.7, 113.5, 63.5, 37.6, 14.2, 12.4; HRMS (ESI): $C_{12}H_{14}N_2NaO_2$ $[M+Na]^+$ calculated: 241.0947, found: 241.0965.

(3bc) 3-Butoxy-1-ethylquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.42 – 7.37 (m, 1H), 7.31 – 7.26 (m, 2H), 4.47 (t, *J* = 6.8 Hz, 2H), 4.34 (q, *J* = 7.2 Hz, 2H), 1.92 – 1.85 (m, 2H), 1.58 – 1.48 (m, 2H), 1.38 (t, *J* = 7.2 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 150.6, 131.6, 130.4, 127.8, 126.9, 123.7, 113.5, 67.4, 37.6, 30.6, 19.2, 13.9, 12.4; ATR-FTIR (cm^{-1}): 2959, 1671, 1470, 1376, 1220, 1125, 1063, 753; HRMS (ESI): $C_{14}H_{18}N_2NaO_2$ $[M+Na]^+$ calculated: 269.1260, found: 269.1278.

(3bd) 1-Ethyl-3-isobutoxyquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.34 – 7.29 (m, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.23 (d, *J* = 6.8 Hz, 2H), 1.40 (t, *J* = 7.2 Hz,

3H), 1.06 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 150.9, 131.8, 130.0, 127.8, 127.0, 124.1, 113.6, 73.8, 37.9, 27.6, 19.3 (2C), 12.4; ATR-FTIR (cm^{-1}):2925, 1698, 1434, 1392, 1259, 1163, 1087; HRMS (ESI): $C_{14}H_{18}N_2NaO_2$ $[M+Na]^+$ calculated: 269.1260, found: 269.1279.

(3ca) 3-isopropoxyquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.23 (s, 1H), 7.60 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.42 – 7.38 (m, 1H), 7.37 – 7.27 (m, 2H), 5.53 (hept, *J* = 6.2 Hz, 1H), 1.50 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7, 153.0, 131.5, 129.0, 126.8, 126.6, 124.3, 115.8, 70.8, 21.6 (2C); ATR-FTIR (cm^{-1}):2975, 1678, 1460, 1383, 1232, 1109; HRMS (ESI): $C_{11}H_{12}N_2NaO_2$ $[M+Na]^+$calculated: 227.0791, found: 227.0812.

(3cc) 3-butoxyquinoxalin-2(1*H*)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.37 (br, 1H), 7.46 – 7.38 (m, 1H), 7.38 – 7.32 (m, 1H), 7.30 (d, *J* = 6.9 Hz, 1H), 4.53 (t, *J* = 6.6 Hz, 2H), 1.97 – 1.84 (m, 2H), 1.60 – 1.53 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 152.8, 131.4, 129.2, 127.0, 126.6, 124.4, 115.9, 67.6, 30.6, 19.3, 13.9; HRMS (ESI): $C_{12}H_{14}N_2NaO_2$ $[M+Na]^+$ calculated: 241.0947, found: 241.0961.

(3ce) 3-(isopentyloxy)quinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.34 (s, 1H), 7.62 (d, *J* = 7. 7 Hz, 1H), 7.48 – 7.28 (m, 3H), 4.55 (t, *J* = 6.6 Hz, 2H), 1. 90 – 1.79 (m, 3H), 1.00 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.4, 152.8, 131.4, 129.2, 127.0, 126.6, 1 24.5, 115.9, 66.4, 37.2, 25.1, 22.6 (2C); ATR-FTIR (cm^{-1}): 2959, 1671, 1495, 1379, 1321, 1272, 1123, 1050; HRMS (ESI): $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ calculated: 255.1104, found: 255.1130.

(3db) 1-benzyl-3-ethoxyquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.34 – 7.17 (m, 8H), 5.52 (s, 2H), 4.58 (q, *J* = 7.1 Hz, 2H), 1.53 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 151.4, 135.2, 131.5, 130.8, 128.9 (2C), 127.7, 127.6, 127.0 (2C), 126.9, 123.9, 114.5, 63.6, 46.2, 14.2; HRMS (ESI): $C_{17}H_{17}N_2O_2$ $[M+H]^+$ calculated: 281.1285, found: 281.1304.

