JOC The Journal of Organic Chemistry

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Palladium-Catalyzed Allylic C−H Oxidative Annulation for Assembly of Functionalized 2-Substituted Quinoline Derivatives

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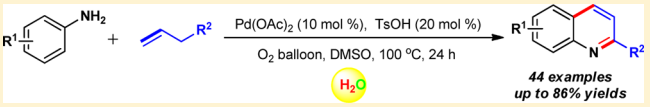
Supporting Information

ABSTRACT: An efficient and practical palladium-catalyzed aerobic oxidative approach to afford functionalized 2-substituted quinolines in moderate to good yields from readily available allylbenzenes with aniline is developed. The present annulation process has high functional-group tolerance and high atom economy, making it a valuable and practical method in synthetic and medicinal chemistry. Moreover, this transformation is supposed to proceed through oxidation of allylic C−H functionalization to form C−C and C−N bonds in one pot.

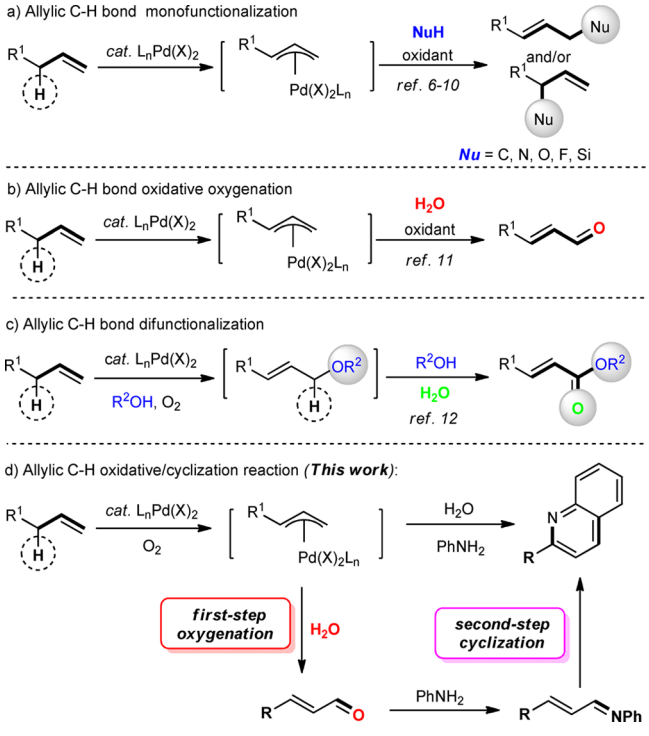


INTRODUCTION

Transition-metal-catalyzed oxidative functionalization of the allylic C−H bond has been an essential strategy for the direct transformation of nonsubstituted simple alkenes into complex molecules in a concise manner.[1] In addition, the practical utility of direct allylic C−H activation and subsequent installation of functionality into hydrocarbon frameworks is highly desirable from atom-economic and environmental perspectives. Among them, metal complexes of copper,[2] iron,[3] ruthenium,[4] and other metals[5] have been defined as markedly efficient catalysts for allylic C−H bond activation. Recently, elegant works have also been reported on Pd-catalyzed oxidation of allylic C−H bonds into more synthetically useful C−C,[6] C−N,[7] C−O,[8] C−F,[9] and C−Si[10] bonds (Scheme 1a). Our group has also reported a facile synthesis of (*E*)-alkenyl aldehydes via palladium-catalyzed aerobic oxidative allylic C−H oxygenation (Scheme 1b).[11] Next, a significant advance in double allylic C−H oxygenation reaction for the expedient and selective synthesis of a broad range of linear aryl α,β-unsaturated esters with alcohol as nucleophile was documented in 2015 (Scheme 1c).[12]

Quinolines and their derivatives are important substructures in a large number of natural or designed products due to their wide spectrum of biological activities.[13] 2-Arylquinoline skeletons, for instance, are associated with a wide range of biological properties, such as P-selectin antagonism, antimalarial, and antitumor activties.[14] As a consequence of their proven potential bioactivity, a great deal of advanced methods for the synthesis of substituted quinolines have been well-developed over these years. Generically, two distinctive methods are employed: (*i*) the traditional metal-free, including Skraup, Friedländer, and Doebner−Miller reactions, cascade condensation/cyclization reactions;[15] and (*ii*) the transition-metal-catalyzed cross-coupling reactions from readily available materials like alkenes or alkynes.[16] Despite the significant progress that has been achieved along this line, most of these elegant developments suffer from certain limitations such as troublesome operation, harsh reaction conditions, or low yields, prohibiting their wider applications in organic synthesis. Therefore, the development of novel and expeditious approaches for the preparation of a diverse range of substituted quinolines, based on the idea of high efficiency and atom economy, remains an active research area.

Scheme 1. Pd-Catalyzed Oxidative Functionalization of Allylic C−H Bonds



Received: August 5, 2016
Published: October 28, 2016

ACS Publications © 2016 American Chemical Society

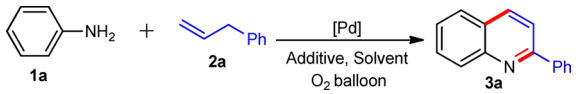
DOI: 10.1021/acs.joc.6b01909
J. Org. Chem. 2016, 81, 12189−12196

On the basis of these precedents, we envision that the allyl−Pd intermediate could be captured by water (H_2O),[11] which would undergo the subsequent cascade condensation/oxidative cyclization to generate 2-arylquinolines in the presence of aniline.[15h] Moreover, the use of molecular oxygen as a terminal oxidant realized the goal of high atom economy and green chemisty.[17,18] Herein we would like to report a strategically distinct approach to synthesize 2-arylquinolines through palladium-catalyzed aerobic oxidative allylic C−H functionalization of terminal olefins (Scheme 1d).

RESULTS AND DISCUSSION

The investigation was initiated by using the reaction of aniline (**1a**) with allylbenzene (**2a**) as a model system to screen the optimal conditions. As shown in Table 1, the reaction did not proceed without palladium catalyst (Table 1, entry 1). Initially, different palladium species such as $Pd(OAc)_2$, $PdCl_2$, $Pd(TFA)_2$, and $Pd(CH_3CN)_2Cl_2$ were tested (entries 2−5), and $Pd(OAc)_2$ proved to be more efficient in this reaction. Subsequently, we also closely examined the solvent effects, and it appears that DMSO was the most suitable solvent for this reaction (entry 2 vs entries 6−9). Finally, several additives were screened, such as H_2SO_4, CF_3SO_3H, $BF_3{\cdot}Et_2O$, $ZnCl_2$, $FeCl_2$, and TsOH, and TsOH was found to be the best one (entries 10−15). Furthermore, the lower or the higher temperature disfavored the reaction, and **3a** was obtained in 67% and 45% yields, respectively (entries 16 and 17). Thus, the optimized reaction conditions are as follows: 10 mol % $Pd(OAc)_2$ and 20 mol % TsOH in 1 mL of DMSO at 110 °C for 24 h.

