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Ru(II)-Catalyzed Chemoselective C(sp3)-H Monoarylation of 8-Methyl Quinolines with Arylboronic Acids

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c01603 • Publication Date (Web): 19 Aug 2020

Ru(II)-Catalyzed Chemoselective C(sp^3)-H Monoarylation of 8-Methyl Quinolines with Arylboronic Acids

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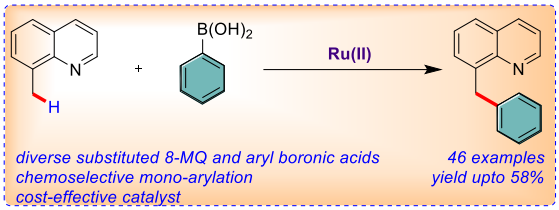
Supporting Information

ABSTRACT: The transition metal promoted C-H activation has grown as an efficient as well as atom economic methodology for the synthesis of wide array of organic molecules but cost of the metal catalyst and selectivity remains the major challenges. Herein, the first $[Cl_2Ru(p\text{-cymene})]_2$-catalyzed direct mono-arylation of unactivated C(sp^3)-H bond of 8-methyl quinolines with aryl boronic acids to synthesize diarylmethane compounds is presented. The transformation shows broad substrate substrate scope with high chemoselectivity for the synthesis of 8-benzyl quinolines. In preliminary mechanistic study- control experiments, deuterium labelling experiments and kinetic studies have been performed.



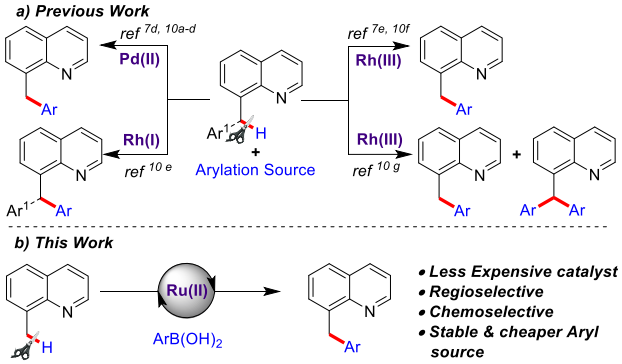
KEYWORDS: *C-H activation, $[Cl_2Ru(p\text{-cymene})]_2$, arylation, 8-methyl quinolines, phenylboronic acids.*

Introduction

Over the years, quinoline has gained a huge attraction of the researchers as it is the most versatile and important *N*-based heterocyclic compound found in the nature particularly in alkaloids.[1] Quinoline scaffolds are used as 'parental moieties' which are integrated to functionalized molecules with a wide range of applications in agrochemicals,[2] pharmaceuticals[1e,3] and ligands in transition metal catalysts.[4] Obeying to the importance of quinolines, various methods have been developed for their functionalization mainly by using Pd-catalyst but necessity of pre-activated substrates, strong bases and stoichiometric amount of metal catalyst remained the main shortcomings.[5] However, development of TM-catalyzed C-H activation eliminates all these requirements and therefore is a desirable methodology for the direct functionalization of quinolines.[6]

The synthesis of C-C_{aryl} bonds are indeed vital in organic chemistry but these transformations are challenging for the substrates having no directing group assistance as uncontrolled regio- and chemo- selectivity leads to the undesired homo- and hetero- couplings and hence formation of side products.[5,7] A number of reactions have been flourished widely for the direct C(sp^2)-H arylation of quinolines *via* transition metal catalysts owing to the availability of *pi*-orbitals and easy formation of their metallacycle intermediates.[8] Significantly, methodologies have also been reported for the direct functionalization[9] and particularly for arylation[7d,7e, 10] of more challenging C(sp^3)-H bond of 8-methyl quinoline (8-MQ) under expensive Pd(II)- and Rh(III)-catalysts. (Scheme 1a) In the pioneering studies, M. S. Sanford,[10a,10c] O. Daugulisfor,[10b] W.Y. Yu[10d] and I. Larrosa[7d] groups have independently developed CH-arylation protocols through costly Pd-catalyst with a limited scope for 8-MQ. In 2015, F. Glorius and co-workers demonstrated a Rh(III)-catalyzed C(sp^3)-H arylation where chemoselectivity remained an issue as both mono- and di-arylation products were observed in case of primary C(sp^3)-H bond.[7e] Later, Rh(I)/NHC-catalyzed site- and enantio- selective direct C(sp^3)-H arylation with aryl bromides[10e] and Rh(III)-catalyzed C(sp^3)-H arylation with diazonaphthalen-2(1H)-ones/quinonediazides[10f] have also been demonstrated but use of costly metal and limited scope permit further investigation in this direction. Recently, our group has reported the rhodium-catalyzed C(sp^3)-H arylation with organoboranes where mono-arylation was achieved only in case of sterically hindered 7-substituted 8-MQs as substrates and otherwise both mono- and di-arylated products were obtained in the reaction.[10g] Although Ru(II)-catalysts have also contributed immensely towards the discovery of efficient catalytic systems for the direct C(sp^2)-H arylation,[11] there are only few reports on C(sp^3)-H arylation.[12] Hence, these considerations led us to search for the cost-effective Ru(II)-catalyzed regio- and chemo- selective direct C(sp^3)-H mono-arylation of 8-MQ with less expensive and bench stable arylboronic acids. (Scheme 1b)

Scheme 1. C(sp^3)-H arylation of 8-methyl quinoline

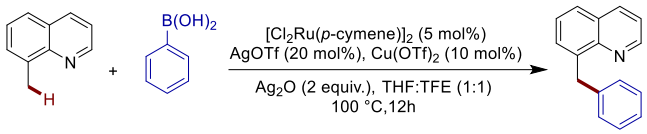


Results and Discussion

In order to explore Ru(II)-catalyzed C(sp^3)-H arylation of 8-MQ, we commenced our studies by reacting 8-MQ (**1a**) with phenyl boronic acid (**2a**) in the presence of $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%) and Ag_2O (2 equiv.) in THF (Tetrahydrofuran) (0.5 ml) at 100 °C for 12h under inert atmosphere. Pleasingly, this reaction afforded the expected 8-benzyl quinoline (**3a**) in 23% isolated yield (Table 1, entry 6). When $[Cl_2Ru(p\text{-cymene})]_2$ was omitted from the reaction, no product was formed and **1a** was recovered as such (Table 1, entry 2). After extensive optimization of various solvents, reaction efficiency was improved to 52% when a combination of solvents (THF : TFE in 1 : 1) was used (Table 1, entry 1, 6). The optimization of additives proved that the efficiency of the reaction was decreased to 35% in the absence

of AgOTf (Table 1, entry 3). Also, control reaction without $Cu(OTf)_2$ or Ag_2O resulted in decreased product yield (Table 1, entry 4-5). Under air atmosphere, reaction efficiency was decreased to 40%. (Table 1, entry 7) No significant improvement was found with decrease or increase in the temperature and 21% product yield was obtained at rt. (Table 1, entry 8, 9) The reaction did not proceed when $[Cl_2Ru(p\text{-cymene})]_2$ was replaced with $CoCp^*(CO)I_2$ metal complex. (Table 1, entry 10) No significant change in reaction efficiency was observed with increase in time of the reaction. (Table 1, entry 11, 12)

Table 1. Optimization study[a]



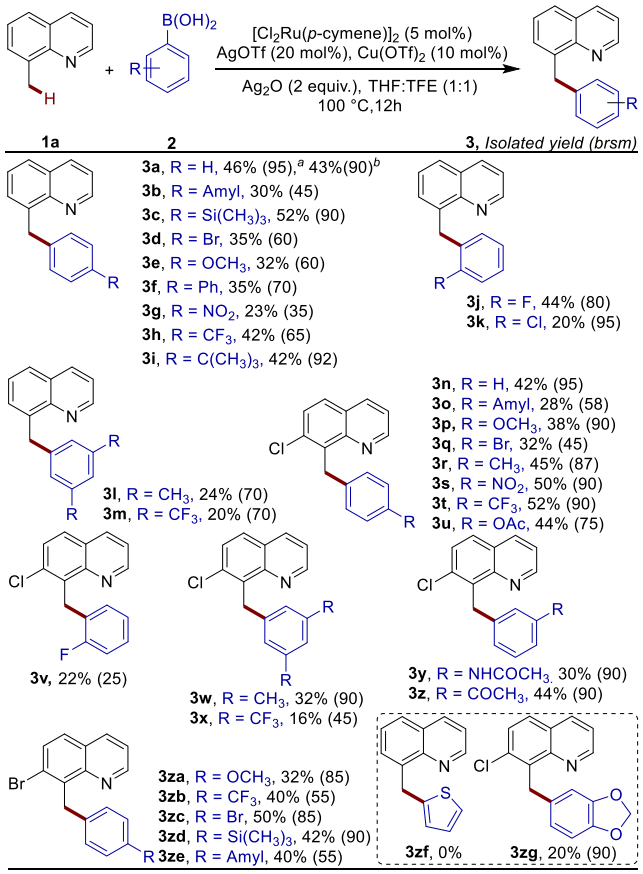
entry	variation in the standard condition	3a yield (%)
1	none	52[b] (95)
2	without $[Cl_2Ru(p\text{-cymene})]_2$	n.r.
3	without AgOTf	35[b]
4	without $Cu(OTf)_2$	31[b]
5	without Ag_2O	9[b]
6	THF instead of THF: TFE (1:1)	23[c]
7	air atmosphere	40[b]
8	at 120 ˚C instead of 100 ˚C	32[b]
9	at rt instead of 100 ˚C	21[b]
10	$CoCp^*(CO)I_2$ in place of $[Cl_2Ru(p\text{-cymene})]_2$	n.r.
11	24 h instead of 12 h	43[b]
12	48 h instead of 12h	42[b]

[a]reaction conditions: **1a** (0.1 mmol), **2a** (2.0 equiv.), $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%), Ag_2O (2 equiv.), THF:TFE (1:1) (0.5 mL) 100 ˚C, 24 h under inert atmosphere. [b]NMR yield (1,1,2,2-tetrachloroethane as an internal standard). [c]Isolated Yield. In parenthesis: Yield based on recovered starting material (brsm).

