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Stereoselective Synthesis of Tetrahydroquinolines Through an Imino-Ene Cyclization Reaction

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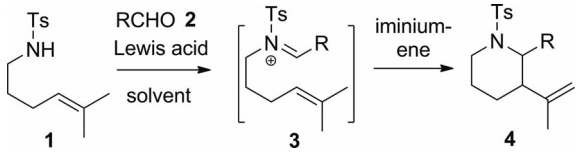
Tetrahydroquinolines have been efficiently synthesized in good yields with excellent stereoselectivity. The reaction between α-allylic anilines and aldehydes proceeds through an imino-ene cyclization that is mediated by boron trifluoride–diethyl ether.

Introduction

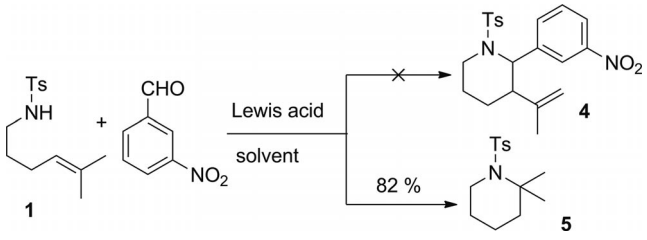
The tetrahydroquinoline unit is important in synthetic chemistry because of its presence in many biologically active natural products[1] and pharmaceuticals.[2] In organic synthesis, some tetrahydroquinolines have been used as ligands.[3] The preparation of 1,2,3,4-tetrahydroquinolines has been accomplished by several methods such as an intramolecular aza-Michael addition,[4] an imino-Diels–Alder reaction,[5] an intramolecular hydroamination,[6] the reduction of quinolines,[7] and other approaches.[8] The imino-ene reaction has been used for the synthesis of homoallylic amines[9] as well as the synthesis of benzimidazole[10] and thiazolidines.[11] Recently, we prepared oxygen[12] and sulfur[13] heterocycles by using the oxonium-ene and thionium-ene cyclization reaction, respectively. Herein, we report a methodology for the synthesis of tetrahydroquinolines. The reaction between an aldehyde and α-allylic aniline proceeds through an imino-ene cyclization that is mediated by boron trifluoride–diethyl ether.

Results and Discussion

In continuation of our interest in the synthesis of heterocyclic compounds through the ene-cyclization reaction,[12,13] we searched for a methodology for the synthesis of substituted piperidines. We envisioned that the reaction between 4-methyl-*N*-(5-methylhex-4-en-1-yl)benzenesulfonamide (**1**) and aldehyde **2** in the presence of a Lewis acid would provide access to 2,3-disubstituted piperidines **4** through an intramolecular iminium-ene cyclization reaction (see Scheme 1). To achieve our goal initially, 4-methyl-*N*-(5-methylhex-4-en-1-yl)benzenesulfonamide (**1**) was treated with *m*-nitrobenzaldehyde at room temperature. In the presence of boron trifluoride–diethyl ether and in dichloromethane, this reaction only furnished self-cyclized product **5** in 82% yield, and the aldehyde coupled product **4** was not detected (see Scheme 2). We explored the reaction further with various Lewis acids such as $In(OTf)_3$, $Bi(OTf)_3$, $Sc(OTf)_3$, TMSOTf, and $FeCl_3$ in different solvents such as CH_2Cl_2 and benzene. However, in contradiction to our hypothesis, the reaction gave only the self-cyclized product in all of the cases. These structures were confirmed by ^1H NMR analysis. In addition, the free amine did not undergo any cyclization reaction.[14]



Scheme 1. Proposed reaction for piperidine synthesis.



Scheme 2. Formation of piperidine from 4-methyl-*N*-(5-methylhex-4-en-1-yl)benzenesulfonamide.

