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Graphical Abstract

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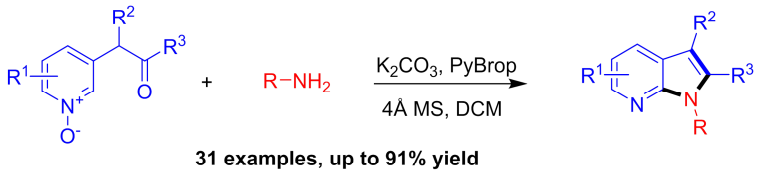

31 examples, up to 91% yield

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Transition-Metal-Free Access to 7-Azaindoles

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ABSTRACT

A novel method for transition-metal-free synthesis of 7-azaindoles is developed through a one-pot synthesis involving amination of pyridine *N*-oxides and intramolecular enamine formation. Remarkable features of the method include simple operation, mild reaction conditions, wide substrate scope, and easily accessible starting materials.

1. Introduction

7-Azaindoles, indole bioisosteres, are the key scaffold for variolins family (Figure 1),[1] many of which are potent kinase inhibitors.[2] 7-Azaindole frameworks exhibit more favorable physicochemical properties and enhanced potency than the corresponding indoles because of the additional nitrogen atom,[3] which serves as efficient hydrogen bond acceptors. Accordingly, they have been widely used as key scaffolds for a variety of drug candidates[4] and chemical probes.[5] There are one on market drug (vemurafenib, Figure 1) and several drugs (fevipiprant and pexidartinib) in clinical phase III containing this structure.

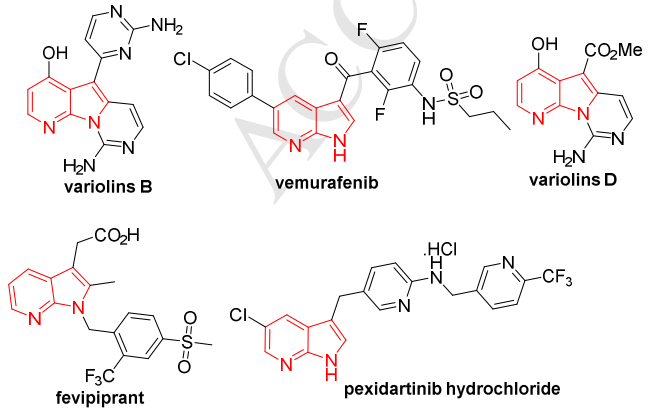
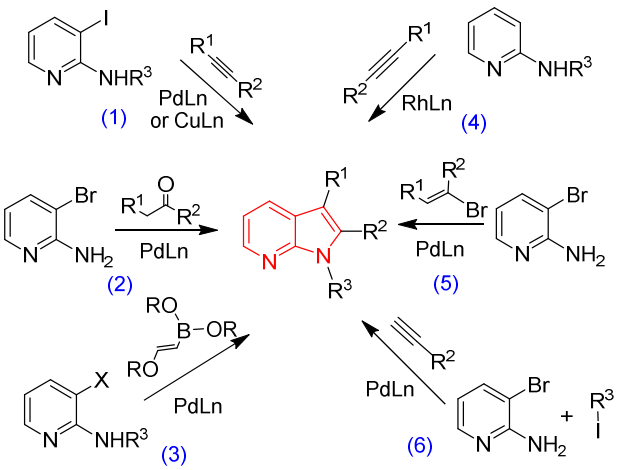


Figure 1. Representative Bioactive Molecules bearing 7-Azaindoles.

Similar to the indole synthesis starting from anilines, common synthetic strategies to prepare 7-azaindoles rely on the use of 2-amino-3-halidepyridines as starting material under the catalysis of Pd or Rh (Scheme 1).[6] For example, the Larock indole synthesis (eq 1),[7] Heck (eq 2),[8] Suzuki (eq 3),[9] C-H activation/annulative coupling (eq 4),[10] Buchwald-Heck (eq 5),[11] and Buchwald-Sonogashira method reported by Marques (eq 6).[12] These approaches, however, suffer from limited substrate scope, harsh reaction conditions, or low yields.

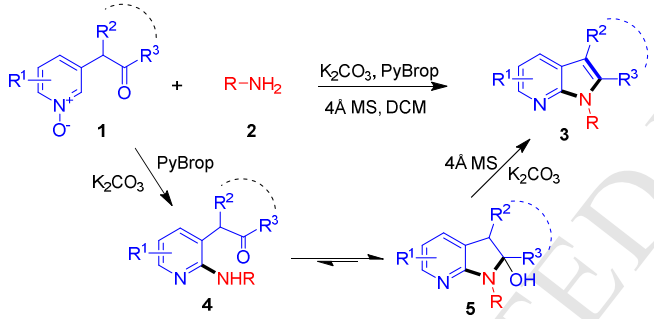


Scheme 1. Synthetic Approaches to 7-Azaindoles.

First, aminopyridines are challenging starting materials in metal-catalyzed reactions[13] due to the strong chelating properties and the low reactivity. Second, transition-metal-catalyzed reactions are problematic in terms of their

environmental impact and operational costs.[14] On the other hand, metal-free access to 7-azaindoles has been scarcely reported.[15] The only metal-free method suffers from 3 steps synthesis, and difficult to access starting material (substituted 2-fluoropyridines). Therefore, the development of new, more versatile procedures under metal-free conditions is highly demanded.

Due to the electronic-deficient nature of pyridines, the majority of synthetic approaches to complex pyridine derivatives largely rely on the manipulation of prefunctionalized building blocks. Completely different from the conventional methods, our group has been exploring reaction conditions that will enable the direct functionalization of pyridines through substrate design and mechanism study, utilizing easily accessible pyridine *N*-oxides as substrates. For example, concise synthetic methods for azacoumarins[16] and azachromones[17] have been established. Herein, we report a transion-metal-free synthetic method to prepare 7-azaindoles, from the easily accessible pyridine *N*-oxides (**1**) and amines (**2**) via a cascade amination of *N*-oxides/enamine formation sequence (Scheme 2). It was expected that **1** and **2** would react to give **4** under PyBrop activation conditions,[18] after which the enamine would be formed to afford **3**. To the best of our knowledge, this general synthetic method based on *N*-oxides chemistry is unprecedented.

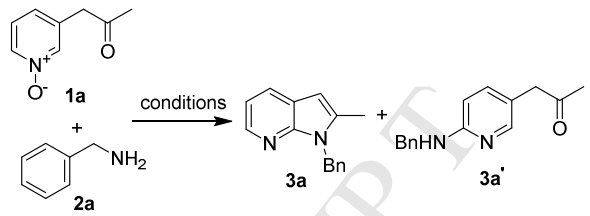


Scheme 2. Transition-Metal-Free Access to 7-Azaindoles.

2. Results and Discussion

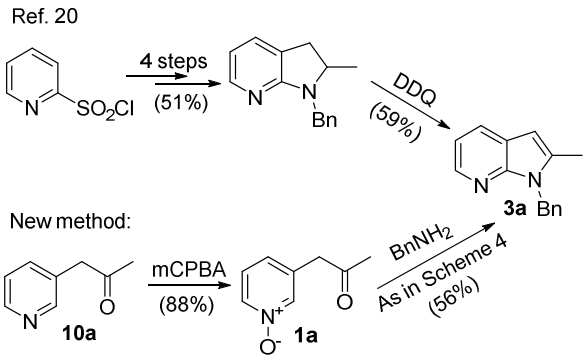
In order to establish the reaction conditions, 3-(2-oxopropyl) pyridine *N*-oxide (**1a**) and benzyl amine were selected as model substrates using PyBrop (bromotripyrrolidinophosphonium hexafluorophosphate) as activation agent (Table 1). Gratifyingly, the desired product was formed in 31% yield using DIEA as base and DCM as solvent (entry 1). Although several byproducts, including the regioisomeric amination byproduct (**3a'**), were detected, **3a** could be easily separated by a flash column because its polarity was much less than other products. It is worth noting that **4a** was not observed, indicating that the enamine formation reaction is fast. A careful screen of base/solvent pair (entries 2 to 7) led to the identification of K_2CO_3/DCM as the optimum combination for this reaction (56% yield, entry 6). Those aforementioned byproducts were still produced under the optimum reaction conditions. The molar ratio of **3a**/**3a'**≈ 6:1 according to ^{1}H NMR of the crude product. It's found that other activation agents, including Ac_2O, Ts_2O and BF_3, are ineffective for this transformation (entries 8 to 10). Although Ts_2O has been proved to be an effective activation agent for the amination of pyridine *N*-oxides,[19] no reaction could be detected for this transformation. Moreover, higher reaction temperature (entry 11) or more concentrated conditions (entry 12) led to decreased product yield.