Table 1. Optimization of the Reaction Conditions[a]

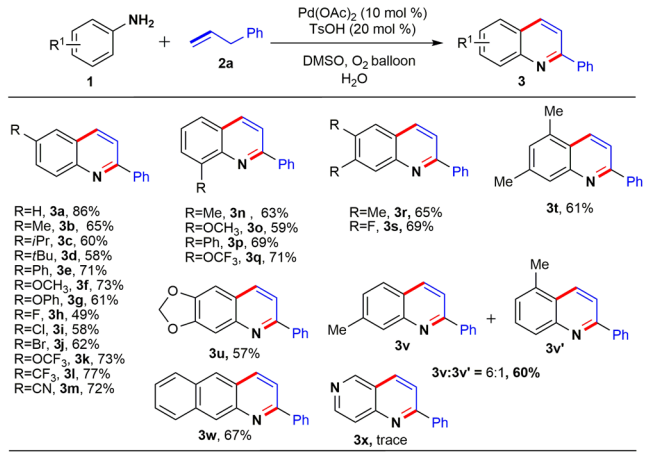


entry	catalyst	additive	solvent	yield (%)[b]
1	-	AcOH	DMSO	-
2	$Pd(OAc)_2$	AcOH	DMSO	30
3	$PdCl_2$	AcOH	DMSO	8
4	$Pd(TFA)_2$	AcOH	DMSO	trace
5	$Pd(CH_3CN)_2Cl_2$	AcOH	DMSO	7
6	$Pd(OAc)_2$	AcOH	toluene	5
7	$Pd(OAc)_2$	AcOH	DMF	trace
8	$Pd(OAc)_2$	AcOH	dioxane	9
9	$Pd(OAc)_2$	AcOH	DMA	8
10	$Pd(OAc)_2$	H_2SO_4	DMSO	17
11	$Pd(OAc)_2$	CF_3SO_3H	DMSO	trace
12	$Pd(OAc)_2$	$BF_3{\cdot}Et_2O$	DMSO	27
13	$Pd(OAc)_2$	$ZnCl_2$	DMSO	16
14	$Pd(OAc)_2$	$FeCl_2$	DMSO	12
15	$Pd(OAc)_2$	TsOH	DMSO	86
16[c]	$Pd(OAc)_2$	TsOH	DMSO	67
17[d]	$Pd(OAc)_2$	TsOH	DMSO	45

[a]Unless otherwise noted, all reactions were performed with **1a** (0.25 mmol), **2a** (0.5 mmol), Pd catalyst (10 mol %), additive (20 mol %), and H_2O (0.25 mL) in the indicated solvent (1.0 mL) under 1 atm oxygen at 110 °C for 24 h. [b]Determined by GC using dodecane as the internal standard. [c]The reaction was performed at 100 °C. [d]The reaction was performed at 120 °C.

Next, the substrate scope of various anilines **1** with allylbenzene (**2a**) was performed under the optimized condition, and the representative results are summarized in Scheme 2.

Scheme 2. Substrate Scope of Various Anilines[a]



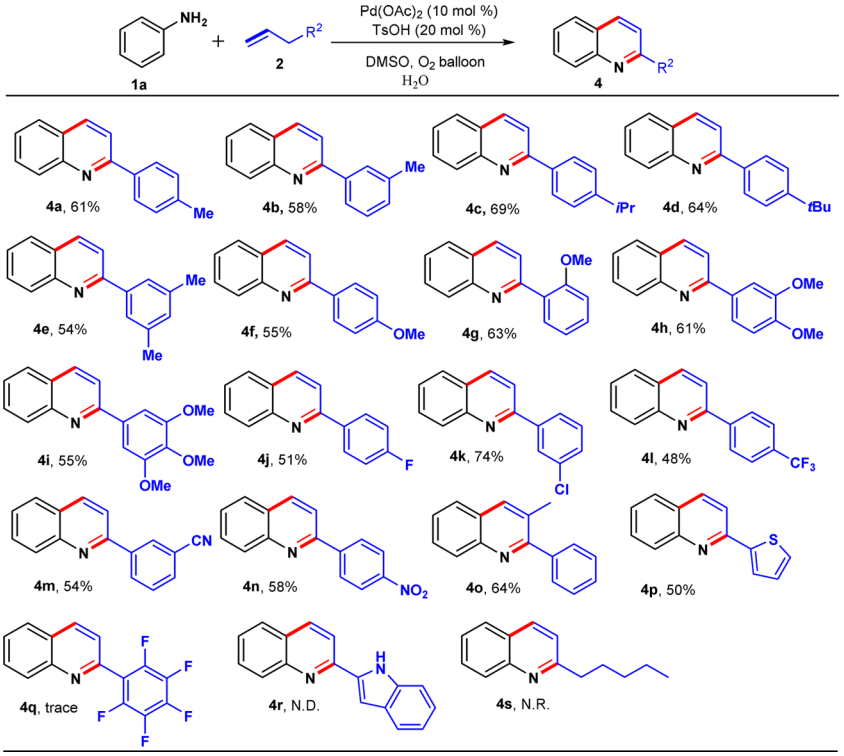
[a]Reactions were performed with **1** (0.25 mmol), **2a** (0.5 mmol), $Pd(OAc)_2$ (10 mol %), TsOH (20 mol %), H_2O (0.25 mL), and DMSO (1 mL) under 1 atm oxygen at 110 °C for 24 h. Yields referred to isolated yield.

Gratifyingly, both electron-deficient and electron-rich aniline components delivered the corresponding products in moderate to good yields. Delightfully, a series of *para*-substituted anilines, including some with electron-donating groups (Me, *i*Pr, *t*Bu, Ph, OMe, and OPh) and some with electron-withdrawing groups (F, Cl, Br, CF_3, and CN), were converted into the corresponding 2-substituted quinolines in moderate to excellent yields (**3a−3m**). Furthermore, various *ortho*-substituted anilines could transfer to the corresponding products **3n−3q** in moderate yields under the optimized condition. As expected, this transformation could be successfully extended to some disubstituted anilines, furnishing the corresponding quinoline derivatives **3r−3u** in 57%−69% yields. These results showed that this new transformation was tolerant toward electronic and steric effects of the aromatic ring. In addition, when 3-methylaniline (**1v**) was employed under the optimized conditions, two regioisomeric products **3v** and **3v′** were obtained with poor selectivity (6:1 d.r.), and the 8-substituted regioisomer **3v** was the major product. Notably, naphthalen-2-amine (**1w**) was also suitable for the current procedure to furnish the corresponding product **3w** in 67% yield. Disappointingly, only trace desired product was observed by GC-MS when pyridin-4-amine (**1x**) was employed in this reaction. Despite the significance of this currently catalytic system, as the byproducts of this transformation, a small amount of cinnamaldehyde derivatives were observed by GC-MS analysis when the reaction was finished.

To expand the scope of this method, we subsequently investigated a variety of allylbenzenes, and the results are presented in Scheme 3. Generally, almost all of the allylbenzenes used in this study were successfully coupled under our optimized conditions (**4a−4p**). Moreover, allylbenzenes bearing electron-donating groups (Me, *i*Pr, *t*Bu, and OMe) at the *para*, *meta*, and *ortho* positions of the phenyl ring could react smoothly and afford the corresponding products **4a−4i** in moderate yields ranging from 54% to 69%. Similarly, allylbenzenes possessing electron-withdrawing groups are also good coupling partners (**4j−4m**). Notably, this transformation was compatible with the Cl-substituted aryl ring, which might allow for further synthetic transformations by transition-metal-catalyzed coupling. Pleasingly, as for the sterically hindered (2-methylallyl)benzene (**2o**),

DOI: 10.1021/acs.joc.6b01909
J. Org. Chem. 2016, 81, 12189−12196

Scheme 3. Substrate Scope of Various Allylbenzenes[a]



[a]Reactions were performed with **1a** (0.25 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (10 mol %), TsOH (20 mol %), H_2O (0.25 mL), and DMSO (1 mL) under 1 atm oxygen at 110 °C for 24 h. Yields referred to isolated yield.

