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Quinoline Synthesis

Three-Component Povarov Reaction with Alcohols as Alkene Precursors: Efficient Access to 2-Arylquinolines

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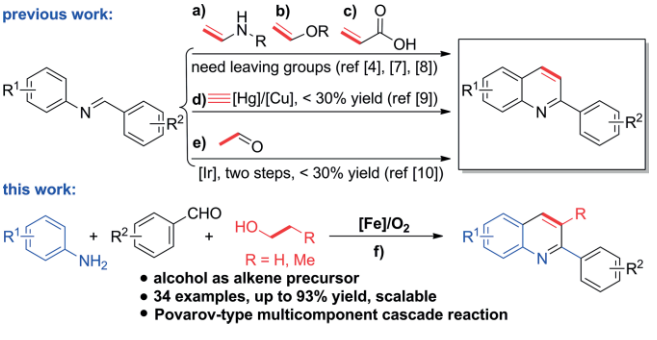
Abstract: An atom-economic and efficient approach to the synthesis of 2-arylquinolines has been developed. The protocol involves an iron-catalysed cascade *N*-alkylation/aerobic oxidation/Povarov reaction, and the desired quinolines were prepared in moderate to excellent yields from readily accessible anilines, aldehydes, and EtOH/*n*PrOH, with water as the only side-product. The aniline substrates also act as a recyclable transfer medium for EtOH/*n*PrOH through an in-situ *N*-alkylation/oxidation process. This makes EtOH/*n*PrOH an economical and environmentally friendly precursor of alkenes as well as the solvent.

Introduction

Multicomponent cascade reactions are powerful protocols that allow the synthesis of series of complex heterocycles.[1] Among these domino processes, the Povarov-type reaction represents an elegant method for the construction of the quinoline skeleton.[2] This transformation involves: 1) imine formation from an aniline and a carbonyl compound; 2) Mannich-type reaction of the imine with an activated alkene; 3) intramolecular aromatic electrophilic substitution and subsequent oxidation to give the quinoline nucleus. This process is compatible with a range of anilines and carbonyl derivatives, and over the years much effort has been put into expanding the range of activated olefin substrates that can be used in the reaction.[3] To date, alkynes, aldehydes, and α-keto esters have also been successfully used in this reaction in place of alkenes.[4] However, these methods generally provide 3- or 4-substituted quinolines. In contrast, research related to the synthesis of quinolines substituted at the 2-position but unsubstituted at the 3- and 4-positions remains rare.[5] Since the substitution patterns on quinoline rings have a great influence on the properties of these compounds,[6] the development of new and efficient methods for the preparation of differently substituted quinolines, based on the ideas of high efficiency and atom economy, is highly desirable.

For several of these rare reports of the synthesis of 2-substituted quinolines, electron-rich vinyl ethers and enamines bearing leaving groups were needed as starting materials (Scheme 1a and b).[7] Recently, Jiang and coworkers achieved the construction of 2-substituted quinolines from arylamines, aldehydes, and electron-deficient acrylic acid through a palladium-catalysed reaction involving a decarboxylation process (Scheme 1c).[8] Furthermore, as early as in 1938, acetylene was used in place of alkenes for the construction of 2-substituted quinolines, with a copper or mercury catalyst, although low yields were obtained (Scheme 1d).[9] Recently, Shimizu et al. reported an iridium-catalysed two-step cyclization/oxidation reaction with acetaldehyde as the alkene surrogate, which gave 2-substituted quinolines in quite low yields (Scheme 1e).[10a] Very recently, alcohols were successfully used as the precursors for aldehydes by Khusnutdinov's group in the synthesis of 2-phenylquinolines; an argon atmosphere was needed, and only three examples were reported.[10b] Despite the progress that has been made in the synthesis of 2-substituted quinolines, the reactions suffer from low yields, and require precious or toxic metal catalysts and/or activated alkene substrates bearing leaving groups. Therefore, there is still a need to explore the use of greener and more atom-economical starting materials as well as efficient catalyst systems to avoid these drawbacks.



Scheme 1. Synthesis of 2-arylquinolines.

Alcohols are easily available, and have been widely used for the synthesis of alkenes. Based on previous elegant work on quinoline synthesis, we wondered whether we could construct quinolines from easily accessible anilines, aldehydes, and alco-

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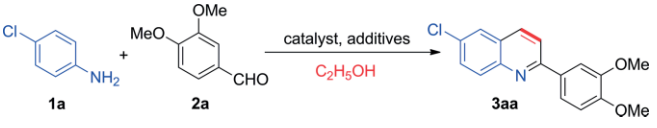
hols through a Povarov-type multicomponent reaction, in which the alcohols act as green and efficient precursors for alkenes. C–N bond construction between amines and alcohols has been intensively investigated, and great successes have been achieved.[11] Inspired by this, we assumed that in-situ C–N-bond coupling between anilines and alcohols and subsequent oxidation might provide an indirect route for the construction of electron-rich enamines, which could be used as the alkene components for the Povarov-type reaction to construct the corresponding quinoline skeleton. The aniline leaving group would return to the reaction system for another circulation; this could simultaneously avoid the waste generated through the use of traditional leaving groups and also the preparation of activated alkenes. As we know, iron, an inexpensive, abundant, and nontoxic metal, offers a wide range of oxidation and spin states.[12] These features make it a potential catalyst for oxidation through single-electron catalysis under an oxygen atmosphere.[13] In a continuation of our previous research into heterocycle synthesis, in this paper we report an iron-catalysed aerobic oxidative Povarov reaction for quinoline synthesis from anilines, aldehydes, and alcohols (Scheme 1f). In this reaction, alcohols were used as precursors of alkenes for the first time, and good results were achieved.

