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Note

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Ru-Catalyzed Deoxygenative Regioselective C8–H Arylation of Quinoline *N*-Oxides

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Supporting Information

ABSTRACT: Regioselective C–H functionalization on quinolines is of high interest to lead to value-added products. Herein, we describe the development of Ru-catalyzed deoxygenative regioselective C8 arylation of quinoline *N*-oxides with arylboronic esters. Mechanistic studies revealed that it proceeds in a tandem process of arylation and then deoxygenation, wherein both steps were found to be catalytic with the ruthenium species.

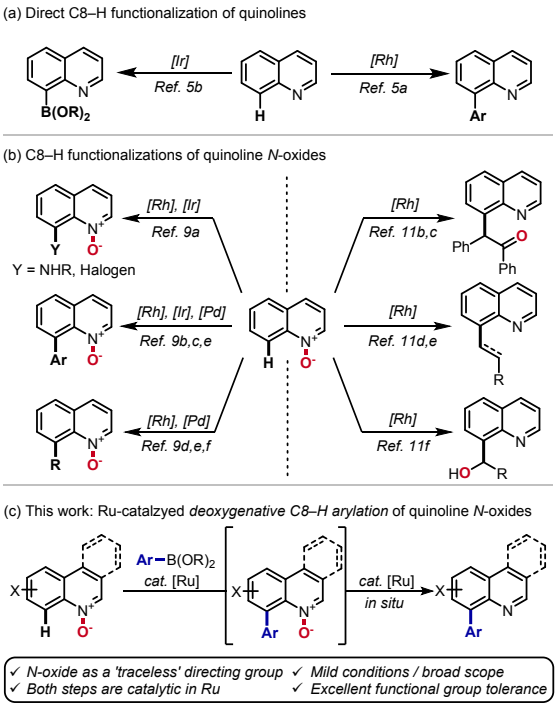
Quinoline is present in a broad range of natural and pharmaceutical compounds,[1] thus receiving special attention towards the introduction of functional groups in a more efficient and selective manner.[2] In the conventional approaches, the regioselective modifications often depend on the pre-functionalization or the *de novo* preparation of the core structure.[3] On the other hand, synthesis of quinoline derivatives via site-specific C–H bond activation has been scrutinized in recent years.[4] For instance, direct C8–H-arylation and borylation of quinolines were shown to be achieved by Rh and Ir catalysis, respectively, albeit with limited substrate scope (Scheme 1a).[5]

An alternative approach is to utilize quinoline *N*-oxides as the substrates, where *N*-oxide serves as an effective directing group to lead to the regioselective C–H bond activation.[6] While C2 functionalization of quinoline *N*-oxides is governed mainly by the high electrophilicity of C2 carbon and acidic nature of that C–H bond,[7,8] C8–H bond activation can be successfully carried out by the facile formation of the corresponding metallacyclic intermediates (Scheme 1b, left).[9] In these procedures, an additional deoxygenation step is often required after the installation of the desired functional groups.[10] A few examples bypassing such a separate reduction process have been reported.[11] However, to our best knowledge, deoxygenative C8 arylation is unprecedented to date (Scheme 1b, right).

Herein we present the first example of Ru-catalyzed deoxygenative C8–H arylation of quinoline *N*-oxides by using arylboronic esters. (*p*-Cymene)Ru^{II} was found to effectively catalyze both C–H arylation and subsequent deoxygenation. The reaction is featured to display broad substrate scope and high functional group compatibility under mild conditions.

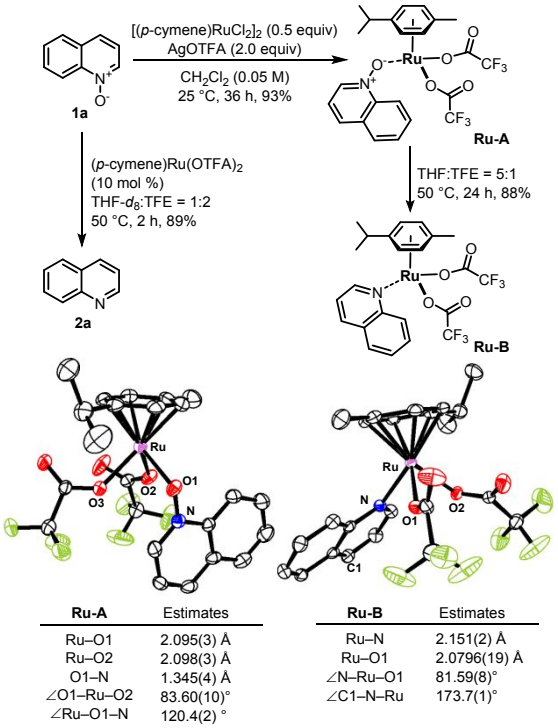
At the outset of this study, we investigated reactivity of quinoline *N*-oxide **1a** with $[(p\text{-cymene})RuCl_2]_2$ (Scheme 2). A stable adduct complex **Ru-A** was obtained in 93% yield in the presence of silver trifluoroacetate (AgOTFA).

Scheme 1. Regioselective C8–H functionalization of quinolines and their *N*-oxides.



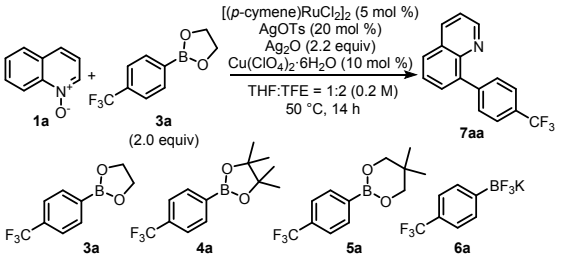
Interestingly, deoxygenative complexation occurred when **Ru-A** is heated at 50 °C in THF/trifluoroethanol (TFE) to give a Ru-quinoline complex **Ru-B**. Deoxygenation of **1a** also took place catalytically by *in situ* generated (*p*-cymene)$Ru(OTFA)_2$ species leading to quinoline **2a** (89%). The N–O bond distance of **Ru-A** is 1.345(4) Å, being slightly longer than that of **1a** (1.310 Å).[12] In **Ru-B**, the Ru–N bond is 2.151(2) Å, well consistent with the reported values of the similar Ru complexes.[13]

Scheme 2. Deoxygenation of quinoline *N*-oxide with (*p*-cymene)Ru^{II}.



We next wondered whether the facile deoxygenation activity of Ru catalyst can be combined with an envisioned C–H arylation to establish a tandem deoxygenative arylation of quinoline *N*-oxides (Table 1).[14] Pleasingly, the (*p*-cymene)Ru^{II} catalyst system enabled a reaction of **1a** with aryl ethyleneglycol boronic ester **3a** to furnish C8-arylated quinoline product **7aa** in excellent yield along with trace amount of quinoline **2a** (2%) under optimized conditions (entry 1). In this reaction, Ag_2O (2.2 equiv) serves as an oxidant and copper cocatalyst (10 mol %) is proposed to facilitate a presumed aryl transmetalation from boronates.[15] On the other hand, quinoline **2a** was not reactive under the same conditions (entry 2).[8a] Interestingly, the reaction efficiency was found to be highly affected by the structure of boronic esters. For instance, pinacol boronate (**4a**), neopentyl glycol boronate (**5a**), and potassium trifluoroborate (**6a**) were much less effective than glycolborate **3a** (entries 3–5). Likewise, the type of copper cocatalyst significantly influenced the product yields (entries 6–9).[16,14] Trifluoroethanol (TFE) was an exceptionally effective solvent in combination with THF (entries 10 and 11). On the other hand, $[Cp^*RhCl_2]_2$ and $[Cp^*IrCl_2]_2$ catalysts were unproductive for the current deoxygenative arylation (entries 12 and 13).

