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Dimethyl Sulfoxide Participated One-pot Synthesis of Quinoxaline Derivatives

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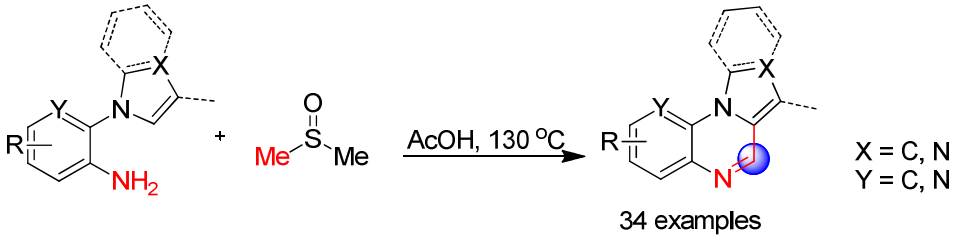


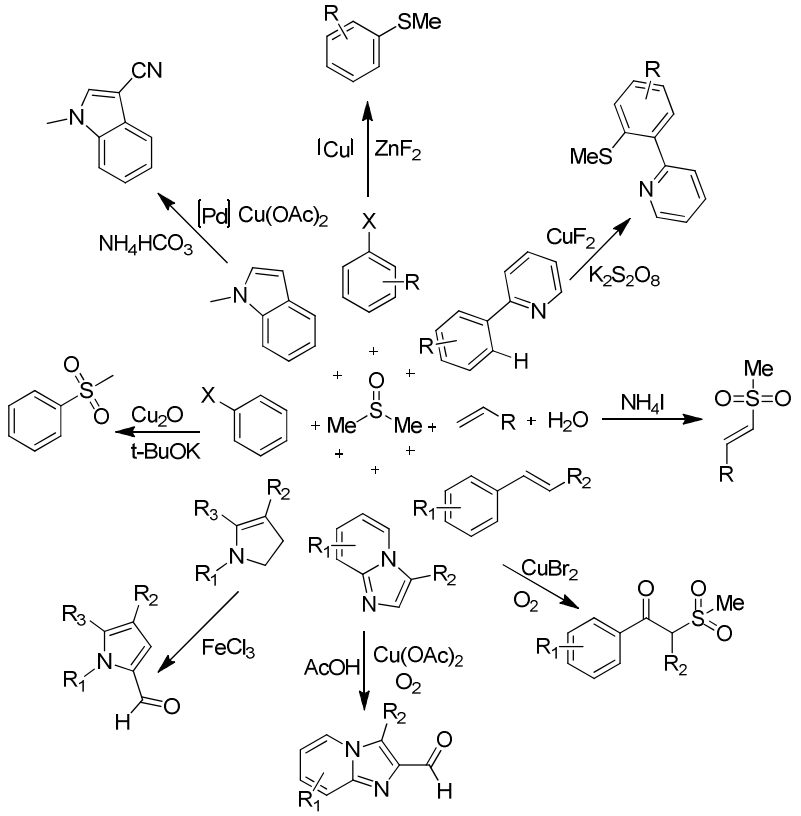
An efficient, green and novel method for the synthesis of N-heterocycle fused quinoxalines is reported herein. Dimethyl sulfoxide was used as both a reactant and a solvent in this reaction. A wide range of products in moderate to excellent yields was obtained including, pyrrolo[1,2-*a*]quinoxalines, indolo[1,2-*a*]quinoxalines, 1*H*-pyrrolo[3,2-*c*]quinolines and benzo[4,5]imidazo[1,2-*c*]quinazolines.

INTRODUCTION

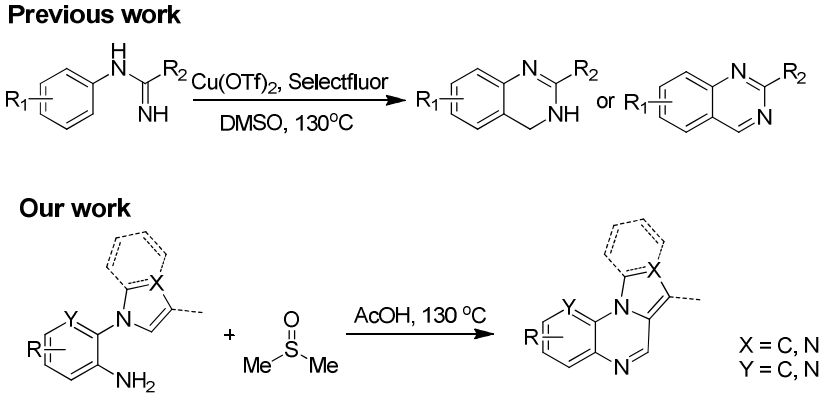
Dimethyl sulfoxide is an important polar solvent and mild oxidant that is routinely used in the synthesis of organic compounds and pharmaceuticals[1] due to its low toxicity and ready availability. In addition, it has been used as reactant in organic synthesis in recent years as well, especially in the transformation of DMSO into –SMe,[2] -CHO,[3] -CN[4] and -SO_2Me[5] for the synthesis of more complex organic compounds, which are the key to production of medicinal and natural products (Scheme 1). Although DMSO has been used in syntheses to introduce functional groups, to the best of our knowledge, only a few[6] researchers have used DMSO to synthesize heterocyclic compounds such as Zhang`s work[6a] published in 2013 using $Cu(OTf)_2$ as catalyst (Scheme 2).

Pyrrolo[1,2-*a*]quinoxaline derivatives are indispensable in heterocyclic organic chemistry and have enjoyed extensive application in organic functional materials, pharmaceuticals and biological studies. Many unique and excellent properties in a

number of products have been revealed, such as the D-loop activity of RAD51 inhibitors,[7] 5-HTR affinities,[8] the human protein kinase CK2 inhibitors,[9] glucagon receptor antagonists,[10] antimalarial activities[11] and others.[12] For this reason, numerous methods have been reported to construct this structural skeleton.[13] However, many inevitable drawbacks have been encountered, such as the use of expensive and toxic reactants,[14] transition-metal catalysts[15] and harsh conditions of microwave irradiation[16] and amberlite.[17] Our group has devoted continuously to explore the



Scheme 1 Reactions employing DMSO as a reactant



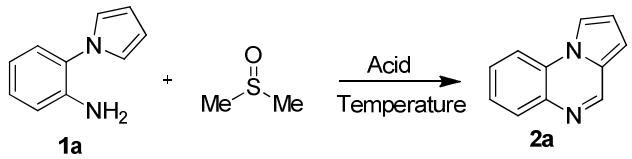
Scheme 2 Synthesis of heterocyclic compounds employing DMSO

efficient and simple methods to resolve these challenges.[18] Based on our previous work[19] on heterocyclic synthesis and the referenced literature reports, we herein describe a simple, metal- free and environmental-friendly method to obtain this class of compounds using 2-(1*H*-pyrrol-1-yl)anilines and DMSO as reactants.

RESULTS AND DISCUSSION

Our initial experiment began with the observation that 2-(1*H*-pyrrol-1-yl)aniline could react with DMSO at 130 ºC in the presence of $TsOH·H_2O$. And the desired product was obtained in a 41% yield (Table 1, entry 1). Hence, several Bronsted acids were examined for use in this reaction strategy. It was found that AcOH was the most effective Bronsted acid with a yield of 87% (Table 1, entries 2-9). The next step entailed optimizing the concentration of AcOH in the reaction, but no improvement in product yield occurred (Table 1, entries 1 and 10-11). Besides, the reaction temperature had an obvious influence (Table 1, entries 12-13). A long reaction time was required to yield the desired product when the reaction temperature was less than 130 ^oC. At 140 ^oC the quantity of by-products was high resulting in a low yield of the desired product. Interestingly, the reaction occurred without the presence of an acid

Table 1 Optimization of the reaction conditions[a]

