

Facile Three-Component Synthesis of Substituted Quinolines Catalyzed by Iridium(III) Complex

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A convenient and efficient synthesis of substituted quinolines via a simple one-pot reaction of an aniline, an aromatic aldehyde, and an enolizable aliphatic aldehyde in the presence of the iridium catalyst $[IrCl_2H(cod)]_2$ under oxygen as an oxidant was developed. The reaction proceeds with Mannich-type imine formation followed by nucleophilic addition to give β-amino aldehydes. Dehydrative cyclization takes place to give dihydroquinoline, which is then dehydrogenated by aerobic oxidation to give 2-aryl-3-alkylquinolines. Dialkylquinolines were obtained by the reaction with anilines and aliphatic aldehydes in good yields.

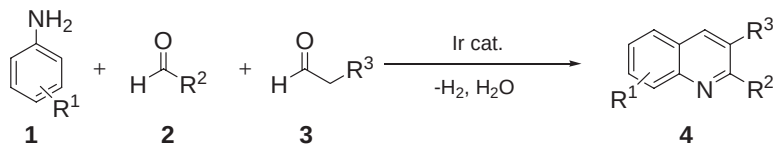
Designing and synthesizing functionalized compounds or materials are essential for innovation in industrial technology. Quinolines are one of the most used heterocyclic compounds for functionalized materials, and substituted quinolines have a wide variety of applications, such as pharmaceutical agents and organic electroluminescence materials. Several synthetic methods of quinolines are known; for example, Skraup,[1] Döbner–von Miller,[2] Friedländer,[3] and Pfitzinger[4] syntheses are recognized as fundamental methods. However, applicability of these classical methods is limited to simple quinolines without functional groups because a large amount of acids or bases are necessary. Therefore, for preparation of functionalized quinolines, appropriate functional groups are introduced to preexisting quinoline rings. In contrast, recently several quinoline syntheses under mild conditions using transition metals[5] or Lewis acids[6] have been reported. We have focused on convergent methods, which involve the coupling of functionalized moieties, because it is possible to prepare chemically diverse quinolines.

Previously, we reported a novel substituted quinoline synthesis by the reaction of an aniline, an aromatic aldehyde, and an aliphatic aldehyde in the presence of iridium catalysts, such as $[Ir(cod)Cl]_2$ (Scheme 1).[7] The formation of the quinolines is considered to proceed via a Mannich reaction (**A** → **B**) followed by aromatic substitution and dehydration to form dihydroquinoline **C**, and finally, dehydrogenation of **C** proceeds to afford quinolines as shown in Scheme 2. The final dehydrogenation step seems to proceed either via a hydrogen-transfer mechanism with hydrogen acceptors or an autoxidation mechanism. If the reaction proceeds via an autoxidation mechanism, the dehydrogenation step may be better under aerobic conditions, instead of under inert atmospheres. In the course of our studies, we have found that the reaction proceeds more effectively under air or oxygen.[8] Furthermore, the reaction was found to proceed using $[IrCl_2H(cod)]_2$ as a catalyst with much higher reactivity than $[IrCl(cod)]_2$. We describe, here, the details of the iridium(III)-catalyzed quinoline synthesis.

Results and Discussion

Optimization of the Iridium-Catalyzed Reaction with Aniline, Benzaldehyde, and Butanal Using Dehydrogenating Agents. The results of the reactions with $[IrCl_2H(cod)]_2$ under various atmospheres are summarized in Table 1. A mixture of aniline (**1a**) and benzaldehyde (**5a**) in DMSO was stirred in the presence of the iridium catalyst at room temperature for 1 h, and then butanal (**3a**) was added. The resulting mixture was heated at 90 °C for 12 h under argon to give the desired product **6a** in 46% yield along with 3-ethyl-2-propylquinoline (**7a**) and *N*-benzylaniline (**8a**) in 18 and 31% yields, respectively (Entry 1). Amine **8a** was considered to form from *N*-benzylideneaniline intermediate **10a** by hydrogen transfer with the dihydroquinoline **C**. This hydrogen transfer was found to proceed without catalysts under argon in an NMR tube. Indeed, the reaction of the 1,2-dihydroquinoline **9**,[9] as a model compound of the dihydroquinoline **C**, and the imine **10a** proceeded to give 2-phenylquinoline (**6b**) and secondary amine **8a** (Scheme 3). In other words, a more efficient dehydrating agent is needed to prevent the secondary amine formation.

We examined the reaction with several dehydrating agents, such as nitrobenzene and 2,3-dichloro-5,6-dicyano-1,4-benzo-



Scheme 1. Iridium-catalyzed three component coupling reaction.

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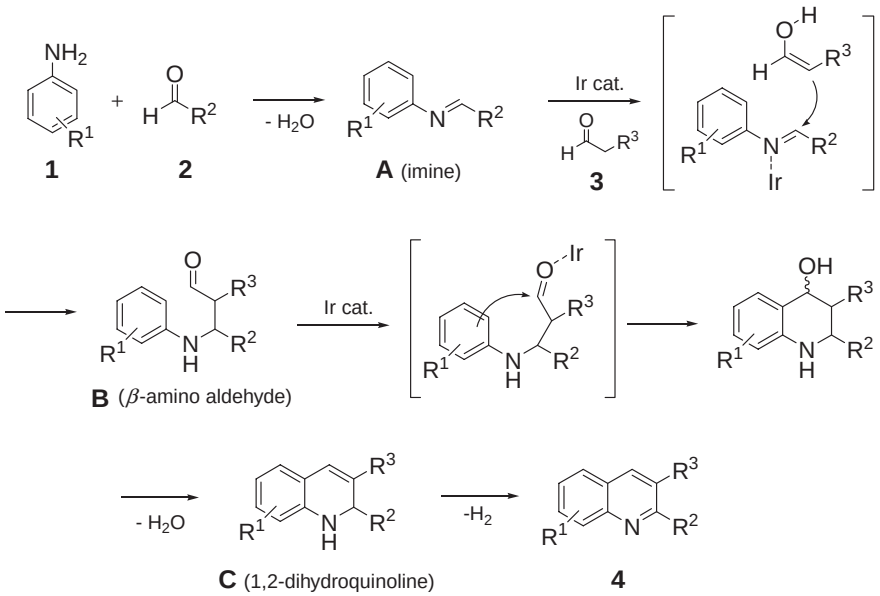
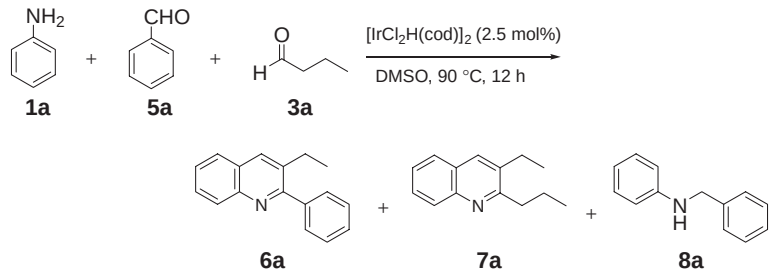


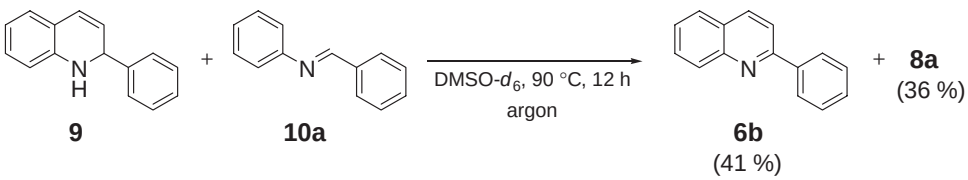
Scheme 2. Plausible mechanism for quinoline synthesis.

Table 1. Three Component Coupling Reaction under Various Atmospheres



Entry	Cat.	Condition	Yield/%[a)]		
			6a	**7a**	**8a**
1	$[IrCl_2H(cod)]_2$	Under Argon	46	18	31
2		Under Air	51	22	25
3		Under O_2	79	8	Trace
4	$[IrCl(cod)]_2$	Under O_2	38	28	Trace
5	HCl	Under O_2	63	Trace	Trace

a) Isolated yield based on aniline **1a**.