Table 1. Reaction optimization for the Cascade Amination/Enamine Formation Reaction[a].



entry	act.	base	solvent	[M]	yield, %
1	PyBroP	DIEA	DCM	0.25	31
2	PyBroP	NaOAc	DCM	0.25	28
3	PyBroP	Na_2CO_3	DCM	0.25	42
4	PyBroP	Na_2CO_3	THF	0.25	19
5	PyBroP	Na_2CO_3	EA	0.25	37
6	PyBroP	K_2CO_3	DCM	0.20	56
7	PyBroP	Cs_2CO_3	DCM	0.20	21
8[b]	Ac_2O	Na_2CO_3	DCM	0.25	n/a
9[b]	Ts_2O	n/a	$PhCF_3$	0.25	n/a
10[b]	BF_3	Na_2CO_3	THF	1.0	n/a
11[c]	PyBroP	K_2CO_3	DCE	0.20	30
12	PyBroP	K_2CO_3	DCM	0.80	49

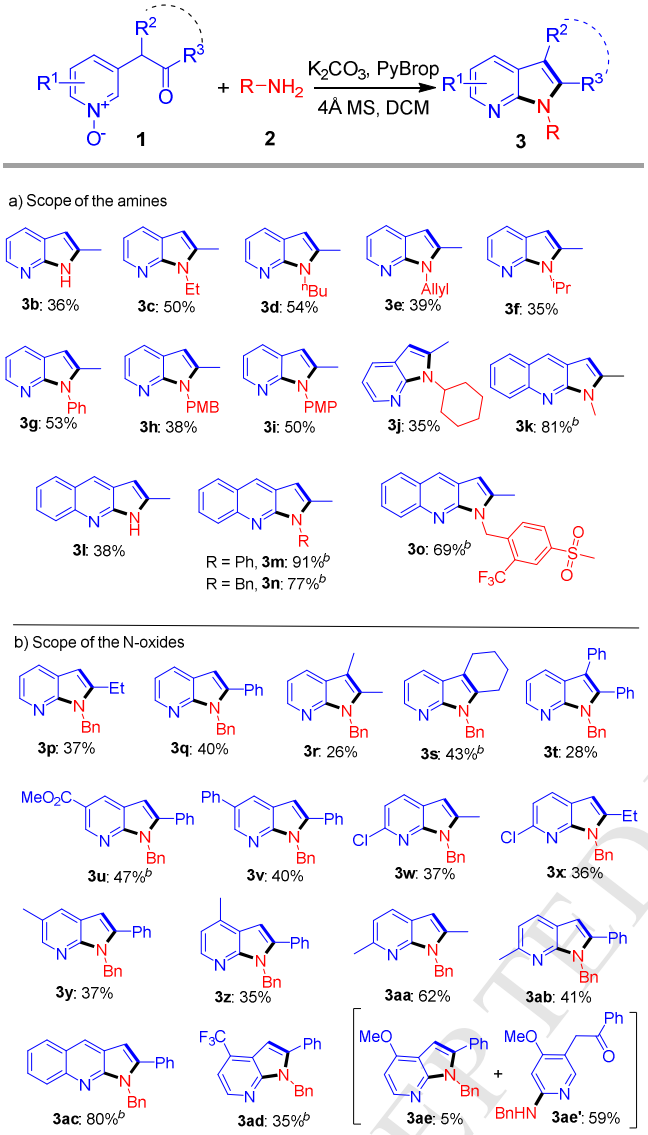
[a] Unless otherwise noted, all reactions were conducted at 0.20 M concentration with *N*-oxide (120 mg, 1.0 equiv), activation agent (1.3 equiv), base (3.0 equiv) and 4Å molecular sieves at r.t. [b] 3.0 equiv of activation agent was used. [c] Reaction temperature was 85 □.



Scheme 3. Preparation of **3a**.

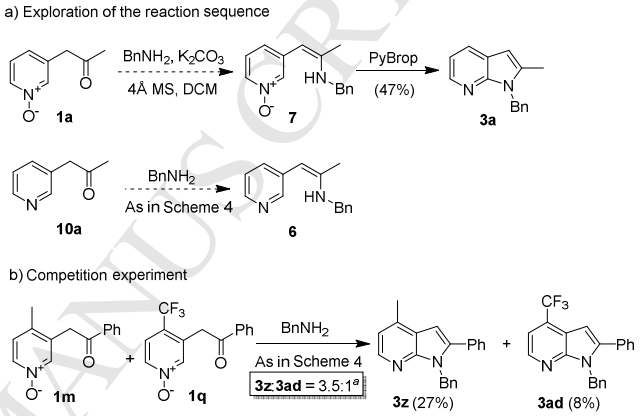
It's worth noting that **3a** was delivered in only 2 steps with 49% overall yield using commercially available 1-(pyridin-3-yl)propan-2-one (**10a**), compared with the known method, which resulted in 30% overall yield after five steps (Scheme 3).[20] Besides, this reported procedure requires using very toxic CuCN. Therefore, this newly developed one-pot reaction is likely to be a very useful method for the preparation of 7-azaindoles.

Scheme 4. Substrate Scope for the Cascade Amination/Enamine Formation Reaction[a].



[a] Unless otherwise noted, all reactions were conducted at 0.20 M concentration with *N*-oxide (1.0 equiv), amines (1.5 equiv), PyBrop (1.3 equiv), K_2CO_3 (3.0 equiv) and 4Å molecular sieves in DCM at r.t. [b] The reaction were conducted at 0.20 M concentration with *N*-oxide (1.0 equiv), amines (2.0 equiv), PyBrop (2.0 equiv), K_2CO_3 (3.0 equiv) and 4Å molecular sieves in DCE at reflux.

With the optimized conditions in hand, we then investigated the scope of this cascade amination/enamine formation and found that a variety of pyridine and quinoline *N*-oxides can be successfully converted to the desired product in modest to good yields (up to 91%, Scheme 4). Excellent regioselectivity (C2 vs. C4) was also observed. With regard to the scope of amines, ammonia (**3b**, **3l**), alkyl and aryl amines (**3g**, **3i**, **3m**) are all good substrates. Generally, aryl amines afforded better yields than alkyl amines (i.e., **3i** > **3h**, **3m** > **3n**). Moreover, the reaction works for those steric hindered amines (**3f**, **3j**, **3o**), although slightly lower yields were observed. The reaction can well tolerate alkyl, cycloalkyl, and aryl groups for R^2 and R^3 groups in the pyridine *N*-oxides part. Furthermore, pyridine rings carrying ester groups (**3u**), chloro (**3w**, **3x**), C2- (**3aa**, **3ab**), C3- (**3y**) and C4- methyl (**3z**) substituents are compatible with the reaction, thus providing additional handles for further functionalization at the halogenated and benzylic positions using cross coupling reactions or nucleophilic aromatic substitutions. It seems that the reaction is very sensitive to R^2 groups. Low yields were observed for both **3r** and **3t**, probably due to steric hindrance. Surprisingly, in sharp contrast to most electron neutral or poor substrates, the regioisomeric amination byproduct (**3ae'**) predominates (59% yield, Scheme 4) for methoxy substituted substrate, indicating that this new synthetic method is not suitable for those strong EDG substituted pyridine *N*-oxides.



Scheme 5. Mechanism Investigations. [a] The ratio is determined by ^{1}H NMR of the crude product.

