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The synthesis of quinolines *via* denitrogenative palladium-catalyzed cascade reaction of *o*-aminocinnamonitriles with arylhydrazines†

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The first example of the palladium-catalyzed cascade reaction of *o*-aminocinnamonitriles with arylhydrazines has been achieved, providing an efficient synthetic pathway to access quinolines with moderate to good yields. Preliminary mechanistic experiments indicate that this cascade process involves sequential denitrogenative addition followed by an intramolecular cyclization.

Introduction

Quinoline derivatives have become increasingly popular in the past few years due to their ubiquity in natural products, bioactive compounds, and other functional molecules. For example, quinoline scaffolds are privileged structures in medicinal chemistry, and therapeutic agents with such cores on the market or in clinical trials for the treatment of urological malignancies such as renal cell carcinoma (*e.g.*, lenvatinib,[1] cabozantinib[2]) and the treatment of head and neck cancer (*e.g.*, camptothecin[3]) (Fig. 1). Therefore, the development of the effective methods for the synthesis of quinolines has been actively pursued during the past several decades.[4] However, less attention has been paid to the preparation of quinolines from nitriles.

Nitriles are well-known as solvents or ligands in organometallic reactions because of the inherently inert nature of the C≡N bond.[5] For example, acetonitrile or benzonitrile are usually used as solvents or ligands in many transition-metal-catalyzed reactions.[6] The development of transition-metal-catalyzed inert C≡N bond activation and further transformation has received significant attention from organic chemists because nitriles are normally very stable and abundant and cheap feedstock chemicals. Substantial progress towards this goal made in recent years, the transition-metal-catalyzed transformation of nitriles offers an attractive route for the synthesis of arylketones or further cyclization products by several other groups.[7] Our group also developed transition-metal-catalyzed a series of tandem addition/cyclization reaction of nitriles with organoboron reagents for the synthesis of structurally diverse 5-membered, 6-membered, and 7-membered *N*-heterocycles.[8] In addition, arylhydrazines are used as an important class of molecular building blocks in both synthetic and medicinal chemistry for preparing various nitrogen-containing compounds because of their high reactivity, low cost, and ready availability.[9] Recent progresses in the development of using arylhydrazines as aryl source by denitrogenation have been documented.[10] Despite the remarkable advances in transition-metal-catalyzed addition reactions of nitriles with arylating reagents into a valuable array of products to date, less attention has been paid to the using arylhydrazines as aryl sources by denitrogenation presumably due to the high dissociation energy from direct activation of the C–N bond.[11] To our knowledge, only two examples of denitrogenative palladium-catalyzed reaction of nitriles with arylhydrazines for the synthesis of aryl ketones have been reported (Scheme 1a).[12]

We envisioned that a Pd-catalyzed sequential denitrogenative addition followed by an intramolecular dehydrative cyclization of readily available *o*-aminocinnamonitriles with arylhydrazines would result in a tandem procedure for the preparation of 2-arylquinolines (Scheme 1b). It is worth noting that the amino group cannot approach the carbonyl group to achieve the intramolecular cyclization because of the steric configuration. Recently, Cheon group developed the synthesis of 2-substituted quinolines by the dehydrative cyclization of 2-aminostyryl ketones.[13] These strategies involve the change of unreactive (*E*)-2-aminostyryl ketones into the unstable but reactive *Z*-configuration intermediate to undergo dehydrative cyclization reaction by using iodide[13a] or benzylamine[13b] as the nucleophilic catalyst. Recently, we reported the Pd-catalyzed tandem reaction of 2-aminostyryl nitriles with arylboronic acids for the synthesis of 2-arylquinolines.[14] As part of the continuing efforts in our laboratory toward the development of novel transformations of nitriles,[8,14] we herein report the first example of the denitrogenative Pd-catalyzed cascade reaction of

