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# Ruthenium-Catalyzed Direct and Selective C−H Cyanation of *N*-(Hetero)aryl-7-azaindoles

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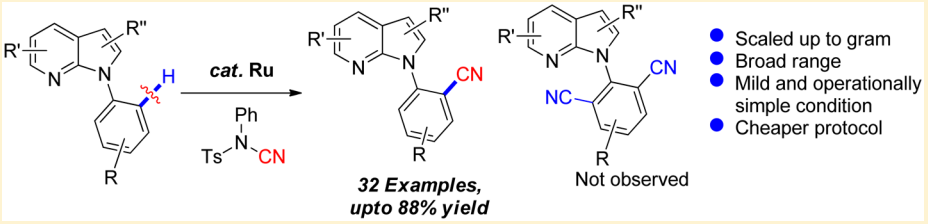
Supporting Information




**ABSTRACT:** An efficient, highly regioselective, and scalable ruthenium-catalyzed *o*-aryl C−H mono-cyanation of *N*-aryl-7-azaindoles to form *N*-(2-cyanoaryl)-7-azaindoles has been developed through N-directed ortho C−H activation using *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide as cyanating reagent in the presence of AgOTf and NaOAc in DCE. A range of substrates has furnished cyanated azaindoles in good to excellent yields under the simple reaction conditions. Involvement of C−H metalation has been supported by a kinetic study. This methodology provides easy access to a class of pharmaceutically significant molecules and their precursors.

## INTRODUCTION

Azaindole is a unique heterocyclic moiety present in various biologically active molecules[1] and novel synthetic materials[2] and has been found in various marketed drugs,[3] including vemurafenib. On the other hand, the nitrile group is of great research interest in the area of organic and medicinal chemistry and plays an important role in organic synthesis due to its easy conversion into many other important functional groups, like amine, aldehyde, amide, ester, and various heterocyclic scaffolds.[4] A large number of bioactive natural products and drug molecules, such as letrozole, fadrozole, and citalopram, also feature cyano group(s) (Figure 1).[5]

Over the past decades, direct C−H/C−X functionalization has been considered as a practical alternate catalytic approach to conventional cyanation reactions such as the Rosenmund−von Braun[6] reaction and diazotization followed by Sandmeyer reaction,[7] which uses an excess amount of hazardous cyanating reagents. In this context, various methods employing transition-metal catalysis have been developed.[8] Several organo-cyanating reagents, including cyanohydrin, DMF−$NH_3$, PhTsNCN, MeCN, and $MeNO_2$ have been reported for the cyanation reaction.[9] During the past few years, transition metals, mainly rhodium and cobalt, catalyzed chelating groups, such as oxime,[10] pyridine,[11] pyrimidine,[12] amide,[13] azo,[14] nitrileoxide,[15] and phosphonate;[16] thus, assisted catalytic C−H activation has emerged as a powerful approach for C−H cyanation using *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS). Though ruthenium catalysis[17] is well-known for C−H bond functionalization, directing-group-assisted C−H cyanation employing ruthenium remains less explored.[13a] In spite of the known importance of the azaindole scaffold in medicinal chemistry and in material chemistry, only a limited number of metal-catalyzed functional group incorporations have been achieved. For example, palladium-catalyzed amination, C2−C3 arylation, C3-alkenylation, and selective C6 arylation of azaindoles have been reported.[18]

Recently, 7-azaindole-directed catalytic C−H chlorination using DCE as a chloride source, oxidative annulation with alkyne, C−C coupling with vinyl acetate, and alkynylation have been reported using expensive rhodium or iridium catalysts (Scheme 1, eq 1).[19] However, to date, azaindole-directed catalytic and selective C−H cyanation using transition metals has not been reported. Thus, a catalytic approach for the direct and selective C−H cyanation of azaindole appeared highly desirable. In continuation of our research interest in metal-catalyzed C−H bond functionalization,[20] herein we wish to reveal the N-directed selective C−H cyanation reaction of *N*-aryl-7-azaindole using the relatively less expensive $[RuCl_2(p\text{-cymene})]_2$ catalyst and the easily accessible NCTS (**2**) as the cyanating reagent in the presence of additives AgOTf and NaOAc in DCE (Scheme 1, eq 2).

## RESULTS AND DISCUSSION

We initiated our study by performing the cyanation reaction of arenes using *N*-phenyl-7-azaindole (**1a**) as a substrate under different conditions. To our delight, screening of different nitrile sources, such as benzyl cyanide, isocyanide, and *N*-

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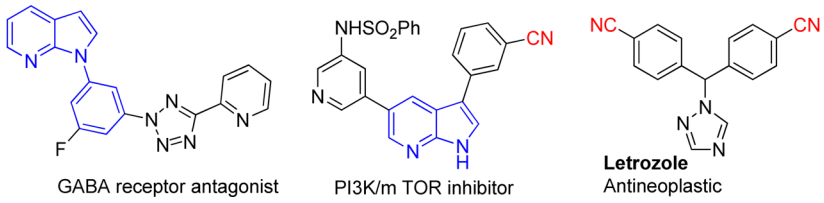
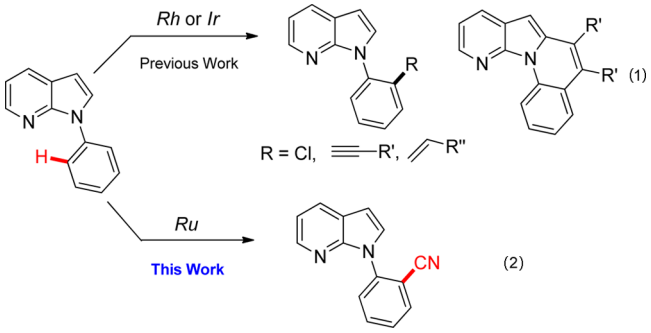


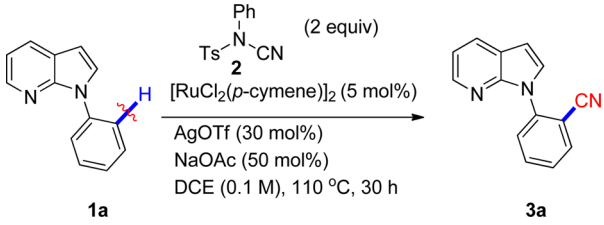

**Figure 1.** Bioactive molecules.

**Scheme 1. 7-Azaindole-Directed C−H Bond Functionalization**




cyanosuccinimide (see the Supporting Information (SI), Table S1], revealed NCTS to be an efficient cyanating reagent to provide ortho-cyanated *N*-phenyl-7-azaindole (**3a**) in 84% yield at 110 °C (Table 1, entry 1) in the presence of [$RuCl_2$(*p*-cymene)]$_2$ (5 mol %) as catalyst and AgOTf (30 mol %) and NaOAc (50 mol %) as cocatalysts in DCE without the formation of any C2 or C3 cyanation product. The use of other catalytic conditions for cyanation did not give satisfactory results (see the SI, Table S1). No cyanation reaction occurred in the absence of catalysts and silver salt (Table 1, entries 14 and 15). Screening of different solvents (chlorobenzene, toluene, and 1,4-dioxane) other than DCE resulted in poor yield of the cyanated product (Table 1, entries 4 and 5). On the other hand, replacement of NaOAc with other additives [CsOAc, $Cu(OAc)_2$, and AgOAc] (see SI, Table S1) proved less effective or not effective at all. Decreasing the amount of AgOTf (10 mol %) and NaOAc (30 mol %) did not improve the yield, while increasing the proportion of NaOAc (100 mol %) also furnished less product (Table 1, entries 8, 10, and 11).

**Table 1. Optimization of Condition for Cyanation of *N*-Aryl-7-azaindoles**[a]




| entry | deviation from standard condition | yield (%)[b] of **3a** |
|---|---|---|
| 1 | none | 84 |
| 2 | $RuCl_3$ (10 mol %) instead of [$RuCl_2$(*p*-cymene)]$_2$ | nr |
| 3 | [Cp(*p*-cymene)Ru(II)]$PF_6$ (5 mol %) instead of [$RuCl_2$(*p*-cymene)]$_2$ (5 mol %) | nr |
| 4 | toluene or 1,4-dioxane instead of DCE | trace |
| 5 | chlorobenzene instead of DCE | 32 |
| 6 | 3 mol % of [$RuCl_2$(*p*-cymene)]$_2$ | 67 |
| 7 | 50 mol % of AgOTf | 63 |
| 8 | 10 mol % of AgOTf | 64 |
| 9 | $AgSbF_6$ instead of AgOTf | 82 |
| 10 | 30 mol % of NaOAc | 78 |
| 11 | 100 mol % of NaOAc | 68 |
| 12 | 80 °C | 52 |
| 13 | omitting NaOAc | 61 |
| 14 | omitting AgOTf | nr |
| 15 | omitting [$RuCl_2$(*p*-cymene)]$_2$/AgOTf/NaOAc | nr |

[a]Reaction conditions: unless otherwise mentioned all reactions were performed with a mixture of **1a** (0.2 mmol), **2** (2 equiv), [$RuCl_2$(*p*-cymene)]$_2$ (5 mol %), AgOTf (30 mol %), and NaOAc (50 mol %) in DCE (0.1 M) at 110 °C, under $N_2$ for 30 h. [b]Isolated yield. nr: no reaction.

Lowering the catalyst loading [Ru(II), 3 mol %] furnished the product to the extent of 67% only (Table 1, entry 6). Although use of $AgSbF_6$ (30 mol %) gave the product in 82% yield (Table 1, entry 9), the relatively less hygroscopic AgOTf (30 mol %) was considered more economical. A decrease in the reaction temperature to 80 °C lowered the yield (Table 1, entry 12). Although the reaction proceeds well in the absence of NaOAc (Table 1, entry 13), which is common in ruthenium catalysis,[17] the presence of NaOAc is essential to obtain the cyanated product in excellent yield, which might be due the formation of the relatively more active carboxylate complex of ruthenium.