(3eb) 3-ethoxy-1-phenethylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.34 (d, *J* = 4.8 Hz, 4H), 7.32 – 7.27 (m, 3H), 4.55 (q, *J* = 7.1 Hz, 2H), 4.50 – 4.41 (m, 2H), 3.07 – 3.01 (m, 2H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 150.9, 137.9, 131.7, 130.6, 128.9 (2C), 128.9 (2C), 128.0, 127.1, 127.0, 124.0, 113.5, 63.6, 44.1, 33.4, 14.3; ATR-FTIR (cm^{-1}): 2975, 1667, 1609, 1491, 1339, 1237, 1128, 745, 702; HRMS (ESI): $C_{18}H_{19}N_2O_2$ $[M+H]^+$ calculated: 295.1441, found: 295.1443.

(3fb) tert-butyl 2-(3-ethoxy-2-oxoquinoxalin-1(2H)-yl)acetate

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.29 (d, *J* = 7.0 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 4.95 (s, 2H), 4.55 (q, *J* = 7.1 Hz, 2H), 1.50 (t, *J* = 7.1 Hz, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 153.7, 150.9, 131.2, 130.8, 127.8, 127.0, 124.1, 113.1, 83.1, 63.6, 44.5, 28.0 (3C), 14.2; HRMS (ESI): $C_{16}H_{20}N_2NaO_4$ $[M+Na]^+$ calculated: 327.1315, found: 327.1341.

(3gb) 3-ethoxy-1-(prop-2-yn-1-yl)quinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.42 (m, 2H), 7.32 (ddd, *J* = 8.3, 6.2, 2.4 Hz, 1H), 5.07 (d, *J* = 2.4 Hz, 2H), 4.55 (q, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 2.5 Hz, 1H), 1.50 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.9, 149.9, 131.0, 130.4, 127.5, 127.4, 124.5, 115.3, 78.4, 75.6, 63.5, 32.0, 14.5; HRMS (ESI): $C_{13}H_{12}N_2NaO_2$ $[M+Na]^+$ calculated: 251.0791, found:251.0807.

(3hb) 3-ethoxy-1-octylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 1H), 7.42 – 7.35 (m, 1H), 7.30 – 7.24 (m, 2H), 4.53 (q, *J* = 7.1 Hz, 2H), 4.26 (t, *J* = 7.6 Hz, 2H), 1.75 (quint, *J* = 7.6 Hz, 2H), 1.50 (t, *J* = 7.1 Hz, 3H), 1.40 – 1.20 (m, 10H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 150.9, 131.6, 130.7, 127.8, 126.8, 123.7, 113.7, 63.4, 42.6, 31.8, 29.3, 29.2, 27.2, 26.9, 22.6, 14.2, 14.1; ATR-FTIR (cm^{-1}): 2927, 2855, 1674, 1610, 1470, 1369, 1277, 1126, 1061, 752; HRMS (ESI): $C_{18}H_{27}N_2O_2$ $[M+H]^+$ calculated: 303.2067, found:303.2061.

(3ib) 7-bromo-3-ethoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 2.1 Hz, 1H), 7.49 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 4.54 (q, *J* = 7.0 Hz, 2H), 3.69 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.5, 150.9, 132.4, 130.7, 130.0, 129.6, 116.5, 114.9, 63.8, 29.6, 14.1; HRMS (ESI): $C_{11}H_{11}BrN_2NaO_2$ $[M+Na]^+$ calculated: 304.9896, found: 304.9919.

(3jb) 6-bromo-3-ethoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.44 (m, 1H), 7.40 – 7.36 (m, 2H), 4.52 (q, *J* = 7.1 Hz, 2H), 3.68 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 150.9, 132.7, 130.3, 128.8, 127.1, 120.3, 116.7, 63.8, 29.7, 14.2; HRMS (ESI): $C_{11}H_{11}BrN_2NaO_2$ $[M+Na]^+$ calculated: 304.9896, found: 304.9887.