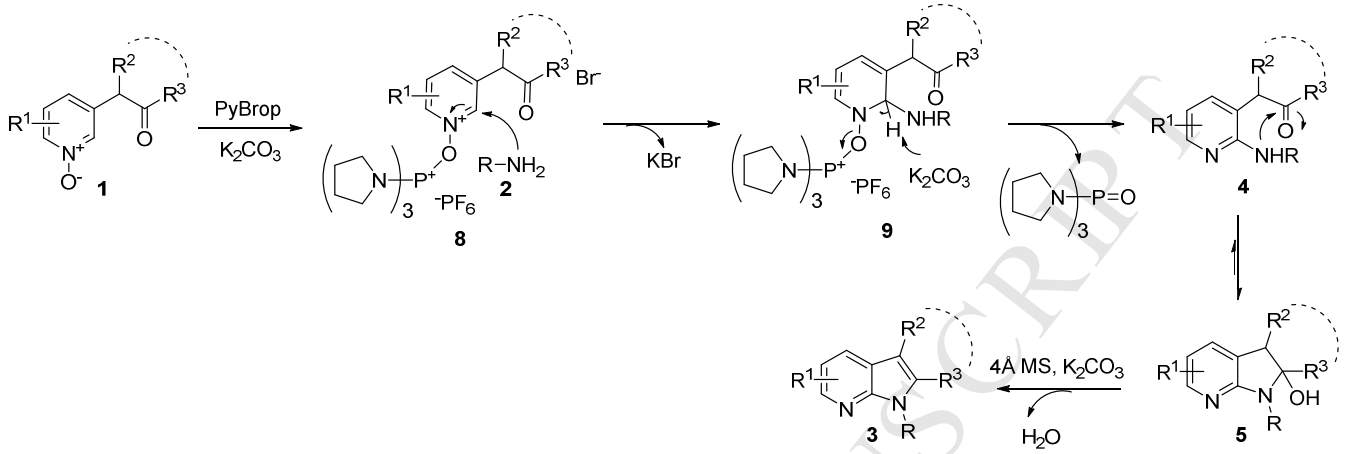
In order to determine the reaction sequence of this cascade transformation, compound **1a** was subjected to enamine formation conditions (Scheme 5a). However, both **1a** and benzyl amine remained in the mixture and no reaction could be detected. In contrast, the reaction was triggered once PyBrop was added. Moreover, it has been confirmed that PyBrop cannot trigger the formation of enamine because no reaction could be detected with **10a** under the reaction conditions (Scheme 5a). These observations indicate that the amination of *N*-oxides occurs first, followed by the intramolecular enamine formation. Since pyridine *N*-oxides are known to react via S_EAr in some reactions,[21] a competition experiment was performed to verify if this pathway was operative. Benzyl amine was reacted in the presence of both electron-rich pyridine *N*-oxide (**1m**) and electron-deficient pyridine *N*-oxide (**1q**) under the standard conditions (Scheme 5b). It was found that product **3z** predominates, indicating a complex reaction manifold, and the rate-determining step is governed by S_EAr.

Based on the above observations and the reactivity of *N*-oxides, the proposed mechanism for this transformation is outlined in Scheme 6. Replacement of the bromine atom of PyBrop with **1** produces the activated pyridine complex **8**. Nucleophilic attack of amines **2** to the C2 position of **8** yields **9**, followed by basic rearomatization to yield **4** and phosphoryltripyrrolidine. Nucleophilic attack of the amino group to the carbonyl group produces **5**. Finally, elimination of water affords product **3**.

3. Conclusions

In conclusion, an efficient and tranisition-metal-free synthesis of 7-azaindoles is developed through a one-pot

operation, involving amination of pyridine *N*-oxides and intramolecular enamine formation. The present reaction has broad substrate scope, including alkyl amines, aryl amines and pyridines carrying various substituents. Moreover, most of the substrates required in this methodology, without any C2-amino group, is cheap and easy to access. The reaction had only moderate overall yield (46% average yield) but it was nevertheless remarkably effective given that it generated three new bonds (~77% average yield per bond formation). This new method would also refresh strategy to prepare complex pyridine derivatives via conventional methods.



Scheme 6. Proposed Reaction Mechanism.

4. Experimental section

General Remarks. The preparation experiments were performed under air or an argon atmosphere in oven dried glassware. Solvents used as reaction media were distilled immediately before use: THF was distilled from Na/benzophenone ketyl, DCM and DCE were distilled from calcium hydride. All reagents were purchased at the highest commercial quality and used without further purification. Reactions were monitored by thin layer chromatography (TLC) using ultra violet light (UV) as the visualizing agent. Nuclear magnetic resonance spectra (NMR) were recorded on Bruker AV-400 instruments and were calibrated using residual undeuterated solvent as an internal reference (^{1}H NMR: $CHC1_3$ 7.26 ppm, ^{13}C NMR: $CHC1_3$ 77.16 ppm). High resolution mass spectra (HRMS) were recorded on a hybrid IT-TOF mass spectrometer (Shimadzu LCMS-IT-TOF, Kyoto, Japan). The following abbreviations were used to indicate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, sep = septet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, m = multiplet).

See the Supplenmentary Data for general reaction schemes.

General Procedure I (for the Preparation of 9a-c): To a stirred solution of compound **8** (1.0 eq.) in deoxygenated DMF (1 M) was added CuI (0.05 eq.), Et_3N (4.0 eq.), alkyne (1.2 eq.) and $Pd(PPh_3)_2Cl_2$ (0.05 eq.), the resulting mixture was stirred at r.t. overnight. After filtration through Celite, the organic layer was diluted with H_2O and extracted with DCM. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford the crude product, which was purified by flash column chromatography using PE/EA (50:1~10:1) as eluent.

General Procedure II (for the Preparation of 10h, 10o-q): A solution of alkyne **9** in toluene and conc. sulfuric acid (V_{PhMe}/V_{H2SO4} =1:4, 0.5 M) was heated to 80□ for four hours until the reaction was complete as indicated by TLC. After cooled down to r.t., the reaction mixture was basified to pH 7~8 with ammonia, then diluted with water and extracted with EA. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated in vacuo and chromatographed gradiently on silica gel with PE/EA (10:1~1:1) to afford the product.

General Procedure III (for the Preparation of 1a-q): Compound **10** (1.0 eq) was dissolved in DCM (0.3 M) and *m*CPBA (1.2 eq) was added and stirred at room temperature overnight until the reaction was complete as indicated by TLC. The reaction mixture was concentrated in vacuo and chromatographed gradiently on silica gel with DCM/MeOH (100:1~30:1) to afford product **1**.

General Procedure IV (for the Preparation of 3a-ad): To a solution of compound **1** (1.0 eq.) and compound **2** (1.5 eq.) in dry DCM (0.2 M) was added K_2CO_3 (3.0 eq.), 4Å molecular sieves (same weight as cpd.**1**), and PyBrop (1.3 eq.) in this order. The resulting mixture was stirred at r.t. for several hours until the reaction was complete as indicated by TLC. The reaction mixture was filtrated. The mother liquor was diluted with sat. aqueous NH_4Cl and extracted with EA. The combined organic phase was dried over Na_2SO_4, concentrated in vacuo and the crude product was purified by flash column chromatography using PE/EA (50:1~10:1) to afford product **3**.

Methyl 5-(phenylethynyl)nicotinate (9a). Following General Procedure □, using methyl 5-bromonicotinate (4 g, 18.516 mmol), phenylacetylene (2.27 g, 22.220 mmol), the title compound was obtained (4.05 g, 92% yield) as a yellow solid. The spectroscopic data are consistent with material from commercial sources. ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.04 (s, 1H), 8.97 (s, 1H), 8.37 (s, 1H), 7.62 (d, *J* = 3.6 Hz, 2H), 7.47 (d, *J* = 1.6 Hz, 3H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 164.6, 155.2, 149.0, 138.8, 131.7, 129.6, 128.9, 125.5, 121.4, 119.7, 93.5, 85.1, 52.7.

3-(Phenylethynyl)quinoline (9b). Following General Procedure I, using 3-bromoquinoline (2.08 g, 10.0 mmol), phenylacetylene (1.23 g, 12.0 mmol), the title compound was obtained (1.66 g, 72% yield) as a yellow solid. The spectroscopic data are consistent with material from

commercial sources. ^{1}H NMR (400 MHz, d_6-DMSO) δ 9.01 (s, 1H), 8.63 (s, 1H), 8.01-8.06 (m, 2H), 7.82 (t, *J* = 6.8 Hz, 1H), 7.65-7.69 (m, 3H), 7.47 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 151.6, 146.3, 138.4, 131.5, 130.6, 129.3, 128.9, 128.8, 128.1, 127.6, 126.9, 121.8, 116.4, 92.3, 86.8.

3-(phenylethynyl)-4-(trifluoromethyl)pyridine (9c). Following General Procedure □, using 3-bromo-4-(trifluoromethyl)pyridine (2.3g, 10.18 mmol) and phenylacetylene (1.25 g, 12.2 mmol), compound **9c** was obtained (1.75 g, 70% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.69 (d, *J* = 4.4 Hz, 1H), 7.55-7.59 (m, 3H), 7.39-7.40 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 149.0, 132.0, 129.6, 128.6, 123.8, 122.1, 121.1, 119.4 (q, *J* = 4.0 Hz), 117.7, 98.4, 82.3. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_9NF_3$ 248.0682, found 248.0664.

1-(pyridin-3-yl)propan-2-one (10a). This compound was obtained from commercial sources.

1-(quinolin-3-yl)propan-2-one (10b). This compound was obtained from commercial sources.

1-(pyridin-3-yl)butan-2-one (10c). This compound was obtained from commercial sources.

1-phenyl-2-(pyridin-3-yl)ethan-1-one (10d). This compound was obtained from commercial sources.

