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Synthesis of 4-Aryl Pyrrolo[1,2-α]quinoxalines *via* Iron-Catalyzed Oxidative Coupling from an Unactivated Methyl Arene

Jiwon Ahn, Seok Beom Lee, Injae Song, Simin Chun, Dong-Chan Oh, and Suckchang Hong*

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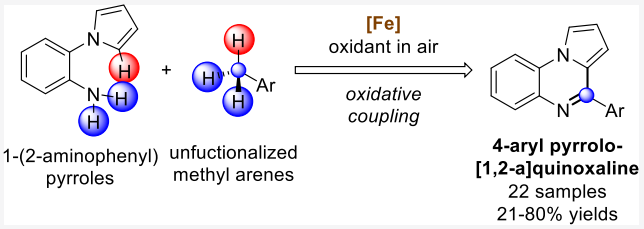
ABSTRACT: Herein, we describe the direct synthesis of pyrrolo[1,2-α]quinoxaline *via* oxidative coupling between methyl arene and 1-(2-aminophenyl) pyrroles. Oxidation of the benzylic carbon of the methyl arene was achieved by di-*t*-butyl peroxide in the presence of an iron catalyst, followed by conversion to an activated aldehyde *in situ*. Oxygen played a crucial role in the oxidation process to accelerate benzaldehyde formation. Subsequent Pictet–Spengler-type annulation completed the quinoxaline structure. The protocol tolerated various kinds of functional groups and provided 22 4-aryl pyrrolo[1,2-α]quinoxalines when various methyl arene derivatives were used. The developed method proceeded in air, and all catalysts, reagents, and solvents were easily accessible.



INTRODUCTION

Among nitrogen-containing heterocycles, pyrrolo[1,2-α]-quinoxalines are important building blocks found in biologically active compounds and are considered to be privileged substructures for drug design.[1] In particular, substitution at the C-4 position of the pyrrolo[1,2-α]quinoxaline motif results in derivatives that possess a variety of biological activities (Figure 1), such as anticancer,[2] antimalarial,[3] and antiproliferative activities.[4] They can also act as human protein kinase CK2 inhibitors,[5] glucagon receptor antagonists,[6] and 5-HT$_3$ receptor antagonists.[7] In addition to exhibiting biological activity, some derivatives of 4-aryl pyrrolo[1,2-α]quinoxalines have excellent fluorescence and photophysical properties that are of great importance in the synthesis of biomarkers, dyes, and materials.[8]

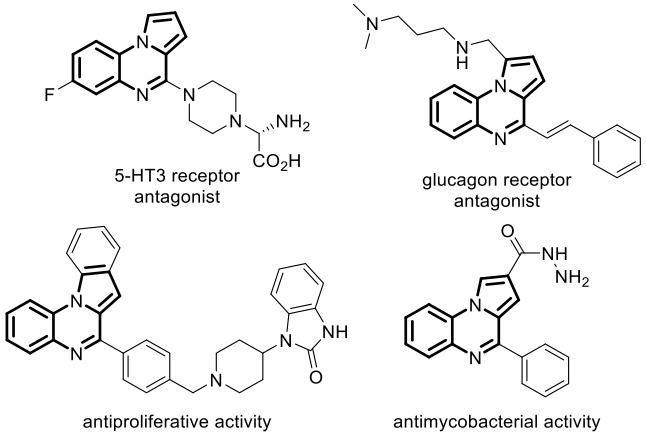


Figure 1. Selected examples of biologically active pyrrolo[1,2-α]quinoxalines.

Owing to these characteristic features, various methods have been developed for the synthesis of 4-aryl pyrrolo[1,2-α]quinoxalines (**3**) in recent decades (Scheme 1). The most common synthetic approach is oxidative cyclization of 1-(2-aminophenyl)pyrrole (**1**) with aromatic aldehyde.[9] These modified Pictet–Spengler reactions can be achieved under aerobic heating,[9a] catalyzed by Lewis or Brønsted acids,[9b–e] or mediated by TEMPO oxoammonium salts.[9f] Even though aldehyde substrates have been applied well for the synthesis of pyrrolo[1,2-α]quinoxalines, they have some shortcomings because of their lability. Several research groups have reported the synthesis of 4-aryl pyrrolo[1,2-α]quinoxalines from benzyl amine instead of aldehyde.[10] In addition, the condensation of 1-(2-aminophenyl)-pyrrole with ketone,[11] carboxylic acid,[12] 1,3-diketone,[13] amino acid,[14] or ether[15] was also reported for the synthesis of 4-aryl pyrrolo[1,2-α]quinoxalines. Although the various synthetic methods mentioned above have provided 4-aryl pyrrolo[1,2-α]quinoxalines, they also involve an electrophilic carbon synthon with specific functional groups such as carbonyl, hydroxyl, and amine groups, which limits the substrate scope. To the best of our knowledge, no direct synthetic strategy has been explored for 4-aryl pyrrolo[1,2-α]quinoxalines by employing unactivated methyl arene. Over

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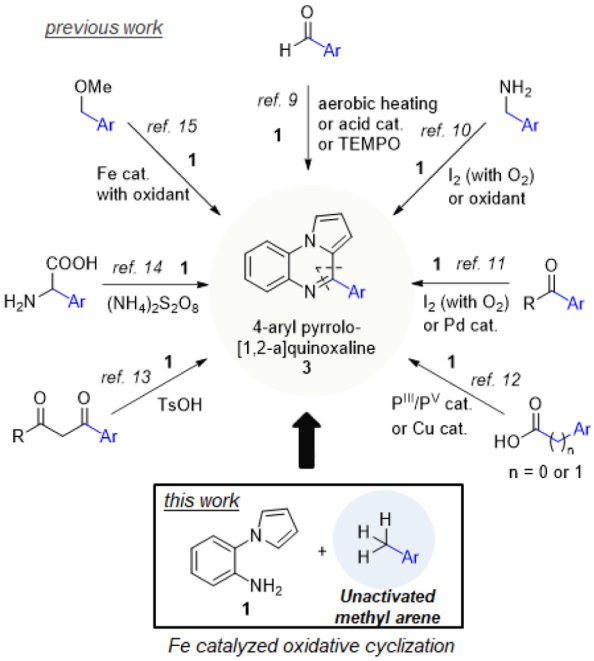
Scheme 1. Synthesis of 4-Aryl Pyrrolo[1,2-α]quinoxalines (3) from 1-(2-Aminophenyl)-pyrrole (1)

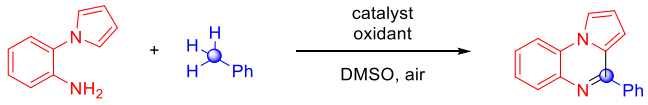


the years, various types of base-metal-catalyzed oxidative annulations using peroxide have been applied to the construction of heterocycles.[16] Recently, our group also reported the direct synthesis of quinazolinone and quinolone *via* iron-catalyzed oxidative cyclization from unactivated methyl arene.[17] In this strategy, direct functionalization of C−H bonds forms C−C or C−heteroatom bonds and offers substantial benefits owing to the remarkable potential for atom economy and environmental sustainability. In particular, iron has attracted considerable attention because of its low cost, abundance, and low toxicity. As part of our program on developing a new synthetic method for N-heterocycles, we investigated iron-catalyzed oxidative reactions for the synthesis of pyrrolo[1,2-α]quinoxalines. In this report, we disclose a new one-pot annulation between 1-(2-aminophenyl)pyrrole and methyl arene through *in situ* oxidative activation of a benzylic sp^3 C−H bond (Scheme 1 down).

RESULTS AND DISCUSSION

We began our studies by optimizing various parameters of the reaction of 1-(2-aminophenyl)-pyrrole (**1a**) with toluene (**2a**). Based on our previous study on the synthesis of quinazolinone,[17a] $FeCl_3·6H_2O$ and di-*t*-butyl peroxide (DTBP) were employed as a preliminary catalyst and oxidant, respectively, in an air environment. As shown in Table 1, the desired quinoxaline product **3aa** was obtained in 61% yield when 15 mol % $FeCl_3·6H_2O$ and 3 equiv of DTBP were used in the reaction (entry 1). Based on this promising result, various types of catalysts and oxidants were employed in the reaction to improve the formation of **3aa** (entries 2−5). However, we could not find more efficient ones. Interestingly, the yield of **3aa** could be increased depending on the amount of DTBP. As we decreased the amount of DTBP to 1 equiv relative to **1a**, clear conversion was observed by thin-layer chromatography (TLC), and **3aa** was obtained in higher yield (entries 6−7). However, at least 1 equiv of DTBP was necessary to achieve satisfactory conversion (entry 8). The highest yield of **3aa** was

Table 1. Optimization of the Reaction Conditions[a]



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

entry	catalyst	oxidant (equiv)	T (°C)	time (h)	yield[b] (%)
1	$FeCl_3·6H_2O$	DTBP (3)	110	16	61
2	$FeCl_3·6H_2O$	TBHP[c] (3)	110	41	49
3	$FeCl_3·6H_2O$	H_2O_2[d] (3)	110	46	10
4	$FeCl_2·4H_2O$	DTBP (3)	110	19	57
5	$Fe(NO_3)_3·9H_2O$	DTBP (3)	110	22	53
6	$FeCl_3·6H_2O$	DTBP (2)	110	18	62
7	$FeCl_3·6H_2O$	DTBP (1)	110	18	68
8	$FeCl_3·6H_2O$	DTBP (0.5)	110	20	57
9	**$FeCl_3·6H_2O$**	**DTBP (1)**	**120**	**40**	**77**
10	no catalyst	DTBP (1)	120	44	47
11	no catalyst	DTBP (2)	120	40	29

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (18 mmol), the catalyst (15 mol %), and the oxidant in DMSO (0.5 mL) in air. [b]Isolated yield. [c]70% aqueous solution. [d]35% aqueous solution.

achieved when the reaction temperature was increased to 120 °C and the reaction time was increased to 40 h (entry 9). A control experiment was also performed, and a significant decrease in yield was observed in the absence of the catalyst (entries 10 and 11). Similar to the iron catalytic system (entries 6−7), excess DTBP showed a lower yield of **3aa** with a messy mixture in TLC. We predicted that this excessive use of DTBP induces various side reactions *via* a radical pathway. Based on the above results, we chose 1-(2-aminophenyl)-pyrrole **1** (0.3 mmol), methyl arene **2** (18 mmol), $FeCl_3·6H_2O$ (15 mol %), and DTBP (0.3 mmol) in dimethyl sulfoxide (DMSO, 0.5 mL) at 120 °C for 40 h in air as the optimal reaction conditions.

We applied the optimized conditions for the annulation of **1a** with a wide range of methyl arenes **2** to explore the reaction scope (Table 2). A diverse array of methyl arenes bearing electron-donating and electron-withdrawing groups could react with **1a**, and the corresponding quinoxaline products **3** were obtained. Generally, methyl arenes with electron-donating groups, such as methyl groups, showed better results than those with electron-withdrawing groups (**3ab**−**3ae** vs **3ag**−**3al**). This tendency might occur because the electron-donating group could stabilize the benzyl cationic charge that is generated during benzylic carbon activation. However, methyl arene substituted with a methoxy group gave the desired product **3af** in low yield with many side products. Strong electron-withdrawing groups, such as nitrile-substituted methyl arene, could also be applied in the reaction system to afford quinoxaline product **3al** in moderate yield. The steric effect also influenced the formation of the desired product. The para-substituted methyl arene showed higher yields than ortho- and meta-substituted analogues (**3ab**−**3ae**). Additionally, naphthalene and heteroaromatic groups, such as thiophene and pyridine, could be substituted at the 4-position of pyrrolo[1,2-α]quinoxalines (**3am**−**3ao**).