(3kb) 6,7-dichloro-3-ethoxy-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.32 (s, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 3.67 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 150.6, 131.0, 130.6, 130.5, 128.3, 127.5, 115.0, 64.0, 29.8, 14.1; HRMS (ESI): $C_{11}H_{10}Cl_2N_2NaO_2$ $[M+Na]^+$ calculated: 295.0012, found: 295.0028.

(3lb) 3-ethoxy-1-methyl-6-nitroquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1H), 8.2 6 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.36 (d, *J* = 9.1 Hz, 1H), 4.59 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 1.52 (t, *J* = 7.1 Hz, 3H); ^{13} C NMR (151 MHz, $CDCl_3$) δ 155.1, 150.8, 143.8, 136.3, 1 31.1, 123.0, 121.7, 114.0, 64.4, 30.1, 14.l; HRMS (ESI): C $_{11}H_{12}N_3O_4$ $[M+H]^+$ calculated: 250.0822, found: 250.0816.

(3mb) 3-ethoxy-1,6,7-trimethylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.01 (s, 1H), 4.51 (q, *J* = 7.1 Hz, 2H), 3.69 (s, 3H), 2.38 (s, 3H), 2.32 (s, 3H), 1.49 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 151.2, 136.1, 132.6, 129.4, 129.2, 127.8, 114.3, 63.2, 29.4, 20.2, 19.2, 14.2; HRMS (ESI): $C_{13}H_{16}N_2NaO_2$ $[M+Na]^+$ calculated: 255.1104, found: 255.1101.

(3nb) 3-ethoxy-6-fluoro-1-methylquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.22 – 7.18 (m, 1H), 7.16 – 7.11 (m, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 1.50 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1 (d, *J* = 242.7 Hz), 154.8

(s), 150.8 (s), 132.2 (d, *J* = 11.9 Hz), 128.2 (d, *J* = 2.3 Hz), 114.5 (d, *J* = 9.2 Hz), 114.2 (d, *J* = 23.8 Hz), 113.4 (d, *J* = 23.1 Hz), 63.8 (s), 29.7 (d, *J* = 5.3 Hz), 14.1 (s); ATR-FTIR (cm^{-1}): 2965, 1669, 1619, 1576, 1458, 1372, 1275, 1119, 1078; HRMS (ESI): $C_{11}H_{11}FN_2NaO_2$ $[M+Na]^+$ calculated: 245.0697, found: 245.0693.

(3ob) 3-ethoxy-1-methyl-6-(trifluoromethyl)quinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.47 (m, 2H), 4.60 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 1.53 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 150.9, 133.6, 131.6, , 128.7 (q, *J* = 33.0 Hz), 128.0, 123.9 (q, *J* = 273.2 Hz), 120.5 (q, *J* = 3.7 Hz), 111.0 (q, *J* = 4.1 Hz) , 64.1, 29.7, 14.1; HRMS (ESI): $C_{12}H_{12}F_3$ N_2O_2 $[M+H]^+$ calculated: 273.0845, found: 273.0840.

(3pb) 8-chloro-3-ethoxy-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 1H), 7.31 – 7.27 (m, 1H), 7.21 – 7.09 (m, 1H), 4.65 – 4.59 (m, 2H), 3.72 – 3.71 (m, 3H), 1.55 – 1.51 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.8, 150.8, 132.8, 132.0, 128.1, 126.7, 124.7, 112.4, 64.1, 29.9, 14.0; ATR-FTIR (cm^{-1}): 2979, 2357, 1663, 1605, 1466, 1370, 1275, 1134, 1014, 785; HRMS (ESI): $C_{11}H_{12}ClN_2O_2$ $[M+H]^+$ calculated: 239.0582, found: 239.0581; HRMS (ESI): $C_{11}H_{12}ClN_2O_2$ $[M+Na]^+$ calculated: 261.0401, found: 261.0405.