After establishing the optimal reaction conditions, to assess the generality of developed strategy several substituted phenyl boronic acids with 8-MQ were tested (Table 2). A range of *para*-substituted phenyl boronic acids with electron donating and electron withdrawing groups provided the mono-arylated products in yield up to 95% on the basis of recovered starting material (**3b-i**). Also, the *ortho*- and *meta*- substituted phenyl boronic acids furnished products in satisfactory yields and high selectivity. (**3j-m**). Therefore, in case of unsubstituted 8-MQ, selectively mono-arylated products were obtained which was not feasible in the previously reported protocol **(3a-m)**.[10g] We further examined the scope for 7-substituted 8-MQs with various substituted phenyl boronic acids. When 7-chloro-8-MQ was reacted with a range of *para*-substituted phenyl boronic acids, desired arylated products were obtained in good yields (**3n-u**). While *ortho*- and *meta*-substituted phenyl boronic acids also afforded the desired products (**3v-3z**). Similarly, 7-bromo-8-MQ also furnished the desired mono-arylated products with various *para*-substituted phenyl boronic acids in moderate yields (**3za-e**). Unfortunately, when the reaction of thiophen-2-ylboronic acid was conducted with 8-MQ, no arylated product was obtained and **1a** was recovered (**3zf**) whereas, benzo[*d*][1,3]dioxol-5-ylboronic acid provided the desired product with 7-chloro-8-MQ in low yield (**3zg**).

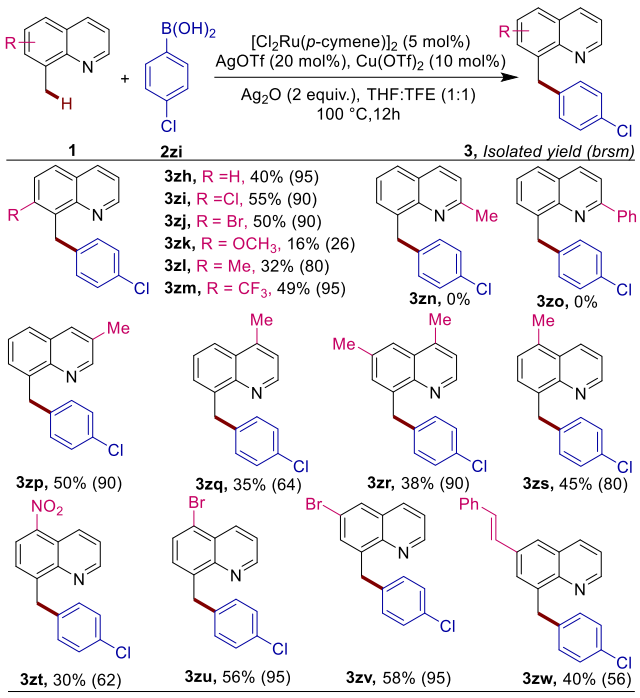
Scope of the reaction was further investigated by reacting different substituted 8-MQs with *para*-chloro phenylboronic acid to access diverse functionalized quinoline derivatives (Table 3). It was observed that substituents like -Cl, -Br, -OMe, -Me, CF_3 at C7 position of 8-MQ were well tolerable and provided the desired 7-substituted 8-benzyl quinolines in good yields (**3zh-m**). However, 2-methyl- and 2-phenyl-8-MQ didn't underwent the reaction which might be due to the steric hindrance (**3zn-o**). Methyl substituted 8-MQ at C3, C4, C5 and C6 position reacted smoothly with *para*-chloro phenyl boronic acid and afforded the desired products with yields up to 50% (**3zp-s**). The reaction of 5-nitro- and 5-bromo-8-MQ with *para*-chloro phenyl boronic acid afforded the products in acceptable yields **(3zt-u)** and 6-substituted 8-MQ with -Br and styrene were also amiable to provide the desired arylated products **(3zv-w)**.

Table 2. Substrate scope with phenyl boronic acids



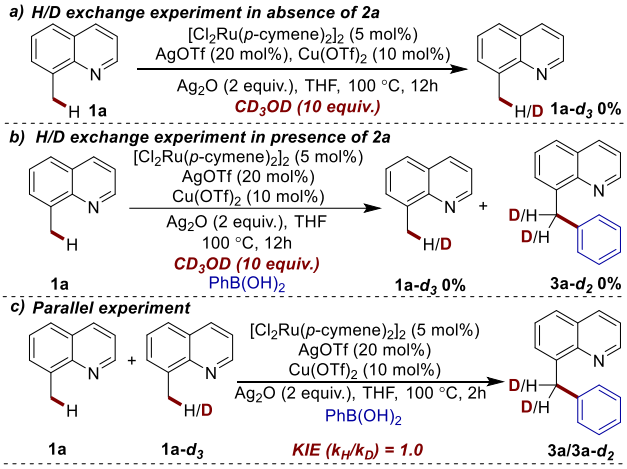
reaction conditions: **1** (0.2 mmol), **2** (2.0 equiv.), $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%), Ag_2O (2 equiv.), THF:TFE (1:1) (0.5 mL) 100 ˚C, 24 h under inert atmosphere. [b]Use of 2,4,6-triphenylboroxin instead of phenyl boronic acid. In parenthesis: Yield based on recovered starting material (brsm).

Table 3. Substrate scope with 8-methyl quinoline



reaction conditions: **1a** (0.2 mmol), **2i** (2.0 equiv.), $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%), Ag_2O (2 equiv.), THF:TFE (1:1) (0.5 mL) 100°C, 24 h under inert atmosphere. [b]NMR yield (1,1,2,2-tetrachloroethane as an internal standard). In parenthesis: Yield based on recovered starting material (brsm)

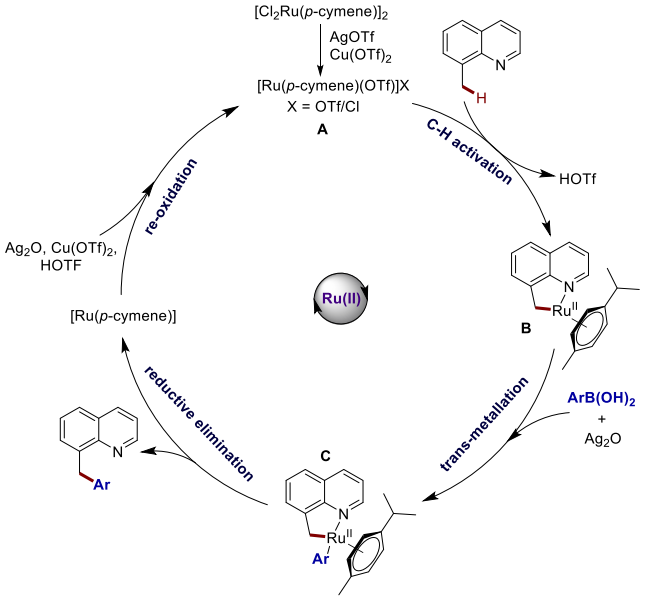
Scheme 2. Deuterium labelling experiments



Further, preliminary experiments to understand the mechanistic pathway of reaction were carried out. When deuterium labelling experiment was carried out without **2a** in the presence of CD_3OD, no deuterium incorporation was observed (Scheme 2a). When the same experiment was repeated with **2a,** 0% deuteration was observed in the recovered reactant as well as in the product. Both these experiments confirmed the irreversible nature of CH-activation step as well no formation of diarylated product (Scheme 2b). Next, competition and parallel experiments were performed by reacting the equimolar amount of **1a** and deuterated 8-MQ (**1a-*d*$_3$**) with **2a** for 2h. In both these experiments KIE value of 1.0 was observed (Scheme 2c-d) which confirmed that the C-H bond activation is not involved in the rate limiting step. In order to check the possibility of formation of Ru(0) nanoparticles, SEM analysis of crude reaction mixture was carried out however, no NPs were observed.