Next, we employed various types of 2-aminophenyl-pyrroles for further extension of the reaction scope (Table 3). 6-Methyl-substituted **1b** afforded the corresponding products **3ba** in good yield. Regardless of the electron density, the position of the substituent played a crucial role in the reaction.

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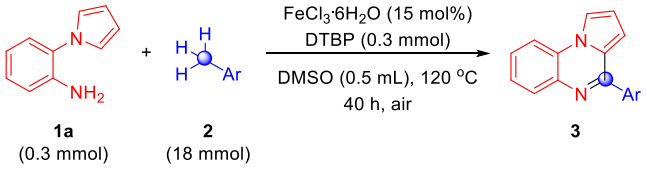
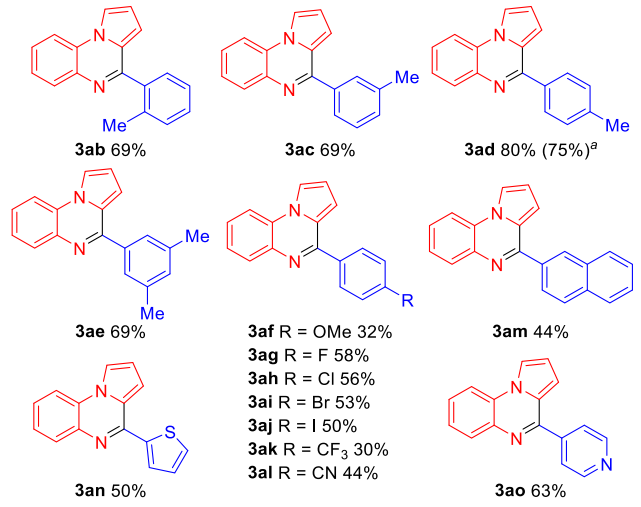
Table 2. Scope of Methyl Arenes 2[a]

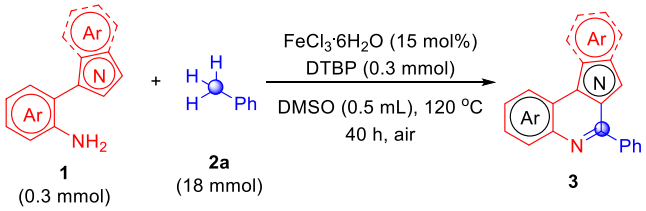


1a (0.3 mmol) + **2** (18 mmol) → **3**

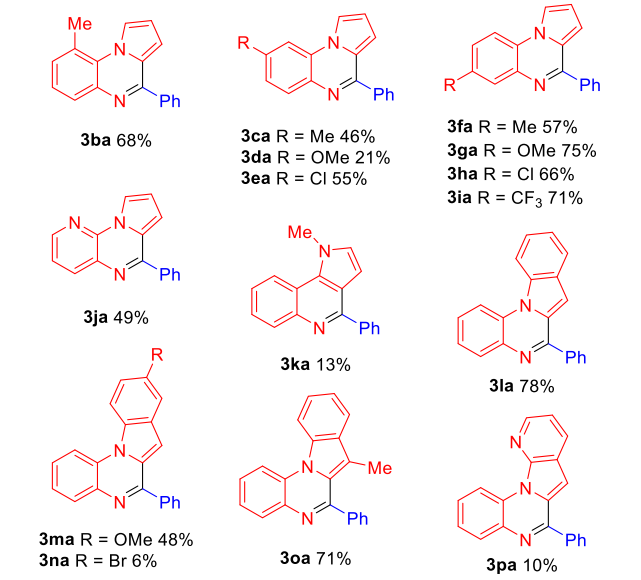


[a]All presented yields are isolated yields. [b]1 mmol scale reaction of **1a**, DTBP (1.2 mmol) was used.

Table 3. Scope of 2-Aminoaryl-pyrroles and -Indoles (1)[a]



1 (0.3 mmol) + **2a** (18 mmol) → **3**



[a]All presented yields are isolated yields.

The 4-substituted 1-(2-aminophenyl)-pyrroles were more reactive than the 5-substituted analogues (**3ca**–**3ea** vs **3fa**–**3ia**). Additionally, 1-(2-amino-6-pyridyl)-pyrrole could also be applied in the reaction to yield annulated product **3ja**. We hypothesized that the 3-position of the pyrrole can participate in the annulation instead of the 2-position of pyrrole. However, because of the low nucleophilicity of the 3-position of the pyrrole, 1-methyl-2-(2-aminophenyl)-pyrrole gave pyrrolo[3,2-*c*]quinoline product **3ka** in low yield. In addition to pyrrole substrates, 1-(2-aminophenyl)-indole substrates were also explored in the reaction system. Depending on the substituents on the indole moiety, the corresponding 4-phenyl indolo[1,2-*α*]quinoxaline products were synthesized in a wide range of yields. The desired products were obtained in moderate to good yields from simple and 3-methyl/5-methoxy indole substrates (**3la**, **3ma**, **3oa**), whereas very poor yields were observed from 5-bromo indole and pyrrolo[2,3-*b*]pyridine substrates (**3na**, **3pa**). Based on these results, we expected that the electron density of indole is significantly influenced in the annulation step, which would affect the whole reaction procedure.

After exploration of the reaction scope, the fluorescence characteristics of **3aa**, **3af**, **3ah**, **3ak**, **3al**, **3ao**, **3ga**, **3ia**, and **3la** were evaluated systematically (Figures 2 and 3). The maximum

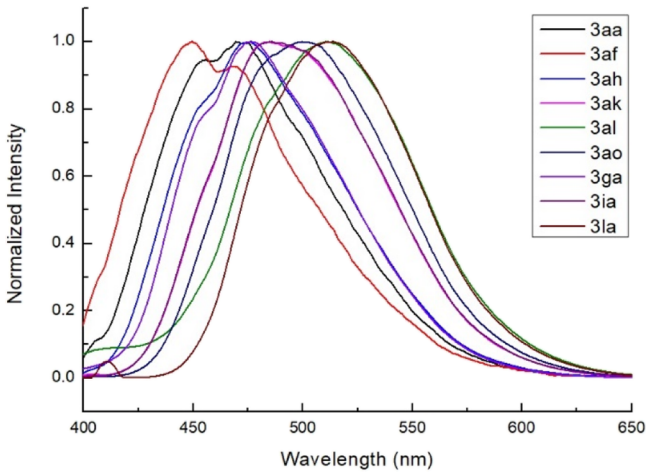


Figure 2. Normalized fluorescence emission spectra of pyrrolo[1,2-*α*]quinoxalines in DMSO.

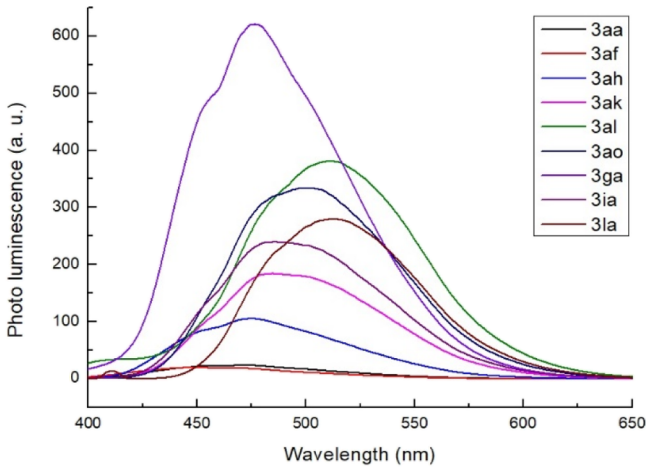


Figure 3. Fluorescence emission spectra of pyrrolo[1,2-*α*]-quinoxalines in DMSO.

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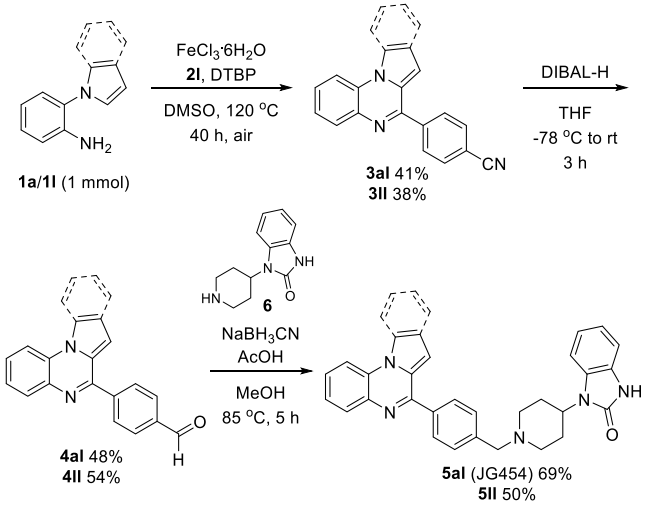
wavelengths and intensities of the emission spectra varied depending on the substituents. As shown in Figure 2, these quinoxaline products showed fluorescence within the range of 445−515 nm. A red shift was induced by electron-withdrawing substituents. For example, nitrile- or pyridine-substituted pyrrolo[1,2-α]quinoxalines showed a large red shift to give maximum wavelengths over 500 nm (**3al**, **3ao**). In the case of indolo[1,2-α]quinoxaline, a red shift in the emission was also observed over 500 nm (**3la**). Interestingly, most of the quinoxaline derivatives exhibited stronger fluorescence emission than simple pyrrolo[1,2-α]quinoxaline **3aa** (Figure 3). Substitution at the 7-position (para-position to pyrrole) pyrrolo[1,2-α]quinoxalines appeared to enhance the fluorescence intensity, regardless of the electron density (**3ga**, **3ia**). In the case of the substituent of the 4-phenyl group, electron-withdrawing groups increased the fluorescence emission (**3al**, **3ao**, **3ak**, **3ah**), whereas electron-donating groups decreased the fluorescence emission (**3af**). Moreover, indolo[1,2-α]-quinoxaline **3la** showed more than 10 times higher emission than pyrrolo[1,2-α]quinoxaline **3aa**. All these findings suggest potential applications of the products in the design of functional materials or biosensors.

To show the additional synthetic applications, we also tried to convert pyrrolo[1,2-α]quinoxaline products **3al** and **3ll** to antiproliferative compounds[4] (Scheme 2). Large-scale (1 mmol) reaction was carried out to prepare quinoxaline **3al** and **3ll**. DIBAL-H reduction of the nitrile group afforded the corresponding aldehydes **4al** and **4ll**, respectively. After reductive amination with **6**, antiproliferative compound JG454 (**5al**) and its indole analogue **5ll** were obtained. Compared with the previous synthesis, the total yield is relatively low. However, the strength of this synthetic method is a shortcut to the integrated route for the JG454 family.

Scheme 2. Synthetic Application for Antiproliferative Compounds



To investigate the mechanism of the reaction, we focused on the aldehyde intermediate because the corresponding aldehydes were observed in most reactions. The representative substrate, toluene, was alternated to 2-methylnaphthalene **2m** due to the volatility and instability of benzaldehyde. Initially, we assumed oxygen as an oxidizing agent along with DTBP and not DMSO. According to our previous synthesis of quinazolinone,[17a] DMSO reacted with nucleophilic substrates as a coupling partner rather than being an oxidizing agent under similar reaction conditions. Since a carbon radical adjacent to the sulfur was generated by DTBP, the radical directly participated in the intermolecular annulation. Based on this hypothesis, we illustrated a correlation graph showing the aldehyde formation depending on the oxygen and the iron catalyst as shown in Figure 4. Both the iron catalyst and the oxygen affected the oxidation process. Comparing the two variables, the role of oxygen was more important.