(3qb) 8-bromo-3-ethoxy-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.25 – 7.18 (m, 2H), 4.63 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 3H), 1.53 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 150.9, 132.6, 129.2, 128.0, 127.2, 122.8, 113.1, 64.3, 29.9, 14.0; ATR-FTIR (cm^{-1}): 2922, 1622, 1464, 1368, 1273, 1204, 1131, 1051; HRMS (ESI): $C_{11}H_{12}BrN_2O_2$ $[M+H]^+$ calculated: 283.0077, found, 283.0075.

(3rb) 3-ethoxy-6-methoxy-1-methylquinoxalin-2(1H)-one

(3rb') 3-ethoxy-7-methoxy-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 9.1 Hz, 1H), 7.13 – 6.66 (m, 2H), 4.56 – 4.47 (m, 2H), 3.89 – 3.87 (m, 3H), 3.69 – 3.67 (m, 3H), 1.52 – 1.47 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 156.3, 154.4, 152.2, 151.4, 150.7, 132.6, 132.1, 128.4, 125.6, 125.4, 115.2, 114.4, 110.2, 110.0, 98.7, 63.5, 63.1, 55.7, 55.7, 29.6, 29.5, 14.2, 14.2; ATR-FTIR (cm^{-1}): 2963, 2363, 1670, 1598, 1466, 1303, 1261, 1096, 1027, 802; HRMS (ESI): $C_{12}H_{15}N_2O_3$ $[M+H]^+$ calculated: 235.1077, found: 235.1077; HRMS (ESI): $C_{12}H_{15}N_2O_3$ $[M+Na]^+$ calculated: 257.0879, found, 257.0884.

(3sb) 3-ethoxy-6,7-difluoro-1-methylpyrazino[2,3-b]pyrazin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 1H), 7.09 – 7.05 (m, 1H), 4.53 (q, *J* = 7.0 Hz, 2H), 3.68 (s, 3H), 1.50 (t, *J* = 7.1 Hz, 3H);^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1 (d, *J* = 2.2 Hz), 150.7 (s), 149.2 (dd, *J* = 227.9, 14.0 Hz), 146.7 (dd, *J* = 224.8, 14.0 Hz), 128.2 (dd, *J* = 8.4, 2.2 Hz), 127.5 (dd, *J* = 9.8, 2.9 Hz), 115.3 (dd, *J* = 18.7, 1.4 Hz), 102.4 (d, *J* = 23.2 Hz), 63.8 (s), 30.0 (s), 14.1 (s); ATR-FTIR (cm^{-1}): 2965, 1667, 1611, 1516, 1445, 1384, 1285, 1108, 0.38, 798; HRMS (ESI): $C_{11}H_{11}F_2N_2O_2$ $[M+H]^+$ calculated:241.0783, found:241.0787.

(3tb) methyl 2-ethoxy-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate

^1H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.93 (m, 2H), 7.63 (d, *J* = 8.7 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 3.97 (s, 3H), 3.76 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 155.2, 151.0, 134.7, 131.3, 128.1, 127.4, 124.9, 115.3, 64.0, 52.5, 29.7, 14.1; ATR-FTIR (cm^{-1}): 2922, 1677, 1591, 1456, 1313, 1234, 1114, 1048, 768; HRMS (ESI): $C_{13}H_{15}N_2$ O_4 $[M+H]^+$ calculated:263.1026, found: 263.1026.

(3ub) 2-ethoxy-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile

^1H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 1H), 7.58 – 7.51 (m, 2H), 4.58 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 150.7, 134.5, 132.0, 128.3, 127.2, 118.5, 117.7, 110.0, 64.4, 29.7, 14.1; ATR-FTIR (cm^{-1}): 2925, 2233, 1683, 1613, 1559, 1460, 1312, 1251, 1129, 1045; HRMS (ESI): $C_{12}H_{12}N_3O_2$ $[M+H]^+$ calculated:230.0924, found: 230.0921.