Table 1. Reaction optimization for deoxygenative C8–H arylation of quinoline *N*-oxide.[a]



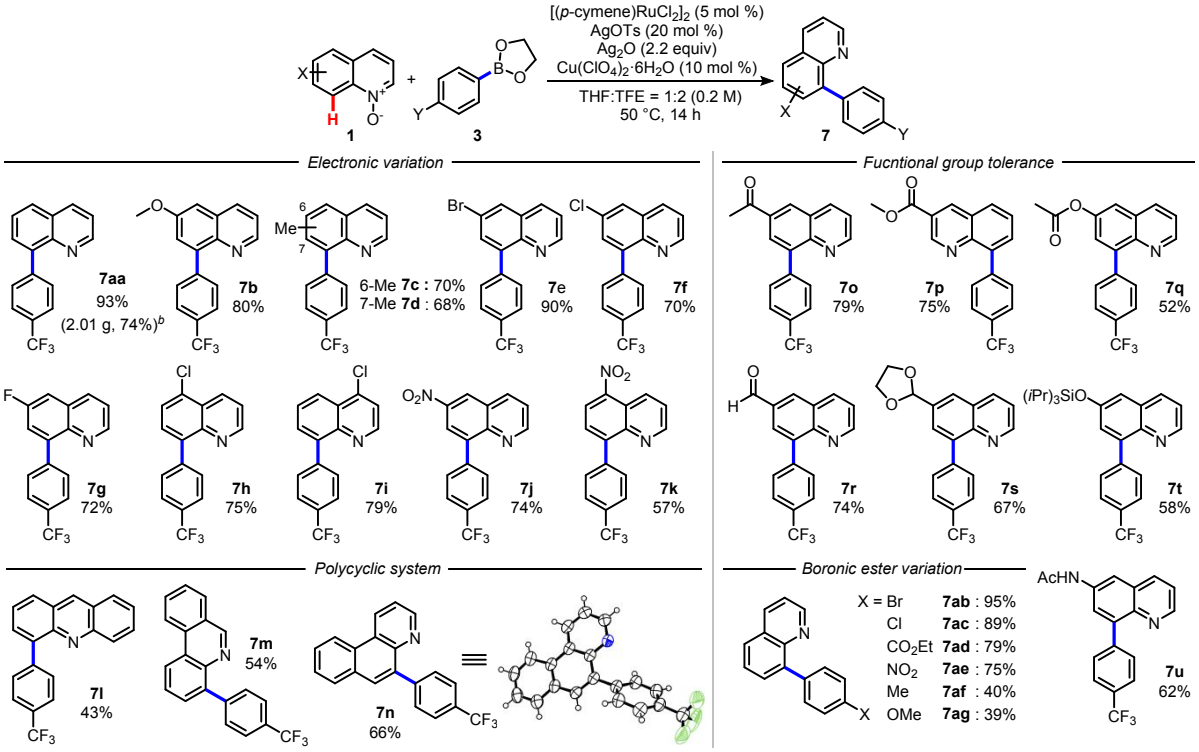
entry	variation from the "standard" conditions	yield (%)[b]	**2a** (%)[b]
1	none	95 (93)[c]	<5
2	**2a** instead of **1a**	0	99
3	**4a** instead of **3a**	39	59
4	**5a** instead of **3a**	70	30
5	**6a** instead of **3a**	0	75
6	No $Cu(ClO_4)_2·6H_2O$	51	49
7	$CuBr_2$ instead of $Cu(ClO_4)_2·6H_2O$	6	81
8	$Cu(OTf)_2$ instead of $Cu(ClO_4)_2·6H_2O$	69	30
9	$Cu(OAc)_2$ instead of $Cu(ClO_4)_2·6H_2O$	35	41
10	EtOH instead of TFE	9	74
11	$(CF_3)_2CHOH$ instead of TFE	7	71
12	$[Cp^*IrCl_2]_2$ instead of $[(p\text{-cymene})RuCl_2]_2$	9	<5
13	$[Cp^*RhCl_2]_2$ instead of $[(p\text{-cymene})RuCl_2]_2$	0	0

[a]Reaction conditions: **1a** (0.10 mmol), boronic ester (2.0 equiv), catalyst (5 mol %), AgOTs (20 mol %), Cu salt (10 mol %), and Ag_2O (2.2 equiv) in THF/TFE (1:2, 0.5 mL) for 14 h at 50 °C. [b]Yields were determined by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as the internal standard. [c]Isolated yield.

With the optimized conditions in hand, we then explored the substrate scope of the Ru-catalyzed deoxygenative C8-arylation of quinoline *N*-oxides (Table 2). Electronic variation on the quinoline skeleton did not much alter the reaction efficiency (**7b–7d**). Halides and nitro substituents were totally compatible with the present conditions (**7e–7k**). Substrate scope was further examined using polycyclic *N*-oxides. For instance, acridine *N*-oxide was arylated albeit in moderate yield (**7l**). The arylation of benzo[*c*]quinoline *N*-oxide and benzo[*f*]quinoline *N*-oxide also proceeded smoothly (**7m** and **7n**), and the regioselectivity of **7n** was confirmed by an XRD analysis.

We subsequently examined the compatibility of more labile but synthetically versatile functional groups to the current deoxygenative arylation conditions. A number of carbonyl moieties such as acetyl, ester, and aldehyde were all tolerated, and the arylation took place in high to moderate yields (**7o–7r**). Protecting groups for aldehyde, phenol, and amine were also well compatible with the current conditions (**7s–7u**). In addition, the scope of arylboronic esters was briefly surveyed to see that various substituents could be incorporated on the aryl coupling partner (**7ab–7ag**).[14,17]

Table 2. Substrate scope of the deoxygenative C8–H arylation of quinoline *N*-oxides.[a]

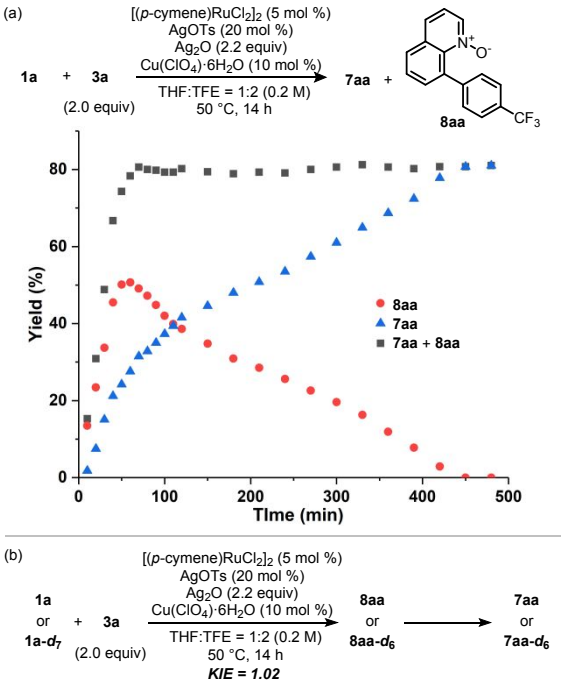


[a]Reaction conditions: **1** (0.10 mmol), **3** (2.0 equiv), [(*p*-cymene)$RuCl_2$]$_2$ (5 mol %), AgOTs (20 mol %), $Cu(ClO_4)_2{\cdot}6H_2O$ (10 mol %), and Ag_2O (2.2 equiv) in THF/TFE (1:2, 0.5 mL) for 14 h at 50 °C. Isolation yields are reported. [b]**1a** (1.45 g, 10.0 mmol), **3a** (2.0 equiv), [(*p*-cymene)$RuCl_2$]$_2$ (5 mol %), AgOTs (20 mol %), $Cu(ClO_4)_2{\cdot}6H_2O$ (10 mol %), and Ag_2O (2.2 equiv) in THF/TFE (1:2, 60 mL) for 36 h at 50 °C.

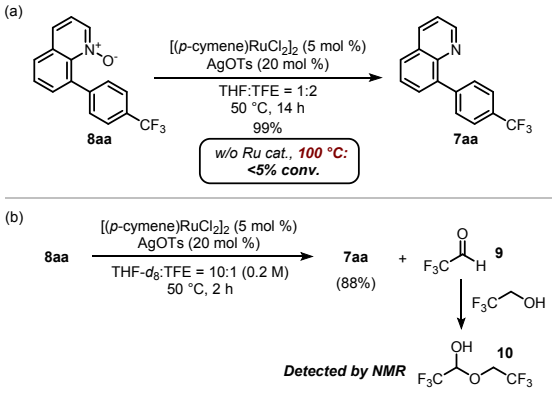
To gain mechanistic insights, we first obtained a reaction profile of the arylation of **1a** (Scheme 3a). The C8-arylated *N*-oxide intermediate **8aa** was found to initially form and then deoxygenation proceeded to afford **7aa**, eventually reaching a full conversion after 10 h at 50 °C. No kinetic isotope effect (KIE) of the first C–H arylation process was observed (k_H/k_D=1.02) from a parallel rate comparison between **1a** and **1a-*d*$_7$** (Scheme 3b).

