JOC The Journal of Organic Chemistry

Note

Visible-Light Promoted C2 Selective Arylation of Quinoline and Pyridine N-Oxides with Diaryliodonium Tetrafluoroborate

Dazhi Li, Ce Liang, Zaixing Jiang, JunZheng Zhang, Wang-Tao Zhuo, Fan-Yue Zou, Wan-Peng Wang, Guo-Lin Gao, and Jinzhu Song

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02933 • Publication Date (Web): 07 Jan 2020

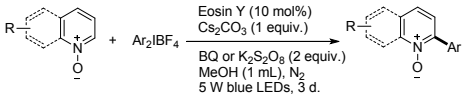
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Visible-Light Promoted C2 Selective Arylation of Quinoline and Pyridine *N*-Oxides with Diaryliodonium Tetrafluoroborate

Dazhi Li,[†,§] Ce Liang,[‡,§] Zaixing Jiang,[‡] Junzheng Zhang,[‡] Wang-Tao Zhuo,[‡] Fan-Yue Zou,[‡] Wan-Peng Wang,[‡] Guo-Lin Gao,*[,‡] and Jinzhu Song*[,†]

[†] School of Life Science and Technology, Harbin Institute of Technology, Harbin 150001, Heilongjiang, China.

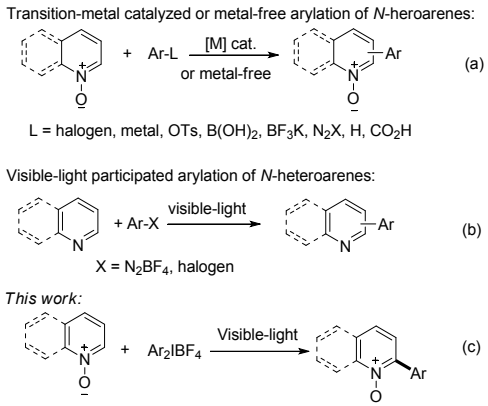
[‡] MIIT Key Laboratory of Critical Materials Technology for New Energy Conversion and Storage, School of Chemistry and Chemical Engineering, Harbin Institute of Technology, Harbin, 150001, Heilongjiang, China.



ABSTRACT: A protocol of visible-light promoted C2 selective arylation of quinoline and pyridine *N*-oxides, with diaryliodonium tetrafluoroborate as arylation reagent, using eosin Y as photo-catalyst for the construction of *N*-heterobiaryls was presented. This methodology provided an efficient way for the synthesis of 2-aryl substituted quinoline and pyridine *N*-oxides. And this strategy advantaged of its specific regioselectivity, simple operation, good functional group tolerance, and high to moderate yields under mild conditions.

Quinoline and pyridine motifs contained *N*-heterobiaryls are very important subunits widely existed in natural products,[1] bioactive compounds,[2] pharmaceuticals,[3] ligands,[4] and functional materials.[5] Therefore, significant efforts had been made for the efficient synthesis of these functional molecules in the last decades. Conventional methodologies commonly utilize transition-metal-catalyzed cross-coupling reactions, such as Stille,[6] Suzuki,[7] Negishi,[8] Kumada,[9] Hiyama[10] and others.[11] Among which, quinoline or pyridine coupling precursors usually needed to be prefunctionalized by halogenation, boronation or metallization, which was neither step nor atom

Scheme 1. Selected direct arylation of *N*-heteroarenes.

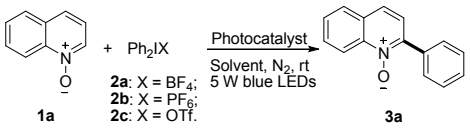


economy. And the usage of air and moisture sensitive organometallic compounds in stoichiometric also bad for the operation. All these defects limited their application in organic chemistry.

Recently, direct selective arylation of quinoline and pyridine *N*-oxides have emerged as a powerful strategy to build C-C bond between quinoline and pyridine *N-oxide* with arene for the construction of *N*-heterobiaryls, in which various transition-metal catalysts were used, e.g. Pd,[12] Cu,[13] Ir,[14] Ag,[15] Rh,[16] as well as metal-free processes were employed (Scheme 1, a).[17] All these protocols were very useful, but there were still some disadvantages, such as high temperature,[12b-d, 13b, c, 15] use of explosive diazonium compound,[14, 16] use of water and moisture sensitive organometallic compounds.[13a, 17] To our best knowledge, there was no visible-light promoted or induced direct arylation of quinoline or pyridine *N*-oxide was reported. Only rare of visible-light induced selective C-H arylation of pyridine or quinoline was reported (Scheme 1, b).[18] In these processes, there have some defects too, such as explosive diazonium compounds were used,[18a-e] or bad regioselectivity were given.[18a, 18d-f] There's still room for inspiration in developing mild, efficient, regioselective and benign methods for the preparation of quinoline or pyridine *N*-oxide contained *N*-heterobiaryls. Herein, we present visible-light promoted C2 selective arylation of quinoline and pyridine *N*-oxides using diaryliodonium tetrafluoroborate as arylation reagent with simple operation in room temperature to give C2 arylation products with good group tolerance (Scheme 1, c).

Our initial investigation was carried out by using quinoline *N*-oxide (**1a**) as substrate, Ph_2IBF_4 (**2a**, 1 equiv.) as arylation reagent, K_2CO_3 (1 equiv.) as base in the presence of $Ru(bpy)_3Cl_2{\cdot}6H_2O$ (5 mol%), in 1 mL of MeCN under N_2 atmosphere, which led to the desired product **3a** in 12% yield after irradiation with 5 W blue LEDs (light emitting diodes) for 3 days (Table 1, entry 1). The preliminary result urges us for the further condition optimization. Subsequently, different photo-catalysts were screened, and eosin Y gave the best result to give **3a** in 20% yield (Table 1, entries 2 - 7). Other common bases were also tested, and Cs_2CO_3 was the ideal base for this transformation in which the yield of **3a** was increased to 25% (Table 1, entries 8 - 9). Further investigation showed that methanol was the best solvent, and the yield of **3a** was improved to 35% (Table 1, entry 10). When the reaction time was shortened to 2 days, the yield of **3a** was decreased to 24%, but if the reaction time was prolonged to 7 days, the yield of the desired product was almost the same as 3 days (Table 1, entries 11 - 12). Other diphenyliodonium salts, such as Ph_2IPF_6 (**2b**) and Ph_2IOTf (**2c**) were also used as arylation reagents, but failed to improve the yield of **3a** (Table 1, entries 13 - 14). Furthermore, different additives were tested, and BQ (1,4-benzoquinone) was helpful for improving the yield of **3a** to 40% (Table 1, entries 15 - 18), probably with deprotonation of intermediate. Different loadings of photo-catalyst, arylation reagent **2a** and additive were investigated, and the yield of **3a** was improved up to 76% (Table 1, entries 19 - 21). When this reaction was run

Table 1. Reaction conditions screening.[a]



1a **3a**

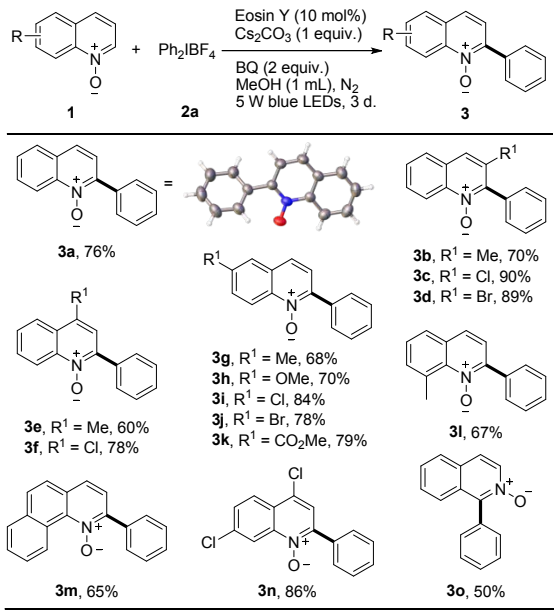
Entry	Photocatalyst (mol%)	**2** (equiv.)	Base (1 equiv.)	Solvent (1 mL)	Additive (equiv.)	Time (d)	Yield (%)
1	$Ru(bpy)_3Cl_2•6H_2O$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	12
2	*fac*-Ir(ppy)$_3$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	17
3	$Ru(phen)_3(PF_6)_2$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	12
4	$Ru(phen)_3Cl_2$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	12
5	$Ru(bpz)_3(PF_6)_2$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	13
6	$[Ir(bpy)(ppy)_2](PF_6)$ (5)	**2a** (1)	K_2CO_3	MeCN	---	3	15
7	Eosin Y (5)	**2a** (1)	K_2CO_3	MeCN	---	3	20
8	Eosin Y (5)	**2a** (1)	NEt_3	MeCN	---	3	18
9	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeCN	---	3	25
10	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	---	3	35
11	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	---	2	24
12	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	---	7	34
13	Eosin Y (5)	**2b** (1)	Cs_2CO_3	MeOH	---	3	33
14	Eosin Y (5)	**2c** (1)	Cs_2CO_3	MeOH	---	3	20
15	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	Ag_2CO_3 (1)	3	29
16	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	$K_2S_2O_8$ (1)	3	38
17[b]	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	DDQ (1)	3	32
18[c]	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	BQ (1)	3	40
19	Eosin Y (5)	**2a** (1)	Cs_2CO_3	MeOH	BQ (2)	3	50
20	Eosin Y (5)	**2a** (2)	Cs_2CO_3	MeOH	BQ (2)	3	65
21	Eosin Y (10)	**2a** (2)	Cs_2CO_3	MeOH	BQ (2)	3	76
22	---	**2a** (2)	Cs_2CO_3	MeCN	BQ (2)	3	trace
23[d]	Eosin Y (10)	**2a** (2)	Cs_2CO_3	MeCN	BQ (2)	3	trace

[a] Reaction condition: **1a** (0.1 mmol), **2**, photocatalyst, base, additive, 1 mL solvent, N_2 atmosphere, room temperature under the irradiation of 5 W blue LEDs for a certain time. [b] DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. [c] BQ = 1,4-benzoquinone. [d] In darkness.

without light or photo-catalyst, only trace amount of product was detected (Table 1, entries 22 - 23), suggesting either the photo-catalyst or light is necessary for the process. The best conditions that we got for this reaction were: **1a** (1 equiv.) reacted with **2a** (2 equiv.), in the presence of photo-catalyst eosin Y (10 mol%), with base Cs_2CO_3 (1 equiv.) and additive BQ (2 equiv.) in 1 mL of methanol under N_2 atmosphere, with the irradiation of 5 W LEDs for 3 days.