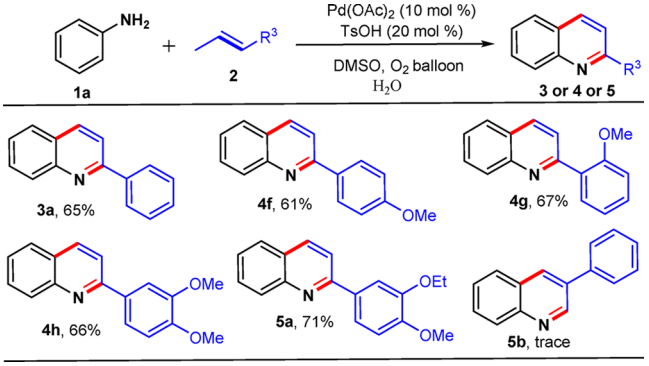
the reaction also furnished the corresponding products **4o** in 64% yield. Significantly, when 2-allylthiophene was employed as substrate, the desired product **4p** was isolated in 50% yield. Unfortunately, functionalized allylbenzene derivatives, such as 1-allyl-2,3,4,5,6-pentafluorobenzene (**2q**) and 2-allyl-1*H*-indole (**2r**), failed to afford the desired products. Finally, long-chain alkenes, such as 1-octene (**2s**), were also investigated, but no desired product was obtained under the optimal conditions.

Remarkably, as shown in Scheme 4, when *trans*-*β*-methylstyrenes were used as the substrates, the desired 2-substituted quinoline derivatives were obtained, which was in good agreement with the result obtained when the corresponding reactions were performed with allylbenzenes (**3a**, **4f**–**4h**). However, when we subjected prop-1-en-2-ylbenzene to the standard reaction conditions, only a trace amount of the desired product **5b** was detected by GC-MS.

Several control experiments were carried out to get further insights into this unique transformation (Scheme 5). Under the standard conditions, the control experiment without aniline was performed, and cinnamaldehyde **6** was observed in 89% GC yield (eq 1).[11] Furthermore, when **6** was reacted with aniline (**1a**) under the standard conditions, product **3a** was detected in 79% GC yield (eq 2).[15] These observations indicated that the reaction might proceed via cinnamaldehyde **6** as the key intermediate. Finally, when super dry DMSO was used as solvent, only a trace amount of the desired product **3a** was detected by GC-MS (eq 3). We reasoned that water played a vital role and was indispensable for the present method.

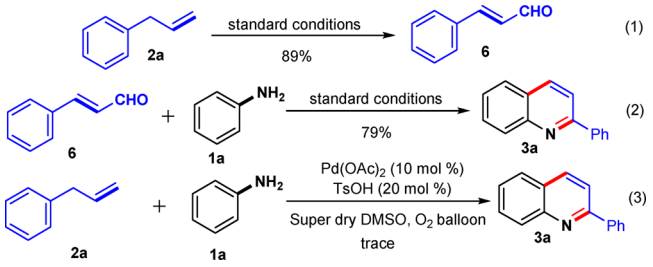
Based on the current results and previous literature, a plausible mechanism was proposed which is shown in Scheme 6. First, the corresponding *π*-allylpalladium species intermediate **I** is formed

Scheme 4. Synthesis of 2-Substituted Quinoline Derivatives from *trans*-*β*-Methylstyrene with 1a[a]



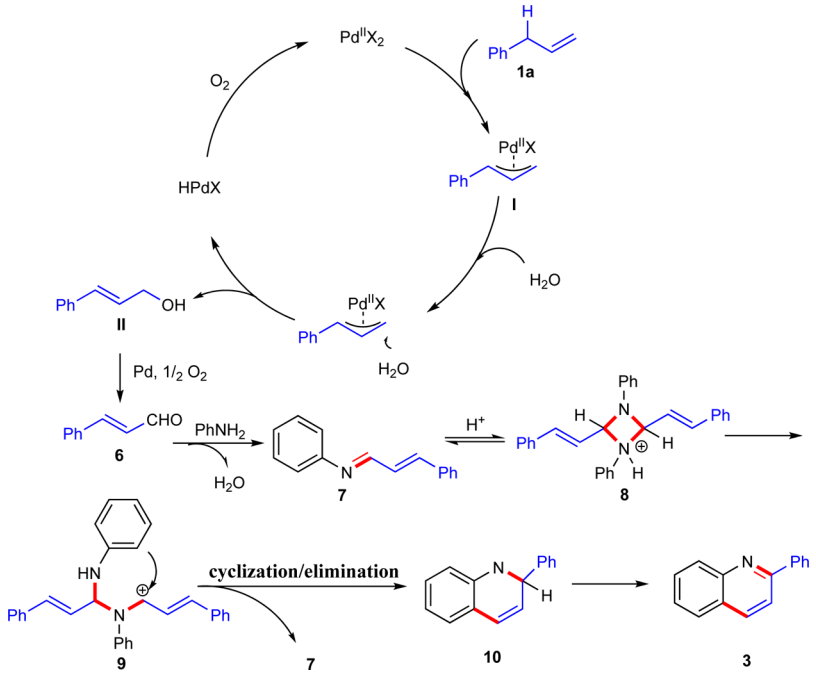
[a]Reactions were performed with **1a** (0.25 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (10 mol %), TsOH (20 mol %), H_2O (0.25 mL), and DMSO (1 mL) under 1 atm oxygen at 110 °C for 24 h. Yields referred to isolated yield.

Scheme 5. Control Experiments



DOI: 10.1021/acs.joc.6b01909
J. Org. Chem. 2016, 81, 12189–12196

Scheme 6. Proposed Mechanism



through the coordination of the allylic C−H bond of the olefin to palladium.[19,20] Then, nucleophilic attack by H_2O subsequently occurs to afford the cinnamic alcohol intermediate **II**. Oxidation of **II** by O_2 affords the cinnamaldehyde **6**.[11] Then, the next step was a traditional condensation leading to the formation of an imine,[21a] followed by a conjugate addition of a second molecule of imine in the presence of TsOH. Therefore, the labile diazetidinium cation intermediate **8** was formated. Then following the irreversible cyclization and elimination of **7**, 2-phenyl-1,2-dihydroquinolin **10** was generated with the subsquent oxidation to afford the desired product.[21b] Finally, Pd(0) is oxidized to regenerate the active species Pd(II) by dioxygen.[12]

In conclusion, we report the Pd(II)/TsOH/O_2-catalyzed oxidative/cyclization of simple alkenes with water and simple amines to afford 2-aryl-substituted quinolines in moderate to good yields. More importantly, this method provides a new tool for the construction of biologically important 2-aryl-substituted quinoline derivatives from inexpensive starting materials with broad substrate scope and excellent functional group compatibility.

EXPERIMENTAL SECTION

General Method. Melting points were measured using a melting point instrument and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.24 and 77.0 ppm, respectively, and chloroform was used as a solvent with TMS as the internal standard. IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets. GC−MS data were obtained using electron ionization. HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed using commercially available 100−400 mesh silica gel plates (GF_{254}). Unless otherwise noted, purchased chemicals were used without further purification.

General Procedure for Synthesis of Quinoline Derivatives. Amine (0.25 mmol), allylbenzene derivatives (0.50 mmol), $Pd(OAc)_2$ (10 mol %), TsOH (20 mol %), and water (0.25 mL) were added to DMSO (1 mL) under 1 atm oxygen. The mixture was stirred under 1 atm oxygen at 110 °C for the desired reaction time. After that, water was added and extracted with ethyl acetate twice. The combined organic phase was dried over $MgSO_4$ and concentrated. The residue was eventually purified by flash column chromatography on a silica gel (hexane/ethyl acetate) to afford the product. Compounds **3c**−**3d**, **3g**, **3k**, **3m**, **3q**, **3s**, **4c**, **4d**, **4i**, and **5a** are all new compounds.