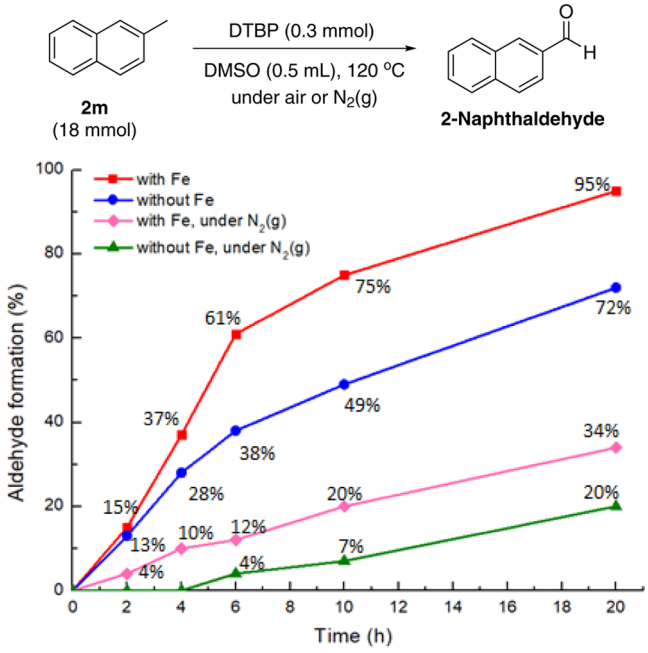


Figure 4. Formation of 2-naphthaldehyde depending on reaction parameters.

Further control experiments were also performed to understand the mechanism (Scheme 3). The radical scavenger TEMPO disrupted the reaction, and benzylated TEMPO was obtained (eq 1). This result confirmed that a benzyl radical intermediate was generated during oxidation. We presumed that *t*-butoxy benzyl ether **2a−O*t*Bu** might be another possible intermediate that can be generated from benzyl radicals. However, it gave a lower yield of **3aa** (eq 2, left). Thus, we can assume that the oxidation pathway *via* **2a−O*t*Bu** is not preferred under the reaction conditions. In addition, since the reaction did not proceed at all without DTBP, the direct N-alkylation of **2a−O*t*Bu** could be excluded. When preoxidized benzaldehyde reacted with **1a** without DTBP, **3aa** was obtained in a yield similar to that obtained under standard conditions (eq 2, right). Therefore, the final oxidation and aromatization process readily occurred under aerobic conditions to afford a pyrrolo[1,2-α]quinoxaline structure. To explore synthetic possibility for dihydropyrrolo[1,2-α]-quinoxaline, we also applied ethylbenzene and diphenylmethane under standard conditions instead of toluene substrates (eq 3). As expected, the oxidation process occurred, and a significant amount of ketones was obtained. However, no dihydropyrrolo[1,2-α]quinoxaline products were observed in the reaction. This result indicates that the ketone intermediate could not participate in the subsequent annulation process. Next, the reaction was performed in the presence of argon gas. Significant formation of **3aa** was observed, and benzylated **1a**−

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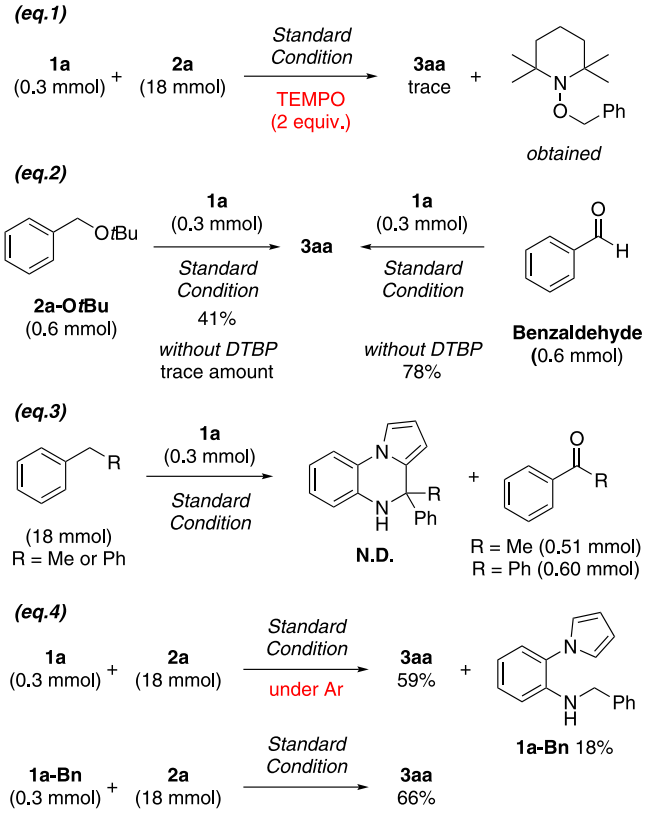
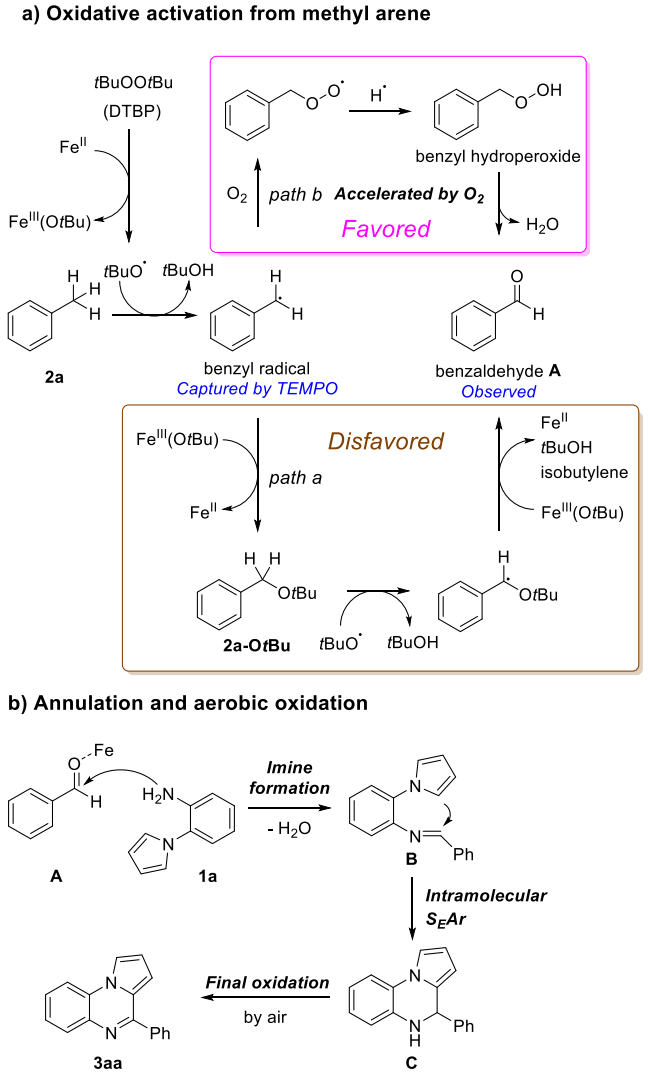
Scheme 3. Investigation of the Reaction Mechanism



Bn was also obtained as a side product (eq 4). In the absence of oxygen, we could not observe clear benzaldehyde spots by TLC during the reaction. Thus, direct N-alkylation from benzyl radicals, followed by annulation, could not be ruled out as a background reaction. Additionally, it was supposed that anilic amine reacts faster in the annulation than the pyrrole group. Our hypothesis was confirmed by the formation of **3aa** from **1a**−**Bn** under the standard conditions.

Based on the above control experiments and previous studies,[17] we proposed a rational mechanism (Scheme 4). There are two possible pathways to generate benzaldehyde intermediates from toluene **2a** (*path a* and *path b*). First, a *t*-butoxy radical is generated from DTBP with the assistance of an iron catalyst. The *t*-butoxy radical abstracts H•, which is located at the benzyl position of toluene **2a**, to form a benzyl radical. As mentioned above, DMSO, used as a solvent, can also generate a methyl radical by DTBP. We expected that this radical species helps to form the benzyl radical through radical propagation. In *pathway a*, *t*-butoxy benzyl ether **2a**−**OtBu** can be formed as an intermediate by the coupling of benzyl radicals with the iron *t*-butoxy salt. One more oxidation process occurs by DTBP and the iron catalyst to produce benzaldehyde **A**. However, **2a**−**OtBu** is considered an insufficient substrate in the oxidation process (refer to eq 2 in Scheme 2), and 2 equiv of DTBP is required theoretically in *pathway a*, whereas only 1 equiv of DTBP was used in the developed reaction; another alternative oxidation *pathway b* is suggested. In the presence of oxygen gas, benzyl hydrogen peroxide was generated *via* the coupling of benzyl radicals with O_2, followed by the abstraction of H• from the solvent (**2a** or DMSO). Then, benzyl hydrogen peroxide liberates water and is converted to benzaldehyde **A** under the reaction conditions. Based on the results shown in Figure 4, oxygen played a crucial role in oxidation; thus,

Scheme 4. Proposed Mechanism



pathway b is more preferred than *pathway a* under an air atmosphere. After the formation of benzaldehyde **A**, it reacted with 1-(2-aminophenyl)pyrrole **1a**, and imine **B** was generated. Subsequently, annulation of imine **B** through intramolecular electrophilic aromatic substitution of the pyrrole moiety, followed by aerobic oxidation, gave final product **3aa**. However, we could not exclude direct amination of **1a** with a benzyl radical intermediate.

■ CONCLUSIONS

In summary, we have developed an iron-catalyzed oxidative annulation of 1-(2-aminophenyl)pyrrole with an unreactive methyl arene for the synthesis of 4-aryl pyrrolo[1,2-α]-quinoxalines. Benzaldehyde was suggested as a key intermediate generated by oxidation of methyl arene in the presence of DTBP and an iron catalyst, and we found that oxygen plays a crucial role in this oxidative process. The benzaldehyde intermediate underwent Pictet−Spengler-type annulation, condensation with 1-(2-aminophenyl)pyrrole, followed by electrophilic aromatic substitution, to afford the annulated pyrrolo[1,2-α]quinoxaline product. Based on control experiments and previous studies, we suggested a possible reaction mechanism, especially describing the oxidation process, including the formation of benzaldehyde

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as a key intermediate. Importantly, this is the first report on the synthesis of 4-aryl pyrrolo[1,2-α]quinoxalines *via* intermolecular oxidative coupling from methyl arene. The reaction was performed under an air atmosphere, and all reagents and catalysts are inexpensive and readily available. The developed method also tolerates various functional groups, allowing further functionalization. Further expansion of the oxidative annulation from methyl arene to approach other aryl-substituted N-heterocycles is under investigation by our group.

EXPERIMENTAL SECTION

General Information. *Experimental Details.* All commercially available reagents and solvents (purchased from Sigma-Aldrich, TCI, Alfa Aesar, Acros, Combi-Blocks) were used without further purification unless otherwise noted. All reactions were carried out in an oven-dried round-bottom flask or borosilicate glass tubes purchased from Fisher Scientific (Fisherbrand disposable borosilicate glass tubes with threaded end). Reactions were monitored by TLC on a silica gel 60 F_{254} plate (Merck, Darmstadt, Germany) using UV illumination at 254 and 365 nm (VL-4.LC, Vilber Lourmat, Eberhardzell, Germany). Column chromatography was performed on silica gel (230−400 mesh; Zeochem, Lake Zurich, Switzerland) using a mixture of hexane and EtOAc as eluents.