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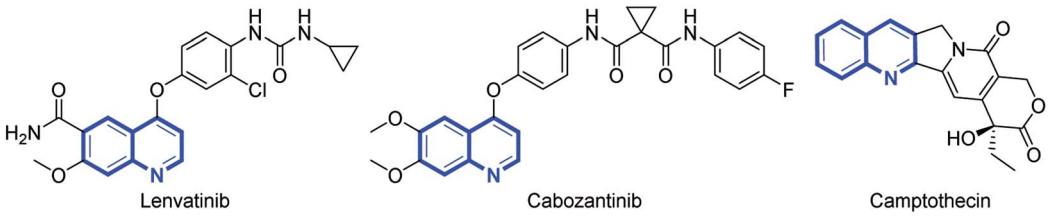
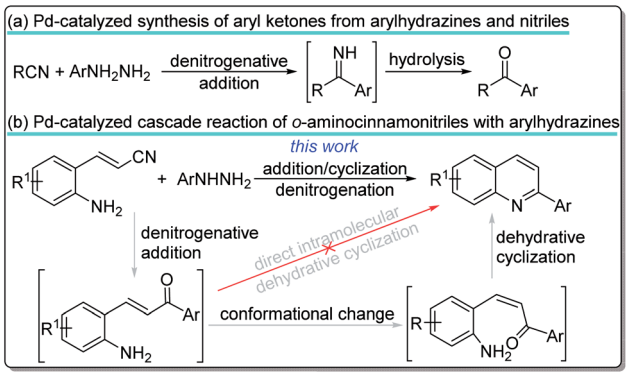


Fig. 1 Representative bioactive quinoline derivatives.



Scheme 1 Design of new approach to quinolines.

o-aminocinnamonitriles with arylhydrazines to afford 2-arylquinolines (Scheme 1b).

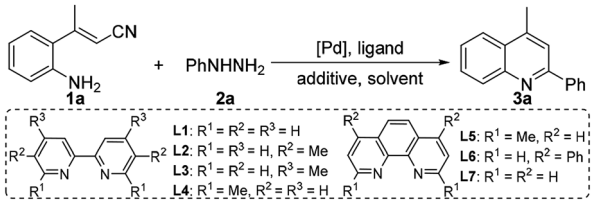
Results and discussion

We begin our investigation with readily available (*E*)-3-(2-aminophenyl)but-2-enenitrile (**1a**) and phenylhydrazine (**2a**) for the optimization of reaction conditions (Table 1).

We initially found that the desired product 2-phenylquinoline (**3a**) could be obtained in 12% yield under the combination of $Pd(OAc)_2$, trifluoroacetic acid (TFA) and 2,2′-bipyridine (**L1**) in THF under air atmosphere (entry 2). Various palladium catalysts were tested (entries 3–7) and $PdCl_2$ exhibited the highest catalytic reactivity in 31% yield (entry 5). Delightedly, the yield of **3a** could be improved to 56% using toluene as the solvent. Other solvents, including DMF, dimethylacetamide (DMA), 1,4-dioxane and H_2O were less efficient (entries 8–13). Replacement of **L1** with other bidentate *N*-ligands (entries 13–19), resulted in lower yields. However, trace amounts of **3a** was detected when sterically hindered ligands, such as 6,6′-dimethyl-2,2′-bipyridine (**L4**) and 2,9-dimethyl-1,10-phenanthroline (**L5**) were used (entries 16–17). An investigation of the effect of additive revealed that the yield of **3a** was greatly increased to 81% under O_2 atmosphere (entry 23). The product **3a** was not observed if either Pd catalyst or ligand was absent (entries 24 and 25).

Having the optimized reaction conditions in hand, we examined the substrates scope of this cascade reaction. First, the cascade reaction of (*E*)-3-(2-aminophenyl)but-2-enenitrile (**1a**) with different arylhydrazines were evaluated under optimized conditions (Table 2). The reactivities of *para*-, *meta*-, and *ortho*-tolylhydrazine were evaluated, and the results demonstrated that the steric effect of the substituent had an obvious impact on the reaction. For example, the reactions of **1a** with *para*- and *meta*-tolylhydrazine afforded 85% and 79% yields of **3b** and **3c**, respectively, while the *ortho*-tolylhydrazine gave the desired product **3d** with a diminished yield of 52%. Moderately electron-withdrawing halogens, such as fluoro (**3e**–**3f**), chloro (**3g**), and bromo (**3h**) groups, were compatible with this reaction, providing 42–76% yields. The substrate bearing

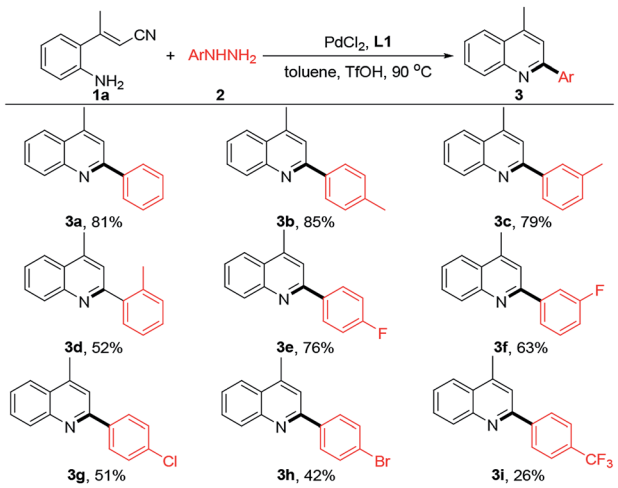
Table 1 Optimization of reaction conditions[a]