Based on the preliminary experiments we have performed and precedent literature,[13] a tentative mechanistic pathway for this coupling reaction was proposed (Scheme 3). The initial step likely involves the conversion of ruthenium catalyst to the active cationic ruthenium species **A** in the presence of AgOTf and $Cu(OTf)_2$. This active catalytic species reacts with **1a** to give intermediate **B** which undergoes transmetallation with arylboronic acid to afford the intermediate **C**. Reductive elimination from **C** results in the formation of desired arylated product and Ru(0) species which undergoes re-oxidation to generate the active species **A** for the continuation of the catalytic cycle.

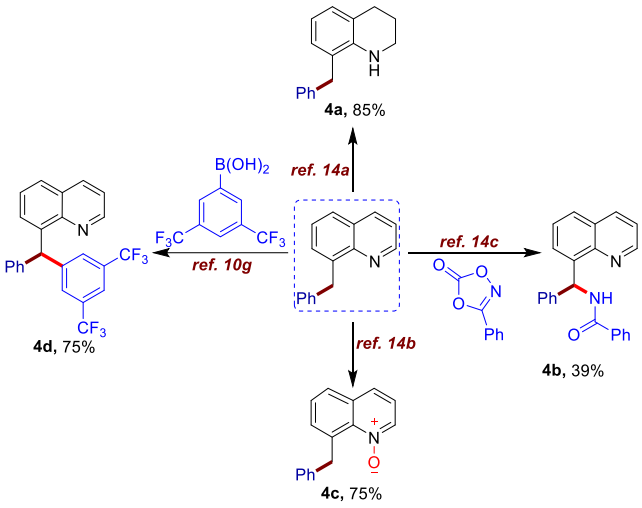
Scheme 3. Plausible mechanistic cycle



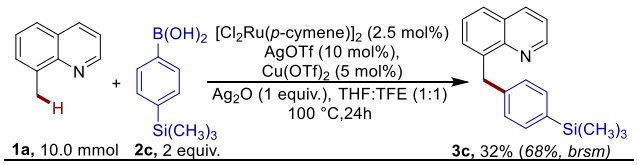
Next, the synthetic utility of arylated product **3a** was illustrated by subjecting it to different post transformation reactions (Scheme 4).[14] The reaction of **3a** was performed in the presence of Ni(II)-catalyst and $NaBH_4$ to obtain the corresponding reduced product (**4a**),[14a] whereas secondary C(sp^3)-H amidation was carried out with dioxazolone to obtain the amidated product (**4b**).[14c] Oxidation of **3a** was carried out with *m*-CPBA to synthesize corresponding *N*-oxide derivative (**4c**).[14b] Also, secondary C(sp^3)-arylation was carried out with phenylboronic acid to obtain the corresponding triarylmethane **(4d)**.[10g]

Gram scale experiment was carried out with 8-methyl quinoline (10.0 mmol) and 4-(Trimethylsilyl)phenylboronic acid (2.0 equiv.) using $[Cl_2Ru(p\text{-cymene})]_2$ (2.5 mol%), AgOTf (10 mol%), $Cu(OTf)_2$ (5 mol%) and Ag_2O (1 equiv.) in THF:TFE (1:1) 25mL at 100 °C for 24h under inert atmosphere. Arylated product was isolated in 32% (933 mg) yield. (Scheme 5)

Scheme 4. Synthetic utility of arylated product 3a



Scheme 5. Gram scale experiment



Conclusion

In summary, a catalytic method has been developed for the synthesis of 8-benzyl quinolines *via* direct regio- and chemo-selective C(sp^3)-H arylation with bench stable aryl boronic acids under cost effective Ru(II)-catalysis. This method provides access to broad array of 8-benzyl quinolines in moderate to good yields with easy recovery of the unreacted starting material.

EXPERIMENTAL SECTION

Reagent Information. All the reactions were performed under inert atmosphere in the screw cap reaction vials unless otherwise stated. All the solvents in sure-seal bottles and chemicals were bought from TCI and Sigma-Aldrich whereas silica gel (230-400 mesh) and C-18 reversed phase silica used for column chromatography were procured from Merck. For normal phase column chromatography, gradient elution using ethyl acetate : *n*-hexane and for reversed phase column chromatography. methanol : water was performed based on Merck aluminium TLC sheets (silica gel 60F254 and 60 RP-18 F_{254}s)

Analytical Information. For heating, IKA magnetic hot plate stirrers are used. Bronsted Electro thermal 9100 was used to record the melting point. For characterization of all the compounds, ^{1}H NMR, ^{13}C NMR, FTIR, LC-MS & HRMS were performed. Q-TOF-Micromass and maXis Impact mass spectrometers were used to perform the mass spectrometry of new compounds. Copies of ^{1}H, ^{13}C NMR are attached in the NMR supporting information. Shimadzu IR Prestige-21with ZnSe Single reflection ATR accessory was used to perform the IR spectroscopy of new compounds. Bruker-Avance 600 MHz instrument was used to perform the NMR of all the compounds. All ^{1}H and proton decoupled- ^{13}C NMR spectrums are reported in parts per million (ppm) units, and measured relative to the deuterated chloroform signal- 7.260 (for ^{1}H NMR) and 77.16 (for $^{13}C\{^1H\}$). Optimization studies were carried out with NMR yields calculated by using TCE (1, 1, 2, 2-tetrachloroethane) as internal standard.

Synthesis of substituted 8-methyl quinolines: Substituted 8-methyl quinolines **1n**, **1za**, **1zk**, **1zl**, **1zm**, **1zs**, **1zt**, **1zu**, and **1zv** were prepared by following the literature procedure, [15] compounds **1zn**, **1zo**, **1zp**, **1zq** and **1zw** were prepared by following the literature procedure, [16] and **1zr** was used from commercially available source.

General procedure for the arylation of 8-methyl quinolines with phenyl boronic acid: To a 10 mL oven-dried reaction vial-8-methylquinoline (0.2 mmol), phenyl boronic acid (0.4 mmol), $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%), Ag_2O (2 equiv.) and THF:TFE (1:1) 1.0 mL were added under argon atmosphere. The crude mixture was stirred at 100 °C for 12 h. Under reduced pressure, solvent was evaporated and the reaction mixture was directly purified by flash chromatography using silica gel (230−400 mesh size) and EtOAc : *n*-hexane as the eluent otherwise mentioned in reverse phase silica using MeOH : H_2O as eluent.

Characterization Data. *8-benzylquinoline (Table 2, Entry **3a**)*[10g] White solid, yield = 20 mg (46%). Mp = 51 – 53 ℃. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.15 (dd, J = 8.4, 1.8 Hz, 1H), 7.69 (dd, J = 7.2, 2.4 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.35 – 7.33 (m, 2H), 7.30 – 7.28 (m, 2H), 7.21 – 7.20 (m, 1H), 4.70 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 149.7, 146.9, 141.5, 140.3, 136.4, 129.6, 129.52, 129.51, 128.5, 126.5, 126.4, 126.0, 121.1, 36.9.

*8-(4-amylbenzyl)quinoline (Table 2, Entry **3b**)*[10g] Colourless liquid, yield = 17.3 mg (30%). Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ) : 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.15 (dd, J = 8.4, 1.8 Hz, 1H), 7.69 – 7.68 (m, 1H), 7.46 – 7.43 (m, 2H), 7.41 (dd, J = 8.4, 4.2 Hz, 1H), 7.24 (d, J = 7.2 Hz, 2H), 7.11 (d, J = 7.8 Hz, 2H), 4.67 (s, 2H), 2.57 (t, J = 7.8 Hz, 2H), 1.63 – 1.58 (m, 2H), 1.37 – 1.30 (m, 4H), 0.91 – 0.89 (m, 3H). $^{13}C\{^1H\}$NMR (150 MHz, $CDCl_3$, δ): 149.6, 146.9, 140.6, 140.5, 138.5, 136.4, 129.5, 129.3, 128.52, 128.50, 126.5, 126.3, 121.1, 36.5, 35.7, 31.7, 31.4, 22.7, 14.2.

*8-(4-(trimethylsilyl)benzyl)quinoline (Table 2, Entry **3c**)*[10g] Yellow solid, yield = 30.2 mg (52%). Mp = 92 – 95 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.98 – 8.97 (m, 1H), 8.15 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.71 – 7.68 (m, 1H), 7.46 – 7.45 (m, 4H), 7.42 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.33 (d, *J* = 7.2 Hz, 2H), 4.70 (s, 2H), 0.25 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.7, 146.9, 142.1, 140.2, 137.5, 136.4, 133.6, 129.6, 129.0, 128.5, 126.5, 126.4, 121.1, 36.9, -0.91.

*8-(4-bromobenzyl)quinoline (Table 2, Entry **3d**)*[10g] White solid, yield = 20.8 mg (35%). Mp = 44 – 46 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.95 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.70 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.47 – 7.43 (m, 2H), 7.41 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 4.63 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.7, 146.8, 140.6, 139.7, 136.4, 131.5, 131.2, 129.6, 128.6, 126.7, 126.5, 121.2, 119.8, 36.4.