(5aa) 3-(Ethylthio)-1-methylquinoxalin-2(1*H*)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.37 – 7.35 (m, 1H), 7.33 – 7.31 (m, 1H), 3.71 (s, 3H), 3.19 (q, *J* = 7.4 Hz, 2H), 1.42 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 153.4, 133.6, 131.4, 128.3, 128.2, 123.8, 113.8, 29.3, 24.0, 13.8; ATR-FTIR (cm^{-1}): 2961, 1654, 1600, 1534, 1464. 1343, 1251, 1172, 1079, 755; HRMS (ESI): $C_{11}H_{12}N_2NaOS$ $[M+Na]^+$ calculated: 243.0563, found: 243.0589.

(5ab) 3-(isopropylthio)-1-methylquinoxalin-2(1H)-one

^1H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 8.3 Hz, 1H), 4.00 (hept, *J* = 6.8 Hz, 1H), 3.70 (s, 3H), 1.46 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.0, 153.3, 133.6, 131.3, 128.2, 128.1, 123.8, 113.7, 34.5, 29.3, 22.6 (2C); ATR-FTIR (cm^{-1}): 2985, 1646, 1466, 1384, 1175, 1080, 748; HRMS (ESI): $C_{12}H_{14}N_2NaOS$ $[M+Na]^+$ calculated: 257.0719, found : 257.0740.

(5ac) 3-(tert-butylthio)-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.27 – 7.25 (m, 1H), 3.68 (s, 3H), 1.68 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 153.4, 133.3, 131.3, 128.3, 128.2, 123.8, 113.8, 47.3, 29.7 (3C), 29.4; ATR-FTIR (cm^{-1}): 2954, 1655, 1530, 1466, 1364, 1166, 1077; HRMS (ESI): $C_{13}H_{16}N_2NaOS$ $[M+Na]^+$ calculated: 271.0876, found: 271.0863.

(5ad) 3-(cyclohexylthio)-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.34 – 7.27 (m, 1H), 7.26 – 7.24 (m, 1H), 3.91-3.85 (m, 1H), 3.67 (s, 3H), 2.13 – 2.11 (m, 2H), 1.82 – 1.79 (m, 2H), 1.66 – 1.34 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 153.3, 133.5, 131.3, 128.2, 128.0, 123.7, 113.7, 42.2, 32.5 (2C), 29.3, 26.0 (2C), 25.9; ATR-FTIR (cm^{-1}): 2923, 1647, 1599, 1466, 1313, 1269, 1175, 1079, 749; HRMS (ESI): $C_{15}H_{18}N_2NaOS$ $[M+Na]^+$ calculated: 297.1032, found: 297.1032.

(5ae) 3-(heptylthio)-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.32 – 7.26 (m, 2H), 3.69 (s, 3H), 3.16 (t, *J* = 7.0 Hz, 2H), 1.80 – 1.44 (m, 4H), 1.37 – 1.22 (m, 6H), 0.89 (t, *J* = 6.0 Hz,, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 153.4, 133.5, 131.4, 128.3, 128.1, 123.8,

113.8, 31.8, 29.7, 29.3, 29.1, 28.9, 28.6, 22.7, 14.2; ATR-FTIR (cm^{-1}): 2920, 1644, 1600, 1467, 1346, 1173, 1079, 750; HRMS (ESI): $C_{16}H_{22}N_2NaOS$ $[M+Na]^+$ calculated: 313.1345, found: 313.1336.

(5af) 1-methyl-3-(tetradecylthio)quinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 8.3 Hz, 1H), 7.34 – 7.28 (m, 2H), 3.71 (s, 3H), 3.17 (t, *J* = 7.4 Hz, 2H), 1.75 (quint, *J* = 7.4 Hz, 2H), 1.48 (quint, *J* = 6.8 Hz, 2H), 1.36 – 1.23 (m, 20H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 153.4, 133.5, 131.4, 128.3, 128.1, 123.8, 113.7, 31.9, 29.7, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 28.6, 22.7, 14.1; ATR-FTIR (cm^{-1}): 2917, 1643, 1599, 1469, 1345, 1173, 1078, 749; HRMS (ESI): $C_{23}H_{37}N_2OS$ $[M+H]^+$ calculated: 389.2621, found: 389.2622.