Spectral Data. Melting points were measured on a Büchi B-540 melting point apparatus and were not corrected. Nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were recorded on a JEOL JNM-ECZ400s [400 MHz (^{1}H), 100 MHz (^{13}C), 376 MHz (^{19}F)] spectrometer. The chemical shifts are given in parts per million on the delta (δ) scale. The solvent peak was used as a reference value; for ^{1}H NMR: $CDCl_3$ = 7.26 ppm, DMSO-d_6 = 2.50 ppm; for ^{13}C NMR: $CDCl_3$ = 77.16 ppm, DMSO-d_6 = 39.52 ppm. Coupling constants (J) are expressed in hertz. All high-resolution mass spectra (HRMS) were recorded using the fast atom bombardment (FAB) ionization method on a JMS-700 MStation mass spectrometer (JEOL, Tokyo, Japan).

Optical Characterization. The UV−vis absorption spectra of the synthesized compounds were recorded at ambient temperature using a Lambda 25 UV−vis spectrometer (PerkinElmer, Waltham, MA, United States). Fluorescence emission spectra were recorded with an FP-6500 spectrofluorometer (JASCO, Tokyo, Japan) with slit widths of 3 nm for excitation and also 3 nm for emission. UV−vis absorption and fluorescence emission spectra were both recorded at a concentration of 10 μM in the DMSO solvent.

Preparation of 2-Aminoaryl-pyrroles Substrate. Starting compounds **1a**−**1f** and **1h**−**1l** were synthesized from the corresponding 2-nitroaryl-pyrroles through the similar procedures with the literature. **1g** is commercially available.

Method A:[18] Dissolve 1-(2-nitrophenyl)-1*H*-pyrroles in ethanol (0.3 M), and add Pd/C (10 mol % Pd) to the mixture. Purge the reaction with H_2 (1 atm) for 10 min, and hold under a H_2 atmosphere at room temperature overnight. After complete consumption of 1-(2-nitrophenyl)-1*H*-pyrrole, filtrate the reaction mixture over Celite, and then remove the solvent under reduced pressure thoroughly. Recrystallization of the mixture was performed using diethylether.

Method B:[9a] 1-(2-Nitrophenyl)-1*H*-pyrroles were dissolved in ethanol (0.08 M), and powdered zinc (10.2 equiv) was added to the vigorously stirred solution. 90% formic acid (11.8 equiv) was slowly added to the reaction mixture at room temperature while stirring vigorously. After refluxing at 80 °C for 2 h, cool it to room temperature and filtrate the reaction mixture over Celite. After removing the solvent under reduced pressure thoroughly, the reaction mixture was poured into water (100 mL) and extracted with EtOAc three times. The residue was purified by flash column chromatography using hexane/EtOAc as the eluent.

*2-(1H-Pyrrol-1-yl)aniline (**1a**).* Following method A, 1-(2-nitrophenyl)-1*H*-pyrrole (12.8 mmol, 2.41 g) was used as the starting material. After recrystallization, **1a** was obtained as a white solid (1.58 g, 78% yield); mp 93−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14−7.19 (m, 2H), 6.84 (t, J = 2.2 Hz, 2H), 6.77−6.82 (m, 2H), 6.34 (t, J = 2.2 Hz, 2H), 3.71 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.6, 128.7, 128.0, 127.3, 121.9, 119.0, 116.6, 109.6; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{10}H_{10}N_2$, 158.0844; found, 158.0845.

*3-Methyl-2-(1H-pyrrol-1-yl)aniline (**1b**).* Following method A, 1-(2-methyl-6-nitrophenyl)-1*H*-pyrrole (4.95 mmol, 1 g) was used as the starting material. After recrystallization, **1b** was obtained as a white solid (791 mg, 93% yield); mp 37−39 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, J = 7.8 Hz, 1H), 6.64−6.67 (m, 4H), 6.36 (d, J = 1.8 Hz, 2H), 3.51 (s, 2H), 2.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.0, 137.1, 128.9, 126.9, 121.6, 119.9, 113.3, 109.4, 17.3; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{11}H_{13}N_2$, 173.1079; found, 173.1074.

*4-Methyl-2-(1H-pyrrol-1-yl)aniline (**1c**).* Following method A, 1-(5-methyl-2-nitrophenyl)-1*H*-pyrrole (8.41 mmol, 1.7 g) was used as the starting material. After recrystallization, **1c** was obtained as a white solid (525 mg, 36% yield); mp 59−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 6.4 Hz, 2H), 6.83 (t, J = 2.1 Hz, 2H), 6.73 (dd, J = 6.7, 2.1 Hz, 1H), 6.33 (t, J = 2.1 Hz, 2H), 3.59 (s, 2H), 2.27 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 139.5, 129.2, 128.1, 127.7, 127.6, 121.8, 116.4, 109.4, 20.4; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{11}H_{12}N_2$, 172.1000; found, 172.0997.

*4-Methoxy-2-(1H-pyrrol-1-yl)aniline (**1d**).* Following method B, 1-(5-methoxy-2-nitrophenyl)-1*H*-pyrrole (4.583 mmol, 1 g) was used as the starting material. After column chromatography (hexane/EtOAc = 10:1), **1d** was obtained as a white solid (385 mg, 45% yield); mp 91−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (t, J = 2.3 Hz, 2H), 6.75−6.81 (m, 3H), 6.35 (q, J = 2.0 Hz, 2H), 3.75 (s, 3H), 3.46 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.6, 135.5, 128.2, 121.8, 117.4, 114.9, 112.5, 109.6, 56.0; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{11}H_{12}N_2O$, 188.0950; found, 188.0949.

*4-Chloro-2-(1H-pyrrol-1-yl)aniline (**1e**).* Following method B, 1-(5-chloro-2-nitrophenyl)-1*H*-pyrrole (2.695 mmol, 600 mg) was used as the starting material. After column chromatography (hexane/EtOAc = 10:1), **1e** was obtained as a white solid (306 mg, 59% yield); mp 92−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11−7.15 (m, 2H), 6.82 (t, J = 2.1 Hz, 2H), 6.73 (d, J = 8.7 Hz, 1H), 6.34 (t, J = 2.3 Hz, 2H), 3.73 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 140.8, 128.5, 128.2, 127.1, 122.7, 121.6, 117.0, 110.0; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{10}H_9ClN_2$, 192.0454; found, 192.0454.

*5-Methyl-2-(1H-pyrrol-1-yl)aniline (**1f**).* Following method A, 1-(4-methyl-2-nitrophenyl)-1*H*-pyrrole (7.42 mmol, 1.5 g) was used as the starting material. After recrystallization, **1f** was obtained as a beige solid (1.08 g, 85% yield); mp 88−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 (d, J = 7.8 Hz, 1H), 6.81 (t, J = 2.1 Hz, 2H), 6.59−6.63 (m, 2H), 6.33 (t, J = 2.1 Hz, 2H), 3.64 (s, 2H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 141.9, 138.8, 127.1, 125.3, 122.0, 119.3, 116.7, 109.3, 21.3; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{11}H_{13}N_2$, 173.1079; found, 173.1081.

*5-Chloro-2-(1H-pyrrol-1-yl)aniline (**1h**).* Following method B, 1-(4-chloro-2-nitrophenyl)-1*H*-pyrrole (2.695 mmol, 600 mg) was used as the starting material. After column chromatography (hexane/EtOAc = 10:1), **1h** was obtained as a white solid (447 mg, 86% yield); mp 85−87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J = 8.3 Hz, 1H), 6.79 (q, J = 1.4 Hz, 3H), 6.74 (dd, J = 8.3, 2.3 Hz, 1H), 6.34 (t, J = 2.1 Hz, 2H), 3.79 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.3, 134.1, 128.3, 126.1, 121.8, 118.4, 115.7, 109.9; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{10}H_9ClN_2$, 192.0454; found, 192.0453.

*2-(1H-Pyrrol-1-yl)-5-(trifluoromethyl)aniline (**1i**).* Following method A, 1-(2-nitro-4-(trifluoromethyl)phenyl)-1*H*-pyrrole (5.62 mmol, 1.44 g) was used as the starting material. After recrystallization, **1i** was obtained as a white solid (772 mg, 61% yield); mp 91−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 7.8 Hz, 1H), 7.03 (d, J = 7.4 Hz, 2H), 6.85 (t, J = 2.1 Hz, 2H), 6.38 (t, J = 2.1 Hz, 2H), 3.94 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 142.3, 131.2 (q, $^2J_{C-F}$ = 32.6 Hz), 130.9 (q, $^2J_{C-F}$ = 32.6 Hz), 130.5 (q, $^2J_{C-F}$ = 32.6 Hz), 130.2 (q, $^2J_{C-F}$ = 32.6 Hz), 129.9, 128.1 (q, $^1J_{C-F}$ = 271.0 Hz), 127.5, 125.4 (q, $^1J_{C-F}$ = 271.0 Hz), 122.7 (q, $^1J_{C-F}$ = 271.0 Hz), 121.5, 119.9 (q, $^1J_{C-F}$ = 271.0 Hz), 115.2 (q, $^3J_{C-F}$ = 3.8 Hz), 115.1 (q, $^3J_{C-F}$ = 3.8 Hz), 115.1 (q, $^3J_{C-F}$ = 3.8 Hz), 115.0 (q, $^3J_{C-F}$ = 3.8 Hz), 112.9 (q,

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$^4J_{C-F}$ = 3.8 Hz), 112.9 (q, $^4J_{C-F}$ = 3.8 Hz), 112.8 (q, $^4J_{C-F}$ = 3.8 Hz), 112.8 (q, $^4J_{C-F}$ = 3.8 Hz), 110.2; ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.68 ppm; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{11}H_{10}F_3N_2$, 227.0796; found, 227.0797.

*2-(1H-Pyrrol-1-yl)pyridin-3-amine (**1j**).* Following method A, 3-nitro-2-(1*H*-pyrrol-1-yl)pyridine (6.872 mmol, 1.3 g) was used as the starting material. After recrystallization, **1j** was obtained as a brown solid (646 mg, 59% yield); mp 84−87 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.72 (dd, J = 4.6, 1.4 Hz, 1H), 7.25 (dd, J = 8.0, 1.6 Hz, 1H), 7.18 (t, J = 2.3 Hz, 2H), 7.10 (q, J = 4.1 Hz, 1H), 6.24 (t, J = 2.3 Hz, 2H), 5.11 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 138.3, 137.1, 136.1, 124.0, 122.9, 120.0, 109.1; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_9H_{10}N_3$, 160.0875; found, 160.0873.

*2-(1-Methyl-1H-pyrrol-2-yl)aniline (**1k**).* Following method A, 1-methyl-2-(2-nitrophenyl)-1*H*-pyrrole (7.418 mmol, 1.5 g) was used as the starting material. After recrystallization, **1k** was obtained as a white solid (1.21 g, 95% yield); mp 38−40 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (td, J = 7.7, 1.6 Hz, 1H), 7.15 (dd, J = 7.4, 1.8 Hz, 1H), 6.77−6.84 (m, 3H), 6.27 (t, J = 3.1 Hz, 1H), 6.21 (q, J = 1.6 Hz, 1H), 3.77 (s, 2H), 3.52 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.9, 131.8, 130.6, 129.2, 122.7, 118.8, 118.0, 115.1, 108.8, 107.7, 34.3; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{11}H_{13}N_2$, 173.1079; found, 173.1082.

