A NOVEL SOLID-PHASE SYNTHESIS OF QUINOLINES

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Abstract – A method for synthesizing substituted-quinolines using TMSOTf-catalyzed polystyrene-supported succinimidyl selenide-induced intramolecular seleno-arylation of tethered alkenes as a key step has been developed. The catalytic process provides an efficient method for the stereoselective and regioselective synthesis of tetrahydroquinoline possessing a seleno-functionality, followed by deprotection of tosyl group and syn-elimination of selenoxides to provide quinolines in good yields and purities.

The regioselective and stereoselective solid-phase synthesis of heterocycles and its application to the generation of drug-like molecules has attracted widespread attention.1 Various Lewis acid-catalyzed carbon-carbon bond forming reactions have been adapted to solid-phase synthesis as a way of constructing a wide range of heterocyclic structures.2 Quinolines are one of the major classes of heterocycles and the quinoline ring system is found in many natural products.3 Substituted quinolines are widely used in medicinal chemistry particularly as antituberculosis,4 antimalaria,5 anticancer6 and antiviral7 agents. Quinoline derivatives also find significant applications as agrochemicals8 and dyes.9 Numerous literatures have grown up relating to preparation of combinatorial library of quinolines. Most of them are focused on the intermolecular reaction to form supported tetrahydroquinolines10 and subsequent oxidation reaction with oxidants11 to give quinolines. The solid-phase synthesis of quinolines based on the Friedländer reaction between the resin-bound azomethine and a ketone has been developed, the yields are high and the polymer-bound aniline moiety of the azomethine is easily recycled.12 Quinolines have also been prepared by modification of quinoline skeleton.13 However, few solid-phase synthesis of quinolines by intramolecular cyclization reaction has been reported.14 In recent years, we
have been keen to study the solid-phase synthesis of heterocyclic compounds, using organoselenium resin as the linker and reagent since organoselenium compounds can be utilized as synthetic intermediates and selenium-carbon bond can be easily broken by various methods. Herein, we report an efficient solid-phase synthesis of quinolines by Lewis acid-catalyzed polymer-supported selenium-mediated intramolecular carbon-carbon bond forming reaction and the subsequent deprotection of tosyl group and oxidative cleavage of selenium resins. Advantages of this method are easy operations, odorlessness, and easy preparation of the substrates.

Firstly, N-allyl-toluene-4-sulfonanilide (1a) was synthesized by the treatment of aniline with allyl bromide in refluxing DMF in the presence of anhydrous potassium carbonate and then with p-toluenesulfonyl chloride in pyridine. The solid phase cyclization of 1a with polystyrene-supported selenenyl bromide (Br: 0.99 mmol/g) was explored at -78 °C to 40 °C in dry CH₂Cl₂ for 48 h. But the selenium resin-bound cyclized intermediate 5a was not produced, since no cyclized product 7a and 8a were obtained by treatment of the selenium resin-bound intermediate with 30% H₂O₂ at 0 °C to room temperature. Hajra et al. reported a convenient method for the synthesis of benzoheterocycles by Lewis acid-catalyzed intramolecular halo-arylation of tethered alkenes using N-halosuccinimide (NXS) as the halogen source. Inspired by Hajra’s work, we envisioned that in the presence of Lewis acid, the intramolecular seleno-arylation of 1a might be induced by polystyrene-supported succinimidyl selenide (PSSS) 3. Then polystyrene-supported allyl selenide 2 was prepared by allylation of the dark-red polystyrene-supported selenenyl bromide (Br: 0.99 mmol/g) with NaBH₄ and allyl bromide. The pale-yellow resin 2 was obtained almost quantitatively (FTIR: 3019 cm⁻¹). As shown in Scheme 1, resin 2 reacted smoothly with N-chlorosuccinimide (NCS) to give polystyrene-supported succinimidyl selenide (PSSS) 3 (FTIR: 1707 cm⁻¹ with the disappearance of 3019 cm⁻¹). Like N-phenyl-selenosuccinimide (NPSS), PSSS is a good electrophilic selenium reagent. With the help of Lewis acid, PSSS could react with 1a to form seleniranium ion intermediate 4a which was subsequently attacked by the intramolecular aromatic carbon-centered nucleophile from the anti-side to form a new carbon-carbon bond and offer the cyclized product 5a (Scheme 2). In the synthesis of PSSS, we found that in addition to excessive NCS, allyl chloride was the only by-product (Scheme 1). Considering PSSS is sensitive to moisture, a one-pot synthesis of polymer-supported cyclized product 5 was employed. After completion of the reaction of resin 2 with NCS, PSSS was directly washed by dry CH₂Cl₂ under nitrogen without being removed from

