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Iodine Catalyzed C-N bond Formation: Synthesis of 3-Aminoquinoxalinones Under Ambient Conditions

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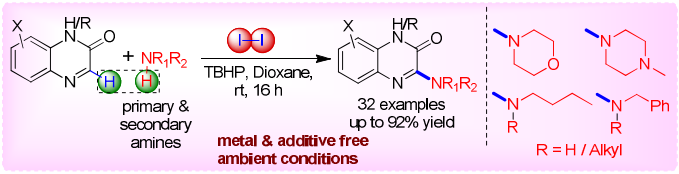
KEYWORDS: Metal-free, C-H activation, Quinoxalinone, Iodine, Ambient Condition

ABSTRACT

A metal-free cross-dehydrogenative coupling between quinoxalinones (sp^2 C-H) and amines (N-H) in presence of catalytic iodine is reported. The reaction yields 3-aminoquinoxalinones in moderate to high yields under ambient conditions in dioxane as solvent, and aqueous *tert*-butyl hydroperoxide (aq. TBHP) as the terminal oxidant. The reaction is highly versatile, and exhibits good functional group tolerance with a range of primary and secondary amines. It provides a practical access to pharmaceutically active 3-aminoquinoxalinone derivatives. Preliminary mechanistic studies reveal *in-situ* iodination of the amine as the putative mode of activation.



INTRODUCTION

Substituted quinoxalin-2(1*H*)-ones represent an important class of fused heterocyclic compounds due to their diverse pharmacological properties,[1] and have been synthesized through diverse chemical routes.[1c,2] 3-Aminoquinoxalin-2(1*H*)-one, in particular, is an important sub-family known to possess potent biological activities such as antimicrobial,[3] antiviral,[4] antihypertensive,[5] anticancer,[6] antidiabetic,[7] and anti-inflammatory.[8] A wide variety of 3-aminoquinoxalinone derivatives have recently been explored for their therapeutic applications such as calcium

channel blockers,[5] aldose reductase inhibitors,[7a] modulators of PAS kinase,[7c] and histamine receptor antagonists[8c] (**Figure 1**).

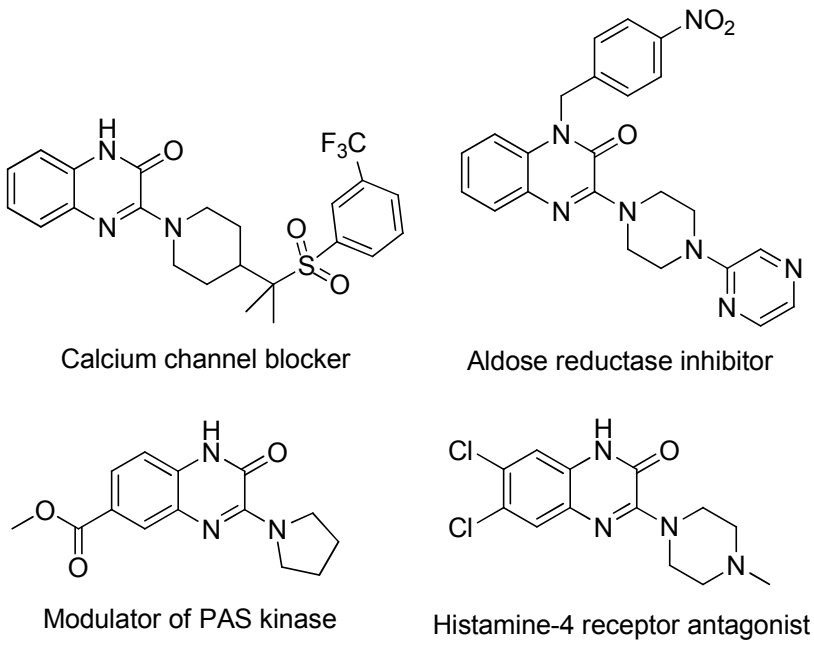
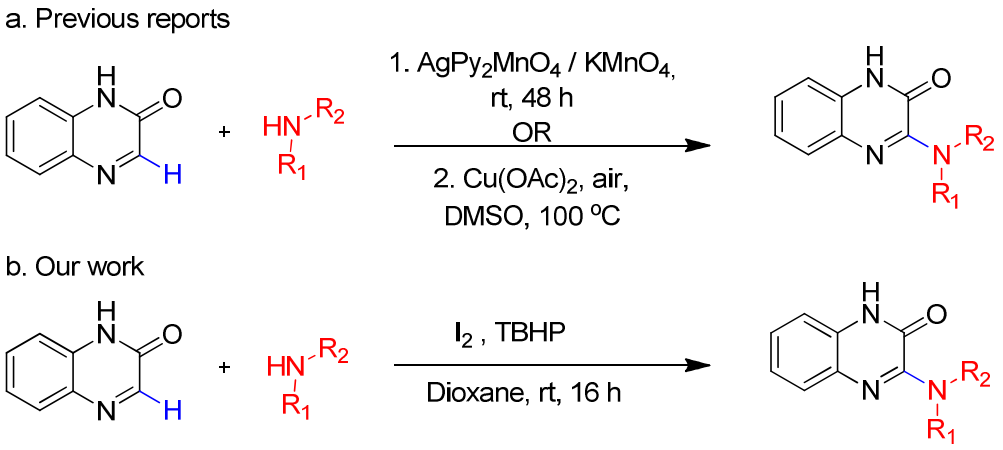


Figure 1. Pharmaceutically Active 3-Aminoquinoxalinones

In view of such pharmaceutical and therapeutic significance of 3-aminoquinoxalinones, several methods targeting their synthesis have been developed. Conventional methods involve construction of the heterocyclic ring, or functionalization of quinoxalinones *via* nucleophilic aromatic substitution (S_NAr) of a halo or other leaving group with an amine nucleophile.[7b,9] Both the strategies, however, suffer from limitations such as requirement of pre-functionalized starting materials, harsh reaction conditions, and low atom economy. More recent approaches for heteroarene amination rely on direct C-H functionalization using transition metal catalysts such as palladium, copper, cobalt, manganese, iridium, silver, iron, rhodium and ruthenium.[10] Though useful, direct C-H amination of quinoxalinones has only two reports (Scheme 1). Gulevskaya *et al*. reported the first oxidative alkylamination of quinoxalinone using an excess of strong oxidants such as $KMnO_4$ or $AgPy_2MnO_4$.[11] A more recent report by Cui *et al*. demonstrates a $Cu(OAc)_2$ catalysed direct amination of quinoxalinones in DMSO at 100 ºC.[12] While, the first one is challenged by the use of strong oxidant, low efficiency (15-68%), and hazardous by-products; the second employs metal catalyst and high temperatures, thus reducing the practical

applicability of these methods. Till date, a simple, mild, and efficient metal-free method for synthesizing 3-aminoquinoxalinones does not exist.

Scheme 1. Synthesis of 3-Aminoquinoxalinones by Direct C-H Amination

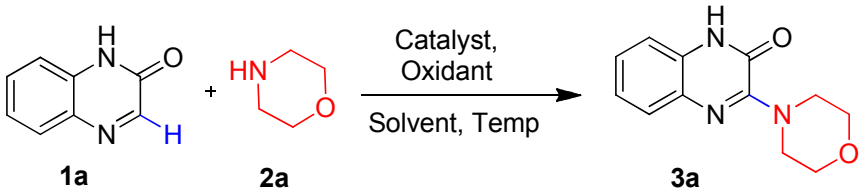


Of late, iodine assisted C-H bond activation has emerged as a useful method for heteroarene functionalization.[13] This has primarily been applied to benzoxazoles, which have been aminated using molecular iodine,[14] tetraalkylammonium iodide,[15] and *N*-iodosuccinimide.[16] However, unlike benzoxazoles, the C_3-H of quinoxalinone is far less reactive and challenging to functionalize. With an intention of developing a metal-free strategy for the synthesis of 3-aminoquinoxalinones, we embarked upon an iodine catalyzed oxidative C-H amination at room temperature with TBHP as the oxidant. To the best of our knowledge, there is no precedence of a direct C3-amination of quinoxalinones catalyzed by molecular iodine.

RESULTS AND DISCUSSION

We initiated our work with the reaction of quinoxalinone (**1a**) with morpholine (**2a**) in presence of iodine, TBHP and acetic acid in dioxane at room temperature for 12 h. Pleasantly as expected, the C-N cross-coupled product **3a**, was isolated albeit in low yield (55%, Table 1, entry 1).