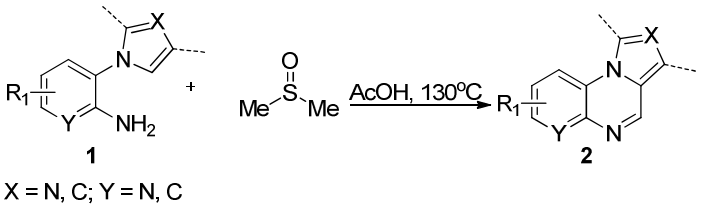


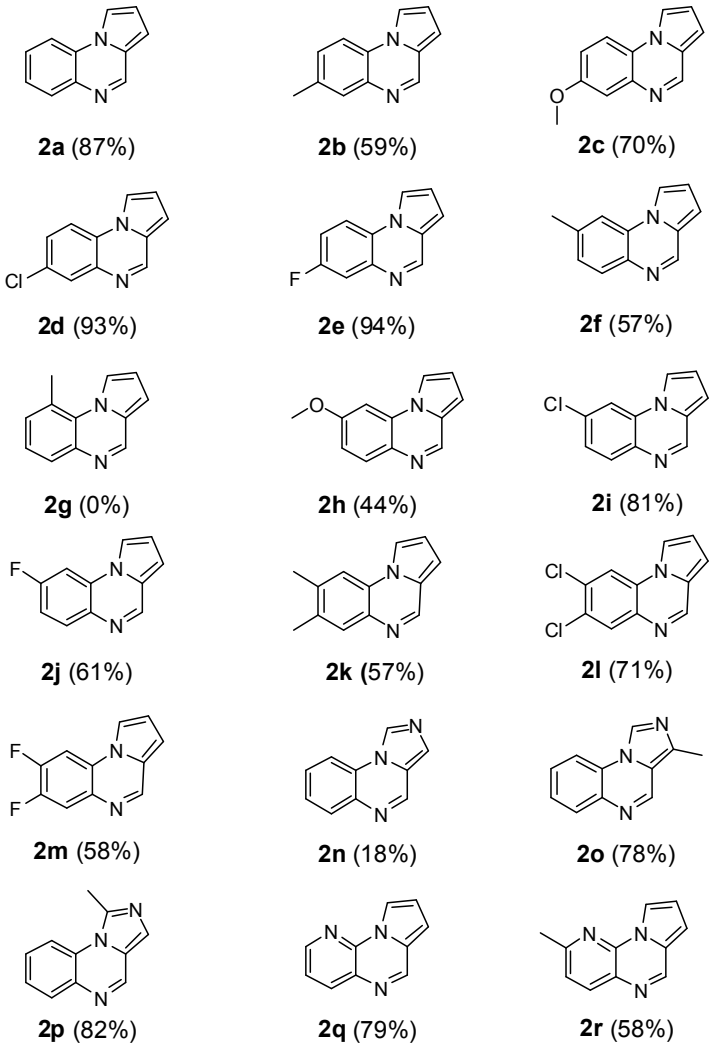
Entry	Acid	Equiv	Solvent	T / ^oC	Yield / %[b]
1	$TsOH·H_2O$	1	DMSO	130	41
2	MsOH	1	DMSO	130	63
3	**CH_3COOH**	**1**	**DMSO**	**130**	**87**
4	CF_3COOH	1	DMSO	130	22
5	Ph_2PO_2H	1	DMSO	130	58
6	$HOCH_2COOH$	1	DMSO	130	66
7	$NCCH_2COOH$	1	DMSO	130	50
8	$ClCH_2COOH$	1	DMSO	130	41
9	$C(CH_3)_3COOH$	1	DMSO	130	50
10	CH_3COOH	0.5	DMSO	130	73
11	CH_3COOH	2	DMSO	130	77
12	CH_3COOH	1	DMSO	120	41
13	CH_3COOH	1	DMSO	140	65
14	None	----	DMSO	130	42
15	CH_3COOH	1	$DMSO/H_2O$	130	21[c]
16	CH_3COOH	1	DMSO	130	54[d]
17	CH_3COOH	1	DMSO	130	N.R.[e]

[a]**1a** (0.5 mmol, 0.079 g), DMSO (2 mL), acid (0.5 mmol), in a sealed tube, 130 ^oC (TLC monitored); [b]Isolated yields; [c]DMSO / H_2O = 1:1; [d]under oxygen atmosphere; [e]under nitrogen atmosphere.

and a yield of 42% was obtained after three days of reaction at 130 °C (Table 1, entry 14). No product was detected when the reaction was performed under nitrogen atmosphere (Table 1, entry 17). This result indicated that oxygen played an essential role in this reaction. However, the reaction proceeded well under O_2 atmosphere with a lower yield, possibly because of the side reactions (Table 1, entry 16). It was worth noting that the reaction was hindered when water was present in the reaction system

Scheme 3 Substrate scope of 2-(1*H*-pyrrol-1-yl)aniline **1**[a,b]



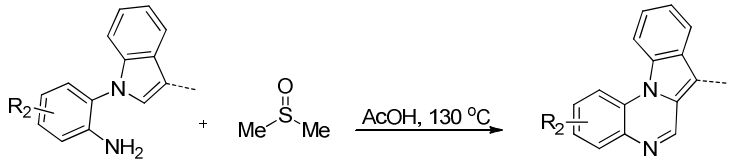


[a]**1** (0.5 mmol), DMSO (2 mL), CH_3COOH (0.5 mmol), 130 °C in a sealed tube for about 20 h, (TLC monitored); [b]Isolated yields.

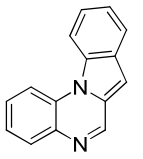
(Table 1, entry 15). Under the optimized reaction conditions (Table 1, entry 3), the desired product **3a** was isolated in a yield of 87%.

With these established reaction conditions , the scope of the 2-(1*H*-pyrrol-1-yl)aniline reaction was evaluated. It was found that compounds **1** bearing electron-withdrawing groups gave better yields than those bearing electron-donating groups (Scheme 3, **2b**-**2e**). Among the compounds with

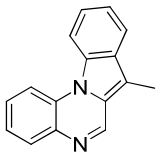
Scheme 4 Substrate scope of 2-(1*H*-indol-1-yl)aniline[a,b]



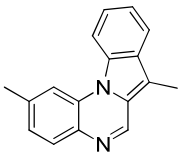
3 **4**



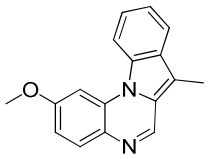
4a (12%)



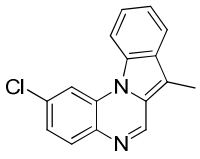
4b (82%)



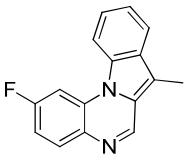
4c (73%)



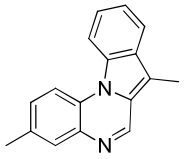
4d (74%)



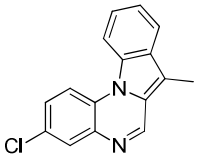
4e (78%)



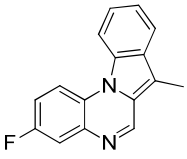
4f (79%)



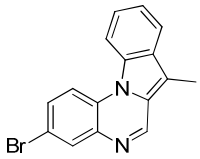
4g (93%)



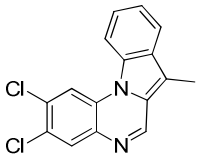
4h (68%)



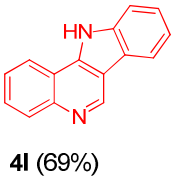
4i (81%)



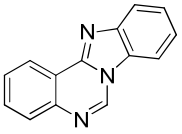
4j (55%)



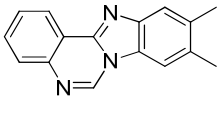
4k (68%)



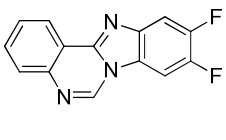
4l (69%)



4m (68%)



4n (62%)

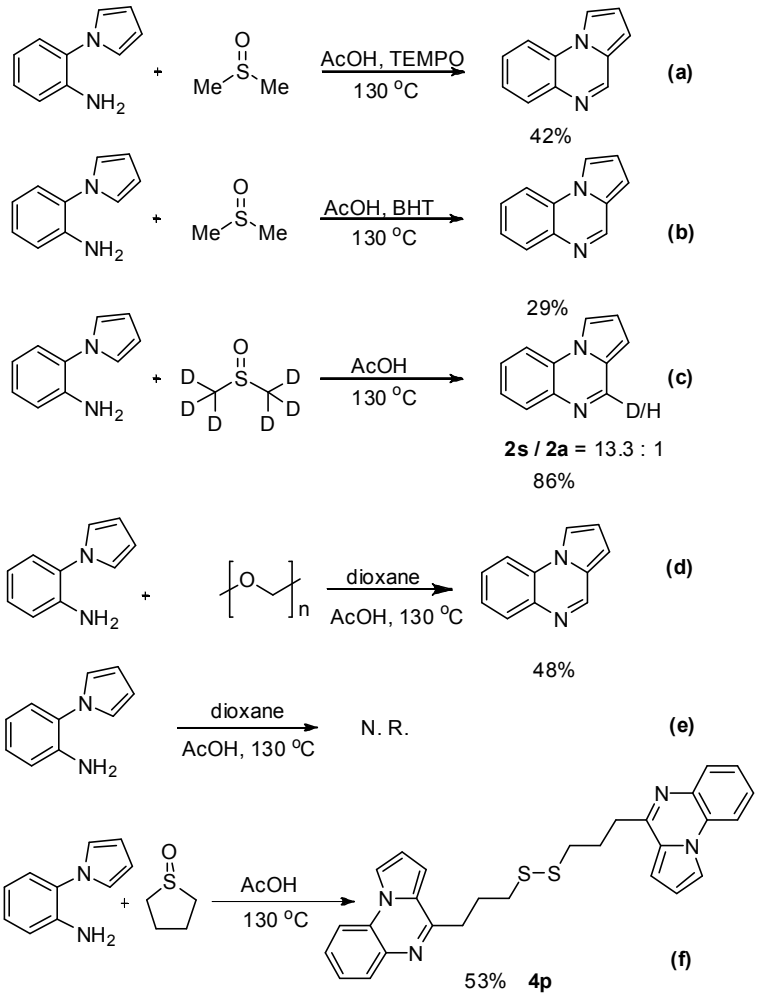


4o (34%)