3-(pyridin-3-yl)butan-2-one (10e). To an ice cold suspension of $NaNH_2$ (0.79 g, 20.35 mmol) in anhydrous THF (40 ml) was added a solution of 1-(pyridin-3-yl)propan-2-one (2.5 g, 18.50 mmol) in THF (46 ml) slowly under argon. After stirring for 1.5 hours at 0□, a solution of iodomethane (3.15 g, 22.19 mmol) in THF (4 ml) was added. The resulting reaction mixture was warmed to r.t. and stirred for several hours until the reaction was complete as indicated by TLC. The reaction was quenched by water, and the water phase was extracted with EA for three times. The combined organic phase was washed with brine, dried over Na_2SO_4, concentrated in vacuo and chromatographed gradiently on silica gel with PE/EA (20:1~10:1) to give **10e** (1.49 g, 54% yield) as a yellow oil. The spectroscopic data are consistent with data previously reported.[22] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 3.6 Hz, 1H), 3.80 (q, *J* = 7.2 Hz, 1H), 2.10 (s, 3H), 1.43 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 149.7, 148.9, 136.1, 135.0, 123.9, 51.0, 28.7, 17.4.

2-(pyridin-3-yl)cyclohexan-1-one (10f). This compound was obtained from commercial sources.

1,2-diphenyl-2-(pyridin-3-yl)ethan-1-one (10g). This compound was prepared following a known procedure[23] with slightly modification. To a suspension of $PdCl_2(D^tBPF)$ (223 mg, 5mol%), t-BuONa (987 mg, 10.27 mmol) in degassed anhydrous toluene (27 ml) was added 1-phenyl-2-(pyridin-3-yl)ethan-1-one（1.35 g, 6.85 mmol）and iodobenzene (1.54 g, 7.54 mmol) under argon. The resulting mixture was heated to reflux for 16 hurs. After cooled down to r.t., the mixture was diluted with EA, filtered through Celite, and the filtrate was concentrated in vacuo, which was chromatographed gradiently on silica gel with PE/EA (15:1~5:1) to afford **10g** (1.08 g, 58% yield) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 2.0 Hz, 1H), 8.46 – 8.45 (m, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 8..0 Hz, 2H), 7.35 – 7.21 (m, 6H), 6.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 150.1, 148.4, 138.1, 137.0, 136.3, 135.1, 133.5, 129.2, 129.0, 128.9, 128.8, 127.7, 123.5, 56.8. HRMS (+ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}NO$ 274.1226; found 274.1222.

methyl 5-(2-oxo-2-phenylethyl)nicotinate (10h). Following General Procedure Ⅱ, using **9a** (2.0 g, 8.43 mmol), compound **10h** was obtained (541 mg, 25% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (d, *J* = 1.6 Hz, 1H), 8.68 (d, *J* = 2.0 Hz, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 8.02-8.04 (m, 2H), 7.60-7.70 (m, 1H), 7.44-7.55 (m, 2H), 4.38 (s, 2H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 165.8, 154.6, 149.6, 138.5, 136.3, 133.9, 130.2, 129.0, 128.5, 126.0, 52.6, 42.1. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{15}H_{13}NO_3Na$ 278.0788, found 278.0784.

1-phenyl-2-(5-phenylpyridin-3-yl)ethan-1-one (10i). In a sealed tube equipped with magnetic stir bar was combined $Pd(OAc)_2$ (67 mg, 0.3 mmol), $P(^tBu)_3{\cdot}HBF_4$ (35 mg, 0.12 mmol), t-BuONa (1.44 g, 14.95 mmol) and degassed anhydrous THF (31 ml). After stirring for 5 min under argon, 3-bromo-5-phenylpyridine (1.40 g, 5.98 mmol) and acetophenone (1.08 g, 8.97 mmol) were added. The resulting mixture was heated to reflux for 15 hours. After cooled down to r.t., the mixture was diluted with DCM and water, filtered through Celite, and the filtrate was separated. Water phase was extracted with DCM. The combined organic phase was dried, concentrated in vacuo to give the crude product, which was chromatographed gradiently on silica gel with PE/EA (30:1~10:1) to afford **10i** (750 mg, 46% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 2.0 Hz, 1H), 8.51 (d, *J* = 2.0 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 2H), 7.80 (s, 1H), 7.63-7.57 (m, 3H), 7.52-7.45 (m, 4H), 7.40 (d, *J* = 7.2 Hz, 1H), 4.37 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 149.4, 147.1, 137.8, 136.6, 136.4, 135.8, 133.7, 130.2, 129.2, 129.0, 128.6, 128.3, 127.4, 42.4. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{19}H_{16}NO$ 274.1226; found 274.1217.

1-(6-chloropyridin-3-yl)propan-2-one (10j). This compound was obtained from commercial sources.

1-(6-chloropyridin-3-yl)butan-2-one (10k). To a solution of 2-(6-chloropyridin-3-yl)-*N*-methoxy-*N*-methylacetamide (2 g, 9.3 mmol) in dry tetrahydrofuran (20 ml) at 0 ℃ was added ethylmagnesium bromide (1.36 g, 10.2 mmol) and stirred for 1 h at r.t. The reaction mixture was quenched with aqueous ammonium chloride solution and then extracted thrice with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography using PE/EA (10:1~3:1) as eluent. The title compound was obtained (776 mg, 45% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 2.4 Hz, 1H), 7.51 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 3.69 (s, 2H), 2.54 (q, *J* = 7.2 Hz, 2H), 1.08 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.0, 150.4, 150.3, 140.0, 128.9, 124.2, 45.4, 36.1, 7.8. HRMS(+ESI-TOF) m/z: $[M + H]^+$ calcd for $C_9H_{11}ClNO$ 184.0524, found 184.0517.

2-(5-methylpyridin-3-yl)-1-phenylethan-1-one (10l). This compound was obtained from commercial sources.

2-(4-methylpyridin-3-yl)-1-phenylethan-1-one (10m). Following the procedure for **10i**, using 3-bromo-4-methylpyridine (2 g, 11.627 mmol), the title compound was obtained (646 mg, 26%) as a black solid. The spectroscopic data are consistent with material from commercial sources. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.8 Hz, 1H), 8.34 (s, 1H), 8.03-8.06 (m, 2H), 7.60-7.63 (m, 1H), 7.49-7.53 (m, 2H), 7.14 (d, *J* = 4.8 Hz, 1H), 4.34 (s, 2H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 150.9, 148.5, 146.9, 136.5, 133.7, 129.8, 128.9, 128.4, 125.4, 40.7, 19.4. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{14}NO$ 212.1070, found 212.1066.

1-(6-methylpyridin-3-yl)propan-2-one (10n). This compound was obtained from commercial sources.

2-(6-methylpyridin-3-yl)-1-phenylethan-1-one (10o). Following Following General Procedure □, using 2-methyl-5-(phenylethynyl)pyridine (2.30 g, 11.9 mmol), the title compound was obtained (880 mg, 35% yield) as a yellow oil. The spectroscopic data are consistent with material from commercial sources. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.0 Hz, 1H), 8.02-7.99 (m, 1H), 7.60-7.56 (m, 1H), 7.50-7.45 (m, 3H), 7.13 (d, *J* = 8.0 Hz, 1H), 4.26 (s, 2H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 157.1, 149.9, 137.6, 136.4, 133.5, 128.9, 128.5, 127.1, 123.2, 42.1, 24.1. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{14}NO$ 212.1070, found 212.1078.

1-phenyl-2-(quinolin-3-yl)ethan-1-one (10p). Following General Procedure □, using **9b** (1.0 g, 4.36 mmol), compound **10p** was obtained (450 mg, 42% yield) as a yellow solid. The spectroscopic data are consistent with material from commercial sources. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.83 (d, *J* = 2.0 Hz, 1H), 8.21 (d, *J* = 1.6 Hz, 1H), 8.11-8.13 (m, 2H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.71-7.76 (m, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.56-7.62 (m, 3H), 4.70 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 197.3, 152.7, 146.4, 136.3, 136.1, 133.5, 129.0, 128.8, 128.7, 128.5, 128.3, 127.7, 127.6, 126.6, 42.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{17}H_{14}NO$ 248.1070, found 248.1072.

1-phenyl-2-(4-(trifluoromethyl)pyridin-3-yl)ethan-1-one (10q). Following General Procedure □, using **9c** (1.75 g, 7.079 mmol), compound **10q** was obtained (1.7 g, 91% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.8 Hz, 1H), 8.62 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 5.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.52 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 154.1, 149.5, 136.9 (q, *J* = 32.0 Hz), 136.2, 133.9, 129.0, 128.3, 127.7, 124.6 (q, *J* = 273.0 Hz), 119.7 (q, *J* = 4.0 Hz), 40.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{11}NOF_3$ 266.0787, found 266.0777.