Entry	[Pd]	Ligand	Additive	Solvent	Yield[b] (%)
1	$Pd(PPh_3)_4$	**L1**	TFA	THF	0
2	$Pd(OM)_2$	**L1**	TFA	THF	12
3	$Pd(CF_3CO_2)_2$	**L1**	TFA	THF	19
4	$Pd(PPh_3)_2Cl_2$	**L1**	TFA	THF	17
5	$PdCl_2$	**L1**	TFA	THF	31
6	$Pd_2(dba)_3$	**L1**	TFA	THF	21
7	$Pd(acac)_2$	**L1**	TFA	THF	23
8	$PdCl_2$	**L1**	TFA	2-MeTHF	37
9	$PdCl_2$	**L1**	TFA	DMF	41
10	$PdCl_2$	**L1**	TFA	DMA	47
11	$PdCl_2$	**L1**	TFA	1,4-Dioxane	23
12	$PdCl_2$	**L1**	TFA	Toluene	56
13	$PdCl_2$	**L1**	TFA	H_2O	18
14	$PdCl_2$	**L2**	TFA	Toluene	53
15	$PdCl_2$	**L3**	TFA	Toluene	51
16	$PdCl_2$	**L4**	TFA	Toluene	Trace
17	$PdCl_2$	**L5**	TFA	Toluene	Trace
18	$PdCl_2$	**L6**	TFA	Toluene	41
19	$PdCl_2$	**L7**	TFA	Toluene	51
20	$PdCl_2$	**L1**	AcOH	Toluene	Trace
21	$PdCl_2$	**L1**	$TsOH \cdot H_2O$	Toluene	33
22	$PdCl_2$	**L1**	MsOH	Toluene	21
23	$PdCl_2$	**L1**	TfOH	Toluene	79(81)[c]
24		**L1**	TfOH	Toluene	0
25	$PdC1_2$		TfOH	Toluene	0

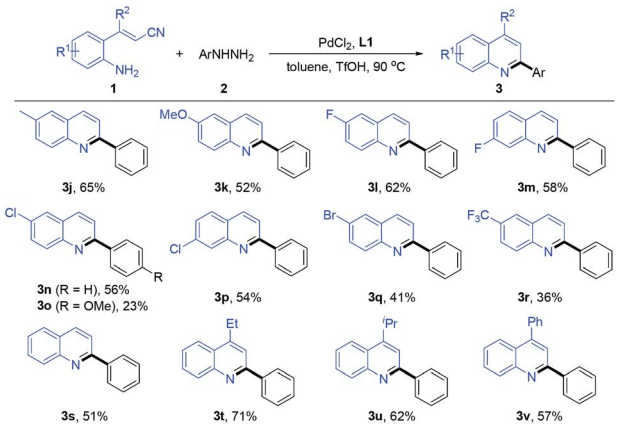
[a] Conditions: **1a** (0.3 mmol), **2a** (0.6 mmol), Pd catalyst (10 mol%), ligand (20 mol%), additive (2 equiv.), solvent (2 mL), 90 °C, 24 h, air. [b] Isolated yield. [c] Under O_2.

Table 2 Denitrogenative Pd-catalyzed cascade reaction of **1a** with arylhydrazines[a]



[a] Conditions: **1a** (0.3 mmol), **2** (0.6 mmol), $PdCl_2$ (10 mol%), **L1** (20 mol%), toluene (2 mL), TfOH (2 equiv.), 90 °C, 24 h, O_2, isolated yield.

Table 3 Denitrogenative Pd-catalyzed reaction of *o*-amino-cinnamonitriles with arylhydrazines[a]



[a] Conditions: **1** (0.3 mmol), **2** (0.6 mmol), $PdCl_2$ (10 mol%), **L1** (20 mol%), toluene (2 mL), TfOH (2 equiv.), 90 °C, 24 h, O_2, isolated yield.

a strong electron-withdrawing group (*e.g.*, CF_3) could also be well tolerated, albeit giving the desired **3i** in a slightly lower yield.