For more details on the subsequent deoxygenation step, an isolated C8-arylated *N*-oxide **8aa** was subjected to various conditions (Scheme 4a). The deoxygenation was enabled by the action of a cationic Ru(II) species, *in situ* generated from [(*p*-cymene)$RuCl_2$]$_2$ and AgOTs (Scheme 4a). Neither Ag_2O oxidant nor Cu additive mediated the catalytic deoxygenation in the absence of Ru catalyst.[10b,c] Moreover, the reaction was not thermally driven. We further observed the formation of trifluoroethoxy hemiacetal **10** from the reaction mixture, which was assumed to be formed from trifluoroacetaldehyde **9** and TFE (Scheme 4b),[18] implying that TFE solvent is likely involved in the catalysis as a reducing agent.

Scheme3. Kinetic study of the Ru-catalyzed deoxygenative C8–H arylation

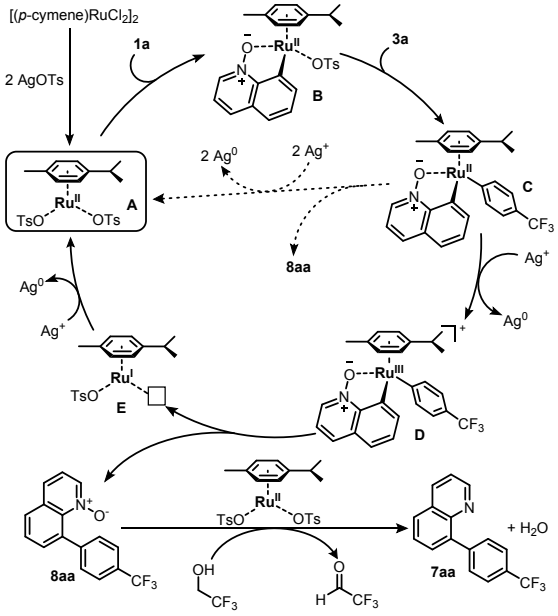


Scheme 4. Mechanistic investigations on the Ru-catalyzed deoxygenation.



A plausible catalytic cycle of the present Ru-catalyzed deoxygenative C8-arylation of quinoline *N*-oxides is depicted in Scheme 5. The *in situ*-generated active species **A** undergoes the C8–H bond activation to form a ruthenacycle **B**. A subsequent transmetalation from arylboronic ester, presumably through an aryl cuprate species, is assumed to follow to give rise to a Ru aryl intermediate **C**. The oxidation of **C** to the high-valent Ru(III) species **D** by Ag^+ oxidant is proposed to facilitate the reductive elimination to afford C8-arylated quinoline *N*-oxide **8aa**.[14] The resulting Ru(I) species **E** will be subsequently oxidized to **A** to close the catalytic cycle. Alternatively, a direct reductive elimination from a neutral Ru(II) intermediate **C** cannot be completely excluded at the present. The second deoxygenation process is proposed also to be catalyzed by (*p*-cymene)Ru(OTs)$_2$ species **A**, wherein trifluoroethanol cosolvent acts as a reducing agent.

Scheme 5. A plausible pathway of the current Ru-catalyzed deoxygenative arylation.



In conclusion, we have developed a Ru-catalyzed deoxygenative C8-arylation of quinoline *N*-oxides for the first time. The reaction was found to be a tandem process consisted of an initial arylation and subsequent deoxygenation, both of which is enabled by the ruthenium catalyst. A broad range of substrates was successfully applied with excellent functional group tolerance under mild conditions.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all commercial reagents were used without additional purifications. Quinoline *N*-oxide (**1a**) was purchased from Tokyo Chemical Industry Co. and used without further purification. The water content of *N*-oxides was analyzed by Karl Fischer titration before use. All the chemical reaction was performed under Ar atmosphere. Analytical thin layer chromatography (TLC) was performed on Merck pre-coated silica gel F_{254} plates. NMR spectra were recorded on Bruker Ascend 400 (400 MHz) or Agilent Technologies DD2 (600 MHz). ^{1}H NMR chemical shifts were quoted in parts per million (ppm) referenced to the residual solvent peak or 0.0 ppm for tetramethylsilane. ^{13}C{^{1}H} NMR was fully decoupled by broad band proton decoupling and the chemical shifts were reported in ppm referenced to the residual solvent peaks. All coupling constant (*J*) values are reported in hertz. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), triplet (t), quartet (q), heptet (hept), and multiplet (m). Infrared spectra were acquired on Bruker Alpha ATR FT-IR spectrometer. Frequencies are given in wave numbers (cm^{-1}) and only selected peaks were reported. High resolution mass spectra were obtained from the Korea Basic Science Institute (Daegu) by EI and FAB method using Jeol JMS 700 high resolution mass spectrometer with a quadrupole mass analyzer. The HRMS data of **7d** and **7ag** were obtained from KAIST Analysis Center for Research Advancement (Daejeon) by ESI method using Bruker microQTOF-QII with a quadrupole mass analyzer. X-ray diffraction data was collected on a Bruker D8 QUEST coated with Parabar oil under a stream of N_2 (g) at 173 K. The PAL BL2D-SMDC program was used for data collection (detector distance is 66 mm, omega scan; $\Delta\omega = 3°$, exposure time is 0.7 sec per frame) and HKL3000sm (Ver 716.7) was used for cell refinement, reduction and absorption correction.

Synthesis of an Ru-Quinoline *N*-oxide Adduct (Scheme 2, Ru-A). To a mixture of quinoline *N*-oxide (284 mg, 1.96 mmol), silver trifluoroacetate (432 mg, 1.96 mmol), and Li_2CO_3 (144 mg, 1.95 mmol) in CH_2Cl_2 (40 mL) was added [(*p*-cymene)$RuCl_2$]$_2$ (600 mg, 0.978 mmol) and the mixture was stirred at 25 °C. After 12 h, additional portion of silver trifluoroacetate (432 mg, 1.96 mmol) was added and the reaction mixture was further stirred at 25 °C for 24 h. The suspension was filtered through a pad of celite and the filtrate was concentrated under reduced pressure. The residue was recrystallized in CH_2Cl_2/*n*-hexane to obtain **Ru-A**. Orange crystal (874 mg, 93%); decompose at >250 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.61 (d, *J* = 8.8 Hz, 1H), 8.53 (d, *J* = 6.1 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.98 – 7.91 (m, 2H), 7.76 – 7.71 (m, 1H), 7.26 (dd, *J* = 8.4, 6.2 Hz, 1H), 6.06 (d, *J* = 5.9 Hz, 2H), 5.82 (d, *J* = 5.8 Hz, 2H), 2.98 (hept, *J* = 7.0 Hz, 1H), 2.26 (s, 3H), 1.34 (d, *J* = 7.0 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 162.4 (q, *J* = 35.9 Hz), 143.6, 141.3, 135.8, 132.6, 130.2, 129.4, 128.7, 120.3, 119.4, 115.4 (q, *J* = 291.8 Hz), 99.9, 95.9, 80.0, 77.7, 31.6, 22.5, 18.5; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -75.56; IR (cm^{-1}) 3122, 3075, 2969, 2934, 2880, 1713, 1697, 1397, 1181; HRMS (FAB) m/z calcd. for $C_{23}H_{21}F_6NO_5Ru$ [*M*]$^+$: 607.0374, found:

607.0371.