Table 1. Optimization of Reaction Conditions[a]



1a **2a** **3a**

entry	catalyst (equiv)	oxidant (equiv)	temp (°C)	additive	solvent	yield (%)
1	iodine (0.5)	TBHP (1.5)	rt	AcOH	Dioxane	55
2	iodine (0.5)	TBHP (1.5)	60	AcOH	Dioxane	67
3	iodine (0.5)	TBHP (1.5)	120	AcOH	Dioxane	68
4	iodine (0.5)	TBHP (1.5)	120	TEA	Dioxane	68
5	iodine (0.5)	TBHP (1.5)	rt	--	Dioxane	86
6	iodine (0.5)	TBHP (2)	rt	--	Dioxane	95
7	iodine (0.1)	TBHP (2)	rt	--	Dioxane	95
8	iodine (0.05)	TBHP (2)	rt	--	Dioxane	95, 78[b]
9	KI (0.1)	TBHP (2)	rt	--	Dioxane	89
10	n-Bu_4NI (0.1)	TBHP (2)	rt		Dioxane	84
11	iodine (0.1)	$K_2S_2O_8$ (2)	rt	--	Dioxane	86
12	iodine (0.1)	H_2O_2 (2)	rt	--	Dioxane	NR
13	iodine (0.1)	O_2	rt	—	Dioxane	74
14	iodine (0.1)	air	rt	--	Dioxane	45
15	iodine (0.05)	TBHP (2)	rt	--	DMF	71[c]
16	iodine (0.05)	TBHP (2)	rt	--	DMSO	77[d]
17	--	TBHP (2)	rt	--	Dioxane	NR
18	iodine (0.05)	--	rt	--	Dioxane	6[e]

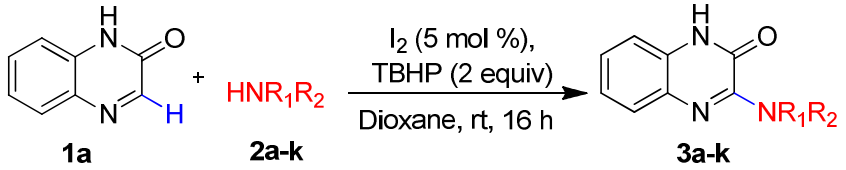
[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), catalyst, additive (1.0 mmol), oxidant in 1,4-dioxane (3.0 mL) stirred at room temperature for 16 h. % yields are HPLC yields. [b]Reaction time was 8h. [c]DMF was used as solvent. [d]DMSO was used as solvent. [e]Reaction performed under argon atmosphere.

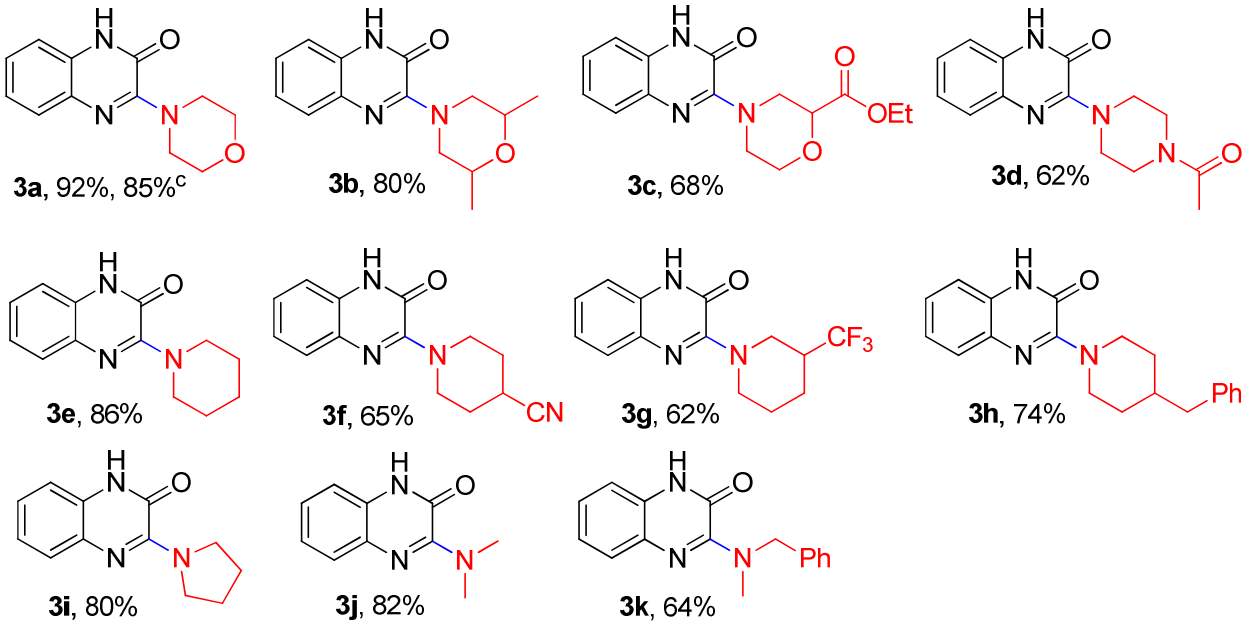
To improve the product yield, reaction optimization with respect to catalyst, oxidant, additive, temperature and solvent was performed (Table 1). Raising the temperature from room temperature to 60 ºC increased the yield from 55 to 67%, but increasing it further to 120 ºC had no influence (Table 1, entries 2 and 3). The reaction was not affected by replacing acetic acid

with triethyl amine, suggesting the additive to have no direct role (Table 1, entry 4). Notably, the product yield improved significantly in the absence of any additive (Table 1, entry 5). Further, increasing the amount of TBHP to 2.0 equiv facilitated the reaction, and furnished the product in 95% yield (Table 1, entry 6). Reducing the amount of iodine from 0.5 to 0.1 equiv (10 mol %) and further to 0.05 equiv (5 mol %) did not show any negative effect on the yield suggesting that iodine was required only in catalytic amounts (Table 1, entries 7 and 8). Screening of other iodine sources such as KI (yield 89%) and Bu_4NI (yield 84%) did not provide any edge over molecular iodine (Table 1, entries 9 and 10). Other oxidants such as $K_2S_2O_8$ and H_2O_2 were also tested, but TBHP was found to be the best (Table 1, entries 11 and 12). Notably, the reaction also worked in presence of oxygen as well as air as oxidant, though lower yields were obtained in either case (Table 1, entries 13 and 14). Changing to polar solvents like DMF and DMSO affected the reaction adversely, and the yields diminished (Table 1, entries 15 and 16). Control experiment in absence of iodine did not gave any product (Table 1, entry 17). The reaction in absence of TBHP under argon atmosphere resulted in significant drop in yield (6%, Table 1, entry 18). These results clearly indicated that both iodine and TBHP were essential for the C-N coupling, and the best conditions were found to be with 5 mol % iodine and 2 equiv TBHP in dioxane at room temperature for 16 h.

With the optimized condition in hand, the scope of amination on quinoxalinone was explored. A variety of secondary aliphatic amines ranging from cyclic to acyclic derivatives were tried, and the corresponding products were obtained in moderate to high yields (Table 2, **3a-3k**). In general, it was found that cyclic amines such as morpholine and piperidine substituted with electron withdrawing groups such as $COOCH_2CH_3$, $COCH_3$, CN, and CF_3 (**3c, 3d, 3f, 3g**) gave lower yields of the aminated products compared to the unsubstituted amines (**3a, 3e, 3i**) or those with electron releasing methyl or benzyl substituents (**3b, 3h**). This could be attributed to the reduced nucleophilicity at the reaction centre with electron withdrawing substituents. The scalability of the reaction was confirmed by carrying out a gram scale synthesis starting from 1 g of **1a**. The desired product **3a**, was obtained in 85% yield (1.34g) after of reaction time (Table 2).

Table 2. Substrate Scope with Secondary Amines[a,b]



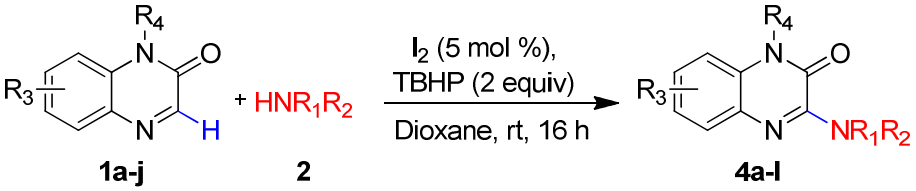


[a]Reaction conditions: **1a** (0.5 mmol), **2a-k** (0.75 mmol), iodine (0.025 mmol), TBHP (70 % aq. solution) (1.0 mmol) in 1,4-dioxane (3.0 mL) stirred at room temperature for 16 h. [b]% yields are isolated yields. [c]reaction carried out on gram scale with 1g of **1a**.