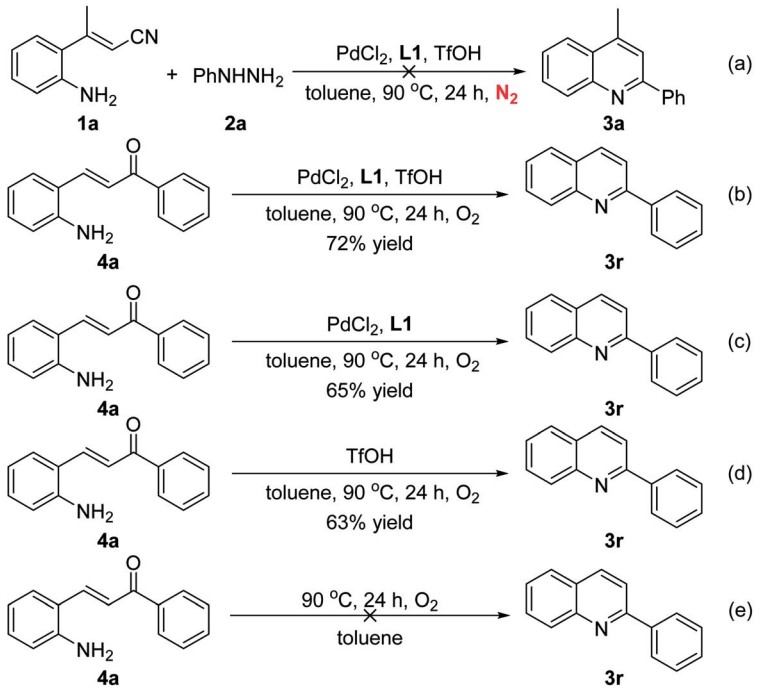
We next turned our attention to the effect of the reactions between substituted *o*-aminocinnamonitriles (**1**) and phenylhydrazine (**2a**) under standard conditions (Table 3). First, the influence of a variety of functional groups (R^1) on the phenyl ring of the 2-(benzylideneamino)benzonitriles was evaluated. Both electron-donating groups, such as methyl (**3j**) and methoxy (**3k**) moieties, and electron-withdrawing groups, such as fluoro (**3l–3m**), chloro (**3n–3p**) and bromo (**3q**) moieties, were also compatible, affording the corresponding desired products with moderate to good yields. Treatment of a strong electron-withdrawing trifluoromethyl substituent with **2a** delivered product **3r** in 36% yield. Finally, several representative examples of substituents (R^2) on the carbon–carbon double bond were investigated. The R^2-substituted products **3t**, **3u** and **3u** was obtained in 71%, 62% and 57% yields, respectively, compared to relatively low yield of the product **3s** in 51% yield. It is worth noting that the presence of the halogen in the products (*e.g.*, **3h**, **3q**) is very useful for further synthetic elaborations by cross-coupling reaction thereby broadening the diversity of the products.

To gain insight into the mechanism of this cascade reaction, several control experiments were conducted (Scheme 2). The desired product **3a** was not detected when the reaction was performed under N_2 atmosphere (Scheme 2a), which revealed that the reaction required the presence of oxygen. As expected, the reactions of (*E*)-3-(2-aminophenyl)-1-phenylprop-2-en-1-one (**4a**) under optimized conditions in the absence of phenylhydrazine achieved the product 2-phenylquinoline (**3r**) in 72% yield, indicating that **4a** was proposed as a possible intermediate for this transformation (Scheme 2b). The cyclization of **4a** gave the desired product **3r** in 65% yield in the absence of TfOH (Scheme 2c). The cyclization of **4a** could also proceed to afford **3r** in 63% yield in the absence of $PdCl_2$/**L1** (Scheme 2d). However, we attempted to perform the reaction in the absence of palladium catalyst and additive failed to give **3r** (Scheme 2e).