*2-Phenylquinoline (**3a**).*[16a] Yield: 86% (44.3 mg) as yellow solid; mp = 86−87 °C; R_f = 0.69 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.8 Hz, 2H), 8.17 (d, J = 7.2 Hz, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 7.2 Hz, 1H), 7.53 (t, J = 6.8 Hz, 3H), 7.49−7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 148.1, 139.5, 136.9, 129.8, 129.6, 129.4, 128.9, 127.6, 127.5, 127.2, 126.4, 119.1 ppm; ν_{max}(KBr)/cm^{-1} 3450, 2923, 1625, 1603, 1021, 830, 799, 688; MS (EI) m/z 51, 76, 88, 102, 113, 128, 151, 164, 176, 205, 206; HRMS-ESI (m/z): calcd for $C_{15}H_{12}N$, $[M + H]^+$: 206.0964, found 206.0969.

*6-Methyl-2-phenylquinoline (**3b**).*[16f] Yield: 65% (35.6 mg) as yellow solid; mp = 91−92 °C; R_f = 0.59 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46−7.91 (m, 4H), 7.83 (d, J = 8.0 Hz, 1H), 7.62−7.48 (m, 4H), 7.51−7.40 (m, 1H), 2.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 146.8, 139.7, 136.2, 136.2, 132.2, 129.3, 129.2, 128.8, 127.5, 127.2, 126.3, 119.0, 21.5 ppm; ν_{max}(KBr)/cm^{-1} 3448, 2920, 1628, 1504, 1448, 1271, 965, 840; MS (EI) m/z 219, 204, 189, 165, 140, 115, 108, 95, 89, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1125.

*6-(iso-Propyl)-2-phenylquinoline (**3c**).* Yield: 60% (37.4 mg) as yellow solid; mp = 96−97 °C; R_f = 0.52 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 16.0, 8.0 Hz, 4H), 7.85 (d, J = 8.0 Hz, 1H), 7.67−7.63 (m, 2H), 7.53 (t, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 1H), 3.11 (dt, J = 13.2, 6.4 Hz, 1H), 1.37 (d, J = 4.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 147.1, 146.8, 139.5, 136.8 129.8, 129.3, 129.1, 127.6, 127.3, 123.6, 119.0, 34.1, 23.9 ppm; ν_{max}(KBr)/cm^{-1} 3727, 3059, 2958, 2349, 1592, 1458, 1306, 1025, 885; MS (EI) m/z 248, 232, 204, 176, 154, 127, 108, 77; HRMS-ESI (m/z): calcd for $C_{18}H_{18}N$, $[M + H]^+$: 248.1434, found 248.1435.

*6-(tert-Butyl)-2-phenylquinoline (**3d**).* Yield: 58% (38.1 mg) as yellow solid; mp = 103−104 °C; R_f = 0.62 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 18.0, 8.0 Hz, 4H), 7.86−7.82 (m, 2H), 7.74 (s, 1H), 7.52 (t, J = 6.4 Hz, 2H), 7.46 (d, J = 8.0 Hz, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 149.3, 146.5, 137.0, 129.3, 129.0, 128.8, 128.1, 127.9, 127.6, 126.9, 122.5, 119.0, 34.9, 31.2 ppm; ν_{max}(KBr)/cm^{-1} 3428, 3061, 2960, 2865, 1597, 1456, 889,

DOI: 10.1021/acs.joc.6b01909
J. Org. Chem. 2016, 81, 12189−12196

796, 692; MS (EI) m/z 261, 246, 230, 218, 206, 168, 152, 128, 108, 95; HRMS-ESI (m/z): calcd for $C_{19}H_{20}N$, $[M + H]^+$: 262.1590, found 262.1595.

*2,6-Diphenylquinoline (**3e**).* Yield: 71% (50.1 mg) as yellow solid; mp = 196−197 °C; R_f = 0.54 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 8.0 Hz, 2H), 7.90 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.55−7.48 (m, 5H), 7.40 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 147.6, 140.4, 139.6, 139.1, 137.0, 130.1, 129.4, 129.4, 128.9, 128.9, 127.7, 127.6, 127.4, 127.4, 125.2, 119.4 ppm; ν_{max}(KBr)/cm^{-1} 3052, 2955, 1600, 1455, 1069, 957, 765, 696; MS (EI) m/z 281, 280, 278, 226, 139, 126, 113, 100, 76, 51; HRMS-ESI (m/z): calcd for $C_{21}H_{16}N$, $[M + H]^+$: 282.1277, found 282.1277.

*6-Methoxy-2-phenylquinoline (**3f**).*[16a] Yield: 73% (42.3 mg) as yellow solid; mp = 128−129 °C; R_f = 0.42 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 9.2 Hz, 1H.), 7.86 (d, J = 8.0 Hz, 1H), 7.55 (t, J = 6.0 Hz, 2H), 7.49−7.40 (m, 2H), 7.12 (s, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 155.1, 144.4, 139.8, 135.5, 131.2, 128.9, 128.8, 128.2, 127.3, 122.3, 119.3, 105.0, 55.6 ppm; ν_{max}(KBr)/cm^{-1} 3060, 2921, 2851, 1595, 1494, 832, 758, 694; MS (EI) m/z 235, 220, 204, 192, 176, 165, 139, 117, 95, 88; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1074.

*6-Phenoxy-2-phenylquinoline (**3g**).* Yield: 61% (45.5 mg) as yellow solid; mp = 196−197 °C; R_f = 0.50 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 16.0, 8.0 Hz, 3H), 8.07 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 6.4 Hz, 3H), 7.49−7.35 (m, 3H), 7.20−7.10 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 156.1, 155.6, 144.9, 139.5, 136.0, 131.5, 129.9, 129.3, 128.9, 127.9, 127.5, 123.9, 123.4, 119.6, 119.5, 112.6 ppm; ν_{max}(KBr)/cm^{-1} 3441, 2922, 2852, 1632, 1486, 1229, 755, 694; MS (EI) m/z 297, 268, 243, 220, 203, 191, 165, 148, 115, 77; HRMS-ESI (m/z): calcd for $C_{21}H_{16}NO$, $[M + H]^+$: 298.1226, found 298.1227.

*6-Fluoro-2-phenylquinoline (**3h**).*[16d] Yield: 49% (27.5 mg) as yellow solid; mp = 106−107 °C; R_f = 0.61 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.14 (m, 4H), 7.88 (d, J = 8.0 Hz, 2H), 7.54−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4 (d, J = 246.0 Hz), 156.7 (d, J = 3.0 Hz), 145.4, 139.4, 136.2 (d, J = 5.3 Hz), 132.2 (d, J = 9.0 Hz), 129.4, 128.9, 127.7 (d, J = 10.0 Hz), 127.5, 119.9, 119.7, 110.5 (d, J = 21.0 Hz) ppm; ν_{max}(KBr)/cm^{-1} 3063, 2970, 1552, 1499, 1235, 870, 692; MS (EI) m/z 223, 204, 194, 175, 169, 146, 126, 101, 88, 75; HRMS-ESI (m/z): calcd for $C_{15}H_{11}NF$, $[M + H]^+$: 224.0870, found 224.0871.

*6-Chloro-2-phenylquinoline (**3i**).*[16d] Yield: 58% (34.8 mg) as yellow solid; mp = 108−109 °C; R_f = 0.52 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (t, J = 6.0 Hz, 4H), 7.90 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H), 7.66 (d, J = 9.0 Hz, 1H), 7.55−7.48 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 146.6, 139.1, 135.9, 131.9, 131.3, 130.6, 129.6, 128.9, 127.7, 127.6, 126.2, 119.8 ppm; ν_{max}(KBr)/cm^{-1} 3450, 2922, 2852, 1636, 1547, 879, 785, 694; MS (EI) m/z 239, 204, 176, 151, 119, 102, 88, 74; HRMS-ESI (m/z): calcd for $C_{15}H_{11}ClN$, $[M + H]^+$: 240.0575, found 240.0575.