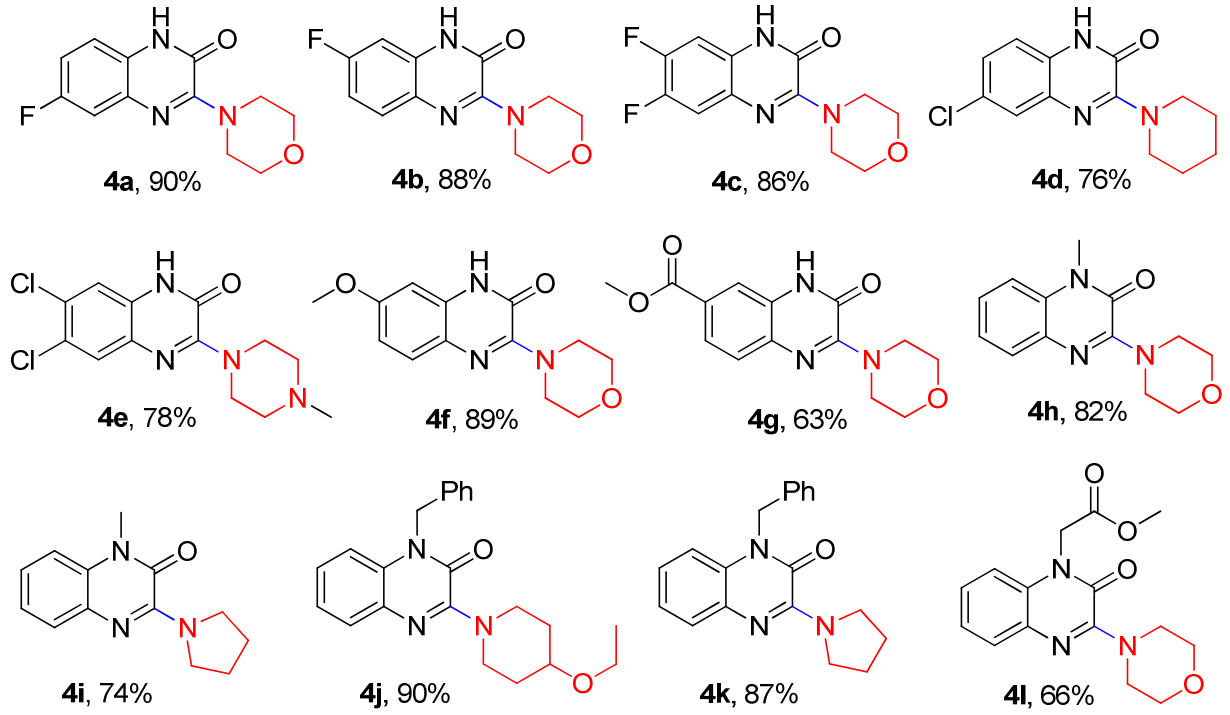
Next, we examined the versatility of this reaction with various quinoxalinones (Table 3). The influence of substituents in aryl ring of quinoxalinone was screened first. Quinoxalinones substituted with fluoro, chloro, methoxy and ester groups in the aryl ring were treated with secondary amines under the optimized conditions, and the desired products (**4a-4g**) were obtained in all the cases. The yields, however, varied from 63-90%, and were higher for quinoxalinones substituted with fluoro, chloro and methoxy compared to the ester functionality. The availability of halogen in the aryl ring provided a handle for functionalization. Further, to examine the compatibility with *N*-substituted quinoxalinones, the reaction was tried with *N*-methyl, *N*-benzyl and *N*-acetate protected derivatives. Pleasantly, as expected, the C-N coupled

products (**4h-4l**) were isolated in moderate to high yields suggesting no direct involvement of the amide hydrogen in the oxidative amination process.

Table 3. Scope with Substituted Quinoxalin-2(1*H*)-ones[a,b]



1a-j **2** **4a-l**

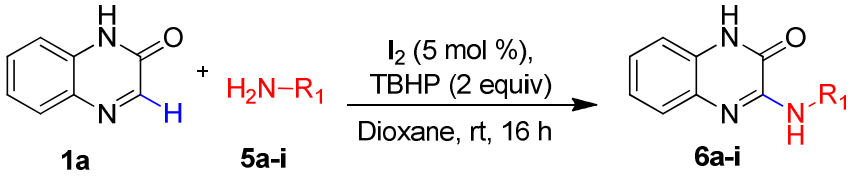


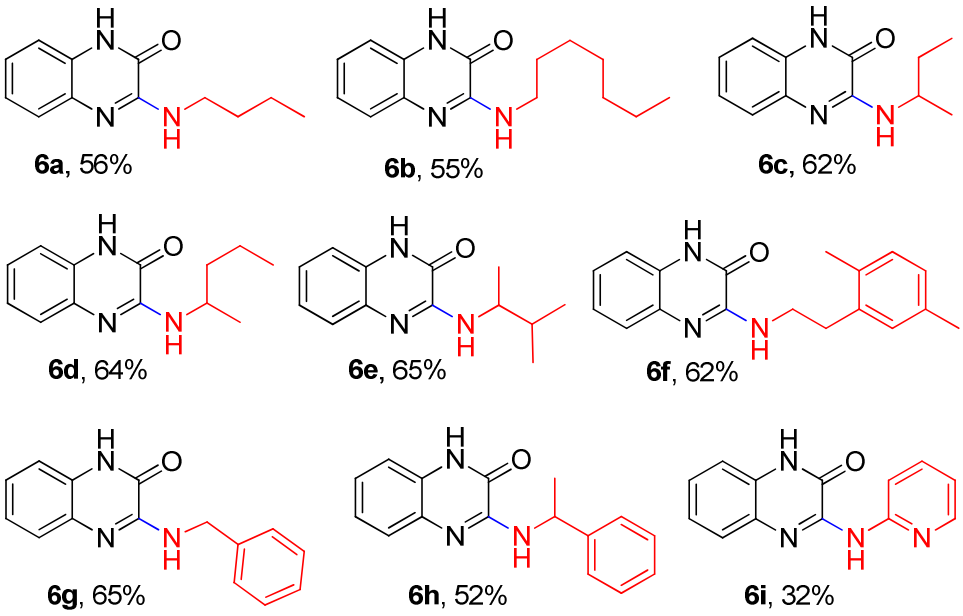
[a]Reaction conditions: **1** (0.5 mmol), **2** (0.75 mmol), iodine (0.025 mmol), TBHP (70 % aq. solution) (1.0 mmol) in 1,4-dioxane (3.0 mL) stirred at room temperature for 16 h. [b]% yields are isolated yields.

After successful demonstration of oxidative amination of quinoxalinones with secondary amines, it was explored with primary amines as substrates (Table 4). A range of primary aliphatic amines with varied alkyl chains were screened, and were found to give moderate yields of the corresponding 3-aminoquinoxalinones (**6a-6h**). The yields, in general, were lower compared to

secondary amines. The branched primary amines gave slightly better yields (**6c-6f**) than the linear primary amines (**6a, 6b**). The reaction was also compatible with primary benzyl amines, and gave the products **6g** and **6h** in 52 and 65% yields. Interestingly, 2-amino pyridine reacted with quinoxalinone, and gave the C-N coupled product (**6i**) in 32% yield. The lower reactivity of aryl amines could be attributed to the lower nucleophilicity of the reactive nitrogen.

Table 4. Substrate Scope with Primary Amines[a,b]



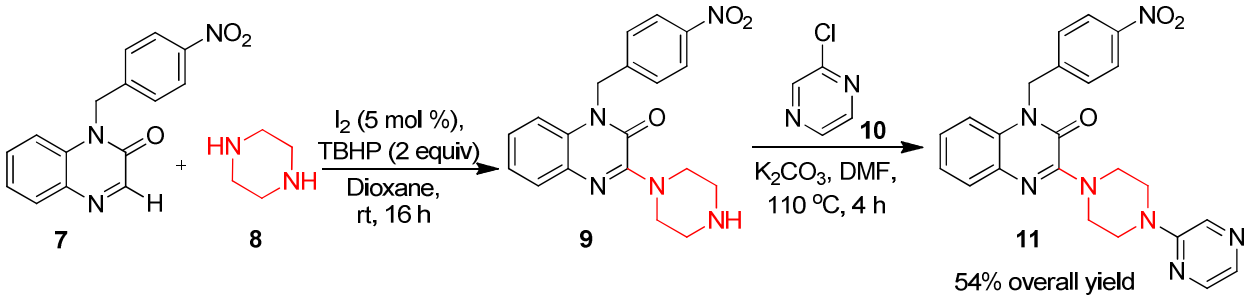


[a]Reaction conditions: **1a** (0.5 mmol), **5a-j** (0.75 mmol), iodine (0.025 mmol), TBHP (70 % aq. solution) (1.0 mmol) in 1,4-dioxane (3.0 mL) stirred at rt for 16 h. [b]%yields are isolated yields.