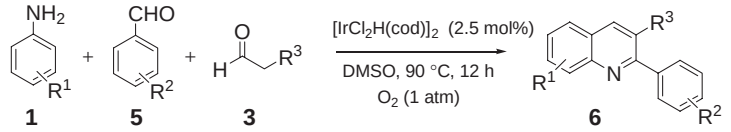


Scheme 3.

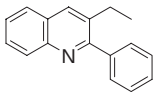
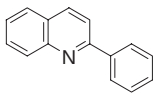
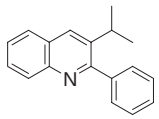
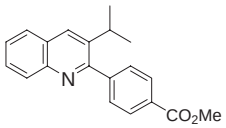
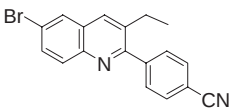
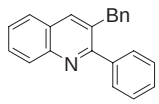
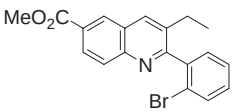
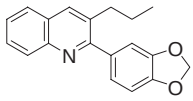
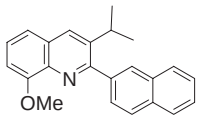
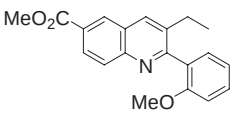
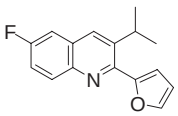
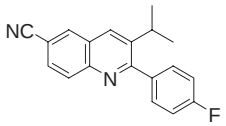
quinone (DDQ), but these organic oxidants were not effective.[10] However, the reaction was somewhat improved when performed in air to give **6a** (51%), **7a** (22%), and **8a** (25%).[8a] Oxygen proved to give the best yield of **6a** (79%) and a small amount of **7a** (8%). However, the Ir^I complex $[IrCl(cod)]_2$ gave low yields even under O_2. The optimal conditions, Entry 3 in Table 1, were employed in the most of the syntheses for a wide variety of quinolines in this paper. During our investigations, another synthetic method involving the reaction of imines and aldehydes in DMSO under acidic conditions was reported by Baba et al.[8a] The method was applied to this reaction to give the same product **6a** in 63% yield (Entry 5).

Synthesis of Various 2-Arylquinolines. A wide range of functionalized anilines, aromatic aldehydes, and aliphatic aldehydes were subjected to the procedure to synthesize the corresponding quinolines in yields as shown in Table 2. Functional groups, such as halogen, ester, methyl ether, and cyano, were used. The yield of quinoline in the case of acetaldehyde was

Table 2. Iridium-Catalyzed Synthesis of 2-Arylquinolines **6** from Anilines **1**, Aromatic Aldehydes **5**, and Aliphatic Aldehydes **3**

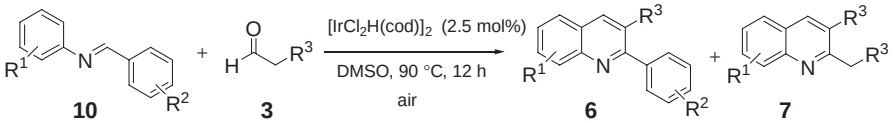


1 **5** **3** **6**

Product (Yield)[a)]		
 **6a** (79%)	 **6b** (28%)	 **6c** (63%)
 **6d** (65%)	 **6e** (63%)	 **6f** (48%)
 **6g** (52%)	 **6h** (38%)	 **6i** (22%)
 **6j** (69%)	 **6k** (54%)	 **6l** (55%)

a) Isolated yield based on the aniline **1**.

Table 3. Iridium-Catalyzed Synthesis of 2-Arylquinolines **6** from Imines **10** and Aliphatic Aldehydes **3**



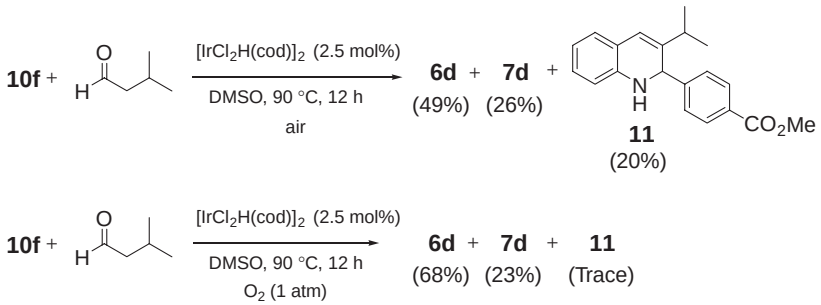
10 **3** **6** **7**

Entry	Imines **10**	R^3	**6** (Yield/%)[a)]	**7** (Yield/%)[a)]
1	**10a** ($R^1 = R^2 = H$)	H	**6b** (25)	**7b** (18)
2	**10a**	Me	**6m** (52)	**7c** (25)
3	**10a**	Et	**6a** (43)	**7a** (8)
4	**10a**	*i*-Pr	**6c** (53)	**7d** (27)
5	**10b** ($R^1 = p$-OMe, $R^2 = H$)	Me	**6n** (21)	**7e** (35)
6	**10b**	*i*-Pr	**6o** (32)	**7f** (42)
7	**10c** ($R^1 = p$-OMe, $R^2 = p$-OMe)	*i*-Pr	**6p** (14)	**7f** (46)
8	**10d** ($R^1 = p$-OMe, $R^2 = p$-CO_2Me)	*i*-Pr	**6q** (48)	**7f** (35)
9	**10e** ($R^1 = p$-CO_2Me, $R^2 = H$)	*i*-Pr	**6r** (55)	**7g** (35)
10	**10f** ($R^1 = H$, $R^2 = p$-CO_2Me)	*i*-Pr	**6d** (49)	**7d** (26)

a) Isolated yield based on the imine **10**.

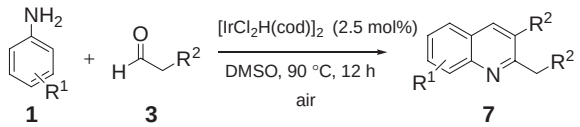
low, and oily polymeric by-products were formed. Other aliphatic aldehydes could be used, and 3-substituted quinolines were obtained in satisfactory yields.

Reaction of Imine and Aliphatic Aldehyde. The other crucial problem for the substituted quinoline synthesis was formation of the by-product dialkylquinoline **7**. To avoid dialkylquinoline formation, a two step synthesis was examined.[8a,8b] The reaction of aliphatic aldehyde **3** and the imine **10**, obtained from an aromatic aldehyde and an aniline, was carried out. However, 2,3-dialkylquinolines **7** still formed in considerable yields along with the desired quinolines **6** as shown in Table 3. This results indicate that iridium-catalyzed hydrolysis of imine **10** occurred in the reaction. Actually, when *N*-benzylideneaniline in DMSO-d_6 was added to an NMR tube in the presence of a catalytic amount of iridium catalyst (2.5 mol %), hydrolysis of the imine to form an aldehyde was observed by using



Scheme 4.

Table 4. Iridium-Catalyzed Synthesis of Substituted Quinolines **7** from Anilines **1** and Aliphatic Aldehydes **3**



Entry	R^1	R^2	**7** (Yield/%)[a]	Entry	R^1	R^2	**7** (Yield/%)[a]
1	H	Et	**7a** (59)	8	*p*-MeO	H	**7n** (41)
2	*o*-MeO	Et	**7h** (55)	9	*p*-MeO	Me	**7e** (47)
3	*p*-MeO	Et	**7i** (53)	10	*p*-MeO	*n*-Pr	**7o** (49)
4	*o*-F	Et	**7j** (41)	11	*p*-MeO	*i*-Pr	**7f** (83)
5	*p*-F	Et	**7k** (55)	12	*p*-MeO	*i*-Pr	**7f** (81)[b]
6	*o*-CO_2Et	Et	**7l** (17)	13	H	*i*-Pr	**7d** (>99)
7	*p*-CO_2Me	Et	**7m** (68)	14	*m*-MeO	*i*-Pr	**7p** (40)[c]

a) Isolated yield based on the aniline **1**. b) The reaction was carried out at rt. c) The ratio of 5- and 7-isomers was 1:9.