*6-Bromo-2-phenylquinoline (**3j**).*[16a] Yield: 62% (44.0 mg) as yellow solid; mp = 123−124 °C; R_f = 0.63 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (t, J = 8.0 Hz, 3H), 8.05 (d, J = 8.0 Hz, 1H), 7.98 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 12.0 Hz, 1H), 7.50 (dt, J = 13.2, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 146.8, 139.1, 135.8, 133.2, 131.4, 129.7, 129.5, 128.9, 128.3, 127.6, 120.1, 119.8 ppm; ν_{max}(KBr)/cm^{-1} 3433, 2922, 2854, 1594, 1483, 830, 694; MS (EI) m/z 283, 204, 176, 164, 151, 127, 102, 88, 75, 51; HRMS-ESI (m/z): calcd for $C_{15}H_{11}BrN$, $[M + H]^+$: 284.0069, found 284.0066.

*2-Phenyl-6-(trifluoromethoxy)quinoline (**3k**).* Yield: 76% (55.1 mg) as yellow solid; mp = 123−124 °C; R_f = 0.59 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 2H), 8.16 (d, J = 8.0 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.65 (s, 1H), 7.59−7.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 146.8 (q, J = 4.0 Hz), 139.1, 136.6, 131.9, 129.7 (q, J = 241.2 Hz), 128.9, 127.6, 127.2, 123.8, 121.9, 119.9, 119.3, 117.5 ppm; ν_{max}(KBr)/cm^{-1} 3444, 2924, 1605, 1255, 1164, 839, 754, 697; MS (EI) m/z 289, 207, 204, 191, 165, 139, 115, 89, 69; HRMS-ESI (m/z): calcd for $C_{16}H_{11}F_3NO$, $[M + H]^+$: 290.0787, found 290.0792.

*2-Phenyl-6-(trifluoromethyl)quinoline (**3l**).*[16d] Yield: 77% (52.7 mg) as yellow solid; mp = 132−133 °C; R_f = 0.63 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 8.0 Hz, 2H), 8.12 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.52 (dq, J = 14.4, 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 149.2, 138.9, 137.6, 130.8, 130.0 (q, J = 265.1 Hz), 128.9, 128.2, 127.9, 127.7, 126.09, 125.4 (q, J = 4.0 Hz), 122.8, 120.1 ppm; ν_{max}(KBr)/cm^{-1} 3449, 2922, 1636, 1162, 1119, 836, 758, 692; MS (EI) m/z 273, 252, 204, 169, 151, 136, 126, 102, 88, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{11}F_3N$, $[M + H]^+$: 274.0838, found 274.0834.

*2-Phenylquinoline-6-carbonitrile (**3m**).* Yield: 72% (41.2 mg) as yellow solid; mp = 137−138 °C; R_f = 0.26 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (dd, J = 14.4, 8.4 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.57−7.51 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 149.2, 138.5, 137.1, 133.7, 131.1, 130.5, 130.4, 129.1, 127.8, 126.5, 120.5, 118.6, 109.8 ppm; ν_{max}(KBr)/cm^{-1} 3438, 2924, 2853, 1627, 1595, 1458, 833, 751, 694; MS (EI) m/z 230, 201, 175, 164, 153, 126, 114, 101, 88, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{10}N_2$, $[M + H]^+$: 231.0917, found 231.0914.

*8-Methyl-2-phenylquinoline (**3n**).*[16a] Yield: 63% (34.6 mg) as yellow oil; R_f = 0.78 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.0 Hz, 2H), 8.18 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.58−7.51 (m, 3H), 7.45−7.39 (m, 2H), 2.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 147.2, 139.9, 137.7, 136.7, 129.7, 129.2, 128.8, 127.5, 127.1, 126.0, 125.4, 118.2, 17.9 ppm; ν_{max}(KBr)/cm^{-1} 3448, 2920, 1628, 1504, 965, 840, 756, 690; MS (EI) m/z 219, 204, 191, 165, 141, 109, 95, 89, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1118.

*8-Methoxy-2-phenylquinoline (**3o**).*[15d] Yield: 59% (34.8 mg) as yellow oil; R_f = 0.32 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 4.0 Hz, 3H), 7.94 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 8.0 Hz, 2H), 7.45 (dd, J = 15.2, 8.0 Hz, 3H), 7.11 (d, J = 4.0 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 155.6, 140.1, 139.7, 136.8, 129.1, 128.8, 128.3, 127.7, 126.5, 119.5, 119.4, 108.2, 56.2 ppm; ν_{max}(KBr)/cm^{-1} 3474, 2921, 2852, 1465, 1257, 840, 761, 704; MS (EI) m/z 235, 204, 191, 176, 163, 128, 117, 102, 88, 76; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1070.

*2,8-Diphenylquinoline (**3p**).*[16e] Yield: 69% (34.8 mg) as yellow oil; R_f = 0.74 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 4.0 Hz, 2H), 7.93 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.79 (t, J = 8.0 Hz, 2H), 7.58−7.54 (m, 3H), 7.50−7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 145.6, 140.8, 139.6, 139.5, 137.1, 131.2, 130.4, 129.3, 128.8, 127.7, 127.4, 127.2, 126.2, 118.1 ppm; ν_{max}(KBr)/cm^{-1} 3052, 2955, 1600, 1455, 1069, 957, 765, 696; MS (EI) m/z 281, 280, 278, 226, 139, 126, 113, 100, 76, 51; HRMS-ESI (m/z): calcd for $C_{21}H_{16}N$, $[M + H]^+$: 282.1277, found 282.1272.

*2-Phenyl-8-(trifluoromethoxy)quinoline (**3q**).* Yield: 71% (51.5 mg) as yellow oil; R_f = 0.57 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 19.2, 8.0 Hz, 4H), 7.92 (d, J = 8.0 Hz, 1H), 7.65 (s, 1H), 7.59−7.48 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 146.8, 146.5, 139.2, 136.6, 131.9, 129.7 (q, J = 220.1 Hz), 128.9, 127.6, 127.2, 123.7, 121.9, 119.9, 119.3, 117.5 ppm; ν_{max}(KBr)/cm^{-1} 3444, 2924, 1605, 1255, 1164, 839, 754, 697; MS (EI) m/z 289, 268, 203, 202, 191, 176, 139, 115, 88, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{11}F_3NO$, $[M + H]^+$: 290.0787, found 290.0786.

*6,7-Dimethyl-2-phenylquinoline (**3r**).*[16a] Yield: 65% (38.0 mg) as yellow solid; mp = 109−110 °C; R_f = 0.68 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 18.4 Hz, 8.0 Hz, 3H), 7.99 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.56 (dd, J = 14.4, 8.0 Hz, 3H), 7.47 (t, J = 8.0 Hz, 1H), 2.52 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 147.4, 139.9, 136.3, 135.8, 129.1, 128.8, 127.5, 126.7, 125.8, 118.2, 20.5, 20.4 ppm; ν_{max}(KBr)/cm^{-1} 3457, 2972, 2932, 1632, 1447, 872, 756, 690; MS (EI) m/z 233, 218, 204, 189, 154, 128, 115, 108, 95, 77; HRMS-ESI (m/z): calcd for $C_{17}H_{16}N$, $[M + H]^+$: 234.1277, found 234.1280.

*6,7-Difluoro-2-phenylquinoline (**3s**).* Yield: 69% (41.8 mg) as yellow solid; mp = 94−95 °C; R_f = 0.63 (10:1 hexanes/ethyl acetate); ^{1}H NMR

DOI: 10.1021/acs.joc.6b01909
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(400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.0 Hz, 3H), 7.92−7.75 (m, 2H), 7.52−7.34 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7 (d, J = 3.0 Hz), 152.5 (dd, J = 253.1, 15.1 Hz), 148.8 (d, J = 16.1 Hz), 145.5 (d, J = 10.0 Hz), 139.0, 135.9 (dd, J = 5.1, 1.6 Hz), 129.7, 128.9, 127.5, 123.9 (d, J = 8.3 Hz), 119.1 (d, J = 2.2 Hz), 115.9 (d, J = 16.0 Hz), 112.6 (dd, J = 17.6, 1.5 Hz) ppm; ν_{max}(KBr)/cm^{-1} 3445, 2924, 1636, 1501, 1297, 882, 754, 696; MS (EI) m/z 241, 222, 212, 193, 164, 144, 120, 110, 87, 75; HRMS-ESI (m/z): calcd for $C_{15}H_{10}F_2N$, $[M + H]^+$: 242.0776, found 242.0775.