Results and Discussion

Initially, the reaction of *p*-chloroaniline (**1a**) and 3,4-dimethoxybenzaldehyde (**2a**) in ethanol was chosen as a model reaction to optimize the reaction conditions. To our delight, when substrates **1a** and **2a** were treated with $FeCl_3·6H_2O$ (10 mol-%) in ethanol under an oxygen atmosphere, the desired product **3aa** was obtained in 24 % yield (Table 1, entry 1). On the basis of previous work on *N*-alkylation, we assumed that the aromatic amine could react with the alcohol to give an *N*-alkyl amine derivative with the assistance of acid and halide anions. So we mixed **1a** with a catalytic amount (20 mol-%) of *p*-toluenesulfonic acid (PTSA) and KI in ethanol, and a 32 % yield of 4-chloro-*N*-ethylaniline was isolated, along with a trace amount of 4-chloro-*N*,*N*-diethylaniline (Equation S2 in the Supporting Information). Encouraged by this result, we added PTSA (20 mol-%) and KI (20 mol-%) to the reaction system, and the yield increased dramatically from 24 to 81 % (Table 1, entry 2). Significantly diminished yields were obtained in the absence of PTSA or KI; this indicates that acid and KI are both essential for this transformation (Table 1, entries 3 and 4). Furthermore, a control experiment was carried out without the iron catalyst, and the desired product was formed in poor yield (Table 1, entry 5). Subsequently, several metal salts were investigated to examine their catalytic efficiency in the reaction. When iron salts with different anions were used, such as $Fe(acac)_3$, $Fe(OTf)_3$, or $Fe(OTf)_2$, yields of **3aa** of only 9–14 % were obtained; while a moderate yield was obtained with $FeCl_2$ as the catalyst (Table 1, entries 6–9). Thus, the anion component of the iron salt has a pronounced effect on its catalytic performance. Significantly, under similar reaction conditions, other metal salts such as $CuCl_2$, $AlCl_3$, and $ZnCl_2$ all showed lower reactivities, and yields of **3aa** of only 10–16 % were obtained (Table 1, entries 10–12). Next, we studied the influence of different halide species. NaI and I_2 gave yields similar to that obtained with KI, but TBAI (tetrabutylammonium iodide) and KBr proved to be less efficient (Table 1, entries 13–16). TfOH also gave an efficient reaction, while the use of TFA (trifluoroacetic acid) caused a slight decrease in the yield (Table 1, entries 17 and 18). In addition, lowering the reaction temperature to 120 °C resulted in a decreased yield (Table 1, entry 19). It is notable that the reaction could also be smoothly carried out under an air atmosphere, although this gave a slightly lower yield (Table 1, entry 20).

Table 1. Optimization of reaction conditions.[a]



Entry	Metal catalyst	Acid	Halide salt	Yield [%]
1	$FeCl_3·6H_2O$	–	–	24
2	$FeCl_3·6H_2O$	PTSA	KI	81 (81)[b]
3	$FeCl_3·6H_2O$	PTSA	–	48
4	$FeCl_3·6H_2O$	–	KI	26
5	–	PTSA	KI	17
6	$Fe(acac)_3$	PTSA	KI	9
7	$Fe(OTf)_3$	PTSA	KI	14
8	$Fe(OTf)_2$	PTSA	KI	14
9	$FeCl_2$	PTSA	KI	58
10	$CuCl_2$	PTSA	KI	10
11	$AlCl_3$	PTSA	KI	16
12	$ZnCl_2$	PTSA	KI	14
13	$FeCl_3·6H_2O$	PTSA	NaI	81
14	$FeCl_3·6H_2O$	PTSA	I_2	78
15	$FeCl_3·6H_2O$	PTSA	TBAI	52
16	$FeCl_3·6H_2O$	PTSA	KBr	31
17	$FeCl_3·6H_2O$	TfOH	KI	81
18	$FeCl_3·6H_2O$	TFA	KI	71
19[c]	$FeCl_3·6H_2O$	PTSA	KI	52
20[d]	$FeCl_3·6H_2O$	PTSA	KI	77

[a] Reaction conditions: **1a** (0.66 mmol), **2a** (0.30 mmol), catalyst (10 mol-%), acid (20 mol-%), halide salt (20 mol-%), ethanol (3 mL), oxygen atmosphere (1 atm), 140 °C, 12 h. HPLC yields. [b] Isolated yield. [c] 120 °C. [d] 1 atm air was used instead of O_2. TFA = trifluoroacetic acid.

With optimal reaction conditions identified, we went on to investigate the scope of the reaction. We first investigated the scope of the reaction with respect to the aldehyde component. As shown in Scheme 2, the reaction of 4-chloroaniline with unsubstituted benzaldehyde proceeded smoothly, giving **3ab** in 63 % yield. For substituted benzaldehydes, both electron-donating (-Me, -OMe, -*t*Bu) and electron-withdrawing (-Cl, -Br, $-NO_2$) substituents on the benzene ring of benzaldehyde derivatives were well tolerated under the standard conditions, giving the desired products **3ac**–**3ai** in moderate to good yields. For example, *p*-methoxybenzaldehyde underwent the reaction smoothly, providing **3ad** in yields as high as 93 %. The sterically hindered 2-methoxybenzaldehyde also reacted with 4-chloroaniline to give the corresponding product **3af** in 72 % yield. To our delight, the strongly electron-withdrawing nitro group was also well tolerated, and **3ai** was formed in 72 % yield. Notably, benzaldehyde substituted with an active halogen group (-Br) gave the corresponding halogen-substituted 2-phenylquinoline

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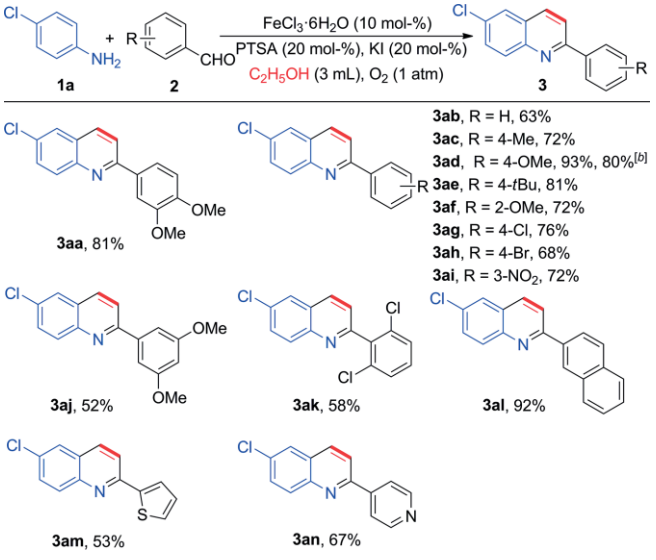
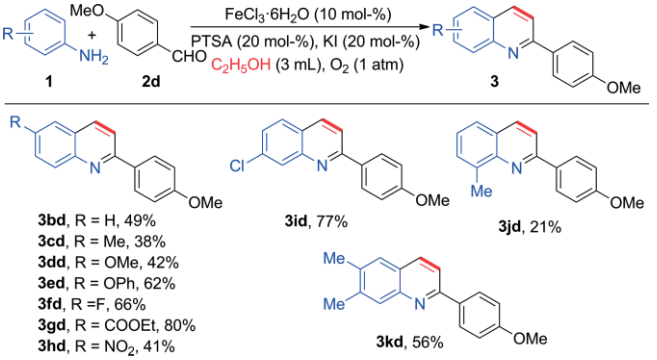
3ah in excellent yield, thus providing the potential for further functionalization. Disubstituted (3,5-dimethoxy, 2,6-dichloro) benzaldehydes were also suitable for this reaction, providing the corresponding products **3aj** and **3ak** in moderate to good yields. We were delighted to find that 2-naphthaldehyde also underwent the reaction efficiently to give **3al** in up to 92 % yield. Heterocyclic aldehydes also gave the target products **3am**, **3an** in moderate yields, but aliphatic aldehydes were not suitable for this reaction. A scaled-up reaction of *p*-methoxybenzaldehyde and *p*-chloroaniline worked well under the standard conditions to give the target product **3ad** in 80 % yield (1.07 g); this demonstrates the high efficiency of this transformation.