^{1}H NMR spectroscopy. Even the addition of drying agents, such as $MgSO_4$ or molecular sieves, did not increase the selectivity. Compared with the results in Table 2, the yields of quinolines **6a** and **6c** prepared by the reaction of **10** and **3** (Entries 3 and 4 in Table 3) were lower than those by the reaction of **1**, **5**, and **3** (Table 2), which is explained by the different ratio of aromatic imines **10** that formed in situ in the reaction of the aromatic aldehydes and anilines under the three-component coupling reaction conditions.

In the reaction of imine **10f** and 3-methylbutanal, 1,2-dialkylquinoline **7d** was obtained along with quinoline **6d** as normal; however, a considerable amount of **11** (20%) was obtained (Scheme 4). Dihydroquinoline **11** was oxidized into quinoline **6d** slowly in air, which indicates that the methoxycarbonyl substituent at the para position decreases the rate of the autoxidation from **11** to **6d**. However, the reaction under oxygen proceeded smoothly to give **6d** in good yield (68%), and the dihydroquinoline **11** was almost completely oxidized.

Synthesis of 2,3-Dialkylquinolines. It is difficult to synthesize 2,3-dialkylquinolines using two different aliphatic aldehydes. However, the iridium-catalyzed three-component coupling reaction with two equivalents of an aliphatic aldehyde gives 2,3-dialkylquinolines in moderate to good yields. Reaction of aniline **1** (1 mmol) and aliphatic aldehyde **3** (2.5 mmol) in the presence of a catalytic amount of $[IrCl_2H(cod)]_2$ at 90 °C for 12 h under an air atmosphere afforded 2,3-dialkyl-substituted quinolines **7** as shown in Table 4. Reaction of various substituted anilines **1**, such as anisidine and fluoroaniline, with propanal was carried out, and the corresponding quinolines were obtained in moderate yields (Entries 1–7), except for ethyl 2-aminobenzoate (17%). In the case of the reaction of 2-aminobenzoate the starting aniline was recovered, which can be explained by steric effects of the ester group at the ortho position. Next, several aliphatic aldehydes were used for 6-methoxyquinoline from *p*-methoxyaniline (Entries 8–11). With 3-methylaldehyde, the corresponding quinoline **7f** was obtained in high yield (Entry 11). When *p*-anisidine and 3-methylaldehyde were used even at room temperature, quinoline **7f** was obtained in high yield (Entry 12). The reaction of *m*-anisidine with 3-methylaldehyde afforded a 1:9 mixture of 5- and 7-isomers (**7p** and **7p′**), which is a similar selectivity to the rhodium-catalyzed reaction at 180 °C reported by Watanabe and co-workers.[5a]

Conclusion

In summary, we have developed an efficient and general route to substituted quinolines via a one-pot synthesis from an aniline, an aromatic aldehyde, and an aliphatic aldehyde in the presence of a catalytic amount of an iridium(III) complex under aerobic conditions. This reaction is a promising method to prepare various functional quinolines. Further development is underway.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ as a solvent using TMS as an internal standard on a JEOL Lambda 500 spectrometer. Multiplicities are indicated as br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet).

High-resolution mass spectroscopy (HRMS) and elemental analysis were performed by the Material Characterization Central Laboratory of Waseda University.

General Procedure for the Reaction of Aniline (1a), Benzaldehyde (2a), and Butanal (3a) in Table 1. A mixture of aniline (**1a**) (1.0 mmol), benzaldehyde (**2a**), (2.0 mmol), and $[IrCl_2H(cod)]_2$ (0.025 mmol) in DMSO (3 mL) was stirred at room temperature for 1 h, and butanal (**3a**) (1.5 mmol) was added to the mixture. After the resulting mixture was stirred at 90 °C for 12 h, the mixture was washed with phosphate buffer saline (PBS, 50 mL) and extracted with AcOEt (20 mL × 3). The organic layer was dried over $MgSO_4$. Removal of the solvent in vacuo, followed by chromatographic purification on silica gel (AcOEt/Hexane = 5/95) afforded **6a**, **7a**, and **8a**.

General Procedure for the Synthesis of 2-Arylquinolines 6 in Table 2. A mixture of an aniline **1** (1.0 mmol), an aromatic aldehyde **2** (2.0 mmol), and $[IrCl_2H(cod)]_2$ (0.025 mmol) in DMSO (3 mL) was stirred at room temperature for 1 h, and an aliphatic aldehyde **3** (1.5 mmol) was added to the mixture. After the resulting mixture was stirred at 90 °C under oxygen (1 atm) for 12 h, the mixture was washed with PBS (50 mL) and extracted with AcOEt (20 mL × 3). The organic layer was dried over $MgSO_4$. Removal of the solvent in vacuo, followed by chromatographic purification on silica-gel column (AcOEt/Hexane = 5/95) afforded **6**.

3-Ethyl-2-phenylquinoline (6a) (Table 2): Yellow oil (185 mg, 79%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (t, J = 7.5 Hz, 3H, CH_3), 2.80 (q, J = 7.5 Hz, 2H, CH_2), 7.42–7.56 (m, 6H, aromatic H), 7.66 (td, J = 7.7, 1.5 Hz, 1H, aromatic H), 7.81 (d, J = 8.2 Hz, 1H, aromatic H), 8.05 (s, 1H, aromatic H), 8.13 (d, J = 8.4 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7 (CH_3), 26.0 (CH_2), 126.3, 126.9, 127.7, 128.0, 128.3, 128.7, 128.7, 129.3, 134.9, 135.3, 140.9, 146.3, 160.6 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{16}N$ $[M + H]^+$ 234.1283, found 234.1251.

2-Phenylquinoline (6b) (Table 2): Colorless needles (58 mg, 28%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.48 (m, 1H, aromatic H), 7.52–7.55 (m, 3H, aromatic H), 7.73 (td, J = 6.8, 1.5 Hz, 1H, aromatic H), 7.83 (dd, J = 8.2, 1.1 Hz, 1H, aromatic H), 7.88 (d, J = 8.6 Hz, 1H, aromatic H), 8.16–8.18 (m, 3H, aromatic H), 8.22 (d, J = 8.6 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.0, 126.3, 127.2, 127.4, 127.6, 128.8, 129.3, 129.6, 129.8, 136.7, 139.7, 148.3, 157.3 (aromatic C); HRMS (FAB) calcd for $C_{15}H_{12}N$ $[M + H]^+$ 206.0970, found 206.0978; Anal. Calcd for $C_{15}H_{11}N$: C, 87.77; H, 5.40; N, 6.82%. Found: C, 87.60; H, 5.66; N, 6.67%.

3-Isopropyl-2-phenylquinoline (6c) (Table 2): White solid (155 mg, 63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (d, J = 7.0 Hz, 6H, CH_3), 3.23–3.26 (m, 1H, CH), 7.44–7.53 (m, 6H, aromatic H), 7.65 (td, J = 7.7, 1.1 Hz, 1H, aromatic H), 7.82 (d, J = 8.1 Hz, 1H, aromatic H), 8.12 (m, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 29.2 (CH), 126.3, 127.0, 127.8, 127.9, 128.2, 128.7, 128.8, 129.2, 132.7, 140.3, 141.0, 146.1, 160.4 (aromatic C); HRMS (FAB) calcd for $C_{18}H_{18}N$ $[M + H]^+$ 248.1439, found 248.1432; Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66%. Found: C, 86.84; H, 7.03; N, 5.49%.

3-Isopropyl-2-(4-methoxycarbonylphenyl)quinoline (6d) (Table 2): Colorless crystals (200 mg, 65%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (d, J = 7.0 Hz, 6H, CH_3), 3.17–3.19 (m, 1H, CH), 3.96 (s, 3H, OCH_3), 7.54 (td, J = 7.1, 0.7 Hz, 1H, aromatic H), 7.61 (d, J = 8.2 Hz, 2H, aromatic H), 7.68 (td, J = 7.0, 1.3 Hz, 1H, aromatic H), 7.83 (d, J = 8.1 Hz, 1H, aromatic H), 8.11 (d, J = 8.6 Hz, 1H, aromatic H), 8.15–8.18 (m, 3H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.0 (CH_3), 29.2 (CH_2), 52.1 (OCH_3), 126.6, 127.1, 127.9, 128.9, 129.1, 129.2, 129.6, 129.7, 133.0, 140.0, 145.5, 146.1, 159.2 (aromatic C), 166.9 (CO); HRMS (FAB) calcd for $C_{20}H_{20}NO_2$ $[M + H]^+$ 306.1494, found 306.1461; Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59%. Found: C, 78.66; H, 6.46; N, 4.41%.