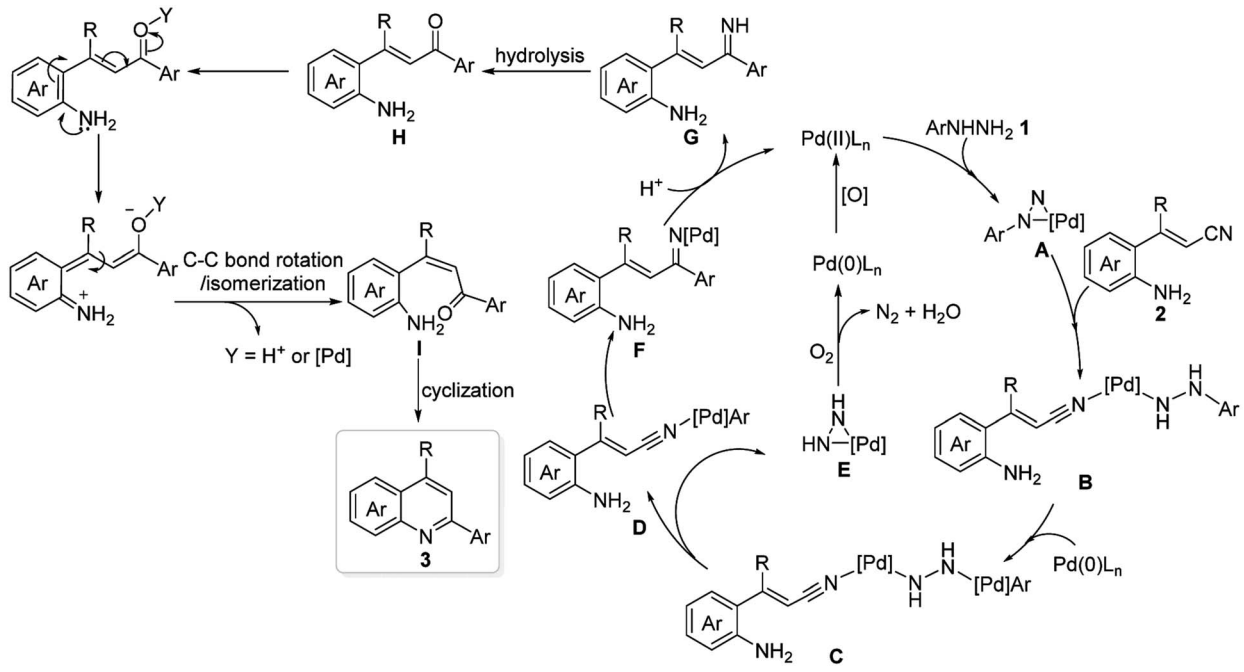
On the basis of the above experimental results and previous reports,[12a] a possible reaction mechanism for the formation of quinolines is shown in Scheme 3. The first step may involve metathesis between the palladium catalyst and arylhydrazide to form the palladiaziridine intermediate **A**, which is followed by the coordination of cyano group affording intermediate **B**. Oxidative addition of the intermediate **B** to palladium(0) species to give the corresponding two palladium(II) centered intermediate **C** *via* C–N bond cleavage. Thereafter, cracking of the intermediate **C** gives the intermediate **D** and the palladiaziridine intermediate **E**, which would be decomposed into palladium(0), N_2 and H_2O in the presence of oxygen. Then, carbopalladation of the cyano group affords the imine-Pd intermediate **F**. Protonation of **F** by TfOH gives the imine intermediate **G** and regenerates palladium(II) species. Hydrolysis of **G** under acidic conditions would deliver the ketone intermediate **H**. Finally, the ketone intermediate **H** undergoes C–C bond *E*/*Z* configurational tautomerization to give **I** in the presence of TfOH and/or palladium(II) species, which is followed by intramolecular cyclization to generate the desired quinolines **3**.

Conclusions

In summary, we have developed a new and complementary strategy for the synthesis of 2-arylquinolines in moderate to good yields by palladium-catalyzed cascade denitrogenative addition and intramolecular cyclization of *o*-amino-cinnamonitriles with arylhydrazines.



Scheme 2 Control experiments.



Scheme 3 Plausible reaction mechanism for the formation of quinolines.

Experimental section

General methods

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz spectrometer using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given *n* δ relative to TMS, and the coupling constants *J* are given in hertz. The starting materials *o*-aminocinnamonitriles[15] and **4a**[16] were synthesized according to the method described in the literatures. Column chromatography was performed using EM silica gel 60 (300–400 mesh).

General procedure for the synthesis of quinolines

Under O_2 atmosphere, a Teflon-valve-sealed Schlenk tube was charged with *o*-aminocinnamonitriles and arylhydrazines, $PdCl_2$, **L1**, TfOH and toluene at room temperature. The reaction mixture was stirred for 10 minutes at room temperature for proper mixing of the reactants, and then heated at 90 °C (oil bath) with vigorous stirring for 24 hours. After the reaction equilibrium, the mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (10 mL). The aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the desired products.