Scheme 2. Scope of the reaction in terms of aromatic aldehydes.[a] Reaction conditions: [a] **1a** (0.66 mmol), **2** (0.30 mmol), $FeCl_3$·$6H_2O$ (0.03 mmol), PTSA (0.06 mmol), KI (0.06 mmol), oxygen atmosphere (1 atm), C_2H_5OH (3 mL), 12 h. Isolated yields. [b] **1a** (11 mmol), **2d** (5 mmol), $FeCl_3$·$6H_2O$ (0.5 mmol), PTSA (1 mmol), KI (1 mmol), oxygen atmosphere (1 atm), C_2H_5OH (20 mL), 24 h; 1.07 g of **3ad** was isolated.

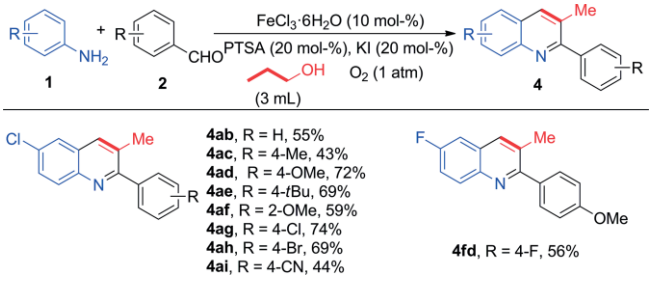
We next investigated the scope of the reaction in terms of the aniline component. As shown in Scheme 3, anilines with electron-donating groups and electron-withdrawing groups were generally tolerated, and gave the desired quinoline derivatives **3bd**–**3hd** in moderate to good yields. The reaction of 3-chloroaniline also proceeded smoothly at the less sterically hindered position, selectively giving **3id** in 77 % yield.

We also investigated the reactivity of other alcohols. To our delight, *n*-propanol also participated efficiently in this reaction. Similarly to the reaction with ethanol, both electron-donating and electron-withdrawing substituents were tolerated in this reaction, and a series of 2,3-disubstituted quinoline derivatives were formed selectively in moderate to good yields (Scheme 4). Unfortunately, other alcohols could not act as alkene precursors for this transformation, though *N*-alkylation of anilines with other alcohols did proceed smoothly under the same reaction conditions (Equation S15 in the Supporting Information). Control experiments (Equations S16–22 in the Supporting Information) indicated that Fe catalysts were not effective for the aerobic oxidative dehydrogenation of the in-situ-generated *N*-alkyl-



Scheme 3. Scope of the reaction in terms of aromatic amines. Reaction conditions: **1** (0.66 mmol), **2d** (0.30 mmol), $FeCl_3$·$6H_2O$ (0.03 mmol), PTSA (0.06 mmol), KI (0.06 mmol), oxygen atmosphere (1 atm), C_2H_5OH (3 mL), 12 h. Isolated yields.

ated anilines to yield imine intermediates, except for *N*-ethyl anilines and *N*-propyl anilines. As a result, the cascade reaction stopped at this oxidation step, so the reaction could not be used with other alcohols.



Scheme 4. The cascade reaction in *n*-propanol instead of ethanol. Reaction conditions: **1** (0.66 mmol), **2** (0.30 mmol), $FeCl_3$·$6H_2O$ (0.03 mmol), PTSA (0.06 mmol), KI (0.06 mmol), oxygen atmosphere (1 atm), *n*-propanol (3 mL), 12 h. Isolated yields.

A series of control experiments was carried out to gain information about the reaction mechanism (Scheme 5). Firstly, when methanol was used instead of ethanol, none of the target product was generated [Equation (1)]. This result confirms that ethanol participates in the reaction as a carbon source. In the beginning, we envisioned a possibility that aromatic amines might react with alcohols in the presence of PTSA and KI to form *N*-ethylaniline, which could then be converted into an enamine through oxidative dehydrogenation. To verify this speculation, we replaced KI with ethyl iodide (50 mol-%). As expected, the reaction proceeded well, and provided the desired product in 88 % yield [Equation (2)]. Furthermore, a reaction mixture of aniline, imine, and *N*-ethylaniline in ethanol under the standard conditions gave the desired product in 71 % yield [Equation (3)]. Here, aniline was present to prevent the hydrolysis of the imine. Similarly, a good yield was also achieved when methanol was used instead of ethanol [Equation (4)]. These results confirm the involvement of *N*-ethylaniline and imine intermediates in the reaction. To obtain more information about the reaction mechanism, we carried out the reaction of aniline, imine, and *N*-ethylaniline without an Fe^{III} catalyst, and found the yield of the desired product **3ad** decreased a lot [Equation (5)]. In contrast, when this reaction was carried out with an iron cata-