6-Bromo-2-(4-cyanophenyl)-3-ethylquinoline (6e) (Table 2): White solid (212 mg, 63%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, J = 7.5 Hz, 3H, CH_3), 2.77 (q, J = 7.5 Hz, 2H, CH_2), 7.67 (d, J = 8.1 Hz, 2H, aromatic H), 7.75 (dd, J = 9.0, 2.2 Hz, 1H, aromatic H), 7.79 (d, J = 8.2 Hz, 2H, aromatic H), 7.95 (d, J = 9.0 Hz, 1H, aromatic H), 7.99 (m, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6 (CH_3), 25.8 (CH_2), 112.2 (aromatic C), 118.6 (CN), 121.0, 129.0, 129.1, 129.6, 131.0, 132.2, 132.8, 134.5, 135.8, 144.9, 145.0, 158.7 (aromatic C); HRMS (FAB) calcd for $C_{18}H_{14}BrN_2$ $[M + H]^+$ 337.0340, found 337.0346; Anal. Calcd for $C_{18}H_{13}BrN_2$: C, 64.11; H, 3.89; N, 8.31%. Found: C, 64.01; H, 4.21; N, 7.84%.

3-Benzyl-2-phenylquinoline (6f) (Table 2): Yellow crystals (143 mg, 48%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05 (s, 2H, CH_2), 6.91–6.92 (m, 2H, aromatic H), 7.10–7.17 (m, 3H, aromatic H), 7.34–7.37 (m, 3H, aromatic H), 7.39–7.43 (m, 3H, aromatic H), 7.60 (td, J = 7.7, 1.5 Hz, 1H, aromatic H), 7.67 (dd, J = 8.2, 1.1 Hz, 1H, aromatic H), 7.84 (s, 1H, aromatic H), 8.06 (d, J = 8.4 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1 (CH_2), 126.2, 126.5, 127.1, 127.5, 128.2, 128.3, 128.5, 128.8, 129.0, 129.1, 129.3, 132.5, 137.0, 139.9, 140.6, 146.6, 160.7 (aromatic C); HRMS (FAB) calcd for $C_{22}H_{18}N$ $[M + H]^+$ 296.1439, found 296.1433; Anal. Calcd for $C_{22}H_{17}N$: C, 89.46; H, 5.80; N, 4.74%. Found: C, 89.33; H, 5.82; N, 4.51%.

2-(2-Bromophenyl)-3-ethyl-6-methoxycarbonylquinoline (6g) (Table 2): Pale yellow oil (200 mg, 52%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.11 (t, J = 7.5 Hz, 3H, CH_3), 2.46–2.48 (m, 1H, CH_2), 2.59–2.61 (m, 1H, CH_2), 3.89 (s, 3H, OCH_3), 7.20–7.23 (m, 1H, aromatic H), 7.27–7.29 (m, 1H, aromatic H), 7.33–7.36 (m, 1H, aromatic H), 7.58 (d, J = 8.1 Hz, 1H, aromatic H), 8.06–8.07 (m, 2H, aromatic H), 8.16 (dd, J = 8.9, 1.5 Hz, 1H, aromatic H), 8.52 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8 (CH_3), 25.3 (CH_2), 52.3 (OCH_3), 122.1, 127.1, 127.4, 128.0, 128.2, 129.4, 129.8, 130.0, 130.2, 132.6, 135.5, 136.5, 141.0, 147.8, 162.0 (aromatic C), 166.6 (CO); HRMS (FAB) calcd for $C_{19}H_{17}BrNO_2$ $[M + H]^+$ 370.0443, found 370.0443.

2-(3,4-Methylenedioxyphenyl)-3-propylquinoline (6h) (Table 2): Pale yellow oil (110 mg, 38%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, J = 7.3 Hz, 3H, CH_3), 1.54–1.59 (m, 2H, CH_2), 2.76 (t, J = 8.1 Hz, 2H, CH_2), 6.00 (s, 2H, OCH_2O), 6.90 (d, J = 7.9 Hz, 1H, aromatic H), 7.00–7.03 (m, 2H, aromatic H), 7.47–7.50 (m, 1H, aromatic H), 7.62–7.65 (m, 1H, aromatic H), 7.76 (d, J = 8.1 Hz, 1H, aromatic H), 7.98 (s, 1H, aromatic H), 8.09 (d, J = 8.4 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9 (CH_3), 23.6, 34.9 (CH_2), 101.0 (OCH_2O), 108.1, 109.5, 122.5, 126.2, 126.8, 127.5, 128.7, 129.1, 133.8, 134.9, 135.7, 146.3, 147.4, 147.5, 160.1 (aromatic C); HRMS (FAB) calcd for $C_{19}H_{18}NO_2$ $[M + H]^+$ 292.1338, found 292.1327.

3-Isopropyl-8-methoxy-2-(naphthalen-2-yl)quinoline (6i) (Table 2): White solid (80 mg, 22%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (d, J = 6.9 Hz, 6H, CH_3), 3.28–3.34 (m, 1H, CH), 4.04 (s, 3H, OMe), 7.01 (d, J = 7.3 Hz, 1H, aromatic H), 7.41–7.47 (m, 2H, aromatic H), 7.51 (q, J = 3.3 Hz, 2H, aromatic H), 7.66 (d, J = 8.3 Hz, 1H, aromatic H), 7.89–7.92 (m, 3H, aromatic H), 8.04 (s, 1H, aromatic H), 8.12 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 29.3 (CH), 56.0 (OCH_3), 107.0, 119.0, 126.1, 126.1, 126.5, 127.2, 127.5, 127.6, 128.3, 128.4,

129.0, 132.7, 132.9, 133.2, 138.2, 138.6, 141.1, 155.4, 159.0 (aromatic C); HRMS (FAB) calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.1693, found 328.1678; Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28%. Found: C, 84.29; H, 6.41; N, 4.34%.

3-Ethyl-6-methoxycarbonyl-2-(2-methoxyphenyl)quinoline (6j) (Table 2): Yellow oil (220 mg, 69%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.15 (t, $J = 7.5$ Hz, 3H, CH_3), 2.56–2.58 (m, 1H, CH_2), 2.66–2.68 (m, 1H, CH_2), 3.70 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 6.96 (d, $J = 8.4$ Hz, 1H, aromatic H), 7.04–7.08 (m, 1H, aromatic H), 7.30 (dd, $J = 7.3$, 1.3 Hz, 1H, aromatic H), 7.38–7.41 (m, 1H, aromatic H), 8.06 (s, 1H, aromatic H), 8.13 (d, $J =$ 8.8 Hz, 1H, aromatic H), 8.19–8.21 (m, 1H, aromatic H), 8.57 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9 (CH_3), 25.1 (CH_2), 52.2 (OCH_3), 55.3 (OCH_3), 110.8, 120.8, 127.0, 127.6, 127.9, 129.4, 129.6, 129.8, 130.1, 130.2, 134.6, 137.6, 148.1, 156.4, 161.3 (aromatic C), 166.8 (CO); HRMS (FAB) calcd for $C_{20}H_{20}NO_3$ $[M+H]^+$ 322.1443, found 322.1437.

6-Fluoro-2-(furan-2-yl)-3-isopropylquinoline (6k) (Table 2): Yellow oil (138 mg, 54%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (d, $J = 6.8$ Hz, 6H, CH_3), 3.66–3.68 (m, 1H, CH), 6.50 (dd, $J = 3.5$, 1.8 Hz, 1H, aromatic H), 6.94 (dd, $J = 3.5$, 0.7 Hz, 1H, aromatic H), 7.28–7.35 (m, 2H, aromatic H), 7.55 (m, 1H, aromatic H), 7.95 (s, 1H, aromatic H), 8.01 (dd, $J = 9.2$, 5.3 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.7 (CH_3), 28.8 (CH), 109.9 (d, $J_{CF} = 21.0$ Hz, aromatic C), 111.5, 111.8 (aromatic C), 119.2 (d, $J_{CF} = 25.8$ Hz, aromatic C), 128.2 (d, $J_{CF} = 9.7$ Hz, aromatic C), 131.6 (d, $J_{CF} = 8.9$ Hz, aromatic C), 132.4 (d, $J_{CF} = 5.6$ Hz, aromatic C), 140.7, 143.4 (aromatic C), 148.3 (d, $J_{CF} = 3.2$ Hz, aromatic C), 153.5, 159.5, 161.5 (aromatic C); HRMS (FAB) calcd for $C_{16}H_{15}FNO$ $[M+H]^+$ 256.1138, found 256.1128; Anal. Calcd for $C_{16}H_{14}FNO$: C, 75.28; H, 5.53; N, 5.49%. Found: C, 75.22; H, 5.83; N, 5.45%.