With the optimized condition in hand, we investigated the scope of this reaction, and the results were elucidated in Scheme 2. As depicted in Scheme 2, for all the quinoline *N*-oxide substrates investigated, desired products were obtained in good to moderate yields, and substrates with electron-withdrawing group (Cl, Br, or CO_2Me) gave relatively higher yield than electron-donating group (Me or OMe). And the structure of **3a** was further established by X-ray crystallographic analysis (preparation and details in SI, CCDC: 1858700).[19] As shown

Scheme 2. Scope study of quinoline *N*-oxide.[a]

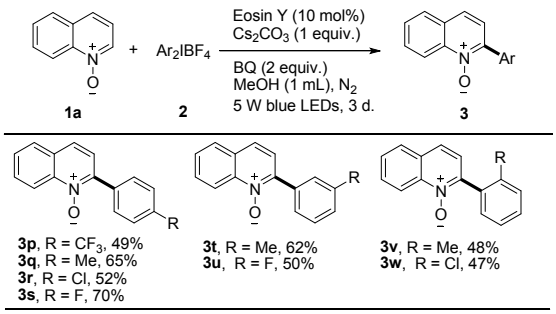


[a] Reaction conditions: **1** (0.1 mmol), Ph_2IBF_4 (0.2 mmol, 2 equiv.), Cs_2CO_3 (0.1 mmol, 1 equiv.), BQ (0.2 mmol, 2 equiv.), MeOH (1 mL) under N_2 atmosphere, irradiation with 5 W blue LEDs for 3 days.

in Scheme 2, substituted groups at C3 position of pyridine ring didn't hinder the reaction, to form the final products in good yields (Scheme 2, **3b** - **3d**). It's also worth to notice that 3-chloroquinoline *N*-oxide gave the expected product up to 90% yield (Scheme 2, **3c**). C4 substituted quinoline *N*-oxides substrates could converted into corresponding products smoothly in good yields (Scheme 2, **3e** - **3f**). Different substituents on the phenyl ring fragment of the quinoline *N*-oxide were also tested, to give the corresponding products in good to moderate yields. For example, substitution group at C6 or C8 position with Me, OMe, Cl, or Br group was tolerated with the reaction conditions to produce the corresponding products in 67 - 84% yields (Scheme 2, **3g** - **3j**, **3l**). Interestingly, the ester group was suitable for the reaction conditions to furnish the desired product in 79% yield (Scheme 2, **3k**). In addition, when benzo[*h*]quinoline *N*-oxide and 4,7-dichloroquinoline *N*-oxide were submitted to the reaction, desired products were isolated in 65% and 86% yield, respectively (Scheme 2, **3m** - **3n**). It was also worth noting that when isoquinoline *N*-oxide submitted to this reaction, only 1-phenylisoquinoline *N*-oxide was isolated as the main product in 50% yield, probably because of electronic effects (Scheme 2, **3o**).

To extend the scope of the reaction, different substituted diaryliodonium tetrafluoroborate was subjected to the reaction conditions (Scheme 3). As seen from Scheme 3, different substituents in *para*-position of the diaryl-iodonium tetrafluoroborate, such as CF_3, Cl, Me, and F, to give the desired products in 49-70% yields (Scheme 3, **3p** - **3s**). Different substituents in *meta*-position of the diaryliodonium salts were also converted into the final products in 62% and 50% yields, respectively (Scheme 3, **3t**, **3u**). It worth to noticed that, *ortho*-position

Scheme 3. Scope study of diaryliodonium tetrafluoroborate.[a]

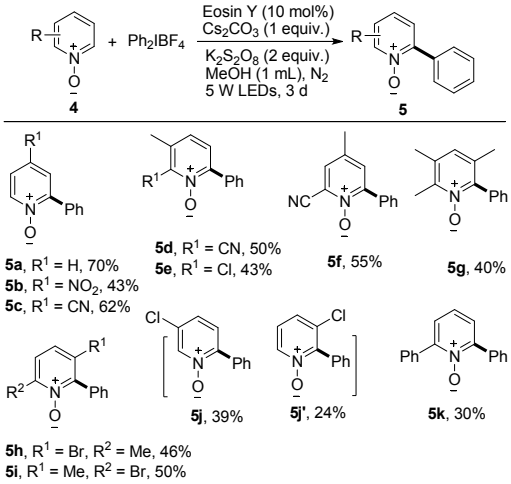


[a] Reaction conditions: **1a** (0.1 mmol), Ar_2IBF_4 (0.2 mmol, 2 equiv.), Cs_2CO_3 (0.1 mmol, 1 equiv.), BQ (0.2 mmol, 2 equiv.), MeOH (1 mL) under N_2 atmosphere, irradiation with 5 W blue LEDs for 3 days.

(2-Cl, 2-Me) substituted substrates didn't hinder the reaction, to give the corresponding products in 48% and 47% yield, respectively (**3v**, **3w**). The yield were relative lower probably because the steric hindrance.

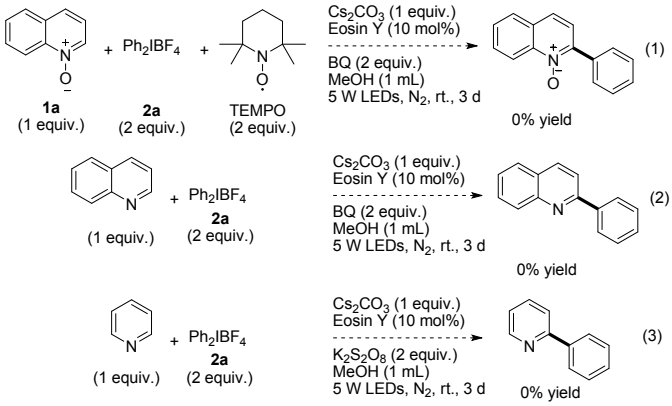
Then we tried this protocol for the arylation of pyridine *N*-oxide, and results were listed in Scheme 4. Further investigation showed that $K_2S_2O_8$ was a better additive for the arylation of pyridine *N*-oxide than BQ in the reaction, probably with the oxidation of photo-catalyst. Pyridine *N*-oxide could convert to its corresponding 2-phenylpyridine *N*-oxide in 70% yield (Scheme 4, **5a**). When pyridine *N*-oxides bearing strong withdrawing groups, such as 4-nitro- or 4-cyanopyridine *N*-oxides, were also suitable for the reaction, to give the corresponding products in 43% and 62% yield, respectively (Scheme 4, **5b**, **5c**). The yield of **5b** was isolated in a relative lower probably because the nitro group. Di- or tri-substituents on the pyridine ring did not hinder the reaction, to form the desired products in acceptable yield (Scheme 4, **5d** - **5i**). **5g** gave a lower yield probably because the steric hindrance. It is worth to point out that the halogen substituted pyridine *N*-oxide, such as Br, Cl, that were normally

Scheme 4. Scope study of pyridine *N*-oxide.[a]



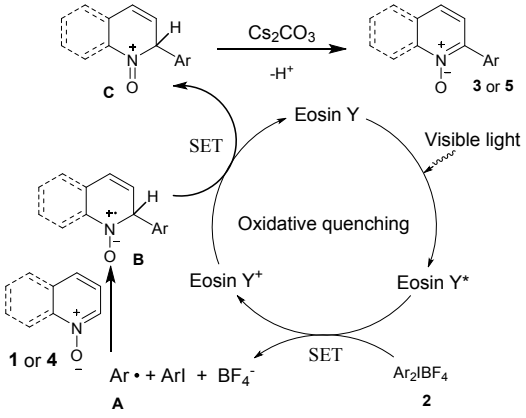
[a] Reaction conditions: **4** (0.1 mmol), Ph_2IBF_4 (0.2 mmol, 2 equiv.), Cs_2CO_3 (0.1 mmol, 1 equiv.), $K_2S_2O_8$ (0.2 mmol, 2 equiv.), MeOH (1 mL) under N_2 atmosphere, irradiation with 5 W LEDs for 3 days.

sensitive to the metal catalytic arylation reaction conditions, could be suitable for this protocol. The yield of **5e** was not so good probably because of electron effect. The yield of **5h** was a bit low probably as electron and steric effects. It was not surprise that 3-chloropyridine *N*-oxide gave the expected products in two structure isomers (**5j** and **5j'**) in 63% yield, and the ratio is 13:8. Interestingly, when the product 2-phenylpyridine *N*-oxide (**5a**) was subjected to the standard conditions, the expected product 2,6-diphenylpyridine *N*-oxide was obtained in 30% yield (Scheme 4, **5k**).