[a]**3** (0.5 mmol), DMSO (2 mL), CH_3COOH (0.5 mmol), 130 °C in a sealed tube for about 20 h, (TLC monitored); [b]Isolated yields.

electron-withdrawing groups, substituents at various positions on the benzene ring produced obvious differences and substituents at the 5-position on the ring were found to have a better effect on the reaction than groups located at the 4-position (Scheme 3, **2d**-**2j**). However, none of the desired product was obtained when 3-methyl-2-(1*H*-pyrrol-1-yl)aniline was used in this reaction, which might be the result of steric effects (Scheme 3, **2g**). In addition, when imidazolyl was used in place of pyrrolyl, low yields of the desired product resulted. A great improvement in the yield resulted when there was a methyl group in imidazole ring (Scheme 3, entries **2n**-**2p**).[20] 2-(1*H*-pyrrol-1-yl)pyridin-3-amine could also react with DMSO and provided the desired product in moderate yields (Scheme 3, entries **2q**, **2r**).

Encouraged by these results, 2-(1*H*-indol-1-yl)aniline was used as the reactant and a 12% yield of the desired product was obtained (Scheme 4, **4a**). To our delight, the yield was significantly improved when 2-(3-methyl-1*H*-indol-1-yl)aniline was used as a substrate (Scheme 4, **4b**). This was probably due to the competitive reaction



Scheme 5 Control experiments

between the 2-position and 3-position of indolyl and the electron-donating effect of alkyl group.[20] A wide range of 2-(3-methyl-1*H*-indol-1-yl)anilines with different substituents were tolerated in our protocol (Scheme 4, **4c**-**4k**). Interestingly, the desired product was also obtained when 2-(1*H*-indol-2-yl)aniline was selected as substrate (Scheme 4, **4l**). And substituted 2-(1*H*-benzo[d]imidazol-2-yl)anilines also proceeded well in this reaction (Scheme 4, **4m**-**4o**), which greatly extended the scope of this synthesis strategy.

To obtain further insight into the reaction mechanism, several control experiments were conducted (Scheme 5). Initially, radical inhibitors (TEMPO and BHT) were added to the reaction and the yields were found to be reduced to 42% and 29% (Eq **a**, Eq **b**). Thus, it appeared that a radical process cannot be excluded in this reaction. Then to determine the source of the carbon, an isotope experiment was performed and the product **2s** was obtained with the radio of **2s**:**2a** = 13.3: 1 (Eq **c**, **^{1}H NMR** of **2s** see supporting information). This result suggested that the C-H bond cleavage of DMSO had occurred and the carbon atom in the desired product was obtained from DMSO. Next, paraformaldehyde was reacted with 2-(1*H*-pyrrol-1-yl)aniline in dioxane and the desired product was obtained, but in the absence of paraformaldehyde, no desired product resulted(Eq **d**, Eq **e**). To further explore this mechanism, tetrahydrothiophene 1-oxide was used as a solvent and the desired product 3-(pyrrolo[1,2-*a*]quinoxalin-4-yl)propane-1-thiol was not obtained, but a coupling product of S-S bond was detected in a yield of 53% (Eq **f**).

Based on the control experiments and the previous literature, we suspect that two mechanistic pathways may be possible in this reaction. The first one may be a radical process,[21, 3b, d, f, e] where $\cdot CH_3$ may be produced by DMSO participated by O_2 at high temperature and then, CH_2O was produced through a process that $\cdot CH_3$ was trapped by oxygen to give peroxy radical. Then the imine formation and electrophilic aromatic substitutions occur to produce the desired products.[22] In addition, according to the previous literature,[23, 5b] DMSO could decompose and produce CH_2O directly at high temperature, which may form a second reaction pathway to the desired product.

CONCLUSION

In conclusion, a simple, green and efficient way to construct pyrrolo[1,2-*a*]quinoxalines was developed as well as other N-heterocycle fused quinoxalines under mild conditions. In particular, it was found that oxygen could be used as a cheap oxidant and no metal catalysts were needed. This new reaction strategy can provide access to a wide range of processes in organic and medicinal chemistry synthesis.

EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR spectra of the products were recorded using a 300 MHz or a 400 MHz MNR instrument in $CDCl_3$ or DMSO-d_6, and tetramethylsilane (TMS) as the internal standard. HRMS spectra were determined using a Q-TOF spectrograph.

Compounds **1a-1r** and **3a-3o** were prepared according to the literature. Other reagents were commercially available and were used without further purification. All reactions were monitored using thin-layer chromatography (TLC).

General experimental procedures for the synthesis of pyrrolo [1,2-*a*]quinoxalines

A mixture of 2-(1*H*-pyrrol-1-yl)aniline (0.5 mmol) and DMSO (2mL) with AcOH (0.5 mmol) were stirred at 130 ^{o}C for 20-25 h (TLC monitored). Then the mixture was extracted with ethyl acetate three times (3×30 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to produce a residue. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate to provide the desired product.

Pyrrolo[1,2-a]quinoxalines (2a)[13b]

Light yellow solid. 73 mg (87% yield). Mp: 137-139 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.78 (s, 1H), 7.95 (dd, *J* = 7.8 Hz, 1.5 Hz, 1H), 7.87 (d, *J* = 1.2 Hz, 1H), 7.81 (d, *J* = 6.3 Hz, 1H), 7.50-7.38 (m. 2H), 6.87-6.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.7, 135.8, 130.1, 128.0, 127.7, 126.4, 125.1, 114.1, 113.7, 113.7, 107.2; HRMS (ESI) calcd for $C_{11}H_8N_2$ [$(M+H)^+$]:169.0760; found, 169.0761.

7-Methylpyrrolo[1,2-*a*]quinoxaline (2b)[24]

Light yellow solid. 54 mg (59% yield). Mp: 112-113 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1H), 7.87 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 8.3 Hz, 1.2 Hz, 1H), 6.87-6.94 (m, 2H), 2.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7, 135.7, 13, 128. 9, 128.9, 126.4, 125.9, 114.0, 113.7, 113.5, 107.0; HRMS (ESI) calcd for $C_{12}H_{10}N_2$ [$(M+H)^+$]: 183.0917; found,183.0913.

7-Methoxypyrrolo[1,2-*a*]quinoxaline (2c)[13c]

Yellow solid. 69 mg (70% yield). Mp: 99-101 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.79 (s, 1H), 7.86 (t, *J* = 1.4 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.15 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 6.89-6.84 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.1, 146. 0, 136.9, 126.2, 122.3, 116.8, 114.7, 113.9, 113.7, 111.4, 107.1, 55.7; HRMS (ESI) calcd for $C_{12}H_{10}N_2O$ [$(M+H)^+$]: 199.0866; found, 199.0869.

7-Chloropyrrolo[1,2-*a*]quinoxaline (2d)[18a]

Yellow solid. 94 mg (93% yield). Mp: 135-137 ^{o}C.^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 2.4 Hz, 1H), 7.88 (t, *J* = 1.2 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.47 (dd, 8.7 Hz, 2.4 Hz, 1H), 6.92-6.87 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.7, 136.7, 130.3, 129.5, 127. 8, 126.6, 126.3, 114.9, 114.5, 114.4, 108.0; HRMS (ESI) calcd for $C_{11}H_7N_2Cl$ [$(M+H)^+$]: 203.0371; found, 203.0372.