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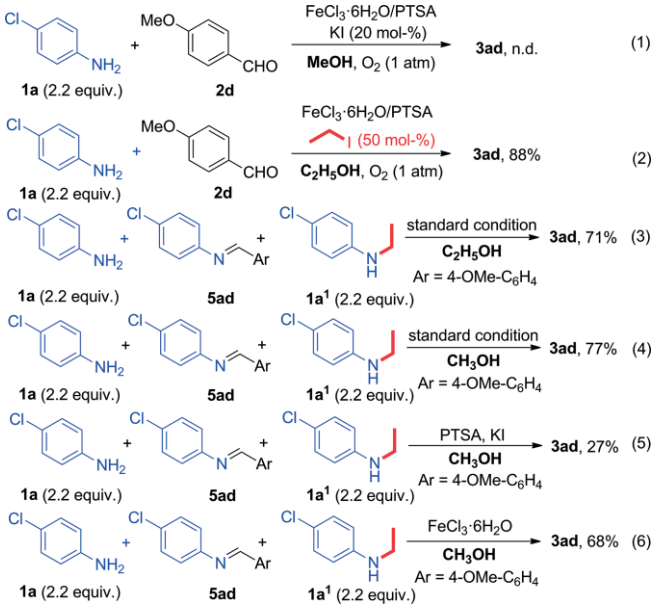
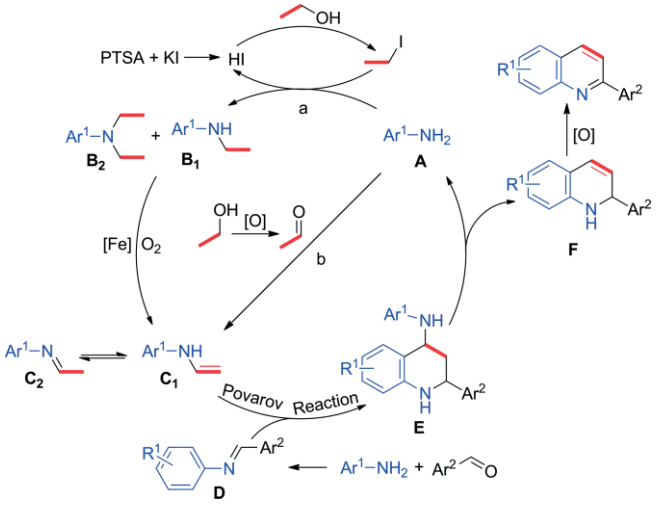
lyst in the absence of PTSA (20 mol-%) and KI (20 mol-%), **3ad** was obtained in good yield (68 %) [Equation (6)]. These results indicate that the Fe catalyst might play an important role in the oxidation of **1a**[1]. In addition, a series of control experiments was also carried out by using the reactant mixture of *p*-chloroaniline (**1a**) with acetaldehyde (Equation S9 in the Supporting Information). The results indicated that the *N*-vinylalinine might be an intermediate of this reaction, and that the Fe catalyst does play a key role in the oxidation of **1a**[1].



Scheme 5. Control experiments to investigate the mechanism.

Based on the above experimental results, we propose a plausible mechanism as shown in Scheme 6. Initially, aniline (**A**) reacts with ethyl iodide, generated from ethanol and KI under acidic conditions, to produce B^1 and B^2. Subsequently, B^1 was oxidized by O_2 under the catalysis of the iron catalyst to give C^2 (path a). Intermediate C^2 could also be generated through the reaction of amines and acetaldehyde (generated from the oxidation of ethanol; path b). Then, C^1 reacts with imine **D**, generated from the corresponding amine and aldehyde, through a Povarov process to generate tetrahydroquinoline derivative **E**. Under acidic conditions, **E** is converted into dihydroquinoline derivative **F**, and aniline is released for the next cycle. Finally, **F** undergoes further oxidative aromatization to give the target compound.



Scheme 6. Proposed reaction mechanism.

Conclusions

In conclusion, we have developed a simple, new, and efficient catalytic approach for the synthesis of 2-arylquinoline derivatives from readily accessible anilines, aldehydes, and alcohols. In this reaction, environmentally benign oxygen and a salt of naturally abundant iron were used as the oxidant and catalyst, respectively. In addition, alcohols were used as precursors of alkenes in this transformation for the first time. The reaction proceeds through an in-situ *N*-alkylation/oxidation process. Good results were achieved, and the reaction was also carried out on a gram scale. Further investigations into the application of this method in organic synthesis are currently underway in our laboratory.

Experimental Section

General Procedure for Quinoline Synthesis: A Schlenk tube (50 mL) with a magnetic stirrer bar was loaded with **1** (0.66 mmol), **2** (0.30 mmol), $FeCl_3$·$6H_2O$ (10 mol-%), PTSA (20 mol-%), KI (20 mol-%), and C_2H_5OH (3 mL). Then a gas exchange was carried out three times, and the Schlenk tube was filled with oxygen gas. The mixture was stirred at 140 °C for 12 h, then it was cooled to room temperature, and transferred into a flask (100 mL). The solvent was removed, and the residue was purified by column chromatography (petroleum ether/EtOAc) to give the desired quinoline **3** and **4**.

General Procedure for the Large-Scale Reaction: Compound **1a** (11 mmol), **2d** (5 mmol), $FeCl_3$·$6H_2O$ (10 mol-%), PTSA (20 mol-%), KI (20 mol-%), and C_2H_5OH (20 mL) were put into a Schlenk tube (250 mL) with a magnetic stirrer bar. Then the general procedure for quinoline synthesis was followed, but the reaction time was increased to 24 h. This gave **3ad** (1.07 g, 80 %).

6-Chloro-2-(3,4-dimethoxyphenyl)quinoline (3aa): Yellow solid; m.p. 117–119 °C. R_f = 0.16 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.02 (m, 2 H), 7.87–7.81 (m, 2 H), 7.76 (d, J = 2.3 Hz, 1 H), 7.66–7.59 (m, 2 H), 6.97 (d, J = 8.4 Hz, 1 H), 4.04 (s, 3 H), 3.95 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 150.5, 149.4, 146.5, 135.6, 132.0, 131.5, 131.0, 130.4, 127.4, 126.1, 120.2, 119.3, 111.0, 110.2, 56.0, 56.0 ppm. HRMS (ESI): calcd. for $C_{17}H_{15}ClNO_2$ $[M + H]^+$ 300.0786; found 300.0774.

6-Chloro-2-phenylquinoline (3ab):[14] White solid; m.p. 111–114 °C. R_f = 0.74 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18–8.08 (m, 4 H), 7.90 (d, J = 8.6 Hz, 1 H), 7.81 (d, J = 2.3 Hz, 1 H), 7.66 (dd, J = 9.0, 2.3 Hz, 1 H), 7.58–7.45 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 146.7, 139.2, 135.8, 131. 9, 131.3, 130.6, 129.6, 128.9 (two peaks overlapping), 127.7, 127.5 (two peaks overlapping), 126.1, 119.78 ppm. HRMS (ESI): calcd. for $C_{15}H_{11}ClN$ $[M + H]^+$ 240.0575; found 240.0578.

6-Chloro-2-(*p*-tolyl)quinoline (3ac): White solid; m.p. 1623–171 °C. R_f = 0.74 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.03 (m, 4 H), 7.87 (d, J = 8.7 Hz, 1 H), 7.79 (d, J = 2.1 Hz, 1 H), 7.64 (dd, J = 9.0, 2.3 Hz, 1 H), 7.34 (d, J = 7.9 Hz, 2 H), 2.44 (s,

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3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 146.7, 139.7, 136.4, 135.7, 131.6, 131.2, 130.4, 129.6 (two peaks overlapping), 127.6, 127.4 (two peaks overlapping), 126.1, 119.6, 21.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}ClN$ $[M + H]^+$ 254.0731; found 254.0729.