6-Cyano-2-(4-fluorophenyl)-3-isopropylquinoline (6l) (Table 2): Yellow crystals (160 mg, 55%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.18 (d, $J = 6.8$ Hz, 6H, CH_3), 3.18–3.21 (m, 1H, CH), 7.10–7.13 (m, 2H, aromatic H), 7.43–7.45 (m, 2H, aromatic H), 7.71 (d, $J = 8.8$ Hz, 1H, aromatic H), 8.07–8.10 (m, 2H, aromatic H), 8.15 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.9 (CH_3), 29.3 (CH), 110.0 (CN), 111.4 (d, $J_{CF} = 22.5$ Hz, aromatic C), 118.6, 127.1, 129.5, 130.5, 130.5 (aromatic C), 133.4 (d, $J_{CF} =$ 15.3 Hz, aromatic C), 135.9 (d, $J_{CF} = 3.2$ Hz, aromatic C), 142.4, 146.8, 161.9, 162.2, 163.9 (aromatic C); HRMS (FAB) calcd for $C_{19}H_{16}FN_2$ $[M+H]^+$ 291.1298, found 291.1303; Anal. Calcd for $C_{19}H_{15}FN_2$: C, 78.60; H, 5.21; N, 9.65%. Found: C, 78.39; H, 5.11; N, 9.66%.

General Procedure for the Synthesis of Imines 10b–10f. A mixture of an aniline (10 mmol) and an aromatic aldehyde (15 mmol) in anhydrous MeOH (30 mL) was stirred at room temperature. After 10 min, a yellow precipitate was formed. The precipitate was collected by filtration, and the filtrate was washed with cold MeOH (10 mL × 3).

***N*-Benzylidene-4-methoxyaniline (10b):** Colorless crystals (1.47 g, 70%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.83 (s, 3H, OCH_3), 6.93 (d, $J = 8.8$ Hz, 2H, aromatic H), 7.23 (d, $J = 8.8$ Hz, 2H, aromatic H), 7.45–7.47 (m, 3H, aromatic H), 7.89 (m, 2H, aromatic H), 8.48 (s, 1H, azomethine H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5 (OCH_3), 114.4, 122.2, 128.6, 128.7, 131.0, 136.4, 144.9, 158.3 (aromatic C), 158.4 (azomethine C); HRMS (FAB) calcd for $C_{14}H_{13}NNaO$ $[M+Na]^+$ 234.0895, found 234.0928; Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63%. Found: C, 79.61; H, 6.27; N, 6.60%.

***N*-(4-Methoxybenzylidene)-4-methoxyaniline (10c):** Pale yellow crystals (2.38 g, 99%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.92 (d, $J = 8.8$ Hz, 2H, aromatic H), 6.97 (d, $J = 8.6$ Hz, 2H, aromatic H), 7.20 (d, $J =$ 8.6 Hz, 2H, aromatic H), 7.83 (d, $J = 8.6$ Hz, 2H, aromatic H), 8.40 (s, 1H, azomethine H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4, 55.5 (OCH_3), 114.1, 114.3, 122.0, 129.5, 130.2, 145.3, 157.8, 157.9 (aromatic C), 162.0 (azomethine C); HRMS (FAB) calcd for $C_{15}H_{16}NO_2$ $[M+H]^+$ 242.1181, found 242.1183; Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81%. Found: C, 74.76; H, 6.30; N, 5.78%.

***N*-(4-Methoxycarbonylbenzylidene)-4-methoxyaniline (10d):** Pale yellow crystals (2.61 g, 97%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 6.94 (d, $J = 8.8$ Hz, 2H, aromatic H), 7.27 (d, $J = 8.8$ Hz, 2H, aromatic H), 7.95 (d, $J = 8.2$ Hz, 2H, aromatic H), 8.12 (d, $J = 8.2$ Hz, 2H, aromatic H), 8.53 (s, 1H, azomethine H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.2 (CO_2CH_3), 55.5 (OCH_3), 114.4, 122.4, 128.3, 129.9, 131.9, 140.3, 144.3, 156.7 (aromatic C), 158.7 (azomethine C), 166.6 (CO_2CH_3); HRMS (FAB) calcd for $C_{16}H_{16}NO_3$ $[M+H]^+$ 270.1130, found 270.1135; Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20%. Found: C, 71.35; H, 5.55; N, 5.16%.

***N*-Benzylidene-4-methoxycarbonylaniline (10e):** Colorless crystals (1.43 g, 60%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.93 (s, 3H, CO_2CH_3), 7.21 (d, $J = 8.2$ Hz, 2H, aromatic H), 7.49–7.51 (m, 3H, aromatic H), 7.91 (d, $J = 6.8$ Hz, 2H, aromatic H), 8.07 (d, $J = 8.2$ Hz, 2H, aromatic H), 8.44 (s, 1H, azomethine H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.0 (CO_2CH_3), 120.7, 127.4, 128.9, 129.0, 130.9, 131.9, 135.8, 156.3 (aromatic C), 161.6 (s, azomethine C), 166.8 (CO_2CH_3); HRMS (FAB) calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.1025, found 240.0994; Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85%. Found: C, 75.25; H, 5.46; N, 5.82%.

***N*-(4-Methoxycarbonylbenzylidene)aniline (10f):** Colorless crystals (2.20 g, 92%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94 (s, 3H, CO_2CH_3), 7.22–7.27 (m, 3H, aromatic H), 7.40 (t, $J = 7.5$ Hz, 2H, aromatic H), 7.96 (d, $J = 7.9$ Hz, 2H, aromatic H), 8.13 (d, $J = 8.1$ Hz, 2H, aromatic H), 8.49 (s, 1H, azomethine H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.2 (CO_2CH_3), 120.9, 126.4, 128.6, 129.2, 129.9, 132.3, 140.0, 151.5 (aromatic C), 159.0 (azomethine C), 166.5 (CO_2CH_3); HRMS (FAB) calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.1025, found 240.1016; Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85%. Found: C, 75.33; H, 5.45; N, 5.78%.

General Procedure for the Reaction of Imine 10 and Aliphatic Aldehyde 3 in Table 3. A mixture of an imine **10** (1.0 mmol), an aliphatic aldehyde **3** (1.5 mmol), and $[IrCl_2H(cod)]_2$ (0.025 mmol) in DMSO (3 mL) was stirred at 90 °C for 12 h under an air atmosphere. The resulting mixture was washed with PBS (50 mL) and extracted with AcOEt (20 mL × 3). The organic layer was dried over $MgSO_4$. Removal of the solvent in vacuo, followed by chromatographic purification on silica gel (AcOEt/Hexane = 5/95) afforded **6** and **7**.

3-Methyl-2-phenylquinoline (6m) (Table 3, Entry 2): Pale yellow oil (114 mg, 52%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.45 (s, 3H, CH_3), 7.42–7.56 (m, 4H, aromatic H), 7.41–7.60 (m, 2H, aromatic H), 7.65 (td, $J = 7.7$, 1.5 Hz, 1H, aromatic H), 7.77 (d, $J = 8.1$ Hz, 1H, aromatic H), 8.00 (s, 1H, aromatic H), 8.12 (d, $J = 8.4$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6 (CH_3), 126.3, 126.6, 127.5, 128.1, 128.2, 128.7, 128.8, 129.1, 129.3, 136.7, 140.8, 146.6, 160.5 (aromatic C); HRMS (FAB) calcd for $C_{16}H_{14}N$ $[M+H]^+$ 234.1283, found 234.1251.