7-Fluoropyrrolo[1,2-*a*]quinoxaline (2e)[13b]

Light yellow solid. 87 mg (94% yield). Mp: 166-168 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (t, *J* = 1.2 Hz, 1H),7.84 (dd, *J* = 9.0 Hz, 5.0 Hz, 1H), 7.65 (dd, *J* =

9.4 Hz, 2.8 Hz, 1H), 7.29-7.24 (m, 1H), 6.93 (dd, J = 4.0 Hz, 1.1 Hz, 1H), 6.89-6.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0 (d, $^{1}J_{C,F}$ = 242 Hz), 146. 8, 137.1 (d, $^{3}J_{C,F}$ = 11 Hz), 126.27, 124.68, 115.7 (d, $^{2}J_{C,F}$ = 22 Hz), 115.5 (d, $^{2}J_{C,F}$ = 22 Hz), 115.0 (d, $^{3}J_{C,F}$ = 9 Hz), 114.5, 114.2, 107.8; HRMS (ESI) calcd for $C_{11}H_7N_2F$ [$(M+H)^+$]: 187.0666; found, 187.0660.

8-Methylpyrrolo[1,2-*a*]quinoxaline (2f)[24]

Light yellow solid. 52 mg (57% yield). Mp: 127-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.79 (s, 1H), 7.91 (s, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.68 (s, 1H), 7.29 - 7.27 (m, 1H), 6.90 (d, J = 1.8 Hz, 2H), 2.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.9, 138.3, 133.8, 129.8, 127.8, 126.6, 126.4, 113.9, 113.8, 106.9, 21.8; HRMS (ESI) calcd for $C_{12}H_{10}N_2$ [$(M+H)^+$]: 183.0917; found, 183.0917.

8-Methoxypyrrolo[1,2-*a*]quinoxaline (2h)[15b]

Light yellow solid. 44 mg (44% yield). Mp: 110-112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (s, 1H), 7.89 (d, J = 8.9 Hz, 1H), 7.82 (s, 1H), 7.26 (d, J = 2.7 Hz, 1H), 7.05 (dd, J = 8.9 Hz, 2.6 Hz, 1H), 6.89-6.86 (m, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 143.3, 131.3, 130.2, 128.8, 126.4, 114.1, 113.7, 112.7, 106.7, 97.6, 55.8; HRMS (ESI) calcd for $C_{12}H_{10}N_2O$ [$(M+H)^+$]: 199.0866; found, 199.0862.

8-Chloropyrrolo[1,2-*a*]quinoxaline (2i)[24]

Light yellow solid. 82 mg (81% yield). Mp: 224-226 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.78 (s, 1H), 7.89 (d, J = 9.3 Hz, 3H), 7.41 (d, J = 7.2 Hz, 1H), 6.91 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.8, 134.4, 133.2, 131.3, 128.6, 126.3, 125.6, 114.6, 114.4, 113.9, 107.8; HRMS (ESI) calcd for $C_{11}H_7N_2Cl$ [$(M+H)^+$]: 203.0371; found, 203.0374.

8-Fluoropyrrolo[1,2-*a*]quinoxaline (2j)[24]

White solid. Mp: 57 mg (61% yield). 174-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 7.96-7.92 (m, 1H), 7.81 (d, J = 1.6 Hz, 1H), 7.54 (dd, J = 9.2 Hz, 2.7 Hz, 1H), 7.19 (td, J = 8.5 Hz, 2.7 Hz, 1H), 6.91 (d, J = 1.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8 (d, $^{1}J_{C,F}$ = 247 Hz), 144.9 (d, $^{4}J_{C,F}$ = 2 Hz), 132.4, 132.0 (d, $^{3}J_{C,F}$ = 9 Hz),128.8, 126.1, 114.5, 114.4, 113.2 (d, $^{2}J_{C,F}$ = 23 Hz), 107.6, 100.8 (d, $^{2}J_{C,F}$ = 26 Hz); HRMS (ESI) calcd for $C_{11}H_7N_2F$ [$(M+H)^+$]: 187.0666; found, 187.0669.

7,8-Dimethylpyrrolo[1,2-*a*]quinoxaline (2k)

Light yellow solid. 56 mg (57% yield). Mp: 127-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.73 (s, 1H), 7.83 (s, 1H), 7.69 (s, 1H), 7.59 (s, 1H), 6.84 (dd, J = 6.0 Hz, 3.6 Hz, 2H), 2.43 (s, 3H), 2.38 (s, 3H); ^{1}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 137.3, 134.0, 134.0, 130.2, 126.5, 125.9, 114,2, 113.6, 106.7, 20.3, 19.6; HRMS (ESI) calcd for $C_{13}H_{12}N_2$ [$(M+H)^+$]: 197.1073; found, 197.1071

7,8-Dichloropyrrolo[1,2-*a*]quinoxaline (2l)

Light yellow solid. 84 mg (71% yield). Mp: 235-236 °C. ^{1}H NMR (400 MHz, $CDCl_3$):

δ = 8.78 (s, 1H), 8.04 (s,1H), 7.95 (s,1H), 7.85 (s, 1H), 6.96-6.91 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =146.74, 135.2, 131.5, 131.0, 128.9, 127.1, 126.2, 115.5, 115.0, 108.7; HRMS (ESI) calcd for $C_{11}H_6Cl_2N_2$ [$(M+H)^+$]: 236.9981; found,236.9980.

7,8-Difluoropyrrolo[1,2-*a*]quinoxaline (2m)

Light yellow solid. 59 mg (58% yield). Mp: 190-192 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (s, 1H), 7.77 (dd, *J* = 10.4 Hz, 8 Hz, 2H), 7.65 (dd, *J* = 10.4 Hz, 5.4 Hz, 1H), 6.93-6.90 (m, 2H); ^{1}C NMR (100 MHz, $CDCl_3$): δ = 151.0 (dd, $^1J_{C,F}$ = 250 Hz, $^2J_{C,F}$ = 15 Hz), 149.2 (dd, $^1J_{C,F}$ = 246 Hz, $^2J_{C,F}$ = 13 Hz), 146.0 (dd, $^3J_{C,F}$ = 12 Hz),132.6 (dd, $^3J_{C,F}$ =9 Hz, $^4J_{C,F}$ = 3 Hz), 126.0, 124.5 (d, $^3J_{C,F}$ =9 Hz), 117.7, 114.7, 114.5, 108.0, 102.5 (d, $^2J_{C,F}$ =22 Hz); HRMS (ESI) calcd for $C_{11}H_6N_2F_2$ [$(M+H)^+$]: 205.0572; found, 205.0573.

Imidazo[1,5-*a*]quinoxaline (2n)[25]

Light yellow solid. 15 mg (18% yield). Mp: 175-177 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.28 (s, 1H), 9.06 (s, 1H), 8.41 (dd, *J* = 6Hz, 0.9 Hz, 1H), 7.95-7.92 (m, 2H), 7.70 (td, *J* = 6.0 Hz, 0.9 Hz, 1H), 7.61-7.57 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 146.0, 135.8, 131.3, 130.0, 129.3, 127.6, 127.4, 125.5, 124.4, 116.1; HRMS (ESI) calcd for $C_{10}H_7N_3$ [$(M+H)^+$]: 170.0713 ; found, 170.0714.

3-Methylimidazo[1,5-*a*]quinoxaline (2o)

Light yellow solid. 71 mg (78% yield). Mp: 147-149 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.15 (s, 1H), 9.03 (s, 1H), 8.33 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 7.90 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 7.65 (td, *J* = 7.5 Hz, 1.5 Hz, 1H), 7.57 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 145.3, 136.2, 135.4, 129.4, 129.3, 128.4, 126.7, 125.1, 120.5, 115.3, 12.5; HRMS (ESI) calcd for $C_{11}H_9N_3$ [$(M+H)^+$]: 184.0869; found, 184.0873.

1-Methylimidazo[1,5-*a*]quinoxaline (2p)

Light yellow solid. 75 mg (82% yield). Mp: 111-113 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.93 (s, 1H), 8.29 (dd, *J* = 8.2 Hz, 1.1 Hz, 1H), 7.91 (dd, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.77 (s, 1 H), 7.64-7.54 (m, 2 H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 146.2, 142.3, 137.0, 129.9, 128.6, 127.4, 126.8, 126.1, 126.0, 116.9, 18.5; HRMS (ESI) calcd for $C_{11}H_9N_3$ [$(M+H)^+$]: 184.0869 ; found, 184.0870.

Pyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (2q)[13c]

Light yellow solid. 67 mg (79% yield). Mp: 94-95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.80 (s, 1H), 8.56 (dd, *J* = 4.5 Hz, 1.5 Hz, 1H), 8.39 (t, *J* = 0.9 Hz, 1H), 8.26 (dd, *J* = 7.8 Hz, 1.5 Hz, 1H), 7.46 (dd, *J* = 8.1 Hz, 4.5 Hz, 1H), 7.00-6.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.0, 146.5, 137.4, 130.7, 127.9, 121.5, 115.6, 114.6, 108.9; HRMS (ESI) calcd for $C_{10}H_7N_3$ [$(M+H)^+$]:170.0713; found, 170.0732.