*2-(1H-Indol-1-yl)aniline (**1l**).* Following method B, 1-(2-nitrophenyl)-1*H*-indole (4.197 mmol, 1.0 g) was used as the starting material. After column chromatography (hexane/EtOAc = 10:1), **1l** was obtained as a yellow oil (536 mg, 61% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.71 (m, 1H), 7.14−7.29 (m, 6H), 6.86−6.93 (m, 2H), 6.70 (d, J = 3.2 Hz, 1H), 3.40 (br s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.2, 136.5, 129.3, 128.7, 128.7, 128.7, 124.9, 122.3, 121.1, 120.3, 118.6, 116.3, 110.9, 103.3; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{14}H_{12}N_2$, 208.1000; found, 208.0999.

Preparation of 2-Aminoaryl-indole Substrates.[19] To a screw-cap pressure tube, indole (1.0 equiv), CuI (20 mol %), 2-iodoaniline (1.5 equiv), *N*,*N*′-dimethylethylenediamine (80 mol %), K_3PO_4 (2.1 equiv), and toluene (0.6 M) were added. The reaction vessel was fitted with a rubber septum and was evacuated and backfilled with argon gas. The reaction tube was sealed and stirred in a preheated oil bath at 110 °C for 24 h. After completion of the reaction, the mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and filtered through Celite. The filtrate was concentrated under reduce pressure, and the resulting residue was purified by flash column chromatography on silica gel to give the desired substrates.

*2-(5-Methoxy-1H-indol-1-yl)aniline (**1m**).* Following the procedure above, 5-methoxyindole (9.0 mmol, 1.325 g) was used as the starting material. After column chromatography (hexane/EtOAc = 25:1), **1m** was obtained as a sticky orange oil (1.90 g, 89% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16−7.27 (m, 4H), 7.06 (d, J = 8.6 Hz, 1H), 6.83−6.88 (m, 3H), 6.63 (d, J = 3.1 Hz, 1H), 3.88 (s, 3H), 3.53 (br s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.7, 143.2, 131.8, 129.2, 129.2, 129.1, 128.7, 125.1, 118.6, 116.3, 112.6, 111.6, 103.0, 102.8, 56.0; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{15}H_{14}N_2O$, 238.1106; found, 238.1100.

*2-(3-Methyl-1H-indol-1-yl)aniline (**1o**).* Following the procedure above, 3-methylindole (9.0 mmol, 1.18 g) was used as the starting material. After column chromatography (hexane/EtOAc = 25:1), **1o** was obtained as a pale-orange oil (1.926 g, 96% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.59 (dd, J = 6.7, 1.2 Hz, 1H), 7.03−7.19 (m, 5H), 7.00 (dd, J = 6.7, 1.2 Hz, 1H), 6.94 (dd, J = 8.6, 1.2 Hz, 1H), 6.69 (td, J = 7.7, 1.2 Hz, 1H), 4.73 (s, 2H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 144.3, 136.3, 128.6, 128.5, 127.9, 126.6, 123.6, 121.8, 119.1, 118.8, 116.4, 115.9, 111.0, 110.4, 9.5; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{15}H_{14}N_2$, 222.1157; found, 222.1154.

*2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)aniline (**1p**).* Following the procedure above, 1*H*-pyrrolo[2,3-*b*]pyridine (12.0 mmol, 1.418 g) was used as the starting material. After column chromatography (hexane/EtOAc = 25:1), **1p** was obtained as a pale-pink solid (971 mg, 39% yield); mp 103−106 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22 (dd, J = 4.6, 1.5 Hz, 1H), 8.06 (dd, J = 8.0, 1.8 Hz, 1H), 7.55 (d, J = 3.7 Hz, 1H), 7.14−7.20 (m, 2H), 7.09 (dd, J = 7.7, 1.5 Hz, 1H), 6.92 (dd, J = 8.0, 1.2 Hz, 1H), 6.68−6.72 (m, 2H), 4.79 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 147.5, 144.5, 142.9, 130.2, 129.0, 128.7, 128.5, 123.6, 120.4, 116.5, 116.3, 116.2, 101.2; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{13}H_{12}N_3$, 210.1031; found, 210.1033.

*Preparation of 2-(5-Bromo-1H-indol-1-yl)aniline (**1n**).*[20] To a stirred solution of 5-bromoindole (1.18 g, 6 mmol) in DMSO (6 mL), NaOH (6.0 mmol) and 1-fluoro-2-nitrobenzene (6 mmol) were added slowly. The reaction mixture was stirred vigorously for 2 h at room temperature. After completion of the reaction, the reaction mixture was extracted with EtOAc and saturated brine. Then, the organic layer was combined and dried with anhydrous Na_2SO_4. The solvent was evaporated to obtain the desired product which was directly used for the next step without further purification. The residue was added to iron powder (24 mmol) and NH_4Cl (2.4 mmol) in water (72 mL) and refluxed for overnight. After cooling, the reaction mixture was poured into water (100 mL) and extracted with EtOAc three times (3 × 60 mL). The combined organic layers were dried with anhydrous Na_2SO_4, and the solvent was removed *in vacuo* to afford the residue. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc (30:1 to 20:1) as the eluent to provide the desired product **1n** as a pale-yellow oil (1.162 g, 67% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.84 (d, J = 1.8 Hz, 1H), 7.45 (d, J = 3.1 Hz, 1H), 7.24 (dd, J = 8.6, 1.8 Hz, 1H), 7.17−7.21 (m, 1H), 7.06 (dd, J = 7.9, 1.2 Hz, 1H), 6.96 (d, J = 8.6 Hz, 1H), 6.91 (dd, J = 8.6, 1.2 Hz, 1H), 6.65−6.70 (m, 2H), 4.79 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 144.5, 134.8, 130.9, 130.1, 129.1, 128.1, 124.2, 122.8, 116.4, 116.0, 112.6, 112.2, 102.3; HRMS (FAB) m/z: $[M]^+$ calcd for $C_{14}H_{11}BrN_2$, 286.0106; found, 286.0105.

General Procedure for the Synthesis of Quinoxaline Products. To a mixture of anilines **1** (0.3 mmol) and $FeCl_3{\cdot}6H_2O$ (0.045 mmol, 12.16 mg) in 0.5 mL of DMSO, methyl arenes **2** (18 mmol) were added in borosilicate glass tubes. While stirring the mixture, DTBP (0.3 mmol, 55 μL) was added in a dropwise manner. The reaction tube was capped with a rubber septum, and two needles (18/24 gauge) were injected on top of the septum to induce air circulation. The reaction mixture was stirred at 120 °C and monitored by TLC. After stirring for 40 h, the reaction mixture was cooled to room temperature and diluted with diethyl ether (5 mL). The mixture was extracted with diethyl ether (5 mL × 3), and the organic phase was washed with water (1 mL). The combined organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc as the eluent.

*4-Phenylpyrrolo[1,2-a]quinoxaline (**3aa**).* Following the general procedure, 2-(1*H*-pyrrol-1-yl)aniline **1a** (47.46 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3aa** was obtained as a pale-yellow solid (56.3 mg, 77% yield); mp 88−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, J = 8.0, 1.6 Hz, 1H), 7.99−8.02 (m, 3H), 7.90 (dd, J = 8.0, 1.4 Hz, 1H), 7.51−7.57 (m, 4H), 7.45−7.49 (m, 1H), 7.00 (dd, J = 4.1, 1.4 Hz, 1H), 6.91 (dd, J = 4.0, 2.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.5, 138.5, 136.3, 130.3, 130.0, 128.7, 128.7, 127.6, 127.3, 125.5, 125.4, 114.8, 114.1, 113.7, 108.9; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{17}H_{13}N_2$, 245.1079; found, 245.1080.

*4-(o-Tolyl)pyrrolo[1,2-a]quinoxaline (**3ab**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and *o*-xylene (**2b**, 2.17 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ab** was obtained as a pale-yellow solid (53.1 mg, 69% yield); mp 111−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 1.4 Hz, 1H), 7.92 (dd, J = 8.0, 1.1 Hz, 1H), 7.56 (td, J = 7.8, 1.4 Hz, 1H), 7.46−7.51 (m, 2H), 7.30−7.42 (m, 3H), 6.87 (q, J = 2.3 Hz, 1H), 6.61 (d, J = 3.7 Hz, 1H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.6, 136.6, 131.0, 130.1, 129.3, 129.1, 127.8, 127.3, 126.4, 125.8, 125.5, 114.9, 114.3, 113.9, 109.3, 19.9; HRMS (FAB) m/z: $[M + H]^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1229.

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*4-(m-Tolyl)pyrrolo[1,2-a]quinoxaline (**3ac**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and *m*-xylene (**2c**, 2.21 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ac** was obtained as a sticky yellow oil (53.8 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 7.8 Hz, 1H), 8.00 (t, J = 1.4 Hz, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.80 (d, J = 11.9 Hz, 2H), 7.41−7.54 (m, 3H), 7.34 (d, J = 7.4 Hz, 1H), 7.01 (d, J = 4.1 Hz, 1H), 6.90 (t, J = 3.2 Hz, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.6, 138.6, 138.1, 136.0, 130.9, 130.1, 129.4, 128.5, 127.6, 127.2, 125.9, 125.5, 115.0, 114.2, 113.8, 109.3, 21.7; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1240.

*4-(p-Tolyl)pyrrolo[1,2-a]quinoxaline (**3ad**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and *p*-xylene (**2d**, 2.21 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ad** was obtained as a sticky yellow oil (61.8 mg, 80% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 1.8 Hz, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.88 (dd, J = 8.0, 1.2 Hz, 1H), 7.44−7.54 (m, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 3.7 Hz, 1H), 6.91 (t, J = 3.4 Hz, 1H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 140.3, 135.8, 135.2, 130.0, 129.5, 128.8, 127.6, 127.2, 125.5, 125.4, 115.1, 114.3, 113.8, 109.5, 21.6; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1234.

*For 1 mmol Scale Reaction (**3ad** in Table 2).* To a mixture of 2-(1*H*-pyrrol-1-yl)aniline **1a** (1.0 mmol, 158.2 mg) and $FeCl_3{\cdot}6H_2O$ (0.15 mmol, 40.14 mg) in 1.7 mL of DMSO, *p*-xylene **2d** (18.0 mmol, 7.40 mL) was added in an Ace pressure tube. While stirring the mixture, DTBP (1.2 mmol, 224 μL) was added in a dropwise manner. The reaction mixture was stirred at 120 °C under open air conditions and monitored by TLC. After stirring for 40 h, the reaction mixture was cooled to room temperature and diluted with diethyl ether (20 mL). The mixture was extracted with diethyl ether (10 mL × 3), and the organic phase was washed with water (10 mL). The combined organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc (20:1) as the eluent. After purification, **3ad** was obtained as a sticky yellow oil (193.4 mg, 75%).

*4-(3,5-Dimethylphenyl)pyrrolo[1,2-a]quinoxaline (**3ae**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 1,3,5-trimethylbenzene (**2e**, 2.5 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ae** was obtained as a yellow solid (53.1 mg, 69% yield); mp 83−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, J = 7.8, 1.4 Hz, 1H), 7.99 (q, J = 1.2 Hz, 1H), 7.88 (dd, J = 8.3, 1.4 Hz, 1H), 7.60 (s, 2H), 7.51 (td, J = 7.7, 1.5 Hz, 1H), 7.46 (td, J = 7.6, 1.2 Hz, 1H), 7.16 (s, 1H), 7.00 (q, J = 1.8 Hz, 1H), 6.89 (dd, J = 3.8, 2.9 Hz, 1H), 2.44 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.9, 138.3, 136.3, 131.7, 130.3, 127.5, 127.3, 126.5, 125.6, 125.4, 114.8, 114.1, 113.8, 109.2, 21.6; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{19}H_{17}N_2$, 273.1392; found, 273.1392.