6-Chloro-2-(4-methoxyphenyl)quinoline (3ad): Yellow solid; m.p. 162 °C. R_f = 0.54 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, J = 8.8 Hz, 2 H), 8.06 (d, J = 8.8 Hz, 2 H), 7.83 (d, J = 8.6 Hz, 1 H), 7.76 (s, 1 H), 7.63 (dd, J = 9.0, 2.3 Hz, 1 H), 7.04 (d, J = 8.8 Hz, 2 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 157.0, 146.6, 135.6, 131.7, 131.4, 131.1, 130.4, 128.8 (two peaks overlapping), 127.4, 126.1, 119.3, 114.3 (two peaks overlapping), 55.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}ClNO$ $[M + H]^+$ 270.0680; found 270.0683.

2-[4-(*tert*-Butyl)phenyl]-6-chloroquinoline (3ae): White solid; m.p. 174–176 °C. R_f = 0.82 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.06 (m, 4 H), 7.88 (t, J = 8.2 Hz, 1 H), 7.78 (d, J = 2.0 Hz, 1 H), 7.65 (dd, J = 9.0, 2.3 Hz, 1 H), 7.56 (d, J = 8.5 Hz, 2 H), 1.39 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 152.8, 146.7, 136.4, 135.6, 131.6, 131.3, 130.4, 127.6, 127.2 (two peaks overlapping), 126.1, 125.9 (two peaks overlapping), 119.7, 34.7, 31.3 ppm. HRMS (ESI): calcd. for $C_{19}H_{19}ClN$ $[M + H]^+$ 296.1201; found 296.1199.

6-Chloro-2-(2-methoxyphenyl)quinoline (3af): Yellow solid; m.p. 103–107 °C. R_f = 0.56 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 9.0 Hz, 1 H), 8.04 (d, J = 8.6 Hz, 1 H), 7.93 (d, J = 8.6 Hz, 1 H), 7.86 (d, J = 7.5 Hz, 1 H), 7.80 (s, 1 H), 7.63 (dd, J = 9.0, 2.3 Hz, 1 H), 7.43 (ddd, J = 8.3, 7.5, 1.8 Hz, 1 H), 7.18–7.11 (m, 1 H), 7.04 (d, J = 8.3 Hz, 1 H), 3.87 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 157.2, 146.6, 134.1, 131.7, 131.4, 131.21, 130.5, 130.0, 129.2, 127.5, 126.0, 124.3, 121.3, 111.4, 55.6 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}ClNO$ $[M + H]^+$ 270.0680; found 270.0670.

6-Chloro-2-(4-chlorophenyl)quinoline (3ag): White solid; m.p. 162–168 °C. R_f = 0.70 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.05 (m, 4 H), 7.84 (d, J = 8.7 Hz, 1 H), 7.79 (d, J = 2.3 Hz, 1 H), 7.66 (dd, J = 9.0, 2.3 Hz, 1 H), 7.49 (dd, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 146.6, 137.5, 136.0, 135.8, 132.1, 131.3, 130.7, 129.1 (two peaks overlapping), 128.7 (two peaks overlapping), 127.7, 126.1, 119.3 ppm. HRMS (ESI): calcd. for $C_{15}H_{10}Cl_2N$ $[M + H]^+$ 274.0185; found 274.0173.

2-(4-Bromophenyl)-6-chloroquinoline (3ah): Yellow solid; m.p. 180–184 °C. R_f = 0.70 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, J = 8.6 Hz, 1 H), 8.08 (d, J = 9.0 Hz, 1 H), 8.06–8.02 (m, 2 H), 7.85 (d, J = 8.7 Hz, 1 H), 7.81 (d, J = 2.3 Hz, 1 H), 7.69–7.63 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156. 2, 146.6, 138.0, 136.0, 132.2, 132.0 (two peaks overlapping), 131.3, 130.8, 129.0 (two peaks overlapping), 127.8, 126.2, 124.2, 119.3 ppm. HRMS (ESI): calcd. for $C_{15}H_{10}BrN$ $[M + H]^+$ 317.9680; found 317.9665.

6-Chloro-2-(3-nitrophenyl)quinoline (3ai):[15] White solid; m.p. 101–118 °C. R_f = 0.42 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (t, J = 1.9 Hz, 1 H), 8.52–8.47 (m, 1 H), 8.29 (ddd, J = 8.2, 2.2, 0.9 Hz, 1 H), 8.17 (d, J = 8.6 Hz, 1 H), 8.08 (d, J = 9.0 Hz, 1 H), 7.91 (d, J = 8.6 Hz, 1 H), 7.80 (d, J = 2.3 Hz, 1 H), 7.72–7.63 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 148.8, 146.5, 140.7, 136.4, 133.1, 132.8, 131.4, 131.1, 129. 8, 128.0, 126.2, 124.0, 122.3, 119.0 ppm. HRMS (ESI): calcd. for $C_{15}H_{10}ClN_2O_2$ $[M + H]^+$ 385.0425; found 385.0426.

6-Chloro-2-(3,5-dimethoxyphenyl)quinoline (3aj): Yellow solid; m.p. 115–119 °C. R_f = 0.44 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, J = 9.0 Hz, 1 H), 8.04 (d, J = 8.7 Hz, 1 H), 7.80 (d, J = 8.6 Hz, 1 H), 7.74 (d, J = 2.2 Hz, 1 H), 7.63 (dd, J = 9.0, 2.3 Hz, 1 H), 7.30 (d, J = 2.3 Hz, 2 H), 6.58 (t, J = 2.2 Hz, 1 H), 3.89 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 157.2, 146.5, 141.3, 135.8, 132.0, 131.3, 130.5, 127.9, 126.1, 119.9, 105.6, 101.8, 55.5 (two peaks overlapping) ppm. HRMS (ESI): calcd. for $C_{17}H_{15}ClNO_2$ $[M + H]^+$ 300.0786; found 300.0788.