2-(4-methoxypyridin-3-yl)-1-phenylethan-1-one (10r). Following the procedure for **10i**, using 3-bromo-4-methoxypyridine (4 g, 21.27 mmol), the title compound was obtained (1.45 g, 30%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 5.6 Hz, 1H), 8.31 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 2H), 6.83 (d, *J* = 5.6 Hz, 1H), 4.27 (s, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 164.1, 151.4, 150.7, 136.7, 133.4, 128.8, 128.4, 120.1, 106.3, 55.5, 37.6. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{14}NO_2$ 228.1019, found 228.1016.

3-(2-oxopropyl)pyridine 1-oxide (1a). Following General Procedure □, using **10a** (2 g, 14.8 mmol), compound **1a** was obtained (1.97 g, 88% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.4 Hz, 1H), 8.12 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.15-7.16 (m, 1H), 3.73 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 140.0, 137.9, 133.5, 127.9, 125.8, 46.7, 30.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_8H_{10}NO_2$ 152.0706, found 152.0709.

3-(2-oxopropyl)quinoline 1-oxide (1b). Following General Procedure □, using **10b** (444 mg, 2.397 mmol), compound **1b** was obtained (367 mg, 76% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.8 Hz, 1H), 8.44 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 3.83 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 140.6, 137.0, 130.4, 130.2, 129.2, 128.0, 127.9, 126.6, 119.8, 47.4, 30.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{12}H_{12}NO_2$ 202.0863, found 202.0856.

3-(2-oxobutyl)pyridine 1-oxide (1c). Following General Procedure □, using 1-(pyridin-3-yl)butan-2-one (430 mg, 2.88 mmol), compound **1c** was obtained (343 mg, 72% yield) as a yellow oil. ^{1}H NMR (400 MHz, CD_3OD) δ 8.25 (s, 2H), 7.51 – 7.45 (m, 2H), 3.92 (s, 2H), 2.63 (q, *J* = 7.2 Hz, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 208.3, 141.2, 138.6, 136.8, 132.9, 127.4, 45.5, 36.6, 7.9. HRMS (+ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_9H_{11}NO_2Na$ 188.0682; found 188.0677.

3-(2-oxo-2-phenylethyl)pyridine 1-oxide (1d). Following General Procedure □, using **10d** (600 mg, 3.042 mmol), compound **1d** was obtained (465 mg, 72% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.19 (s, 1H), 8.13 (d, *J* = 6.4 Hz, 1H), 8.04-8.06 (m, 2H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 4.49 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 196.2, 139.7, 136.9, 136.1, 134.7, 133.6, 128.8, 128.2, 127.3, 125.8, 41.3. HRMS (-ESI-TOF) *m/z:* $[M - H]^-$ calcd for $C_{13}H_{10}NO_2$ 212.0717, found 212.0719.

3-(3-oxobutan-2-yl)pyridine 1-oxide (1e). Following General Procedure □, using **10e** (1.49 g, 10 mmol), the title compound **1e** was obtained (1.38 g, 86% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.18 (d, *J* = 6.0 Hz, 1H), 7.30 (d, *J* = 6.0 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.75 (q, *J* = 6.8 Hz, 1H), 2.17 (s, 3H), 1.45 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.2, 139.8, 139.1, 138.1, 126.1, 125.9, 50.5, 28.7, 17.2. HRMS (+ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_9H_{12}NO_2$ 166.0836; found 166.0859.

3-(2-oxocyclohexyl)pyridine 1-oxide (1f). Following General Procedure □, using 2-(pyridin-3-yl)cyclohexan-1-one (500 mg, 2.85 mmol), the title compound was obtained (360 mg, 66% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 6.4 Hz, 1H), 8.04 (s, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 3.57 (dd, *J* = 12.0, 5.2 Hz, 1H), 2.46-2.60 (m, 2H), 2.29-2.34 (m, 1H), 2.19-2.23 (m, 1H), 2.05-2.06 (m, 1H), 1.79-2.04 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.7, 139.5, 138.2, 137.7, 127.1, 125.5, 54.6, 42.2, 35.0, 27.7, 25.4. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{11}H_{13}NO_2Na$ 214.0839, found 214.0832.

3-(2-oxo-1,2-diphenylethyl)pyridine 1-oxide (1g). Following General Procedure □, using **10g** (1.5 g, 5.49 mmol) and *m*-CPBA (1.23 g, 6.04 mmol, 85%), the title compound was obtained (947 mg, 60% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 2H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 2H), 7.22 – 7.19 (m, 3H), 7.12 (d, *J* = 4.0 Hz, 2H), 5.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.0, 140.1, 139.1, 137.7, 136.4, 135.8, 133.7, 129.6, 129.0, 128.9, 128.8,

128.2, 127.3, 125.4, 56.4. HRMS (+ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{16}NO_2$ 290.1176; found 290.1170.

3-(methoxycarbonyl)-5-(2-oxo-2-phenylethyl)pyridine 1-oxide (1h). Following General Procedure □, using **10h** (480 mg, 1.880 mmol), compound **1h** was obtained (252 mg, 49% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.29 (s, 1H), 7.99-8.01 (m, 2H), 7.78 (s, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 2H), 4.32 (s, 2H), 3.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 165.8, 154.6, 149.6, 138.5, 136.3, 133.9, 130.2, 129.0, 128.5, 126.0, 52.6, 42.1. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{15}H_{14}NO_4$ 272.0917, found 272.0911.

3-(2-oxo-2-phenylethyl)-5-phenylpyridine 1-oxide (1i). Following General Procedure □, using **10i** (370 mg, 1.463 mmol), the title compound was obtained (360 mg, 92% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.16 (s, 1H), 8.03-8.00 (m, 2H), 7.65-7.61 (m, 1H), 7.54-7.40 (m, 8H), 4.32 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 140.0, 138.4, 136.2, 135.9, 135.1, 134.1, 133.7, 129.5, 129.4, 129.1, 128.5, 127.1, 126.9, 41.9. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{19}H_{16}NO_2$ 290.1176; found 290.1165.

2-chloro-5-(2-oxopropyl)pyridine 1-oxide (1j). Following General Procedure □, using **10j** (400 mg, 2.36 mmol), the title compound was obtained (320 mg, 73% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 3.70 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 141.1, 140.7, 131.3, 127.5, 126.7, 46.2, 30.1. HRMS (-ESI-TOF) *m/z*: $[M - H]^-$ calcd for $C_8H_7NO_2Cl$ 184.0171; found 184.0180.

2-chloro-5-(2-oxobutyl)pyridine 1-oxide (1k). Following General Procedure □, using **10k** (1.1 g, 6.0 mmol), the title compound was obtained (410 mg, 34% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 3.65 (s, 2H), 2.55 (q, *J* = 7.2 Hz, 2H), 1.09 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6, 141.1, 140.6, 131.6, 127.6, 126.7, 45.0, 36.3, 7.8. HRMS(+ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_9H_{10}ClNO_2Na$ 222.0292, found 222.0285.

3-methyl-5-(2-oxo-2-phenylethyl)pyridine 1-oxide (1l). Following General Procedure □, using **10l** (400 mg, 1.893 mmol), compound **1l** was obtained (356 mg, 83% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 5.2 Hz, 2H), 7.98-8.00 (m, 2H), 7.61-7.65 (m, 1H), 7.49-7.53 (m, 2H), 7.06 (s, 1H), 4.22 (s, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 137.8, 137.3, 136.4, 135.9, 133.9, 133.1, 129.4, 129.0, 128.4, 41.7, 18.3. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_2Na$ 250.0839, found 250.0835.

4-methyl-3-(2-oxo-2-phenylethyl)pyridine 1-oxide (1m). Following General Procedure □, using **10m** (600 mg, 2.840 mmol), compound **1m** was obtained (469 mg, 73% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.11 (m, 2H), 8.01-8.03 (m, 2H), 7.63-7.67 (m, 1H), 7.51-7.55 (m, 2H), 7.14 (d, *J* = 6.4 Hz, 1H), 4.28 (s, 2H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 140.0, 138.4, 137.5, 136.0, 134.1, 133.1, 129.1, 128.4, 127.4, 40.6, 18.6. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_2Na$ 250.0839, found 250.0827.

2-methyl-5-(2-oxopropyl)pyridine 1-oxide (1n). Following General Procedure □, using **10n** (420 mg, 2.815 mmol), the title compound was obtained (360 mg, 77% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 3.66 (s, 2H), 2.51 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.6, 147.7, 139.8, 130.7, 127.5, 126.3, 46.5, 29.9, 17.5. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_9H_{12}NO_2$ 166.0863; found 166.0871.