Employing the optimized catalytic conditions, an array of *N*-aryl-7-azaindoles were subjected to cyanation to evaluate the scope of the reaction (Scheme 2). The results showed that various substituents at different positions were tolerated and no bis-cyanated product resulted. Electron-donating groups on arenes undergoing C−H functionalization are generally favorable for this cyanation reaction, except in the case of the 2-substituted aryl substrate **3g**. Gratifyingly, meta-substituted substrates **1b−1e** yielded the cyanated products **3b−3d** in excellent yields and excellent regioselectivity, the less sterically hindered site of the substrates being favored for functionalization. In the case of para-substituted substrates, the desired cyanated products **3j−3p** were obtained in better yields when the group was electron-donating (except **3n**). Pleasingly, heteroarenes **1r−1t** were also efficiently cyanated using the optimized catalytic system and provided the corresponding cyanated benzothiophene **3r**, thiophene **3s**, and furans **3t** in good yields; compound **3u**, however, was obtained in moderate yield.

In general, substrates bearing electron-withdrawing groups provided the cyanation products in moderate yields. The single-crystal X-ray study of **3q** confirmed the structure of the cyanated product (SI).

Next, we turned our attention to substituted 7-azaindoles. Using the optimized conditions, substrates **1v−1af** were successfully converted to cyanated products **3v−3af** in good



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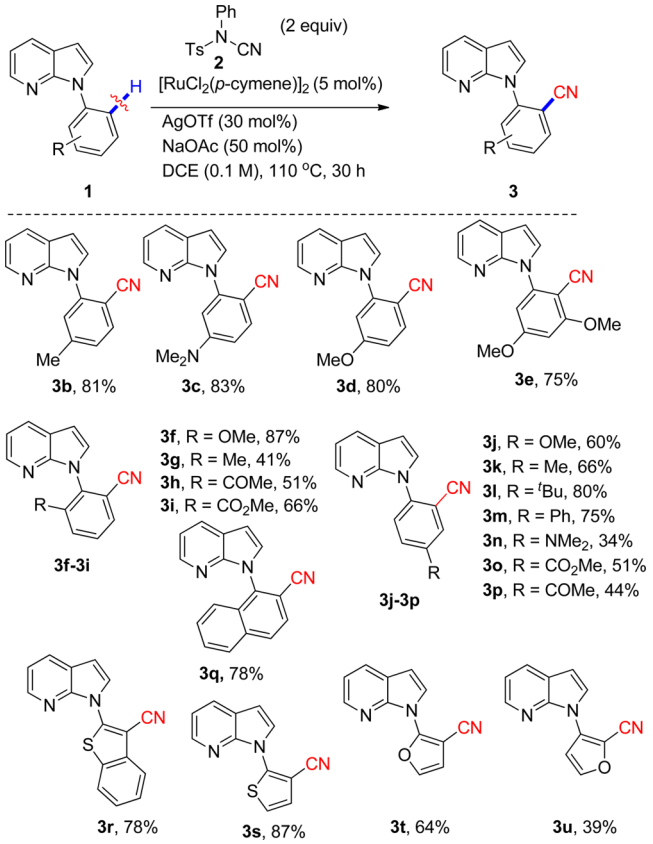
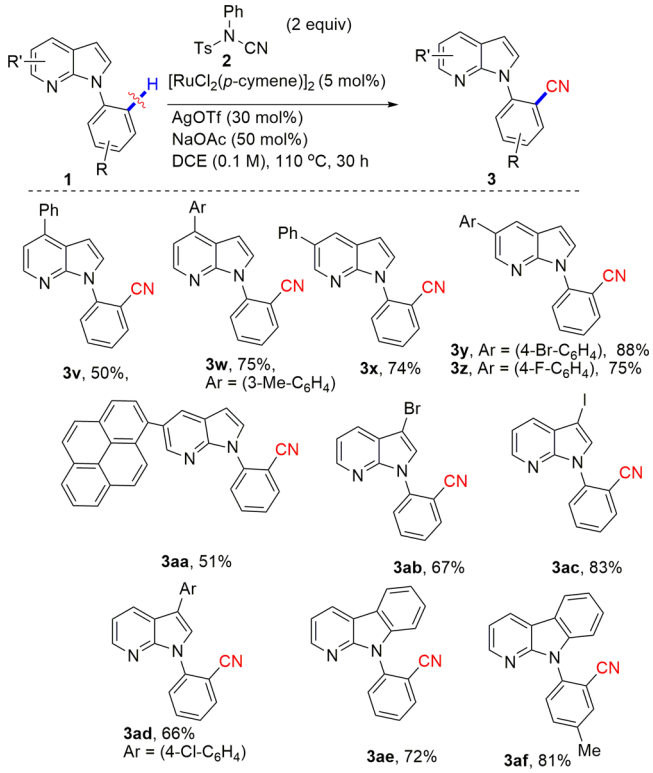
**Scheme 2. Scope of Cyanation of *N*-Aryl-7-azaindoles**[a]




[a]Reaction condition: mixture of **1** (0.2 mmol), **2** (2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), AgOTf (30 mol %), and NaOAc (50 mol %) in DCE (0.1 M) at 110 °C, under $N_2$ for 30 h. Yields refer to isolated products.

**Scheme 3. Scope of Cyanation of *N*-Aryl-7-azaindoles**[a]




[a]Reaction condition: mixture of **1** (0.2 mmol), **2** (2 equiv), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), AgOTf (30 mol %), and NaOAc (50 mol %) in DCE (0.1 M) at 110 °C, under $N_2$ for 30 h. Yields refer to isolated products.

to excellent yields (Scheme 3). Substrates possessing aryl groups reacted smoothly to afford the products **3v**–**3aa** and **3ad** in good yields. It should be noted that a halide such as iodo or bromo at the 3-position of the 7-azaindole ring exerted only a minor effect on the yields of **3ab** and **3ac**. This finding encouraged us to extend this methodology and explore whether *N*-aryl-*α*-carbolines **1ae** and **1af** could also be cyanated. Substrates **1ae** and **1af** indeed participated in the reaction and afforded the desired cyanated *N*-aryl-*α*-carboline products **3ae** and **3af** in 72% and 81% yields, respectively (Scheme 3).

To illustrate the scalability of the cyanation, we conducted a gram-scale experiment using the substrate **1a** (1 g) and obtained the cyanated product **3a** (0.79 g) in 70% yield. The nitrile-bearing *N*-aryl-7-azaindole **3a** underwent smooth synthetic transformations to provide amine **4** and amide **5** in good yields (Scheme 4), underlining the utility of the cyanide product as a synthetic intermediate.

To prove the possible mechanism of the cyanation reaction, several experiments were conducted (Scheme 5). Rapid ortho H–D exchange of **1a** in the presence of excess amount of $D_2O$ clearly suggested that reversible cleavage of the C–H bond may be involved in the C–H cyanation. Low kinetic isotope effect values of 1.6 and 1.2 were found in both parallel and competitive experiments between **1a** and **1a**-$d_5$, implying that the cleavage of the ortho C–H bond may not be the rate-limiting step in the mechanism. No significant substituent effect was observed in competitive experiment of the substrates **1a** and **1f**.

On the basis of the mechanistic studies shown in Scheme 5 and a previous report,[13a] it appears that the reaction involved is the formation of monomeric active cationic ruthenium complex **A** from $[RuCl_2(p\text{-cymene})]_2$ in the presence of AgOTf and NaOAc, followed by reversible C–H ruthenation of *N*-aryl-7-azaindole **1a**, producing ruthenacycle **B** (Scheme 6). Coordination of NCTS (**2**) with **B** forms the intermediate **C**, which upon migratory insertion leads the formation of **D**. The intermediate **D** undergoes *β*-amine elimination to afford the desired cyanated product **3** and the intermediate **E**. The active catalytic species **A** is regenerated to continue the redox neutral catalytic cycle by elimination of tosylaniline from **E** via proto-demetalation.

## CONCLUSIONS

In summary, we have demonstrated a direct and selective C–H cyanation of *N*-aryl-7-azaindoles with a broad range of substrate scope using the relatively less expensive $[RuCl_2(p\text{-cymene})]_2$ catalyst and the easily accessible *N*-cyano-*N*-phenyl-*p*-toluenesulfonamide (NCTS, **2**) as an electrophilic cyanating reagent in the presence of additives AgOTf and NaOAc in DCE solvent.