6-Chloro-2-(2,6-dichlorophenyl)quinoline (3ak): Brown solid; m.p. 91–96 °C. R_f = 0.58 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 8.4 Hz, 1 H), 8.12 (d, J = 9.0 Hz, 1 H), 7.88 (d, J = 2.2 Hz, 1 H), 7.69 (dd, J = 9.0, 2.3 Hz, 1 H), 7.48–7.42 (m, 3 H), 7.32 (dd, J = 8.7, 7.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 146.3, 138.3, 135.6, 134.5, 132.9, 131.3, 130.7, 130.1, 128.3, 127.9, 126.3, 123.4 ppm. HRMS (ESI): calcd. for $C_{15}H_9Cl_3N$ $[M + H]^+$ 307.9795; found 307.9784.

6-Chloro-2-(naphthalen-2-yl)quinoline (3al): White solid; m.p. 171–176 °C. R_f = 0.62 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.60 (d, J = 1.0 Hz, 1 H), 8.35 (dd, J = 8.6, 1.8 Hz, 1 H), 8.14 (dd, J = 8.8, 2.1 Hz, 2 H), 8.06–7.97 (m, 3 H), 7.93–7.87 (m, 1 H), 7.81 (d, J = 2.3 Hz, 1 H), 7.68 (dd, J = 9.0, 2.3 Hz, 1 H), 7.58–7.51 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 146.7, 136.5, 135.8, 133.9, 133.4, 131.9, 131.3, 130.6, 128.8, 128.6, 127.7 (two peaks overlapping), 127.2, 126.8, 126.4, 126.2, 124.8, 119.9 ppm. HRMS (ESI): calcd. for $C_{19}H_{13}ClN$ $[M + H]^+$ 290.0731; found 290.0719.

6-Chloro-2-(thiophen-2-yl)quinoline (3am): White solid; m.p. 107–109 °C. R_f = 0.6 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 7.4 Hz, 2 H), 7.84–7.67 (m, 3 H), 7.61 (d, J = 7.1 Hz, 1 H), 7.48 (s, 1 H), 7.15 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 146.4, 144.9, 135.6, 131.6, 130.7, 130.6, 128.9, 128.1, 127.6, 126.1, 126.1, 118.4 ppm. HRMS (ESI): calcd. for $C_{13}H_9ClNS$ $[M + H]^+$ 246.0139; found 246.0137.

6-Chloro-2-(pyridin-4-yl)quinoline (3an):[16] Yellow solid; m.p. 167–169 °C. R_f = 0.12 (petroleum ether/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.79 (d, J = 4.0 Hz, 2 H), 8.20 (d, J = 8.5 Hz, 1 H), 8.12 (d, J = 8.9 Hz, 1 H), 8.05 (d, J = 4.5 Hz, 2 H), 7.93 (d, J = 8.5 Hz, 1 H), 7.84 (s, 1 H), 7.70 (d, J = 8.3 Hz, 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 154.7, 150.6, 146.6, 146.1, 136.3, 133.0, 131.6, 131.1, 128.3, 126.2, 121.5, 119.3 ppm. HRMS (ESI): calcd. for $C_{14}H_{10}ClN_2$ $[M + H]^+$ 241.0527; found 241.0521.

2-(4-Methoxyphenyl)quinoline (3bd):[17] White solid; m.p. 126–129 °C. R_f = 0.48 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.11 (m, 4 H), 7.85–7.77 (m, 2 H), 7.71 (dd, J = 8.2, 7.1 Hz, 1 H), 7.50 (t, J = 7.5 Hz, 1 H), 7.05 (d, J = 8.7 Hz, 2 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 156.8, 148.3, 136.6, 132.2, 129.5, 129.5, 128.8 (two peaks overlapping), 127.4, 126.9, 125.8, 118.5, 114.2 (two peaks overlapping), 55.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{14}NO$ $[M + H]^+$ 236.1070; found 236.1064.

2-(4-Methoxyphenyl)-6-methylquinoline (3cd):[18] White solid; m.p. 138 °C. R_f = 0.46 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15–8.10 (m, 2 H), 8.08 (d, J = 8.6 Hz, 1 H), 8.03 (d, J = 8.4 Hz, 1 H), 7.79 (d, J = 8.6 Hz, 1 H), 7.54 (m, 2 H), 7.07–7.02 (m, 2 H), 3.88 (s, 3 H), 2.54 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 156.1, 146.9, 135.9, 135.7, 132.4, 131.8, 129.2, 128.7 (two peaks overlapping), 126.9, 126.3, 118.5, 114.2 (two peaks overlapping), 55.4, 21.5 ppm. HRMS (ESI): calcd. for $C_{17}H_{16}NO$ $[M + H]^+$ 250.1226; found 250.1228.

6-Methoxy-2-(4-methoxyphenyl)quinoline (3dd):[19] White solid; m.p. 178–183 °C. R_f = 0.30 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.02 (m, 4 H), 7.78 (d, J = 8.6 Hz, 1 H), 7.37 (dd, J = 9.1, 2.7 Hz, 1 H), 7.07 (d, J = 2.5 Hz, 1 H), 7.04 (d, J = 8.7 Hz, 2 H), 3.94 (s, 3 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz,

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$CDCl_3$): δ = 160.5, 157.4, 154.7, 144.3, 135.4, 132.4, 130.9, 128.5 (two peaks overlapping), 127.8, 122.1, 118.8, 114.2 (two peaks overlapping), 105.1, 55.5, 55.4 ppm. HRMS (ESI): calcd. for $C_{17}H_{16}NO_2$ [M + H]$^+$ 266.1176; found 266.1165.

2-(4-Methoxyphenyl)-6-phenoxyquinoline (3ed): White solid; m.p. 140–145 °C. R_f = 0.48 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15–8.10 (m, 3 H), 8.02 (d, J = 8.7 Hz, 1 H), 7.80 (d, J = 8.7 Hz, 1 H), 7.48 (dd, J = 9.1, 2.7 Hz, 1 H), 7.40 (t, J = 7.9 Hz, 2 H), 7.23 (d, J = 2.6 Hz, 1 H), 7.18 (t, J = 7.4 Hz, 1 H), 7.11 (d, J = 7.8 Hz, 2 H), 7.05 (d, J = 8.8 Hz, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7, 156.8, 155.7, 155.1, 145.1, 135.7, 132.2, 131.4, 129.9 (two peaks overlapping), 128.7 (two peaks overlapping), 127.6, 123.8, 123.2, 119.4 (two peaks overlapping), 118.9, 114.2 (two peaks overlapping), 112.9, 55.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{18}NO_2$ [M + H]$^+$ 328.1332; found 328.1327.