2-methyl-5-(2-oxo-2-phenylethyl)pyridine 1-oxide (1o). Following General Procedure □, using **10o** (400 mg, 1.893 mmol), the title compound was obtained (360 mg, 84% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.00 (s, 1H), 7.98 (t, *J* = 1.6 Hz , 1H), 7.63-7.59 (m, 1H), 7.52-7.48 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.11 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 4.22 (s, 2H), 2.51 (d, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 147.6, 140.1, 136.0, 133.9, 131.2, 129.0, 128.5, 127.4, 126.2, 41.7, 17.6. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_2Na$ 250.0839; found 250.0830.

3-(2-oxo-2-phenylethyl)quinoline 1-oxide (1p). Following General Procedure □, using **10p** (450 mg, 1.820 mmol), compound **1p** was obtained (400 mg, 84% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.8 Hz, 1H), 8.54 (s, 1H), 8.04 (d, *J* = 7.6 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.74 (t, *J* = 8.0 Hz, 1H), 7.61-7.67 (m, 3H), 7.52 (t, *J* = 7.6 Hz, 2H), 4.40 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 140.5, 137.3, 136.1, 134.0, 130.4, 130.3, 129.12, 129.10, 128.6, 128.4, 128.1, 127.0, 119.8, 42.4. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{17}H_{14}NO_2$ 264.1019, found 264.1010.

3-(2-oxo-2-phenylethyl)-4-(trifluoromethyl)pyridine 1-oxide (1q). Following General Procedure □, using **10q** (1.7 g, 6.413 mmol), compound **1q** was obtained (1.0g, 55% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.20 (m, 2H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.51-7.54 (m, 3H), 4.43 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 142.5, 138.0, 135.7, 134.1, 132.4, 129.0, 128.3, 125.9 (q, *J* = 32.0 Hz), 123.3 (q, *J* = 5.0 Hz), 122.8 (q, *J* = 271.0 Hz), 39.6. HRMS (+ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{10}NO_2F_3Na$ 304.0556, found 304.0544.

4-methoxy-3-(2-oxo-2-phenylethyl)pyridine 1-oxide 1-oxide (1r). Following General Procedure □, using **10r** (640 mg, 2.82 mmol), compound **1r** was obtained (300 mg, 44% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 6.8 Hz, 1H), 8.09 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 6.80 (d, *J* = 6.8 Hz, 1H), 4.23 (s, 2H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 157.0, 141.2, 139.1, 136.2, 133.8, 128.9, 128.4, 123.3, 107.7, 56.5, 37.3. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{14}NO_3$ 244.0968, found 244.0953.

1-benzyl-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3a). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and benzylamine (128 mg, 1.191 mmol), compound **3a** was obtained (99 mg, 56% yield) as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.16 (d, *J* = 4.8 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.26-7.30 (m, 2H), 7.20-7.23 (m, 1H), 7.05 (d, *J* = 7.2 Hz, 3H), 6.30 (s, 1H), 5.50 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.1, 141.2, 138.4, 137.7, 128.6, 127.1, 127.0, 126.4, 120.0, 115.8, 98.0, 44.0, 12.7. The spectroscopic data are consistent with data previously reported.[20]

2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3b). Following General Procedure □, using **1a** (120 mg, 0.79 mmol) and

ammonia (0.4 M in 1,4-dioxane) (3 ml, 1.2 mmol), compound **3b** was obtained (38 mg, 36% yield) as a yellow solid. The spectroscopic data are consistent with material from commercial sources. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.20 (dd, *J* = 4.8 Hz, 1.2 Hz, 1H), 7.82 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.04 (dd, *J* = 8.0 Hz, 5.2 Hz, 1H), 6.18 (s, 1H), 2.53 (d, *J* = 0.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 140.3, 137.0, 127.8, 122.3, 115.6, 98.2, 14.2.

1-ethyl-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3c). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and ethylamine (2.0 M in THF) (0.6 ml, 1.191 mmol), compound **3c** was obtained (64 mg, 50% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 5.2 Hz, 1H), 8.31 (d, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 6.4 Hz, 1H), 6.56 (s, 1H), 4.76 (q, *J* = 6.8 Hz, 2H), 2.58 (s, 3H), 1.54 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0, 138.5, 135.3, 131.5, 126.0, 115.2, 101.6, 40.7, 15.7, 13.1. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{10}H_{13}N_2$ 161.1073, found 161.1073.

1-butyl-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3d). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and butylamine (87 mg, 1.191 mmol), compound **3d** was obtained (80 mg, 54% yield) as a colorless oil. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.13 (d, *J* = 4.8 Hz, 1H), 7.80 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.00 (dd, *J* = 7.6 Hz, 4.8 Hz, 1H), 6.22 (s, 1H), 4.21 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.63-1.70 (m, 2H), 1.25-1.34 (m, 2H) , 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 147.8, 140.9, 137.5, 126.7, 119.9, 115.4, 97.5, 40.8, 31.9, 19.6, 13.7, 12.7. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{12}H_{17}N_2$ 189.1386, found 189.1376.

1-allyl-2-methyl-1H-pyrrolo[2,3-b]pyridine (3e). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and allylamine (111 mg, 1.191 mmol), compound **3e** was obtained (53 mg, 39% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.78 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.01 (dd, *J* = 7.6 Hz, 4.8 Hz, 1H), 6.20 (d, *J* = 0.8 Hz, 1H), 5.95-6.05 (m, 1H), 5.08-5.12 (m, 1H), 4.89-4.91 (m, 2H), 4.75-4.81 (m, 1H), 4.43 (d, *J* = 0.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 141.7, 137.7, 134.0, 127.3, 120.7, 115.9, 115.8, 98.2, 43.7, 13.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{11}H_{13}N_2$ 173.1073, found 173.1072.

1-isopropyl-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3f). Following General Procedure □, using **1a** (100 mg, 0.662 mmol) and isopropylamine (59 mg, 0.993 mmol), compound **3f** was obtained (40 mg, 35% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.74 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 6.97 (dd, *J* = 7.6 Hz, 4.8 Hz, 1H), 6.15 (d, *J* = 0.8 Hz, 1H), 5.03 (qui, *J* = 6.8 Hz, 1H), 2.51 (s, 3H), 1.66 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 139.9, 136.1, 125.7, 119.7, 114.2, 97.6, 45.2, 20.6, 13.5. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{11}H_{15}N_2$ 175.1230, found 175.1221.

2-methyl-1-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (3g). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and aniline (111 mg, 1.191 mmol), compound **3g** was obtained (85 mg, 53% yield) as a yellow oil. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.08 (dd, *J* = 4.8 Hz, 1.2 Hz, 1H), 7.91 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.57 (t, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.43-7.45 (m, 2H), 7.09 (dd, *J* = 8.0 Hz, 4.8 Hz, 1H), 6.44 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.8, 141.7, 137.7, 136.2, 129.1, 128.2, 127.7, 127.2, 120.2, 116.5, 99.2, 13.5. HRMS (+ESI-TOF) *m/z:* $[M + Na]^+$ calcd for $C_{14}H_{12}N_2Na$ 231.0893, found 231.0883.

1-(4-methoxybenzyl)-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3h). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and 4-methoxybenzylamine (163 mg, 1.191 mmol), compound **3h** was obtained (76 mg, 38% yield) as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.17 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.85 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.02-7.07 (m, 3H), 6.83-6.85 (m, 2H), 6.27 (d, *J* = 0.8 Hz, 1H), 5.42 (s, 2H), 3.69 (s, 3H), 2.35 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 158.3, 148.0, 141.2, 137.6, 130.3, 127.9, 127.0, 120.0, 115.7, 114.0, 98.0, 55.0, 43.5, 12.8. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{16}H_{17}N_2O$ 253.1335, found 253.1334.

1-(4-methoxyphenyl)-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3i). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and *p*-anisidine (147 mg, 1.191 mmol), compound **3i** was obtained (94 mg, 50% yield) as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.07 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.89 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.32-7.36 (m, 2H), 7.06-7.12 (m, 3H), 6.41 (d, *J* = 0.8 Hz, 1H), 3.84 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 158.6, 149.0, 141.6, 138.0, 129.4, 128.8, 127.1, 120.1, 116.3, 114.3, 98.7, 55.4, 13.4. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{15}H_{15}N_2O$ 239.1179, found 239.1190.

1-cyclohexyl-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3j). Following General Procedure □, using **1a** (120 mg, 0.794 mmol) and cyclohexylamine (118 mg, 1.19 mmol), compound **3j** was obtained (60 mg, 35% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.74 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 6.96 (dd, *J* = 8.0 Hz, 4.8 Hz, 1H), 6.15 (d, *J* = 0.8 Hz, 1H), 4.43-4.58 (m, 1H), 2.46-2.51 (m, 5H), 1.84-1.95 (m, 4H), 1.76 (d, *J* = 12.0 Hz, 1H), 1.25-1.54 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 141.0, 137.4, 126.9, 120.8, 115.4, 98.8, 55.1, 31.7, 26.6, 25.6, 15.0. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{14}H_{19}N_2$ 215.1543, found 215.1533.