2-Methylpyrido[3,2-*e*]pyrrolo[1,2-*a*]pyrazine (2r)[26]

Light yellow solid. 53 mg (58% yield). Mp: 108-110 °C. ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 8.75 (s, 1H), 8.39 (s, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.29-7.26 (m, 1H), 6.96 (dd, *J* = 3.9 Hz, 1.0 Hz, 1H), 6.91-6.89 (m, 1H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 145.4, 139.1, 137.4, 128.3, 128.0, 121.5, 115.3, 114.3, 108.4, 24.6; HRMS (ESI) calcd for $C_{11}H_9N_3$ [$(M+H)^+$]: 184.0869; found, 184.0864.

4-D-pyrrolo[1,2-a]quinoxaline (2s)

Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (s, 0.07H), 7.98-7.94 (m, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.55-7.51 (m, 1H), 7.48-7.43 (m, 1H), 6.92-6.88 (m, 2H).

Indolo[1,2-*a*]quinoxaline (4a)[13b]

Yellow solid. 13 mg (12% yield). Mp: 104-106 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.95 (s, 1H), 8.48-8.42 (m, 2H), 8.02-7.96 (m, 2H), 7.65-7.54 (m, 2H), 7.48-7.41 (m, 2H), 7.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.9, 135.8, 132.7, 131.0, 130.4, 129.8, 129.2, 128.8, 124.5, 124.2, 122.9, 122.7, 114. 9, 114.6, 101.0; HRMS (ESI) calcd for $C_{15}H_{10}N_2$ [$(M+H)^+$]: 219.0917; found, 219.0919.

7-Methylindolo[1,2-*a*]quinoxaline (4b)

Yellow solid. 95 mg (82% yield).Mp: 149-150 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33-8.30 (m, 2H), 7.94 (dd, *J* = 8.1 Hz, 1.8 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.56-7.49 (m, 2H), 7.45-7.40 (m, 1H), 7.39-7.33 (m, 1H), 2.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.5, 135.9, 131.9, 131.1, 130.2, 129.3, 128.5, 126.6, 124.50, 123.7, 122.0, 120.7, 114.5, 114.3, 109.6, 8.0; HRMS (ESI) calcd for $C_{16}H_{12}N_2$ [$(M+H)^+$]: 233.1073; found,233.1073.

2,7-Dimethylindolo[1,2-*a*]quinoxaline (4c)

Yellow solid. 90 mg (73% yield).Mp: 179-181 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.88 (s, 1H), 8.38 (d, *J* = 8.4 Hz, 1H), 8.16 (s, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.57-7.52(m, 1H), 7.47-7.42 (m, 1H), 7.20 (dd, *J* = 8.1 Hz, 0.9 Hz, 1H), 2.65 (s, 3H), 2.59 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.5, 139.0, 133.8, 131.9, 131.0, 129.9, 129.5, 126.7, 124.8, 124.3, 122.0, 120.7, 114.9, 114.5, 109.3, 22.2, 8.0; HRMS (ESI) calcd for $C_{17}H_{14}N_2$ [$(M+H)^+$]: 247.1230 ; found,247.1237.

2-Methoxy-7-methylindolo[1,2-*a*]quinoxaline (4d)

Yellow solid. 97 mg (74% yield). Mp: 126-128 ^{o}C. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 8.77 (s, 1H), 8.29 (m, 1H), 7.92-7.88 (m, 1H), 7.84 (d, *J* = 9.0Hz, 7.78 (d, *J* = 2.7 Hz, 1H), 7.56-7.43 (m, 2 H), 6.96 (dd, *J* = 8.7 Hz, 2.7 Hz, 1H), 4.00 (s, 3H), 2.62 (S, 3H); ^{1}C NMR (75 MHz, CD_2Cl_2): δ = 159.8, 143.6, 131.8, 131.6, 131.0, 130.4, 129.6, 126.6, 123.9, 121.9, 120.4, 114.1, 109.4, 108.7, 100.0, 55.70, 7.6; HRMS (ESI) calcd for $C_{17}H_{14}N_2O$ [$(M+H)^+$]: 263.1179; found, 263.1194.

2-Chloro-7-methylindolo[1,2-*a*]quinoxaline (4e)

Yellow solid. 104 mg (78% yield). Mp: 179-181 ^{o}C. ^{1}H NMR (300 MHz, CD_2Cl_2): δ

= 8.60 (d, *J* = 4.5 Hz, 1H), 8.23-8.18 (m, 2H), 7.89-7.79 (m, 2H), 7.57-7.52 (m, 1H), 7.47-7.42 (m, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 2.61 (s, 3H); ^{1}C NMR (75 MHz, CD_2Cl_2): δ = 146.5, 134.5, 133.8, 131.8, 131.6, 131.0, 129.5, 126.3, 125.0, 123.8, 122.4, 120.8, 114.6, 114.1, 110.4, 8.0; HRMS (ESI) calcd for $C_{16}H_{11}N_2Cl$ [$(M+H)^+$]: 267.0684; found, 267.0686.

2-Fluoro-7-methylindolo[1,2-*a*]quinoxaline (4f)

Yellow solid. 99 mg (79% yield). Mp: 192-194 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (s, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.00 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.09 (td, *J* = 8.4 Hz, 2.0Hz, 1H), 2.63 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.3 (d, $^{1}J_{C,F}$ = 247 Hz), 145.6 (d, $^{4}J_{C,F}$ = 2 Hz), 132.4, 131.8, 131.6 (d, $^{3}J_{C,F}$ = 10 Hz), 129.6 , 126.1, 124.8, 122.4, 120.81, 114.0, 111.0 (d, $^{2}J_{C,F}$ = 22 Hz), 110.0, 102.0 (d, $^{2}J_{C,F}$ = 28 Hz), 8.0; HRMS (ESI) calcd for $C_{16}H_{11}FN_2$ [$(M+H)^+$]: 251.0979; found, 251.0976.

3,7-Dimethylindolo[1,2-*a*]quinoxaline (4g)

Yellow solid. 114 mg (93% yield). Mp: 131-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.87 (s, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H),7.70 (d, *J* = 1.2 Hz, 1H), 7.52-7.47 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.32 (dd, *J* = 8.4 Hz, 1.2 Hz, 1H), 2.61 (s, 3H), 2,46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.4, 135.8, 133.4, 131.8, 130.3, 129.3, 129.2, 128.8, 126.6, 124.3, 121.8, 120.6, 114.3, 114.2, 109.2, 20.8, 8.0; HRMS (ESI) calcd for $C_{17}H_{14}N_2$ [$(M+H)^+$]: 247.1230 ; found,247.1235.

3-Chloro-7-methylindolo[1,2-*a*]quinoxaline (4h)

Yellow solid. 90 mg (68% yield). Mp: 208-210 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.81 (s, 1H), 8.24 (dd, *J* = 15.2 Hz, 8.8 Hz, 2H), 7.91-7.88 (m, 2H), 7.57-7.43 (m, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.5, 136.8, 131.9, 129.7, 129.6, 129.4, 128.6, 128.2, 126.4, 125.0, 122.3, 121.0, 115.4, 114.1, 110.6, 8.0; HRMS (ESI) calcd for $C_{16}H_{11}ClN_2$ [$(M+H)^+$]: 267.0684 ; found, 267.0688.

3-Fluoro-7-methylindolo[1,2-*a*]quinoxaline (4i)

Yellow solid. 101 mg (81% yield). Mp: 127-129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.91 (s, 1H), 8.28-8.23 (m, 2H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.64 (dd, *J* = 9.1 Hz, 3.0 Hz, 1H), 7.57-7.52 (m, 1H), 7.29-7.22 (m, 1H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.2 (d, $^{1}J_{C,F}$ = 242 Hz), 147.5, 137.2 (d, $^{3}J_{C,F}$ = 11 Hz), 131.8, 129.2, 127.7, 126.4, 125.0, 122.1, 121.0, 116.1 (d, $^{2}J_{C,F}$ = 22 Hz), 115.5 (d, $^{2}J_{C,F}$ = 22 Hz), 115.4 (d, $^{3}J_{C,F}$ = 9 Hz), 113.9, 110.2, 8.0; HRMS (ESI) calcd for $C_{16}H_{11}N_2F$ [$(M+H)^+$]: 251.0979; found, 251.0990.

3-Bromo-7-methylindolo[1,2-*a*]quinoxaline (4j)

Yellow solid. 85 mg (55% yield).Mp: 215-217 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (s, 1H), 8.24 (d, *J* = 8.8 Hz, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 2.4 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.61-7.53 (m, 2H), 7.48- 7.44 (m, 1H), 2.63 (s, 3H); ^{13}C

NMR (100 MHz, $CDCl_3$): δ = 147.5， 137.2, 132.6, 131.9，131.0, 130.1, 129.4, 126.4, 125.0, 122.3, 121.0, 115.9, 115.7, 114.2, 110.6, 8.0; HRMS (ESI) calcd for $C_{16}H_{11}BrN_2$ [$(M+H)^+$]: 311.0170; found, 311.0170.