Next, to establish the synthetic utility of this methodology, we employed it for preparing an aldose reductase inhibitor **11** known to possess anti-diabetic activity.[7a] The synthesis involved a straightforward two-step process starting with 1-(4-nitrobenzyl)quinoxalin-2(1*H*)-one (**7**) as the

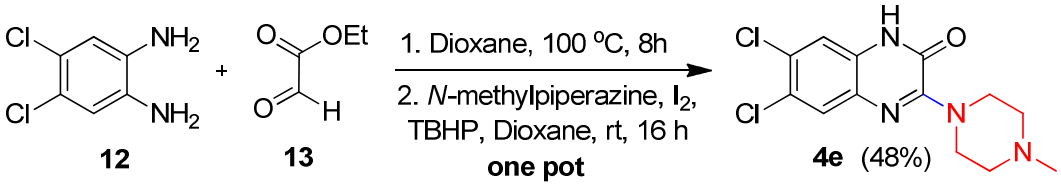
substrate. An initial iodine catalyzed direct C-H amination yielded **9** which on reaction with 2-chloropyrazine (**10**) furnished the desired product **11** with an overall yield of 54% (Scheme 2). The earlier report for its synthesis started from the 3-chloro derivative of **7**, which upon nucleophilic aromatic substitution with *N*-pyrazinopiperazine under basic conditions yielded **11**.[7a]

Scheme 2. Synthesis of Aldose Reductase Inhibitor



Notably, the feasibility of our methodology towards a sequential one-pot format was tested, and a direct synthesis of histamine-4 receptor antagonist **4e** starting from 1,2-diamino-4,5-dichlorobenzene (**12**) was successfully achieved (Scheme 3). The earlier reported method involved a ytterbium triflate catalyzed condensation of 1,2-diamino-4,5-dichlorobenzene **12** with methyl trimethoxy-acetate in toluene at 100 °C, followed by substitution of 3-methoxy group with *N*-methylpiperazine in toluene at 120 °C.[8c] Alternately, **4e** was also synthesized by lithium hydroxide mediated partial hydrolysis of intermediate 2,3,6,7-tetrachloroquinoxaline to 3,6,7-trichloroquinoxalin-2(1*H*)-one, followed by reaction with *N*-methylpiperazine.[9d]

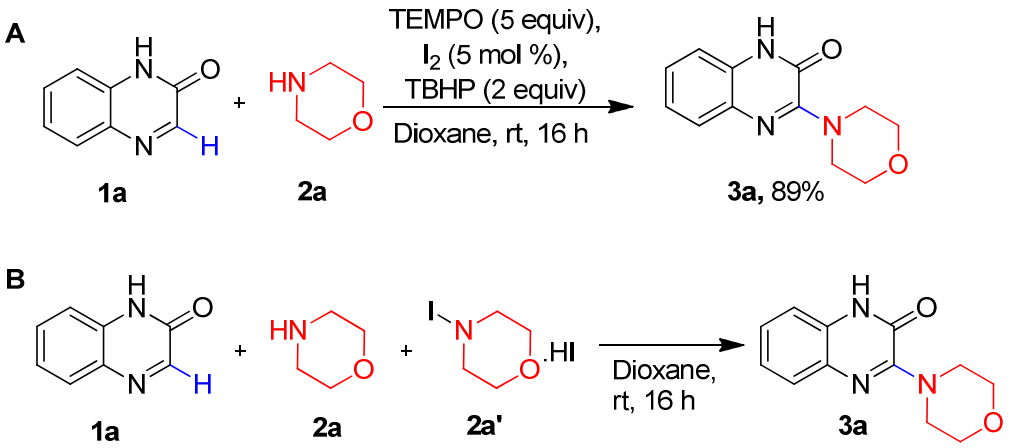
Scheme 3. Sequential One-pot Synthesis of Histamine-4 Receptor Antagonist



To understand the reaction mechanism, several control experiments were carried out. Addition of radical scavenger, TEMPO (2,2,6,6-tetramethyl piperidine-*N*-oxyl) to the standard reaction did not affect the product yield, and no TEMPO bound adduct was observed either suggesting that the reaction probably followed an ionic pathway (Scheme 4A). During the reaction optimization

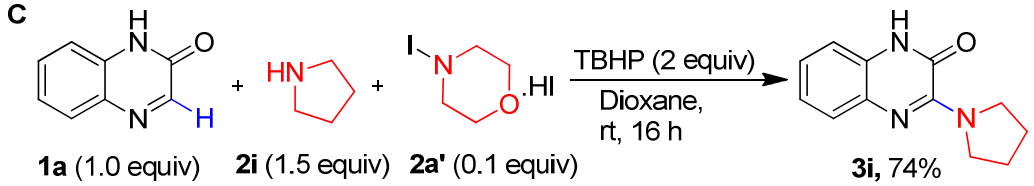
studies, it was noticed that both iodine and oxidant were essential for the reaction, and the product yield dropped significantly in absence of either of them. Based on this observation, we wanted to ascertain if *N*-iodomorpholine was the actual reactive species involved in the reaction.[9a] For this, a reaction of **1a** was carried out with preformed *N*-iodomorpholine hydroiodide (**2a'.HI**) in place of morpholine and iodine (Scheme 4B). Surprisingly, no product was formed and the starting material **1a** was recovered completely (Scheme 4B, entry 1). We modified the conditions, and treated **1a** and **2a** in presence of catalytic amount of **2a'** (10 mol %) under air atmosphere. Interestingly, we got the desired product **3a** in 46% yield (Scheme 4B, entry 2). Further, on adding TBHP to this reaction, the yield increased to 92% (Scheme 4B, entry 3). Furthermore, the reaction of **1a** and **2i** in presence of catalytic amount of **2a'** gave the desired product **3i** in 74% yield (Scheme 4C). This suggested that stoichiometric amount of free amine was crucial for the reaction, and **2a'** was required only in catalytic amounts to affect the transformation. However, with stoichiometric amount of **2a'** in absence of TBHP, a mixture of **3i** and **3a** was formed in 56 and 24% yields respectively as determined by HPLC analysis (Scheme 4D). This indicated that during the reaction, **2a** was being generated from **2a'**, and competed with **2i** to yield **3a**. The putative formation of reactive *N*-iodomorpholine species was also probed by taking the ^{1}HNMR of the reaction mixture after 4 h of reaction time. As shown in Figure 2, appearance of new peaks at 3.75 ppm indicated formation of **2a'**.

Scheme 4. Mechanistic Studies (A) Reaction in Presence of TEMPO (B) Reactions with *N*-iodomorpholine hydroiodide (2a') (C) Cross-over Experiment

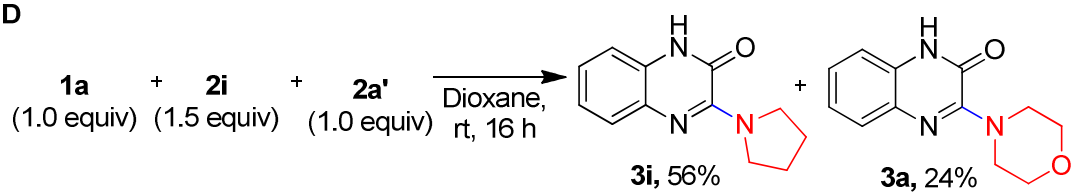


Entry	**1a** (equiv)	**2a** (equiv)	**2a'** (equiv)	TBHP (equiv)	**3a** (%yield)
1	1.0	0	1.0	2.0	0
2	1.0	1.5	0.1	0	46
3	1.0	1.5	0.1	2.0	92