Synthesis of Ru-B (Scheme 2). A solution of **Ru-A** (30.4 mg, 0.0500 mmol) in THF-d_8/TFE=5:1 (0.5 mL) was heated in a preheated oil bath at 50 °C for 24 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was recrystallized in CH_2Cl_2/*n*-hexane to obtain **Ru-B**. Yellow crystal (25.9 mg, 88%); decompose at >250 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.16 (dd, *J* = 5.3, 1.5 Hz, 1H), 8.67 (dd, *J* = 8.8, 1.0 Hz, 1H), 8.32 (d, *J* = 8.1 Hz, 1H), 7.91 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.85 (ddd, *J* = 8.7, 6.9, 1.5 Hz, 1H), 7.67 (ddd, *J* = 8.1, 6.9, 1.0 Hz, 1H), 7.51 (dd, *J* = 8.2, 5.3 Hz, 1H), 6.22 (d, *J* = 5.7 Hz, 2H), 5.78 (d, *J* = 5.9 Hz, 2H), 2.77 (hept, *J* = 6.9 Hz, 1H), 1.85 (s, 3H), 1.21 (d, *J* = 6.9 Hz, 6H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 163.6 (q, *J* = 36.3 Hz), 156.2, 148.3, 140.2, 131.6, 130.2, 129.4, 129.1, 128.1, 121.9, 115.3 (q, *J* = 291.3 Hz), 103.7, 97.7, 82.4, 79.6, 31.5, 22.4, 18.6; ^{19}F NMR (376 MHz, CD_2Cl_2) δ -75.34; IR (cm^{-1}) 3080, 3057, 2974, 1696, 1681, 1181, 1126; HRMS (FAB) m/z calcd. for $C_{23}H_{21}F_6NO_4Ru$ [*M*]$^+$: 591.0425, found: 591.0415.

Catalytic Deoxygenation of 1a with (*p*-cymene)Ru^{II} Species (Scheme 2). A mixture of [(*p*-cymene)$RuCl_2$]$_2$ (3.1 mg, 0.0050 mmol) and silver trifluoroacetate (4.4 mg, 0.020 mmol) in THF-d_8/TFE=10:1 (0.5 mL) was stirred at 25 °C for 30 min. The mixture was filtered through syringe filter and **1a** (14.5 mg, 0.100 mmol) was added to the filtrate. The mixture was taken into J-Young NMR tube and heated in a preheated oil bath at 50 °C for 24 h. The crude yield of deoxygenated product **2a** was determined by ^{1}H NMR spectroscopy using 1,1,2,2-tetrachloroethane as the internal standard (89%).

General Procedure for the Reaction Condition Screening (Table 1). A mixture of catalyst (0.0050 mmol) and AgOTs (5.8 mg, 0.020 mmol) in solvents (0.5 mL) was stirred at 25 °C for 30 min. To the solution were added **1a** (14.5 mg, 0.100 mmol), boronic ester (0.200 mmol), Ag_2O (51.0 mg, 0.220 mmol), and Cu salt (0.010 mmol) and the reaction mixture was stirred in a preheated heating mantle at 50 °C for 14 h. The mixture was cooled to 25 °C, diluted with EtOAc (30 mL), quenched with sat. aq. Na_2CO_3 (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layer was dried over $MgSO_4$, concentrated, and the crude yield of **7aa** was determined by ^{1}H NMR spectroscopy using 1,1,2,2-tetrachloroethane as the internal standard.

Preparation of Quinoline *N*-Oxides (Table 2). Quinoline *N*-oxides **1b–1k**, **1m–1p**, and **1u** were prepared following the reference procedures.[9a,11b]

*Acridine N-oxide (Table 2, **1l**).*[19] To a mixture of acridine (300 mg, 1.67 mmol) and $MeReO_3$ (12.5 mg, 0.050 mmol) was added 50% aqueous solution of H_2O_2 (227 mg, 3.34 mmol) and the reaction mixture was stirred at 25 °C for 12 h. The mixture was diluted with CH_2Cl_2 (50 mL) and H_2O (20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (20 mL x 3). The combined organic layer was washed with brine (5 mL), dried over Na_2SO_4, concentrated, and the residue was purified by SiO_2 column chromatography (CH_2Cl_2/acetone = 3:1, R_F = 0.3) to obtain the product. The spectral data was well matched with the previous report.[9a] Yellow solid (201 mg, 62%); ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.79 (dd, *J* = 9.1, 0.6 Hz, 2H), 8.25 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.76 (ddd, *J* = 9.0, 6.7, 1.2 Hz, 2H), 7.58 (ddd, *J* = 8.0, 6.7, 0.9 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 140.0, 130.9, 129.1, 128.2, 127.5, 123.5, 119.9; IR (cm^{-1}) 3048, 2920, 2851, 1620, 1560, 1530, 1471, 1435, 1401, 1327.

*6-Acetoxyquinoline N-oxide (Table 2, **1q**).* The same procedure for the synthesis of **1l** was followed by using 6-acetoxyquinoline (187 mg, 1.00 mmol) as starting material (CH_2Cl_2/acetone = 2:1, R_F = 0.3). White solid (91.4 mg, 45%); mp 89 – 91 °C; δ 8.68 (d, *J* = 9.4 Hz, 1H), 8.43 (d, *J* = 5.7 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 2.4 Hz, 2H), 7.48 (d, *J* = 9.4 Hz, 1H), 7.33 – 7.28 (m, 2H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 169.4, 150.8, 140.1, 135.5, 131.7, 125.7, 125.1, 122.5, 121.8, 119.5, 21.3; IR (cm^{-1}) 3073, 3053, 2994, 2923, 1748, 1572, 1371, 1199; HRMS (EI) m/z calcd. for $C_{11}H_9NO_3$ [*M*]$^+$: 203.0582, found: 203.0581

*6-(1,3-Dioxolan-2-yl)quinoline 1-oxide (Table 2, **1s**).* The same procedure for the synthesis of **1l** was followed by using 6-(1,3-dioxolan-2-yl)quinoline[5a] (503 mg, 2.50 mmol) as the starting material (acetone, R_F = 0.1). Yellow solid (395 mg, 73%); mp 81 – 83 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.67 (d, *J* = 9.0 Hz, 1H), 8.46 (dd, *J* = 6.1, 0.9 Hz, 1H), 7.99 (d, *J* = 1.4 Hz, 1H), 7.83 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.30 (dd, *J* = 8.4, 6.1 Hz, 1H), 5.96 (s, 1H), 4.19 – 4.03 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 142.4, 139.4, 136.0, 130.7, 128.7, 126.6, 125.7, 121.9, 120.3, 103.1, 66.9; IR (cm^{-1}) 3096, 3049, 2939, 2887, 1716, 1571, 1507, 1275; HRMS (EI) m/z calcd. for $C_{12}H_{11}NO_3$ [*M*]$^+$: 217.0739, found 217.0738.

*6-[(Triisopropylsilyl)oxy]quinoline N-oxide (Table 2, **1t**).* The same procedure for the synthesis of **1l** was followed by using 6-[(triisopropylsilyl)oxy]quinoline[5a] (302 mg, 1.00 mmol) as the starting material (CH_2Cl_2/acetone = 4:1, R_F = 0.2). Yellow solid (317 mg, 91%); mp 63 – 65 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.54 (d, *J* = 9.5 Hz, 1H), 8.30 (dd, *J* = 6.0, 1.0 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.33 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.23 – 7.18 (m, 2H), 1.39 – 1.24 (m, *J* = 7.5 Hz, 3H), 1.11 (d, *J* = 7.6 Hz, 18H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 156.5, 137.8, 134.0, 132.5, 126.2, 124.5, 121.9, 121.7, 114.9, 18.0, 13.1; ^{29}Si NMR (79 MHz, CD_2Cl_2) δ 17.87; IR (cm^{-1}) 3063, 2941, 2892, 2863, 1617, 1205; HRMS (FAB) m/z calcd. for $C_{18}H_{28}NO_2Si$ [*M*]$^+$ 318.1889, found: 318.1892.