![Scheme 1](image-url)

**Scheme 1.** Synthesis of polystyrene-supported succinimidyl selenide (PSSS)
the reaction flask. PSSS was then treated in turn with 10 mol% TMSOTf and 1a in dry CH₂Cl₂ at -78 °C for 2 h. And then the reaction mixture was kept at -20 °C for 8 h to afford 3-polystyrene-supported selenotetrahydroquinoline (5a). The treatment of 5a with H₂O₂ in THF at 0 °C to room temperature gave a mixture of quinoline (7a) in 26% isolated yield and 1-tosyl-1, 2-dihydroquinoline (8a) in 48% isolated yield. However, 7a could be obtained in the yield of 95% by the treatment of 8a with sodium hydroxide in methanol. Therefore, the intermediate resin 5a was firstly deprotected with 1, 8-diazabicyclo[5, 4, 0]undec-7-ene (DBU) in THF at room temperature to give 3-polystyrene-supported selenotetrahydroquinoline (6a). The reaction was monitored by FT-IR. The strong peak of the sulfonyl absorption at 1321 cm⁻¹ disappeared in the FT-IR spectrum of resulting resin 6a. Then, the treatment of 6a with H₂O₂ at 0 °C to room temperature afforded quinoline (7a) in 78% total yield (Scheme 2).

In the step to afford 5a, a range of cyclization reaction conditions involving 1a and PSSS (3) were explored. The results are depicted in Table 1. The employment of 10 mol% BF₃·Et₂O, AlCl₃, FeCl₃ and

![Scheme 2. Solid-phase synthesis of quinoline 7a](image)

**Table 1.** Optimization of solid-phase conditions of cyclization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Lewis acid</th>
<th>Amount of catalyst (mol%)</th>
<th>Total yield of 7a (%)</th>
<th>Purity of 7a (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>-</td>
<td>nr</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>TiCl₄</td>
<td>10</td>
<td>nr</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Sm(OTf)₃</td>
<td>10</td>
<td>nr</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>AgOTF</td>
<td>10</td>
<td>nr</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>BF₃·Et₂O</td>
<td>10</td>
<td>&lt;5</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>AlCl₃</td>
<td>10</td>
<td>&lt;5</td>
<td>-</td>
</tr>
</tbody>
</table>
ZnCl₂ afforded the product in very low yield when the cyclization reaction was performed at -78 °C for 2 h and then -20 °C for 8 h in dry CH₂Cl₂ (Table 1, entries 5-8). Addition of double dose of TMSOTf did not improve the yield of 7a (Table 1, entries 11). The yield and the purity of 7a decreased when 5 mol% of TMSOTf was employed (Table 1, entries 10). No product was obtained when other Lewis acids such as TiCl₄, Sm(OTf)₃, and AgOTf were used (Table 1, entries 2-4). It is noteworthy that substrate 1a did not undergo any reaction with PSSS (3) in the absence of a Lewis acid (Table 1, entry 1).