To give further insight into the reaction mechanism, the control experiment was conducted by addition of 2 equiv. of TEMPO ((2,2,6,6-Tetramethylpiperidin-1-yl)oxyl) into the reaction, and no desired product was isolated (eq. 1), and with HRMS (high resolution mass spectrometer) test for the reaction mixture, Ph-OTEMP was detected. And in our reaction mixture without TEMPO, diphenyl was also detected by GC-Mass, which suggested that radical pathway involved in the process. We also tried the same condition use quinoline and pyridine as substrates, but to find no reaction (eq. 2 and 3), that means the *N*-oxide group was essential for this reaction. And Stern-Volmer experiments were carried out with **1a**, **2a**, and BQ (details in SI).

Scheme 5. Proposed reaction mechanism.



Accordingly the reaction mechanism was proposed based upon the above results and previous literatures as depicted in Scheme 5.[20] Firstly, eosin Y was activated by visible light to its excited state eosin Y* under the

irradiation of 5 W blue LEDs, which was oxidized by Ar_2IBF_4 (**2**) through a SET (single electron transfer) reaction, to give eosin Y^+ and phenyl radical (**A**).[21] Subsequently the radical intermediate **A** was selectively added to C2 position of quinoline or pyridine *N*-oxide (**1** or **4**) to generate intermediate **B** which went through another SET reaction to give intermediate **C** and regenerated photo-catalyst. Finally, intermediate **C** loss one proton with the assistant of base (Cs_2CO_3) to afford the final products **3** or **5**. The additives, BQ probably help with the deprotonation of intermediate **C** to give final product **3**, and $K_2S_2O_8$ probably with the oxidation of photo-catalyst in pyridine *N*-oxide examples.

In summary, we have developed a strategy of visible-light promoted C2 selective arylation of quinoline and pyridine *N*-oxides under mild reaction conditions. Compared with previous methodologies, this strategy has attracted special attention due to its operational simplicity, good functional group tolerance, good regioselectivity, and high to moderate yields under mild conditions.

EXPERIMENTAL SECTION

1. General information:

^1H and ^{13}C NMR spectra were obtained on Bruker AV-400 or AV-600 instrument in $CDCl_3$ or DMSO-d_6 with TMS ($SiMe_4$) as internal standard. And chemical shift values were reported in ppm relative to dimethyl TMS (δ = 0.00 ppm) or DMSO (δ = 2.50 ppm) for ^1H NMR, chloroform (δ = 77.0 ppm) or DMSO (δ = 39.5 ppm) for ^{13}C NMR. The reported δ of ^{13}C NMR were $^{13}C\{^1H\}$ proton-decoupled carbons data. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. HRMS (ESI) spectra were recorded on a 1200-6520 Q-TOF/Agilent mass spectrometer using electrospray ionization. The single crystal data was collected on an Agilent Technology Super Nova Eos Dual system with a (Mo-Kα, λ = 0.71073 Å) micro focus source and focusing multilayer mirror optics. All materials and solvents were used as received from commercial sources without further purification. Flash column chromatography was performed using 200-300 mesh silica gel. The 5W LEDs tape lights were made by NVC lighting CO., LTD, the wave length is 450-480 nm, the distance from light source to vessel is about 5 cm, no filters was used.

2. Preparation and characterization of substrates

2.1. Preparation of substituted quinoline or pyridine *N*-oxide.

Quinoline and pyridine *N*-oxides were synthesized according previous report. [22]

2.2. Preparation of diaryliodonium tetrafluoroborate.

Diaryliodonium tetrafluoroborates were synthesized according previous report.[23]

2.3. Preparation of diphenyliodonium hexafluorophosphate.

Diphenyliodonium hxeaflurophosphates was synthesized according previous report.[24]

2.4. Preparation of diphenyliodonium trifluoromethanesulfonate.

Diphenyliodonium trifluoromethanesulfonate was synthesized according previous report.[25]

2.5. Characterization of substrates.

1a, quinoline *N*-oxide, white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (d, *J* = 8.8 Hz, 1H), 8.55 (d, *J* = 5.9 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.78 –7.74 (m, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 141.4, 135.5, 130.4, 130.3, 128.7, 128.0, 126.0, 120.9, 119.6.

1b, 3-methylquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.7 Hz, 1H), 8.41 (s, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.51 (s, 1H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 139.5, 136.8, 131.1, 130.1, 129.2, 128.6, 127.3, 125.4, 119.4, 18.6.

1c, 3-chloroquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.7 Hz, 1H), 8.51 (d, *J* = 1.7 Hz, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.76 – 7.72 (m, 2H), 7.68 – 7.65 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 140.3, 135.2, 130.2, 129.8, 129.6, 127.4, 127.3, 124.3, 119.7.

1d, 3-bromoquinoline *N*-oxide, white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (d, *J* = 8.8 Hz, 1H), 8.65 (d, *J* = 1.5 Hz, 1H), 7.90 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.68 – 7.65 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 140.3, 137.1, 130.5, 130.1, 129.7, 127.8, 127.3, 119.7, 114.2.

1e, 4-methylquinoline *N*-oxide, brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 8.7 Hz, 1H), 8.43 (d, *J* = 6.1 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.77 (t, *J* = 7.4 Hz, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 6.1 Hz, 1H), 2.66 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 140.8, 134.8, 134.5, 130.0, 129.7, 128.4, 124.6, 121.3, 120.2, 18.2.

1f, 4-chloroquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 8.7 Hz, 1H), 8.44 (d, *J* = 6.5 Hz, 1H), 8.20 (d, *J* = 8.3 Hz, 1H), 7.83 (t, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 6.5 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 142.0, 135.0, 131.1, 129.9, 129.6, 127.9, 125.1, 120.9, 120.2.

1g, 6-methylquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.9 Hz, 1H), 8.46 (d, *J* = 6.0 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.61 (s, 1H), 7.58 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.25 (dd, *J* = 8.4, 6.0 Hz, 1H), 2.54 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 139.8, 138.8, 134.8, 132.4, 130.5, 126.8, 125.4, 120.8, 119.3, 21.3.

1h, 6-methoxyquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 9.5 Hz, 1H), 8.39 (dd, *J* = 6.0, 0.7 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.37 (dd, *J* = 9.5, 2.7 Hz, 1H), 7.24 (dd, *J* = 8.5, 6.0 Hz, 1H), 7.10 (d,

J = 2.6 Hz, 1H), 3.94 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 159.3, 137.1, 133.7, 131.9, 124.9, 122.7, 121.4, 121.3, 105.6, 55.6.

1i, 6-chloroquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 9.3 Hz, 1H), 8.50 (d, *J* = 6.0 Hz, 1H), 7.85 (d, *J* = 2.1 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.33 (dd, *J* = 8.5, 6.1 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 139.9, 135.5, 134.9, 131.1, 131.0, 126.7, 124.6, 122.1, 121.6.

1j, 6-bromoquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 9.3 Hz, 1H), 8.51 (d, *J* = 6.0 Hz, 1H), 8.04 (d, *J* = 1.5 Hz, 1H), 7.82 (dd, *J* = 9.3, 1.7 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 8.4, 6.2 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 140.3, 135.7, 133.6, 131.5, 130.0, 124.5, 123.2, 122.1, 121.7.

1k, 6-(methoxycarbonyl)quinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (d, *J* = 9.1 Hz, 1H), 8.62 – 8.59 (m, 2H), 8.32 (dd, *J* = 9.1, 1.6 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.39 (dd, *J* = 8.4, 6.1 Hz, 1H), 4.01 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 165.6, 143.1, 137.0, 130.9, 130.3, 129.8, 129.7, 126.5, 121.8, 120.3, 52.6.

1l, 8-methylquinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 6.0 Hz, 1H), 7.64 – 7.61 (m, 2H), 7.43 – 7.39 (m, 2H), 7.16 (dd, *J* = 8.3, 6.1 Hz, 1H), 3.19 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 141.2, 137.1, 133.4, 133.2, 132.3, 127.9, 126.7, 126.3, 120.5, 24.8.

1m, benzo[*h*]quinoline *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (d, *J* = 7.6 Hz, 1H), 8.65 (d, *J* = 6.2 Hz, 1H), 7.92 – 7.89 (m, 1H), 7.83 – 7.71 (m, 4H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.37 (dd, *J* = 7.9, 6.4 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 139.2, 138.3, 133.9, 131.1, 130.4, 128.9, 128.2 (d, *J* = 7.6 Hz), 127.9, 127.6, 125.9, 125.7, 124.9, 121.1.

1n, 4,7-dichloroquinoline *N*-oxide, white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (d, *J* = 2.0 Hz, 1H), 8.43 (d, *J* = 6.6 Hz, 1H), 8.14 (d, *J* = 8.9 Hz, 1H), 7.69 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.38 (d, *J* = 6.6 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 142.2, 138.1, 135.8, 130.7, 129.6, 126.7, 126.4, 121.2, 119.8.

1o, isoquinoline *N*-oxide, white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.15 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.1 Hz, 1H), 7.64 – 7.58 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 136.6, 136.0, 129.4, 129.3, 128.9, 128.6, 126.5, 124.8, 124.1.

2a, diphenyliodonium tetrafluoroborate, off-white solid. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.25 (d, *J* = 7.5 Hz, 4H), 7.66 (t, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 4H). $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d6) δ 135.2, 132.1, 131.8, 116.6.

2b, diphenyliodonium hexafluorophosphate, off-white solid. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.21 (d, *J* = 7.7 Hz, 4H), 7.63 (t, *J* = 7.3 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 4H). $^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO-d6) δ 135.1, 131.7, 131.6,

118.1.