6-Methoxy-3-methyl-2-phenylquinoline (6n) (Table 3, En-

try 5): Colorless crystals (52 mg, 21%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.47 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 7.04 (d, J = 2.6 Hz, 1H, aromatic H), 7.31 (dd, J = 9.2, 2.6 Hz, 1H, aromatic H), 7.40–7.43 (m, 1H, aromatic H), 7.46–7.49 (m, 2H, aromatic H), 7.57 (d, J = 7.5 Hz, 2H, aromatic H), 7.91 (s, 1H, aromatic H), 8.01 (d, J = 9.2 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6 (CH_3), 55.5 (OCH_3), 104.2, 121.4, 128.0, 128.2, 128.5, 128.9, 129.4, 130.8, 135.6, 141.0, 142.7, 157.8, 158.0 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{16}NO$ $[M+H]^+$ 250.1232, found 250.1224; Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62%. Found: C, 81.88; H, 6.00; N, 5.53%.

3-Isopropyl-6-methoxy-2-phenylquinoline (6o) (Table 3, Entry 6): White crystals (75 mg, 32%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (d, J = 6.8 Hz, 6H, CH_3), 3.21–3.24 (m, 1H, CH), 3.92 (s, 3H, OCH_3), 7.08 (d, J = 2.7 Hz, 1H, aromatic H), 7.31 (dd, J = 4.6, 2.7 Hz, 1H, aromatic H), 7.40–7.51 (m, 5H, aromatic H), 8.00–8.01 (m, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 29.2 (CH_2), 55.4 (OCH_3), 104.5, 121.6, 127.7, 128.2, 128.7, 128.8, 130.7, 131.5, 140.5, 141.1, 142.3, 157.7, 157.8 (aromatic C); HRMS (FAB) calcd for $C_{19}H_{20}NO$ $[M+H]^+$ 278.1545, found 278.1540; Anal. Calcd for $C_{19}H_{19}NO$: C, 82.28; H, 6.90; N, 5.05%. Found: C, 82.28; H, 7.09; N, 4.89%.

3-Isopropyl-6-methoxy-2-(4-methoxyphenyl)quinoline (6p) (Table 3, Entry 7): White solid (43 mg, 14%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (d, J = 6.8 Hz, 6H, CH_3), 3.25–3.30 (m, 1H, CH), 3.87 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 7.01 (d, J = 8.4 Hz, 2H, aromatic H), 7.08 (d, J = 2.7 Hz, 1H, aromatic H), 7.31 (dd, J = 9.2, 2.7 Hz, 1H, aromatic H), 7.46 (d, J = 8.2 Hz, 2H, aromatic H), 7.98–8.00 (m, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.2 (CH_3), 29.2 (CH_2), 55.4, 55.5 (OCH_3), 104.5, 113.7, 121.5, 128.6, 130.1, 130.6, 131.5, 133.6, 140.7, 142.4, 157.6, 157.6, 159.4 (aromatic C); HRMS (FAB) calcd for $C_{20}H_{22}NO_2$ $[M+H]^+$ 308.1651, found 308.1653; Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56%. Found: C, 78.17; H, 6.97; N, 4.38%.

3-Isopropyl-6-methoxy-2-(4-methoxycarbonylphenyl)quinoline (6q) (Table 3, Entry 8): Colorless crystals (161 mg, 48%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (d, J = 7.0 Hz, 6H, CH_3), 3.15–3.18 (m, 1H, CH), 3.95 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 7.11 (d, J = 2.7 Hz, 1H, aromatic H), 7.34 (dd, J = 9.2, 2.7 Hz, 1H, aromatic H), 7.60 (d, J = 8.1 Hz, 2H, aromatic H), 7.99 (d, J = 9.2 Hz, 1H, aromatic H), 8.05 (s, 1H, aromatic H), 8.16 (d, J = 8.2 Hz, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 29.2 (CH_2), 55.2, 55.5 (OCH_3), 104.5, 122.0, 128.9, 129.1, 129.5, 129.6, 130.7, 131.8, 140.3, 142.3, 145.7, 156.7, 157.9 (aromatic C), 167.0 (CO); HRMS (FAB) calcd for $C_{21}H_{22}NO_3$ $[M+H]^+$ 336.1600, found 336.1609; Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18%. Found: C, 75.15; H, 6.41; N, 4.03%.

3-Isopropyl-6-methoxycarbonyl-2-phenylquinoline (6r) (Table 3, Entry 9): Colorless crystals (168 mg, 55%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (d, J = 6.8 Hz, 6H, CH_3), 3.27–3.29 (m, 1H, CH), 4.00 (s, 3H, OCH_3), 7.46–7.54 (m, 5H, aromatic H), 8.14 (d, J = 8.8 Hz, 1H, aromatic H), 8.23–8.26 (m, 2H, aromatic H), 8.61 (d, J = 1.6 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (CH_3), 29.3 (CH_2), 52.3 (OCH_3), 126.9, 127.8, 128.3, 128.3, 128.3, 128.6, 129.5, 130.4, 134.1, 140.5, 141.4, 147.9, 162.6 (aromatic C), 166.8 (CO); HRMS (FAB) calcd for $C_{20}H_{20}NO_2$ $[M+H]^+$ 306.1494, found 306.1461; Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59%. Found: C, 78.37; H, 6.63; N, 4.31%.

2-Ethyl-3-methylquinoline (7c) (Table 3, Entry 2): Yellow crystals (43 mg, 25%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (t, J = 7.5 Hz, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.99 (q, J = 7.5 Hz, 2H, CH_2), 7.44 (m, 1H, aromatic H), 7.59–7.62 (m, 1H, aromatic H), 7.69 (d, J = 8.1 Hz, 1H, aromatic H), 7.82 (s, 1H, aromatic H), 8.01 (d, J = 8.4 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.8, 19.1 (CH_3), 29.5 (CH_2), 125.6, 126.6, 127.3, 128.2, 128.5, 129.4, 135.7, 146.7, 163.3 (aromatic C); HRMS (FAB) calcd for $C_{12}H_{14}N$ $[M+H]^+$ 172.1126, found 172.1099; Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18%. Found: C, 84.05; H, 7.65; N, 8.03%.

2-Isobutyl-3-isopropyl-6-methoxycarbonylquinoline (7g) (Table 3, Entry 9): White crystals (99 mg, 35%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (d, J = 6.6 Hz, 6H, CH_3), 1.26 (d, J = 6.8 Hz, 6H, CH_3), 2.19–2.25 (m, 1H, CH), 2.86 (d, J = 7.3 Hz, 2H, CH_2), 3.23–3.28 (m, 1H, CH), 3.90 (s, 3H, OCH_3), 7.94–7.96 (m, 2H, aromatic H), 8.12 (dd, J = 9.0, 1.8 Hz, 1H, aromatic H), 8.45 (d, J = 1.8 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 23.7 (CH_3), 28.8, 29.2 (CH), 44.2 (CH_2), 52.2 (OCH_3), 126.4, 127.0, 127.9, 128.8, 130.4, 132.6, 141.7, 148.0, 163.4 (aromatic C), 166.9 (CO); HRMS (FAB) calcd for $C_{18}H_{24}NO_2$ $[M+H]^+$ 286.1807, found 286.1801; Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91%. Found: C, 75.28; H, 8.36; N, 4.67%.

General Procedure for the Synthesis of 1,2-Dialkylquinolines 7 in Table 4. A mixture of an aniline **1** (1.0 mmol), an aliphatic aldehyde **3** (2.5 mmol), and $[IrCl_2H(cod)]_2$ (0.025 mmol) in DMSO (3 mL) was stirred at 90 °C for 12 h under an air atmosphere. The mixture was washed with PBS (50 mL) and extracted with AcOEt (20 mL × 3). The organic layer was dried over $MgSO_4$. Removal of the solvent in vacuo, followed by chromatographic purification on silica gel (AcOEt/Hexane = 5/95), afforded 1,2-dialkylquinoline **7**.