*4-(4-Methoxyphenyl)pyrrolo[1,2-a]quinoxaline (**3af**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-methoxytoluene (**2f**, 2.3 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3af** was obtained as a pale-yellow solid (26.0 mg, 32% yield); mp 111−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (ddd, J = 12.6, 7.4, 1.6 Hz, 4H), 7.86 (dd, J = 8.0, 1.1 Hz, 1H), 7.49 (td, J = 7.6, 1.4 Hz, 1H), 7.44 (td, J = 7.5, 1.4 Hz, 1H), 7.06 (dt, J = 9.5, 2.5 Hz, 2H), 7.00 (dd, J = 3.9, 1.1 Hz, 1H), 6.88 (dd, J = 4.0, 2.9 Hz, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 161.1, 154.0, 136.5, 131.2, 130.2, 127.3, 127.2, 125.5, 125.4, 114.6, 114.1, 114.0, 113.7, 108.7, 55.6; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2O$, 275.1184; found, 275.1183.

*4-(4-Fluorophenyl)pyrrolo[1,2-a]quinoxaline (**3ag**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-fluorotoluene (**2g**, 1.98 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ag** was obtained as a pale-yellow solid (45.7 mg, 58% yield); mp 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01−8.12 (m, 4H), 7.90 (d, J = 8.3 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.22−7.27 (m, 2H), 6.94−7.01 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.2 (d, $^1J_{C-F}$ = 249.2 Hz), 162.7 (d, $^1J_{C-F}$ = 249.2 Hz), 153.3, 136.0 (d, $^2J_{C-F}$ = 156.2 Hz), 134.4 (d, $^2J_{C-F}$ = 156.2 Hz), 130.8 (d, $^4J_{C-F}$ = 8.7 Hz), 130.7 (d, $^4J_{C-F}$ = 8.7 Hz), 130.1, 127.8, 127.2, 125.6, 125.2, 115.9 (d, $^3J_{C-F}$ = 21.1 Hz), 115.7 (d, $^3J_{C-F}$ = 21.1 Hz), 115.1, 114.3, 113.8, 109.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ −110.52 ppm; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}FN_2$, 263.0985; found, 263.0979.

*4-(4-Chlorophenyl)pyrrolo[1,2-a]quinoxaline (**3ah**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-chlorotoluene (**2h**, 2.13 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ah** was obtained as a white solid (46.8 mg, 56% yield); mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01−8.05 (m, 2H), 7.96−7.98 (m, 2H), 7.88 (dd, J = 8.3, 0.9 Hz, 1H), 7.45−7.55 (m, 4H), 6.97 (dd, J = 3.9, 1.1 Hz, 1H), 6.91 (dd, J = 3.7, 2.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.2, 136.9, 136.1, 136.1, 130.3, 130.1, 129.0, 127.9, 127.2, 125.6, 125.2, 115.1, 114.3, 113.8, 108.8; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}ClN_2$, 279.0689; found, 279.0698.

*4-(4-Bromophenyl)pyrrolo[1,2-a]quinoxaline (**3ai**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-bromotoluene (**2i**, 2.21 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ai** was obtained as a pale-yellow solid (51.5 mg, 53% yield); mp 157−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01−8.04 (m, 2H), 7.88−7.91 (m, 3H), 7.68 (d, J = 7.9 Hz, 2H), 7.52−7.56 (m, 1H), 7.45−7.49 (m, 1H), 6.96 (d, J = 4.3 Hz, 1H), 6.91 (t, J = 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.3, 137.4, 136.2, 131.9, 130.4, 130.3, 127.9, 127.3, 125.6, 125.1, 124.4, 115.0, 114.3, 113.8, 108.7; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}BrN_2$, 323.0184; found, 323.0190.

*4-(4-Iodophenyl)pyrrolo[1,2-a]quinoxaline (**3aj**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-iodotoluene (**2j**, 2.34 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3aj** was obtained as a pale-yellow solid (55.7 mg, 50% yield); mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 7.9 Hz, 1H), 8.02 (d, J = 1.2 Hz, 1H), 7.89 (d, J = 8.6 Hz, 3H), 7.76 (d, J = 8.6 Hz, 2H), 7.52−7.56 (m, 1H), 7.45−7.49 (m, 1H), 6.98 (d, J = 3.7 Hz, 1H), 6.92 (t, J = 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.3, 137.9, 137.9, 136.1, 130.5, 130.3, 127.9, 127.2, 125.5, 125.1, 115.0, 114.3, 113.8, 108.7, 96.3; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}IN_2$, 371.0045; found, 371.0048.

*4-(4-(Trifluoromethyl)phenyl)pyrrolo[1,2-a]quinoxaline (**3ak**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-methylbenzotrifluoride (**2k**, 2.51 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ak** was obtained as a pale-yellow solid (28.5 mg, 30% yield); mp 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 7.9 Hz, 2H), 8.04 (dd, J = 8.1, 1.4 Hz, 1H), 8.02 (q, J = 1.3 Hz, 1H), 7.88 (dd, J = 8.3, 1.2 Hz, 1H), 7.81 (d, J = 8.3 Hz, 2H), 7.52−7.57 (m, 1H), 7.46−7.50 (m, 1H), 6.96 (dd, J = 4.0, 1.2 Hz, 1H), 6.92 (dd, J = 4.1, 2.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.0, 142.0, 136.2, 132.2 (q, $^2J_{C-F}$ = 32.6 Hz), 131.9 (q, $^2J_{C-F}$ = 32.6 Hz), 131.6 (q, $^2J_{C-F}$ = 32.6 Hz), 131.2 (q, $^2J_{C-F}$ = 32.6 Hz), 130.5, 129.1, 128.1, 127.3, 125.7 (q, $^3J_{C-F}$ = 3.8 Hz), 125.7 (q, $^3J_{C-F}$ = 3.8 Hz), 125.7 (q, $^3J_{C-F}$ = 3.8 Hz), 125.6 (q, $^3J_{C-F}$ = 3.8 Hz), 125.6, 125.5 (d, $^1J_{C-F}$ = 271.2 Hz), 125.1, 122.8 (d, $^1J_{C-F}$ = 271.2 Hz), 120.1, 115.1, 114.4, 113.8, 108.5; ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.67 ppm; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{12}F_3N_2$, 313.0953; found, 313.0953.

*4-(Pyrrolo[1,2-a]quinoxalin-4-yl)benzonitrile (**3al**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and *p*-tolunitrile (**2l**, 2.15 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3al** was obtained as a light-yellow solid (35.9 mg, 44% yield); mp 224−226 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.7 Hz, 2H), 8.02−8.04 (m, 2H), 7.91 (d, J = 8.3 Hz, 1H), 7.84 (d, J = 8.3 Hz, 2H), 7.57 (td, J = 7.8, 1.4 Hz, 1H), 7.47−7.51 (m, 1H), 6.94−6.95 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.3, 142.8, 136.1, 132.5, 130.5, 129.4, 128.4, 127.3, 125.7, 124.9, 118.8, 115.2, 114.5, 113.9, 113.4, 108.4; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{12}N_3$, 270.1031; found, 270.1033.

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*4-(Naphthalen-2-yl)pyrrolo[1,2-a]quinoxaline (**3am**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 2-methylnaphthalene (**2m**, 2.56 g) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3am** was obtained as a pale-yellow solid (38.7 mg, 44% yield); mp 93−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.13 (qd, J = 4.1, 1.6 Hz, 2H), 8.01−8.03 (m, 2H), 7.99 (t, J = 4.8 Hz, 1H), 7.94 (t, J = 4.6 Hz, 1H), 7.90 (dd, J = 8.3, 1.4 Hz, 1H), 7.47−7.60 (m, 4H), 7.10 (dd, J = 3.9, 1.1 Hz, 1H), 6.93 (q, J = 2.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 136.2, 135.7, 134.2, 133.3, 130.2, 128.9, 128.6, 128.5, 127.9, 127.7, 127.2, 127.1, 126.6, 126.2, 125.6, 125.5, 115.0, 114.3, 113.8, 109.2; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{21}H_{15}N_2$, 295.1235; found, 295.1229.

*4-(Thiophen-2-yl)pyrrolo[1,2-a]quinoxaline (**3an**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 2-methylthiophene (**2n**, 1.74 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3an** was obtained as a yellow solid (37.7 mg, 50% yield); mp 102−104 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.58 (q, J = 1.3 Hz, 1H), 8.32 (dd, J = 8.1, 1.1 Hz, 1H), 8.14 (dd, J = 3.8, 1.1 Hz, 1H), 7.89 (dd, J = 7.8, 1.4 Hz, 1H), 7.85 (dd, J = 5.0, 1.1 Hz, 1H), 7.57−7.62 (m, 1H), 7.50 (ddd, J = 8.3, 6.9, 1.1 Hz, 1H), 7.46 (dd, J = 4.0, 1.2 Hz, 1H), 7.29 (dd, J = 5.2, 3.7 Hz, 1H), 7.04 (dd, J = 4.3, 2.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 146.3, 142.1, 134.9, 130.1, 129.1, 128.9, 128.5, 127.9, 126.6, 125.7, 122.6, 116.8, 114.8, 114.6, 108.1; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{15}H_{11}N_2S$, 251.0643; found, 251.0636.

*4-(Pyridin-4-yl)pyrrolo[1,2-a]quinoxaline (**3ao**).* Following the general procedure, **1a** (47.46 mg) was used as aniline and 4-methylpyridine (**2o**, 1.75 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ao** was obtained as a light-yellow solid (46.1 mg, 63% yield); mp 188−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (q, J = 2.1 Hz, 2H), 8.03−8.05 (m, 2H), 7.90 (d, J = 6.1 Hz, 3H), 7.56 (t, J = 7.7 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 6.99 (d, J = 4.3 Hz, 1H), 6.93 (t, J = 2.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.9, 150.4, 145.8, 136.0, 130.6, 128.5, 127.4, 125.7, 124.8, 123.1, 115.2, 114.5, 113.9, 108.3; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{16}H_{12}N_3$, 246.1031; found, 246.1034.

*9-Methyl-4-phenylpyrrolo[1,2-a]quinoxaline (**3ba**).* Following the general procedure, 3-methyl-2-(1*H*-pyrrol-1-yl)aniline (**1b**, 51.67 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ba** was obtained as a light-yellow solid (52.5 mg, 68% yield); mp 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (q, J = 1.4 Hz, 1H), 7.96−7.99 (m, 2H), 7.93 (dd, J = 7.4, 2.3 Hz, 1H), 7.50−7.56 (m, 3H), 7.31−7.37 (m, 2H), 7.00 (dd, J = 4.1, 0.9 Hz, 1H), 6.88 (dd, J = 4.1, 3.2 Hz, 1H), 2.99 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 138.6, 138.1, 131.1, 129.8, 128.9, 128.8, 128.7, 127.6, 126.9, 125.4, 124.8, 120.4, 113.4, 108.3, 24.1; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1240.