6-Fluoro-2-(4-methoxyphenyl)quinoline (3fd): White solid; m.p. 142–144 °C. R_f = 0.70 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–8.07 (m, 4 H), 7.83 (d, J = 8.6 Hz, 1 H), 7.51–7.44 (m, 1 H), 7.40 (dd, J = 8.8, 2.8 Hz, 1 H), 7.08–7.02 (m, 2 H), 3.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 160.1 (d, $J_{C,F}$ = 247.3 Hz), 156.2, 145.3, 135.9 (d, $J_{C,F}$ = 5.2 Hz), 131.9, 131.9 (d, $J_{C,F}$ = 9.0 Hz), 128.7, 127.3 (d, $J_{C,F}$ = 9.9 Hz), 119.6 (d, $J_{C,F}$ = 25.6 Hz), 119.2, 114.2, 110.4 (d, $J_{C,F}$ = 21.7 Hz), 55.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}FNO$ [M + H]$^+$ 254.0976; found 254.0981.

Ethyl 2-(4-Methoxyphenyl)quinoline-6-carboxylate (3gd): Yellow solid; m.p. 132–153 °C. R_f = 0.32 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (s, 1 H), 8.33–8.24 (m, 2 H), 8.21–8.10 (m, 3 H), 7.89 (d, J = 8.6 Hz, 1 H), 7.05 (d, J = 8.6 Hz, 2 H), 4.45 (q, J = 7.0 Hz, 2 H), 3.91 (s, 3 H), 1.46 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 161.2, 158.8, 150.2, 137.8, 131.6, 130.5, 129.6, 129.1 (two peaks overlapping), 127.6, 126.0, 119.1, 114.3 (two peaks overlapping), 61.2, 55.4, 14.4 ppm. HRMS (ESI): calcd. for $C_{19}H_{18}NO_3$ [M + H]$^+$ 308.1281; found 308.1268.

2-(4-Methoxyphenyl)-6-nitroquinoline (3hd): Yellow solid; m.p. 228–230 °C. R_f = 0.32 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.77 (d, J = 2.5 Hz, 1 H), 8.47 (dd, J = 9.2, 2.5 Hz, 1 H), 8.34 (d, J = 8.7 Hz, 1 H), 8.25–8.17 (m, 3 H), 8.01 (d, J = 8.7 Hz, 1 H), 7.10–7.05 (m, 2 H), 3.91 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.8, 160.1, 150.6, 138.2, 131.1, 130.9, 129.3 (two peaks overlapping), 125.5, 124.3, 124.3, 123.1, 120.1, 114.5 (two peaks overlapping), 55.5 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}N_2O_3$ [M + H]$^+$ 281.0921; found 281.0934.

7-Chloro-2-(4-methoxyphenyl)quinoline (3id): Yellow solid; m.p. 176–179 °C. R_f = 0.58 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.10 (m, 4 H), 7.83 (d, J = 8.7 Hz, 1 H), 7.73 (d, J = 8.6 Hz, 1 H), 7.44 (dd, J = 8.6, 2.0 Hz, 1 H), 7.08–7.02 (m, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1, 157.8, 148.7, 136.4, 135.4, 131.7, 129.0 (two peaks overlapping), 128.6, 128.5, 126.9, 125.2, 118.6, 114.3 (two peaks overlapping), 55.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}ClNO$ [M + H]$^+$ 270.0680; found 270.0684.

2-(4-Methoxyphenyl)-8-methylquinoline (3jd): White solid; m.p. 85–88 °C. R_f = 0.68 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27–8.21 (m, 2 H), 8.14 (d, J = 8.6 Hz, 1 H), 7.85 (d, J = 8.6 Hz, 1 H), 7.64 (d, J = 8.1 Hz, 1 H), 7.56 (d, J = 6.9 Hz, 1 H), 7.41–7.36 (m, 1 H), 7.08–7.02 (m, 2 H), 3.90 (s, 3 H), 2.90 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7, 155.1, 147.1, 137.4, 136.8, 132.5, 129.6, 128.7 (two peaks overlapping), 126.8, 125.6, 125.3, 117.7, 114.1 (two peaks overlapping), 55.4, 17.9 ppm. HRMS (ESI): calcd. for $C_{17}H_{16}NO$ [M + H]$^+$ 250.1226; found 250.1219.

2-(4-Methoxyphenyl)-6,7-dimethylquinoline (3kd): Yellow solid; m.p. 155–160 °C. R_f = 0.50 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.09 (m, 2 H), 8.05 (d, J = 8.6 Hz, 1 H), 7.90 (s, 1 H), 7.74 (d, J = 8.6 Hz, 1 H), 7.53 (s, 1 H), 7.06–7.01 (m, 2 H), 3.88 (s, 3 H), 2.48 (s, 3 H), 2.44 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 156.0, 147.4, 139.7, 135.7, 135.5, 132.6, 128.9, 128.7 (two peaks overlapping), 126.7, 125.5, 117.7, 114.1 (two peaks overlapping), 55.4, 20.4, 20.0 ppm. HRMS (ESI): calcd. for $C_{18}H_{18}NO$ [M + H]$^+$ 264.1383; found 264.1386.

6-Chloro-3-methyl-2-phenylquinoline (4ab): Yellow solid; m.p. 76–80 °C. R_f = 0.56 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, J = 9.0 Hz, 1 H), 7.90 (s, 1 H), 7.74 (d, J = 2.3 Hz, 1 H), 7.61–7.56 (m, 3 H), 7.53–7.42 (m, 3 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.7, 144.9, 140.4, 135.7, 132.0, 130. 9, 130.3, 129.6, 128.7 (two peaks overlapping), 128.3, 128.3 (two peaks overlapping), 128.1, 125.3, 20.6 ppm. HRMS (ESI): calcd. for $C_{16}H_{13}ClN$ [M + H]$^+$ 254.0731; found 254.0736.

6-Chloro-3-methyl-2-(*p*-tolyl)quinoline (4ac): Yellow solid; m.p. 85–89 °C. R_f = 0.60 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, J = 9.0 Hz, 1 H), 7.88 (s, 1 H), 7.73 (d, J = 2.3 Hz, 1 H), 7.57 (dd, J = 9.0, 2.3 Hz, 1 H), 7.51–7.47 (m, 2 H), 7.30 (d, J = 7.8 Hz, 2 H), 2.47 (s, 3 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 145.0, 138.2, 137.6, 135.6, 131.8, 130.9, 130.3, 129.5, 129.0 (two peaks overlapping), 128.7 (two peaks overlapping), 128.0, 125.3, 21.3, 20.7 ppm. HRMS (ESI): calcd. for $C_{17}H_{15}ClN$ [M + H]$^+$ 268.0888; found 268.0887.