3-Ethyl-2-propylquinoline (7a) (Table 4, Entry 1): Pale yellow oil (118 mg, 59%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (t, J = 7.1 Hz, 3H, CH_3), 1.33 (t, J = 7.5 Hz, 3H, CH_3), 1.82–1.86 (m, 2H, CH_2), 2.82 (q, J = 7.5 Hz, 2H, CH_2), 2.94–2.97 (m, 2H, CH_2), 7.42–7.45 (m, 1H, aromatic H), 7.59–7.62 (m, 1H, aromatic H), 7.71 (d, J = 8.2 Hz, 1H, aromatic H), 7.84 (s, 1H, aromatic H), 8.01 (d, J = 8.2 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 14.4 (CH_3), 22.8, 25.1, 37.8 (CH_2), 125.5, 126.9, 127.3, 128.3, 128.5, 133.8, 135.3, 146.4, 162.0 (aromatic C); HRMS (FAB) calcd for $C_{14}H_{17}NNa$ $[M+Na]^+$ 222.1259, found 222.1282.

2-Isobutyl-3-isopropylquinoline (7d) (Table 4, Entry 13): Colorless oil (225 mg, 99%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (d, J = 6.6 Hz, 6H, CH_3), 1.33 (d, J = 6.8 Hz, 6H, CH_3), 2.25–2.28 (m, 1H, CH), 2.92 (d, J = 7.3 Hz, 2H, CH_2), 3.31–3.34 (m, 1H, CH), 7.43–7.46 (m, 1H, aromatic H), 7.59–7.62 (m, 1H, aromatic H), 7.72–7.74 (m, 1H, aromatic H), 7.94 (s, 1H, aromatic H), 8.01 (d, J = 8.6 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 23.8 (CH_3), 28.8, 29.4 (CH), 44.1 (CH_2), 125.5, 127.0, 127.3, 128.3, 128.5, 131.5, 140.7, 146.2, 160.8 (aromatic C); HRMS (FAB) calcd for $C_{16}H_{22}N$ $[M+H]^+$ 228.1752, found 228.1727; Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16%. Found: C, 84.48; H, 9.30; N, 6.14%.

2-Ethyl-6-methoxy-3-methylquinoline (7e) (Table 4, Entry 9): Pale yellow oil (95 mg, 47%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (t, J = 7.5 Hz, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.94 (q, J = 7.5 Hz, 2H, CH_2), 3.87 (s, 3H, OCH_3), 6.94 (d, J = 2.8 Hz, 1H, aromatic H), 7.25 (dd, J = 4.6, 2.8 Hz, 1H, aromatic H), 7.69 (s, 1H, aromatic H), 7.91 (d, J = 9.0 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.8, 19.0 (CH_3), 29.1 (CH_2),

55.3 (OCH_3), 104.4, 120.6, 128.1, 129.6, 129.9, 134.7, 142.6, 157.1, 160.6 (aromatic C); HRMS (FAB) calcd for $C_{13}H_{16}NO$ $[M + H]^+$ 202.1232, found 202.1222.

2-Isobutyl-3-isopropyl-6-methoxyquinoline (7f) (Table 4, Entry 11): Colorless crystals (213 mg, 83%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (d, $J = 6.8$ Hz, 6H, CH_3), 1.32 (d, $J = 6.8$ Hz, 6H, CH_3), 2.21–2.24 (m, 1H, CH), 2.88 (d, $J = 7.3$ Hz, 2H, CH_2), 3.28–3.32 (m, 1H, CH), 3.91 (s, 3H, OCH_3), 7.03 (m, 1H, aromatic H), 7.26–7.28 (m, 1H, aromatic H), 7.85 (s, 1H, aromatic H), 7.90 (d, $J = 9.2$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 23.9 (CH_3), 28.8, 29.4 (CH), 43.9 (CH_2), 55.5 (OCH_3), 104.6, 120.9, 128.0, 130.0, 130.5, 141.0, 142.3, 157.1, 158.1 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{24}NO$ $[M + H]^+$ 258.1858, found 258.1830; Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N, 5.44%. Found: C, 79.28; H, 9.09; N, 5.42%.

3-Ethyl-8-methoxy-2-propylquinoline (7h) (Table 4, Entry 2): Colorless crystals (126 mg, 55%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (t, $J = 7.3$ Hz, 3H, CH_3), 1.33 (t, $J = 7.5$ Hz, 3H, CH_3), 1.82–1.84 (m, 2H, CH_2), 2.84 (q, $J = 7.5$ Hz, 2H, CH_2), 2.99–3.02 (m, 2H, CH_2), 4.06 (s, 3H, OCH_3), 6.96 (d, $J = 7.5$ Hz, 1H, aromatic H), 7.26–7.35 (m, 2H, aromatic H), 7.83 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.4, 14.4 (CH_3), 23.1, 25.1, 38.0 (CH_2), 56.1 (OCH_3), 106.8, 118.9, 125.5, 128.5, 133.9, 135.8, 138.3, 155.0, 161.0 (aromatic C); HRMS (FAB) calcd for $C_{15}H_{20}NO$ $[M + H]^+$ 230.1545, found 230.1514; Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11%. Found: C, 78.62; H, 8.61; N, 6.01%.

3-Ethyl-6-methoxy-2-propylquinoline (7i) (Table 4, Entry 3): Pale yellow oil (122 mg, 53%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (t, $J = 7.3$ Hz, 3H, CH_3), 1.33 (t, $J = 7.5$ Hz, 3H, CH_3), 1.79–1.84 (m, 2H, CH_2), 2.80 (q, $J = 7.3$ Hz, 2H, CH_2), 2.89–2.93 (m, 2H, CH_2), 3.90 (s, 3H, OCH_3), 7.00 (d, $J = 2.7$ Hz, 1H, aromatic H), 7.26 (dd, $J = 4.6$, 2.7 Hz, 1H, aromatic H), 7.76 (s, 1H, aromatic H), 7.90 (d, $J = 9.2$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 14.4 (CH_3), 22.9, 25.2, 37.5 (CH_2), 55.4 (OCH_3), 104.6, 120.7, 128.1, 129.9, 132.9, 135.6, 142.5, 157.1, 159.3 (aromatic C); HRMS (FAB) calcd for $C_{15}H_{20}NO$ $[M + H]^+$ 230.1545, found 230.1549.

3-Ethyl-8-fluoro-2-propylquinoline (7j) (Table 4, Entry 4): Colorless oil (90 mg, 41%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (t, $J = 7.5$ Hz, 3H, CH_3), 1.35 (t, $J = 7.5$ Hz, 3H, CH_3), 1.82–1.87 (m, 2H, CH_2), 2.85 (q, $J = 7.5$ Hz, 2H, CH_2), 2.98–3.02 (m, 2H, CH_2), 7.26–7.31 (m, 1H, aromatic H), 7.34–7.38 (m, 1H, aromatic H), 7.51 (d, $J = 8.1$ Hz, 1H, aromatic H), 7.89 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3 (CH_3), 22.8, 25.2, 37.8 (CH_2), 112.3 (d, $J_{CF} = 19.3$ Hz, aromatic C), 122.5 (d, $J_{CF} = 4.8$ Hz, aromatic C), 125.2 (d, $J_{CF} = 8.1$ Hz, aromatic C), 129.1 (d, $J_{CF} = 2.4$ Hz, aromatic C), 133.4 (d, $J_{CF} = 2.4$ Hz, aromatic C), 136.5, 156.7, 158.7, 162.5 (aromatic C); HRMS (FAB) calcd for $C_{14}H_{17}FN$ $[M + H]^+$ 218.1345, found 218.1318.

3-Ethyl-6-fluoro-2-propylquinoline (7k) (Table 4, Entry 5): Yellow oil (120 mg, 55%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (t, $J = 7.3$ Hz, 3H, CH_3), 1.34 (t, $J = 7.5$ Hz, 3H, CH_3), 1.81–1.85 (m, 2H, CH_2), 2.82 (q, $J = 7.3$ Hz, 2H, CH_2), 2.92–2.95 (m, 2H, CH_2), 7.32–7.38 (m, 2H, aromatic H), 7.79 (s, 1H, aromatic H), 7.97–8.00 (m, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3 (CH_3), 22.7, 25.1, 37.6 (CH_2), 109.8 (d, $J_{CF} = 21.7$ Hz, aromatic C), 118.3 (d, $J_{CF} = 25.8$ Hz, aromatic C), 127.8 (d, $J_{CF} = 9.7$ Hz, aromatic C), 130.8 (d, $J_{CF} = 9.7$ Hz, aromatic C), 133.1 (d, $J_{CF} = 4.8$ Hz, aromatic C), 136.2, 143.5, 159.0 (aromatic C), 161.1 (d, $J_{CF} = 36.2$ Hz, aromatic C); HRMS (FAB) calcd for $C_{14}H_{16}FNNa$ $[M + Na]^+$ 240.1164, found 240.1151.