*6-Formylquinoline N-oxide (Table 2, **1r**).*[5a] To a solution of 6-(1,3-dioxolan-2-yl)quinoline *N*-oxide (217 mg, 1.00 mmol) in THF (4 mL) were added formaldehyde (2.1 mL, 37 wt. % in water) and *p*-toluenesulfonic acid monohydrate (190 mg, 1.00 mmol). The resulting mixture was stirred at room temperature for 36 h. The solution was quenched with sat. aq. $NaHCO_3$ solution (20 mL) and then extracted with dichloromethane (20 mL x 3). The solution was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by SiO_2 column chromatography (acetone, R_F = 0.2) to obtain the product. Yellow solid (139 mg, 80%); mp 169 – 171 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 10.19 (d, *J* = 0.8 Hz, 1H), 8.78 (d, *J* = 9.0 Hz, 1H), 8.55 (dd, *J* = 6.1, 1.0 Hz, 1H), 8.40 (d, *J* = 1.7 Hz, 1H), 8.17 (dd, *J* = 9.0, 1.7 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.40 (dd, *J* = 8.5, 6.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 191.3, 144.4, 137.7, 136.4, 133.5, 130.9, 127.7, 126.2, 122.9, 121.4; IR (cm^{-1}) 3104, 3046, 3010, 2923, 2852, 1679, 1573, 1450, 1356, 1268; HRMS (EI) m/z calcd. for $C_{10}H_7NO_2$ [*M*]$^+$: 173.0477, found 173.0474.

Preparation of Arylboronic Esters (Table 1 and Table 2). Arylboronic esters **3a**,[20] **4a**,[21] **5a**,[22] **6a**,[23] and **3b–3g**[20] were prepared according to the reference procedure.

General Procedure for the Ru-Catalyzed Tandem Deoxygenative C–H Arylation (Table 2). A mixture of [(*p*-cymene)$RuCl_2$]$_2$ (3.1 mg, 0.0050 mmol) and AgOTs (5.8 mg, 0.020 mmol) in THF/TFE (1:2, 0.5 mL) was stirred at 25 °C for 30 min. To the solution were added **1** (0.100 mmol), **3** (0.200 mmol), Ag_2O (51.0 mg, 0.220 mmol), and $Cu(ClO_4)_2 \cdot 6H_2O$ (3.7 mg, 0.010 mmol) and the reaction mixture was stirred in a preheated heating mantle at 50 °C for 14 h. The mixture was cooled to 25 °C, diluted with EtOAc (30 mL), quenched with sat. aq. Na_2CO_3 (20 mL), and extracted with EtOAc (20 mL x 3). The

combined organic layer was dried over $MgSO_4$, concentrated, and purified by SiO_2 column chromatography to obtain the product.

8-[4-(Trifluoromethyl)phenyl]quinoline (Table 2, ***7aa****).* EtOAc/*n*-hexane = 1:4, R_F = 0.4; White solid (25.3 mg, 93%); mp 115 – 117 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.90 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.26 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.91 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.79 – 7.73 (m, 3H), 7.67 – 7.63 (m, 1H), 7.46 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.8, 146.2, 144.0, 139.7, 136.7, 131.6, 130.6, 129.4 (q, *J* = 32.2 Hz), 129.2, 128.9, 126.7, 125.01 (q, *J* = 271.8 Hz), 124.99 (q, *J* = 3.7 Hz), 121.8; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.66; IR (cm^{-1}) 3069, 3046, 2953, 2918, 2849, 1586, 1322, 1107; HRMS (EI) m/z calcd. for $C_{16}H_{10}F_3N$ [*M*]$^+$: 273.0765, found: 273.0761.

6-Methoxy-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7b****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; White solid (24.1 mg, 80%); mp 85 – 87 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.73 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.18 (d, *J* = 2.8 Hz, 1H), 3.97 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 157.6, 148.2, 143.5, 142.5, 141.1, 135.4, 131. 5, 130.4, 129.5 (q, *J* = 32.2 Hz), 124.98 (q, *J* = 3.8 Hz), 124.94 (q, *J* = 271.9 Hz), 123.1, 122.1, 106.1, 56.0; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.69; IR (cm^{-1}) 3077, 3022, 2938, 2836, 1608, 1597, 1322, 1212, 1148, 1105; HRMS (EI) m/z calcd. for $C_{17}H_{12}F_3NO$ [*M*]$^+$: 303.0871, found: 303.0868.

6-Methyl-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7c****).* EtOAc/*n*-hexane = 1:4, R_F = 0.7; White solid (20.1 mg, 70%); mp 103 – 105 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.82 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.70 – 7.65 (m, 1H), 7.60 (d, *J* = 2.0 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 1H), 2.59 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 149.9, 144.8, 144.1, 139.3, 136.6, 136.0, 132.9, 131.5, 129.3 (q, *J* = 32.3 Hz), 129.2, 127.6, 125.00 (q, *J* = 271.8 Hz), 124.95 (q, *J* = 3.8 Hz), 121.7, 21.7; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.66; IR (cm^{-1}) 2959, 2922, 2854, 1739, 1616, 1593, 1574, 1486, 1321, 1160; HRMS (EI) m/z calcd. for $C_{17}H_{12}F_3N$ [*M*]$^+$: 287.0922, found: 287.0920.

7-Methyl-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7d****).* EtOAc/*n*-hexane = 1:10, R_F = 0.4; White solid (19.6 mg, 68%); mp 114 – 116 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.77 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 7.9 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.36 (dd, *J* = 8.2, 4.2 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 150.5, 147.4, 144.0, 138.6, 137.8, 136.1, 131.4, 129.8, 129.1 (q, *J* = 32.2 Hz), 127.8, 127.0, 125.2 (q, *J* = 3.7 Hz), 125.0 (q, *J* = 271.8 Hz), 120.7, 21.1; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.58; IR (cm^{-1}) 3053, 3006, 2923, 2853, 1607, 1318, 1106; HRMS (ESI) m/z calcd. for $C_{17}H_{12}F_3N$ [*M*+H]$^+$: 288.0995, found: 288.0993.

6-Bromo-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7e****).* EtOAc/*n*-hexane = 1:4, R_F = 0.6; White solid (31.7 mg, 90%); mp 110 – 112 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.90 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.07 (d, *J* = 2.2 Hz, 1H), 7.84 (d, *J* = 2.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.48 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 151.1, 145.0, 142.5, 141.7, 135.8, 133.6, 131.5, 130.6, 130.4, 129.9 (q, *J* = 32.3 Hz), 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 272.0 Hz), 122.6, 120.3; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.77; IR (cm^{-1}) 3071, 2925, 1615, 1586, 1482, 1415, 1322, 1158, 1105, 1066; HRMS (EI) m/z calcd. for $C_{16}H_9BrF_3N$ [*M*]$^+$: 350.9870, found: 350.9866.

6-Chloro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7f****).* EtOAc/*n*-hexane = 1:4, R_F = 0.6; White solid (21.5 mg, 70%); mp 115 – 117 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.89 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.89 (d, *J* = 2.4 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 2.3 Hz, 1H), 7.48 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 151.0, 144.8, 142.6, 141.6, 135.9, 132.2, 131.5, 131.1, 129.92 (q, J = 32.3 Hz), 129.92, 127.2, 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 272.0 Hz), 122.6; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.78; IR (cm^{-1}) 3057, 3034, 2959, 2920, 2849, 1615, 1315, 1105; HRMS (EI) m/z calcd. for $C_{16}H_9ClF_3N$ [*M*]$^+$: 307.0376, found: 307.0371.

6-Fluoro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7g****).* EtOAc/*n*-hexane = 1:10, R_F = 0.4; White solid (20.9 mg, 72%); mp 100 – 102 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.86 (dd, *J* = 4.0, 1.8 Hz, 1H), 8.21 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.58 – 7.51 (m, 2H), 7.47 (dd, *J* = 8.4, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 160.2 (d, *J* = 247.5 Hz), 150.1 (d, *J* = 2.8 Hz), 143.5, 142.7, 142.5 (d, *J* = 8.9 Hz), 136.2 (d, *J* = 5.5 Hz), 131.5, 130.1 (d, *J* = 10.2 Hz), 129.9 (q, *J* = 32.4 Hz), 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 271.9 Hz), 122.5, 120.5 (d, *J* = 26.5 Hz), 111.4 (d, *J* = 21.3 Hz); ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.79 (s, 3F), -114.01 – -114.37 (m, 1F); IR (cm^{-1}) 3080, 2922, 1610, 1497, 1395, 1318, 1164, 1118, 1067, 841; HRMS (EI) m/z calcd. for $C_{16}H_9F_4N$ [*M*]$^+$: 291.0671, found: 291.0668.