Table 2. Solid-phase synthesis of quinolines 7 by route A

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>R¹</th>
<th>R²</th>
<th>Product</th>
<th>Total yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Purity (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1c</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>7a</td>
<td>78</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>H</td>
<td>MeO</td>
<td>7b</td>
<td>82</td>
<td>&gt; 95</td>
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<tr>
<td>3</td>
<td>Me</td>
<td>H</td>
<td>H</td>
<td>7c</td>
<td>75</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>4</td>
<td>Me</td>
<td>Me</td>
<td>H</td>
<td>7d</td>
<td>76</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>5</td>
<td>Me</td>
<td>MeO</td>
<td>H</td>
<td>7e</td>
<td>81</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>6</td>
<td>Me</td>
<td>H</td>
<td>MeO</td>
<td>7f</td>
<td>82</td>
<td>&gt; 95</td>
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<tr>
<td>7</td>
<td>Me</td>
<td>H</td>
<td>Cl</td>
<td>7g</td>
<td>75</td>
<td>&gt; 90</td>
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<tr>
<td>8</td>
<td>Me</td>
<td>H</td>
<td>Br</td>
<td>7h</td>
<td>73</td>
<td>&gt; 90</td>
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<tr>
<td>9</td>
<td>Ph</td>
<td>H</td>
<td>H</td>
<td>7i</td>
<td>78</td>
<td>&gt; 90</td>
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<tr>
<td>10</td>
<td>Ph</td>
<td>H</td>
<td>MeO</td>
<td>7j</td>
<td>85</td>
<td>&gt; 95</td>
</tr>
<tr>
<td>11</td>
<td>4'-MeC₆H₄</td>
<td>H</td>
<td>H</td>
<td>7k</td>
<td>78</td>
<td>&gt; 90</td>
</tr>
</tbody>
</table>

<sup>a</sup> Yields of the crude products based on the loading of polystyrene-supported selenenyl bromide (Br, 0.99 mmol/g); nr = no reaction; 7a was synthesized by route A.

<sup>b</sup> Determined by HPLC analysis.
Then the polystyrene-supported selenium-mediated cyclization reactions of a series of substituted N-allyl-toluene-4-sulfonanilides 1 in the one-pot procedure were studied. The products 7 were obtained in good yields and high purities by route A. The results are summarized in Table 2. It was quite obvious that when R^1 and R^2 were H, electron-donating substituents such as alkoxyl and alkyl and halide substituents, the carbon-based ring-closure reaction proceeded smoothly to give cyclized compounds (Table 2, entries 1-6, 9-15). Good results were also obtained when R was H, alkyl, phenyl, and electron-donating group substituted phenyl (Table 2). No cyclized products were obtained when R^1 and R^2 were electron-withdrawing substituents such as formyl (Table 2, entry 16). It is interesting that the TMSOTf-catalyzed PSSS-mediated cyclization reaction of compounds 1 and the subsequent deprotection of p-toluenesulfonyl group gave rise to the six-membered cyclic compounds 6 as a result of 6-endo-trig cyclization of compounds 1. The five-membered cyclic compounds were not obtained.

In conclusion, we have developed a highly regioselective selenium-mediated intramolecular Friedel-Crafts alkylation of substituted N-allyl-toluene-4-sulfonanilides using polymer-supported organoselenium reagent as a selenium source. Among the catalysts investigated, TMSOTf was found to be the best one. The target products were obtained in good yields and purities by the cleavage of the selenium linker. Furthermore, the easy workup procedure and easily prepared substrates provide an approach that is well-suited for building the parallel libraries upon the basis of further transformation of polymer-supported tetrahydroquinoline 6. The further modifications of resin 6 are still underway.

**EXPERIMENTAL**

Melting points were measured with a X-6 micro-melting apparatus and were uncorrected. ^1^H NMR (300 MHz or 400MHz) and ^13^C NMR (75 MHz or 100 MHz) spectra were recorded on a Bruker Avance 300 or 400 spectrometer in CDCl₃ with TMS as the internal standard; chemical shifts were quoted in ppm and J values were given in Hz. IR spectra were recorded on a Thermo Nicolet Avatar 360 spectrometer. HRMS were performed on an Agilent LC/Msd TOF instrument. HPLC were run on an Agilernt 1100
High performance liquid chromatograph with a tunable UV detector. Dry CH₂Cl₂ and DMF were distilled from CaH₂. Dry THF was distilled from Na. Purities and yields of the products are determined by the crude products and NMR, HRMS, FTIR, are determined by the purified products (the crude products were subjected to TLC on silica gel with ethyl acetate and light petroleum (1:4-1:25) as eluent to give the purified products).