8-Ethoxycarbonyl-3-ethyl-2-propylquinoline (7l) (Table 4, Entry 6): Yellow oil (45 mg, 17%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (t, $J = 7.5$ Hz, 3H, CH_3), 1.29 (t, $J = 7.5$ Hz, 3H, CH_3), 1.44 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 1.91–1.95 (m, 2H, CH_2), 2.77 (q, $J = 7.5$ Hz, 2H, CH_2), 2.92 (t, $J = 7.5$ Hz, 2H, CH_2), 4.50 (q, $J = 7.2$ Hz, 2H, OCH_2CH_3), 7.40 (t, $J = 7.6$ Hz, 1H, aromatic H), 7.76–7.78 (m, 2H, aromatic H), 7.83 (dd, $J = 7.2$, 1.4 Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.1 (CH_3), 14.3 (OCH_2CH_3), 21.0, 25.0, 37.1 (CH_2), 61.1 (OCH_2CH_3), 124.4, 127.3, 128.2, 129.8, 131.7, 133.1, 136.0, 143.3, 162.3 (aromatic C), 168.9 (CO); HRMS (FAB) calcd for $C_{17}H_{22}NO_2$ $[M + H]^+$ 272.1651, found 272.1652.

3-Ethyl-6-methoxycarbonyl-2-propylquinoline (7m) (Table 4, Entry 7): Colorless crystals (175 mg, 68%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (t, $J = 7.3$ Hz, 3H, CH_3), 1.36 (t, $J = 7.3$ Hz, 3H, CH_3), 1.84–1.88 (m, 2H, CH_2), 2.84–2.86 (m, 2H, CH_2), 2.95–2.99 (m, 2H, CH_2), 3.98 (s, 3H, OCH_3), 7.95 (s, 1H, aromatic H), 8.02–8.04 (m, 1H, aromatic H), 8.20 (dd, $J = 8.8$, 1.8 Hz, 1H, aromatic H), 8.51 (d, $J = 1.8$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3 (CH_3), 22.6, 25.1, 37.9 (CH_2), 52.2 (OCH_3), 126.4, 127.0, 127.9, 128.7, 130.2, 134.8, 136.3, 148.3, 164.6 (aromatic C), 166.9 (CO); HRMS (FAB) calcd for $C_{16}H_{20}NO_2$ $[M + H]^+$ 258.1494, found 258.1457; Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44%. Found: C, 74.60; H, 7.51; N, 5.32%.

6-Methoxy-2-methylquinoline (7n) (Table 4, Entry 8): Yellow crystals (71 mg, 41%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.70 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 7.03 (d, $J = 2.7$ Hz, 1H, aromatic H), 7.23 (d, $J = 8.4$ Hz, 1H, aromatic H), 7.33 (dd, $J = 4.6$, 2.7 Hz, 1H, aromatic H), 7.92 (d, $J = 4.6$ Hz, 1H, aromatic H), 7.93 (d, $J = 3.7$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9 (CH_3), 55.4 (OCH_3), 105.2, 121.8, 122.2, 127.3, 129.9, 135.0, 143.8, 156.3, 157.2 (aromatic C); HRMS (FAB) calcd for $C_{11}H_{12}NO$ $[M + H]^+$ 174.0919, found 174.0907.

2-Butyl-6-methoxy-3-propylquinoline (7o) (Table 4, Entry 10): Yellow oil (126 mg, 49%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, $J = 7.3$ Hz, 3H, CH_3), 1.04 (t, $J = 7.3$ Hz, 3H, CH_3), 1.48 (m, 2H, CH_2), 1.69–1.79 (m, 4H, alkyl H), 2.73 (t, $J = 7.8$ Hz, 2H, CH_2), 2.93 (t, $J = 8.1$ Hz, 2H, CH_2), 3.89 (s, 3H, OCH_3), 6.98 (d, $J = 2.9$ Hz, 1H, aromatic H), 7.26 (dd, $J = 9.2$, 2.7 Hz, 1H, aromatic H), 7.73 (s, 1H, aromatic H), 7.91 (d, $J = 9.2$ Hz, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.0 (CH_3), 23.0, 23.6, 31.9, 34.4, 35.3 (CH_2), 55.4 (OCH_3), 104.5, 120.7, 127.9, 129.8, 133.8, 134.0, 142.5, 157.0, 159.6 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{24}NO$ $[M + H]^+$ 258.1858, found 258.1864.

2-Isobutyl-3-isopropyl-7-methoxyquinoline (7p) (Table 4, Entry 14): Colorless oil (93 mg, 36%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (d, $J = 6.6$ Hz, 6H, CH_3), 1.31 (d, $J = 6.8$ Hz, 6H, CH_3), 2.23–2.27 (m, 1H, CH), 2.90 (d, $J = 7.3$ Hz, 2H, CH_2), 3.28–3.31 (m, 1H, CH), 3.93 (s, 3H, OMe), 7.10 (d, $J = 8.8$ Hz, 1H, aromatic H), 7.35 (s, 1H, aromatic H), 7.61 (d, $J = 8.8$ Hz, 1H, aromatic H), 7.87 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 23.9 (CH_3), 28.6, 29.5 (CH), 44.0 (CH_2), 55.4 (OMe), 106.5, 118.6, 122.4, 128.0, 131.3, 138.3, 147.6, 159.9, 160.7 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{24}NO$ $[M + H]^+$ 258.1858, found 258.1852.

2-Isobutyl-3-isopropyl-5-methoxyquinoline (7p′) (Table 4, Entry 14): Colorless oil (10 mg, 4%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (d, $J = 6.6$ Hz, 6H, CH_3), 1.34 (d, $J = 6.8$ Hz, 6H, CH_3), 2.23–2.26 (m, 1H, CH), 2.91 (d, $J = 7.3$ Hz, 2H, CH_2), 3.22–3.34 (m, 1H, CH), 4.00 (s, 3H, OMe), 6.77 (d, $J = 7.7$ Hz,

1H, aromatic H), 7.48–7.52 (m, 1H, aromatic H), 7.60 (d, $J =$ 8.6 Hz, 1H, aromatic H), 8.37 (s, 1H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 24.0 (CH_3), 29.0, 29.4 (CH), 44.1 (CH_2), 55.6 (OMe), 103.2, 119.6, 120.9, 126.1, 128.1, 139.9, 147.0, 154.7, 160.9 (aromatic C); HRMS (FAB) calcd for $C_{17}H_{24}NO$ $[M + H]^+$ 258.1858, found 258.1857.

1,2-Dihydro-3-isopropyl-2-(4-methoxycarbonylphenyl)quinoline (11). Yellow oil (62 mg, 20%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, $J = 6.8$ Hz, 3H, CH_3), 0.98 (t, $J = 6.8$ Hz, 3H, CH_3), 1.94–1.97 (m, 1H, CH), 3.78 (s, 3H, OCH_3), 4.08 (br, 1H, NH), 5.06 (s, 1H, NHC*H*), 6.22 (d, $J = 7.2$ Hz, 1H, aromatic H), 6.28 (s, 1H, vinyl H), 6.54 (td, $J = 7.3$, 0.9 Hz, 1H, aromatic H), 6.81–6.86 (m, 2H, aromatic H), 7.29 (d, $J = 8.2$ Hz, 2H, aromatic H), 7.85 (d, $J = 8.2$ Hz, 2H, aromatic H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.9 (CH_3), 31.4 (CH_2), 52.0 (OCH_3), 59.2 (NH*C*H), 112.2 (4-C), 117.8, 119.0, 120.4, 126.4, 126.6, 128.2, 129.5, 130.1, 141.1, 142.0 (aromatic C), 148.9 (3-C); HRMS (FAB) calcd for $C_{20}H_{22}NO_2$ $[M + H]^+$ 308.1651, found 308.1643.

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