2c, diphenyliodonium trifluoromethanesulfonate, off-white solid. ^{1}H NMR (400 MHz, DMSO-d6) δ 8.25 (d, *J* = 7.8 Hz, 4H), 7.67 (t, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 4H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 135.2, 132.1, 131.8, 116.6.

2d, bis[4-(trifluoromethyl)phenyl]iodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.52 (d, *J* = 7.3 Hz, 4H), 7.94 (d, *J* = 7.4 Hz, 4H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 136.3, 132.1 (q, *J* = 32.7 Hz), 128.6 (d, *J* = 2.9 Hz), 123.4 (q, *J* = 273.7 Hz), 121.0. ^{19}F NMR (376 MHz, DMSO-d6) δ -61.77, -148.19 (d, *J* = 19.9 Hz).

2e, di-*p*-tolyliodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.09 (d, *J* = 8.1 Hz, 4H), 7.32 (d, *J* = 8.0 Hz, 4H), 2.33 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 142.5, 135.0, 132.3, 113.1, 20.9.

2f, bis(4-chlorophenyl)iodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.26 (d, *J* = 7.3 Hz, 4H), 7.59 (d, *J* = 7.3 Hz, 4H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 137.5, 137.1, 131.8, 115.1.

2g, bis(4-fluorophenyl)iodonium tetrafluoroborate, gray solid.[26] ^{1}H NMR (600 MHz, DMSO-d6) δ 8.32 (dd, *J* = 8.0, 5.2 Hz, 4H), 7.42 (d, *J* = 8.6 Hz, 4H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 164.0 (d, *J* = 251.6 Hz), 138.0 (d, *J* = 9.1 Hz), 119.3 (d, *J* = 22.8 Hz), 111.2. ^{19}F NMR (376 MHz, DMSO-d6) δ -106.57, -148.12 (d, *J* = 21.8 Hz).

2h, di-*m*-tolyliodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.11 (s, 2H), 8.05 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 2.33 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 141.8, 135.4, 132.7, 132.3, 131.5, 116.2, 20.8.

2i, bis(3-fluorophenyl)iodonium tetrafluoroborate, gray solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.32 (d, *J* = 5.3 Hz, 2H), 8.12 (d, *J* = 5.8 Hz, 2H), 7.63 (d, *J* = 5.9 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 161.8 (d, *J* = 252.3 Hz), 133.6 (d, *J* = 7.9 Hz), 131.6, 122.4 (d, *J* = 24.8 Hz), 119.6 (d, *J* = 21.0 Hz), 116.4 (d, *J* = 7.7 Hz). ^{19}F NMR (376 MHz, DMSO-d6) δ -107.44, -148.23 (d, *J* = 21.8 Hz).

2j, di-*o*-tolyliodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.33 (d, *J* = 7.9 Hz, 2H), 7.59 – 7.55 (m, 4H), 7.32 – 7.29 (m, 2H), 2.61 (s, 6H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 140.6, 137.2, 132.8, 131.6, 129.3, 120.6, 25.0. **HRMS** (ESI) *m/z* calcd for $C_{14}H_{14}I^{+}$ [M-BF_4]$^{+}$ 309.0140, found 309.0145.

2k, bis(4-chlorophenyl)iodonium tetrafluoroborate, white solid. ^{1}H NMR (600 MHz, DMSO-d6) δ 8.53 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.70 (t, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d6) δ 139.0, 136.0, 134.8, 130.5, 130.3, 119.6.

4a, pyridine *N*-oxide, colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.22 (m, 2H), 7.30 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 139.3, 126.1, 125.9.

4b, 4-nitropyridine *N*-oxide, pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 6.3 Hz, 2H), 8.13 (d, *J* = 6.4 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 142.1, 140.1, 120.8.

4c, 4-cyanopyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 6.1 Hz, 2H), 7.53 (d, *J* = 6.0 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 140.2, 128.9, 115.8, 107.6.

4d, 2-cyano-3-methylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.5 Hz, 1H), 7.40 (dd, *J* = 7.8, 6.7 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 2.56 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 142.4, 137.3, 127.9, 126.3, 126.2, 111.0, 19.0.

4e, 2-chloro-3-methylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 6.4 Hz, 1H), 7.17 – 7.11 (m, 2H), 2.44 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 142.2, 138.0, 136.0, 127.2, 122.3, 19.9.

4f, 2-cyano-4-methylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 6.8 Hz, 1H), 7.49 (d, *J* = 1.9 Hz, 1H), 7.30 (dd, *J* = 6.4, 2.2 Hz, 1H), 2.41 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 139.4, 136.6, 131.4, 130.0, 125.1, 111.7, 20.0.

4g, 2,3,5-trimethylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 6.90 (s, 1H), 2.46 (s, 3H), 2.30 (s, 3H), 2.23 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 145.1, 136.9, 134.0, 132.1, 128.7, 19.3, 17.7, 13.3.

4h, 5-bromo-2-methylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 1.1 Hz, 1H), 7.31 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 147.9, 140.5, 128.2, 126.4, 117.2, 17.3.

4i, 2-bromo-5-methylpyridine *N*-oxide, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.54 (d, *J* = 8.3 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 2.30 (s, 3H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 140.2, 135.5, 129.9, 129.6, 127.5, 17.9.

4j, 3-chloropyridine *N*-oxide, white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.14 (d, *J* = 6.3 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.29 – 7.23 (m, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 138.6, 137.6, 133.2, 125.7, 125.7.

3. Preparation and characterization of products

3.1 The preparation of products.

To a 10 mL vial, magnetic stir bar, substrate **1** (0.1 mmol), Ph_2IBF_4 (0.2 mmol, 2 equiv.), BQ or $K_2S_2O_8$ (0.2 mmol, 2 equiv.), Cs_2CO_3 (0.1 mmol, 1 equiv.), eosin Y (0.01 mmol, 10 mol%), MeOH (1 mL) were added in sequence and sealed the flask. Evacuated and backfilled it with nitrogen (3 cycles) under -78 ^{o}C. Then the vial was irradiated by 5 W blue LEDs at room temperature for 3 days. After the substrate was consumed (monitored by

TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by precipitation thin-layer chromatography (PTLC) using hexanes: ethyl acetate (10:1 to 1:1 depending on the substrates) as the eluant to afford the desired products **3** and **5**.

3.2. Characterization of products.

3a, 2-phenylquinoline *N*-oxide, 16.8 mg, yield 76%, white solid.[27] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 7.3 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 7.5 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.46 (t, *J* = 7.4 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 144.9, 142.2, 133.4, 130.5, 129.5, 129.5, 129.4, 128.3, 128.2, 127.9, 125.2, 123.2, 120.2. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{12}NO^+$ $[M+H]^+$ 222.0919, found 222.0919.

3b, 3-methyl-2-phenylquinoline *N*-oxide, 16.5 mg, yield 70%, white solid.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 8.7 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.72 – 7.68 (m, 1H), 7.63 – 7.59 (m, 2H), 7.57 – 7.53 (m, 2H), 7.49 – 7.45 (m, 1H), 7.43 – 7.41 (m, 2H), 2.23 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 147.2, 140.4, 133.1, 131.3, 129.5, 129.2, 128.9, 128.8 (2C), 128.5, 127.2, 125.6, 120.2, 20.6. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1078.

3c, 3-chloro-2-phenylquinoline *N*-oxide, 23.0 mg, yield 90%, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.7 Hz, 1H), 7.88 (s, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.76 (t, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.58 – 7.49 (m, 5H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 145.4, 141.1, 131.4, 130.5, 129.5 (3C), 128.6, 128.6, 128.5, 127.2, 124.9, 120.4. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ 256.0529, found 256.0530.

3d, 3-bromo-2-phenylquinoline *N*-oxide, 26.7 mg, yield 89%, white solid.[29] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 8.7 Hz, 1H), 8.08 (s, 1H), 7.81 – 7.74 (m, 2H), 7.68 – 7.64 (m, 1H), 7.58 – 7.47 (m, 5H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 146.3, 141.3, 133.3, 130.6, 129.4, 129.4, 129.3, 129.2, 128.6, 128.2, 127.1, 120.5, 117.2. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}BrNO^+$ $[M+H]^+$ 300.0024, found 300.0023.

3e, 4-methyl-2-phenylquinoline *N*-oxide, 14.1 mg, yield 60%, brown solid.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, *J* = 8.7 Hz, 1H), 7.97 (d, *J* = 7.3 Hz, 3H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.34 (s, 1H), 2.69 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 144.4, 141.7, 133.7, 133.5, 130.3, 129.6, 129.4, 129.1, 128.2, 128.2, 124.6, 123.8, 120.8, 18.3. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1076.

3f, 4-chloro-2-phenylquinoline *N*-oxide, 19.9 mg, yield 78%, white solid.[30] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, *J* = 8.7 Hz, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 7.97 (d, *J* = 6.9 Hz, 2H), 7.86 (t, *J* = 7.4 Hz, 1H), 7.76 (t, *J* = 7.6 Hz, 1H), 7.62 (s, 1H), 7.55 – 7.47 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 145.0, 142.9, 132.4, 131.4, 130.0,

129.5 (2C), 129.2, 128.4, 127.1, 125.0, 123.1, 120.8. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ 256.0529, found 256.0523.

3g, 6-methyl-2-phenylquinoline *N*-oxide, 16.0 mg, yield 68%, white solid.[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, *J* = 8.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.61 (d, *J* = 10.4 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 2.56 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 144.3, 140.7, 138.6, 133.6, 132.7, 129.7, 129.6, 129.4, 128.2, 126.9, 124.8, 123.3, 120.1, 21.4. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1076.