**Typical procedure for the preparation of allyl polystyrene-supported selenide (2):** To a suspension of the swollen polystyrene-supported selenenyl bromide (Br: 0.99 mmol/g, 2.5 g) in dry THF/DMF (V/V=5:1, 30 mL) was added NaBH₄ (5 mmol) under nitrogen atmosphere at 40 °C. After stirring for 8 h at 40 °C, allyl bromide (5.5 mmol) was added dropwise under nitrogen atmosphere, and stirred for another 12 h. The resin 2 was collected by filtration, washed with THF (20 mL×2), MeOH (20 mL×2) and CH₂Cl₂ (20 mL×2) and dried in vacuum. IR (KBr): \( \nu_{\text{max}} = 3068, 3019, 2847, 1565, 1415, 1185, 1016, 907, 751, 694 \text{ cm}^{-1} \).

**General procedure for the preparation of 3-poly styrene-supported seleno-1-tosyl-1, 2, 3, 4-tetrahydroquinolines (5):** To a suspension of the swollen resin 2 (1.0 g) in dry CH₂Cl₂ (15 mL) was added NCS (0.668 g, 5.0 mmol) at 0 °C. The mixture was stirred for 0.5 h at 0 °C and 2 h at room temperature. After filtrating and washing with dry CH₂Cl₂ (15 mL×3), resin 3 was suspended with dry CH₂Cl₂ (15 mL) and cool at -78 °C. Trimethylsilyl trifluoromethanesulfonate (0.022 g, 0.10 mmol) was added. After stirring for 0.5 h at -78 °C, substituted N-allyltoluene-4-sulfonanilide 1 (5.0 mmol) was added under nitrogen atmosphere. The suspension was stirred for another 2 h at -78 °C and then stored in a freezer at -20 °C for 8 h. Saturated aqueous NaHCO₃ (5 mL) was poured into the flask to quench reaction mixture. The resin 5 was collected by filtration, washed with THF (20 mL×2), ether (20 mL×2), THF/H₂O (3:1) (20 mL×2), H₂O (20 mL×2), THF (20 mL×2), MeOH (20 mL×2), and CH₂Cl₂ (20 mL×2), and dried under vacuum.

**Typical procedure for the preparation of quinoline (7a) by route B:** The washed resin 5 was suspended in THF (15 mL). To the mixture was added 30% aqueous H₂O₂ (1.2 mL) and stirred for 1 h at 0 °C, and then stirred for another 20 min at room temperature. The mixture was filtered and the resin was washed with CH₂Cl₂ (15 mL×2). The filtrate was washed with H₂O (30 mL×2), dried over MgSO₄. After removal of the solvent, the residue was purified by column chromatography on silica gel (n-hexane/AcOEt (V/V) =10:1) to give 33.3 mg (26% isolated yield) of quinoline (7a) and 135.6 mg (48% isolated yield) of 1-tosyl-1, 2-dihydroquinoline (8a). A mixture of 8a (135.6 mg, 0.475 mmol), 2.4 mL of aq NaOH, and 10 mL MeOH was refluxed overnight. The reaction was quenched by water and the mixture was extracted with CH₂Cl₂. Combined extracts were washed with brine and dried over MgSO₄. After removal of the solvent, the residue was purified by column chromatography on silica gel (n-hexane/AcOEt (V/V) =10:1) to give 58.3 mg (95% isolated yield) of 7a.
General procedure for the preparation of quinolines 7 by route A: The washed resin 5 was suspended in THF (15 mL). To the mixture was added 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) (2.0 mL) and stirred for 24 h at room temperature. The resin 6 was collected by filtration, washed with THF/H_2O (3:1) (20 mL×2), H_2O (20 mL×2), THF (20 mL×2), MeOH (20 mL×2), and CH_2Cl_2 (20 mL×2), and dried under vacuum. The washed resin 6 was suspended in THF (15 mL). To the mixture was added 30% aqueous H_2O_2 (1.2 mL) and stirred for 1 h at 0 °C, and then stirred for another 20 minutes at room temperature. The mixture was filtered and the resin was washed with CH_2Cl_2 (15 mL×2). The filtrate was washed with H_2O (30 mL×2), dried over MgSO_4, and evaporated to dryness in vacuum to afford quinolines 7.