C



D



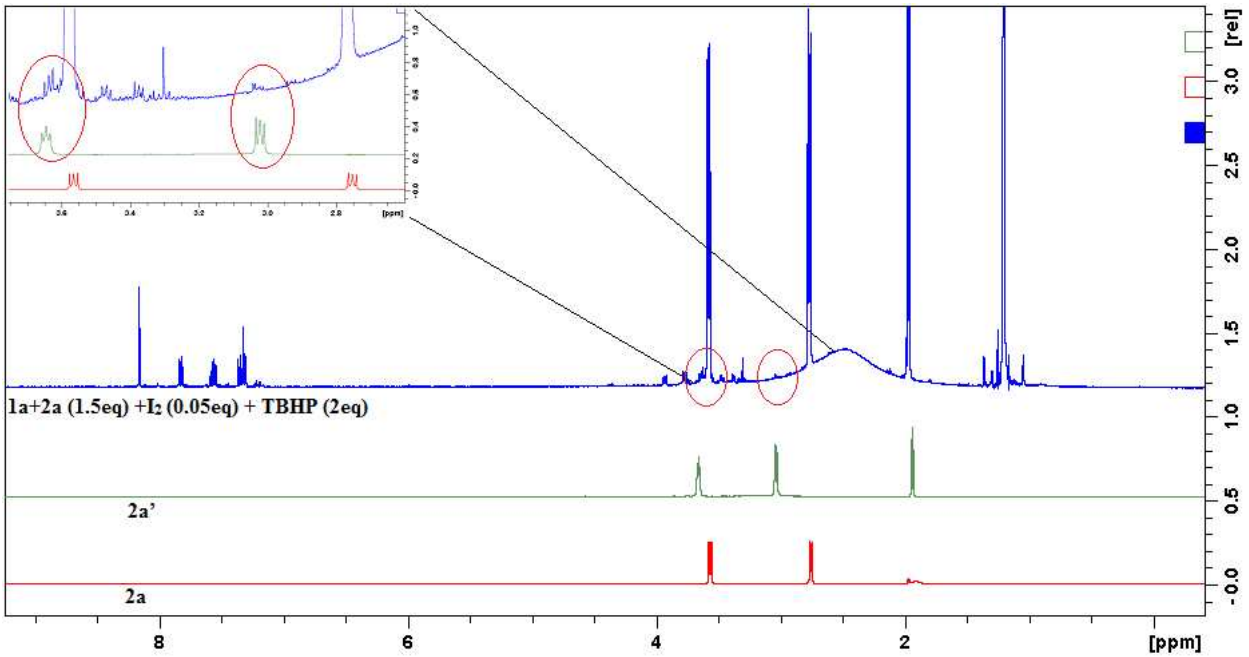


Figure 2. Evidence for *in-situ* Generation of 2a' by ^{1}HNMR

Based on the experimental findings and ^{1}H NMR study, a mechanism is proposed in Figure 3. We believe that initially, iodine reacts with amine (**2**) and generates the reactive *N*-iodoamine species (**2'**),[14a] which coordinates with quinoxalinone N4 and polarizes the C3-N4 double bond

(**14**). This is followed by nucleophilic attack of amine on C-3 to generate **15** which undergoes elimination of HI to furnish the product **3.** Further, HI is oxidized by TBHP to regenerate iodine back to the catalytic cycle. Our mechanism is different from the earlier two mechanisms on amination of benzoxazoles with TBAI/TBHP/AcOH and I_2/TBHP/AcOH reported by Nachtsheim[15a] and Prabhu[14a] respectively.

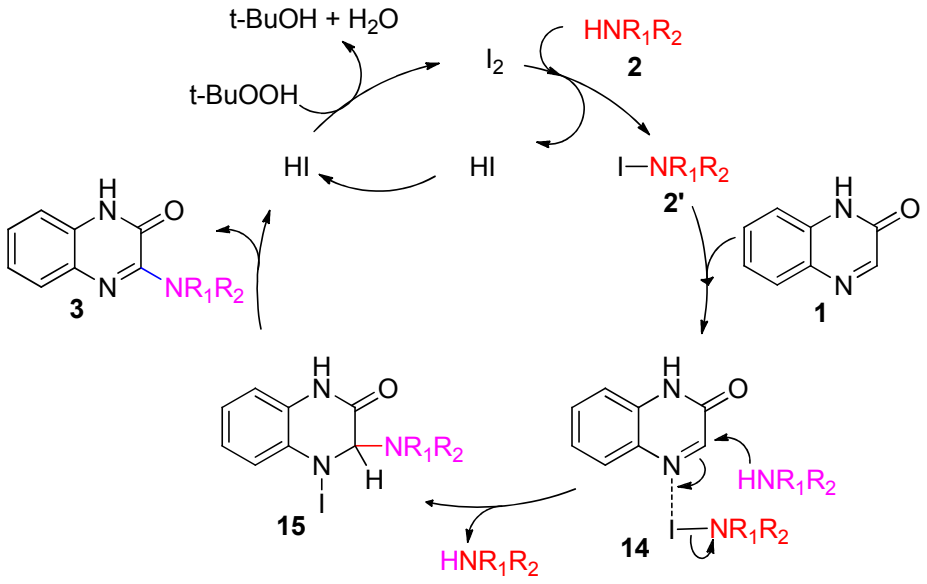


Figure 3. **Proposed Mechanism for Iodine Catalyzed Amination of Quinoxalinones**

CONCLUSION

An iodine catalyzed cross-dehydrogenative coupling between sp2 C-H of quinoxalinone and N-H of amines has been developed under ambient conditions. This is the first example of a metal-free synthesis of 3-aminoquinoxalinones starting from unfunctionalized quinoxalinones and amines. The reaction is highly versatile, exhibits good functional group tolerance with a range of primary and secondary amines, and gives the 3-aminoquinoxalinones in moderate to high yields. The C-N coupling works efficiently under metal-free conditions, does not require any ligand or additive, and generates non-hazardous by products like *tert*-butanol and water. The practical utility of this method has been demonstrated through synthesis of pharmaceutically active aldolase reductase inhibitor and histamine-4 receptor antagonist. The mechanistic studies reveal the reaction to proceed through an ionic mechanism, and involve iodination of amine as the putative mode of activation. Considering the pharmaceutical importance of these molecules, the current methodology features atom economy and provides an efficient access to them.

Experimental Section

All reagents and solvents were of pure analytical grade and were used as received from commercial sources. Thin layer chromatography (TLC) was performed on 60 F254 silica gel, pre-coated on aluminium plates and revealed with a UV lamp (λmax = 254 nm). The products were purified by column chromatography employing pre-packed silica gel columns. The reported yields are the actual isolated yields of pure materials. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on 400 MHz spectrometer using tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are reported in δ (ppm) relative to TMS and the coupling constants (*J*) in Hz. High resolution mass spectra (HRMS) were recorded on a Mass spectrometer using electrospray ionization-time of flight (ESI-TOF) reflectron experiments.

General Procedure for Preparation of 3-Aminoquinoxalinones (3a-3k), (4a-4l) and (6a-6i):

To a well stirred solution of quinoxalinone (0.5 mmol) and amine (0.75 mmol) in 1,4-dioxane (3.0 mL), TBHP (70% solution in water, 1.0 mmol), and molecular iodine (0.025 mmol) were added at room temperature. The resulting reaction mixture was stirred at room temperature for 16 h. After complete conversion as indicated by TLC, the reaction mixture was poured in water (10 mL) and extracted with EtOAc (50 mL x 2). The combined organic extract was washed with water (50 mL × 2) and saturated brine solution, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The impure product thus obtained was purified by column chromatography using pre-packed silica gel column eluting with a gradient of MeOH/DCM (0-6%).

Synthesis of 1-(4-Nitrobenzyl)-3-[4-(pyrazin-2-yl)piperazin-1-yl]quinoxalin-2(1H)-one (11):

To a well stirred solution of 1-(4-nitrobenzyl)quinoxalinone **7** (250 mg, 0.89 mmol) and piperazine **8** (115 mg, 1.34 mmol) in 1,4-dioxane (10 mL), TBHP (70% solution in water, 229 μL, 1.78 mmol), and molecular iodine (11 mg, 0.045 mmol) were added at room temperature. The resulting reaction mixture was stirred at same temperature for 16 h. After complete conversion as indicated by TLC, the reaction mixture was poured in water (30 mL). The precipitated solid was filtered, washed with water, dried under vacuum and used for next step without further purification. The crude 1-(4-nitrobenzyl)-3-(piperazin-1-yl)quinoxalin-2(1H)-one) (250 mg, 0.684 mmol) and K_2CO_3 (283 mg, 2.05 mmol) were suspended in DMF (5 mL), and 2-chloropyrazine (122 μL, 1.368 mmol) was added drop by drop at room temperature. The

contents were stirred at 110 ºC for 4 h. After complete conversion, it was cooled to room temperature, poured in water (10 mL) and extracted with EtOAc (50 mL x 2). The combined organic extract was washed with water (50 mL × 2) and saturated brine solution, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The impure product thus obtained was purified by column chromatography using pre-packed silica gel column eluting with a gradient of MeOH/DCM (0-6%).

Sequential One-pot Synthesis of 6,7-Dichloro-3-(4-methylpiperazin-1-yl)quinoxalin-2(1H)-one (4e):

To a stirred solution of 4,5-dichlorobenzene-1,2-diamine (250 mg, 1.421 mmol) in dioxane (10 mL), ethyl 2-oxoacetate (50% in toluene, 580 µL, 2.842 mmol) was added drop by drop. After complete addition, the resultant reaction mixture was stirred at 100 ºC for 8 h. After complete conversion as indicated by TLC, the reaction mixture was cooled to room temperature, and *N*-methylpiperazine (236 µL, 2.132 mmol), iodine (18 mg, 0.071 mmol) and TBHP (365 µL, 2.842 mmol) were added at room temperature. The resultant reaction mixture was stirred at same temperature for 16 h. After complete conversion, the reaction mixture was poured in water (25 mL) and extracted with EtOAc (50 mL x 2). The combined organic extract was washed with water (30 mL × 2) and saturated brine solution, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The impure product thus obtained was purified by column chromatography using pre-packed silica gel column using a mixture of MeOH/DCM (0-6%) as eluent.