2,3-Dichloro-7-methylindolo[1,2-*a*]quinoxaline (4k)

Yellow solid. 102 mg (68% yield).Mp: 219-220 °C. ^{1}H NMR (300 MHz, CD_2Cl_2): δ = 8.92 (s, 1H), 8.38 (s, 1H), 8.25 (d, *J* = 8.7 Hz, 1H), 7.98 (s, 1H), 7,96 (d, *J* = 8.4 Hz, 1H), 7.64-7.58 (m, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 2,66 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ = 147.4, 135.1, 132.1, 131.7, 130.4, 130.2, 129.6, 126.8, 126.1, 125.6, 122.7, 121.2, 116.0, 113.9, 7.8; HRMS (ESI) calcd for $C_{16}H_{10}N_2Cl_2$ [$(M+H)^+$]: 301.0294; found, 301.0297.

11*H*-indolo[3,2-c]quinoline (4l)[27]

White solid. 75 mg (69% yield). Mp: >300 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.62 (s, 1H), 8.56 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 7.8 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.78-7.68 (m, 3H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 145.4, 144.8, 139.7, 138.7, 129.5, 127.9, 125.6, 125.5, 122.0, 121.8, 120.5, 120.0, 117.0, 114.2, 111.8; HRMS (ESI) calcd for $C_{15}H_{10}N_2$ [$(M+H)^+$]: 219.0919; found, 219.0914.

Benzo[4,5]imidazo[1,2-*c*]quinazoline (4m)[28]

White solid. 74 mg (68% yield). Mp: 229-231 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.14 (s, 1H), 8.71 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 8.04-7.96 (m, 3H), 7.83 (td, *J* = 7.5 Hz, 1.6 Hz, 1H), 7.73 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 7.61 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 7.53 (td, *J* = 8.1 Hz, 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3, 143.9, 142.6, 136.1, 131.8, 128.7, 128.5, 128.1, 126.2, 124.3, 123.3, 120.3, 119.3, 110.1; HRMS (ESI) calcd for $C_{14}H_9N_3$ [$(M+H)^+$]: 220.0869; found, 220.0863.

9,10-Dimethylbenzo[4,5]imidazo[1,2-*c*]quinazoline (4n)[29]

White solid. 77 mg (62% yield).Mp: 229-231 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.58 (s, 1H), 8.51 (d, *J* = 7.0 Hz, 1H), 8.11 (s, 1H), 7.94 (dd, *J* = 7.5 Hz, 1H), 7.83 (t, *J* = 6.8 Hz, 1H), 7.73-7.67 (m, 2H), 2.42 (d, *J* =6.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 142.5, 138.9, 135.1, 132.4, 131.9, 128.7, 128.6, 127.3, 124.0, 119.8, 119.4, 112.3, 20.7; HRMS (ESI) calcd for $C_{16}H_{13}N_3$ [$(M+H)^+$]: 248.1182; found, 248.1183.

9,10-Difluorobenzo[4,5]imidazo[1,2-*c*]quinazoline (4o)

White solid. 43 mg (34% yield).Mp: 185-187 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.41 (s, 1H), 8.34 (t, *J* = 9.0 Hz, 1H), 8.26 (d, *J* = 7.6 Hz, 1H), 7.76 (m, 2H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.57 (t, *J* = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ =150.5 (dd, $^1J_{C,F}$ = 241 Hz, $^2J_{C,F}$ = 15 Hz), 148.5 (dd, $^1J_{C,F}$ = 240 Hz, $^2J_{C,F}$ = 15 Hz), 147.5, 142.2, 139.7, 138.6, 132.5, 129.0, 128.6, 124.4 (d, $^3J_{C,F}$ = 11 Hz), 124.0, 118.8, 107.4 (d, $^2J_{C,F}$ = 20 Hz), 101.5 (d, $^2J_{C,F}$ = 24 Hz); HRMS (ESI) calcd for $C_{14}H_7N_3F_2$[$(M+H)^+$]: 256.0681; found, 256.0687.

1,2-bis(3-(pyrrolo[1,2-*a*]quinoxalin-4-yl)propyl)disulfane (4p)

White solid. 64 mg (53% yield).Mp: 185-187 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87-7.86 (m, 4H), 7.79-7.77 (m, 2H), 7.46-7.37 (m, 4H), 6.91 (dd, *J* = 4.0 Hz, 1.1 Hz, 2H), 6.82 (dd, *J* = 3.8 Hz, 2.8 Hz, 2H), 3.13 (t, *J* = 7.3 Hz, 4H), 2.87 (t, *J* = 7.0 Hz, 4H), 2.35-2.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 135.9, 129.5, 127.2, 127.0, 125.9, 125.1, 114.3, 113.6, 113.6, 106.3, 38.5, 34.0, 27.4. HRMS (ESI) calcd for $C_{28}H_{26}N_4S_2$[$(M+H)^+$]: 483.1672; found, 483.1672.

General experimental procedures for the starting materials.

A mixture of substituted 2-nitroaniline (20 mmol) and 2, 5-dimethoxytetrahydrofuran(20 mmol) in acetic acid (100 mL) was refluxed for 2 h with vigorous stirring. After cooling, the reaction mixtures were poured into water (300 mL) and extracted with EtOAc three times (3×50 mL). The organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was added to iron powder (80 mmol) and NH_4Cl (20 mmol) in water (50 mL) and reflux for 4 h. After cooling, the reaction mixtures were poured into water (300 mL) and extracted with ethyl acetate three times (3×50 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether / EtOAc = 100: 1 as eluent to provide the desired product(**1a-1m, 1q** and **1r**)[18b].

2-(1*H*-pyrrol-1-yl)aniline (1a)[18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16-7.12 (m, 2H), 6.82 (t, *J* = 2.1 Hz, 2H), 6.79-6.75 (m, 2H), 6.33 (t, *J* = 2.0, 2H), 3.68 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 128.6, 127.5, 127.2, 121.7, 118.4, 116.1, 109.4.

General experimental procedures for the synthesis of starting materials

5-Methyl-2-(1*H*-pyrrol-1-yl)aniline (1b)[18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (d, *J* = 7.7 Hz, 1H), 6.80 (t, *J* = 2.1 Hz, 2H), 6.60 (d, *J* = 9.2 Hz, 2H), 6.32 (t, *J* = 2.0Hz, 2H), 3.61 (s, 2H)，2.29 (s. 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =141.9, 138.6, 127.0, 125.3, 121.9, 119.2, 116.6, 109.3, 21.2.

5-Methoxy-2-(1*H*-pyrrol-1-yl)aniline (1c) [18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (dd, *J* = 8.8 Hz, 3.6 Hz, 1H), 6.77 (t, *J* = 2.8Hz, 2H), 6.35-6.31 (m, 4H), 3.78 (s, 3H), 3.67 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 143.4, 128.2, 122.1, 121.2, 109.2, 103.7, 102.1, 55.4.

5-Chloro-2-(1*H*-pyrrol-1-yl)aniline (1d) [18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, *J* = 8.3 Hz, 1H), 6.78-6.76 (m, 3H), 6.74 (dd, *J* = 8.3 Hz, 2.2 Hz, 1H), 6.34 (t, *J* = 2.06 Hz, 2H), 3.76 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.152, 134.0, 128.2, 126.0, 121.7, 118.2, 115.6, 109.8.

5-Fluoro-2-(1*H*-pyrrol-1-yl)aniline (1e) [18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ =7.08-7.04 (m, 1H), 6.76 (t, *J*=2.0 Hz, 2H), 6.47-6.42 (m, 2H), 6.33 (t, *J* = 2.0 Hz, 2H), 3.78 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0 (d, $^1J_{C,F}$ = 243 Hz), 143.9 (d, $^3J_{C,F}$ = 12 Hz), 128.6 (d, $^3J_{C,F}$ = 11 Hz), 123.6, 121.9, 109.6, 104.9 (d, $^2J_{C,F}$ = 23 Hz), 102.6 (d, $^2J_{C,F}$ = 26 Hz).

4-Methyl-2-(1*H*-pyrrol-1-yl)aniline (1f)[30]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.97 (d, *J* = 5.4 Hz, 2H), 6.82 (d, *J* = 1.8 Hz, 2H), 6.71 (dd, *J* = 5.7 Hz, 3.0 Hz, 1H), 6.33 (d, *J* = 1.8 Hz, 2H), 3.55 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.4, 129.1, 128.0, 127.6, 127.5, 121.7, 116.3, 109.3, 20.3.