## EXPERIMENTAL SECTION

**General Information.** All reactions were carried out in oven-dried reaction vessels under nitrogen atmosphere unless otherwise mentioned. TLC analysis was performed on Merck 60 $F_{254}$ silica gel TLC plates. Column chromatography was done using 230–400 mesh silica gel or neutral alumina (activity I–II) by applying pressure



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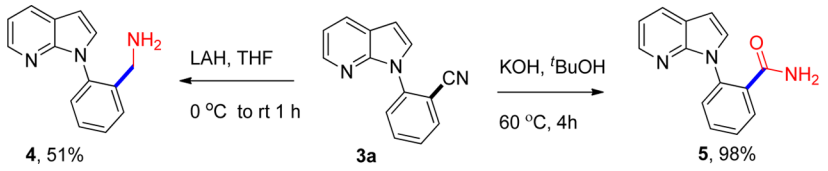
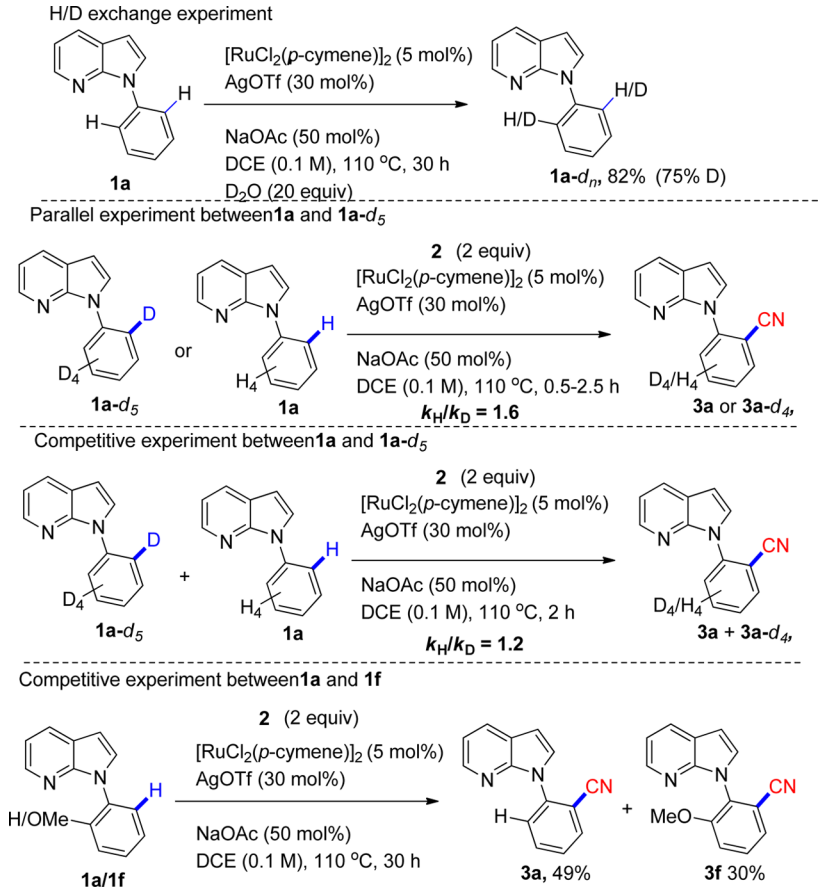
**Scheme 4. Synthetic Transformations of Cyanated *N*-Phenyl-7-azaindole**




**Scheme 5. Mechanistic Experiments**




through an air pump. $^1$H and $^{13}$C NMR spectra were recorded on 300 and 600 MHz spectrometers and are reported as chemical shifts ($\delta$) in parts per million (ppm), and multiplicities are abbreviated as s = singlet, d = doublet, t = triplet, m = multiplet, comp = complex. Internal standards or residual solvent signals were used as reference. HRMS ($m/z$) was recorded using ESI (Q-Tof, positive ion) and EI (magnetic sector, positive ion) mode. Melting points were determined in a capillary melting point apparatus and are uncorrected. GC analysis was done on a GC system with a flame ionizing detector (FID). Single-crystal X-ray data were recorded in a diffractometer with Mo K$\alpha$ radiation. The CIF file was submitted to CCDC (1472438) and can be obtained at https://summary.ccdc.cam.ac.uk/structure-summary-form.

**Preparation of Starting Materials.** All 7-azaindoles are commercially available. *N*-Aryl-7-azaindoles were prepared by *N*-arylation of 7-azaindoles using appropriate aryl iodides (**1a**, **1b**, **1d**, **1f**, **1g**, **1h**, **1i**, **1j**, **1k**, **1l**, **1o**, **1p**, **1q**, **1s**, **1ab**, **1ae**, and **1af**)[19a,21] or aryl bromides (**1a**-$d_5$, **1c**, **1e**, **1n**, **1r**, **1t**, and **1u**)[22] following the literature procedure. **1ac** was prepared by iodination of **1a** with NIS.[19a] *N*-Aryl-7-azaindoles (**1m**, **1v**, **1w**, **1x**, **1y**, **1z**, **1aa**, and **1ad**) were prepared using the appropriate bromo-*N*-aryl-7-azaindoles and appropriate boronic acids following the Suzuki cross-coupling method.[19a] Characterization data of newly synthesized *N*-aryl-7-azaindoles are given below. Data for all of the reported (**1a**,[19a] **1b**,[19a] **1d**,[19a] **1j**,[19a] **1k**,[19a] **1m**,[19a] **1o**,[19a] **1p**,[19a] **1s**,[23] **1v**,[19a] **1x**,[19a] **1ab**,[19a] **1ac**,[19a] **1ad**,[19a] **1ae**,[24] and **1af**[24]) *N*-aryl-7-azaindoles are in good agreement with literature data.

NCTS was prepared by following a literature procedure and its characterization data are in good agreement with literature data.[10]

**Characterization Data of Starting Materials.** *N,N-Dimethyl-3-(1H-pyrrolo[2,3-b]pyridin-1-yl)aniline (**1c**).* Yield 71%; colorless solid; mp 78−79 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.03 (s, 6 H), 6.62 (d, $J$ = 3.6 Hz, 1 H), 6.73 (dd, $J$ = 8.1 Hz, 2.6 Hz, 1 H), 7.03−7.10 (comp, 2 H), 7.14 (dd, $J$ = 7.8 Hz, 4.6 Hz, 1 H), 7.38 (t, $J$ = 7.2 Hz, 1 H), 7.54 (d, $J$ = 3.6 Hz, 1 H), 7.98 (dd, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 8.39 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 40.5, 100.9, 108.4, 110.6, 112.2, 116.3, 121.3, 128.2, 128.8, 129.7, 139.2, 143.4, 147.5, 151.2; HRMS (EI, $m/z$) calcd for $C_{15}H_{15}N_3$ $[M]^+$ 237.1266, observed 237.1253.

*1-(3,5-Dimethoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (**1e**).* Yield 11%; colorless solid; mp 54−55 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.88 (s, 6 H), 6.47 (t, $J$ = 2.4 Hz, 1 H), 6.64 (d, $J$ = 3.6 Hz, 1 H), 6.99 (d, $J$ = 1.8 Hz, 1 H), 7.16 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.53 (d, $J$ = 4.2 Hz, 1 H), 7.99 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.40 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 55.5, 98.4, 101.6, 102.6, 116.6, 121.6, 127.9, 129.0, 140.0, 143.6, 147.5, 161.1; HRMS (EI, $m/z$) calcd for $C_{15}H_{14}N_2O_2$ $[M]^+$ 254.1055, observed 254.1049.

*1-(2-Methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (**1f**).* Yield 67%; pale brown solid; mp 87−88 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.79



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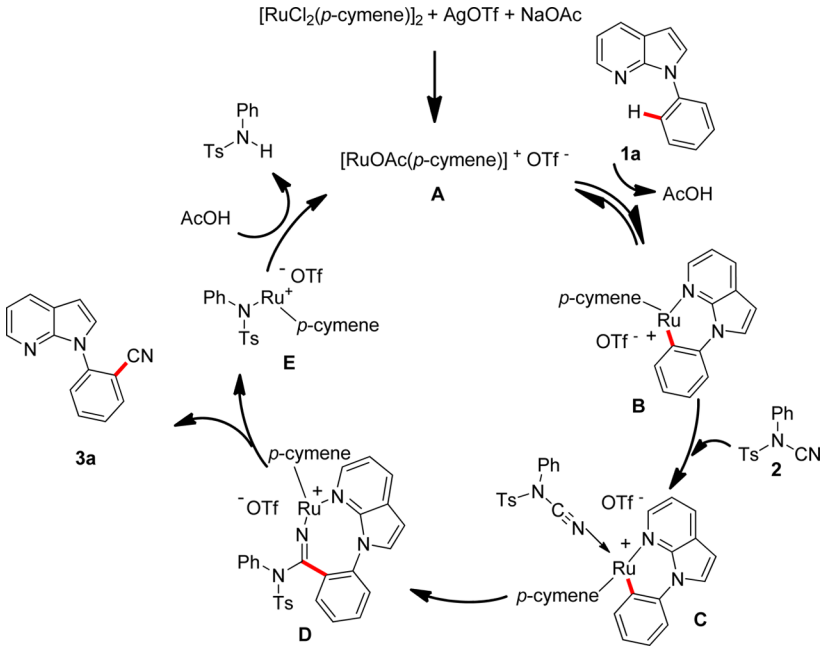
**Scheme 6. Plausible Reaction Mechanism**




(s, 3 H), 6.61 (d, $J$ = 3.6 Hz, 1 H), 7.08−7.15 (comp, 3 H), 7.37−7.43 (comp, 2 H), 7.56 (dd, $J$ = 7.5 Hz, 1.8 Hz, 1 H), 7.97 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.33 (dd, $J$ = 4.8 Hz, 1.5 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 55.8, 100.3, 112.4, 116.2, 120.6, 120.9, 126.7, 128.7, 128.7, 128.8, 130.1, 143.4, 148.2, 154.4; HRMS (EI, $m/z$) calcd for $C_{14}H_{12}N_2O$ $[M]^+$ 224.0950, observed 224.0940.

*1-(o-Tolyl)-1H-pyrrolo[2,3-b]pyridine* (**1g**). Yield 27%; yellow oil; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.11 (s, 3 H), 6.64 (d, $J$ = 3.6 Hz, 1 H), 7.12 (dd, $J$ = 7.5 Hz, 4.8 Hz, 1 H), 7.29 (d, $J$ = 3.3 Hz, 1 H), 7.34−7.41 (comp, 4 H), 8.00 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.35 (dd, $J$ = 4.8 Hz, 1.5 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 17.9, 100.6, 116.0, 120.4, 126.6, 128.1, 128.4, 128.8, 129.1, 131.1, 135.8, 137.1, 143.6, 148.0; HRMS (ESI, $m/z$) calcd for $C_{14}H_{12}N_2Na$ $[M + Na]^+$ 231.0898, observed 231.0893.