Physical Properties and Characterization Data of the Synthesized Compounds:

3-(Morpholin-4-yl)quinoxalin-2(1H)-one ***(3a)***.[12] yield 92% (107 mg); off-white solid, MeOH/DCM = 2/98; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.14 (br. s., 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 6.88-7.27 (m, 3H), 3.87 (t, *J* = 4.4 Hz, 4H), 3.71 (t, *J* = 4.4 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 152.5, 151.6, 132.6, 129.8, 125.7, 125.3, 123.6, 114.9, 66.5, 47.2. HRMS-ESI calcd. for $C_{12}H_{13}N_3O_2^+$ $[M+H]^+$ 232.1081, found 232.1086.

3-(2,6-Dimethylmorpholin-4-yl)quinoxalin-2(1H)-one ***(3b).*** yield 80% (104 mg); off-white solid, MeOH/DCM = 2/98, mp 186-188 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.14 (br. s., 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.28 - 7.04 (m, 3H), 4.77 (d, *J* = 12.4 Hz, 2H), 3.82 - 3.58 (m, 2H), 2.66-2.50 (m, 2H) 1.14 (d, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.5, 151.3,

132.7, 129.8, 125.6, 125.2, 123.6, 114.8, 71.4, 52.0,19.2. HRMS-ESI calcd. for $C_{14}H_{17}N_3O_2^+$ $[M+H]^+$ 260.1394, found 260.1391.

*Ethyl 4-(3-oxo-3,4-dihydroquinoxalin-2-yl)morpholine-2-carboxylate (**3c**)*. yield 68% (103 mg); yellowish solid, MeOH/DCM = 2/98, mp 129-131 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.18 (br. s., 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.18 - 7.06 (m, 3H), 4.59 (d, *J* = 12.8 Hz, 1H), 4.40 - 4.22 (m, 2H), 4.14 (q, *J* = 6.8 Hz, 2H), 4.00 (d, *J* = 11.6 Hz, 1H), 3.77 - 3.43 (m, 3H), 1.20 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 169.7, 152.4, 151.4, 132.4, 129.9, 125.8, 125.6, 123.7, 114.9, 73.6, 65.1, 61.1, 48.2, 46.4, 14.5. HRMS-ESI calcd. for $C_{15}H_{17}N_3O_4^+$ $[M+H]^+$ 304.1292, found 304.1293.

*3-(4-Acetylpiperazin-1-yl)quinoxalin-2(1H)-one (**3d**)*. yield 62% (72 mg); yellowish solid, MeOH/DCM = 2/98, mp 188-190 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.15 (br. s., 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.23 - 7.11 (m, 3H), 3.92 (s., 2H), 3.85 (s., 2H), 3.63 - 3.51 (m, 4H), 2.05 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 168.9, 152.5, 151.5, 132.6, 129.8, 125.6, 125.3, 123.6, 114.9, 46.8, 46.4, 45.9, 41.2, 21.7. HRMS-ESI calcd. for $C_{14}H_{16}N_4O_2^+$ $[M+H]^+$ 273.1346, found 273.1343.

*3-(Piperidin-1-yl)quinoxalin-2(1H)-one (**3e**)*.[17] yield 86% (99 mg); yellowish solid, MeOH/DCM = 2/98; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.99 (br. s., 1H), 7.36 (d, J = 6.8 Hz, 1H), 7.18-7.06 (m, 3H), 3.85 (s, 4H), 1.62 (s., 6H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 152.6, 151.7, 133.0, 129.7, 125.4, 124.7, 123.5, 114.7, 47.7, 26.1, 24.8. HRMS-ESI calcd. for $C_{13}H_{15}N_3O^+$ $[M+H]^+$ 230.1288, found 230.1287.

*1-(3-Oxo-3,4-dihydroquinoxalin-2-yl)piperidine-4-carbonitrile (**3f**)*. yield 65% (83 mg); brown solid, MeOH/DCM = 2/98, mp 159-161 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.12 (br. s., 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.29 - 6.94 (m, 3H), 4.38 - 4.09 (m, 2H), 3.78-3.50 (m, 2H), 3.25-3.04 (m, 1H), 2.11-1.92 (m, 2H), 1.91 - 1.67 (m, 2H);^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 151.4, 150.5, 131.6, 128.8, 124.6, 124.2, 122.5, 121.6, 113.7, 43.9, 27.4, 24.9. HRMS-ESI calcd. for $C_{14}H_{14}N_4O^+$ $[M+H]^+$ 255.1240, found 255.1240.

*3-[3-(Trifluoromethyl)piperidin-1-yl]quinoxalin-2(1H)-on (**3g**)*. yield 62% (92 mg); yellowish solid, MeOH/DCM = 2/98, mp 128-130 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.29 (br. s., 1H), 7.56 - 7.41 (m, 1H), 7.18 - 7.04 (m, 3H), 5.08 (d, *J* = 12.8 Hz, 1H), 4.91 (d, *J* = 13.2 Hz, 1H), 3.00 - 2.79 (m, 2H), 2.48 (br. s, 1H), 2.06 (d, *J* = 10.0 Hz, 1H), 1.84 (d, *J* = 12.0 Hz, 1H), 1.71 - 1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.5, 150.9, 133.1, 128.6, 126.7 (q, J_{CF} = 277.0 Hz), 126.1, 125.5, 124.3, 114.5, 47.3, 46.2 (d, J_{CF} = 3.0 Hz), 40.3 (q, J_{CF} = 26.0 Hz), 24.3, 23.8. HRMS-ESI calcd. for $C_{14}H_{14}F_3N_3O^+$ $[M+H]^+$ 298.1162, found 298.1168.

3-(4-Benzylpiperidin-1-yl)quinoxalin-2(1H)-one ***(3h)***. yield 74% (118 mg); yellow solid, MeOH/DCM = 2/98, mp 127-128 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (br. s., 1H), 7.50 (d, *J* = 7.2, Hz, 1H), 7.31 - 7.28 (m, 2H), 7.22 - 7.17 (m, 5H),7.40 (d, *J* = 7.2, Hz, 1H), 4.95 (d, *J* = 12.8 Hz, 2H), 2.97-2.82 (m, 2H), 2.58 (d, *J* = 7.2 Hz, 2H), 1.78 (d, *J* = 13.6, Hz, 2H), 1.48-1.36 (m, 2H) 1.25 (br.s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.1, 151.2, 140.4, 133.3, 129.2, 128.4, 128.3, 125.9, 125.8, 124.6, 124.1, 114.0, 47.3, 43.2, 38.5, 32.4. HRMS-ESI calcd. for $C_{20}H_{21}N_3O^+$ [M+H]+ 320.1757, found 320.1751.

3-(Pyrrolidin-1-yl)quinoxalin-2(1H)-one ***(3i)***.[17] yield 80% (86 mg); yellowish solid, MeOH/DCM = 2/98; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.86 (br. s., 1H), 7.32-7.24 (m, 1H), 7.12-6.98 (m, 3H), 3.81 (br. s., 4H), 1.86 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.6, 148.9, 133.0, 127.9, 123.6, 122.4 (2C), 113.6, 48.5, 24.9. HRMS-ESI calcd. for $C_{12}H_{13}N_3O^+$ [M+H]+ 216.1131, found 216.1133.

3-(Dimethylamino)quinoxalin-2(1H)-one ***(3j)***.[18] yield 82% (78 mg); pale yellow solid, MeOH/DCM = 2/98; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.94 (br. s., 1H), 7.35-7.33 (m, 1H), 7.19-7.02 (m, 3H), 3.28 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 152.7, 151.9, 133.3, 129.5, 125.0, 124.2, 123.5, 114.7, 40.2. HRMS-ESI calcd. for $C_{10}H_{11}N_3O^+$ $[M+H]^+$ 190.0975, found 190.0972.

3-[Benzyl(methyl)amino]quinoxalin-2(1H)-one ***(3k)***. yield 64% (85 mg); white solid, MeOH/DCM = 2/98, mp 118-120 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.07 (br. s., 1H), 7.40-7.21 (m, 6H), 7.18-7.11 (m, 3H), 5.16 (s, 2H), 3.14 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 152.7, 151.3, 139.2, 133.2, 129.6, 128.9, 127.9, 127.4, 125.3, 124.5, 123.6, 114.8, 54.4, 38.2. HRMS-ESI calcd. for $C_{16}H_{15}N_3O^+$ $[M+H]^+$ 266.1288, found 266.1287.