(5ag) 1-methyl-3-(phenethylthio)quinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 1H), 7.35 – 7.32 (m, 5H), 7.28 – 7.22 (m, 2H), 3.67 (s, 3H), 3.40 (t, *J* = 8.0 Hz, 2H), 3.05 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 153.4, 140.6, 133.5, 131.4, 128.7 (2C), 128.6 (2C), 128.3 (2C), 126.5, 123.9, 113.8, 35.2, 31.1, 29.3; ATR-FTIR (cm^{-1}): 2925, 1644, 1580, 1460, 1346, 1279, 1174, 1077, 754; HRMS (ESI): $C_{17}H_{16}N_2NaOS$ $[M+Na]^+$ calculated: 319.0876. found: 319.0882.

(5ah) ethyl 2-((4-methyl-3-oxo-3,4-dihydroquinoxalin-2-yl)thio)acetate

^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.33 – 7.27 (m, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 2H), 3.68 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 158.4, 153.1, 133.2, 131.6, 128.7, 128.3, 124.0, 113.9, 61.7, 32.5, 29.3, 14.3; ATR-FTIR (cm^{-1}): 2972, 1644, 1598, 1463, 1383, 1306, 1159, 1095, 755; HRMS (ESI): $C_{13}H_{14}N_2NaO_3S$ $[M+Na]^+$ calculated: 301.0617, found: 301.0620.

(5ai) 3-((3-mercaptopropyl)thio)-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.37 – 7.28 (m, 2H), 3.72 (s, 3H), 3.31 (t, *J* = 7.0 Hz, 2H), 2.71 (q, *J* = 7.1 Hz, 2H), 2.08 (quint, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 153.4, 133.4, 131.4, 128.4, 128.3, 123.9, 113.8, 32.8, 29.3, 27.8, 23.7; ATR-FTIR (cm^{-1}): 2923, 1640, 1598, 1463, 1315, 1173, 1079, 753; HRMS (ESI): $C_{12}H_{14}N_2NaOS_2$ $[M+Na]^+$ calculated: 289.0440, found: 289.0454.

(5aj) 3-(allylthio)-1-methylquinoxalin-2(1H)-one

^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.36 – 7.29 (m, 2H), 6.05 – 5.94 (m, 1H), 5.41 – 5.15 (m, 2H), 3.85 (d, *J* = 6.9 Hz, 2H), 3.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 153.3, 133.4, 133.0, 131.5, 128.4 (2C), 123.9, 118.2, 113.8, 32.5, 29.3; ATR-FTIR (cm^{-1}): 2921, 1638, 1600, 1535, 1464, 1344, 1173, 1079, 969, 754; HRMS (ESI): $C_{12}H_{12}N_2NaOS$ $[M+Na]^+$ calculated: 255.0563, found: 255.0565.

(5bk) 3-(propylthio)-6-(trifluoromethyl)quinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.59 – 7.58 (m, 2H), 3.16 (t, *J* = 7.2 Hz, 2H), 1.79 – 1.70(m, 2H), 1.06 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.5, 153.2, 134.5, 130.7, 128.3, 128.0 (q, *J* = 32.1 Hz), 124.3 (q, *J* = 272.2 Hz), 120.1 (q, *J* = 3.5 Hz), 113.2 (q, *J* = 4.1 Hz), 31.2, 21.9, 13.9; ATR-FTIR (cm^{-1}): 2920, 1679, 1523, 1458, 1349, 1228, 1127, 1079; HRMS (ESI): $C_{12}H_{11}F_3N_2OS$ $[M+H]^+$ calculated:289.0617, found:289.0612.