*1-(2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)phenyl)ethanone* (**1h**). Yield 67%; yellow solid; mp 57−59 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.97 (s, 3 H), 6.68 (d, $J$ = 3.6 Hz, 1 H), 7.13 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.34 (d, $J$ = 3.6 Hz, 1 H), 7.46−7.52 (comp, 2 H), 7.64 (td, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.76 (dd, $J$ = 7.5 Hz, 2.1 Hz, 1 H), 7.98 (dd, $J$ = 8.1 Hz, 1.8 Hz, 1 H), 8.31 (dd, $J$ = 4.5 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 28.4, 102.2, 116.9, 120.9, 127.9, 128.0, 128.8, 129.1, 129.3, 132.3, 135.7, 137.5, 143.9, 148.0, 200.7; HRMS (EI, $m/z$) calcd for $C_{15}H_{12}N_2O$ $[M]^+$ 236.0950, observed 236.0945.

*Methyl 2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)benzoate* (**1i**). Yield 57%; brown solid; mp 60−63 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.46 (s, 3 H), 6.65 (d, $J$ = 3.6 Hz, 1 H), 7.10 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.38 (d, $J$ = 3.6 Hz, 1 H), 7.47−7.52 (comp, 2 H), 7.68 (td, $J$ = 7.8 Hz, 1.5 Hz), 7.97 (dd, $J$ = 7.8 Hz, 1.5 Hz), 8.03 (dd, $J$ = 7.8 Hz, 1.5 Hz), 8.29 (dd, $J$ = 4.8 Hz, 1.5 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 52.0, 101.4, 116.4, 120.8, 127.5, 128.0, 128.6, 128.8, 129.0, 131.2, 132.8, 137.2, 143.4, 148.3, 166.7; HRMS (EI, $m/z$) calcd for $C_{15}H_{12}N_2O_2$ $[M]^+$ 252.0899, observed 252.0902.

*1-(4-(tert-Butyl)phenyl)-1H-pyrrolo[2,3-b]pyridine* (**1l**). Yield 98%; colorless solid; mp 89−90 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.37 (s, 9 H), 6.62 (d, $J$ = 3.6 Hz, 1 H), 7.12 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.50 (d, $J$ = 3.6 Hz, 1 H), 7.52−7.57 (comp, 2 H), 7.63−7.67 (comp, 2 H), 7.98 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.38 (dd, $J$ = 4.5 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 31.3, 34.5, 101.2, 116.4, 121.3, 123.6, 126.2, 127.9, 128.9, 135.7, 143.4, 147.4, 149.1; HRMS (EI, $m/z$) calcd for $C_{17}H_{18}N_2$ $[M]^+$ 250.1470, observed 250.1476.

*N,N-Dimethyl-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)aniline* (**1n**). Yield 88%; brown solid; mp 92−93 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.02 (s, 6 H), 6.60 (d, $J$ = 3.3 Hz, 1 H), 6.85−6.90 (comp, 2 H), 7.11 (dd, $J$ = 7.8 Hz, 4.5 Hz, 1 H), 7.45 (d, $J$ = 3.6 Hz, 1 H), 7.51−7.56 (comp, 2 H), 7.98 (dd, $J$ = 8.1 Hz, 1.8 Hz, 1 H), 8.37 (dd, $J$ = 4.5 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 40.7, 100.3, 113.0, 116.0, 121.0, 125.4, 127.8, 128.5, 128.7, 143.3, 147.6, 149.3; HRMS (EI, $m/z$) calcd for $C_{15}H_{15}N_3$ $[M]^+$ 237.1266, observed 237.1264.

*1-(Naphthalen-1-yl)-1H-pyrrolo[2,3-b]pyridine* (**1q**). Yield 83%; colorless solid; mp 98−99 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.73 (d, $J$ = 3.3 Hz, 1 H), 7.15 (dd, $J$ = 7.8 Hz, 4.5 Hz, 1 H), 7.38−7.42 (comp, 2 H), 7.46 (d, $J$ = 3.6 Hz, 1 H), 7.50−7.56 (m, 1 H), 7.61−7.64 (comp, 2 H), 7.59−7.66 (comp, 2 H), 8.06 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.31 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 100.9, 116.4, 120.5, 123.1, 125.4, 125.6, 126.4, 126.8, 128.2, 128.8, 129.0, 130.3, 130.7, 134.4, 134.7, 143.8, 149.0; HRMS (ESI, $m/z$) calcd for $C_{17}H_{12}N_2Na$ $[M + Na]^+$ 267.0898, observed 267.0892.

*1-(Benzo[b]thiophen-3-yl)-1H-pyrrolo[2,3-b]pyridine* (**1r**). Yield 84%; yellow solid; mp 66−67 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.70 (d, $J$ = 3.6 Hz, 1 H), 7.16 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.34−7.45 (comp, 2 H), 7.52 (d, $J$ = 3.6 Hz, 1 H), 7.60 (dd, $J$ = 7.2 Hz, 2.1 Hz, 1 H), 7.67 (s, 1 H), 7.92 (dd, $J$ = 7.2 Hz, 1.2 Hz, 1 H), 8.02 (dd, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 8.36 (dd, $J$ = 4.8 Hz, 1.5 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 101.4, 116.8, 120.8, 121.2, 121.9, 123.1, 124.6, 125.1, 129.0, 129.1, 130.8, 134.9, 138.8, 143.8, 148.2; HRMS (EI, $m/z$) calcd for $C_{15}H_{10}N_2S$ $[M]^+$ 250.0565, observed 250.0573.

*1-(Furan-2-yl)-1H-pyrrolo[2,3-b]pyridine* (**1t**). Yield 97%; brown oil; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.57 (dd, $J$ = 3.0 Hz, 2.1 Hz, 1 H), 6.62 (d, $J$ = 3.6 Hz, 1 H), 6.72 (dd, $J$ = 3.6 Hz, 0.9 Hz, 1 H), 7.16 (dd, $J$ = 7.8 Hz, 4.5 Hz, 1 H), 7.33 (dd, $J$ = 2.1 Hz, 1.2 Hz), 7.61 (d, $J$ = 3.6 Hz, 1 H), 7.96 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.42 (dd, $J$ = 4.5 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 97.0, 102.3, 111.6, 117.0, 121.1, 125.8, 129.0, 137.4, 143.9, 144.9, 146.6; HRMS (ESI, $m/z$) calcd for $C_{11}H_8N_2ONa$ $[M + Na]^+$ 207.0534, observed 207.0527.

*1-(Furan-3-yl)-1H-pyrrolo[2,3-b]pyridine* (**1u**). Yield 98%; brown solid; mp 61−62 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.59 (d, $J$ = 3.6 Hz, 1 H), 6.87 (dd, $J$ = 1.8 Hz, 0.6 Hz, 1 H), 7.12 (dd, $J$ = 7.8 Hz, 4.5 Hz, 1 H), 7.41 (d, $J$ = 3.6 Hz, 1 H), 7.48 (t, $J$ = 1.8 Hz, 1 H), 7.93 (dd, $J$ = 7.8 Hz, 4.5 Hz, 1 H), 8.27 (dd, $J$ = 1.2 Hz, 0.9 Hz, 1 H), 8.40 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 101.6, 105.6, 116.5, 121.2, 125.8, 126.5, 128.9, 133.2, 142.4, 143.6, 147.0; HRMS (EI, $m/z$) calcd for $C_{11}H_8N_2O$ $[M]^+$ 184.0637, observed 184.0624.

*1-Phenyl-4-(m-tolyl)-1H-pyrrolo[2,3-b]pyridine* (**1w**). Yield 98%; colorless solid; mp 143−145°C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.49



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(s, 3 H), 6.84 (d, $J$ = 3.6 Hz, 1 H), 7.22 (app d, $J$ = 4.8 Hz, 1 H), 7.29 (app d, $J$ = 7.5 Hz, 1 H), 7.37 (app t, $J$ = 7.2 Hz, 1 H), 7.44 (app t, $J$ = 7.8 Hz, 1 H), 7.53−7.59 (comp, 5 H), 7.77−7.80 (comp, 2 H), 8.43 (app d, $J$ = 5.1 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 21.6, 101.2, 116.0, 119.6, 124.2, 125.8, 126.4, 128.1, 128.8, 129.2, 129.3, 129.4, 138.6 (2 C), 138.7, 142.6, 143.9, 148.1; HRMS (EI, $m/z$) calcd for $C_{20}H_{16}N_2$ $[M]^+$ 284.1313, observed 284.1317.

*5-(4-Bromophenyl)-1-phenyl-1H-pyrrolo[2,3-b]pyridine* (**1y**). Yield 29%; colorless solid; mp 172−173 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.71 (d, $J$ = 3.6 Hz, 1 H), 7.36−7.41 (m, 1 H), 7.51−7.64 (comp, 7 H), 7.78−7.82 (comp, 2 H), 8.14 (d, $J$ = 2.1 Hz, 1 H), 8.59 (d, $J$ = 2.1 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 101.9, 121.4, 121.6, 123.9, 126.4, 127.2, 128.8, 128.9, 129.2, 129.4, 132.0, 138.3 (2 C), 142.5, 147.1; HRMS (ESI, $m/z$) calcd for $C_{19}H_{13}BrN_2Na$ $[M + Na]^+$ 371.0160, observed 371.0164.