5,7-Dimethyl-2-phenylquinoline (**3t**).[15f] Yield: 61% (35.6 mg) as yellow oil; R_f = 0.29 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 2H), 7.88−7.83 (m, 2H), 7.56 (t, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.23 (s, 1H), 2.69 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 148.8, 139.7, 139.6, 133.9, 133.0, 129.2, 128.8, 127.5, 126.9, 124.6, 117.7, 21.8, 18.5 ppm; ν_{max}(KBr)/cm^{-1} 3701, 2922, 1727, 1497, 1459, 1030, 786, 698; MS (EI) m/z 233, 218, 204, 189, 154, 115, 108, 95, 77; HRMS-ESI (m/z): calcd for $C_{17}H_{16}N$, $[M + H]^+$: 234.1277, found 234.1274.

6-Phenyl-[1,3]dioxolo[4,5-g]quinoline (**3u**).[16d] Yield: 57% (35.6 mg) as yellow solid; mp = 110−111 °C; R_f = 0.38 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.0 Hz, 2H), 8.02 (d, J = 12.0 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.52−7.41 (m, 2H), 7.06 (s, 1H), 6.10 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 150.9, 147.8, 146.5, 139.6, 135.6, 128.9, 128.8, 127.3, 124.2, 117.3, 106.1, 102.6, 101.7 ppm; ν_{max}(KBr)/cm^{-1} 3459, 2921, 1644, 1467, 920, 859, 748, 696; MS (EI) m/z 249, 234, 207, 190, 163, 139, 124, 95, 81; HRMS-ESI (m/z): calcd for $C_{16}H_{12}NO_2$, $[M + H]^+$: 250.0863, found 250.0866.

7-Methyl-2-phenylquinoline (**3v**):*5-Methyl-2-phenylquinoline* (**3v′**) = *6:1*. Yield: 60% (33 mg) as yellow solid; mp = 95−96 °C; R_f = 0.56 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.8 Hz, 0.2H), 8.15 (d, J = 8.0 Hz, 3H), 8.03 (d, J = 8.4 Hz, 0.17H), 7.96 (s, 1H), 7.87 (d, J = 8.8 Hz, 0.22H), 7.79 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.63−7.57 (m, 0.29H), 7.51 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 4.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 2.69 (s, 0.5H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 148.6, 139.9, 139.8, 136.4, 134.4, 133.2, 129.4, 129.3, 129.2, 128.9, 128.8, 128.8, 128.6, 128.1, 127.6, 127.1, 126.8, 125.3, 118.2, 21.9, 18.6 ppm; ν_{max}(KBr)/cm^{-1} 3045, 2921, 2854, 1600, 1489, 835, 767, 693; MS (EI) m/z 219, 204, 189, 165, 147, 115, 108, 95, 89, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1124.

2-Phenylbenzo[g]quinoline (**3w**).[15g] Yield: 67% (41.8 mg) as yellow solid; mp = 195−196 °C; R_f = 0.58 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 4.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 1H), 8.01 (t, J = 8.0 Hz, 2H), 7.94 (d, J = 8.0 Hz, 1H), 7.67 (dt, J = 22.0, 7.2 Hz, 2H), 7.54 (t, J = 6.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 148.2, 139.4, 131.7, 131.6, 131.0, 129.6, 129.3, 128.9, 128.7, 128.6, 127.5, 127.2, 127.1, 124.2, 122.6, 118.8 ppm; ν_{max}(KBr)/cm^{-1} 3366, 2922, 1567, 1457, 1269, 833, 751, 694; MS (EI) m/z 255, 226, 207, 177, 151, 127, 113, 100, 75; HRMS-ESI (m/z): calcd for $C_{19}H_{14}N$, $[M + H]^+$: 256.1121, found 256.1123.

2-(p-Tolyl)quinoline (**4a**).[15e] Yield: 61% (33.6 mg) as yellow solid; mp = 81−82 °C; R_f = 0.55 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (t, J = 8.0 Hz, 2H), 8.07 (d, J = 4.0 Hz, 2H), 7.84 (dd, J = 19.2, 8.0 Hz, 2H), 7.72 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 148.2, 139.5, 136.9, 129.6, 129.6, 129.3, 128.5, 127.5, 127.4, 127.1, 126.1, 118.9, 21.3 ppm; ν_{max}(KBr)/cm^{-1} 2922, 2853, 1600, 1033, 813, 748, 615; MS (EI) m/z 219, 204, 189, 176, 165, 139, 128, 95, 83, 75, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1123.

2-(m-Tolyl)quinoline (**4b**).[15e] Yield: 58% (31.9 mg) as yellow oil; R_f = 0.66 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (t, J = 10.0 Hz, 2H), 8.04 (s, 1H), 7.96 (d, J = 4.0 Hz, 1H), 7.88 (dd, J = 18.2, 8.0 Hz, 2H), 7.76 (t, J = 8.0 Hz, 1H), 7.56 (t, J = 6.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 148.2, 139.6, 138.5, 136.8, 130.2, 129.8, 129.7, 128.7, 128.3, 127.5, 127.2, 126.3, 124.7, 119.2, 21.6 ppm; ν_{max}(KBr)/cm^{-1} 3700, 3058, 2924, 1728, 1028, 831, 786, 704; MS (EI) m/z 219, 204, 189, 165, 128, 108, 95, 83, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1122.

2-(4-(iso-Propyl)phenyl)quinoline (**4c**). Yield: 69% (41.1 mg) as yellow solid; mp = 84−85 °C; R_f = 0.66 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (t, J = 6.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 2H), 7.83 (dd, J = 18.2, 8.0 Hz, 2H), 7.71 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 6.0 Hz, 1H), 7.39 (d, J = 4.0 Hz, 2H), 2.99 (dt, J = 14.4, 7.2 Hz, 1H), 1.31 (d, J = 4.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 150.4, 148.3, 137.3, 136.7, 129.6, 129.6, 127.6, 127.4, 127.1, 126.9, 126.1, 118.9, 34.0, 23.9 ppm; ν_{max}(KBr)/cm^{-1} 3055, 2959, 2924, 1601, 1058, 820, 756, 616; MS (EI) m/z 247, 232, 217, 204, 176, 151, 128, 115, 101, 77; HRMS-ESI (m/z): calcd for $C_{18}H_{18}N$, $[M + H]^+$: 248.1434, found 248.1440.

2-(4-(tert-Butyl)phenyl)quinoline (**4d**). Yield: 64% (41.9 mg) as yellow solid; mp = 84−85 °C; R_f = 0.72 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (t, J = 8.0 Hz, 2H), 8.09 (d, J = 8.0 Hz, 2H), 7.83 (dd, J = 19.2, 8.0 Hz, 2H), 7.71 (t, J = 8.0 Hz, 1H), 7.59−7.47 (m, 3H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 152.6, 148.3, 136.9, 136.7, 129.7, 129.6, 127.4, 127.3, 127.1, 126.1, 125.8, 118.9, 34.8, 31.3 ppm; ν_{max}(KBr)/cm^{-1} 3453, 2959, 1549, 1269, 1019, 821, 755, 569; MS (EI) m/z 261, 246, 230, 217, 204, 191, 176, 128, 108, 101, 77; HRMS-ESI (m/z): calcd for $C_{19}H_{20}N$, $[M + H]^+$: 262.1590, found 262.1590.