*8-(4-methoxybenzyl)quinoline (Table 2, Entry **3e**)*[10g] Yellow liquid, yield = 15.9 mg (32%). Purification by flash chromatography (7% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 9.01 – 8.99 (m, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.69 – 7.67 (m, 1H), 7.46 (d, *J* = 6.0 Hz, 2H), 7.40 – 7.38 (m, 1H), 7.31 – 7.29 (m, 2H), 6.89 –7 6.8 (m, 2H), 4.69 (s, 2H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 157.9, 149.5, 146.7, 140.6, 136.3, 133.4, 130.3, 129.3, 128.4, 126.4, 126.2, 121.0, 113.8, 55.2, 36.0.

*8-([1,1'-biphenyl]-4-ylmethyl)quinoline (Table 2, Entry **3f**)* White solid, yield = 20.6 mg (35%). Mp = 90 – 92 °C. Purification by reverse silica C-18 (80% MeOH/H_2O). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 9.01 – 8.99 (m, 1H), 8.17 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.60 – 7.57 (m, 2H), 7.54 – 7.46 (m, 4H), 7.44 – 7.40 (m, 5H), 7.34 – 7.31 (m, 1H), 4.75 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.7, 146.9, 141.3, 140.7, 140.2, 138.9, 136.4, 129.9, 129.7, 128.8, 128.6, 127.2, 127.14, 127.10, 126.6, 126.5, 121.2, 36.6. IR (ZnSe) ν_{max} (cm^{-1}) 2960, 2922, 1689, 1494, 1485, 1469, 806, 792, 758. HRMS (ESI-TOF) (m/z) $[M + H]^+$ calcd for $C_{22}H_{18}N$ 296.1434; found, 296.1444.

*8-(4-nitrobenzyl)quinoline (Table 2, Entry **3g**)*[10g] Brown solid, yield = 12.1 mg (23%). Mp = 84 – 86 °C. Purification by flash chromatography (7% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.93 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.16 (dd, *J* = 8.4, 1.8 Hz, 1H), 8.10 – 8.08 (m, 2H), 7.75 – 7.74 (m, 1H), 7.51 – 7.45 (m, 4H), 7.43 (dd, *J* = 8.4, 4.2 Hz, 1H), 4.75 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.9, 149.7, 146.6, 146.4, 138.4, 136.5, 130.0, 129.9, 128.7 127.3, 126.5, 123.6, 121.4, 37.1.

*8-(4-(trifluoromethyl)benzyl)quinoline (Table 2, Entry **3h**)*[10g] White solid, yield = 24.1 mg (42%). Mp = 52 – 55 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.96 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.16 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.73 (dd, *J* = 6.6, 3.0 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.49 – 7.45 (m, 2H), 7.43 – 7.41 (m, 3H), 4.73 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.8, 146.7, 145.8, 139.2, 136.5, 129.7, 129.6, 128.6, 128.30 (q, J_{CF} = 31.5 Hz), 126.9, 126.5, 125.34 (q, J_{CF} = 3.0 Hz), 124.54 (q, J_{CF} = 270 Hz), 121.3, 36.9.

*8-(4-(tert-butyl)benzyl)quinoline (Table 2, Entry **3i**)* White solid, yield = 23.1 mg (42%). Mp = 83 – 85 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.12 (dd, J = 8.4, 1.8 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 7.8, 4.2 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 7.24 – 7.22 (m, 2H), 4.84 (s, 2H), 1.26 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 150.6, 148.5, 147.8, 137.7, 137.3, 136.2, 135.4, 128.6, 128.5, 127.2, 127.1, 125.1, 121.1, 34.4, 33.1, 31.5. IR (ZnSe) ν_{max} (cm^{-1}) 2954, 2924, 2910, 2866, 1653, 1595, 1498, 800, 788. HRMS (ESI-TOF) (m/z) $[M + H]^+$ calcd for $C_{20}H_{22}N$ 276.1747; found, 276.1751.

*8-(2-fluorobenzyl)quinoline (Table 2, Entry **3j**)*[10g] Colourless liquid, yield = 20.8 mg (44%). Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.98 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.70 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.46 – 7.44 (m, 2H), 7.41 (dd, *J* = 8.4 Hz, 4.2 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.21 – 7.18 (m, 1H), 7.09 – 7.06 (m, 1H), 7.05 – 7.02 (m, 1H), 4.74 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 161.47 (d, J_{CF} = 244.5 Hz), 149.6, 146.9, 138.8, 136.4, 131.90 (d, J_{CF} = 4.5 Hz), 129.3, 128.5, 128.23 (d, J_{CF} = 16.5 Hz), 127.85 (d, J_{CF} = 7.5 Hz), 126.6, 126.5, 124.05 (d, J_{CF} = 3.0 Hz), 121.1, 115.33 (d, J_{CF} = 21.0 Hz), 29.91 (d, J_{CF} = 3.0 Hz).

*8-(2-chlorobenzyl)quinoline (Table 2, Entry **3k**)* Yellow liquid, yield = 10.1 mg (20%). Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.17 (dd, J = 7.8, 1.8 Hz, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.45 – 7.41 (m, 3H), 7.32 (d, J = 7.2 Hz, 1H), 7.21 – 7.14 (m, 3H), 4.82 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.7, 146.9, 138.9, 138.5, 136.5, 134.7, 131.7, 129.6, 129.2, 128.5, 127.7, 126.9, 126.6, 126.5, 121.2, 34.5. IR (ZnSe) ν_{max} (cm^{-1}) : 2953, 2922, 2850, 1653, 1595, 1496, 806, 788, 742. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{16}H_{13}ClN$ 254.0731; found, 254.0731.

*8-(3,5-dimethylbenzyl)quinoline (Table 2, Entry **3l**)*[10g] White solid, yield = 11.8 mg (24%). Mp = 81 – 84 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.98 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.70 – 7.68 (m, 1H), 7.46 – 7.42 (m, 2H), 7.42 – 7.40 (m, 1H), 6.94 (s, 2H), 6.84 (s, 1H), 4.62 (s, 2H), 2.27 (s, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.6, 146.9, 141.3, 140.5, 137.9, 136.4, 129.6, 128.5, 127.7, 127.4, 126.5, 126.3, 121.1, 36.6, 21.4.

*8-(3,5-bis(trifluoromethyl)benzyl)quinoline (Table 2, Entry **3m**)*[10g] White solid, yield = 14.2 mg (20%). Mp = 49 – 50 °C. Purification by flash chromatography (5% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.95 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.18 – 8.16 (m, 1H), 7.82 (s, 2H), 7.77 – 7.75 (m, 1H), 7.68 (s, 1H), 7.53 – 7.49 (m, 2H), 7.43 (dd, *J* = 7.8 Hz, 4.2 Hz, 1H), 4.76 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, *δ*): 149.9, 146.6, 144.2, 138.2, 136.5, 131.46 (q, J_{CF} = 33.0 Hz), 129.7, 129.52 (q, J_{CF} = 4.5 Hz), 128.8, 127.4, 126.6, 123.61 (q, J_{CF} = 271.5 Hz), 121.5, 120.15 – 120.04 (m), 37.1.

*8-benzyl-7-chloroquinoline (Table 2, Entry **3n**)*[10g] White solid, yield = 21.2 mg (42%). Mp = 65 – 68 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, *δ*): 8.99 (d, *J* = 3.6 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.41 (dd, *J* = 8.4, 4.2 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.22 – 7.20 (m, 2H),

7.14 – 7.12 (m, 1H), 4.89 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.5, 147.5, 140.3, 137.3, 136.5, 135.7, 129.0, 128.6, 128.2, 127.3, 127.2, 126.0, 121.1, 33.6.

*7-chloro-8-(4-amylbenzyl)quinoline (Table 2, Entry **3o**)*[10g] Yellow solid, yield = 18.0 mg (28%). Mp = 40 – 42 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.12 (dd, J = 8.4, 1.8 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 9.0 Hz, 1H), 7.40 (dd, J = 8.4, 4.2 Hz, 1H), 7.24 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 7.8 Hz, 2H), 4.84 (s, 2H), 2.51 (t, J = 7.8 Hz, 2H), 1.57 – 1.54 (m, 2H), 1.31 – 1.27 (m, 4H), 0.88 – 0.85 (m, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.7, 140.4, 137.7, 137.5, 136.2, 135.4, 128.8, 128.5, 128.3, 127.2, 127.1, 121.1, 35.7, 33.2, 31.7, 31.3, 22.7, 14.2.

*7-chloro-8-(4-methoxybenzyl)quinoline (Table 2, Entry **3p**)*[10g] *Pale* yellow solid, yield = 21.5 mg (38%). Mp = 78 – 80 °C. Purification by flash chromatography (6% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.99 (dd, J = 4.2, 1.8 Hz, 1H), 8.10 (dd, J = 8.4, 1.8 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 9.0 Hz, 1H), 7.39 (dd, J = 7.8, 4.2 Hz, 1H), 7.32 – 7.29 (m, 2H), 6.80 – 6.77 (m, 2H), 4.82 (s, 2H), 3.74 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 157.8, 150.6, 147.7 137.8, 136.3, 135.3, 132.5, 130.0, 128.5, 127.2, 127.1, 121.1, 113.7, 55.3, 32.7.