*5-(4-Fluorophenyl)-1-phenyl-1H-pyrrolo[2,3-b]pyridine* (**1z**). Yield 92%; colorless solid; mp 121−123 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.70 (d, $J$ = 3.6 Hz, 1 H), 7.16−7.22 (comp, 2 H), 7.38 (app t, $J$ = 7.2 Hz, 1 H), 7.54−7.63 (comp, 6 H), 7.79−7.82 (comp, 2 H), 8.12 (d, $J$ = 2.1 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 101.8, 115.8 (d, $^2J_{F-C}$ = 21.3 Hz), 121.5, 123.9, 126.4, 127.3, 128.7, 128.9 (d, $^3J_{F-C}$ = 8.0 Hz), 129.5 (d, $^3J_{F-C}$ = 12.9 Hz), 129.4, 135.5, 138.3, 142.7, 146.9, 162.4 (d, $^1J_{F-C}$ = 245.1 Hz); HRMS (ESI, $m/z$) calcd for $C_{19}H_{13}FN_2Na$ $[M + Na]^+$ 311.0960, observed 311.0956.

*1-Phenyl-5-(pyren-1-yl)-1H-pyrrolo[2,3-b]pyridine* (**1aa**). Yield 91%; green solid; mp 130−132°C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.76 (d, $J$ = 3.6 Hz, 1 H), 7.39 (app t, $J$ = 7.5 Hz, 1 H), 7.56−7.62 (comp, 2 H), 7.65 (d, $J$ = 3.6 Hz, 1 H), 7.86−7.89 (comp, 2 H), 8.00−8.06 (comp, 3 H), 8.13 (comp, 2 H), 8.17−8.28 (comp, 5 H), 8.65 (d, $J$ = 2.1 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 101.8, 121.3, 123.9, 124.6, 124.8 (2 C), 124.9, 125.0, 125.1, 126.0, 126.4, 127.3, 127.4, 127.6, 128.1, 128.6, 129.0, 129.4, 129.9, 130.6 (2 C), 130.9, 131.4, 135.1, 138.4, 145.3, 146.7; HRMS (ESI, $m/z$) calcd for $C_{29}H_{19}N_2$ $[M + H]^+$ 395.1548, observed 395.1545.

**General Procedure for Cyanation.** *Small (Milligram) Scale.* To an oven-dried 10 mL Schlenk tube was added 38.8 mg (0.2 mmol) of 1-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (**1a**). To that were added NCTS (109 mg, 0.4 mmol), NaOAc (8.2 mg, 50 mol %), AgOTf (15.4 mg, 30 mol %) and $[RuCl_2(p\text{-cymene})]_2$ (6.1 mg, 5 mol %) were added. Next it was degassed and backfilled with nitrogen. 2.0 mL of anhydrous DCE was added as solvent. Then the tube was degassed and backfilled with nitrogen (3 times). The tube was closed with a Teflon-lined cap and heated at 110 °C (oil bath temperature). After 30 h, the reaction was stopped and cooled to room temperature. The reaction mixture was filtered through a short pad of Celite and concentrated under vacuo. The crude reaction mixture was directly purified by column chromatography on silica gel using pet. ether/ethyl acetate as eluent and isolated the product **3a** in 84% yield (36.8 mg).

*Large (Gram) Scale.* One gram (5.1 mmol) of 1-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine (**1a**) was placed in an oven-dried 100 mL round-bottom flask equipped with a reflux condenser. To that were added NCTS (2.8 g, 10.3 mmol), NaOAc (205 mg, 50 mol %), AgOTf (385 mg, 30 mol %), and $[RuCl_2(p\text{-cymene})]_2$ (154 mg, 5 mol %). Next, it was degassed and backfilled with nitrogen. A 50 mL portion of anhydrous DCE was added. Then the reactipon vessel was degassed, backfilled with nitrogen (three times), and heated at 110 °C (oil bath temperature). After 30 h, the reaction was stopped and cooled to room temperature. The reaction mixture was filtered through a short pad of Celite and concentrated under vacuo. The crude reaction mixture was directly purified by column chromatography on silica gel using pet. ether/ethyl acetate as eluent to give 2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)benzonitrile (**2a**) (0.79 g, 70% yield).

**Characterization Data of Cyanated Products.** *2-(1H-Pyrrolo-[2,3-b]pyridin-1-yl)benzonitrile* (**3a**). Yield 84% (36.8 mg); colorless solid; mp 132−133 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.75 (d, $J$ = 3.6 Hz, 1 H), 7.21 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.53 (td, $J$ = 7.2 Hz, $J$ = 1.2 Hz, 1 H), 7.58 (d, $J$ = 3.6 Hz, 1 H), 7.78−7.83 (comp, 2 H), 7.87 (dd, $J$ = 7.8 Hz, 1.2 Hz), 8.03 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.39 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 102.8, 110.0, 116.7, 117.5, 121.3, 127.5, 128.1, 128.3, 129.5, 133.7, 134.2, 140.4, 143.9, 147.8; HRMS (ESI, $m/z$) calcd for $C_{14}H_9N_3Na$ $[M + Na]^+$ 242.0694, observed 242.0687.

*4-Methyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3b**). Yield 81% (37.7 mg); pale orange solid; mp 88−89 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.51 (s, 3 H), 6.70 (d, $J$ = 3.6 Hz, 1 H), 7.18 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.30 (dd, $J$ = 8.4 Hz, 1.5 Hz, 1 H), 7.52 (d, $J$ = 3.6 Hz, 1 H), 7.58 (d, $J$ = 1.8 Hz, 1 H), 7.72 (d, $J$ = 7.8 Hz, 1 H), 8.00 (dd, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 8.36 (dd, $J$ = 4.8 Hz, 1.5 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 21.9, 102.6, 107.1, 116.9, 117.3, 121.2, 128.4, 128.5, 128.8, 129.4, 113.8, 140.3, 143.8, 145.1, 147.8; HRMS (EI, $m/z$) calcd for $C_{15}H_{11}N_3$ $[M]^+$ 233.0953, observed 233.0948.

*4-(Dimethylamino)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3c**). Yield 83% (43.5 mg); colorless solid; mp 179−180 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.10 (s, 6 H), 6.70−6.72 (comp, 2 H), 6.95 (d, $J$ = 3.0 Hz, 1 H), 7.18 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.57 (d, $J$ = 3.6 Hz, 1 H), 7.62 (d, $J$ = 9.0 Hz, 1 H), 8.01 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.38 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 40.0, 95.1, 102.0, 110.4, 110.5, 117.0, 118.4, 121.2, 128.7, 129.2, 134.8, 141.6, 143.7, 147.9, 153.1; HRMS (EI, $m/z$) calcd for $C_{16}H_{14}N_4$ $[M]^+$ 262.1218, observed 262.1212.

*4-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3d**). Yield 80% (39.9 mg); pale yellow solid; mp 132−135 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.93 (s, 3 H), 6.73 (d, $J$ = 3.6 Hz, 1 H), 7.02 (dd, $J$ = 9.0 Hz, 2.4 Hz, 1 H), 7.21 (dd, $J$ = 9.0 Hz, 2.4 Hz, 1 H), 7.21 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.34 (d, $J$ = 2.4 Hz, 1 H), 7.58 (d, $J$ = 4.2 Hz, 1 H), 7.76 (d, $J$ = 9.0 Hz, 1 H), 8.02 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.39 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 55.9, 101.4, 102.7, 113.6, 113.8, 117.1, 117.4, 121.3, 128.3, 129.4, 135.3, 142.1, 143.9, 147.7, 163.4; HRMS (EI, $m/z$) calcd for $C_{15}H_{11}N_3O$ $[M]^+$ 249.0902, observed 249.0908.

*2,4-Dimethoxy-6-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3e**). Yield 75% (41.9 mg); colorless solid; mp 141−143 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.92 (s, 3 H), 3.98 (s, 3 H), 6.52 (d, $J$ = 1.8 Hz, 1 H), 6.70 (d, $J$ = 3.6 Hz, 1 H), 6.92 (dd, $J$ = 1.8 Hz, 1 H), 7.19 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.57 (d, $J$ = 4.2 Hz, 1 H), 8.00 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.38 (dd, $J$ = 4.8 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 55.9, 56.4, 92.2, 97.3, 102.5, 105.2, 114.6, 117.3, 121.4, 128.4, 129.4, 143.0, 143.8, 147.8, 163.7, 164.4; HRMS (ESI, $m/z$) calcd for $C_{16}H_{13}O_2N_3Na$ $[M + Na]^+$ 302.0905, observed 302.0901.

*3-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3f**). Yield 87% (43.3 mg); gray solid; mp 140−143 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.79 (s, 3 H), 6.73 (d, $J$ = 3.6 Hz, 1 H), 7.17 (dd, $J$ = 8.4 Hz, 4.2 Hz, 1 H), 7.32−7.34 (comp, 2 H), 7.44 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 7.54 (t, $J$ = 8.4 Hz, 1 H), 8.01 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.36 (dd, $J$ = 4.2 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 56.2, 102.2, 114.0, 116.0, 116.8, 116.9, 120.6, 124.9, 129.0, 129.2, 129.3, 129.9, 143.7, 148.3, 156.1; HRMS (EI, $m/z$) calcd for $C_{15}H_{11}N_3O$ $[M]^+$ 249.0902, observed 249.0896.

*3-Methyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3g**). Yield 41% (19.1 mg); yellow solid; mp 86−89 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.11 (s, 3 H), 6.77 (d, $J$ = 4.2 Hz, 1 H), 7.18 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.31 (d, $J$ = 3.6 Hz, 1 H), 7.50 (t, $J$ = 7.8 Hz, 1 H), 7.65 (app d, $J$ = 7.2 Hz, 1 H), 7.69 (app d, $J$ = 7.8 Hz, 1 H), 8.04 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.35 (dd, $J$ = 4.2 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 18.0, 102.6, 113.3, 116.3, 116.9, 120.6, 128.1, 129.0, 129.5, 131.3, 135.6, 138.9, 139.4, 144.0, 148.0; HRMS (EI, $m/z$) calcd for $C_{15}H_{11}N_3$ $[M]^+$ 233.0953, observed 233.0944.