(5ck) 3-(propylthio)-7-(trifluoromethyl)quinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.76 (s, 1H), 7.92 (s, 1H), 7.74 – 7.72 (m, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 3.12 (t, *J* = 7.2 Hz, 2H), 1.76 – 1.66 (m, 2H), 1.02 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 163.2, 153.4, 133.4, 132.0, 124.8 (q, *J* = 3.6 Hz), 124.5 (q, *J* = 272.7 Hz), 124.2 (q, *J* = 32.6 Hz), 124.2 (q, *J* = 3.9 Hz),117.2, 31.1, 22.0, 13.9; ATR-FTIR (cm^{-1}): 2921, 1684, 1624, 1459, 1326, 1123, 1064; HRMS (ESI): $C_{12}H_{11}F_3N_2OS$ $[M+H]^+$calculated: 289.0617, found:289.0621.

(5dc) 3-(tert-butylthio)-6,7-dichloroquinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.55 (s, 1H), 7.91 (s, 1H), 7.40 (s, 1H), 1.61 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.6, 152.8, 131.8, 130.3, 130.1, 128.1, 125.6, 117.0, 47.5, 29.7(3C); ATR-FTIR (cm^{-1}): 2957, 1667, 1541, 1457, 1165, 1067; HRMS (ESI): $C_{12}H_{12}Cl_2N_2NaOS$ $[M+Na]^+$ calculated: 324.9940, found: 324.9944.

(5ek) 2-oxo-3-(propylthio)-1,2-dihydroquinoxaline-6-carbonitrile

^1H NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 7.78 (d, *J* = 8.3 Hz, 1H), 7.66 – 7.64 (m, 1H), 7.60 (d, *J* = 1.7 Hz, 1H), 3.13 (t, *J* = 7.2 Hz, 2H), 1.76 – 1.67 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.2, 153.1, 134.9, 130.9, 128.3, 126.9, 120.1, 118.9, 110.0, 31.2, 21.9, 13.9; ATR-FTIR (cm^{-1}): 2958, 2226, 1673, 1525, 1455, 1383, 1234, 1136, 1077; HRMS (ESI): $C_{12}H_{11}N_3OS$ $[M+H]^+$ calculated: 246.0696, found:246.0699.

(5fc) 3-(tert-butylthio)-6,7-dimethylquinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.28 (s, 1H), 7.45 (s, 1H), 7.02 (s, 1H), 2.28 (s, 6H), 1.61 (s, 9H);^{13}C NMR (101 MHz, DMSO-d_6) δ 159.9, 153.3, 138.0, 132.4, 130.9, 128.0, 127.3, 116.0, 46.7, 29.8(3C), 20.1, 19.3; ATR-FTIR (cm^{-1}): 2920, 1651, 1526, 1450, 1361, 1164, 1073; HRMS (ESI): $C_{14}H_{19}N_2OS$ $[M+H]^+$ calculated: 263.1213, found:263.1204.

(5gc) 3-(tert-butylthio)-8-chloroquinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.00 (s, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.31 – 7.24 (m, 1H), 1.61 (s, 9H).^{13}C NMR (101 MHz, DMSO-d_6) δ 162.8, 153.6, 133.4, 128.7, 127.5, 126.4, 124.2, 119.0, 47.2, 29.7(3C); ATR-FTIR (cm^{-1}): 2961, 1662, 1527, 1458, 1384, 1065, 940, 724; HRMS (ESI): $C_{12}H_{13}ClN_2NaOS$ $[M+Na]^+$ calculated: 291.0329, found: 291.0322.

(5hc) 3-(tert-butylthio)-6,7-difluoroquinoxalin-2(1H)-one

^1H NMR (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), 7.72 – 7.68 (dd, *J* = 11.1, 8.2 Hz, 1H), 7.18– 7.13 (m , 1H), 1.59 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3 (d, *J* = 2.6 Hz), 152.8 (s), 149.4 (dd, *J* = 247.7, 14.6 Hz), 146.2 (dd, *J* = 242.2, 14.2 Hz), 128.7 (dd, *J* = 10.0, 2.4 Hz), 127.3 (d, *J* =9.1， 1.0 Hz), 115.0 (d, *J* = 18.5 Hz), 103.8 (d, *J* = 21.9 Hz), 47.2 (s), 29.7 (3C); ATR-FTIR (cm^{-1}): 2921, 1670, 1510, 1470, 1386, 1292, 1166, 1070, 756; HRMS

(ESI): $C_{12}H_{13}F_2N_2OS$ $[M+H]^+$ calculated: 271.0711, found: 271.0710.