5-Chloro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7h****).* EtOAc/*n*-hexane = 1:4, R_F = 0.7; White solid (22.9 mg, 75%); mp 94 – 96 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.95 (dd, *J* = 4.1, 1.7 Hz, 1H), 8.67 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.78 – 7.72 (m, 3H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.57 (dd, *J* = 8.6, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 151.3, 146.8, 143.2, 139.1, 133.4, 131.8, 131.6, 130.3, 129.6 (q, *J* = 32.3 Hz), 127.0, 126.8, 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 271.8 Hz), 122.5; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.73; IR (cm^{-1}) 3069, 3049, 2959, 2920, 2851, 1615, 1320, 1120; HRMS (EI) m/z calcd. for $C_{16}H_9ClF_3N$ [*M*]$^+$: 307.0376, found: 307.0371.

4-Chloro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7i****).* EtOAc/*n*-hexane = 1:4, R_F = 0.7; White solid (24.1 mg, 79%); mp 97 – 99 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.76 (d, *J* = 4.7 Hz, 1H), 8.34 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.81 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.77 – 7.73 (m, 3H), 7.56 (d, *J* = 4.5 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.1, 147.2, 143.7, 143.1, 140.3, 131.6, 131.6, 129.6 (q, *J* = 32.5 Hz), 127.7, 127.3, 125.0 (q, *J* = 3.8 Hz), 124.94 (q, *J* = 271.8 Hz), 124.94 (s), 121.9; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.71; IR (cm^{-1}) 3112, 3073, 2918, 2851, 1496, 1317, 1107; HRMS (EI) m/z calcd. for $C_{16}H_9ClF_3N$ [*M*]$^+$: 307.0376, found: 307.0377.

6-Nitro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7j****).* EtOAc/*n*-hexane = 1:4, R_F = 0.3; White solid (23.5 mg, 74%); mp 170 – 172 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.08 (d, *J* = 2.5 Hz, 1H), 8.85 (s, 1H), 8.51 (d, *J* = 2.2 Hz, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.63 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 154.1, 148.3, 145.5, 142.0, 141.8, 138.7, 131.6, 130.3 (q, *J* = 32.4 Hz), 128.2, 125.3 (q, *J* = 3.8 Hz), 125.0, 124.8 (q, *J* = 272.0 Hz), 123.6, 123.4; ^{19}F NMR (564 MHz, CD_2Cl_2) -62.85; IR (cm^{-1}) 3085, 1803, 1610, 1533, 1484, 1349, 1318, 1161, 1120, 1107; HRMS (EI) m/z calcd. for $C_{16}H_9F_3N_2O_2$ [*M*]$^+$: 318.0616, found: 318.0617.

5-Nitro-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7k****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; Yellow solid (18.1 mg, 57%); mp 161 – 163 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.03 (d, *J* = 8.9 Hz, 1H), 9.01 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.77 (m, 4H), 7.69 (dd, *J* = 8.9, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 151.8, 146.5, 146.2, 145.8, 142.4, 132.3, 131.6, 130.5 (q, *J* = 32.3 Hz), 128.8, 125.2 (q, *J* = 3.9 Hz), 124.8 (q, *J* = 271.9 Hz), 124.5, 124.3, 122.1; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.88; IR (cm^{-1}) 3067, 2959, 2920, 2851, 1617, 1322, 1095; HRMS (EI) m/z calcd. for $C_{16}H_9F_3N_2O_2$ [*M*]$^+$: 318.0616, found: 318.0613.

4-[4-(Trifluoromethyl)phenyl]acridine (Table 2, ***7l****).* EtOAc/*n*-hexane = 1:5, R_F = 0.6; Yellow solid (13.8 mg, 43%); mp 147 –

149 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.88 (s, 1H), 8.12 – 8.10 (m, 2H), 8.07 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 2H), 7.84 (d, *J* = 6.8 Hz, 1H), 7.82 – 7.75 (m, 3H), 7.66 – 7.63 (m, 1H), 7.59 – 7.57 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 149.3, 147.0, 144.0, 139.3, 136.6, 131.7, 131.3, 130.6, 130.2, 129.34 (q, *J* = 32.1 Hz), 129.33, 128.5, 127.3, 126.9, 126.5, 125.8, 125.1 (q, *J* = 272.0 Hz), 125.0 (q, *J* = 3.8 Hz); ^{19}F NMR (564 MHz, CD_2Cl_2) -62.62; IR (cm^{-1}) 3054, 3039, 2930, 1929, 1613, 1525, 1409, 1326, 1164, 1106; HRMS (EI) m/z calcd. for $C_{20}H_{12}F_3N$ [*M*]$^+$: 323.0922, found: 323.0924.

4-[4-(Trifluoromethyl)phenyl]phenanthridine (Table 2, ***7m****).* EtOAc/*n*-hexane = 1:4, R_F = 0.7; White solid (17.6 mg, 54%); mp 163 – 165 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.26 (s, 1H), 8.73 – 8.67 (m, 2H), 8.08 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.92 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 2H), 7.81 – 7.74 (m, 5H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 153.7, 144.7, 142.2, 140.5, 132.9, 131.7, 131.5, 130.2, 129.3 (q, *J* = 32.3 Hz), 129.1, 128.3, 127.1, 126.7, 125.0 (q, *J* = 271.8 Hz), 124.93 (q, *J* = 4.0 Hz), 124.93 (s), 123.1, 122.5; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.62; IR (cm^{-1}) 3089, 3036, 2959, 2925, 2851, 1613, 1315, 1118; HRMS (EI) m/z calcd. for $C_{20}H_{12}F_3N$ [*M*]$^+$: 323.0922, found: 323.0918.

5-[4-(Trifluoromethyl)phenyl]benzo[f]quinoline (Table 2, ***7n****).* EtOAc/*n*-hexane = 1:4, R_F = 0.4; White solid (21.4 mg, 66%); mp 95 – 97 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.10 – 9.05 (m, 1H), 8.93 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.71 (d, *J* = 8.2 Hz, 1H), 8.04 (s, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.80 – 7.74 (m, 3H), 7.74 – 7.69 (m, 1H), 7.63 (dd, *J* = 8.4, 4.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 149.7, 146.5, 144.1, 138.1, 131.8, 131.6, 131.49, 131.47, 130.2, 129.4 (q, *J* = 32.2 Hz), 129.3, 128.2, 127.9, 126.2, 125.01 (q, *J* = 3.9 Hz), 124.99 (q, *J* = 271.9 Hz), 123.0, 121.9; ^{19}F NMR (564 MHz, CD_2Cl_2) -62.65; IR (cm^{-1}) 3066, 2960, 2926, 2849, 2088, 1919, 1703, 1686, 1615, 1321; HRMS (EI) m/z calcd. for $C_{20}H_{12}F_3N$ [*M*]$^+$: 323.0922, found: 323.0917.

1-{8-[4-(Trifluoromethyl)phenyl]quinolin-3-yl)ethan-1-one (Table 2, ***7o****).* EtOAc/*n*-hexane = 1:4, R_F = 0.2; White solid (24.9 mg, 79%); mp 141 – 143 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 9.38 (d, *J* = 2.2 Hz, 1H), 8.78 (d, *J* = 2.3 Hz, 1H), 8.04 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.88 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.73 (dd, *J* = 8.2, 7.1 Hz, 1H), 2.73 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 197.0, 149.4, 147.6, 143.3, 139.8, 137.9, 133.0, 131.5, 130.3, 129.8, 129.6 (q, *J* = 32.2 Hz), 127.8, 127.7, 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 272.0 Hz), 27.1; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.72; IR (cm^{-1}) 3050, 2922, 2852, 1682, 1607, 1574, 1317, 1248, 1159, 1107; HRMS (EI) m/z calcd. for $C_{18}H_{12}F_3NO$ [*M*]$^+$: 315.0871, found: 315.0869.