4-Methyl-2-phenylquinoline (3a).[17] White solid (53.2 mg, 81%), mp 62–63 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 10.5 Hz, 1H), 8.19–8.17 (m, 2H), 7.97 (d, J = 10.5 Hz, 1H), 7.75–7.70 (m, 2H), 7.56–7.52 (m, 3H), 7.49–7.46 (m, 1H), 2.73 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.0, 148.2, 144.8, 139.8, 130.3, 129.3, 129.2, 128.8, 127.6, 127.3, 126.0, 123.6, 119.7, 19.0.

4-Methyl-2-(*p*-tolyl)quinoline (3b).[18] Yellow oil (59.4 mg, 85%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 10.5 Hz, 1H), 8.09–8.07 (m, 2H), 7.98 (d, J = 10.0 Hz, 1H), 7.74–7.70 (m, 2H), 7.55–7.51 (m, 1H), 7.34 (d, J = 10.0 Hz, 2H), 2.74 (s, 3H), 2.45 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.0, 148.1, 144.7, 139.3, 136.9, 130.2, 129.5, 129.3, 127.4, 127.2, 125.9, 123.6, 119.6, 21.3, 19.0.

4-Methyl-2-(*m*-tolyl)quinoline (3c).[18] Yellow oil (55.2 mg, 79%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 8.02–7.98 (m, 2H), 7.94 (d, J = 8.0 Hz, 1H), 7.74–7.70 (m, 2H), 7.56–7.52 (m, 1H), 7.44–7.41 (m, 1H), 7.29 (d, J = 7.5 Hz, 1H), 2.75 (s, 3H), 2.50 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.3, 148.1, 144.7, 139.8, 138.4, 130.3, 130.0, 129.3, 128.7, 128.3, 127.3, 126.0, 124.7, 123.6, 119.9, 21.6, 19.0.

4-Methyl-2-(*o*-tolyl)quinoline (3d).[19] Yellow oil (36.3 mg, 52%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 8.5 Hz, 1H), 8.04–8.03 (m, 1H), 7.76–7.73 (m, 1H), 7.60–7.57 (m, 1H), 7.51–7.49 (m, 1H), 7.39 (s, 1H), 7.37–7.31 (m, 3H), 2.76 (s, 3H), 2.43 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 160.3, 147.9, 144.3, 140.5, 136.0, 130.3, 130.0, 129.6, 129.3, 128.3, 126.0, 123.6, 123.1, 20.3, 18.8.

2-(4-Fluorophenyl)-4-methylquinoline (3e).[20] Yellow oil (54.1 mg, 76%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 10.5 Hz, 1H), 7.99 (d, J = 10.5 Hz, 1H), 7.92–7.90 (m, 2H), 7.75–7.71 (m, 1H), 7.67 (s, 1H), 7.58–7.54 (m, 1H), 7.50–7.45 (m, 1H), 7.17–7.13 (m, 1H), 2.76 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 163.8 (d, J = 247.5 Hz), 155.9, 148.1, 145.0, 135.9 (d, J = 2.5 Hz), 130.2, 129.4, 129.3 (d, J = 7.5 Hz), 127.2, 126.1, 123.6, 119.4, 115.7 (d, J = 22.5 Hz), 19.0.

2-(3-Fluorophenyl)-4-methylquinoline (3f).[21] Yellow oil (44.8 mg, 63%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.18 (m, 3H), 7.86–7.85 (m, 1H), 7.61–7.50 (m, 2H), 7.43–7.42 (m, 1H), 7.09–7.07 (m, 2H), 2.62 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 163.4 (d, J = 243.8 Hz), 155.5 (d, J = 2.5 Hz), 148.0, 145.1, 142.1 (d, J = 7.5 Hz), 130.4, 130.2 (d, J = 8.8 Hz), 129.5, 127.4, 126.4, 123.6, 123.0 (d, J = 3.8 Hz), 119.4, 116.0 (d, J = 21.3 Hz), 114.4 (d, J = 22.5 Hz), 19.0.

2-(4-Chlorophenyl)-4-methylquinoline (3g).[22] White solid (38.8 mg, 51%), mp 73–74 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.16 (d, J = 10.5 Hz, 1H), 8.11–8.09 (m, 2H), 7.98 (d, J = 10.5 Hz, 1H), 7.74–7.70 (m, 1H), 7.65 (s, 1H), 7.57–7.53 (m, 1H), 7.49–7.47 (m, 2H), 2.74 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 155.5, 147.9, 144.9, 138.0, 135.3, 130.1, 129.4, 128.8, 128.6, 126.2, 126.1, 123.5, 119.1, 18.8.