**Quinoline (7a):** ^{22}_1H NMR (300 MHz, CDCl_3): δ = 8.92 (d, J = 4.2 Hz, 1H), 8.14 (t, J = 8.4 Hz, 2H), 7.80 (d, J = 8.1 Hz, 1H), 7.72 (t, J = 8.1 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.39 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H). IR (KBr): v_max = 1620, 1597, 1529, 1315, 1118 cm^{-1}; HRMS m/z [M]^+ calcd for C_9H_7N 129.0578; found 129.0577.

**6-Methoxyquinoline (7b):** ^{22}_1H NMR (300 MHz, CDCl_3): δ = 8.75 (dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz, 1H), 8.04 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 9.0 Hz, 1H), 7.38–7.33 (m, 2H), 7.06 (d, J = 2.7 Hz, 1H), 3.93 (s, 3H); IR (KBr): v_max = 1618, 1427, 1388, 1255, 1130 cm^{-1}; HRMS m/z [M]^+ calcd for C_10H_9NO 159.0684; found 159.0688.

**4-Methylquinoline (7c):** ^{23}_1H NMR (300 MHz, CDCl_3): δ = 8.75 (d, J = 4.2 Hz, 1H), 8.15–8.05 (m, 1H), 7.93 (dd, J_1 = 8.3 Hz, J_2 = 1.4, 1H), 7.68–7.63 (m, 1H), 7.52–7.47 (m, 1H), 7.15 (d, J = 4.2 Hz, 1H), 2.64 (s, 3H); IR (film): v_max = 1598, 1525, 1454, 1311, 1253 cm^{-1}; HRMS m/z [M]^+ calcd for C_10H_9N 143.0735; found 143.0732.

**4,6-Dimethylquinoline (7d):** ^{23}_1H NMR (300 MHz, CDCl_3): δ = 8.70 (d, J = 4.2 Hz, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.76–7.72 (m, 1H), 7.52–7.47 (m, 1H), 7.16 (d, J = 4.2 Hz, 1H), 2.70 (s, 3H), 2.60 (s, 3H); IR (film): v_max = 1620, 1586, 1528, 1500, 1457, 1383, 1256 cm^{-1}; HRMS m/z [M]^+ calcd for C_{11}H_{11}N 157.0891; found 157.0892.

**8-Methoxy-4-methylquinoline (7e):** ^{24}_1H NMR (300 MHz, CDCl_3): δ = 8.75 (d, J = 4.5 Hz, 1H), 8.00 (d, J = 6.0 Hz, 1H), 7.45 (t, J = 6.0 Hz, 1H), 7.25–7.18 (m, 2H), 3.89 (s, 3H), 2.68 (s, 3H); IR (KBr): v_max = 1618, 1522 cm^{-1}; HRMS m/z [M]^+ calcd for C_{11}H_{11}NO 173.0841; found 173.0840.