3h, 6-methoxy-2-phenylquinoline *N*-oxide, 17.6 mg, yield 70%, brown solid.[22] ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 9.5 Hz, 1H), 7.94 (d, *J* = 7.4 Hz, 2H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.52 – 7.43 (m, 4H), 7.39 (dd, *J* = 9.5, 2.6 Hz, 1H), 7.11 (d, *J* = 2.5 Hz, 1H), 3.95 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 159.2, 143.3, 137.7, 133.5, 130.9, 129.5, 129.3, 128.2, 124.5, 123.8, 122.6, 121.9, 105.8, 55.7. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO_2^+$ $[M+H]^+$ 252.1025, found 252.1025.

3i, 6-chloro-2-phenylquinoline *N*-oxide, 21.5 mg, yield 84%, white solid.[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 9.3 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.85 (s, 1H), 7.70 (d, *J* = 9.3 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.55 – 7.46 (m, 4H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.2, 140.8, 134.6, 133.0, 131.2, 130.3, 129.7, 129.5, 128.4, 126.6, 124.6, 124.0, 122.3. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ 256.0529, found 256.0527.

3j, 6-bromo-2-phenylquinoline *N*-oxide, 23.4 mg, yield 78%, brown solid.[31] ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 9.3 Hz, 1H), 8.03 (d, *J* = 1.9 Hz, 1H), 7.96 (d, *J* = 7.0 Hz, 2H), 7.84 (dd, *J* = 9.3, 1.9 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.54 – 7.46 (m, 4H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.2, 141.1, 133.8, 133.0, 130.7, 129.9, 129.8, 129.5, 128.3, 124.5, 123.9, 122.8, 122.3. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}BrNO^+$ $[M+H]^+$ 300.0024, found 300.0029.

3k, 6-(methoxycarbonyl)-2-phenylquinoline *N*-oxide, 22.1 mg, yield 79%, brown solid.[28] ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 9.1 Hz, 1H), 8.61 (s, 1H), 8.35 (d, *J* = 9.1 Hz, 1H), 7.99 (d, *J* = 7.4 Hz, 2H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.48 (m, 3H), 4.02 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 165.9, 146.6, 144.1, 133.0, 130.8, 130.1, 130.0, 129.9, 129.5, 129.0, 128.4, 125.8, 124.2, 120.9, 52.7. **HRMS** (ESI) *m/z* calcd for $C_{17}H_{14}NO_3^+$ $[M+H]^+$ 280.0974, found 280.0974.

3l, 8-methyl-2-phenylquinoline *N*-oxide, 15.8 mg, yield 67%, white solid.[28] ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 – 7.84 (m, 2H), 7.66 – 7.63 (m, 2H), 7.53 – 7.49 (m, 2H), 7.46 – 7.41 (m, 3H), 7.38 (d, *J* = 8.6 Hz, 1H), 3.21 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.3, 142.1, 134.2, 134.2, 133.8, 131.6, 129.4, 129.1, 128.3, 127.9, 126.8, 125.5, 123.1, 25.6. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1075.

3m, 2-phenylbenzo[*h*]quinoline *N*-oxide, 17.7 mg, yield 65%, brown solid.[27] ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.92 – 10.88 (m, 1H), 7.98 – 7.94 (m, 1H), 7.90 – 7.87 (m, 3H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.51 – 7.47 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 148.6, 139.0, 134.5, 134.4, 130.6, 130.4, 129.6, 129.2, 128.9, 128.6 (d, *J* = 6.5 Hz), 128.3, 128.2, 127.6, 126.6, 125.1 (2C), 123.5. **HRMS** (ESI) *m/z* calcd for $C_{19}H_{14}NO^+$ $[M+H]^+$ 272.1075, found 272.1071.

3n, 4,7-dichloro-2-phenylquinoline *N*-oxide, 24.9 mg, yield 86%, white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.15 (d, *J* = 8.9 Hz, 1H), 7.95 (d, *J* = 7.2 Hz, 2H), 7.69 (d, *J* = 8.9 Hz, 1H), 7.61 (s, 1H), 7.55 – 7.48 (m, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.8, 143.2, 138.2, 132.0, 130.3 (2C), 129.4, 129.1, 128.5, 126. 6, 125.6, 123.2, 120.4. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{10}Cl_2NO^+$ $[M+H]^+$ 290.0139, found 290.0138.

3o, 1-phenylisoquinoline *N*-oxide, 11.1 mg, yield 50%, brown solid.[27] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.61 – 7.45 (m, 8H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.2, 137.4, 130.9, 130.1, 129.6, 129.4, 129.1, 129.0, 128.8, 128.3, 126.8, 125.7, 123.3. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{12}NO^+$ $[M+H]^+$ 222.0919, found 222.0918.

3p, 2-(4-(trifluoromethyl)phenyl)quinoline *N*-oxide, white solid, 14.1 mg, yield 49%.[31] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 8.7 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.78 (m, 4H), 7.69 (t, *J* = 7.4 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 143.6, 142.2, 137.0, 131.2 (q, *J* = 32.7 Hz), 130.9, 130.0, 129.8, 128.9, 128.1, 125.5, 125.3 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 272.7 Hz), 122.9, 120.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.86. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{11}F_3NO^+$ $[M+H]^+$ 290.0793, found 290.0784.

3q, 2-*p*-tolylquinoline *N*-oxide, light yellow solid, 15.2mg, yield 65%.[32] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.86 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.79 – 7.76 (m, 1H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.1, 142.2, 139.7, 130.5, 130.5, 129.4, 129.4, 128.9, 128.2, 127.9, 125.2, 123.2, 120.2, 21.5. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1073.

3r, 2-(4-chlorophenyl)quinoline *N*-oxide, white solid, 13.3 mg, yield 52%.[29] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.51 – 7.48 (m, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 143.9, 142.2, 135.5, 131.8, 131.0, 130.7, 129.6, 128.6, 128.5, 128.0, 125.4, 122.9, 120.2. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ 256.0529, found 256.0519.

3s, 2-(4-fluorophenyl)quinoline *N*-oxide, light yellow solid, 16.7 mg, yield 70%.[15] ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 8.8 Hz, 1H), 8.03 –8.00 (m, 2H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.76 (d, *J* = 8.7 Hz,

1H), 7.67 – 7.64 (m, 1H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.21 (t, *J* = 8.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 163.2 (d, *J* = 250.7 Hz), 144.0, 142.2, 131.8 (d, *J* = 8.5 Hz), 130.7, 129.5, 129.4 (d, *J* = 3.5 Hz), 128.5, 128.0, 125.4, 123.0, 120.2, 115.4 (d, *J* = 21.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.53. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}FNO^+$ $[M+H]^+$ 240.0825, found 240.0817.

3t, 2-*m*-tolylquinoline *N*-oxide, light yellow solid, 14.6 mg, yield 62%.[29] ^1H NMR (600 MHz, $CDCl_3$) δ 8.86 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.83 (s, 1H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.50 (d, *J* = 8.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 145.3, 142.2, 137.9, 133.4, 130.5, 130.3, 130.1, 129.5, 128.3, 128.2, 127.9, 126.6, 125.2, 123.4, 120.3, 21.5. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1077.

3u, 2-(3-fluorophenyl)quinoline *N*-oxide, light yellow solid, 12.0 mg, yield 50%.[31] ^1H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.82 – 7.77 (m, 3H), 7.72 (d, *J* = 7.7 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.18 (td, *J* = 8.4, 2.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 162.4 (d, *J* = 246.1 Hz), 143.7, 142.3, 135.3 (d, *J* = 8.5 Hz), 130.8, 129.9 (d, *J* = 8.3 Hz), 129.7, 128.7, 128.0, 125.4, 125.3(d, *J* = 3.0 Hz), 123.0, 120.3, 116.7 (d, *J* = 23.6 Hz), 116.6 (d, *J* = 21.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.66. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}FNO^+$ $[M+H]^+$ 240.0825, found 240.0816.

3v, 2-*o*-tolylquinoline *N*-oxide, light yellow solid, 11.3 mg, yield 48%.[22] ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (d, *J* = 8.7 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.37 – 7.31 (m, 4H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 146.7, 142.1, 137.7, 133.9, 130.4, 130.1, 129.8, 129.3, 129.1, 128.4, 128.0, 125.9, 124.6, 123.8, 120.3, 19.6. **HRMS** (ESI) *m/z* calcd for $C_{16}H_{14}NO^+$ $[M+H]^+$ 236.1075, found 236.1076.

3w, 2-(2-chlorophenyl)quinoline *N*-oxide, white solid, 12.1 mg, yield 47%.[22] ^1H NMR (600 MHz, $CDCl_3$) δ 8.84 (d, *J* = 8.7 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.78 (m, 1H), 7.77 (d, *J* = 8.6 Hz, 1H), 7.70 – 7.67 (m, 1H), 7.57 – 7.55 (m, 1H), 7.53 – 7.52 (m, 1H), 7.46 – 7.41 (m, 2H), 7.39 (d, *J* = 8.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 143.9, 142.0, 133.8, 133.2, 131.0, 130.6, 130.5, 130.1, 129.8, 128.8, 128.1, 126.9, 124.6, 123.6, 120.3. **HRMS** (ESI) *m/z* calcd for $C_{15}H_{11}ClNO^+$ $[M+H]^+$ 256.0529, found 256.0522.