2-(4-Bromophenyl)-4-methylquinoline (3h).[21] White solid (37.5 mg, 42%), mp 66–67 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22–8.15 (m, 2H), 8.05–8.03 (m, 1H), 8.00–7.98 (m, 1H), 7.74–7.71 (m, 1H), 7.66–7.63 (m, 2H), 7.57–7.51 (m, 2H), 2.77–2.76 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 155.3, 148.0, 145.2, 141.8, 132.1, 130.6, 130.4, 130.3, 129.6, 127.4, 126.4, 126.1, 123.7, 123.1, 119.5, 19.0.

4-Methyl-2-(4-(trifluoromethyl)phenyl)quinoline (3i).[23] Yellow oil (22.4 mg, 26%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 2H), 8.20 (d, J = 8.5 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.78–7.24 (m, 4H), 7.60–7.57 (m, 1H), 2.79 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 155.5, 148.0, 145.5, 143.0, 131.0 (d, J = 32.5 Hz), 130.4, 129.7, 127.9, 127.5, 126.6, 125.7 (q, J = 3.8 Hz), 124.2 (d, J = 270.0 Hz), 123.7, 119.6, 19.0.

6-Methyl-2-phenylquinoline (3j).[24] White solid (42.7 mg, 65%), mp 68–69 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18–8.16 (m, 2H), 8.10 (d, J = 11.0 Hz, 2H), 7.82 (d, J = 11.0 Hz, 1H), 7.57–7.52 (m, 4H), 7.48–7.45 (m, 1H), 2.55 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 156.5, 146.8, 139.8, 136.2, 136.1, 132.0, 129.4, 129.2, 128.8, 127.5, 127.2, 126.3, 119.0, 21.6.

6-Methoxy-2-phenylquinoline (3k).[25] White solid (36.7 mg, 52%), mp 125–126 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.15–8.14 (m, 1H), 8.13 (s, 1H), 8.11 (d, J = 6.0 Hz, 1H), 8.08 (d, J = 6.0 Hz, 1H), 7.83 (d, J = 11.5 Hz, 1H), 7.52 (dd, J_1 = 9.5 Hz, J_2 = 9.0 Hz, 2H), 7.45 (d, J = 9.5 Hz, 1H), 7.39 (dd, J_1 = 3.5 Hz, J_2 = 11.5 Hz, 1H), 7.08 (d, J = 3.5 Hz, 1H), 3.94 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.8, 155.0, 144.4, 139.8, 135.5, 131.2, 128.9, 128.8, 128.2, 127.3, 122.3, 119.2, 105.1, 55.5.

6-Fluoro-2-phenylquinoline (3l).[16] White solid (41.5 mg, 62%), mp 94–95 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.21–8.19 (m, 2H), 8.17–8.15 (m, 2H), 7.91 (d, J = 10.5 Hz, 1H), 7.56–7.44 (m, 5H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 160.4 (d, J = 248.0 Hz), 156.7 (d, J = 2.8 Hz), 145.3, 139.2, 136.2 (d, J = 5.2 Hz), 132.1 (d, J = 9.1 Hz), 129.5, 128.9, 127.7 (d, J = 10.0 Hz), 127.5, 119.9 (d, J = 25.7 Hz), 119.7, 110.5 (d, J = 21.7 Hz).

7-Fluoro-2-phenylquinoline (3m).[25] White solid (38.8 mg, 58%), mp 88–89 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.5 Hz, 2H), 7.86–7.80 (m, 3H), 7.56–7.53 (m, 2H), 7.50–7.47 (m, 1H), 7.34–7.30 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 163.3 (d, J = 249.6 Hz), 158.3, 149.3 (d, J = 12.9 Hz), 139.3, 136.6, 129.6, 129.4 (d, J = 10.0 Hz), 128.9, 127.6, 124.2, 118.3 (d, J = 2.5 Hz), 116.7 (d, J = 25.5 Hz), 113.3 (d, J = 20.2 Hz).

6-Chloro-2-phenylquinoline (3n).[26] White solid (40.3 mg, 56%), mp 109–110 °C. ^{11}H-NMR (500 MHz, $CDCl_3$) δ 8.16–8.11 (m, 4H), 7.89 (d, J = 9.0 Hz, 1H), 7.84–7.80 (m, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.55–7.52 (m, 2H), 7.49–7.47 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.5, 146.6, 139.2, 135.8, 132.0, 131.3, 130.6, 129.6, 128.9, 127.7, 127.5, 126.1, 119.8.