2-(3,5-Dimethylphenyl)quinoline (**4e**).[15e] Yield: 54% (31.6 mg) as yellow oil; R_f = 0.59 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.0 Hz, 2H), 7.84 (dd, J = 16.0, 8.0 Hz, 2H), 7.80−7.69 (m, 3H), 7.52 (t, J = 8.0 Hz, 1H), 7.11 (s, 1H), 2.44 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 148.1, 139.5, 138.4, 136.8, 131.1, 129.7, 129.6, 127.4, 127.2, 126.2, 125.5, 119.3, 21.5 ppm; ν_{max}(KBr)/cm^{-1} 3697, 2922, 1596, 1503, 1266, 1024, 824, 754; MS (EI) m/z 233, 217, 189, 167, 115, 108, 102, 77; HRMS-ESI (m/z): calcd for $C_{17}H_{16}N$, $[M + H]^+$: 234.1277, found 234.1280.

2-(4-Methoxyphenyl)quinoline (**4f**).[16a] Yield: 55% (31.6 mg) as yellow solid; mp = 113−114 °C; R_f = 0.40 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (t, J = 8.0 Hz, 4H), 7.91−7.79 (m, 2H), 7.74 (t, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 156.9, 148.2, 136.8, 132.1, 129.7, 129.4, 128.9, 127.4, 126.9, 125.9, 118.6, 114.3, 55.4 ppm; ν_{max}(KBr)/cm^{-1} 3686, 2921, 1711, 1246, 1028, 820, 787, 727; MS (EI) m/z 235, 220, 204, 192, 165, 128, 117, 96, 88, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1074.

2-(3-Methoxyphenyl)quinoline (**4g**).[15e] Yield: 63% (37.2 mg) as yellow oil; R_f = 0.28 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 18.4, 8.0 Hz, 2H), 7.96−7.78 (m, 3H), 7.69 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.41 (t, J = 8.0 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 157.1, 148.3, 135.1, 131.5, 130.4, 129.8, 129.6, 129.3, 127.4, 127.1, 126.2, 123.5, 121.3, 111.5, 55.7 ppm; ν_{max}(KBr)/cm^{-1} 3413, 2925, 1596, 1249, 965, 831, 754, 692; MS (EI) m/z 235, 206, 190, 176, 139, 130, 102, 95, 89, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1073.

2-(3,4-Dimethoxyphenyl)quinoline (**4h**).[16c] Yield: 61% (40.6 mg) as yellow solid; mp = 121−122 °C; R_f = 0.37 (10:1 hexanes:ethyl acetate); R_f = 0.69 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.0 Hz, 2H), 7.88 (s, 1H), 7.81 (dd, J = 16.0, 8.0 Hz, 2H), 7.75−7.57 (m, 2H), 7.49 (t, J = 8.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 4.04 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 150.4, 149.4, 148.2, 136.6, 132.5, 129.6, 129.5, 127.5, 126.9, 126.0, 120.3, 118.6, 111.1, 110.5, 56.0, 56.0 ppm; ν_{max}(KBr)/cm^{-1} 2922, 2851, 1628, 1503, 1025, 816, 727, 622; MS (EI) m/z 265, 250, 219, 207, 191, 178, 167, 124, 102, 89, 76; HRMS-ESI (m/z): calcd for $C_{17}H_{16}NO_2$, $[M + H]^+$: 266.1176, found 266.1180.

2-(3,4,5-Trimethoxyphenyl)quinoline (**4i**). Yield: 55% (40.2 mg) as yellow solid; mp = 141−142 °C; R_f = 0.16 (10:1 hexanes/ethyl acetate); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24−8.13 (m, 2H), 7.83 (d, J = 8.0 Hz, 2H), 7.73 (t, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.41 (s, 2H), 4.01 (s, 6H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 153.6, 148.1, 139.5, 136.8, 135.3, 129.7, 129.6, 127.5, 127.1, 126.3, 118.9, 104.9, 60.9, 56.3 ppm; ν_{max}(KBr)/cm^{-1} 2929, 1591, 1497, 1419, 1126, 1105,

DOI: 10.1021/acs.joc.6b01909
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822, 782; MS (EI) m/z 295, 280, 249, 222, 219, 166, 140, 132, 89, 83; HRMS-ESI (m/z): calcd for $C_{18}H_{18}NO_3$, $[M + H]^+$: 296.1281, found 296.1285.

*2-(4-Fuorophenyl)quinoline (**4j**)*.[15e] Yield: 51% (28.6 mg) as yellow solid; mp = 99−100 °C; R_f = 0.52 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 16.0, 7.2 Hz, 4H), 7.81 (d, J = 8.0 Hz, 2H), 7.72 (s, 1H), 7.52 (s, 1H), 7.20 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J = 248 Hz), 156.2, 148.2, 136.9, 135.8 (d, J = 3.0 Hz), 129.8, 129.7, 129.4 (d, J = 9.0 Hz), 127.4, 127.1, 126.4, 118.6, 115.8 (d, J = 22.0 Hz) ppm; ν_{max}(KBr)/cm^{-1} 3701, 2922, 2854, 1592, 1459, 828, 786, 698; MS (EI) m/z 223, 202, 175, 169, 128, 111, 101, 75, 74; HRMS-ESI (m/z): calcd for $C_{15}H_{11}FN$, $[M + H]^+$: 224.0870, found 224.0872.

*2-(3-Chlorophenyl)quinoline (**4k**)*.[16d] Yield: 74% (44.4 mg) as yellow solid; mp = 91−92 °C; R_f = 0.31 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22−8.12 (m, 3H), 7.98 (s, 1H), 7.76 (dd, J = 8.0, 5.6 Hz, 2H), 7.70 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.40 (d, J = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 148.2, 141.4, 137.0, 134.9, 130.1, 129.9, 129.8, 129.3, 127.7, 127.5, 127.4, 126.7, 125.6, 118.6 ppm; ν_{max}(KBr)/cm^{-1} 3450, 2923, 1597, 1432, 876, 827, 749, 692; MS (EI) m/z 239, 204, 176, 151, 128, 119, 102, 88, 75; HRMS-ESI (m/z): calcd for $C_{15}H_{11}ClN$, $[M + H]^+$: 240.0575, found 240.0578.

*2-(4-(Trifluoromethyl)phenyl)quinoline (**4l**)*.[16a] Yield: 48% (34.2 mg) as yellow solid; mp = 131−132 °C; R_f = 0.62 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (t, J = 8.0 Hz, 3H), 8.19 (d, J = 8.0 Hz, 1H), 7.87 (dd, J = 12.0, 9.2 Hz, 2H), 7.76 (t, J = 10.0 Hz, 3H), 7.56 (t, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 148.3, 142.9, 137.2, 131.3, 130.9 (q, J = 245.2 Hz), 130.0, 129.9, 127.9, 127.5, 127.5, 126.9, 125.8 (q, J = 3.7 Hz), 125.6, 118.8 ppm; ν_{max}(KBr)/cm^{-1} 2921, 1600, 1330, 1072, 851, 759, 675; MS (EI) m/z 273, 252, 204, 194, 176, 169, 151, 126, 101, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{11}F_3N$, $[M + H]^+$: 274.0838, found 274.0842.

*3-(Quinolin-2-yl)benzonitrile (**4m**)*.[16g] Yield: 54% (31.2 mg) as yellow solid; mp = 99−101 °C; R_f = 0.23 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.41 (d, J = 8.0 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.18 (t, J = 10.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.76 (dd, J = 16.8, 8.0 Hz, 2H), 7.63 (t, J = 7.6 Hz, 2H), 7.58 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 148.3, 140.8, 137.4, 132.5, 131.6, 131.3, 130.1, 129.8, 129.6, 127.6, 127.5, 118.8, 118.3, 113.1 ppm; MS (EI) m/z 230, 201, 175, 151, 128, 115, 101, 88, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{10}N_2$, $[M + H]^+$: 231.0917, found 231.0915.