*8-Methyl-4-phenylpyrrolo[1,2-a]quinoxaline (**3ca**).* Following the general procedure, 4-methyl-2-(1*H*-pyrrol-1-yl)aniline (**1c**, 51.67 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ca** was obtained as a yellow oil (35.9 mg, 46% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dq, J = 6.2, 1.9 Hz, 2H), 7.96 (q, J = 1.4 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.68 (s, 1H), 7.49−7.56 (m, 3H), 7.27 (dd, J = 8.5, 1.6 Hz, 1H), 6.97 (q, J = 1.8 Hz, 1H), 6.88 (q, J = 2.3 Hz, 1H), 2.57 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.6, 138.7, 138.1, 134.4, 130.1, 129.8, 128.7, 128.7, 127.0, 126.7, 125.6, 114.4, 114.0, 113.8, 108.5, 22.0; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1231.

*8-Methoxy-4-phenylpyrrolo[1,2-a]quinoxaline (**3da**).* Following the general procedure, 4-methoxy-2-(1*H*-pyrrol-1-yl)aniline (**1d**, 56.47 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3da** was obtained as a yellow solid (35.9 mg, 46% yield); mp 98−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96−7.99 (m, 3H), 7.90 (q, J = 1.4 Hz, 1H), 7.48−7.56 (m, 3H), 7.29 (d, J = 2.7 Hz, 1H), 7.06 (dd, J = 8.9, 2.5 Hz, 1H), 6.97 (dd, J = 4.1, 0.9 Hz, 1H), 6.90 (q, J = 2.3 Hz, 1H), 3.98 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.3, 152.1, 138.8, 131.6, 130.9, 129.6, 128.7, 128.1, 125.5, 114.2, 114.2, 113.0, 108.3, 97.7, 56.0; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2O$, 275.1184; found, 275.1180.

*8-Chloro-4-phenylpyrrolo[1,2-a]quinoxaline (**3ea**).* Following the general procedure, 4-chloro-2-(1*H*-pyrrol-1-yl)aniline (**1e**, 57.8 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ea** was obtained as a pale-yellow solid (46.0 mg, 55% yield); mp 179−181 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−8.00 (m, 3H), 7.94 (q, J = 1.4 Hz, 1H), 7.88 (d, J = 2.3 Hz, 1H), 7.52−7.58 (m, 3H), 7.42 (dd, J = 8.7, 2.3 Hz, 1H), 7.02 (dd, J = 3.9, 1.1 Hz, 1H), 6.93 (dd, J = 3.9, 3.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.7, 138.3, 135.0, 133.0, 131.6, 130.2, 128.8, 128.7, 127.9, 125.9, 125.4, 115.0, 114.7, 114.0, 109.4; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}ClN_2$, 279.0689; found, 279.0694.

*7-Methyl-4-phenylpyrrolo[1,2-a]quinoxaline (**3fa**).* Following the general procedure, 5-methyl-2-(1*H*-pyrrol-1-yl)aniline (**1f**, 51.67 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3fa** was obtained as a yellow solid (44.4 mg, 57% yield); mp 87−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98−8.01 (m, 2H), 7.96 (q, J = 1.4 Hz, 1H), 7.85 (d, J = 0.9 Hz, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.49−7.57 (m, 3H), 7.34 (dd, J = 8.3, 1.8 Hz, 1H), 6.97 (q, J = 1.8 Hz, 1H), 6.88 (q, J = 2.3 Hz, 1H), 2.51 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.5, 138.7, 136.3, 135.2, 130.2, 129.9, 128.7, 128.7, 125.5, 125.2, 114.5, 113.8, 113.5, 108.6, 21.3; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1233.

*7-Methoxy-4-phenylpyrrolo[1,2-a]quinoxaline (**3ga**).* Following the general procedure, 5-methoxy-2-(1*H*-pyrrol-1-yl)aniline (**1g**, 56.47 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ga** was obtained as a pale-yellow solid (61.4 mg, 75% yield); mp 129−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98−8.00 (m, 2H), 7.94 (m, 1H), 7.81 (d, J = 8.7 Hz, 1H), 7.52−7.57 (m, 4H), 7.14 (dd, J = 8.7, 2.8 Hz, 1H), 6.97 (dd, J = 4.1, 0.9 Hz, 1H), 6.87 (dd, J = 3.7, 2.8 Hz, 1H), 3.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.3, 154.9, 138.7, 137.5, 129.9, 128.7, 125.3, 121.6, 116.9, 114.7, 114.4, 113.8, 111.5, 108.5, 55.9; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2O$, 275.1184; found, 275.1188.

*7-Chloro-4-phenylpyrrolo[1,2-a]quinoxaline (**3ha**).* Following the general procedure, 5-chloro-2-(1*H*-pyrrol-1-yl)aniline (**1h**, 57.8 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ha** was obtained as a white solid (54.8 mg, 66% yield); mp 145−147 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.61 (q, J = 1.4 Hz, 1H), 8.39 (d, J = 8.6 Hz, 1H), 7.97−8.00 (m, 3H), 7.67 (dd, J = 9.2, 2.4 Hz, 1H), 7.58−7.62 (m, 3H), 7.07 (dd, J = 4.3, 1.2 Hz, 1H), 7.02 (q, J = 2.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 154.4, 137.5, 136.6, 130.3, 129.3, 128.6, 128.5, 128.4, 127.6, 125.7, 124.2, 117.3, 116.7, 114.8, 109.2; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{17}H_{12}ClN_2$, 279.0689; found, 279.0687.

*4-Phenyl-7-(trifluoromethyl)pyrrolo[1,2-a]quinoxaline (**3ia**).* Following the general procedure, 2-(1*H*-pyrrol-1-yl)-5-(trifluoromethyl)-aniline (**1i**, 67.86 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ia** was obtained as a light-yellow solid (66.3 mg, 71% yield); mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.99−8.03 (m, 3H), 7.92 (d, J = 8.6 Hz, 1H), 7.71 (d, J = 8.6 Hz, 1H), 7.54−7.59 (m, 3H), 7.06 (d, J = 3.7 Hz, 1H), 6.94 (t, J = 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.8, 138.0, 136.1, 130.4, 129.3, 128.8 (d, $^2J_{C-F}$ = 8.6 Hz), 128.7 (d, $^2J_{C-F}$ = 8.6 Hz), 127.9 (q, $^4J_{C-F}$ = 3.8 Hz), 127.9 (q, $^4J_{C-F}$ = 3.8 Hz), 127.8 (q, $^4J_{C-F}$ = 3.8 Hz), 127.8 (q, $^4J_{C-F}$ = 3.8 Hz), 127.7, 127.4, 127.4, 125.6, 125.5 (d, $^1J_{C-F}$ = 270.2 Hz), 123.9 (q, $^3J_{C-F}$ = 3.9 Hz), 123.9 (q, $^3J_{C-F}$ = 3.9 Hz), 123.8 (q, $^3J_{C-F}$ = 3.9 Hz), 123.8 (q, $^3J_{C-F}$ = 3.9 Hz), 122.8 (d, $^1J_{C-F}$ = 270.2 Hz), 121.4, 115.4, 115.0, 114.4, 110.2, 110.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ −61.89 ppm; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{12}F_3N_2$, 313.0953; found, 313.0953.

*6-Phenylpyrido[3,2-e]pyrrolo[1,2-a]pyrazine (**3ja**).* Following the general procedure, 2-(1*H*-pyrrol-1-yl)pyridin-3-amine (**1j**, 47.76 mg)

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was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ja** was obtained as a pale-yellow solid (36.1 mg, 49% yield); mp 139−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (dd, J = 4.8, 1.6 Hz, 1H), 8.48 (q, J = 1.4 Hz, 1H), 8.32 (dd, J = 8.0, 1.6 Hz, 1H), 7.99−8.04 (m, 2H), 7.54−7.59 (m, 3H), 7.46 (q, J = 4.3 Hz, 1H), 7.07 (q, J = 1.8 Hz, 1H), 6.94 (dd, J = 3.7, 2.7 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.4, 146.8, 139.4, 138.1, 137.5, 131.2, 130.3, 128.8, 128.8, 126.9, 121.8, 116.1, 114.6, 110.5; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{16}H_{12}N_3$, 246.1031; found, 246.1031.

*1-Methyl-4-phenyl-1H-pyrrolo[3,2-c]quinoline (**3ka**).* Following the general procedure, 2-(1-methyl-1*H*-pyrrol-2-yl)aniline (**1k**, 60.66 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ka** was obtained as a beige solid (9.9 mg, 13% yield); mp 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, J = 8.6 Hz, 1H), 8.33 (dd, J = 8.6, 1.2 Hz, 1H), 8.04−8.07 (m, 2H), 7.62−7.66 (m, 1H), 7.53−7.58 (m, 3H), 7.47−7.51 (m, 1H), 7.07 (d, J = 3.1 Hz, 1H), 6.82 (d, J = 3.1 Hz, 1H), 4.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.8, 144.8, 140.4, 134.9, 130.8, 129.8, 129.2, 128.9, 128.6, 126.4, 125.4, 120.5, 120.3, 118.4, 103.2, 38.2; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{15}N_2$, 259.1235; found, 259.1241.

*6-Phenylindolo[1,2-a]quinoxaline (**3la**).* Following the general procedure, 2-(1*H*-indol-1-yl)aniline (**1l**, 62.48 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3la** was obtained as a yellow solid (68.7 mg, 78% yield); mp 162−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48−8.53 (m, 2H), 8.09 (dd, J = 7.7, 1.5 Hz, 1H), 8.01−8.05 (m, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.54−7.64 (m, 5H), 7.43−7.47 (m, 2H), 7.25 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.4, 138.4, 136.4, 133.2, 130.7, 130.3, 130.2, 129.3, 129.3, 128.8, 128.8, 128.5, 124.5, 124.3, 122.9, 122.8, 114.8, 114.7, 102.6; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{21}H_{15}N_2$, 295.1235; found, 295.1238.

*9-Methoxy-6-phenylindolo[1,2-a]quinoxaline (**3ma**).* Following the general procedure, 2-(5-methoxy-1*H*-indol-1-yl)aniline (**1m**, 71.5 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3ma** was obtained as a light-yellow solid (46.4 mg, 48% yield); mp 167−169 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.67 (dd, J = 15.3, 8.6 Hz, 2H), 7.99−8.04 (m, 3H), 7.68−7.72 (m, 1H), 7.63 (t, J = 3.4 Hz, 3H), 7.51 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 2.4 Hz, 1H), 7.26 (s, 1H), 7.21 (dd, J = 9.2, 2.4 Hz, 1H), 3.87 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 155.4, 154.7, 137.7, 135.4, 130.2, 130.1, 129.9, 129.1, 129.1, 128.6, 128.5, 127.7, 124.3, 116.0, 115.7, 114.8, 102.6, 101.8, 55.4; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{22}H_{17}N_2O$, 325.1341; found, 325.1347.

*9-Bromo-6-phenylindolo[1,2-a]quinoxaline (**3na**).* Following the general procedure, 2-(5-bromo-1*H*-indol-1-yl)aniline (**1n**, 86.15 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3na** was obtained as a light-yellow solid (6.6 mg, 6% yield); mp 234−237 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, J = 7.8 Hz, 1H), 8.38 (d, J = 9.2 Hz, 1H), 8.10 (dd, J = 7.8, 1.4 Hz, 1H), 8.06 (d, J = 1.8 Hz, 1H), 8.00−8.02 (m, 2H), 7.57−7.67 (m, 5H), 7.47−7.51 (m, 1H), 7.18 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 156.2, 138.1, 136.5, 131.8, 131.0, 131.0, 130.3, 130.1, 129.9, 128.9, 128.8, 128.7, 127.3, 125.2, 124.8, 116.3, 116.1, 114.7, 101.7; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{21}H_{14}BrN_2$, 373.0340; found, 373.0332.