5a, 2-phenylpyridine *N*-oxide, 12.0 mg, white solid, yield 70%.[13c] ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 6.4, 0.8 Hz, 1H), 7.82 – 7.79 (m, 2H), 7.50 – 7.40 (m, 4H), 7.29 (td, *J* = 7.8, 1.2 Hz, 1H), 7.23 – 7.19 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 149.1, 140.3, 132.5, 129.4, 129.1, 128.1, 127.3, 125.6, 124.4. **HRMS** (ESI) *m/z* calcd for $C_{11}H_{10}NO^+$ $[M+H]^+$ 172.0762, found 172.0764.

5b, 4-nitro-2-phenylpyridine *N*-oxide, 9.3 mg, brown solid, yield 43%.[12a] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 7.2 Hz, 1H), 8.30 (d, *J* = 2.8 Hz, 1H), 8.04 (dd, *J* = 7.1, 2.8 Hz, 1H), 7.82 – 7.80 (m, 2H), 7.54 – 7.53 (m, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 150.3, 142.0, 141.4, 130.8, 130.6, 129.1, 128.7, 121.6, 118.5. **HRMS** (ESI) *m/z* calcd for $C_{11}H_9N_2O_3^+$ $[M+H]^+$ 217.0613, found 217.0615.

5c, 4-cyano-2-phenylpyridine *N*-oxide, 12.2 mg, white solid, yield 62%.[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 6.8 Hz, 1H), 7.78 – 7.74 (m, 2H), 7.69 (d, *J* = 2.4 Hz, 1H), 7.52 – 7.50 (m, 3H), 7.45 (dd, *J* = 6.8, 2.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 150.6, 141.4, 130.6, 130.5, 130.0, 129.1, 128.6, 126.6, 116.0, 107.7. **HRMS** (ESI) *m/z* calcd for $C_{12}H_9N_2O^+$ $[M+H]^+$ 197.0715, found 197.0722.

5d, 2-cyano-3-methyl-6-phenylpyridine *N*-oxide, 10.6 mg, white solid, yield 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.78 (m, 2H), 7.52 – 7.48 (m, 4H), 7.21 (d, *J* = 8.2 Hz, 1H), 2.57 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 147.5, 141.0, 130.9, 130.2, 129.1, 128.9, 128.4, 127.4, 126.0, 111.5, 19.0. **HRMS** (ESI) *m/z* calcd for $C_{13}H_{11}N_2O^+$ $[M+H]^+$ 211.0871, found 211.0875.

5e, 2-chloro-3-methyl-6-phenylpyridine *N*-oxide, 9.5 mg, white solid, yield 43%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.49 – 7.42 (m, 3H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 148.3, 143.3, 134.4, 132.7, 129.6, 129.3, 128.2, 126.4, 123.7, 20.2. **HRMS** (ESI) *m/z* calcd for $C_{12}H_{11}ClNO^+$ $[M+H]^+$ 220.0529, found 220.0527.

5f, 2-cyano-4-methyl-6-phenylpyridine *N*-oxide, 11.6 mg, white solid, yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.78 (m, 2H), 7.49 – 7.48 (m, 3H), 7.43 (d, *J* = 2.6 Hz, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 149.5, 135.9, 130.9, 130.9, 130.4, 130.2, 129.2, 128.4, 126.3, 112.2, 20.2. **HRMS** (ESI) *m/z* calcd for $C_{13}H_{11}N_2O^+$ $[M+H]^+$ 211.0871, found 211.0872.

5g, 2,3,5-trimethyl-6-phenylpyridine *N*-oxide, 8.6 mg, white solid, yield 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.45 (m, 2H), 7.42 – 7.38 (m, 1H), 7.31 – 7.29 (m, 2H), 7.00 (s, 1H), 2.49 (s, 3H), 2.34 (s, 3H), 2.04 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 147.2, 146.0, 133.3, 132.6, 131.3, 129.2, 129.0, 128.6, 128.4, 19.5, 19.4, 14.1. **HRMS** (ESI) *m/z* calcd for $C_{14}H_{16}NO^+$ $[M+H]^+$ 214.1232, found 214.1232.

5h, 3-bromo-6-methyl-2-phenylpyridine *N*-oxide, 12.1 mg, white solid, yield 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.44 (m, 4H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 1H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 150.1, 148.9, 133.1, 129.3, 129.2, 128.7, 128.5, 125.0, 119.2, 18.2. **HRMS** (ESI) *m/z* calcd for $C_{12}H_{11}BrNO^+$ $[M+H]^+$ 264.0024, found 264.0024.

5i, 6-bromo-3-methyl-2-phenylpyridine *N*-oxide, 13.2 mg, white solid, yield 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.0 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.03 (d, *J* = 8.4

Hz, 1H), 2.09 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 151.1, 134.6, 132.4, 130.9, 129.1, 129.0, 128.7, 128.5, 127.1, 19.7. **HRMS** (ESI) *m/z* calcd for $C_{12}H_{11}BrNO^+$ $[M+H]^+$ 264.0024, found 264.0026.

5j, 5-chloro-2-phenylpyridine *N*-oxide, white solid, 8.0 mg, yield 39%. White solid.[33] ^1H NMR (600 MHz, $CDCl_3$) δ 8.38 (s, 1H), 7.78 (d, *J* = 7.1 Hz, 2H), 7.50 – 7.46 (m, 3H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 148.0, 139.65, 131.59, 131.56, 129.91, 129.17, 128.41, 127.06, 125.92. **HRMS** (ESI) *m/z* calcd for $C_{11}H_9ClNO^+$ $[M+H]^+$ 206.0373, found 206.0377.

5j', 3-chloro-2-phenylpyridine *N*-oxide, white solid, 4.9 mg, yield 24%. White solid. ^1H NMR (600 MHz, $CDCl_3$) δ 8.29 (d, *J* = 6.5 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 149.2, 138.8, 133.5, 130.3, 129.7, 129.5, 128.6, 126.6, 124.0. **HRMS** (ESI) *m/z* calcd for $C_{11}H_9ClNO^+$ $[M+H]^+$ 206.0373, found 206.0366.

5k, 2,6-diphenylpyridine *N*-oxide, 7.4 mg, white solid, yield 30%.[27] ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.5 Hz, 4H), 7.48 – 7.41 (m, 8H), 7.33 (t, *J* = 8.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 150.0, 133.3, 129.6, 129.3, 128.1, 126.1, 125.0. **HRMS** (ESI) *m/z* calcd for $C_{17}H_{14}NO^+$ $[M+H]^+$ 248.1075, found 248.1072.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

^1H and ^{13}C NMR spectra of starting materials and products

X-ray crystal structure data for **3a**

AUTHOR INFORMATION

Corresponding Authors

*E-mail: songjinzhulab@hit.edu.cn

*E-mail:gaoguol@hit.edu.cn

ORCID

Junzheng Zhang: 0000-0002-1989-7714

Guo-Lin Gao: 0000-0001-5177-9139

Author Contributions

§ D. L. and C. L. contributed equally to this work.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful for financial support from China NSFC (No. 21302029, 21372055, 21472030 and 21672047),

the Fundamental Research Funds for the Central Universities (HIT.NSRIF.2014064) and the Heilongjiang Postdoctoral Science Foundation (No.LBH-Z14104).

REFERENCES

(1) Michael, J. P. Quinoline, quinazoline and acridone alkaloids. *Nat. Prod. Rep.* **2008**, *25*, 166-187.

(2) (a) Afzal, O.; Kumar, S.; Haider, M. R.; Ali, M. R.; Kumar, R.; Jaggi, M.; Bawa, S. A review on anticancer potential of bioactive heterocycle quinoline. *Eur. J. Med. Chem.* **2015**, *97*, 871-910. (b) Palmer, J. T.; Axford, L. C.; Barker, S.; Bennett, J. M.; Blair, M.; Collins, I.; Davies, D. T.; Ford, L.; Gannon, C. T.; Lancett, P.; Logan, A.; Lunniss, C. J.; Morton, C. J.; Offermann, D. A.; Pitt, G. R. W.; Rao, B. N.; Singh, A. K.; Shukla, T.; Srivastava, A.; Stokes, N. R.; Thomaides-Brears, H. B.; Yadav, A.; Haydon, D. J. Discovery and in vivo evaluation of alcohol-containing benzothiazoles as potent dual-targeting bacterial DNA supercoiling inhibitors. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 4215-4222.

(3) Vitaku, E.; Smith, D. T.; Njardarson, J. T. Analysis of the structural diversity, substitution patterns, and frequency of nitrogen heterocycles among U.S. FDA approved pharmaceuticals. *J. Med. Chem.* **2014**, *57*, 10257-10274.

(4) (a) Nisic, F.; Cariati, E.; Colombo, A.; Dragonetti, C.; Fantacci, S.; Garoni, E.; Lucenti, E.; Righetto, S.; Roberto, D.; Williams, J. A. G. Tuning the dipolar second-order nonlinear optical properties of 5-π-delocalized-donor-1,3-di(2-pyridyl)benzenes, related cyclometallated platinum(II) complexes and methylated salts. *Dalton Trans.* **2017**, *46*, 1179-1185. (b) Sues, P. E.; John, J. M.; Bukhryakov, K. V.; Schrock, R. R.; Müller, P. Molybdenum and tungsten alkylidene complexes that contain a 2-pyridyl-substituted phenoxide ligand. *Organometallics* **2016**, *35*, 3587-3593. (c) Noda, H.; Bode, J. W. Synthesis of chemically and configurationally stable monofluoro acylboronates: effect of ligand structure on their formation, properties, and reactivities. *J. Am. Chem. Soc.* **2015**, *137*, 3958-3966. (d) Veliks, J.; Tseng, J.-C.; Arias, K. I.; Weisshar, F.; Linden, A.; Siegel, J. S. Linear bilateral extended 2,2':6',2"-terpyridine ligands, their coordination complexes and heterometallic supramolecular networks. *Chem. Sci.* **2014**, *5*, 4317-4327. (e) Kozhevnikov, V. N.; Donnio, B.; Heinrich, B.; Bruce, D. W. Morphology-driven absorption and emission colour changes in liquid-crystalline, cyclometallated platinum(II) complexes. *Chem. Commun.* **2014**, *50*, 14191-14193.