6-Fluoro-3-(morpholin-4-yl)quinoxalin-2(1H)-one ***(4a)***. yield 90% (113 mg); off-white solid, MeOH/DCM = 2/98, mp 197-199 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.13 (br. s., 1H), 7.18-7.03 (m, 3H), 3.94 (s, 4H), 3.74 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 157.7 (d, J_{CF} = 236.0 Hz), 151.1, 150.8, 132.5 (d, J_{CF} = 12.0 Hz), 125.4, 114.8 (d, J_{CF} = 9.0 Hz), 111.3 (d, J_{CF} = 24.0 Hz), 109.7 (d, J_{CF} = 23.0 Hz), 65.5, 46.1. HRMS-ESI calcd. for $C_{12}H_{12}FN_3O_2^+$ $[M+H]^+$ 250.0986, found 250.0985.

7-Fluoro-3-(morpholin-4-yl)quinoxalin-2(1H)-one ***(4b)***. yield 88% (110 mg); off-white solid, MeOH/DCM = 2/98, mp 180-183 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.20 (br. s., 1H), 7.44-7.38 (m, 1H), 7.02-6.89 (m, 2H), 3.85-3.81 (m, 4H), 3.68-3.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.5 (d, J_{CF} = 240.0 Hz), 151.4, 149.9, 129.6 (d, J_{CF} = 13.0 Hz), 128.4, 126.2 (d, J_{CF} = 10.0 Hz), 109.9 (d, J_{CF} = 23.0 Hz), 99.9 (d, J_{CF} = 27.0 Hz), 65.4, 46.1. HRMS-ESI calcd. for $C_{12}H_{12}FN_3O_2^+$ $[M+H]^+$ 250.0986, found 250.0985.

*6,7-Difluoro-3-(morpholin-4-yl)quinoxalin-2(1H)-one (**4c**)*. yield 86% (115 mg); off-white solid, MeOH/DCM = 2/98, mp 199-201 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.11 (br. s., 1H),7.38 (dd, *J* = 11.6, 8.0 Hz, 1H), 7.08 (dd, *J* = 11.2, 8.0 Hz, 1H), 3.90-3.87 (m, 4H), 3.72-3.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.1, 150.3, 146.8 (dd, J_{CF} = 14.0, 88.0 Hz), 144.4 (dd, J_{CF} = 14.0, 86.0 Hz), 128.4 (dd, J_{CF} = 2.0, 10.0 Hz), 125.3 (d, J_{CF} = 9.0 Hz), 111.9 (d, J_{CF} = 18.0 Hz), 101.6 (d, J_{CF} = 21.0 Hz), 65.5, 46.1. HRMS-ESI calcd. for $C_{12}H_{11}F_2N_3O_2^+$ $[M+H]^+$ 268.0892, found 268.0892.

*6-Chloro-3-(piperidin-1-yl)quinoxalin-2(1H)-one (**4d**)*. yield 76% (100 mg); brown solid, MeOH/DCM = 3/97, mp 196-198 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.14 (br. s., 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.18-7.05 (m, 2H), 3.91 (s, 4H), 1.62 (br.s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 152.4, 151.9, 134.2, 128.5, 127.2, 124.2, 124.1, 116.1, 47.7, 26.2, 24.8. HRMS-ESI calcd. for $C_{13}H_{14}ClN_3O^+$ $[M+H]^+$ 264.0898, found 264.0894.

*6,7-Dichloro-3-(4-methylpiperazin-1-yl)quinoxalin-2(1H)-one (**4e**)*.[9c] yield 78% (122 mg); yellow solid, MeOH/DCM = 3/97; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.75 (br.s, 1H), 7.53 (s, 1H), 7.27 (s, 1H), 3.94 (br.s, 4H), 2.42 (t, *J* = 4.8 Hz, 4H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 152.2, 151.7, 132.9, 129.5, 125.9, 125.9, 125.2, 115.6, 55.0, 46.4, 46.1. HRMS-ESI calcd. for $C_{13}H_{14}Cl_2N_4O^+$ $[M+H]^+$ 313.0617, found 313.0619.

*7-Methoxy-3-(morpholin-4-yl)quinoxalin-2(1H)-one (**4f**)*. yield 89% (117 mg); off-white solid, MeOH/DCM = 3/97, mp 204-206 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.07 (br.s, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 6.78 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.70 (d, *J* = 2.4 Hz, 1H), 3.76 (s, 3H), 3.73-3.70 (m, 8H); ^{13}C NMR (100 MHz, DMSO- d_6) δ (ppm) 157.5, 152.6, 150.3, 130.9, 126.9, 126.8, 111.5, 98.4, 66.5, 55.8, 47.3. HRMS-ESI calcd. for $C_{13}H_{15}N_3O_3^+$ $[M+H]^+$ 262.1186, found 262.1183.

*Methyl 2-(morpholin-4-yl)-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**4g**)*. yield 63% (91 mg); off-white solid, MeOH/DCM = 3/97, mp 129-131 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 12.27 (br. s, 1H), 7.78 (s, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 4.02 (s, 4H), 3.85 (s, 3H), 3.71 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 166.3, 152.5, 152.1, 136.6, 129.4, 125.3, 125.1, 124.4, 115.9, 66.6, 52.6, 47.2. HRMS-ESI calcd. for $C_{14}H_{15}N_3O_4^+$ $[M+H]^+$ 290.1135, found 290.1139.

*1-Methyl-3-(morpholin-4-yl)quinoxalin-2(1H)-one (**4h**)*.[11] yield 82% (101 mg); yellow solid, MeOH/DCM = 2/98; ^{1}H NMR (400MHz, $CDCl_3$) δ (ppm) 7.48 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.25 - 7.10 (m, 3H), 3.98-3.83 (m, 4H), 3.80-3.71 (m, 4H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.2, 149.7, 132.0, 129.8, 125.8, 124.4, 122.8, 112.3, 65.8, 46.5, 28.3. HRMS-ESI calcd. for $C_{13}H_{15}N_3O_2^+$ $[M+H]^+$ 246.1237, found 246.1237.

1-Methyl-3-(pyrrolidin-1-yl)quinoxalin-2(1H)-one ***(4i)***. yield 74% (90 mg); yellow solid, MeOH/DCM = 2/98, mp 128-130 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.40-7.38(m, 1H), 7.15-7.03 (m, 3H), 3.88 (b, s, 4H), 3.56 (s, 3H), 1.93-1.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.7, 147.9, 133.7, 129.1, 124.7, 122.7, 122.3, 112.1, 48.6, 28.7, 28.0. HRMS-ESI calcd. for $C_{13}H_{15}N_3O^+$ $[M+H]^+$ 230.1288, found 230.1282.

1-Benzyl-3-(4-ethoxypiperidin-1-yl)quinoxalin-2(1H)-one ***(4j)***. yield 90% (164 mg); yellow solid, MeOH/DCM = 3/97, mp 168-170 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.47 (d, J = 7.2 Hz, 1H), 7.23-7.19 (m, 2H), 7.15-7.03 (m, 6H), 5.40 (s, 2H), 4.46-4.34 (m, 2H), 3.57-3.45 (m, 3H), 3.44-3.35 (m, 2H), 2.03-1.88 (m, 2H), 1.74-1.60 (m, 2H), 1.16 (t, J = 6.8 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.2, 150.9, 135.5, 133.4, 129.9, 128.7, 127.3, 126.6, 126.5, 124.8, 123.6, 113.9, 74.5, 62.9, 46.0, 44.7, 31.4, 15.5. HRMS-ESI calcd. for $C_{22}H_{25}N_3O_2^+$ $[M+H]^+$ 364.2020, found 364.2020.

1-Benzyl-3-(pyrrolidin-1-yl)quinoxalin-2(1H)-one ***(4k)***.[12] yield 87% (133 mg); brown solid, MeOH/DCM = 2/98, mp 129-131 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.48 (d, J = 8.0 Hz, 1H), 7.37-7.18 (m, 5H), 7.17-7.10 (m, 1H), 7.09-6.95 (m, 2H), 5.44 (s, 2H), 3.99 (br.s, 4H), 1.96 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.8, 148.9, 135.8, 134.9, 129.3, 128.8, 127.4, 126.7, 125.8, 123.8, 123.3, 113.9, 77.2, 49.8, 45.8. HRMS-ESI calcd. for $C_{19}H_{19}N_3O^+$ $[M+H]^+$ 306.1601, found 306.1600.

Methyl [3-(morpholin-4-yl)-2-oxoquinoxalin-1(2H)-yl]acetate ***(4l)***. yield 66% (100 mg); off-white solid, MeOH/DCM = 3/97, mp 156-158 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.64-7.49 (m, 1H), 7.31-7.17 (m, 2H), 7.06-6.91 (m, 1H), 5.02 (s, 2H), 4.01-3.92 (m, 4H), 3.88-3.80 (m, 4H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 166.8, 151.0, 149.2, 132.1, 128.9, 126.2, 124.5, 123.2, 111.6, 65.9, 51.8, 46.5, 42.7. HRMS-ESI calcd. for $C_{15}H_{17}N_3O_4^+$ $[M+H]^+$ 304.1292, found 304.1295.