6-Chloro-2-(4-methoxyphenyl)-3-methylquinoline (4ad): Yellow solid; m.p. 133–139 °C. R_f = 0.36 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, J = 9.0 Hz, 1 H), 7.86 (s, 1 H), 7.71 (d, J = 2.2 Hz, 1 H), 7.59–7.53 (m, 3 H), 7.01 (d, J = 8.7 Hz, 2 H), 3.86 (s, 3 H), 2.47 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3, 159.8, 145.0, 135.7, 132. 9, 131.7, 130.8, 130.3, 130.2 (two peaks overlapping), 129.5, 127.9, 125.2, 113.7 (two peaks overlapping), 55.3, 20.8 ppm. HRMS (ESI): calcd. for $C_{17}H_{15}ClNO$ [M + H]$^+$ 284.0837; found 284.0836.

2-[4-(*tert*-Butyl)phenyl]-6-chloro-3-methylquinoline (4ae): Yellow solid; m.p. 98–120 °C. R_f = 0.74 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, J = 9.0 Hz, 1 H), 7.90 (s, 1 H), 7.74 (d, J = 2.2 Hz, 1 H), 7.57 (dd, J = 9.0, 2.2 Hz, 1 H), 7.55–7.49 (m, 4 H), 2.50 (s, 3 H), 1.38 (s, 9 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.8, 151.4, 145.0, 137.6, 135.6, 131.8, 130.9, 130.4, 129.5, 128.5, 128.1, 127.0, 125.9, 125.3 (two peaks overlapping), 34.7, 31.3 (three peaks overlapping), 20.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{21}ClN$ [M + H]$^+$ 310.1357; found 310.1345.

6-Chloro-2-(2-methoxyphenyl)-3-methylquinoline (4af): Yellow solid; m.p. 108–117 °C. R_f = 0.32 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, J = 9.0 Hz, 1 H), 7.86 (s, 1 H), 7.75 (d, J = 2.3 Hz, 1 H), 7.56 (dd, J = 9.0, 2.3 Hz, 1 H), 7.45–7.40 (m, 1 H), 7.32 (dd, J = 7.4, 1.7 Hz, 1 H), 7.09 (td, J = 7.4, 0.8 Hz, 1 H), 6.99 (d, J = 8.3 Hz, 1 H), 3.76 (s, 3 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.6, 156.6, 144.9, 134.3, 132.1, 131.8, 130.9, 130.1, 129.9, 129.8, 129.2, 128.4, 125.3, 121.0, 110.8, 55.3, 19.2 ppm. HRMS (ESI): calcd. for $C_{17}H_{15}ClNO$ [M + H]$^+$ 284.0837; found 284.0830.

6-Chloro-2-(4-chlorophenyl)-3-methylquinoline (4ag): Yellow solid; m.p. 177–185 °C. R_f = 0.66 (petroleum ether/EtOAc, 8:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, J = 9.0 Hz, 1 H), 7.92 (s, 1 H), 7.74 (s, 1 H), 7.59 (dd, J = 9.0, 1.0 Hz, 1 H), 7.56–7.51 (m, 2 H), 7.47 (d, J = 8.3 Hz, 2 H), 2.46 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 145.0, 138.8, 136.0, 134.5, 132.3, 130.9, 130.3 (two peaks overlapping), 130.1, 129.8, 128.5 (two peaks overlapping), 128.2,

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125.3, 20.6 ppm. HRMS (ESI): calcd. for $C_{16}H_{16}Cl_2N$ $[M + H]^+$ 288.0341; found 288.0340.

2-(4-Bromophenyl)-6-chloro-3-methylquinoline (4ah): Yellow solid; m.p. 166–184 °C. R_f = 0.68 (petroleum ether/EtOAc, 8:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02 (dd, J = 8.8, 3.5 Hz, 1 H), 7.90 (s, 1 H), 7.73 (d, J = 2.1 Hz, 1 H), 7.64–7.61 (m, 2 H), 7.58 (dd, J = 9.0, 2.2 Hz, 1 H), 7.50–7.45 (m, 2 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 145.0, 139.3, 136.0, 132.3, 132.0, 131.5 (two peaks overlapping), 130.9, 130.5 (two peaks overlapping), 130.0, 129.8, 129.0, 128.1, 125.3, 122.8, 20.6 ppm. HRMS (ESI): calcd. for $C_{16}H_{12}BrClN$ $[M + H]^+$ 331.9836; found 331.9827.

4-(6-Chloro-3-methylquinolin-2-yl)benzonitrile (4ai): Yellow solid; m.p. 200–203 °C. R_f = 0.30 (petroleum ether/EtOAc, 8:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, J = 9.0 Hz, 1 H), 7.95 (s, 1 H), 7.79 (d, J = 8.3 Hz, 2 H), 7.76 (d, J = 2.0 Hz, 1 H), 7.71 (d, J = 8.3 Hz, 2 H), 7.60 (dd, J = 9.0, 2.2 Hz, 1 H), 2.45 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 144.9, 144.8, 136.3, 132.7, 132.1 (two peaks overlapping), 130.9, 130.1, 129.7 (three peaks overlapping), 128.3, 125.4, 118.6, 112.2, 20.3 ppm. HRMS (ESI): calcd. for $C_{17}H_{12}ClN_2$ $[M + H]^+$ 279.0684; found 279.0690.

6-Fluoro-2-(4-methoxyphenyl)-3-methylquinoline (4fd): Yellow solid; m.p. 118–130 °C. R_f = 0.58 (petroleum ether/EtOAc, 8:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09 (dd, J = 9.1, 5.4 Hz, 1 H), 7.92 (s, 1 H), 7.55 (d, J = 8.6 Hz, 2 H), 7.44–7.33 (m, 2 H), 7.02 (d, J = 8.6 Hz, 2 H), 3.87 (s, 3 H), 2.47 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3 (d, $J_{C,F}$ = 247.2 Hz), 159.7, 159.4 (d, $J_{C,F}$ = 2.7 Hz), 143.7, 136.0 (d, $J_{C,F}$ = 5.3 Hz), 133.0, 131.6 (d, $J_{C,F}$ = 9.2 Hz), 130.2, 127.9 (d, $J_{C,F}$ = 10.1 Hz), 118.8 (d, $J_{C,F}$ = 25.7 Hz), 113.7, 109.5 (d, $J_{C,F}$ = 21.6 Hz), 55.3, 20.8 ppm. HRMS (ESI): calcd. for $C_{17}H_{15}FNO$ $[M + H]^+$ 268.1132; found 268.1139.

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