(5) (a) Yang, C.; Mehmood, F.; Lam, T. L.; Chan, S. L.-F.; Wu, Y.; Yeung, C.-S.; Guan, X.; Li, K.; Chung, C. Y.-S.; Zhou, C.-Y.; Zou, T.; Che, C.-M. Stable luminescent iridium(III) complexes with bis(N-heterocyclic carbene) ligands: photo-stability, excited state properties, visible-light-driven radical cyclization and CO_2 reduction, and cellular imaging. *Chem. Sci.* **2016**, *7*, 3123-3136. (b) Obana, M.; Fukino, T.; Hikima, T.; Aida, T. Self-sorting in the formation of metal–organic nanotubes: a crucial role of 2D cooperative interactions. *J. Am. Chem. Soc.* **2016**, *138*, 9246-9250. (c) Chen, D.; Su, S.-J.; Cao, Y. Nitrogen heterocycle-containing materials for highly efficient phosphorescent OLEDs with low operating voltage. *J. Mater. Chem. C* **2014**, *2*, 9565-9578.

(6) (a) Zamorano, A.; Rendón, N.; López-Serrano, J.; Valpuesta, J. E. V.; Álvarez, E.; Carmona, E. Dihydrogen catalysis of the reversible formation and cleavage of C-H and N-H bonds of aminopyridinate ligands bound to ($\eta5$-C_5Me_5)Ir^{III}. *Chem.- Eur. J.* **2015**, *21*, 2576-2587. (b) Iranpoor, N.; Firouzabadi, H.; Etemadi Davan, E.; Rostami, A.; Nematollahi, A. Triphenyltin chloride as a new source of phenyl group for C-heteroatom and C–C bond formation. *J. Organomet. Chem.* **2013**, *740*, 123-130. (c) Louaisil, N.; Pham, P. D.; Boeda, F.; Faye, D.; Castanet, A.-S.; Legoupy, S. Ionic liquid supported organotin reagents: green tools for Stille cross-coupling reactions with brominated substrates. *Eur. J. Org. Chem.* **2011**, 143-149. (d) Kerric, G.; Le Grognec, E.; Zammattio, F.; Paris, M.; Quintard, J.-P. Use of polymer-supported phenyltin for the creation of aryl–aryl or aryl–heteroaryl bonds via Stille cross-coupling reactions. *J. Organomet. Chem.* **2010**, *695*, 103-110.

(7) (a) Ganesamoorthy, S.; Muthu Tamizh, M.; Shanmugasundaram, K.; Karvembu, R. A sustainable heterogenized palladium catalyst for Suzuki-Miyaura cross coupling reaction of azaheteroaryl halides in aqueous media. *J. Organomet. Chem.* **2018**, *862*, 76-85. (b) Jong, H.; Eey, S. T. C.; Lim, Y. H.; Pandey, S.; Iqbal, N. A. B.; Yong, F. F.; Robins, E. G.; Johannes, C. W. One-pot palladium-catalyzed cross-coupling treble of borylation, the Suzuki reaction and amination. *Adv. Synth. Catal.* **2017**, *359*, 616-622. (c) Ramakrishna, V.; Dastagiri Reddy, N. Synthesis of zwitterionic palladium complexes and their application as catalysts in cross-coupling reactions of aryl, heteroaryl and benzyl bromides with organoboron reagents in neat water. *Dalton Trans.* **2017**, *46*, 8598-8610. (d) Braun, C.; Spuling, E.; Heine, N. B.; Cakici, M.; Nieger, M.; Bräse, S. Efficient modular synthesis of isomeric mono- and bispyridyl[2.2]paracyclophanes by palladium-catalyzed cross-coupling reactions. *Adv. Synth. Catal.* **2016**, *358*, 1664-1670.

(8) (a) Price, G. A.; Hassan, A.; Chandrasoma, N.; Bogdan, A. R.; Djuric, S. W.; Organ, M. G. Pd-PEPPSI-IPent-SiO_2: A supported catalyst for challenging Negishi coupling reactions in flow. *Angew. Chem., Int. Ed.* **2017**, *56*, 13347-13350. (b) Roesner, S.; Buchwald, S. L. Continuous-flow synthesis of biaryls by Negishi cross-coupling of fluoro- and trifluoromethyl-substituted (hetero)arenes. *Angew. Chem., Int. Ed.* **2016**, *55*, 10463-10467. (c) Liu, Z.; Dong, N.; Xu, M.; Sun, Z.; Tu, T. Mild Negishi cross-coupling reactions catalyzed by acenaphthoimidazolylidene palladium complexes at low catalyst loadings. *J. Org. Chem.* **2013**, *78*, 7436-7444.

(9) (a) Rull, S. G.; Rama, R. J.; Alvarez, E.; Fructos, M. R.; Belderrain, T. R.; Nicasio, M. C. Phosphine-functionalized NHC Ni(II) and Ni(0) complexes: synthesis, characterization and catalytic properties. *Dalton Trans.* **2017**, *46*, 7603-7611. (b) Clémancey, M.; Cantat, T.; Blondin, G.; Latour, J.-M.; Dorlet, P.; Lefèvre, G. Structural insights into the nature of Fe^0 and Fe^I low-valent species obtained upon the reduction of iron salts by aryl Grignard reagents. *Inorg. Chem.* **2017**, *56*, 3834-3848. (c) Iglesias, M. J.; Prieto, A.; Nicasio, M. C. Kumada–Tamao–Corriu coupling of heteroaromatic chlorides and aryl ethers catalyzed by (IPr)Ni(allyl)Cl. *Org. Lett.* **2012**, *14*, 4318-4321. (d) Jin, Z.; Gu, X.-P.; Qiu, L.-L.; Wu, G.-P.; Song, H.-B.; Fang, J.-X. Air-stable CpPd(NHC)Cl (NHC = N-heterocyclic carbene) complexes as highly active precatalysts for Kumada–Tamao–Corriu coupling of aryl and heteroaryl chlorides. *J. Organomet. Chem.* **2011**, *696*, 859-863.

(10) (a) Gurung, S. K.; Thapa, S.; Vangala, A. S.; Giri, R. Copper-catalyzed Hiyama coupling of (hetero)aryltriethoxysilanes with (hetero)aryl iodides. *Org. Lett.* **2013**, *15*, 5378-5381. (b) Takayoshi, Y.; Shigeki, M.; Yasunari, M.; Hironao, S. Pd/C-Catalyzed and water-mediated Hiyama cross-coupling reaction using an electron-deficient phosphine ligand. *Chem. Lett.* **2011**, *40*, 910-912. (c) Louerat, F.; Tye, H.; Napier, S.; Garrigou, M.; Whittaker, M.; Gros, P. C. TBAF-catalysed silver oxide-mediated cross-coupling of functional trimethysilylpyridines: access to arylpyridines and bihetaryl compounds. *Org. Biomol. Chem.* **2011**, *9*, 1768-1773.

(11) (a) Wei, J.; Liu, K.-M.; Duan, X.-F. Cobalt-catalyzed biaryl couplings via C–F bond activation in the absence of phosphine or NHC ligands. *J. Org. Chem.* **2017**, *82*, 1291-1300. (b) Martinez-Solorio, D.; Melillo, B.; Sanchez, L.; Liang, Y.; Lam, E.; Houk, K. N.; Smith, A. B. Design, synthesis, and validation of an effective, reusable silicon-based transfer agent for room-temperature Pd-catalyzed cross-coupling reactions of aryl and heteroaryl chlorides with readily available aryl lithium reagents. *J. Am. Chem. Soc.* **2016**, *138*, 1836-1839. (c) Becker, M. R.; Knochel, P. High-temperature continuous-flow zincations of functionalized arenes and heteroarenes using $(Cy_2N)_2Zn{\cdot}2LiCl$. *Org. Lett.* **2016**, *18*, 1462-1465. (d) Shrestha, B.; Thapa, S.; Gurung, S. K.; Pike, R. A. S.; Giri, R. General copper-catalyzed coupling of alkyl-, aryl-, and alkynylaluminum reagents with organohalides. *J. Org. Chem.* **2016**, *81*, 787-802. (e) Wang, X.; He, Y.; Ren, M.; Liu, S.; Liu, H.; Huang, G. Pd-catalyzed ligand-free synthesis of arylated heteroaromatics by coupling of N-heteroaromatic bromides with iodobenzene diacetate, iodosobenzene, or diphenyliodonium salts. *J. Org. Chem.* **2016**, *81*, 7958-7962.