*8-(4-bromobenzyl)-7-chloroquinoline (Table 2, Entry **3q**)*[10g] White solid, yield = 21.1 mg (32%). Mp = 99 – 101 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.97 (d, J = 4.2 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.65 (dd, J = 9.0, 1.8 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.41 – 7.39 (m, 1H), 7.32 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 4.81 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.7, 147.5, 139.4, 136.8, 136.3, 135.4, 131.2, 130.8, 128.4, 127.5, 127.2, 121.2, 119.7, 33.1.

*7-chloro-8-(4-methylbenzyl)quinoline (Table 2, Entry **3r**)*[10g] Yellow solid, yield = 24.0 mg (45%). Mp = 72 – 75 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.11 (dd, J = 8.4, 1.8 Hz, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 7.8, 4.2 Hz, 1H), 7.24 (d, J = 7.8 Hz, 2H), 7.03 (d, J = 7.8 Hz, 2H), 4.84 (s, 2H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.7, 137.7, 137.3, 136.2, 135.4, 135.3, 128.9, 128.9, 128.5, 127.2, 127.1, 121.1, 33.2, 21.1.

*7-chloro-8-(4-nitrobenzyl)quinoline (Table 2, Entry **3s**)*[10g] Pale yellow solid, yield = 29.8 mg (50%). Mp = 110 – 112 °C. Purification by flash chromatography (6% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.97 – 8.96 (m, 1H), 8.17 (dd, J = 7.8, 1.8 Hz, 1H), 8.07 – 8.05 (m, 2H), 7.72 (d, J = 9.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 9.6 Hz, 2H), 7.46 – 7.44 (m, 1H), 4.95 (s, 2H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.9, 148.3, 147.4, 146.4, 136.5, 135.8, 135.6, 129.8, 128.4, 128.0 127.3, 123.5, 121.5, 33.7

*7-chloro-8-(4-(trifluoromethyl)benzyl)quinoline (Table 2, Entry **3t**)* Brown crystalline solid, yield = 33.3 mg (52%). Mp = 66 – 68 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.97 (dd, J = 4.2, 1.8 Hz, 1H), 8.15 (dd, J = 8.4, 1.8 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 9.0 Hz, 1H), 7.46 – 7.42 (m, 5H), 4.91 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.8, 147.6, 144.5, 136.5, 136.4, 135.5, 129.3, 128.4, 128.21 (q, J_{CF} = 31.5 Hz), 127.7, 127.3, 125.16 (q, J_{CF} = 3.0 Hz), 124.52 (q, J_{CF} = 270.0 Hz), 121.3, 33.5. IR (ZnSe) ν_{max} (cm^{-1}) 2924, 1606, 1490, 1417, 1321, 1311, 1159, 1109, 1064, 1019, 933. HRMS (ESI-TOF) (m/z) $[M + H]^+$ calcd for $C_{17}H_{12}ClF_3N$ 322.0605; found, 322.0581.

*4-((7-chloroquinolin-8-yl)methyl)phenyl acetate (Table 2, Entry **3u**)*[10g] Yellow solid, yield = 27.3 mg (44%). Mp = 155 – 156 °C. Purification by flash chromatography (10% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.96 (dd, J = 4.2, 1.8 Hz, 1H), 8.14 (dd, J = 8.4, 1.8 Hz, 1H), 7.82 – 7.79 (m, 2H), 7.68 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 9.0 Hz, 1H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 4.91 (s, 2H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 198.0, 150.7, 147.6, 146.2, 136.5, 136.3, 135.6, 135.1, 129.2, 128.4, 128.4, 127.6, 127.2, 121.3, 33.7, 26.6.

*7-chloro-8-(2-fluorobenzyl)quinoline (Table 2, Entry **3v**)*[10g] White sticky, yield = 11.9 mg (22%). Purification by flash chromatography (3% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.94 (dd, J = 4.2, 1.8 Hz, 1H), 8.16 (dd, J = 8.4, 1.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.13 – 7.10 (m, 1H), 7.07 – 7.04 (m, 1H), 6.86 – 6.84 (m, 1H), 6.70 – 6.67 (m, 1H), 4.89 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 161.13 (d, J_{CF} = 243.0 Hz), 150.8, 147.9, 136.3, 136.0, 136.0, 129.74 (d, J_{CF} = 3.0 Hz), 128.4, 127.6, 127.38 (d, J_{CF} = 7.5 Hz), 127.1, 127.06 (d, J_{CF} = 15.0 Hz), 123.80 (d, J_{CF} = 3.0 Hz), 121.3, 115.06 (d, J_{CF} = 22.5 Hz), 26.38 (d, J_{CF} = 4.5 Hz).

*7-chloro-8-(3,5-dimethylbenzyl)quinoline (Table 2, Entry **3w**)*[10g] White solid, yield = 17.9 mg (32%). Mp = 76 – 78 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.99 – 8.98 (m, 1H), 8.13 – 8.12 (m, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.55 (d, J = 9.0 Hz, 1H), 7.40 (dd, J = 8.4, 4.2 Hz, 1H), 6.92 (s, 2H), 6.78 (s, 1H), 4.80 (s, 2H), 2.22 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.8, 140.1, 137.6, 137.5, 136.2, 135.6, 128.5, 127.7, 127.2, 127.1, 126.7, 121.1, 33.4, 21.5.

*8-(3,5-bis(trifluoromethyl)benzyl)-7 chloroquinoline (Table 2, Entry **3x**)*[10g] White solid, yield = 12.4 mg (16%). Mp = 124 – 127 °C. Purification by flash chromatography (3% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 7.86 (s, 2H), 7.72 (d, J = 9.0 Hz, 1H), 7.65 (s, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.45 (dd, J = 8.4, 4.2 Hz, 1H), 4.95 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.9, 147.3, 142.9, 136.5, 135.5, 135.4, 131.31 (q, J_{CF} = 33.0 Hz), 129.43 (q, J_{CF} = 3.0 Hz), 128.4, 128.1, 127.3, 123.60 (q, J_{CF} = 271.5 Hz), 121.5, 120.2 – 120.1 (m), 33.4.

*N-(3-((7-chloroquinolin-8-yl)methyl)phenyl)acetamide (Table 2, Entry **3y**)* Brown solid, yield = 18.6 mg (30%). Mp = 130 – 132 °C. Purification by flash chromatography (25% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 7.8, 4.2 Hz, 1H), 7.26 (d, J = 5.4 Hz, 1H), 7.17 – 7.14 (m, 1H), 7.09 (br s, 1H, N**H**), 7.06 (d, J = 7.8 Hz, 1H), 4.83 (s, 2H), 2.08 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 168.3, 150.7, 147.6, 141.2, 137.9, 137.1, 136.3, 135.6, 128.9, 128.5, 127.4, 127.2, 125.0, 121.2, 120.1, 117.7, 33.5, 24.7. IR (ZnSe) ν_{max} (cm^{-1}): 3288, 3253, 2922, 2852, 1653, 1589, 1489, 800 785. HRMS (ESI-TOF) (m/z): $[M + Na]^+$ calcd for $C_{18}H_{15}ClN_2NaO$ 333.0765; found, 333.0764.

*1-(3-((7-chloroquinolin-8-yl)methyl)phenyl)ethanone (Table 2, Entry **3z**)*[10g] White solid, yield = 25.9 mg (44%). Mp = 86 – 88 °C. Purification by flash chromatography (10% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.99 – 8.97 (m, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.00 (s, 1H), 7.73 (d, J = 7.2 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.43 – 7.41 (m, 1H), 7.29 – 7.26 (m, 1H), 4.91 (s, 2H), 2.53 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 198.5, 150.7, 147.6, 141.0, 137.2, 136.8, 136.4, 135.5, 133.8, 129.2, 128.5, 127.6, 127.3, 126.1, 121.3, 33.5, 26.8.

*7-bromo-8-(4-methoxybenzyl)quinoline (Table 2, Entry **3za**)* Yellow liquid, yield = 20.9 mg (32%). Purification by flash chromatography (10% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.97 (dd, J = 4.2, 1.8 Hz, 1H), 8.10 (dd, J = 8.4, 1.8 Hz, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 7.8, 4.2 Hz, 1H), 7.30 – 7.27 (m, 2H), 6.79 – 6.76 (m, 2H), 4.86 (s, 2H), 3.74 (s, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 157.8, 150.5, 147.7, 139.8, 136.3, 132.3, 131.3, 130.0, 127.6, 127.3, 126.3, 121.2, 113.6, 55.2, 35.4. IR (ZnSe) ν_{max} (cm^{-1}): 3032, 2964, 2922, 1653. 1600, 1581, 1487, 798, 785. HRMS (ESI-TOF) (m/z): [M + H]$^+$ calcd for $C_{17}H_{15}BrNO$ 328.0332; found, 328.0342.