3-Methyl-2-(1*H*-pyrrol-1-yl)aniline (1g)[30]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (dd, *J* = 8.0Hz, 0.6 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 6.66 (t, *J* = 2.1 Hz, 2H), 6.35 (t, *J* = 2.1 Hz, 2H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.3, 139.3, 134.4, 133.1, 128.5, 11.2, 121.7, 110.0, 17.2.

4-Methoxy-2-(1*H*-pyrrol-1-yl)aniline (1h)[30]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.85 (t, *J* = 2.1Hz, 2H), 6.80-6.72 (m, 3H), 6.34 (t, 2.1Hz, 2H), 3.74 (s, 3H), 3.42 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.5, 135.4, 128.1, 121.6, 117.3, 114.8, 112.5, 109.5, 55.9.

4-Chloro-2-(1*H*-pyrrol-1-yl)aniline (1i)[18c]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.13-7.09 (m, 2H), 6.80 (m, *J* = 1.8 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 2.1 Hz, 2H), 3.70 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.7, 128.4, 128.1, 127.0, 122.6, 121.5, 116.9, 109.9.

4-Fluoro-2-(1*H*-pyrrol-1-yl)aniline (1j)[18c]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93-6.86 (m, 2H), 6.83 (t, *J* = 2.1 Hz, 2H), 6.75 (dd, *J* = 9.6 Hz, 5.1 Hz, 1H), 6.34-6.31 (m, 2H), 3.65 (s,2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.1 (d, $^1J_{C,F}$ = 236 Hz), 137.9, 127.9 (d, $^3J_{C,F}$ = 9 Hz), 121.5, 116.9 (d, $^3J_{C,F}$ = 8 Hz), 115.3 (d, $^2J_{C,F}$ = 23 Hz), 114.1 (d, $^2J_{C,F}$ = 23 Hz), 109.9.

4,5-Dimethyl-2-(1*H*-pyrrol-1-yl)aniline (1k)[31]

^{1}H NMR (400 MHz, $CDCl_3$): δ =6.91 (s, 1H), 6.80 (t, *J* = 2.1Hz, 2H), 6.61 (s, 1H), 6.31 (t, *J* = 2.1Hz, 2H), 3.49 (s, 3H), 2.16 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$): δ = 139.5, 137.0, 128.0, 126.6, 125.4, 121.9, 117.6, 109.1, 19.5, 18.6.

4,5-Dichloro-2-(1*H*-pyrrol-1-yl)aniline (1l)[32]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 12.0 Hz, 1H), 6.88 (S,1H), 6.79 (t, *J* = 2.2 Hz, 2H), 6.35 (t, *J* = 2.0 Hz, 2H), 3.79 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.3, 7.2, 6.9, 6.8, 6.8, 6.8, 6.4, 6.3, 6.3.

4,5-Difluoro-2-(1*H*-pyrrol-1-yl)aniline (1m)[33]

^{1}H NMR (400 MHz, $CDCl_3$): δ =7.01 (dd, *J* = 10.2 Hz, 8.2 Hz, 1H), 6.77 (t, *J* = 2.0 Hz, 2H), 6.59(dd, *J* = 11.6 Hz, 7.6 Hz, 1H), 6.34 (t, *J* = 2.1 Hz, 2H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.4 (dd, $^1J_{C,F}$ = 237 Hz, $^2J_{C,F}$ = 13 Hz), 143.8 (dd, $^1J_{C,F}$ = 240 Hz, $^2J_{C,F}$ = 14 Hz), 139.1 (d, $^3J_{C,F}$ = 7 Hz), 122.5 (d, $^3J_{C,F}$ = 5 Hz), 121.7, 116.1, 115.9 (d, $^4J_{C,F}$ = 2 Hz), 110.0, 104.2 (d, $^2J_{C,F}$ = 21 Hz).

2-(1*H*-imidazol-1-yl)aniline (1n)[18c]

^{1}H NMR (300 MHz, DMSO-d_6): δ =7.75 (s, 1H), 7.30 (s, 1H), 7.17-7.11 (m, 1H), 7.11 (s, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 6.67 (t, *J* = 7.5 Hz, 1H), 4.94 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ =143.2, 137.4, 129.0, 128.9, 126.7, 122.4, 120.3, 116.3, 116.1.

2-(4-Methyl-1*H*-imidazol-1-yl)aniline (1o)[18c]

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.59 (s, 1H), 7.14-7.09 (m, 1H), 7.02-6.99 (m, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.65 (m, 1H), 4.93 (s, 2H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 143.2, 137.2, 136.6, 128.8, 126.6, 122.6, 116.5, 116.3, 116.0, 13.6.

2-(2-Methyl-1*H*-imidazol-1-yl)aniline (1p)[18b]

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.18-7.12 (m, 1H), 7.04 (d, *J* = 1.2 Hz, 1H), 6.99 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.93 (d, *J* = 1.2 Hz, 1H), 6.87 (dd, *J* = 8.1 Hz, 1.2 Hz, 1H), 6.66 (td, *J* = 7.5 Hz, 1.2 Hz, 1H), 4,85 (s, 2H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 144.4, 144.2, 129.4, 127.8, 127.4, 122.2, 120.6, 116.1, 115.7, 12.7.

2-(1*H*-pyrrol-1-yl)pyridin-3-amine (1q)[26]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 4.4 Hz, 1.6 Hz, 1H), 7.14-7.13 (m, 2H), 7.09-7.03 (m, 2H), 6.35 (t, *J* = 2.0 Hz, 2H), 3.86 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.7, 138.4, 136.0, 124.2, 123.0, 120.2, 109.9.

2-(1*H*-indol-1-yl)aniline (3a)[18c]

A mixture of 2-nitroaniline (2 mmol), N-heterocycle (2 mmol) and NaOH (2 mmol) in DMSO (4 mL) was stirred vigorously for 2h at room temperature. After cooling, the reaction mixture was poured into water (30 mL) and extracted with ethyl acetate three times (3×30 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was added to iron powder (16 mmol) and NH_4Cl (1 mmol) in water (30 mL) and refluxed for 4 h. After cooling, the reaction mixture was poured into water (100 mL) and extracted with ethyl acetate three times (3×30 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate as eluent to provide the desired product (**3a-3k, 1n-1p**).[18c] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.67 (m, 1H), 7.23-7.14 (m, 6H), 6.83-6.80 (m, 2H), 6.67 (d, *J* = 3.16 Hz, 1H),

3.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.2, 136.4, 129.2, 128.7, 128.6, 124.9, 122.3, 121.0, 120.2, 118.6, 116.3, 110.8, 103.3.

2-(3-Methyl-1*H*-indol-1-yl)aniline (3b)[18c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80-7.77 (m, 1H), 7.35-7.24 (m, 5H), 7.09 (s, 1H), 6.96-6.89 (m, 2H), 3.48 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 136.9, 129.1, 129.0, 128.7, 126.3, 125.2, 122.4, 119.7, 119.2, 118.6, 116.4, 112.5, 110.8, 9.8.

4-Methyl-2-(3-methyl-1*H*-indol-1-yl)aniline (3c)[34]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63-7.60(m, 1H), 7.19-7.09 (m, 3H),7.03-7.00 (m, 1H), 6.95 (d, *J* = 4.2Hz, 2H), 6.75 (d, *J* = 8.1Hz, 1H), 3.41 (s, 2H), 2.37 (s, 3H), 2, 26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 136.7, 129.5, 129.0, 128.9, 128.1, 126.2, 125.2, 122.2, 119.5, 119.1, 116.4, 112.3, 110.7, 20.4, 9.7.

4-Methoxy-2-(3-methyl-1*H*-indol-1-yl)aniline (3d)

Light yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69-7.66 (m, 1H), 7.26-7.14 (m, 3H), 7.07 (d, *J* = 1.2 Hz, 1H), 6.92- 6.85 (m, 2H), 6.82 (d, *J* = 2.4 Hz, 1H), 3.78 (s, 3H), 3.38 (s, 2H), 2.45 (d, *J* = 1.2 Hz, 3H); ^{1}C NMR (74 MHz, $CDCl_3$): δ = 152.5, 136.8, 136.6, 129.0, 126.0, 125.7, 122.1, 119.4, 118.9, 117.3, 115.2, 113.4, 112.4, 110.5, 55.7, 9.3. HRMS (ESI) calcd for $C_{16}H_{16}N_2O$ [$(M+H)^+$]: 253.1335; found, 253.1337.