*3-Acetyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3h**). Yield 51% (26.6 mg); brown solid; mp 86−88 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.92 (s, 3 H), 6.50 (d, $J$ = 3.6 Hz, 1 H), 7.21 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.44 (d, $J$ = 3.6 Hz, 1 H), 7.67 (t, $J$ = 7.8 Hz, 1 H), 7.98 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.00 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.04 (dd,$J$ = 7.2 Hz, 1.2 Hz, 1 H), 8.34 (dd, $J$ = 4.8 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 28.1, 103.7, 113.3, 115.7, 117.6, 120.8, 128.3, 128.8, 129.8, 133.2, 136.3, 138.1, 139.7, 144.2, 148.3, 198.4; HRMS (EI, $m/z$) calcd for $C_{16}H_{11}N_3O$ $[M]^+$ 261.0902, observed 261.0902.

*Methyl 3-Cyano-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzoate* (**3i**). Yield 66% (36.6 mg); colorless solid; mp 92−94 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.41 (s, 3 H), 6.76 (d, $J$ = 3.6 Hz, 1 H), 7.15 (dd, $J$ =



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7.8 Hz, 1.8 Hz, 1 H), 7.45 (d, $J$ = 3.6 Hz, 1 H), 7.64 (t, $J$ = 7.8 Hz, 1 H), 7.98 (app t, $J$ = 2.1 Hz, 1 H), 8.01 (app t, $J$ = 2.1 Hz, 1 H), 8.23−8.29 (comp, 2 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 52.5, 102.9, 113.5, 115.7, 117.2, 120.9, 128.5 (2 C), 131.2, 135.4, 136.9, 139.8, 143.7, 148.7, 164.9; HRMS (EI, $m/z$) calcd for $C_{16}H_{11}N_3O_2$ $[M]^+$ 277.0859, observed 277.0852.

*5-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3j**). Yield 60% (29.9 mg); colorless solid; mp 130−133 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.92 (s, 3 H), 6.71 (d, $J$ = 3.6 Hz, 1 H), 7.19 (dd, $J$ = 8.4 Hz, 4.8 Hz, 1 H), 7.29−7.32 (comp, 2 H), 7.49 (d, $J$ = 3.6 Hz, 1 H), 7.65 (d, $J$ = 8.4 Hz, 1 H), 8.02 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.37 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 56.0, 102.3, 111.2, 116.4, 117.1, 118.0, 120.1, 121.0, 128.5, 129.3, 129.6, 133.4, 143.8, 148.1, 158.5; HRMS (ESI, $m/z$) calcd for $C_{15}H_{11}N_3ONa$ $[M + Na]^+$ 272.0800, observed 272.0811.

*5-Methyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3k**). Yield 66% (30.7 mg); colorless solid; mp 143−146 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.49 (s, 3 H), 6.72 (d, $J$ = 4.2 Hz, 1 H), 7.19 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.54 (d, $J$ = 3.6 Hz, 1 H), 7.58 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 7.66−7.68 (comp, 2 H), 8.02 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.38 (dd, $J$ = 4.2 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 20.8, 102.5, 109.9, 116.8, 117.3, 121.1, 128.0, 128.3, 129.4, 134.2, 134.6, 138.0, 138.1, 143.8, 147.9; HRMS (EI, $m/z$) calcd for $C_{15}H_{11}N_3$ $[M]^+$ 233.0953, observed 233.0948.

*5-(tert-Butyl)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3l**). Yield 80% (44.0 mg); colorless, gummy material; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.38 (s, 9 H), 6.70 (d, $J$ = 3.6 Hz, 1 H), 7.17 (dd, $J$ = 8.1 Hz, 4.8 Hz, 1 H), 7.52 (d, $J$ = 3.6 Hz, 1 H), 7.69 (d, $J$ = 8.4 Hz, 1 H), 7.76−7.83 (comp, 2 H), 8.00 (dd, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 8.36 (dd, $J$ = 4.8 Hz, 1.5 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 31.0, 34.8, 102.5, 109.5, 117.2, 117.3, 121.2, 127.6, 128.4, 129.4, 131.1, 131.2, 137.8, 143.8, 147.8, 151.0; HRMS (ESI, $m/z$) calcd for $C_{18}H_{17}N_3Na$ $[M + Na]^+$ 298.1320, observed 298.1308.

*4-(1H-Pyrrolo[2,3-b]pyridin-1-yl)-[1,1′-biphenyl]-3-carbonitrile* (**3m**). Yield 75% (44.3 mg); colorless solid; mp 150−153 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.77 (d, $J$ = 3.6 Hz, 1 H), 7.23 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.48 (app t, $J$ = 7.2 Hz, 1 H), 7.53−7.55 (comp, 2 H), 7.62−7.65 (comp, 3 H), 7.89 (d, $J$ = 8.4 Hz, 1 H), 7.99 (dd, $J$ = 8.4 Hz, 2.4 Hz, 1 H), 8.04−8.06 (comp, 2 H), 8.42 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 102.9, 110.2, 116.7, 117.5, 121.3, 127.1, 128.2, 128.4, 128.5, 129.2, 129.5, 132.3, 132.5, 138.2, 139.2, 140.9, 143.9, 147.9; HRMS (EI, $m/z$) calcd for $C_{20}H_{13}N_3$ $[M]^+$ 295.1109, observed 295.1104.

*5-(Dimethylamino)-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3n**). Yield 34% (17.8 mg); brown solid; mp 189−191 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.07 (s, 6 H), 6.68 (d, $J$ = 3.6 Hz, 1 H), 7.02−7.04 (comp, 2 H), 7.16 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.46 (d, $J$ = 3.6 Hz, 1 H), 7.52 (dd, $J$ = 7.2 Hz, 2.4 Hz, 1 H), 8.00 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.37 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 40.3, 101.6, 111.2, 115.7, 116.7, 116.8, 117.2, 120.8, 128.6, 128.9, 129.1, 129.2, 143.7, 148.3, 149.4; HRMS (EI, $m/z$) calcd for $C_{16}H_{14}N_4$ $[M]^+$ 262.1218, observed 262.1213.

*Methyl 3-Cyano-4-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzoate* (**3o**). Yield 51% (28.3 mg); colorless solid; mp 156−158 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 4.02 (s, 3 H), 6.79 (d, $J$ = 3.6 Hz, 1 H), 7.25 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.66 (d, $J$ = 4.2 Hz, 1 H), 8.02 (d, $J$ = 8.4 Hz, 1 H), 8.04 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.40 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H), 8.42 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.54 (d, $J$ = 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 52.8, 103.8, 109.2, 116.2, 118.0, 121.6, 127.7 (2 C), 128.9, 129.6, 134.5, 135.7, 143.6, 144.0, 147.7, 164.6; HRMS (EI, $m/z$) calcd for $C_{16}H_{11}N_3O_2$ $[M]^+$ 277.0851, observed 277.0847.

*5-Acetyl-2-(1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3p**). Yield 44% (23 mg); pale orange solid; mp 145−145 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.70 (s, 3 H), 6.79 (d, $J$ = 3.6 Hz, 1 H), 7.25 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.66 (d, $J$ = 4.2 Hz, 1 H), 8.03−8.06 (comp, 2 H), 8.34 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.40 (dd, $J$ = 4.2 Hz, 1.2 Hz, 1 H), 8.44 (d, $J$ = 2.4 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.6, 103.9, 109.3, 116.2, 118.0, 121.6, 127.7, 127.9, 129.7, 133.1, 134.6, 135.2, 143.6, 144.0, 147.7, 194.9; HRMS (EI, $m/z$) calcd for $C_{16}H_{11}N_3O$ $[M]^+$ 261.0902, observed 261.0908.

*1-(1H-Pyrrolo[2,3-b]pyridin-1-yl)-2-naphthonitrile* (**3q**). Yield 78% (42 mg); colorless solid; mp 151−152 °C (crystallization from diethyl ether and pet. ether); $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.87 (d, $J$ = 3.6 Hz, 1 H), 7.22 (dd, $J$ = 8.4 Hz, 4.8 Hz, 1 H), 7.39 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1 H), 7.47 (d, $J$ = 3.6 Hz, 1 H), 7.54 (ddd, $J$ = 8.4 Hz, 7.2 Hz, 1.2 Hz, 1 H), 7.69 (ddd, $J$ = 8.4 Hz, 7.2 Hz, 1.2 Hz, 1 H), 7.80 (d, $J$ = 8.4 Hz, 1 H), 8.02 (d, $J$ = 8.4 Hz, 1 H), 8.08 (d, $J$ = 8.4 Hz, 1 H), 8.10 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.33 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 102.9, 110.4, 116.6, 117.2, 120.6, 124.2, 126.7, 128.4, 128.6, 129.3, 129.5, 129.6, 129.7, 130.8, 135.8, 139.8, 144.2, 149.1; HRMS (ESI, $m/z$) calcd for $C_{18}H_{11}N_3Na$ $[M + Na]^+$ 292.0851, observed 292.0837.

*3-(1H-Pyrrolo[2,3-b]pyridin-1-yl)benzo[b]thiophene-2-carbonitrile* (**3r**). Yield 78% (43 mg); yellow solid; mp 136−137 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.81 (d, $J$ = 3.6 Hz, 1 H), 7.22 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.46 (app t, $J$ = 7.5 Hz, 1 H), 7.54 (d, $J$ = 3.6 Hz, 1 H), 7.60 (m, 1 H), 7.67 (app d, $J$ = 8.4 Hz, 1 H), 7.90 (app d, $J$ = 8.1 Hz, 1 H), 8.05 (dd, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 8.37 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 103.7, 104.3, 113.0, 117.7, 121.1, 123.0, 124.3, 125.9, 128.2, 128.7, 129.6, 133.3, 139.6, 140.1, 144.1, 147.8; HRMS (EI, $m/z$) calcd for $C_{16}H_9N_3S$ $[M]^+$ 275.0517, observed 275.0520.