*7-bromo-8-(4-(trifluoromethyl)benzyl)quinoline (Table 2, Entry **3zb**)* White crystalline, yield = 29.2 mg (40%). Mp = 72 – 74 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.95 (dd, J = 4.2, 1.8 Hz, 1H), 8.14 (dd, J = 8.4, 1.8 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.47 – 7.41 (m, 5H), 4.96 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.7, 147.7, 144.4, 138.5, 136.4, 131.3, 129.3, 128.20 (q, J_{CF} = 33.0 Hz), 127.9, 127.6, 126.6, 125.15 (q, J_{CF} = 4.5 Hz), 124.53 (q, J_{CF} = 271.5 Hz), 121.5, 36.2. IR (ZnSe) ν_{max} (cm^{-1}) 3010, 2924, 1612, 1593, 1588, 1489, 1427, 1315, 1163, 1064, 1056, 827, 792. HRMS (ESI-TOF) (m/z) [M + H]$^+$ calcd for $C_{17}H_{12}BrF_3N$ 366.0100; found, 366.0103.

*7-bromo-8-(4-bromobenzyl)quinoline (Table 2, Entry **3zc**)* White crystalline solid, yield = 37.7 mg (50%). Mp = 93 – 95 °C. Purification by flash chromatography (80% MeOH/H_2O). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.95 (dd, J = 4.2, 1.8 Hz, 1H), 8.13 (dd, J = 8.4, 1.8 Hz, 1H), 7.72 (d, J = 9.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.43 (dd, J = 8.4, 4.2 Hz, 1H), 7.32 – 7.30 (m, 2H), 7.19 – 7.18 (m, 2H), 4.84 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.62, 139.2, 138.9, 136.5, 131.4, 131.3, 130.8, 127.7, 127.6, 126.5, 121.4, 119.7, 35.8. IR (ZnSe) ν_{max} (cm^{-1}) 2924, 2864, 1589, 1485, 1099, 1047, 1010, 800, 786. HRMS (ESI-TOF) (m/z) [M + H]$^+$ calcd for $C_{16}H_{12}Br_2N$ 375.9331; found, 375.9334.

*7-bromo-8-(4-(trimethylsilyl)benzyl)quinoline (Table 2, Entry **3zd**)* Yellow solid, yield = 31.1 mg (42%). Mp = 74 – 76 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.95 (dd, J = 4.2, 1.8 Hz, 1H), 8.12 (dd, J = 8.4, 1.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 9.0 Hz, 1H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.37 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 4.91 (s, 2H), 0.20 (s, 9H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.9, 140.9, 139.4, 137.4, 136.3, 133.3, 131.3, 128.4, 127.6, 127.4, 126.5, 121.3, 36.3, -0.9. IR (ZnSe) ν_{max} (cm^{-1}) 3064, 3012, 2951, 1653, 1521, 1485, 1396, 1247, 1109, 837, 823, 800, 788, 750, 729. HRMS (ESI-TOF) (m/z) [M + H]$^+$ calcd for $C_{19}H_{21}BrNSi$ 370.0621; found, 370.0621.

*7-bromo-8-(4-amylbenzyl)quinoline (Table 2, Entry **3ze**)* Yellow liquid, yield = 29.3 mg (40%). Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.96 (dd, J = 4.2, 1.8 Hz, 1H), 8.12 (dd, J = 8.4, 1.8 Hz, 1H), 7.71 (d, J = 9.0 Hz, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.41 (dd, J = 8.4, 4.2 Hz, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 7.8 Hz, 2H), 4.87 (s, 2H), 2.50 (t, J = 7.8 Hz, 2H), 1.56-1.54 (m, 2H), 1.31 – 1.27 (m, 4H), 0.86 (t, J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.9, 140.4, 139.8, 137.3, 136.3, 131.4, 128.8, 128.3, 127.6, 127.3, 126.5, 121.3, 35.9, 35.7, 31.7, 31.3, 22.7, 14.2. IR (ZnSe) ν_{max} (cm^{-1}): 2956, 2924, 2850, 1653, 1602, 1589, 1558, 1485, 1361, 1121, 921, 837, 796. HRMS (ESI-TOF) (m/z): [M + H]$^+$ calcd for $C_{21}H_{23}BrN$ 368.1008; found, 368.1012.

*8-(benzo[d][1,3]dioxol-5-ylmethyl)-7-chloroquinoline (Table 2, Entry **3zg**)*[10g] Yellow solid, yield = 11.8 mg (20%). Mp = 84 – 87 °C. Purification by flash chromatography (5% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.98 (dd, J = 4.2, 1.8 Hz, 1H), 8.11 (dd, J = 8.4, 1.8 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 7.40 (dd, J = 8.4, 4.2 Hz, 1H), 6.86 – 6.83 (m, 2H), 6.68 (d, J = 8.4 Hz, 1H), 5.85 (s, 2H), 4.78 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.6, 147.6, 147.4, 145.7, 137.5, 136.3, 135.4, 134.2, 128.5, 127.2, 127.2, 122.0, 121.1, 109.7, 108.0, 100.8, 33.18.

*8-(4-chlorobenzyl)quinoline (Table 2, Entry **3zh**)*[10g] White solid, yield = 20.2 mg (40%). Mp = 51 – 53 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.96 (dd, J = 4.2, 1.8 Hz, 1H), 8.15 (dd, J = 8.4, 1.8 Hz, 1H), 7.70 (dd, J = 7.8, 1.8 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.42 (dd, J = 8.4, 4.2 Hz, 1H), 7.26 – 7.22 (m, 4H), 4.65 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 149.7, 146.8, 140.1, 139.8, 136.4, 131.8, 130.7, 129.6, 128.6, 128.5, 126.7, 126.5, 121.2, 36.4.

*7-chloro-8-(4-chlorobenzyl)quinoline (Table 2, Entry **3zi**)*[10g] White solid, yield = 15.8 mg (55%). Mp = 80 – 82 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.98 – 8.97 (m, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 9.0 Hz, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.43 – 7.41 (m, 1H), 7.27 (d, J = 6.6 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 4.82 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.7, 147.6, 138.9, 137.0, 136.3, 135.4, 131.6, 130.4, 128.5, 128.3, 127.5, 127.2, 121.3, 33.0.

*7-bromo-8-(4-chlorobenzyl)quinoline (Table 2, Entry **3zj**)* Yellow liquid, yield = 33.2 mg (50%). Mp = 80 – 82 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.98 – 8.97 (m, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.46 – 7.45 (m, 1H), 7.27 (d, J = 7.8 Hz, 2H), 7.18 (d, J = 7.2 Hz, 2H), 4.88 (s, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.7, 147.7, 139.0, 138.7, 136.4, 131.6, 131.3, 130.4, 128.3, 127.7, 127.6, 126.5, 121.4, 35.7. IR (ZnSe) ν_{max} (cm^{-1}) 2958, 2922, 2852, 1656, 1593, 1487, 1087, 1014, 829, 802. HRMS (ESI-TOF) (m/z) [M + H]$^+$ calcd for $C_{16}H_{12}BrClN$ 331.9836; found, 331.9837.

*8-(4-chlorobenzyl)-7-methoxyquinoline (Table 2, Entry **3zk**)* Brown solid, yield = 9.0 mg (16%). Mp = 99 – 101 °C. Purification by flash chromatography (10% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.92 (dd, J = 4.2, 1.8 Hz, 1H), 8.09 – 8.07 (m, 1H), 7.73 (d, J = 9.0 Hz, 1H), 7.34 (d, J = 9.0 Hz, 1H), 7.29 – 7.25 (m, 3H), 7.14 – 7.12 (m, 2H), 4.64 (s, 2H),

3.95 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 157.5, 150.6, 147.6, 140.8, 136.2, 131.1, 130.4, 128.1, 127.5, 124.7, 123.8, 119.0, 113.9, 56.5, 29.1. IR (ZnSe) ν_{max} (cm^{-1}) 2995, 2958, 2924, 2837, 1612, 1595, 1570, 1502, 1487, 1259, 1082, 823. HRMS (ESI-TOF) (m/z) $[M + Na]^+$ calcd for $C_{17}H_{14}ClNaNO$ 306.0656; found, 306.0656.

*8-(4-chlorobenzyl)-7-methylquinoline (Table 2, Entry **3zl**)* Yellow liquid, yield = 17.1 mg (32%). Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.93 (dd, J = 4.2, 1.8 Hz, 1H), 8.13 (dd, J = 7.8, 1.8 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.36 (dd, J = 8.4, 4.2 Hz, 1H), 7.15 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 4.75 (s, 2H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 149.9, 147.3, 139.7, 138.2, 136.3, 136.2, 131.3, 130.1, 129.9, 128.4, 126.9, 126.2, 120.3, 32.1, 20.6. IR (ZnSe) ν_{max} (cm^{-1}) 2947, 2924, 2858, 2837, 1614, 1598, 1570, 1502, 1489, 1454, 108, 1014, 827, 796, 788. HRMS (ESI-TOF) (m/z) $[M + H]^+$ calcd for $C_{17}H_{15}ClN$ 268.0888; found, 268.0886.