4-Chloro-2-(3-methyl-1*H*-indol-1-yl)aniline (3e)

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68-7.65 (m, 1H), 7.24-7.19 (m, 4H), 7.14-7.12 (m, 1H), 6.97 (d, *J* = 0.9 Hz, 1H), 6.78-6.75 (m, 1H), 3.60 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.8, 136.5, 129.2, 128.8, 128.4, 125.8, 125.8, 122.5, 119.9, 119.3, 117.1, 113.1, 110.6, 9.7. HRMS (ESI) calcd for $C_{15}H_{13}N_2Cl$ [$(M+H)^+$]: 257.0840; found, 257.0846.

4-Fluoro-2-(3-methyl-1*H*-indol-1-yl)aniline (3f)[20]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (dd, *J* = 6.4 Hz, 2.0 Hz, 1H), 7.18-7.12 (m, 1H), 7.09-7.07 (m, 1H), 6.94-6.88 (m, 3H), 6.73 (dd, *J* = 8.8 Hz, 5,2 Hz, 1H), 3.38 (s,1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7 (d, $^1J_{C,F}$ = 237 Hz), 139.4 (d, $^4J_{C,F}$ = 3Hz), 136.6, 129.2, 125.8, 125.6 (d, $^3J_{C,F}$ =10 Hz), 122.5, 119.9, 119.2, 116.9 (d, $^3J_{C,F}$ =7Hz),115.7 (d, $^2J_{C,F}$ = 22 Hz), 115.3 (d, $^2J_{C,F}$ = 23 Hz), 113.1, 110.6, 9.6.

5-Methyl-2-(3-methyl-1*H*-indol-1-yl)aniline (3g)

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 6.4 Hz, 2.4 Hz, 1H), 7.20-7.08 (m, 3H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 0.8 Hz, 1H), 6.64 (d, J= 10.0 Hz, 2H), 3.46 (s, 2H), 2.37 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =142.8, 139.0, 136.9, 129.0, 128.4, 126.3, 122.8, 122.1, 119.5, 119.4, 119.0, 116.8, 112.2, 110.6, 21.3, 9.7. HRMS (ESI) calcd for $C_{16}H_{16}N_2Cl$ [$(M+H)^+$]:

237.1386; found, 237.1389.

5-Chloro-2-(3-methyl-1*H*-indol-1-yl)aniline (3h)

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (dd, *J* = 6.2 Hz, 2.2 Hz, 1H), 7.22-7.15 (m, 2H), 7.08-7.05 (m, 2H), 6.91 (s, 1H), 6.81 (d, *J* = 2.2 Hz, 1H), 6.78 (dd, *J* = 8.3 Hz, 2.2 Hz, 1H), 3.59 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.2, 136.6, 134.3, 129.6, 129.1, 125.9, 123.6, 122.4, 119.8, 119.2, 118.4, 115.8, 112.9, 110.5, 9.7. HRMS (ESI) calcd for $C_{15}H_{13}N_2Cl$ [$(M+H)^+$]: 257.0840; found, 257.0842.

5-Fluoro-2-(3-methyl-1*H*-indol-1-yl)aniline (3i)

Light yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63-7.60 (m, 1H), 7.18-7.14 (m, 2H), 7.09-7.03 (m, 2H), 6.89 (d, *J* = 1.2 Hz, 1H)，6.50-6.45 (m, 2H), 3.56 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.6 (d, $^1J_{C,F}$ = 243 Hz), 145.0 (d, $^3J_{C,F}$ = 11 Hz), 136.9, 130.1 (d, $^3J_{C,F}$ = 11 Hz), 129.0, 126.2, 122.4, 121.1 (d, $^4J_{C,F}$ = 2 Hz), 119.7, 119.2, 112.6, 110.5, 105.2 (d, $^2J_{C,F}$ = 23 Hz), 102.7 (d, $^2J_{C,F}$ = 26 Hz). HRMS (ESI) calcd for $C_{15}H_{13}N_2F$ [$(M+H)^+$]: 241.1136; found, 241.1134.

5-Bromo-2-(3-methyl-1*H*-indol-1-yl)aniline (3j)

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ =7.62 (dd, *J* = 5.8 Hz, 2.6 Hz, 1H), 7.19-7.13 (m, 2H), 7.06 (dd, *J* = 5.8 Hz, 2.6 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 2.4 Hz, 1H), 6.91-6.88 (m, 2H), 3.54 (s,2H), 2.36 (s. 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.4, 136.6, 129.9, 129.1, 125.8, 124.1, 122.5, 122.3, 121.4, 119.8, 119.2, 118.7, 113.0, 110.5, 9.7. HRMS (ESI) calcd for $C_{15}H_{13}N_2Br$ [$(M+H)^+$]: 301.0334; found, 301.0330.

4,5-Dichloro-2-(3-methyl-1*H*-indol-1-yl)aniline (3k)

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 6.4 Hz, 2,4 Hz, 1H), 7.23 (s, 1H), 7.19-7.16 (m, 2H), 7.07 (dd, *J* = 6.0 Hz, 2,0 Hz, 1H), 6.88 (s, 2H), 3.62 (s, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 136.5, 132.4, 129.8, 129.2, 125.6, 124.5, 122.7, 120.6, 120.1, 119.3, 117.0, 113.5, 110.4, 9.7. HRMS (ESI) calcd for $C_{15}H_{12}N_2Cl_2$ [$(M+H)^+$]: 291.0540; found, 291.0448.

2-(1*H*-indol-2-yl)aniline (3l)

A mixture of phenylhydrazine (10 mmol) and 1-(2-aminophenyl)ethanone (10mmol) in 20mL EtOH with AcOH (5 mmol%) were stirred at room temperature for 6 hours, and then 20 mL PPA was added and the temperature rised to 100 ^{o}C for 2h. Next, the reaction mixture was poured into water (100 mL), and Na_2CO_3 was added slowly until the PH =7. And the mixture was extracted with ethyl acetate three times (3×30 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate as eluent = 1:2 to provide the desired product.[35] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.22-7.10 (m, 3H), 6.93-6.84 (m, 2H), 6.72 (t, *J* = 0.9 Hz, 1H), 4.40 (s, 2H);

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.9, 136.2, 135.9, 129.3, 129.1, 128.9, 122.2, 120.4, 120.2, 119.2, 118.9, 116.6, 110.8, 101.6.

2-(1*H*-benzo[*d*]imidazol-2-yl)aniline (3m)[36]

A mixture of benzene-1,2-diamine (10 mmol) and c 1*H*-benzo[d][1,3]oxazine-2,4-dione (10 mmol) were refluxed in AcOH in 100°C for 2h. Then the mixture was extracted with ethyl acetate three times (3×30 mL). The combined organic layers were dried with $MgSO_4$ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate as eluent = 1:2 to provide the desired product (**3m-3o**). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.65 (s, 1H), 7.85 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.58 (s, 2H), 7.20 (m, 5H), 6.85 (dd, J = 8.0Hz, 0.8 Hz, 1H), 6.68 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): δ = 163.0, 148.7, 130.9, 127.7, 122.2, 116.6, 115.4, 110.6.

2-(5,6-Dimethyl-1*H*-benzo[d]imidazol-2-yl)aniline (3n)[36]

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.38 (s, 1H), 7.81 (dd, J = 7.8 Hz, 1.0Hz, 1H), 7.41 (s, 1H)， 7.26-7.21 (m, 3H), 7.14-7.10 (m, 1 H), 6.82 (d, J = 7.6 Hz, 1H), 6.65-6.61 (m, 1H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.2, 148.5, 142.1, 132.5, 131.3, 130.5, 130.0, 127.5, 118.8, 116.5, 115.4, 111.3, 111.0, 20.5.

2-(5,6-Difluoro-1*H*-benzo[d]imidazol-2-yl)aniline (3o)

Light yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.90 (s, 1H), 7.83 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.70 (s, 1H), 7.53 (s, 1H), 7.20 (td, J = 7.6 Hz, 1.2 Hz, 3H), 6.87 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 6.67 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ =155.0, 148.6, 148.6 (dd, $^1J_{C,F}$ = 239 Hz, $^2J_{C,F}$ = 15 Hz), 148.1 (dd, $^1J_{C,F}$ = 235 Hz, $^2J_{C,F}$ = 15 Hz), 138.9 (d, $^3J_{C,F}$ =9 Hz), 131.2, 129.6 (d, $^3J_{C,F}$ = 12 Hz), 127.7, 116.9, 115.5, 110.1, 106.1 (d, $^2J_{C,F}$ = 20 Hz), 99.4 (d, $^2J_{C,F}$ = 21 Hz). HRMS (ESI) calcd for $C_{13}H_{11}N_3F_2$ [$(M+H)^+$]:248.0993; found, 248.0990.

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ASSOCIATED CONTENT

Supporting Information Available: The detailed experimental procedure and copies of ^{1}H NMR and ^{13}C NMR spectra of all compounds is available free of charge via the Internet:// pubs. acs. org.

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