6-Chloro-2-(*p*-methoxyphenyl)quinoline (3o).[27] Pale yellow solid (18.6 mg, 23%), mp 156–158 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.5 Hz, 2H), 8.08 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 1H), 7.77 (s, 1H), 7.64 (d, J = 9.0 Hz, 1H), 7.05 (d, J = 8.5 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 157.1, 146.6, 135.7, 131.5, 131.0, 130.5, 128.9, 127.5, 126.1, 119.3, 114.3, 55.4.

7-Chloro-2-phenylquinoline (3p).[28] White solid (38.8 mg, 54%), mp 106–107 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.21–8.15 (m, 4H), 7.89–7.87 (m, 1H), 7.77–7.75 (m, 1H), 7.56–7.48 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 158.2, 148.5, 139.0, 136.7, 135.6, 129.7, 128.9, 128.7, 128.6, 127.6, 127.4, 125.5, 119.2.

6-Bromo-2-phenylquinoline (3q).[27] White solid (34.9 mg, 41%), mp 113–114 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.0 Hz, 2H), 8.10–8.09 (m, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.96 (s, 1H), 7.88–7.86 (m, 1H), 7.79–7.77 (m, 1H), 7.55–7.52 (m, 2H), 7.50–7.47 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.6, 146.8, 139.1, 135.8, 133.1, 131.4, 129.6, 129.5, 128.9, 128.2, 127.5, 120.0, 119.7.

2-Phenyl-6-(trifluoromethyl)quinoline (3r).[29] White solid (29.5 mg, 36%), mp 118–119 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 10.0 Hz, 2H), 8.20–8.17 (m, 2H), 8.12 (s, 1H), 7.94 (d, J = 10.0 Hz, 1H), 7.90–7.88 (m, 1H), 7.58–7.51 (m, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 159.3, 149.3, 138.9, 137.4, 130.9, 130.0, 129.0, 128.2, 127.9, 127.7, 126.1, 125.4 (q, J = 3.8 Hz), 125.3 (q, J = 3.8 Hz), 123.1, 120.0.

2-Phenylquinoline (3s).[30] White solid (31.4 mg, 51%), mp 84–85 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.24–8.17 (m, 4H), 7.89 (d, J = 10.0 Hz, 1H), 7.84 (d, J = 10.0 Hz, 1H), 7.76–7.72 (m, 1H), 7.56–7.52 (m, 3H), 7.49–7.46 (m, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.4, 148.3, 139.6, 136.8, 129.7, 129.6, 129.4, 128.8, 127.6, 127.4, 127.2, 126.3, 119.0.

4-Ethyl-2-phenylquinoline (3t).[20] Yellow oil (49.6 mg, 71%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 10.5 Hz, 1H), 8.18–8.17 (m, 2H), 8.04 (d, J = 10.5 Hz, 1H), 7.74–7.70 (m, 2H), 7.56–7.52 (m, 3H), 7.49–7.46 (m, 1H), 3.17 (q, J = 9.5 Hz, 2H), 1.45 (t, J = 9.5 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.3, 150.4, 148.5, 140.1, 130.6, 129.2, 128.8, 127.6, 126.4, 126.0, 123.2, 117.8, 25.4, 14.2.

4-Isopropyl-2-phenylquinoline (3u).[31] Yellow oil (45.9 mg, 62%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 10.5 Hz, 1H), 8.17–8.15 (m, 2H), 8.11 (d, J = 10.5 Hz, 1H), 7.79 (s, 1H), 7.73–7.70 (m, 1H), 7.57–7.52 (m, 3H), 7.49–7.45 (m, 1H), 3.84–3.77 (m, 1H), 1.48 (d, J = 9.0 Hz, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 157.4, 154.9, 148.6, 140.3, 130.7, 129.1, 129.0, 128.8, 127.6, 125.9, 125.8, 122.9, 114.9, 28.6, 23.0.

2,4-Diphenylquinoline (3v).[32] White solid (48.1 mg, 57%), mp 104–105 °C. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 10.5 Hz, 1H), 8.21–8.19 (m, 2H), 7.92 (d, J = 10.5 Hz, 1H), 7.83 (s, 1H), 7.77–7.73 (m, 1H), 7.57–7.55 (m, 4H), 7.54–7.48 (m, 5H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 156.9, 149.4, 148.7, 139.6, 138.4, 130.0, 129.6, 129.4, 128.8, 128.6, 128.4, 127.6, 126.4, 125.8, 125.7, 119.4.

Conflicts of interest

There are no conflicts of interest to declare.

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