*8-(4-chlorobenzyl)-7-(trifluoromethyl)quinoline (Table 2, Entry **3zm**)* Yellow solid, yield = 31.4 mg (49%). Mp = 48 – 50 °C. Purification by reverse silica C-18 (80% MeOH/H_2O). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.99 – 8.97 (m, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.51 – 7.49 (m, 1H), 7.13 (d, J = 7.8 Hz, 2H), 7.00 (d, J = 7.8 Hz, 2H), 4.91 (s, 2H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 151.0, 147.0, 139.7, 139.1, 136.3, 131.4, 129.82, 129.6, 128.88 (q, J_{CF} = 16.5 Hz), 128.2, 127.5, 124.60 (q, J_{CF} = 273.0 Hz), 123.05 – 122.9 (m), 122.92, 32.3. ^{19}F NMR (565 MHz, $CDCl_3$) δ 58.28 IR (ZnSe) ν_{max} (cm^{-1}): 2951, 2924, 2852, 1653, 1602, 1489, 1319, 1300, 1107, 837, 798. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{17}H_{22}ClF_3N$ 322.0605; found, 322.0601.

*8-(4-chlorobenzyl)-3-methylquinoline (Table 2, Entry **3zp**)* Yellow solid, yield = 26.7 mg (50%). Mp = 70 – 72 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.80 (s, 1H), 7.91 (s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.43 – 7.40 (m, 1H), 7.36 (d, J = 7.2 Hz, 1H), 7.26 – 7.21 (m, 4H), 4.62 (s, 2H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 151.7, 145.0, 140.1, 139.4, 135.1, 131.7, 130.7, 130.6, 128.6, 128.5, 128.4, 126.6, 126.1, 36.4, 18.8. IR (ZnSe) ν_{max} (cm^{-1}) 2923, 2852, 1602, 1485, 1467, 1435, 1411, 812, 771. HRMS (ESI-TOF) (m/z): $[M + Na]^+$ calcd for $C_{17}H_{14}ClNaN$ 290.0707; found, 290.0706.

*8-(4-chlorobenzyl)-4-methylquinoline (Table 2, Entry **3zq**)* Yellow crystalline solid, yield = 18.7 mg (35%). Mp = 67 – 69 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.81 (d, J = 4.2 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.42 (d, J = 7.2 Hz, 1H), 7.26 – 7.21 (m, 5H), 4.65 (s, 2H), 2.71 (s, 3H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 149.4, 146.4, 140.22, 140.17, 137.9, 131.7, 130.7, 129.3, 128.6, 128.5, 126.2, 122.6, 122.1, 36.7, 19.1. IR (ZnSe) ν_{max} (cm^{-1}): 3037, 2954, 2922, 2852, 1653, 1600, 1489, 1082, 1010, 839, 758. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{17}H_{15}ClN$ 268.0888; found, 268.0887.

*8-(4-chlorobenzyl)-4,6-dimethylquinoline (Table 2, Entry **3zr**)* Yellow crystalline solid, yield = 21.4 mg (38%). Mp = 80 – 82 °C. Purification by flash chromatography y (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.74 (d, J = 4.2 Hz, 1H), 7.65 (s, 1H), 7.26 – 7.20 (m, 6H), 4.61 (s, 2H), 2.68 (s, 3H), 2.49 (s, 3H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 148.5, 145.0, 143.7, 140.3, 139.8, 135.9, 131.6, 131.5, 130.7, 128.6, 128.5, 122.1, 121.6, 36.6, 22.1, 19.1. IR (ZnSe) ν_{max} (cm^{-1}) 2927, 2850, 1653, 1589, 1570, 1489, 1433, 1085, 1016, 866. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{18}H_{17}ClN$ 282.1044; found, 282.1045.

*8-(4-chlorobenzyl)-5-methylquinoline (Table 2, Entry **3zs**)* Brown crystalline solid, yield = 24.0 mg (45%). Mp = 60 – 62 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.95 (dd, J = 4.2, 1.8 Hz, 1H), 8.32 (dd, J = 8.4, 1.8 Hz, 1H), 7.45 – 7.43 (m, 1H), 7.23 (dd, J = 22.2, 7.2 Hz, 2H), 7.25 – 7.21 (m, 4H), 4.61 (s, 2H), 2.66 (s, 3H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 149.2, 147.0, 140.3, 137.7, 133.2, 132.8, 131.6, 130.7, 129.2, 128.5, 127.9, 126.9, 120.8, 36.6, 18.7. IR (ZnSe) ν_{max} (cm^{-1}): 3032, 2964, 2927, 2845, 1653, 1598, 1489, 1471, 1082, 1014, 800, 785. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{17}H_{15}ClN$ 268.0888; found, 268.0887.

*8-(4-chlorobenzyl)-5-nitroquinoline (Table 2, Entry **3zt**)* Yellow crystalline solid, yield = 17.9 mg (30%). Mp = 88 – 90 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 9.06 – 9.03 (m, 2H), 8.29 (d, J = 8.4 Hz, 1H), 7.66 (dd, J = 9.0, 4.2 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.26 – 7.23 (m, 4H), 4.70 (s, 2H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.7, 148.1, 146.3, 138.4, 132.44, 132.38, 130.8, 128.9, 127.5, 124.7, 124.0, 121.5, 37.1. IR (ZnSe) ν_{max} (cm^{-1}) 2920, 2850, 1595, 1514, 1492, 1400, 1336, 1089, 1014, 769, 788. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{16}H_{12}ClN_2O_2$ 299.0582; found, 299.0597.

*5-bromo-8-(4-chlorobenzyl)quinoline (Table 2, Entry **3zu**)* White crystalline solid, yield = 37.2 mg (56%). Mp = 76 – 78 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.96 (dd, J = 4.2, 1.8 Hz, 1H), 8.55 (dd, J = 8.4, 1.8 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.52 (dd, J = 8.4, 4.2 Hz, 1H), 7.30 (d, J = 7.8 Hz, 1H), 7.23 (t, J = 9.6 Hz, 4H), 4.59 (s, 2H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.3, 147.4, 140.0, 139.5, 135.9, 132.0, 130.7, 130.3, 129.9, 128.6, 127.8, 122.4, 120.3, 36.3. IR (ZnSe) ν_{max} (cm^{-1}) 3035, 2927, 2852, 1656, 1591, 1558, 1489, 1031, 1014, 800, 786. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{16}H_{12}BrClN$ 331.9836; found, 331.9836.

*6-bromo-8-(4-chlorobenzyl)quinoline (Table 2, Entry **3zv**)* White crystalline solid, yield = 38.5 mg (58%). Mp = 84 – 86 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.95 – 8.94 (m, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.86 (s, 1H), 7.50 (s, 1H), 7.43 (dd, J = 7.8, 4.2 Hz, 2H), 7.25 (s, 4H), 4.59 (s, 2H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 150.0, 145.4, 142.2, 139.1, 135.4, 132.8, 132.1, 130.7, 129.7, 128.7, 128.6, 122.1, 120.5, 36.1. IR (ZnSe) ν_{max} (cm^{-1}) 2939, 2924, 2854, 1656, 1587, 1558, 1483, 1429, 1359, 1089, 1016, 864, 846, 810, 785. HRMS (ESI-TOF) (m/z): $[M + Na]^+$ calcd for $C_{16}H_{11}BrClNaN$ 353.9656; found, 353.2714.

*(E)-8-(4-chlorobenzyl)-6-styrylquinoline (Table 2, Entry **3zw**)* White solid, yield = 28.4 mg (32%). Mp = 140 – 142 °C. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^1H NMR (600 MHz, $CDCl_3$, δ): 8.89 (dd, J = 4.2, 1.8 Hz, 1H), 8.13 (dd, J = 7.8, 1.8 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.55 (d, J = 7.2 Hz, 2H), 7.41 – 7.37 (m, 3H), 7.30 – 7.25 (m, 5H), 7.23 – 7.16 (m, 2H), 4.66 (s, 2H) $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, δ): 149.5, 146.6, 139.9, 137.1, 136.3, 135.4, 131.8, 130.7, 130.2,

129.0, 128.9, 128.6, 128.96, 128.89, 127.6, 126.8, 124.7, 121.7, 36.5. IR (ZnSe) ν_{max} (cm^{-1}) 3026, 2964, 2821, 1510, 1489, 1375, 1226, 1217, 1043, 9568, 889, 806. HRMS (ESI-TOF) (m/z): $[M + Na]^+$ calcd for $C_{24}H_{18}ClNNa$ 378.1020; found, 378.1019.

General procedure for the synthesis of ***1a-d3****:* To a 10 mL reaction vial- $[Cl_2RhCp^*]_2$ (2.5 mol%) $Cu(OAc)_2$ (2.0 equiv.) & AcOD (1.0 equiv.), 8-methylquinoline (0.1 mmol), D_2O were added and stirred at 100 °C for 20 h. The crude mixture was extracted with EtOAc and purified using flash chromatography, silica gel (230−400 mesh size) and EtOAc : *n*-hexane as eluent. Product with 92% deuteration on the benzylic C(sp^3)-H of 8-methyl quinoline was obtained.