(5ic) 3-(tert-butylthio)-7-fluoroquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 7.49 – 7.46 (m, 1H), 7.37 – 7.23 (m, 2H), 1.61 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.2 (s), 158.5 (d, J = 239.5 Hz), 152.9 (s), 132.6 (d, J = 11.8 Hz), 126.9 (d, J = 1.6 Hz), 117.3 (d, J = 9.4 Hz), 116.4 (d, J = 24.3 Hz), 112.5 (d, J = 22.8 Hz), 47.2 (s), 29.7(3C); ATR-FTIR (cm^{-1}): 2922, 1662, 1558, 1496, 1261, 1117, 1069; HRMS (ESI): $C_{12}H_{13}FN_2NaOS$ $[M+Na]^+$ calculated: 275.0625, found, 275.0617.

(5jc) 3-(tert-butylthio)-7-chloroquinoxalin-2(1H)-one

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.47 (s, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.30 – 7.22 (m, 2H), 1.60 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.0, 153.0, 132.5, 131.2, 131.1, 128.8, 123.9, 115.2, 47.1, 29.7(3C); ATR-FTIR (cm^{-1}): 2961, 1663, 1526, 1383, 1067, 934; HRMS (ESI): $C_{12}H_{13}ClN_2NaOS$ $[M+Na]^+$ calculated: 291.0329, found: 291.0322.

(5kc) methyl 3-(tert-butylthio)-2-oxo-1,2-dihydroquinoxaline-6-carboxylate

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.57 (s, 1H), 7.87 (d, J = 1.5 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.75 – 7.73 (m, 1H), 3.89 (s, 3H), 1.63 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.9, 164.6, 153.1, 134.9, 130.0, 128.9, 127.5, 124.2, 117.3, 52.9, 47.4, 29.6(3C); ATR-FTIR (cm^{-1}): 2923, 2359, 1725, 1661, 1531, 1454, 1384, 1220, 1130, 1064, 760; HRMS (ESI): $C_{14}H_{17}N_2O_3S$ $[M+H]^+$ calculated: 293.0954, found: 293.0951.

(6fb) 2-(3-ethoxy-2-oxoquinoxalin-1(2H)-yl)acetic acid

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.60 (d, J = 7.8 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.37 – 7.28 (m, 1H), 5.01 (s, 2H), 4.45 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.2, 153.8, 150.5, 131.4, 130.8, 127.6, 127.4, 124.3, 114.9, 63.4, 44.3, 14.5; HRMS (ESI): $C_{12}H_{12}N_2NaO_4$ $[M+Na]^+$ calculated: 271.0689, found: 271.0685.

Acknowledgements

We are grateful to the Natural Science Foundation of China (No. 21776254) for financial help.

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[25] During the revision of this manuscript, a closely related paper on visible-light-induced alkoxylation of quinoxalin-2(1H)-ones with alcohol appeared online: L. Zhao, L. Wang, Y. Gao, Z. Wang, P. Li, *Adv. Synth. Catal.* DOI: 10.1002/adsc.201900732

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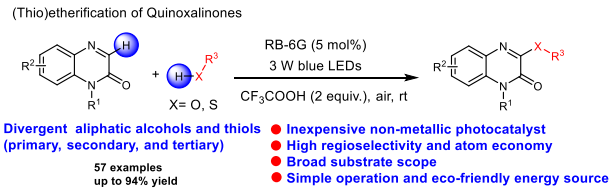
FULL PAPER

(Thio)etherification of Quinoxalinones under Visible-Light Photoredox Catalysis



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Jiadi Zhou,[a] Peng Zhou,[b] Tingting Zhao,[b] Quanlei Ren,[b] and Jianjun Li[a,b*]