**6-Methoxy-4-methylquinoline (7f):** ^{24}_1H NMR (300 MHz, CDCl_3): δ = 8.60 (d, J = 4.2 Hz, 1H), 8.00 (d, J = 9.3 Hz, 1H), 7.34 (dd, J = 2.7, 9 Hz, 1H), 7.14–7.20 (m, 2H), 3.92 (s, 3H), 2.63 (s, 3H); IR (KBr): v_max = 1619, 1497 cm^{-1}; HRMS m/z [M]^+ calcd for C_{11}H_{11}NO 173.0841; found 173.0844.

**6-Chloro-4-methylquinoline (7g):** ^{24}_1H NMR (300 MHz, CDCl_3): δ = 8.76 (d, J = 3.3 Hz, 1H), 8.04 (d, J = 9.0 Hz, 1H), 7.97 (d, J = 2.4 Hz, 1H), 7.65 (dd, J_1 = 9.0 Hz, J_2 = 2.4 Hz, 1H), 7.26 (d, J = 3.3 Hz, 1H), 2.69 (s, 3H); IR (KBr): v_max = 1603, 1506 cm^{-1}; HRMS m/z [M]^+ calcd for C_{10}H_8ClN 177.0345; found
6-Bromo-4-methylquinoline (7h): $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.80 (d, $J$ = 4.5 Hz, 1H), 8.17 (d, $J$ = 2.1 Hz, 1H), 8.05 (d, $J$ = 9.0 Hz, 1H), 7.79 (dd, $J$ = 9.0, 2.1 Hz, 1H), 7.31 (d, $J$ = 4.5 Hz, 1H), 2.69 (s, 3H); IR (KBr): $\nu_{max}$ = 1625, 1512 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{11}$H$_8$BrN 220.984; found 220.987.

4-Phenylquinoline (7i): $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.95 (d, $J$ = 4.5, 1H), 8.23–8.13 (m, 1H), 7.95-7.88 (m, 1H), 7.56–7.44 (m, 6H), 7.32 (d, $J$ = 4.5, 1H); IR (KBr): $\nu_{max}$ = 1588, 1495, 1393 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{15}$H$_{11}$N 205.0891; found 205.0893.

6-Methoxy-4-phenylquinoline (7j): $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.80 (d, $J$ = 4.8 Hz, 1H), 8.09 (d, $J$ = 9.2 Hz, 1H), 7.46–7.56 (m, 5H), 7.39 (d, $J$ = 8.8 Hz, 1H), 7.28 (d, $J$ = 4.5 Hz, 1H), 7.21 (s, 1H), 3.79 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 157.85, 147.46, 147.05, 144.75, 138.29, 131.19, 129.25, 128.61, 128.30, 127.65, 121.69, 121.62, 103.68, 55.35; IR (neat): $\nu_{max}$ = 1620, 1585, 1495, 1429, 1256 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{16}$H$_{13}$NO 235.0997; found 235.0997.

4-($p$-Tolyl)quinoline (7k): $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 8.95 (d, $J$ = 4.5 Hz, 1H), 8.19 (d, $J$ = 8.4 Hz, 1H), 7.96 (d, $J$ = 8.4 Hz, 1H), 7.74 (m, 1H), 7.47–7.55 (m, 1H), 7.39–7.47 (m, 2H), 7.31–7.41 (m, 3H), 2.49 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 149.7, 148.5, 148.2, 138.1, 134.7, 129.6, 129.1, 128.9, 128.7, 126.6, 126.2, 125.7, 121.1, 21.1; IR (neat): $\nu_{max}$ = 1616, 1586, 1504, 1461, 1422, 1391 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{16}$H$_{13}$N 219.1048; found 219.1051.