3-(Butylamino)quinoxalin-2(1H)-one ***(6a)***. yield 56% (61 mg); brown solid, MeOH/DCM = 3/97, mp 119-121 ºC; ^{1}H NMR (400MHz, DMSO-d_6) δ (ppm) 12.10 (br. s., 1H), 7.43 (t, J = 5.8 Hz, 1H), 7.37 - 7.30 (m, 1H), 7.20 - 7.06 (m, 3H), 3.39 (q, J = 7.0 Hz, 2H), 1.59 (quint, J = 7.2 Hz, 2H), 1.34 (sext, J = 7.6 Hz, 2H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 150.8, 149.3, 132.9, 127.2, 123.8, 122.6, 122.4, 114.3, 39.2, 29.9, 19.1, 13.2. HRMS-ESI calcd. for $C_{12}H_{15}N_3O^+$ $[M+H]^+$ 218.1288, found 218.1287.

3-(Heptylamino)quinoxalin-2(1H)-one ***(6b)***. yield 55% (72 mg); off-white solid, MeOH/DCM = 2/98, mp 116-118 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (br. s, 1H), 7.46 (t, J = 5.6 Hz, 1H), 7.32-7.31 (m, 1H), 7.11-7.09 (m, 3H), 3.38-3.37 (m, 2H), 1.60 (s, 2H), 1.31-1.26 (m, 8H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 151.9, 150.4, 134.0, 128.2,

124.9, 123.7, 123.4, 115.3, 40.5, 31.7, 28.9, 28.8, 26.9, 22.6, 14.4. HRMS-ESI calcd. for $C_{15}H_{21}N_3O^+$ $[M+H]^+$ 260.1757, found 260.1757.

3-(Butan-2-ylamino)quinoxalin-2(1H)-one ***(6c)***. yield 62% (68 mg); off-white solid, MeOH/DCM = 2/98, mp 125-127 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.53 (d, *J* = 7.6 Hz, 1H), 7.28 - 7.20 (m, 1H), 7.19-7.13 (m, 2H), 6.16 (d, *J* = 8.4 Hz, 1H), 4.26-4.15 (m, 1H), 1.73 - 1.60 (m, 2H), 1.30 (d, *J* = 6.4 Hz, 3H), 1.00 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.9, 148.9, 134.3, 126.8, 125.4, 124.5, 123.7, 115.2, 47.7, 29.4, 20.0, 10.4. HRMS-ESI calcd. for $C_{12}H_{15}N_3O^+$ $[M+H]^+$ 218.1288, found 218.1289.

3-(Pentan-2-ylamino)quinoxalin-2(1H)-one ***(6d)***. yield 64% (74 mg); light brown solid, MeOH/DCM = 2/98, mp 120-122 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.53 (d, *J* = 8.0 Hz, 1H), 7.31-7.06 (m, 3H), 6.15 (d, *J* = 8.4 Hz, 1H), 4.40-4.15 (m, 1H), 1.71-1.52 (m, 2H), 1.51-1.38 (m, 2H), 1.30 (d, *J* = 6.4 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 151.9, 147.8, 133.3, 125.8, 124.4, 123.4, 122.6, 114.2, 45.0, 37.9, 19.6, 18.3, 13.1. HRMS-ESI calcd. for $C_{13}H_{17}N_3O^+$ $[M+H]^+$ 232.1444, found 232.1442.

3-[(3-Methylbutan-2-yl)amino]quinoxalin-2(1H)-one ***(6e).*** yield 65% (75 mg); off-white solid, MeOH/DCM = 2/98, mp 125-127 ºC; ^{1}H NMR (400MHz, $CDCl_3$) δ (ppm) 7.52 (d, *J* = 8.0 Hz, 1H), 7.26 - 7.18 (m, 1H), 7.17 - 7.11 (m, 2H), 6.23 (d, *J* = 8.8 Hz, 1H), 4.24-4.08 (m, 1H), 2.01-1.87 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.01 (dd, *J* = 12.0, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.9, 148.9, 134.3, 126.8, 125.4, 124.4, 123.7, 115.2, 51.1, 32.8, 18.9, 18.4, 17.0. HRMS-ESI calcd. for $C_{13}H_{17}N_3O^+$ $[M+H]^+$ 232.1444, found 232.1444.

3-{[2-(2,5-Dimethylphenyl)ethyl]amino}quinoxalin-2(1H)-one ***(6f).*** yield 62% (91 mg); yellow solid, MeOH/DCM = 2/98, mp 156-158 ºC; ^{1}H NMR (400MHz, DMSO-d_6) δ (ppm) 12.13 (s, 1H), 7.64 (t, *J* = 6.0 Hz, 1H), 7.41-7.28 (m, 1H), 7.18-7.07 (m, 3H), 7.07-6.97 (m, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.63-3.44 (m, 2H), 2.92-2.82 (m, 2H), 2.34 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 151.9, 150.3, 137.9, 135.1, 133.9, 133.4, 130.4, 130.3, 128.3, 127.3, 124.9, 123.7, 123.6, 115.4, 41.4, 32.5, 21.1, 18.9. HRMS-ESI calcd. for $C_{18}H_{19}N_3O^+$ $[M+H]^+$ 294.1601, found 294.1599.

3-(Benzylamino)quinoxalin-2(1H)-one ***(6g).*** yield 65% (82 mg); pale yellow solid, MeOH/DCM = 2/98, mp 160-162 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 11.92 (br.s, 1H), 8.04 (t, *J* = 6.4 Hz, 1H), 7.49-7.34 (m, 2H), 7.33-7.27 (m, 3H), 7.24-7.19 (m, 1H), 7.17-7.12 (m, 1H), 7.11-7.05 (m, 2H), 4.61 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 150.3, 148.7, 138.5, 132.2, 127.1, 126.9, 126.3, 125.6, 123.5, 122.2, 122.1, 113.8, 42.2. HRMS-ESI calcd. for $C_{15}H_{13}N_3O^+$ $[M+H]^+$ 252.1131, found 252.1129.

3-[(1-Phenylethyl)amino]quinoxalin-2(1H)-one ***(6h).*** yield 52% (69 mg); viscous brown liquid, MeOH/DCM = 2/98; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.52 (br.s, 1H), 7.49 (dd, *J* = 7.6, 1.2

Hz, 1H), 7.47-7.40 (m, 2H), 7.39-7.31 (m, 2H), 7.29-7.27 (m, 1H), 7.23-7.12 (m, 2H), 7.03 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 5.38 (quint, *J* = 7.6 Hz, 1H), 1.65 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.0, 148.5, 143.5, 133.9, 128.6, 127.3, 126.9, 126.4, 125.8, 124.4, 124.0, 114.7, 49.9, 22.1. HRMS-ESI calcd. for $C_{16}H_{15}N_3O^+$ $[M+H]^+$ 266.1288, found 266.1287.

3-(Pyridin-2-ylamino)quinoxalin-2(1H)-one ***(6i).*** yield 32% (38 mg); light brown solid, MeOH/DCM = 4/96, mp 270-272; ^{1}H NMR (400MHz, DMSO-d_6) δ (ppm) 12.65 (br.s, 1H), 8.85 (s, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.36 (s, 1H), 7.92 (t, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.35-7.25 (m, 3H), 7.14 (t, *J* = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d6) δ (ppm) 150.1, 149.9, 147.1, 144.8, 137.3, 130.5, 127.6, 124.7, 124.6, 122.5, 117.7, 114.2, 111.2. HRMS-ESI calcd. for $C_{13}H_{10}N_4O^+$ $[M+H]^+$ 239.0927, found 239.0924.

1-(4-Nitrobenzyl)-3-[4-(pyrazin-2-yl)piperazin-1-yl]quinoxalin-2(1H)-one ***(11).***[7a] yield 54% (213 mg); off-white solid, MeOH/DCM = 2/98, mp 222-224 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.22-8.14 (m, 3H), 8.11 (s, 1H), 7.90 (d, *J* = 2.4 Hz, 1H), 7.64-7.60 (m, 1H), 7.40 (d, *J* = 8.8 Hz, 2H) 7.26-7.24 (m, 1H), 7.21-7.16 (m, 1H), 7.05-7.01 (m, 1H) 5.58 (s, 2H), 4.18-4.11 (m, 4H), 3.84-3.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.9, 151.2, 149.4, 141.9, 140.8, 132.4, 132.3, 129.9, 128.7, 127.2, 126.6, 126.3, 124.7, 123.4, 123.2, 112.5, 45.5, 44.7, 43.4; HRMS-ESI calcd. for $C_{23}H_{21}N_7O_3^+$ $[M+H]^+$ 444.1779, found 444.1763.

ASSICIATED CONTENT

SUPPORTING INFORMATION

Characterization data are available (including copies of ^{1}H and ^{13}CNMR spectra) of all the products. This material is available free of charge via the internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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