General procedure for the synthesis of 8-benzyl-1,2,3,4-tetrahydroquinoline (Scheme 4, entry ***4a****)*:[14a] To a 10 mL reaction vial- 8-benzyl quinoline (0.2 mmol) $NiCl_2.6H_2O$ (10 mol%) in MeOH (1.0 mL), followed by the addition of $NaBH_4$ (40 equiv.) in portions with stirring at 0 °C for 0.5 h. The stirring was continued further for another 2h. The crude mixture was filtered through the celite pad and filterate was purified using flash chromatography, silica gel (230−400 mesh size), (2% EtOAc/*n*-hexane) as eluent. White solid, yield = 38 mg (85%). Mp = 55 – 57 ℃. Purification by flash chromatography (2% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 7.33 – 7.30 (m, 2H), 7.27 – 7.20 (m, 3H), 6.93 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.65 – 6.62 (m, 1H), 3.84 (s, 2H), 3.62 (s, 1H), 3.25 (t, *J* = 5.4 Hz, 2H), 2.82 – 2.80 (m, 2H), 1.93 – 1.90 (m, 2H) ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 142.8, 139.6, 129.7, 128.7, 128.74, 128.70, 128.5, 128.2, 126.4, 124.0, 121.8, 116.6, 42.4, 37.8, 27.5, 22.1. IR (ZnSe) ν_{max} (cm^{-1}) 2924, 2835, 1597, 1492, 1475, 1444, 1431, 1375, 1315, 1265, 765, 734, 698. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{16}H_{18}N$ 224.1434; found, 224.1433.

General procedure for the synthesis of (S)-N-(phenyl(quinolin-8-yl)methyl)benzamide (Scheme 4, entry ***4b****)*:[14c] To a 10 mL reaction vial- 8-benzyl quinoline (0.2 mmol), dioxazolone (1.2 equiv.), $[Cp^*RhCl_2]_2$ (4 mol%), $AgSbF_6$ (16 mol%), H_2-BHTL (8 mol%) were added in DCM (1.0 mL) with stirring at 80 °C for 5 h. The product was purified using flash chromatography, silica gel (230−400 mesh size), (2% EtOAc/*n*-hexane) as eluent. White solid, yield = 26.4 mg (39%). Mp = 185 – 187 ℃. Purification by flash chromatography (8% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 10.03 (d, *J* = 9.0 Hz, 1H), 8.91 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.21 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 2H), 7.87 (d, *J* = 7.2 Hz, 1H), 7.81 (dd, *J* = 0.6, 7.8 Hz, 1H), 7.58 – 7.56 (m, 1H), 7.50 –7.47 (m, 1H), 7.44 – 7.42 (m, 3H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.22 (t, *J* = 7.8 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 9.0 Hz, 1H).^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 166.4, 149.3, 146.6, 143.0, 137.7, 137.2, 135.0, 131.4, 130.6, 129.5, 128.6, 128.3, 128.2, 127.3, 127.0, 126.9, 126.7, 121.2, 57.9. IR (ZnSe) ν_{max} (cm^{-1}) 1714, 1651, 1512, 1481, 1467, 1346, 804, 790, 763, 717, 694. HRMS (ESI-TOF) (m/z): $[M + H]^+$ calcd for $C_{23}H_{19}N_2O$ 339.1492; found, 339.1497.

General procedure for the synthesis of 8-benzylquinoline 1-oxide (Scheme 4, entry ***4c****)*:[14b] To a 10 mL reaction vial- 8-benzyl quinoline (0.2 mmol) and *m*-CPBA (3.0 equiv.) were added in (1.0 mL) DCM with stirring at rt for 24h. The product was purified using flash chromatography, silica gel (230−400 mesh size), (90% EtOAc/*n*-hexane) as eluent. Sticky brown, yield = 35.3 mg (75%). Purification by flash chromatography (100% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.43 (d, *J* = 6.0 Hz, 1H), 7.71 (dd, *J* = 17.4, 7.8 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.28 – 7.26 (m, 2H), 7.22 – 7.20 (m, 3H), 7.17 (t, *J* = 7.2 Hz, 1H), 5.08 (s, 2H) ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 142.0, 140.8, 138.0, 135.7, 134.3, 132.8, 129.1, 128.5, 128.3, 127.8, 127.1, 125.9, 120.8, 41.9. IR (ZnSe) ν_{max} (cm^{-1}) 3059, 3024, 2922, 1653, 1600, 1570, 1558, 1492, 1421, 1382, 1300, 1270750, 696. HRMS (ESI-TOF) (m/z): $[M + Na]^+$ calcd for $C_{16}H_{13}NNaO$ 258.0889; found, 258.0887.

General procedure for the synthesis of 8-((3,5-bis(trifluoromethyl)phenyl)(phenyl)methyl)quinoline (Scheme 4, entry ***4d****)*:[10g] To a 10 mL reaction vial- 8-benzyl quinoline (0.2 mmol), 3,5-bis(trifluoromethyl)phenyl boronic acid (3.0 equiv.), $[Cp^*RhCl_2]_2$ (5 mol%), Tf_2O (10 mol%) were added in DCE (1.0 mL) with stirring at 100 °C for 24h. The arylated product was purified using flash chromatography, silica gel (230−400 mesh size), (2% EtOAc/*n*-hexane) as eluent. Yellow liquid, yield = 64.7 mg (75%). Purification by flash chromatography (3% EtOAc/*n*-hexane). ^{1}H NMR (600 MHz, $CDCl_3$, δ): 8.89-8.87 (m, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.73 (s, 1H), 7.65 (d, *J* = 3.0 Hz, 2H), 7.53 – 7.50 (m, 1H), 7.41 (d , *J* = 8.4, 4.2 Hz, 1H), 7.35 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 7.22 (d, J = 3.0 Hz, 1H), 7.17 – 7.15 (m, 2H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, δ): 150.0, 147.3, 146.1, 142.6, 141.1, 136.5, 131.45 (q, J_{CF} = 33 Hz), 131.3, 130.3, 129.71-129.75 (m), 129.7, 128.8, 128.7, 127.5, 127.0, 126.4, 123.57 (q, J_{CF} = 270 Hz), 121.6, 120.38-120.45 (m), 50.03.

Deuterium Labelling Experiment with 8-Methylquinoline (1a) (Scheme 2a). To a 10 mL reaction vial- $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%), AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%) & Ag_2O (2.0 equiv.) were added followed by the addition of 8-methylquinoline (0.1 mmol), CD_3OD (10 equiv.), THF (0.5 mL) under argon atmosphere and stirred at 100 °C for 12h. The crude reaction mixture was analyzed by ^{1}H NMR. 0% deuteration was observed.

Deuterium Labelling Experiment with 8-Methylquinoline (1a) and phenyl boronic acid (2a) (Scheme 2b). To a 10 mL reaction vial- phenylboronic acid (2.0 equiv.), $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%) AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%) & Ag_2O (2.0 equiv.) were added followed by the addition of 8-methylquinoline (0.1 mmol), CD_3OD (10.0 equiv.), THF (0.5 mL) under argon atmosphere and stirred at 100 °C for 12h. The crude reaction mixture was analyzed by ^{1}H NMR. No deuteration was observed on the benzylic C(sp^3)-H of 8-methyl quinoline and benzylic C(sp^3)-H of 8-benzyl quinoline.

Parallel Reaction for KIE Study (Scheme 2c). To a 10 mL reaction vial- $[Cl_2Ru(p\text{-cymene})]_2$ (5 mol%) AgOTf (20 mol%), $Cu(OTf)_2$ (10 mol%) & Ag_2O (2.0 equiv.) were added followed by the addition of 8-methylquinoline (0.1 mmol), THF (0.5 mL) under argon atmosphere. In another reaction vial 8-methyl quinoline-d_3 (0.1 mmol) was used instead of 8-methyl quinoline. The two-reaction mixtures were allowed to stir at 100 ℃ for 2 h. Both reaction mixtures were analyzed through ^{1}HNMR using TCE (0.10 mmol) as an internal standard and the calculated kinetic isotope effect value (k_H/k_D) equal to 1.0 was found.

Competition Reaction for KIE Study (Scheme 2d). To a 10 mL reaction vial- phenylboronic acid (0.4 mmol), $[Cl_2Ru(p$-

cymene)]$_2$ (5 mol%) AgOTf (20 mol%), Cu(OTf)$_2$ (10 mol%) & Ag_2O (2.0 equiv.) were added followed by the addition of 8-methylquinoline (0.1 mmol), 8-methyl quinoline-d_3 (0.1 mmol), THF (1.0 mL) under argon atmosphere and stirred at 100 °C for 2h. Firstly, 1H NMR of the crude mixture was performed and then it was purified by flash chromatography to obtain the arylated product using silica gel (230−400 mesh size) and EtOAc : *n*-hexane as the eluent. The kinetic isotope effect value (P_H/P_D) equal to 1.0 was found.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, details of optimization studies, characterization data for all synthesized compounds including ^{1}H and ^{13}C spectra. FAIR Data is available as Supporting Information for Publication and includes the primary NMR FID files for compounds **3a-3z**, **3za-3zw**, **4a-4d.**

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Notes

The authors declare no competing financial interests

ACKNOWLEDGMENT

We are thankful to the Director, CSIR-IHBT for continuous inspiration. The work described in this manuscript is financially supported by CSIR (MLP0154/MLP0159). DP and RK acknowledge UGC and CSIR for scholarship. Communication no. provided by CSIR-IHBT for this manuscript is 4610.

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