*2-(4-Nitrophenyl)quinoline (**4n**)*.[16a] Yield: 58% (26.8 mg) as yellow solid; mp = 130−131 °C; R_f = 0.27 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 4H), 8.26 (d, J = 8.0 Hz, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.86 (dd, J = 13.6, 8.4 Hz, 2H), 7.76 (t, J = 8.0 Hz, 1H), 7.57 (t, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 148.3, 148.3, 145.4, 137.3, 130.2, 129.9, 128.3, 127.6, 127.3, 123.9, 118.7 ppm; ν_{max}(KBr)/cm^{-1} 3450, 2922, 2228, 1635, 1268, 797, 755, 690; MS (EI) m/z 250, 220, 204, 192, 176, 151, 128, 101, 88, 75; HRMS-ESI (m/z): calcd for $C_{15}H_{11}N_2O_2$, $[M + H]^+$: 251.0815, found 251.0811.

*3-Methyl-2-phenylquinoline (**4o**)*.[16c] Yield: 64% (35.2 mg) as yellow oil; R_f = 0.52 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.0 Hz, 1H), 7.99 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 8.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.53−7.30 (m, 5H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 146.7, 140.9, 136.7, 129.3, 129.2, 128.9, 128.6, 128.3, 128.2, 127.6, 126.7, 126.4, 20.6 ppm; ν_{max}(KBr)/cm^{-1} 3456, 2923, 1626, 1488, 1268, 1007, 758, 703; MS (EI) m/z 219, 189, 140, 115, 108, 95, 83; HRMS-ESI (m/z): calcd for $C_{16}H_{14}N$, $[M + H]^+$: 220.1121, found 220.1125.

*2-(Thiophen-2-yl)quinoline (**4p**)*.[16a] Yield: 50% (26.8 mg) as yellow solid; mp = 130−131 °C; R_f = 0.52 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (t, J = 11.2 Hz, 2H), 7.74 (dt, J = 15.2, 9.0 Hz, 4H), 7.55−7.41 (m, 2H), 7.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 148.0, 136.7, 129.9, 129.3, 129.2, 128.7, 128.1, 127.5, 127.2, 126.2, 125.9, 117.8 ppm; ν_{max}(KBr)/cm^{-1} 3697, 2922, 1593, 1268, 1026, 825, 755, 714; MS (EI) m/z 211, 185, 178, 167, 151, 139, 128, 105, 83, 75; HRMS-ESI (m/z): calcd for $C_{13}H_{10}NS$, $[M + H]^+$: 212.0528, found 212.0524.

*2-Phenylquinoline (**3a**)*.[16a] Yield: 65% (33.5 mg) as yellow solid; mp = 86−87 °C; R_f = 0.69 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (dd, J = 23.2 Hz, 8.0 Hz, 4H), 7.85 (dd, J = 20.0, 8.0 Hz, 2H), 7.73 (t, J = 8.0 Hz, 1H), 7.50 (dt, J = 25.2, 7.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 148.1, 139.5, 136.9, 129.8, 129.6, 129.4, 128.9, 127.6, 127.5, 127.2, 126.4, 119.0 ppm; ν_{max}(KBr)/cm^{-1} 3450, 2923, 1625, 1603, 1021, 830, 799, 688; MS (EI) m/z 206, 205, 176, 164, 151, 128, 113, 102, 88, 76, 51; HRMS-ESI (m/z): calcd for $C_{15}H_{12}N$, $[M + H]$+: 206.0964, found 206.0969.

*2-(4-Methoxyphenyl)quinoline (**4f**)*.[16a] Yield: 61% (35.9 mg) as yellow solid; mp = 113−114 °C; R_f = 0.40 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz, 4H), 7.87−7.81 (m, 2H), 7.74 (t, J = 6.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 156.9, 148.3, 136.7, 132.2, 129.6, 129.5, 128.9, 127.4, 126.9, 125.9, 118.6, 114.3, 55.4 ppm; ν_{max}(KBr)/cm^{-1} 3686, 2921, 1711, 1246, 1028, 820, 787, 727; MS (EI) m/z 235, 220, 204, 192, 165, 128, 117, 96, 88, 75; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1074.

*2-(3-Methoxyphenyl)quinoline (**4g**)*.[15e] Yield: 67% (39.6 mg) as yellow oil; R_f = 0.28 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 16.8, 8.0 Hz, 2H), 7.95−7.78 (m, 3H), 7.70 (t, J = 8.0 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.41 (t, J = 6.0 Hz, 1H), 7.13 (t, J = 6.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 157.1, 148.3, 135.1, 131.5, 130.3, 129.8, 129.2, 127.4, 127.1, 126.2, 123.5, 121.3, 111.5, 55.7 ppm; ν_{max}(KBr)/cm^{-1} 3413, 2925, 1596, 1249, 965, 831, 754, 692; MS (EI) m/z 235, 206, 190, 176, 139, 130, 102, 95, 89, 63; HRMS-ESI (m/z): calcd for $C_{16}H_{14}NO$, $[M + H]^+$: 236.1070, found 236.1073.

*2-(3,4-Dimethoxyphenyl)quinoline (**4h**)*.[16c] Yield: 66% (43.9 mg) as yellow solid; mp = 103−104 °C; R_f = 0.37 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 2H), 7.89−7.80 (m, 3H), 7.74−7.66 (m, 2H), 7.51 (t, J = 8.0 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 4.06 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 150.5, 149.5, 148.0, 136.8, 132.3, 129.7, 129.4, 127.5, 126.9, 126.1, 120.4, 118.7, 111.1, 110.6, 56.1, 56.0 ppm; ν_{max}(KBr)/cm^{-1} 3413, 2925, 1596, 1249, 965, 831, 754, 692; MS (EI) m/z 265, 250, 219, 207, 191, 178, 167, 124, 102, 89, 76; HRMS-ESI (m/z): calcd for $C_{17}H_{16}NO_2$, $[M + H]^+$: 266.1176, found 266.1180.

*2-(4-Ethoxy-3-methoxyphenyl)quinoline (**5a**)*. Yield: 71% (49.7 mg) as yellow solid; mp = 108−109 °C; R_f = 0.17 (10:1 hexanes/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 12.0 Hz,1H), 7.88 (s, 1H), 7.75 (dd, J = 12.0, 8.0 Hz, 2H), 7.68 (t, J = 6.0 Hz, 1H), 4.12 (dd, J = 13.2, 6.4 Hz, 2H), 4.00 (s, 3H), 1.47 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 149.8, 149.7, 148.2, 136.6, 132.4, 129.6, 129.5, 127.5, 126.9, 125.9, 120.3, 118.6, 112.4, 110.7, 64.4, 56.1, 14.8 ppm; ν_{max}(KBr)/cm^{-1} 3058, 2979, 1597, 1505, 1464, 1036, 817, 756; MS (EI) m/z 279, 264, 235, 222, 191, 178, 167, 152, 128, 113, 89; HRMS-ESI (m/z): calcd for $C_{18}H_{18}NO_2$ $[M + H]^+$: 280.1332, found 280.1338.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01909.

Copies of ^{1}H and ^{13}C NMR spectra data for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the National Program on Key Research Project (2016YFA0602900), the National Natural Science Foundation of China (21490572, 21502055 and

21420102003), and the Fundamental Research Funds for the Central Universities (2015ZY001) for financial support.

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NOTE ADDED AFTER ASAP PUBLICATION

The structure of **3t** in Scheme 2 and in the Supporting Information was replaced on November 30, 2016.

DOI: 10.1021/acs.joc.6b01909
J. Org. Chem. 2016, 81, 12189−12196