*2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)thiophene-3-carbonitrile* (**3s**). Yield 87% (39.2 mg); colorless solid; mp 90−92 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.75 (d, $J$ = 3.6 Hz, 1 H), 7.19−7.21 (comp, 2 H), 7.24 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 8.00 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.02 (d, $J$ = 4.2 Hz, 1 H), 8.44 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 99.4, 104.4, 115.1, 118.2, 121.4, 121.5, 126.7, 127.1, 129.6, 143.9, 147.1, 147.8; HRMS (ESI, $m/z$) calcd for $C_{12}H_8N_3S$ $[M + H]^+$ 226.0439, observed 226.0435.

*2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)furan-3-carbonitrile* (**3t**). Yield 64% (26.7 mg); brown solid; mp 62−64 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.76−6.78 (comp, 2 H), 7.26 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.44 (d, $J$ = 2.4 Hz, 1 H), 7.58 (d, $J$ = 3.6 Hz, 1 H), 8.00 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1 H), 8.49 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 86.1, 105.2, 112.8, 112.9, 118.5, 121.3, 126.0, 129.7, 139.4, 144.7, 147.3, 150.4; HRMS (EI, $m/z$) calcd for $C_{12}H_7N_3O$ $[M]^+$ 209.0589, observed 209.0583.

*3-(1H-Pyrrolo[2,3-b]pyridin-1-yl)furan-2-carbonitrile* (**3u**). Yield 39% (16.4 mg); pale yellow solid; mp 133−135 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.75 (d, $J$ = 3.6 Hz, 1 H), 7.23 (dd, $J$ = 8.4 Hz, 4.2 Hz, 1 H), 7.65 (d, $J$ = 1.8 Hz, 1 H), 7.77 (d, $J$ = 2.4 Hz, 1 H), 7.82 (d, $J$ = 4.2 Hz, 1 H), 8.00 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.43 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 104.6, 108.5, 112.0, 115.5, 117.9, 121.4, 125.6, 129.5, 136.0, 144.1, 147.2, 147.6; HRMS (ESI, $m/z$) calcd for $C_{12}H_8N_3O$ $[M + H]^+$ 210.0667, observed 210.0663.

*2-(4-Phenyl-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3v**). Yield 50% (29.5 mg); yellow solid; mp 223−225 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.94 (d, $J$ = 3.6 Hz, 1 H), 7.30 (d, $J$ = 4.8 Hz, 1 H), 7.49−7.59 (comp, 4 H), 7.62 (d, $J$ = 4.2 Hz, 1 H), 7.78−7.85 (comp, 4 H), 7.89 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.45 (d, $J$ = 4.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 102.3, 110.1, 116.6, 116.7, 119.3, 127.6, 128.2, 128.4, 128.5, 128.6, 128.9, 133.7, 134.2, 138.4, 140.5, 142.9, 144.2, 148.4; HRMS (EI, $m/z$) calcd for $C_{20}H_{13}N_3$ $[M]^+$ 295.1109, observed 295.1112.

*2-(4-(m-Tolyl)-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile* (**3w**). Yield 75% (46.4 mg); colorless solid; mp 143−145 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.51 (s, 3 H), 6.94 (d, $J$ = 3.6 Hz, 1 H), 7.29 (t, $J$ = 2.4 Hz, 1 H), 7.32 (app d, $J$ = 7.2 Hz, 1 H), 7.47 (app t, $J$ = 7.2 Hz, 1 H), 7.54 (td, $J$ = 7.2 Hz, 1.2 Hz, 1 H), 7.58−7.60 (comp, 2 H), 7.61 (d, $J$ = 3.6 Hz, 1 H), 7.80−7.86 (comp, 2 H), 7.89 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H), 8.43 (d, $J$ = 4.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 21.5, 102.4, 110.1, 116.6, 116.7, 119.3, 125.7, 127.6, 128.2, 128.3, 128.8, 129.2, 129.3, 133.7, 134.2, 138.3, 138.6, 140.6, 143.1, 144.2, 148.4; HRMS (EI, $m/z$) calcd for $C_{21}H_{15}N_3$ $[M]^+$ 309.1266, observed 309.1251.



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*2-(5-Phenyl-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3x**).* Yield 79% (43.6 mg); colorless solid; mp 142−143 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.80 (d, $J$ = 4.2 Hz, 1 H), 7.42 (app t, $J$ = 7.2 Hz, 1 H), 7.51−7.56 (comp, 3 H), 7.62 (d, $J$ = 3.6 Hz, 1 H), 7.66−7.67 (comp, 2 H), 7.82 (td, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 7.86 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 7.89 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.21 (d, $J$ = 2.4 Hz, 1 H), 8.62 (d, $J$ = 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 103.1, 109.9, 116.7, 121.3, 127.2, 127.4, 127.6, 127.9, 128.1, 129.0 (2 C), 131.3, 133.8, 134.2, 139.1, 140.4, 143.2, 147.3; HRMS (EI, $m/z$) calcd for $C_{20}H_{13}N_3$ $[M]^+$ 295.1109, observed 295.1110.

*2-(5-(4-Bromophenyl)-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3y**).* Yield 88% (65.9 mg); colorless solid; mp 208−210 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.78 (d, $J$ = 3.6 Hz, 1 H), 7.48−7.56 (comp, 3 H), 7.59−7.63 (comp, 3 H), 7.79−7.81 (comp, 2 H), 7.87 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.14 (d, $J$ = 2.1 Hz, 1 H), 8.54 (d, $J$ = 2.1 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 103.1, 110.0, 116.6, 121.3, 121.6, 127.7 (2 C), 128.1, 129.0, 129.2, 130.1, 133.8, 134.2, 138.0, 140.2, 142.9, 147.4; HRMS (EI, $m/z$) calcd for $C_{20}H_{12}N_3Br$ $[M]^+$ 373.0215, observed 373.0216.

*2-(5-(4-Fluorophenyl)-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3z**).* Yield 75% (47 mg); colorless solid; mp 181−183 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 6.79 (d, $J$ = 3.6 Hz, 1 H), 7.19−7.22 (comp, 2 H), 7.55 (td, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 7.59−7.62 (comp, 3 H), 7.89 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.15 (d, $J$ = 2.4 Hz, 1 H), 8.56 (d, $J$ = 2.4 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 103.0, 110.0, 115.9 (d, $^2J_{F-C}$ = 21.3 Hz), 116.7, 121.2, 127.7 (2 C), 128.1, 129.0 (d, $^3J_{F-C}$ = 8.0 Hz), 129.1, 130.4, 133.7, 134.0, 135.2 (d, $^4J_{F-C}$ = 3.4 Hz), 140.3, 143.0, 147.3, 162.4 (d, $^1J_{F-C}$ = 245.0 Hz); HRMS (EI, $m/z$) calcd for $C_{20}H_{12}N_3F$ $[M]^+$ 313.1015, observed 313.1014.

*2-(5-(Pyren-1-yl)-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3aa**).* Yield 51% (42.8 mg); yellow solid; mp 225−227 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.86 (d, $J$ = 3.6 Hz, 1 H), 7.56 (td, $J$ = 7.5 Hz, 1.5 Hz, 1 H), 7.69 (d, $J$ = 3.9 Hz, 1 H), 7.84 (td, $J$ = 7.8 Hz, 1.5 Hz, 1 H), 7.90−7.95 (comp, 2 H), 8.01−8.07 (comp, 3 H), 8.13 (comp, 2 H), 8.18−8.29 (comp, 5 H), 8.63 (d, $J$ = 2.1 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 103.0, 110.0, 116.8, 121.0, 124.7, 124.8, 124.9, 125.2, 126.1, 127.4, 127.6, 127.7, 127.8, 128.2 (2 C), 129.1 (2 C), 130.8, 130.9 (2 C), 131.1, 131.4, 133.8, 134.2, 134.8, 140.4, 145.6, 147.2; HRMS (EI, $m/z$) calcd for $C_{30}H_{17}N_3$ $[M]^+$ 419.1422, observed 419.1424.

*2-(3-Bromo-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3ab**).* Yield 67% (40 mg); colorless solid; mp 214−215 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.30 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.56 (td, $J$ = 7.2 Hz, 1.2 Hz, 1 H), 7.60 (s, 1H), 9.73 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 7.80 (td, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 7.88 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.00 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.43 (dd, $J$ = 4.8 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 92.3, 110.3, 116.3, 118.1, 120.7, 127.0, 128.1 (2 C), 128.3, 133.8, 134.2, 139.4, 145.1, 146.8; HRMS (EI, $m/z$) calcd for $C_{14}H_8BrN_3$ $[M]^+$ 296.9902, observed 296.9889.

*2-(3-Iodo-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3ac**).* Yield 83% (57.3 mg); colorless solid; mp 219−221 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.30 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.55−7.58 (m, 1 H), 7.73 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1 H), 7.78−7.81 (m, 1 H), 7.86 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1 H), 7.88 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.40 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 58.1, 110.3, 116.3, 118.2, 123.7, 128.1 (2 C), 130.0, 131.9, 133.8, 134.2, 139.4, 145.0, 147.4; HRMS (EI, $m/z$) calcd for $C_{14}H_8IN_3$ $[M]^+$ 344.9763, observed 344.9756.

*2-(3-(4-Chlorophenyl)-1H-pyrrolo[2,3-b]pyridin-1-yl)benzonitrile (**3ad**).* Yield 66% (43.5 mg); colorless solid; mp 209−210 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.30 (dd, $J$ = 7.2 Hz, 4.8 Hz, 1 H), 7.47−7.50 (comp, 2 H), 7.56 (td, $J$ = 7.2 Hz, 1.2 Hz, 1 H), 7.64−7.66 (comp, 2 H), 7.74 (s, 1 H), 7.82 (td, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 7.87 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 7.90 (dd, $J$ = 7.2 Hz, 1.2 Hz, 1 H), 8.26 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.45 (dd, $J$ = 4.8 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 109.9, 116.7, 117.1, 118.0, 119.4, 125.1, 127.7, 128.1, 128.5, 128.6, 129.2, 132.2, 132.7, 133.8, 134.2, 140.0, 144.4, 148.2; HRMS (EI, $m/z$) calcd for $C_{20}H_{12}ClN_3$ $[M]^+$ 329.0720, observed 329.0722.