1,2-dimethyl-1H-pyrrolo[2,3-b]quinoline (3k). Following General Procedure □, using **1b** (120 mg, 0.6 mmol) and methylamine (2.0 M in THF) (0.6 ml, 1.2 mmol) in DCE at reflux conditions, compound **3k** was obtained (95 mg, 81% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.35 (s, 1H), 7.95-7.99 (m, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 6.39 (s, 1H), 3.79 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 149.8, 143.5, 143.3, 128.1, 127.4, 127.0, 124.9, 124.4, 122.4, 121.9, 96.5, 27.7, 13.2. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{13}H_{13}N_2$ 197.1073; found 197.1071.

2-methyl-1H-pyrrolo[2,3-b]quinoline (3l). Following General Procedure □, using **1b** (120 mg, 0.6 mmol) and ammonia (0.4 M in 1,4-dioxane) (3 ml, 1.2 mmol), compound **3l** was obtained (42 mg, 38% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 11.41 (s, 1H), 8.29 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.54-7.57 (m, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 6.28 (s, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 150.8, 143.8, 141.9, 128.0, 127.3, 126.7, 124.4, 122.9, 122.3, 97.0, 14.1. HRMS (+ESI-TOF) *m/z:* $[M + H]^+$ calcd for $C_{12}H_{11}N_2$ 183.0917; found 183.0919.

2-methyl-1-phenyl-1H-pyrrolo[2,3-b]quinoline (3m). Following General Procedure □, using **1b** (120 mg, 0.6 mmol) and aniline (111 mg, 1.2 mmol) in DCE at reflux conditions, compound **3m** was obtained (140 mg, 91% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.46 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.51-7.64 (m, 6H), 7.41 (t, *J* = 7.6 Hz, 1H), 6.61 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 150.5, 143.9, 142.7, 136.3, 129.3, 128.6, 128.1, 127.9, 127.5, 127.3, 125.4, 124.9, 122.9, 121.9, 98.8, 14.1. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{18}H_{15}N_2$ 259.1230; found 259.1231.

1-benzyl-2-methyl-1H-pyrrolo[2,3-*b*]quinoline (3n). Following General Procedure □, using **1b** (120 mg, 0.6 mmol) and benzylamine (128 mg, 1.192 mmol) in DCE at reflux conditions, compound **3n** was obtained (126 mg, 77% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.42 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.27-7.30 (m, 2H), 7.21-7.24 (m, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 6.48 (s, 1H), 5.61 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 149.9, 143.7, 142.7, 138.4, 128.6, 128.1, 127.4, 127.1, 126.4, 125.3, 124.7, 122.6, 121.8, 97.6, 44.0, 13.2. The spectroscopic data are consistent with data previously reported.[24]

2-methyl-1-(4-(methylsulfonyl)-2-(trifluoromethyl)benzyl)-1H-pyrrolo[2,3-b]quinoline (3o). Following General Procedure □, using **1b** (120 mg, 0.6 mmol) and (4-(methylsulfonyl)-2-(trifluoromethyl)phenyl)methanamine (302 mg, 1.2 mmol) in DCE at reflux conditions, compound **3o** was obtained (173 mg, 69% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.50 (s, 1H), 8.29 (s, 1H), 8.01-8.05 (m, 2H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 6.61-6.64 (m, 2H), 5.85 (s, 2H), 3.27 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 149.7, 143.8, 142.6, 142.3, 140.3, 132.0, 128.3, 127.9, 127.5, 127.4, 126.7 (q, *J* = 31.0 Hz), 126.0, 125.2 (q, *J* = 5.0 Hz), 125.0, 123.0, 122.3, 121.9, 98.5, 43.3, 41.0, 12.8. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{21}H_{18}N_2O_2F_3S$ 419.1036, found 419.1035.

1-benzyl-2-ethyl-1*H*-pyrrolo[2,3-*b*]pyridine (3p). Following General Procedure □, using **1c** (120 mg, 0.726 mmol) and benzylamine (117 mg, 1.089 mmol), compound **3p** was obtained (63 mg, 37% yield) as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.19 (s, 1H), 8.17 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.90 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.21-7.29 (m, 2H), 7.20 (d, *J* = 4.8 Hz, 1H), 7.07 (dd, *J* = 7.6 Hz, 4.8 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 6.31 (s, 1H), 5.52 (s, 2H), 2.68 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.1, 143.5, 141.4, 138.5, 128.6, 127.2, 127.1, 126.4, 119.9, 115.8, 96.2, 43.9, 19.5, 11.8. HRMS (+ESI-TOF) *m/z:* [M + Na] $^+$ calcd for $C_{16}H_{16}N_2Na$ 259.1206, found 259.1200.

1-benzyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (3q). Following General Procedure □, using **1d** (120 mg, 0.563 mmol) and benzylamine (91 mg, 0.845 mmol), compound **3q** was obtained (64 mg, 40% yield) as a white solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.27 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 8.04 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.42-7.52 (m, 5H), 7.15-7.21 (m, 4H), 7.84 (d, *J* = 7.2 Hz, 2H), 6.68 (s, 1H), 5.59 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 148.8, 142.8, 141.2, 138.5, 131.8, 128.8, 128.7, 128.5, 128.4, 128.3, 126.9, 126.1, 120.1, 116.6, 100.3, 45.2. The spectroscopic data are consistent with data previously reported.[25]

1-benzyl-2,3-dimethyl-1H-pyrrolo[2,3-b]pyridine (3r). Following General Procedure IV, using **1e** (120 mg, 0.727 mmol) and benzylamine (117 mg, 1.1 mmol), the title compound was obtained (45 mg, 26% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 4.4 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.25-7.18 (m, 3H), 7.04-7.00 (m, 3H), 5.50 (s, 2H), 2.25 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 141.8, 138.6, 133.3, 128.7, 127.2, 126.6, 125.7, 121.2, 115.3, 105.4, 45.0, 10.5, 8.7. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{16}H_{17}N_2$ 237.1386; found 237.1380.

9-benzyl-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole (3s). Following General Procedure □, using **1f** (120 mg, 0.628 mmol) and benzylamine (135 mg, 1.256 mmol) in DCE at reflux conditions, compound **3s** was obtained (71 mg, 43% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.15 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.80 (dd, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.21-7.29 (m, 3H), 7.08 (d, *J* = 7.2 Hz, 2H), 7.03 (dd, *J* = 8.0 Hz, 4.8 Hz, 1H), 5.41 (s, 2H), 2.61-2.63 (m, 4H), 1.75-1.82 (m, 4H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 147.7, 141.3, 138.7, 136.2, 128.6, 127.1, 126.7, 125.4, 119.2, 115.2, 107.3, 43.9, 22.6, 22.4, 21.6, 20.4. The spectroscopic data are consistent with data previously reported.[15]

1-benzyl-2,3-diphenyl-1H-pyrrolo[2,3-b]pyridine (3t). Following General Procedure □, using **1g** (120 mg, 0.415 mmol) and benzylamine (67 mg, 0.623 mmol), compound **3t** was obtained (42 mg, 28% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.36 (d, *J* = 4.4 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.37-7.42 (m, 3H), 7.21-7.31 (m, 7H), 7.14-7.19 (m, 4H), 6.83 (d, *J* = 7.2 Hz, 2H), 5.47 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 147.6, 143.4, 138.2, 137.4, 133.7, 130.8, 130.7, 129.2, 128.8, 128.6, 128.4, 128.3, 127.4, 127.0, 126.4, 126.0, 118.9, 117.0, 112.9, 45.1. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{26}H_{21}N_2$ 361.1699, found 361.1700.

methyl 1-benzyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine-5-carboxylate (3u). Following General Procedure □, using **1h** (120 mg, 0.442 mmol) and benzylamine (95 mg, 0.884 mmol) in DCE at reflux conditions, compound **3u** was obtained (71 mg, 47% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.86 (d, *J* = 2.0 Hz, 1H), 8.62 (d, *J* = 2.0 Hz, 1H), 7.45-7.53 (m, 5H), 7.16-7.21 (m, 3H), 6.82-6.85 (m, 3H), 5.63 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 166.2, 150.5, 144.2, 143.1, 137.8, 131.2, 130.0, 128.94, 128.86, 128.81, 128.5, 127.1, 126.1, 119.4, 118.7, 101.7, 52.1, 45.5. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{22}H_{19}N_2O_2$ 343.1441, found 343.1428.