(12) (a) Li, M.; Li, X.; Chang, H.; Gao, W.; Wei, W. Palladium-catalyzed direct C–H arylation of pyridine N-oxides with potassium aryl- and heteroaryltrifluoroborates. *Org. Biomol. Chem.* **2016**, *14*, 2421-2426. (b)

Stephens, D. E.; Lakey-Beitia, J.; Atesin, A. C.; Ateşin, T. A.; Chavez, G.; Arman, H. D.; Larionov, O. V. Palladium-catalyzed C8-selective C–H arylation of quinoline N-oxides: insights into the electronic, steric, and solvation effects on the site selectivity by mechanistic and DFT computational studies. *ACS Catal.* **2015**, *5*, 167-175. (c) Tan, Y.; Barrios-Landeros, F.; Hartwig, J. F. Mechanistic studies on direct arylation of pyridine N-oxide: evidence for cooperative catalysis between two distinct palladium centers. *J. Am. Chem. Soc.* **2012**, *134*, 3683-3686. (d) Xi, P.; Yang, F.; Qin, S.; Zhao, D.; Lan, J.; Gao, G.; Hu, C.; You, J. Palladium(II)-catalyzed oxidative C−H/C−H cross-coupling of heteroarenes. *J. Am. Chem. Soc.* **2010**, *132*, 1822-1824.

(13) (a) Larionov, O. V.; Stephens, D.; Mfuh, A.; Chavez, G. Direct, catalytic, and regioselective synthesis of 2-alkyl-, aryl-, and alkenyl-substituted N-heterocycles from N-oxides. *Org. Lett.* **2014**, *16*, 864-867. (b) Shen, Y.; Chen, J.; Liu, M.; Ding, J.; Gao, W.; Huang, X.; Wu, H. Copper-catalyzed direct C-H arylation of pyridine N-oxides with arylboronic esters: one-pot synthesis of 2-arylpyridines. *Chem. Commun.* **2014**, *50*, 4292-4295. (c) Do, H.-Q.; Khan, R. M. K.; Daugulis, O. A general method for copper-catalyzed arylation of arene C−H bonds. *J. Am. Chem. Soc.* **2008**, *130*, 15185-15192.

(14) Shin, K.; Park, S.-W.; Chang, S. Cp*Ir(III)-catalyzed mild and broad C−H arylation of arenes and alkenes with aryldiazonium salts leading to the external oxidant-free approach. *J. Am. Chem. Soc.* **2015**, *137*, 8584-8592.

(15) Ackermann, L.; Fenner, S. Direct arylations of electron-deficient (hetero)arenes with aryl or alkenyl tosylates and mesylates. *Chem. Commun.* **2011**, *47*, 430-432.

(16) Sharma, R.; Kumar, R.; Sharma, U. Rh/O_2-catalyzed C8 olefination of quinoline N-oxides with activated and unactivated olefins. *J. Org. Chem.* **2019**, *84*, 2786-2797.

(17) (a) Zhang, F.; Duan, X.-F. Facile one-pot direct arylation and alkylation of nitropyridine N-oxides with Grignard reagents. *Org. Lett.* **2011**, *13*, 6102-6105. (b) Andersson, H.; Sainte-Luce Banchelin, T.; Das, S.; Olsson, R.; Almqvist, F. Efficient, mild and completely regioselective synthesis of substituted pyridines. *Chem. Commun.* **2010**, *46*, 3384-3386.

(18) (a) Zhang, S.; Tang, Z.; Bao, W.; Li, J.; Guo, B.; Huang, S.; Zhang, Y.; Rao, Y. Perylenequinonoid-catalyzed photoredox activation for the direct arylation of (het)arenes with sunlight. *Org. Biomol. Chem.* **2019**, *17*, 4364-4369. (b) Fabry, D. C.; Ho, Y. A.; Zapf, R.; Tremel, W.; Panthofer, M.; Rueping, M.; Rehm, T. H. Blue light mediated C-H arylation of heteroarenes using TiO_2 as an immobilized photocatalyst in a continuous-flow microreactor. *Green Chem.* **2017**, *19*, 1911-1918. (c) Zhi, L.; Zhang, H.; Yang, Z.; Liu, W.; Wang, B. Interface coassembly of mesoporous MoS_2 based-frameworks for enhanced near-infrared light driven photocatalysis. *Chem. Commun.* **2016**, *52*, 6431-6434. (d) Zhang, J.; Chen, J.; Zhang, X.; Lei, X. Total syntheses of menisporphine and daurioxoisoporphine C enabled by photoredox-catalyzed direct C–H arylation of isoquinoline with aryldiazonium salt. *J. Org. Chem.* **2014**, *79*, 10682-10688. (e) Xue, D.; Jia, Z.-H.; Zhao, C.-J.; Zhang, Y.-Y.; Wang, C.; Xiao, J. Direct arylation of N-heteroarenes with aryldiazonium salts by photoredox catalysis in water. *Chem.- Eur. J.* **2014**, *20*, 2960-2965. (f) Cheng, Y.; Gu, X.; Li, P. Visible-light photoredox in homolytic aromatic substitution: direct arylation of arenes with aryl halides. *Org. Lett.* **2013**, *15*, 2664-2667.

(19) CCDC 1858700 contains the supplementary crystallographic date for **3a**. This date can be acquired free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(20) (a) Li, Y.; Wang, M.; Jiang, X. Controllable sulfoxidation and sulfenylation with organic thiosulfate salts via dual electron- and energy-transfer photocatalysis. *ACS Catal.* **2017**, *7*, 7587-7592. (b) Yin, K.; Zhang, R. Transition-metal-free direct C–H arylation of quinoxalin-2(1*H*)-ones with diaryliodonium salts at room temperature. *Org. Lett.* **2017**, *19*, 1530-1533. (c) Zhang, W.-M.; Dai, J.-J.; Xu, J.; Xu, H.-J. Visible-light-induced C2 alkylation of pyridine N-oxides. *J. Org. Chem.* **2017**, *82*, 2059-2066. (d) Hartmann, M.; Li, Y.; Mück-Lichtenfeld, C.; Studer, A. Generation of aryl radicals through reduction of hypervalent iodine(III) compounds with TEMPONa: radical alkene oxyarylation. *Chem.- Eur. J.* **2016**, *22*, 3485-3490. (e) Zhang, W.;

Luo, M. Iron-catalyzed synthesis of arylsulfinates through radical coupling reaction. *Chem. Commun.* **2016**, *52*, 2980-2983.

(21) (a) Dektar, J. L.; Hacker, N. P. Photochemistry of diaryliodonium salts. *J. Org. Chem.* **1990**, *55*, 639-647. (b) Der Puy, M. V. Conversion of diaryliodonium salts to aryl fluorides. *J. Fluorine Chem.* **1982**, *21*, 385-392.

(22) Campeau, L.-C.; Stuart, D. R.; Leclerc, J.-P.; Bertrand-Laperle, M.; Villemure, E.; Sun, H.-Y.; Lasserre, S.; Guimond, N.; Lecavallier, M.; Fagnou, K. Palladium-catalyzed direct arylation of azine and azole N-oxides: reaction development, scope and applications in synthesis. *J. Am. Chem. Soc.* **2009**, *131*, 3291-3306.

(23) Bielawski, M.; Aili, D.; Olofsson, B. Regiospecific one-pot synthesis of diaryliodonium tetrafluoroborates from arylboronic acids and aryl iodides. *J. Org. Chem.* **2008**, *73*, 4602-4607.

(24) Kieffer, M. E.; Chuang, K. V.; Reisman, S. E. Copper-catalyzed diastereoselective arylation of tryptophan derivatives: total synthesis of (+)-naseseazines A and B. *J. Am. Chem. Soc.* **2013**, *135*, 5557-5560.

(25) Hong, X.; Tan, Q.; Liu, B.; Xu, B. Isocyanide-induced activation of copper sulfate: direct access to functionalized heteroarene sulfonic esters. *Angew. Chem., Int. Ed.* **2017**, *56*, 3961-3965.

(26) Wagner, A. M.; Sanford, M. S. Palladium-catalyzed C−H arylation of 2,5-substituted pyrroles. *Org. Lett.* **2011**, *13*, 288-291.

(27) Cho, S. H.; Hwang, S. J.; Chang, S. Palladium-catalyzed C−H functionalization of pyridine N-oxides: highly selective alkenylation and direct arylation with unactivated arenes. *J. Am. Chem. Soc.* **2008**, *130*, 9254-9256.

(28) Kumar, R.; Kumar, R.; Dhiman, A. K.; Sharma, U. Regioselective metal-free C2−H arylation of quinoline N-oxides with aryldiazonium salts/anilines under ambient conditions. *Asian J. Org. Chem.* **2017**, *6*, 1043-1053.

(29) Okuma, K.; Seto, J.-i.; Nagahora, N.; Shioji, K. Chemoselective synthesis of quinoline N-oxides from 3-(2-nitrophenyl)-3-hydroxypropanones. *J. Heterocycl. Chem.* **2010**, *47*, 1372-1378.

(30) Colonna, M.; Greci, L.; Poloni, M. Quinoline nitroxide radicals. Ipso-attack in the reaction between 2-methoxy and 2-cyanoquinoline N-oxide, and phenylmagnesium bromide. *J. Heterocycl. Chem.* **1980**, *17*, 293-297.

(31) Yuan, J.-W.; Qu, L.-B. KMnO4-mediated direct selective radical cross-coupling: An effective strategy for C2 arylation of quinoline N-oxide with arylboronic acids. *Chin. Chem. Lett.* **2017**, *28*, 981-985.

(32) Zhao, D.; Wang, W.; Yang, F.; Lan, J.; Yang, L.; Gao, G.; You, J. Copper-catalyzed direct C arylation of heterocycles with aryl bromides: discovery of fluorescent core frameworks. *Angew. Chem., Int. Ed.* **2009**, *48*, 3296-3300.

(33) Dabiri, M.; Alavioon, S. I.; Movahed, S. K. Decarboxylative arylation of pyridine 1-oxides and anilides with benzoic acid via palladium-catalyzed C–H functionalization. *Eur. J. Org. Chem.* **2019**, 1479-1487.