Methyl 8-[4-(trifluoromethyl)phenyl]quinoline-6-carboxylate (Table 2, ***7p****).* EtOAc/*n*-hexane = 1:4, R_F = 0.3; White solid (24.9 mg, 75%); mp 164 – 166 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.98 (dd, *J* = 4.1, 1.9 Hz, 1H), 8.63 (d, *J* = 2.0 Hz, 1H), 8.36 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.33 (d, *J* = 2.0 Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 2H), 7.76 (d, *J* = 7.9 Hz, 2H), 7.52 (dd, *J* = 8.3, 4.1 Hz, 1H), 4.00 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 166.7, 152.8, 148.0, 143.2, 140.1, 138.1, 131.6, 131.5, 129.9, 129.7 (q, *J* = 32.5 Hz), 128.5, 128.3, 125.1 (q, *J* = 3.9 Hz), 124.9 (q, *J* = 271.7 Hz), 122.5, 52.8; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.73; IR (cm^{-1}) 3067, 2954, 2846, 1725, 1613, 1490, 1328, 1249, 1169, 1096, 1067; HRMS (EI) m/z calcd. for $C_{18}H_{12}F_3NO_2$ [*M*]$^+$: 331.0820, found: 331.0816.

8-[4-(Trifluoromethyl)phenyl]quinolin-6-yl acetate (Table 2, ***7q****).* EtOAc/*n*-hexane = 1:4, R_F = 0.3; White solid (17.3 mg, 52%); mp 78 – 80 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.88 (dd, *J* = 4.0, 1.7 Hz, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 1.4 Hz, 1H), 7.52 (d, *J* = 1.3 Hz, 1H), 7.47 (dd, *J* = 8.5, 4.1 Hz, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 169.7, 150.6, 148.5, 144.3, 143.0, 141.3, 136.5, 131.5, 129.8 (q, *J* = 32.3 Hz), 129.6, 125.8, 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 271.8 Hz), 122.3, 119.3, 21.4; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.76; IR (cm^{-1}) 3051, 2918, 1683, 1609, 1576, 1318, 1248, 1157, 1103, 1060; HRMS (EI) m/z calcd. for $C_{18}H_{12}F_3NO_2$ [*M*]$^+$: 331.0820, found: 331.0821.

8-[4-(Trifluoromethyl)phenyl]quinoline-6-carbaldehyde (Table 2, ***7r****).* EtOAc/*n*-hexane = 1:4, R_F = 0.3; White solid (22.4 mg, 74%); mp 100 – 102 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 10.23 (s, 1H), 9.03 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.42 (dd, *J* = 8.3, 1.8 Hz, 2H), 8.21 (d, *J* = 1.8 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.57 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 191.7, 153.4, 148.8, 143.0, 141.0, 138.2, 134.4, 134.2, 131.6, 129.9 (q, *J* = 32.3 Hz), 128.8, 127.4, 125.1 (q, *J* = 3.8 Hz), 124.9 (q, *J* = 271.9 Hz), 122.8; ^{19}F NMR (376 MHz, CD_2Cl_2) -62.68; IR (cm^{-1}) 3042, 2928, 2853, 1738, 1687, 1616, 1492, 1422, 1324, 1104; HRMS (EI) m/z calcd. for $C_{17}H_{10}F_3NO$ [*M*]$^+$: 301.0714, found: 301.0709.

6-(1,3-Dioxolan-2-yl)-8-[4-(trifluoromethyl)phenyl]quinoline (Table 2, ***7s****).* EtOAc/*n*-hexane = 1:4, R_F = 0.3; White solid (23.2 mg, 67%); mp 112 – 114 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.91 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.28 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.00 (d, *J* = 1.7 Hz, 1H), 7.89 – 7.81 (m, 3H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.01 (s, 1H), 4.22 – 4.05 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, CD_2Cl_2) δ 151.2, 146.6, 143.8, 140.1, 137.0, 136.6, 131.6, 129.5 (q, *J* = 32.3 Hz), 128.8, 128.7, 126.9, 124.99 (q, *J* = 3.8 Hz), 124.98 (q, *J* = 271.9 Hz), 122.0, 103.7, 66.0; ^{19}F NMR (376 MHz, CD_2Cl_2) δ -62.62; IR (cm^{-1}) 3066, 2986, 2954, 2926, 2899, 2876, 1616, 1492, 1323, 1158; HRMS (EI) m/z calcd. for $C_{19}H_{14}F_3NO_2$ [*M*]$^+$: 345.0977, found: 345.0972.

8-[4-(Trifluoromethyl)phenyl]-6-[(triisopropylsilyl)oxy]quinoline (Table 2, ***7t****).* EtOAc/*n*-hexane = 1:4, R_F = 0.8; Yellow oil (25.9 mg, 58%); ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.74 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 2.7 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.26 (d, *J* = 2.8 Hz, 1H), 1.37 (hept, *J* = 7.5 Hz, 3H), 1.17 (d, *J* = 7.5 Hz, 18H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 154.1, 148.5, 143.7, 142.4, 141.2, 135.4, 131.5, 130.5, 129.5 (q, *J* = 32.2 Hz), 126.5, 125.02 (q, *J* = 3.8 Hz), 124.94 (q, *J* = 271.8 Hz), 121.9, 114.8, 18.2, 13.2; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.69; ^{29}Si NMR (119 MHz, CD_2Cl_2) δ 17.22; IR (cm^{-1}) 2946, 2867, 1610, 1597, 1487, 1460, 1323, 1219, 1166, 1122; HRMS (EI) m/z calcd. for $C_{25}H_{30}F_3NOSi$ [*M*]$^+$: 445.2049, found: 445.2047.

N-{8-[4-(Trifluoromethyl)phenyl]quinolin-6-yl}acetamide (Table 2, ***7u****).* EtOAc/*n*-hexane = 1:1, R_F = 0.2; White solid (20.4 mg, 62%); mp 95 – 97 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.79 (dd, *J* = 4.0, 1.9 Hz, 1H), 8.32 (d, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.95 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 2.4 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.1 Hz, 1H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 169.2, 149.6, 143.5, 143.3, 140.4, 136.4, 136.3, 131.4, 129.8, 129.6 (q, *J* = 32.3 Hz), 125.0 (q, *J* = 3.9 Hz), 124.9 (q, *J* = 271.9 Hz), 124.2, 122.2, 116.7, 24.8; ^{19}F NMR (564 MHz, CD_2Cl_2) δ -62.72; IR (cm^{-1}) 3272, 3075, 1669, 1542, 1370, 1321, 1158, 1109, 1064, 839; HRMS (EI) m/z calcd. for $C_{18}H_{13}F_3N_2O$ [*M*]$^+$: 330.0980, found: 330.0977.

8-(4-Bromophenyl)quinoline (Table 2, ***7ab****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; Off-white solid (21.5 mg, 95%); mp 97 – 99 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.91 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.24 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.88 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.73 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.68 – 7.60 (m, 3H), 7.59 (d, *J* = 10.7 Hz, 2H), 7.45 (dd, *J* = 8.2, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.6, 146.2, 139.9, 139.1, 136.6, 132.9, 131.2, 130.3, 129.1, 128.4, 126.7, 121.7, 121.6; IR (cm^{-1}) 3046, 2927, 2846, 1590, 1489, 1070, 1002, 958, 818, 792; HRMS (EI) m/z calcd. for $C_{15}H_{10}BrN$ [*M*]$^+$: 282.9997, found: 282.9995.

8-(4-Chlorophenyl)quinoline (Table 2, ***7ac****).* EtOAc/*n*-hexane

= 1:4, R_F = 0.5; White solid (21.3 mg, 89%); mp 95 – 97 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.91 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.25 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.88 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.73 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.64 – 7.61 (m, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.45 (dd, *J* = 8.7, 4.5 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.6, 146.3, 139.9, 138.7, 136.6, 133.5, 132.5, 130.4, 129.2, 128.4, 128.3, 126.7, 121.6; IR (cm^{-1}) 3044, 1594, 1577, 1489, 1458, 1185, 1083, 1013, 960, 819, 789; HRMS (EI) m/z calcd. for $C_{15}H_{10}ClN$ [*M*]$^+$: 239.0502, found: 239.0499.