1-benzyl-2,5-diphenyl-1H-pyrrolo[2,3-b]pyridine (3v). Following General Procedure IV, using **1i** (120 mg, 0.415 mmol) and benzylamine (67 mg, 0.62 mmol), the title compound was obtained (60 mg, 40% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 2.0 Hz, 1H), 7.65-7.63 (m, 2H), 7.49-7.34 (m, 8H), 7.24-7.17 (m, 3H), 7.00-6.98 (m, 2H), 6.61 (s, 1H), 5.59 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 142.8, 142.6, 139.9, 138.6, 132.4, 130.4, 129.4, 129.1, 128.7, 128.64, 128.61, 127.5, 127.2, 127.1, 126.8, 126.6, 120.7, 100.7, 46.3. HRMS (+ESI-TOF) *m/z:* [M + H] $^+$ calcd for $C_{26}H_{21}N_2$ 361.1699; found 361.1685.

1-benzyl-6-chloro-2-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (3w). Following General Procedure □, using **1j** (120 mg, 0.647 mmol) and benzylamine (104 mg, 0.971 mmol), compound **3w**

was obtained (62 mg, 37% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.22-7.29 (m, 4H), 7.03-7.06 (m, 3H), 7.23 (d, *J* = 0.8 Hz, 1H), 5.47 (s, 2H), 2.30 (d, *J* = 0.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 143.4, 138.2, 137.8, 129.6, 128.8, 127.5, 126.8, 119.1, 116.0, 98.8, 45.2, 13.3. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{15}H_{14}N_2Cl$ 257.0840, found 257.0834.

1-benzyl-6-chloro-2-ethyl-1*H*-pyrrolo[2,3-*b*]pyridine (3x). Following General Procedure □, using **1k** (120 mg, 0.601 mmol) and benzylamine (97 mg, 0.902 mmol), compound **3x** was obtained (58 mg, 36% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.28-7.33 (m, 2H), 7.24-7.26 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.00-7.02 (m, 2H), 6.37 (t, *J* = 0.8 Hz, 1H), 5.47 (s, 2H), 2.63-2.69 (m, 2H), 1.20 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 147.1, 144.3, 142.1, 137.8, 130.4, 128.7, 127.2, 126.2, 118.8, 115.5, 96.8, 56.0, 44.2, 19.4, 18.6, 11.7. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{16}H_{16}N_2Cl$ 271.0997, found 271.0991.

1-benzyl-5-methyl-2-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (3y). Following General Procedure □, using **1l** (120 mg, 0.528 mmol) and benzylamine (85 mg, 0.792 mmol), compound **3y** was obtained (58 mg, 37% yield) as a yellow oil. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.13 (d, *J* = 1.6 Hz, 1H), 7.84 (s, 1H), 7.40-7.56 (m, 6H), 7.15-7.21 (m, 3H), 6.83 (d, *J* = 6.8 Hz, 2H), 6.61 (s, 1H), 5.57 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 147.6, 143.6, 141.3, 138.6, 131.9, 128.74, 128.69, 128.43, 128.38, 128. 1, 126.9, 126.0, 125.2, 119.9, 99.8, 45.2, 18.1. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{19}N_2$ 299.1543, found 299.1535.

1-benzyl-4-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (3z). Following General Procedure □, using **1m** (120 mg, 0.528 mmol) and benzylamine (85 mg, 0.792 mmol), compound **3z** was obtained (55 mg, 35% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 4.4 Hz, 1H), 7.37-7.38 (m, 5H), 7.16-7.18 (m, 3H), 6.93-6.95 (m, 3H), 6.58 (s, 1H), 5.56 (s, 2H), 2.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 143.3, 141.2, 139.5, 138.7, 132.7, 129.4, 128.63, 128.57, 128.4, 127.1, 126.6, 121.0, 117.4, 99.0, 46.3, 18.5. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{19}N_2$ 299.1543, found 299.1539.

1-benzyl-2,6-dimethyl-1H-pyrrolo[2,3-b]pyridine (3aa). Following General Procedure IV, using **1n** (120 mg, 0.73 mmol) and benzylamine (117 mg, 1.1 mmol), the title compound was obtained (107 mg, 62% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 1H), 7.26-7.18 (m, 3H), 7.03 (d, *J* = 6.8 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.16 (d, *J* = 0.8 Hz, 1H), 5.50 (s, 2H), 2.59 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.7, 148.7, 138.6, 136.5, 128.7, 127.5, 127.2, 126.8, 118.0, 115.9, 98.2, 44.7, 24.6, 13.3. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{16}H_{17}N_2$ 237.1386; found 237.1373.

1-benzyl-6-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (3ab). Following General Procedure IV, using **1o** (120 mg, 0.528 mmol) and benzylamine (85 mg, 0.79 mmol), the title compound was obtained (65 mg, 41% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 1H), 7.36-7.35 (m, 5H), 7.17-7.13 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.94-6.91 (m, 2H), 6.48 (s, 1H), 5.56 (s, 2H), 2.63 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 149.4, 140.9, 139.0, 132.9, 129.4, 128.6, 128.4, 128.2, 127.0, 126.9, 118.1, 116.6, 100.3, 77.4, 45.9, 24.8. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{19}N_2$ 299.1543; found 299.1530.

1-benzyl-2-phenyl-1H-pyrrolo[2,3-b]quinoline (3ac). Following General Procedure □, using **1p** (120 mg, 0.456 mmol) and benzylamine (98 mg, 0.912 mmol) in DCE at reflux conditions, compound **3ac** was obtained (122 mg, 80% yield) as a yellow solid. ^{1}H NMR (400 MHz, d_6-DMSO) δ 8.61 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.62-7.66 (m, 1H), 7.57-7.59 (m, 2H), 7.43-7.50 (m, 4H), 7.14-7.20 (m, 3H), 6.86-6.89 (m, 3H), 5.70 (s, 2H). ^{13}C NMR (100 MHz, d_6-DMSO) δ 150.6 145.5, 144.4, 138.4, 131.5, 129.0, 128.8, 128.7, 128.43, 128.35, 127.7, 126.9, 126.1, 124.9, 123.0, 121.6, 100.0, 45.3. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{24}H_{19}N_2$ 335.1543, found 335.1534.

1-benzyl-2-phenyl-4-(trifluoromethyl)-1H-pyrrolo[2,3-b]pyridine (3ad). Following General Procedure □, using **1q** (200 mg, 0.711 mmol) and benzylamine (153 mg, 1.424 mmol) in DCE at reflux conditions, compound **3ad** was obtained (88 mg, 35% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.4 Hz, 1H), 7.33-7.34 (m, 5H), 7.27 (d, *J* = 4.8 Hz, 1H), 7.12-7.17 (m, 3H), 6.87 (d, *J* = 6.4 Hz, 2H), 6.67 (s, 1H), 5.53 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 144.3, 142.8, 138.0, 131.7, 129.5, 129.2, 129.1, 128.8, 128.7, 127.4, 126.7, 125.6 (q, *J* = 33.0 Hz), 116.5 (q, *J* = 2.0 Hz), 112.7 (q, *J* = 4.0 Hz), 99.3, 46.4. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{16}N_2F_3$ 353.1260, found 353.1245.

1-benzyl-4-methoxy-2-phenyl-1H-pyrrolo[2,3-b]pyridine (3ae). Following General Procedure □, using **1r** (120 mg, 0.49 mmol) and benzylamine (79 mg, 0.74 mmol), compound **3ae** was obtained (8 mg, 5% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 5.6 Hz, 1H), 7.28-7.31 (m, 4H), 7.19 (s, 1H), 7.08-7.12 (m, 3H), 6.87 (d, *J* = 7.2 Hz, 2H), 6.57 (s, 1H), 5.52 (d, *J* = 5.6 Hz, 1H), 5.48 (s, 2H), 3.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 151.2, 145.2, 139.8, 138.7, 132.6, 129.4, 128.63, 128.58, 128.3, 127.1, 126.6, 110.9, 98.6, 97.8, 55.7, 46.4. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{19}N_2O$ 315.1492, found 315.1486.

The regioisomeric amination byproduct (**3ae'**) was isolated (96 mg, 59% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.76 (s, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.31-7.37 (m, 4H), 7.24-7.28 (m, 1H), 5.85 (s, 1H), 4.99 (brs, 1H), 4.49 (s, 2H), 4.10 (s, 2H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 165.3, 160.2, 149.4, 139.3, 137.0, 133.1, 128.8, 128.7, 128.4, 127.6, 127.4, 110.3, 88.7, 55.1, 46.8, 37.3. HRMS (+ESI-TOF) *m/z:* [M + H]$^+$ calcd for $C_{21}H_{21}N_2O_2$ 333.1598, found 333.1597.

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Supplenmentary Data

Supplementary data (Supplementary data associated with this article, including materials and methods and NMR spectra) associated with this article can be found in the online version at http://dx.doi.org/10.1016/xxx.

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