*7-Methyl-6-phenylindolo[1,2-a]quinoxaline (**3oa**).* Following the general procedure, 2-(3-methyl-1*H*-indol-1-yl)aniline (**1o**, 66.7 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3oa** was obtained as a light-yellow solid (65.6 mg, 71% yield); mp 162−163 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.71 (t, J = 8.3 Hz, 2H), 7.97 (d, J = 7.9 Hz, 1H), 7.90 (dd, J = 7.6, 1.5 Hz, 1H), 7.57−7.70 (m, 7H), 7.45−7.51 (m, 2H), 2.00 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 157.0, 139.2, 135.1, 131.4, 129.7, 129.7, 129.6, 129.3, 129.0, 128.6, 128.3, 125.2, 125.0, 124.1, 122.3, 120.8, 114.9, 114.7, 110.1, 10.9; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{22}H_{17}N_2$, 309.1392; found, 309.1388.

*6-Phenylpyrido[3′,2′:4,5]pyrrolo[1,2-a]quinoxaline (**3pa**).* Following the general procedure, 2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)-aniline (**1p**, 62.8 mg) was used as aniline and toluene (**2a**, 1.913 mL) was used as methyl arene. After column chromatography (hexane/EtOAc = 20:1), **3pa** was obtained as a yellow solid (8.8 mg, 10% yield); mp 178−180 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.93 (dd, J = 7.9, 1.2 Hz, 1H), 8.73 (q, J = 2.0 Hz, 1H), 8.23 (dd, J = 8.3, 1.5 Hz, 1H), 8.07 (dd, J = 7.9, 1.2 Hz, 1H), 8.01−8.05 (m, 2H), 7.68 (td, J = 7.8, 1.4 Hz, 1H), 7.56−7.62 (m, 3H), 7.47−7.51 (m, 1H), 7.40 (q, J = 4.3 Hz, 1H), 7.15 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.9, 145.7, 145.1, 137.9, 135.7, 130.6, 130.3, 129.8, 129.2, 128.9, 128.8, 128.3, 125.0, 121.3, 118.8, 117.7, 99.5; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{20}H_{14}N_3$, 296.1188; found, 296.1186.

Synthetic Procedure for JG454 and Its Indole Analogue. Piperidine compound **6** was synthesized through known procedures, and characterization data were consistent with the literature.[21]

*For 1 mmol Scale Reaction (**3al** in Scheme 2).* To a mixture of 2-(1*H*-pyrrol-1-yl)aniline **1a** (1.0 mmol, 158.2 mg) and $FeCl_3{\cdot}6H_2O$ (0.20 mmol, 54.06 mg) in 1.7 mL of DMSO, *p*-tolunitrile **2l** (18.0 mmol, 7.11 mL) was added in an Ace pressure tube. While stirring the mixture, DTBP (1.2 mmol, 224 μL) was added in a dropwise manner. The reaction mixture was stirred at 120 °C under open air conditions and monitored by TLC. After stirring for 40 h, the reaction mixture was cooled to room temperature and diluted with diethyl ether (20 mL). The mixture was extracted with diethyl ether (10 mL × 3), and the organic phase was washed with water (10 mL). The combined organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc (10:1) as the eluent. **3al** was obtained as a light-yellow solid (110.5 mg, 41% yield).

*4-(Indolo[1,2-a]quinoxalin-6-yl)benzonitrile (**3ll**).* Following the above procedure of 1 mmol scale reaction for **3al**, 2-(1*H*-indol-1-yl)aniline **1l** (1.0 mmol, 208.3 mg) was used as the starting material. After column chromatography (hexane/EtOAc = 20:1), **3ll** was obtained as an orange solid (122.7 mg, 38% yield); mp 253−255 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (dd, J = 11.9, 8.7 Hz, 2H), 8.15 (d, J = 8.3 Hz, 2H), 8.06 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.66 (t, J = 7.3 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.18 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.2, 142.5, 136.0, 133.2, 132.6, 130.9, 130.3, 129.5, 129.3, 129.2, 128.5, 125.0, 124.6, 123.2, 123.0, 118.7, 114.9, 114.7, 113.7, 102.2; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{22}H_{14}N_3$, 320.1188; found, 320.1184.

*4-(Pyrrolo[1,2-a]quinoxalin-4-yl)benzaldehyde (**4al**).* Diisobutylaluminium hydride [0.297 mmol, 297 μL, 1 M solution in dichloromethane (DCM)] was added dropwise to a solution of **3al** (0.149 mmol, 40.0 mg) in tetrahydrofuran (THF, 6.4 mL) using a syringe pump for 1 h at −78 °C. After stirring for additional 1 h at −78 °C, the mixture continued to stir for 3 h at room temperature. Then, 1 M HCl was slowly added to the mixture to adjust the pH to 4−5. The mixture was filtered on Celite, washed with DCM (20 mL), and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc (7:1) as the eluent. **4al** was obtained as a light-yellow solid (19.5 mg, 48% yield); mp 149−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.13 (s, 1H), 8.18 (d, J = 8.3 Hz, 2H), 8.03−8.07 (m, 4H), 7.90 (dd, J = 8.3, 1.4 Hz, 1H), 7.56 (td, J = 7.7, 1.5 Hz, 1H), 7.46−7.51 (m, 1H), 6.98 (q, J = 1.8 Hz, 1H), 6.93 (q, J = 2.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 192.1, 153.0, 144.1, 137.2, 136.1, 130.5, 130.1, 129.5, 128.3, 127.3, 125.7, 125.1, 115.1, 114.5, 113.9, 108.6; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{18}H_{13}N_2O$, 273.1028; found, 273.1022.

*4-(Indolo[1,2-a]quinoxalin-6-yl)benzaldehyde (**4ll**).* Following the above procedure of **4al**, diisobutylaluminium hydride (0.188 mmol, 188 μL, 1 M solution in DCM) was added dropwise to a solution of **3ll** (0.125 mmol, 40.0 mg) in THF (5.4 mL) using a syringe pump for 1 h at −78 °C. After column chromatography (hexane/EtOAc/DCM = 10:1:1), **4ll** was obtained as an orange solid

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(27.1 mg, 54% yield); mp 191−193 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 1H), 8.52 (dd, J = 8.3, 0.9 Hz, 1H), 8.49 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 8.3 Hz, 2H), 8.07−8.10 (m, 3H), 7.94 (d, J = 7.8 Hz, 1H), 7.65 (td, J = 7.9, 1.5 Hz, 1H), 7.56−7.60 (m, 1H), 7.44−7.49 (m, 2H), 7.21 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 192.0, 154.9, 143.9, 137.3, 136.2, 133.2, 130.9, 130.3, 130.1, 129.5, 129.2, 129.1, 128.7, 124.8, 124.5, 123.1, 123.0, 114.9, 114.7, 102.4; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{22}H_{15}N_2O$, 323.1184; found, 323.1182.

*1-(1-(4-(Pyrrolo[1,2-a]quinoxalin-4-yl)benzyl)piperidin-4-yl)-1,3-dihydro-2H-benzo[d]imidazole-2-one (**5al/JG454**).* **4al** (0.045 mmol, 12.0 mg), **6** (0.053 mmol, 11.6 mg), MeOH (2.5 mL), and acetic acid (2 drops) were added to an oven-dried round-bottom flask. Sodium cyanoborohydride (0.225 mmol, 13.9 mg) was added to the mixture, and then, the reaction mixture was heated to 85 °C for 5 h. After finishing reaction, the mixture was concentrated *in vacuo*. The residue was diluted with DCM (5 mL) and washed with H_2O (2 mL) and sat. $NaHCO_3$ (2 mL) sequentially. The organic phase was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using DCM/MeOH (96:4) as the eluent. **5al** was obtained as a white solid (14.7 mg, 69% yield); mp 275−278 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.17 (s, 1H), 8.06 (dd, J = 8.0, 1.6 Hz, 1H), 7.99−8.01 (m, 3H), 7.89 (dd, J = 8.0, 1.1 Hz, 1H), 7.57 (d, J = 7.8 Hz, 2H), 7.50−7.54 (m, 1H), 7.46 (td, J = 7.6, 1.4 Hz, 1H), 7.31 (s, 1H), 7.02−7.10 (m, 4H), 6.91 (dd, J = 3.7, 2.8 Hz, 1H), 4.43 (t, J = 11.7 Hz, 1H), 3.69 (s, 2H), 3.11 (d, J = 6.9 Hz, 2H), 2.52−2.62 (m, 2H), 2.25 (s, 2H), 1.84 (d, J = 10.5 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.3, 154.3, 140.5, 137.5, 136.4, 130.3, 129.4, 129.2, 128.7, 128.2, 127.6, 127.3, 125.5, 125.4, 121.3, 121.2, 114.8, 114.1, 113.8, 110.0, 109.8, 108.9, 62.7, 53.3, 50.9, 29.4; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{30}H_{28}N_5O$ 474.2294; found, 474.2293.

*1-(1-(4-(Indolo[1,2-a]quinoxalin-6-yl)benzyl)piperidin-4-yl)-1,3-dihydro-2H-benzo[d]imidazole-2-one (**5il**).* Following the above procedure of **5al**, sodium cyanoborohydride (0.310 mmol, 19.0 mg) was added to a mixture of **4il** (0.062 mmol, 20.0 mg), **6** (0.074 mmol, 16.2 mg), MeOH (3.4 mL), and acetic acid (2 drops). After column chromatography (hexane/EtOAc/DCM = 1:5:1), **5il** was obtained as a yellow solid (16.3 mg, 50% yield); mp 284−286 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.87 (s, 1H), 8.74 (d, J = 8.7 Hz, 2H), 7.98−8.04 (m, 4H), 7.68−7.73 (m, 1H), 7.58−7.61 (m, 3H), 7.46−7.53 (m, 2H), 7.39 (s, 1H), 7.25 (d, J = 6.4 Hz, 1H), 6.96−7.02 (m, 3H), 4.19 (tt, J = 12.2, 4.2 Hz, 1H), 3.66 (s, 2H), 3.03 (d, J = 11.5 Hz, 2H), 2.42 (qd, J = 12.2, 3.2 Hz, 2H), 2.17 (t, J = 11.0 Hz, 2H), 1.68 (d, J = 9.6 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 155.0, 153.8, 141.0, 136.3, 135.6, 132.4, 129.3, 129.3, 129.0, 128.9, 128.8, 128.5, 128.3, 128.1, 124.7, 124.5, 122.9, 120.5, 120.4, 115.2, 115.0, 108.8, 108.7, 102.4, 61.7, 52.7, 50.2, 28.8; HRMS (FAB) m/z: [M + H]$^+$ calcd for $C_{34}H_{30}N_5O$, 524.2450; found, 524.2452.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00371.

^{1}H and ^{13}C NMR spectra and details for mechanism studies (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Suckchang Hong − *Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea;* orcid.org/0000-0003-4975-9192; Email: schong17@snu.ac.kr

Authors

Jiwon Ahn − *Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea*

Seok Beom Lee − *Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea*

Injae Song − *Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea*

Simin Chun − *Research Institute of Pharmaceutical Sciences, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea*

Dong-Chan Oh − *Natural Products Research Institute, College of Pharmacy, Seoul National University, Seoul 08826, Republic of Korea;* orcid.org/0000-0001-6405-5535

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00371

Author Contributions

J.A. and S.B.L. contributed equally to this work. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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