Ethyl 4-(quinolin-8-yl)benzoate (Table 2, ***7ad****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; White solid (21.8 mg, 79%); mp 91 – 93 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.92 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.26 (dd, *J* = 8.2, 1.9 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 2H), 7.91 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.81 – 7.75 (m, 3H), 7.65 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.46 (dd, *J* = 8.3, 4.1 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 166.8, 150.7, 146.3, 144.8, 140.2, 136.6, 131.2, 130.6, 129.7, 129.2, 129.1, 128.7, 126.6, 121.7, 61.3, 14.6; IR (cm^{-1}) 3045, 2977, 2900, 1712, 1612, 1495, 1362, 1266, 1190, 1101, 792 ; HRMS (EI) m/z calcd. for $C_{18}H_{15}NO_2$ [*M*]$^+$: 277.1103, found: 277.1102.

8-(4-Nitrophenyl)quinoline (Table 2, ***7ae****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; Yellow solid (18.7 mg, 75%); mp 167 – 169 °C; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.91 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.32 (d, *J* = 8.7 Hz, 2H), 8.28 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.95 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.79 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.49 (dd, *J* = 8.3, 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.9, 147.4, 147.0, 146.0, 138.8, 136.7, 132.1, 130.7, 129.4, 129.2, 126.7, 123.2, 121.9; IR (cm^{-1}) 3101, 3049, 2920, 1596, 1511, 1337, 1107, 965, 852, 796; HRMS (EI) m/z calcd. for $C_{15}H_{10}N_2O_2$ [*M*]$^+$: 250.0742, found: 250.0740.

8-(p-Tolyl)quinoline (Table 2, ***7af****).* EtOAc/*n*-hexane = 1:4, R_F = 0.5; Yellow oil (8.8 mg, 40%); ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.90 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.23 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.85 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.72 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.61 (dd, *J* = 8.2, 7.1 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.43 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 150.4, 146.6, 141.3, 137.4, 137.3, 136.5, 131.0, 130.3, 129.1, 128.8, 127.7, 126.6, 121.4, 21.3; IR (cm^{-1}) 3048, 3025, 3003, 2920, 2861, 1594, 1495, 1465, 1379, 818, 792; HRMS (EI) m/z calcd. for $C_{16}H_{13}N$ [*M*]$^+$: 219.1048, found: 219.1044.

8-(4-Methoxyphenyl)quinoline (Table 2, ***7ag****).* EtOAc/*n*-hexane = 1:3, R_F = 0.5; Colorless oil (9.1 mg, 39%); ^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.90 (d, *J* = 4.1 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 7.1 Hz, 1H), 7.66 – 7.56 (m, 3H), 7.43 (dd, *J* = 8.3, 4.1 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CD_2Cl_2) δ 159.5, 150.3, 146.5, 140.8, 136.6, 132.5, 132.2, 130.2, 129.2, 127.5, 126.7, 121.4, 113.6, 55.7; IR (cm^{-1}) 3034, 3002, 2936, 2898, 2834, 1609, 1513; HRMS (ESI) m/z calcd. for $C_{16}H_{13}NO$ [*M*+Na]$^+$: 258.0889, found: 258.0889.

General Procedure for the Gram-Scale Arylation. A mixture of [(*p*-cymene)$RuCl_2$]$_2$ (306 mg, 0.500 mmol) and AgOTs (558 mg, 2.00 mmol) in THF/TFE (1:2, 60 mL) was stirred at 25 °C for 30 min. To the solution were added **1a** (1.45 g, 10.0 mmol), **3a** (4.32 g, 20.0 mmol), Ag_2O (5.10 g, 22.0 mmol), and $Cu(ClO_4)_2{\cdot}6H_2O$ (371 mg, 1.00 mmol) and the reaction mixture was stirred in a preheated heating mantle at 50 °C for 36 h. The mixture was cooled to 25 °C, diluted with EtOAc (100 mL), quenched with sat. aq. Na_2CO_3 (100 mL), and extracted with EtOAc (100 mL x 3). The combined organic layer was dried over $MgSO_4$, concentrated, and purified by SiO_2 column chromatography to obtain the product (2.01 g, 74%).

Procedure for the Reaction Profile Investigation on the Ru-Catalyzed Deoxygenative C8-Arylation (Scheme 3a). A mixture of **3a** (216 mg, 1.00 mmol), Ag_2O (255 mg, 1.10 mmol), and $Cu(ClO_4)_2{\cdot}6H_2O$ (18.5 mg, 0.500 mmol) in THF/TFE (1:2, 2.5 mL) was stirred at 25 °C for 30 min. In another flask, a mixture of [(*p*-cymene)$RuCl_2$]$_2$ (15.5 mg, 0.0250 mmol) and AgOTs (29.0 mg, 0.100 mmol) in THF/TFE=1:2 (2.5 mL) was stirred at 25 °C for 30 min. To the first mixture were added **1a** (72.5 mg, 0.500 mmol) and the solution from the second flask were added sequentially. The reaction mixture was stirred in a preheated oil bath at 50 °C. At selected time points, 100 μL of the reaction mixture was sampled and the reaction progress was determined by ^{19}F NMR spectroscopy using 3,5-bis(trifluoromethyl)benzamide as the internal standard.

Procedure for the Kinetic Isotope Effect Experiment (Scheme 3b). A mixture of **3a** (216 mg, 1.00 mmol), Ag_2O (255 mg, 1.10 mmol), and $Cu(ClO_4)_2{\cdot}6H_2O$ (18.5 mg, 0.500 mmol) in THF/TFE (1:2, 2.5 mL) was stirred at 25 °C for 30 min. In another flask, a mixture of [(*p*-cymene)$RuCl_2$]$_2$ (15.5 mg, 0.0250 mmol) and AgOTs (29.0 mg, 0.100 mmol) in THF/TFE (1:2, 2.5 mL) was stirred at 25 °C for 30 min. To the first mixture were sequentially added **1a** (72.5 mg, 0.500 mmol) or **1a-*d*$_7$** (76.0 mg, 0.500 mmol) and the solution from the second flask. The reaction mixture was stirred in a preheated oil bath at 50 °C. 100 μL portion of the reaction mixture was sampled every 5 minutes for 2.5 h. The initial reaction progress was monitored by ^{19}F NMR spectroscopy using 3,5-bis(trifluoromethyl)benzamide as the internal standard. The sum of **7aa** and **8aa** (or **7aa-*d*$_6$** and **8aa-*d*$_6$**) was plotted and the initial rate of the arylation on **1a** and **1a-*d*$_7$** was determined by linear fitting of the initial five points from each reaction profile. The initial rate for the C–H arylation was found to be 1.57 mM/min and 1.54 mM/min for **1a** and **1a-*d*$_7$**, respectively, yielding KIE value 1.02.

General Procedure for the Condition Screening on Ru-Catalyzed Deoxygenation (Scheme 4a). A mixture of [(*p*-cymene)$RuCl_2$]$_2$ (3.1 mg, 0.0050 mmol) and AgOTs (5.8 mg, 0.020 mmol) in THF/TFE (1:2, 0.5 mL) was stirred at 25 °C for 30 min. To the solution was added **8aa** (28.9 mg, 0.100 mmol) and the reaction mixture was stirred in a preheated heating mantle at 50 °C for 14 h. The mixture was cooled to 25 °C and concentrated under reduced pressure. The yield of **7aa** was determined by ^{1}H NMR spectroscopy using 1,1,2,2-tetrachloroethane as the internal standard.

Procedure for the Reaction Byproduct Analysis (Scheme 4b). A mixture of [(*p*-cymene)$RuCl_2$]$_2$ (3.1 mg, 0.0050 mmol) and AgOTs (5.8 mg, 0.020 mmol) in THF-d_8/TFE (10:1, 0.5 mL) was stirred at 25 °C for 30 min. The solution was added to **8aa** (28.9 mg, 0.100 mmol) placed in a J-Young tube. The reaction mixture was heated in a preheated oil bath at 50 °C for 2 h. The ^{1}H and ^{19}F crude NMR was compared with **10**, which was separately prepared by dissolving **9**[18] in THF-d_8/TFE (10:1, 0.5 mL).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publication website

NMR spectra for products, and detailed experimental procedure for the mechanistic studies (PDF)

Crystallographic data of **Ru-A**, **Ru-B**, and **7n** (CIF)

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Notes
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