*2-(9H-Pyrido[2,3-b]indol-9-yl)benzonitrile (**3ae**).* Yield 72% (38.7 mg); colorless solid; mp 139−140 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.29−7.32 (comp, 2 H), 7.41 (app t, $J$ = 7.2 Hz, 1 H), 7.52 (app t, $J$ = 7.8 Hz, 1 H), 7.64 (app t, $J$ = 7.8 Hz, 1 H), 7.70 (app d, $J$ = 7.8 Hz, 1 H), 7.86 (dt, $J$ = 7.8 Hz, 1.8 Hz, 1 H), 7.97 (dd, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 8.17 (app d, $J$ = 7.8 Hz, 1 H), 8.43 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.52 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 110.1, 123.2, 116.3, 116.7, 116.9, 121.3 (2 C), 121.5, 127.2, 128.6, 128.7, 129.7, 134.1, 134.3, 139.0, 139.6, 146.5, 151.9; HRMS (ESI, $m/z$) calcd for $C_{18}H_{11}N_3Na$ $[M + Na]^+$ 292.0851, observed 292.0858.

*5-Methyl-2-(9H-pyrido[2,3-b]indol-9-yl)benzonitrile (**3af**).* Yield 81% (46 mg); colorless solid; mp 166−168 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.54 (s, 3 H), 7.29−7.31 (comp, 2 H), 7.39 (app t, $J$ = 7.2 Hz, 1 H), 7.52 (app t, $J$ = 7.8 Hz, 1 H), 7.57 (app d, $J$ = 7.8 Hz, 1 H), 7.66 (app d, $J$ = 8.4 Hz, 1 H), 7.76 (d, $J$ = 1.8 Hz, 1 H), 8.16 (app d, $J$ = 7.8 Hz, 1 H), 8.42 (app d, $J$ = 7.8 Hz, 1 H), 8.50 (dd, $J$ = 4.8 Hz, 1.2 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 21.0, 110.1, 113.0, 116.4, 116.6, 116.7, 121.2 (2 C), 121.3, 127.2, 128.6, 129.5, 134.5, 134.9, 136.4, 139.2, 139.8, 146.5, 152.0; HRMS (EI, $m/z$) calcd for $C_{19}H_{13}N_3$ $[M]^+$ 283.1109, observed 283.1110.

**Synthetic Transformation of Cyanated Products 3a.** *Synthesis of (2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)phenyl)methanamine (**4**).* Following a literature procedure,[11a] to a solution of **3a** (43.8 mg, 0.2 mmol) in THF (2 mL) was added $LiAlH_4$ (15.2 mg, 0.4 mmol) portionwise at 0 °C. Then the reaction mixture was allowed to come at room temperature and stirred for 1 h. The reaction mixture was diluted with $Et_2O$, cooled to 0 °C, and quenched with 15% aq NaOH followed by $MgSO_4$. It was stirred for another 15 min and filtered to remove the salts. After regular extraction with ethyl acetate, the combined organic layers were dried over $Na_2SO_4$ and concentrated in vacuo. The crude residue was purified by column chromatography on basic alumina using dichloromethane/methanol as an eluent to obtain **4** (22.7 mg, 51% yield): yield 51% (22.7 mg); brown, gummy material; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 3.62 (s, 2 H), 6.67 (d, $J$ = 3.6 Hz, 1 H), 7.14 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.33−7.34 (comp, 2 H), 7.42 (app t, $J$ = 7.8 Hz, 1 H), 7.50 (app t, $J$ = 7.8 Hz, 1 H), 7.61 (app d, $J$ = 7.8 Hz, 1 H), 8.01 (app d, $J$ = 7.8 Hz, 1 H), 8.32 (app d, $J$ = 4.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 42.5, 101.2, 116.4, 120.5, 127.9, 128.4, 129.0, 129.1, 129.2, 129.5, 136.2, 140.9, 143.7, 148.5; HRMS (ESI, $m/z$) calcd for $C_{14}H_{14}N_3$ $[M + H]^+$ 224.1188, observed 224.1174.

*Synthesis of 2-(1H-Pyrrolo[2,3-b]pyridin-1-yl)benzamide (**5**).* Following a literature procedure,[11a] to a solution of **3a** (43.8 mg, 0.2 mmol) in $^t$BuOH (1 mL) was added solid KOH (210 mg, 3.7 mmol), and the reaction mixture was heated at 60 °C for 4 h. After the mixture cooled to room temperature, $^t$BuOH was removed in vacuo. After regular extraction with ethyl acetate, the combined organic layers were dried over $Na_2SO_4$ and concentrated in vacuo to obtain **5** (46.5 mg, 98%): yield 98% (46.5 mg); colorless solid; mp 160−161 °C; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 5.69 (br s, 1 H), 6.04 (br s, 1 H), 6.67 (d, $J$ = 3.6 Hz, 1 H), 7.15 (dd, $J$ = 7.8 Hz, 4.8 Hz, 1 H), 7.38 (d, $J$ = 3.6 Hz, 1 H), 7.44 (app d, $J$ = 7.8 Hz, 1 H), 7.53 (app t, $J$ = 7.2 Hz, 1 H), 7.60 (td, $J$ = 7.2 Hz, 1.8 Hz, 1 H), 7.84 (dd, $J$ = 8.4 Hz, 1.8 Hz, 1 H), 8.01 (dd, $J$ = 7.8 Hz, 1.2 Hz, 1 H), 8.29 (dd, $J$ = 4.8 Hz, 1.8 Hz, 1 H); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 102.0, 116.8, 120.9, 128.5, 128.7, 129.5, 129.7 (2 C), 131.4, 133.9, 135.0, 143.6, 148.6, 169.1; HRMS (ESI, $m/z$) calcd for $C_{14}H_{11}N_3ONa$ $[M + Na]^+$ 260.0800, observed 260.0795.

**Mechanistic Experiments.** *Procedure for H/D Exchange Experiment.* Into an oven-dried 10 mL Schlenk tube was weighed 150 mg (0.8 mmol) of **1a**. To that were added NaOAc (31 mg, 50 mol %), AgOTf (58 mg, 30 mol %), and $[RuCl_2(p\text{-cymene})]_2$ (23 mg, 5 mol %). Next the tube was degassed and backfilled with nitrogen. Under nitrogen, 3.8 mL of $D_2O$ and 7.7 mL of anhydrous DCE were added. Then the reaction tube was degassed and backfilled with nitrogen (three times). The tube was closed with a Teflon-lined cap, and the contents were kept stirring in an oil bath. The bath temperature was slowly increased to 110 °C. After 30 h, the reaction was stopped and cooled to room temperature. The reaction mixture was filtered through a short pad of Celite and concentrated under vacuo. The


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crude reaction mixture was directly purified by column chromatography on silica gel using pet. ether/ethyl acetate as eluent to recover the starting material (123 mg, 82%). The deuterium incorporation (75%) was determined by $^1$H NMR spectroscopy (see SI for details).

*Procedure for the Parallel Experiment between **1a** and **1a**-$d_5$.* Two sets of parallel reactions (four each) of **1a** (19.4 mg, 0.1 mmol) and **1a**-$d_5$ (20 mg, 0.1 mmol) were subjected to standard condition in 10 mL oven-dried Schlenk tubes. The reactions were quenched with ethyl acetate at four different time intervals, 48 $\mu$L (0.2 mmol) of tridecane (internal standard) was added to each reaction mixture, and the percentage conversion was monitored by GC analysis. The primary kinetic isotopic effect (KIE) was found to be 1.6 (see the SI for details).

*Procedure for the Competitive Experiment between **1a** and **1a**-$d_5$.* In an oven-dried 10 mL Schlenk tube, a mixture of **1a** (19.4 mg, 0.1 mmol) and **1a**-$d_5$ (20 mg, 0.1 mmol) was subjected to standard conditions. After 2 h, the reaction was stopped and cooled to room temperature. The reaction mixture was filtered through a short pad of Celite and concentrated under vacuo. The crude reaction mixture was directly purified by column chromatography on silica gel using pet. ether/ethyl acetate as eluent. The ratio of **3a** to **3a**-$d_4$ was determined by $^1$H NMR spectroscopy. The primary KIE was found to be 1.2 (see the SI for details).

*Procedure for the Competitive Experiment between **1a** and **1f**.* In an oven-dried 10 mL Schlenk tube, a mixture of **1a** (19.4 mg, 0.1 mmol) and **1f** (20 mg mg, 0.1 mmol) was subjected to standard conditions. After 30 h, the reaction was stopped and cooled to room temperature. The reaction mixture was filtered through a short pad of Celite and concentrated under vacuo. The crude reaction mixture was directly purified by column chromatography on silica gel using pet. ether/ethyl acetate as eluent to obtain pure **3a** (10.7 mg) and **3f** (7.6 mg) in 49% and 30% yields, respectively.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01148.

Additional screening data, mechanistic experimental details, X-ray crystal structure of **3q**, and $^1$H and $^{13}$C NMR spectra of all new compounds (PDF)

Single crystal X-ray diffraction data for compound **3q** in CIF format (CIF)

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### Notes

The authors declare no competing financial interest.

The CIF file of **3q** was submitted to CCDC (1472438) and can be obtained at https://summary.ccdc.cam.ac.uk/structure-summary-form.

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