4-(4-Methoxy-2-methylphenyl)quinoline (7l): $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.91 (d, $J$ = 4.4 Hz, 1H), 8.16 (d, $J$ = 4.4 Hz, 1H), 7.62–7.71 (m, 1H), 7.50 (d, $J$ = 8.4 Hz, 1H), 7.40 (t, $J$ = 7.6 Hz, 1H), 7.21 (d, $J$ = 4.4 Hz, 1H), 7.10 (d, $J$ = 8.4 Hz, 1H), 6.87 (d, $J$ = 2.4 Hz, 1H), 6.83 (dd, $J_1$ = 8.4 Hz, $J_2$ = 2.4 Hz, 1H), 3.83 (s, 3H), 2.00 (s, 3H) $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 159.7, 150.2, 148.5, 148.2, 138.1, 134.7, 129.6, 129.1, 128.9, 128.7, 126.8, 126.2, 122.1, 115.7, 111.3, 55.4, 20.5. IR (neat): $\nu_{max}$ = 1609, 1496, 1388, 1297, 1240 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{17}$H$_{15}$NO 249.1154; found 249.1155.

4-(4-Chlorophenyl)quinoline (7m): $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.92 (d, $J$ = 4.4 Hz, 1H), 8.15 (d, $J$ = 4.4 Hz, 1H), 8.05 (d, $J$ = 8.6 Hz, 1H), 7.83 (d, $J$ = 8.6 Hz, 1H), 7.72 (m, 1H), 7.40–7.52 (m, 5H), 1.38 (s, 3H), 2.00 (s, 3H) $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 149.99, 148.74, 147.15, 136.41, 134.69, 130.86, 130.04, 129.49, 128.89, 126.89, 126.53, 125.49, 121.27. IR (neat): $\nu_{max}$ = 1616, 1588, 1460, 1425 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{15}$H$_{10}$ClN 239.0502; found 239.0500.

4-(2-Tolyl)quinoline (7n): $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.92 (d, $J$ = 4.4 Hz, 1H), 8.18 (d, $J$ = 4.4 Hz, 1H), 7.71–7.60 (m, 1H), 7.47 (dd, $J_1$ = 8.8 Hz, $J_2$ = 2.0 Hz, 1H), 7.25–7.44 (m, 4H), 7.25 (d, $J$ = 4.4 Hz, 1H), 7.16 (d, $J$ = 8.8 Hz, 1H), 2.00 (s, 3H) $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 150.1, 148.7, 148.5, 137.5, 136.2, 130.2, 130.0, 129.6, 129.6, 128.6, 127.4, 126.7, 126.2, 126.0, 121.5, 20.0. IR (neat): $\nu_{max}$ = 1615, 1586, 1502, 1461, 1420, 1390 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{16}$H$_{13}$N 219.1048; found 219.1047.

4-(4-Methoxyphenyl)quinoline (7o): $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.94 (d, $J$ = 4.4 Hz, 1H), 8.18 (d, $J$ = 4.4 Hz, 1H), 8.05 (d, $J$ = 9.0 Hz, 1H), 7.79 (dd, $J_1$ = 9.0, 2.1 Hz, 1H), 7.31 (d, $J$ = 4.5 Hz, 1H), 2.69 (s, 3H); IR (KBr): $\nu_{max}$ = 1625, 1512 cm$^{-1}$; HRMS m/z [M]$^+$ calcd for C$_{11}$H$_8$BrN 220.984; found 220.987.
\[ J = 8.4 \text{ Hz, } 1\text{H}), 7.99 \text{ (d, } J = 8.4 \text{ Hz, } 1\text{H}), 7.70–7.76 \text{ (m, } 1\text{H}), 7.44–7.55 \text{ (m, } 2\text{H}), 7.34 \text{ (d, } J = 4.2 \text{ Hz, } 2\text{H}), 7.08 \text{ (d, } J = 8.7 \text{ Hz, } 2\text{H}), 3.93 \text{ (s, } 3\text{H}); \]
\[ \delta = 159.92, 150.08, 148.81, 148.26, 130.86, 130.34, 129.90, 129.31, 127.01, 126.55, 125.97, 121.34, 114.12, 55.48; \]
\[ \nu_{\text{max}} = 2930, 2849, 1617, 1495, 1238, 1110 \text{ cm}^{-1}; \]
\[ \text{HRMS m/z [M]+ calcd for } C_{16}H_{13}NO \text{ 235.0997; found 235.0994.} \]

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