From these results, we speculated on the utility of free aromatic amine **6** to react with aldehyde **2** and produce imine **7** as the reaction intermediate. Imine **7** would then be

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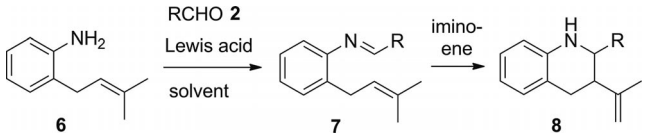
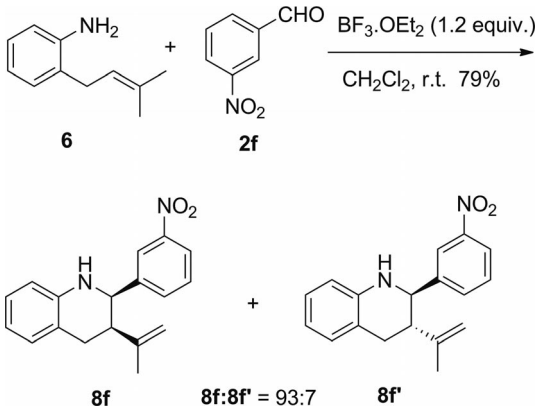
activated by a Lewis acid, which would enable a facile attack by the alkene moiety to afford the corresponding imino-ene product **8** (see Scheme 3).



Scheme 3. Proposed synthesis of tetrahydroquinoline through imino-ene reaction.

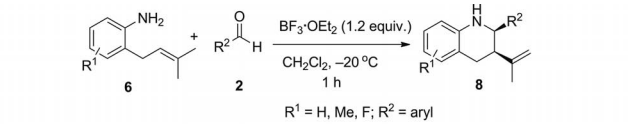
In an initial attempt, arylamine **6** was treated with *m*-nitrobenzaldehyde (**2f**) in the presence of boron trifluoride–diethyl ether at room temperature. The reaction gave the desired product as a mixture of isomers **8f** and **8f′** in a ratio of 93:7. The major and minor isomers were separated by column chromatography, and the products were characterized by NMR spectroscopy (see Scheme 4). The coupling constant of the H-2 proton of **8f** is 4 Hz, whereas the coupling constant of the same proton in **8f′** is 9.2 Hz.

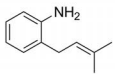
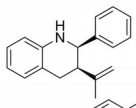
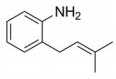
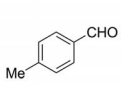
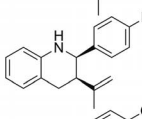
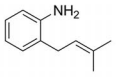
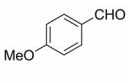
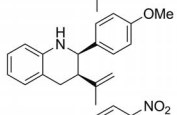
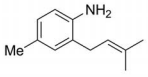
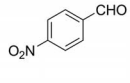
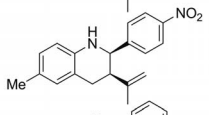
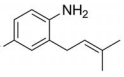
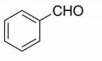
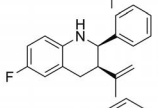
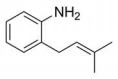
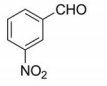
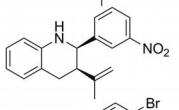
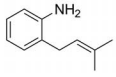
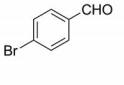
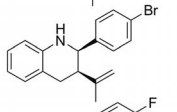
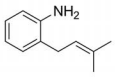
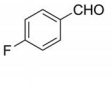
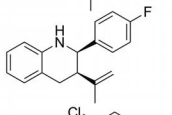
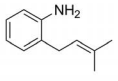
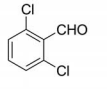
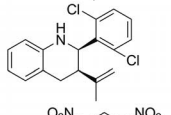
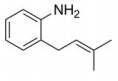
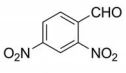
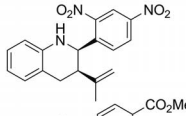
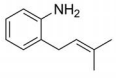
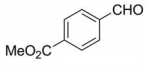
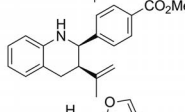
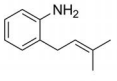
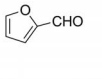
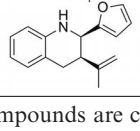


Scheme 4. Synthesis of 1,2,3,4-tetrahydroquinoline.

To improve the diastereoselectivity, the reaction was performed at –20 °C. To our delight, only the single diastereomer **8f** was detected in the ^{1}H NMR of crude reaction mixture. It is noteworthy that the temperature had a significant influence on the diastereoselectivity of the reaction. It was also shown that dichloromethane, in comparison to other solvents such as THF and toluene, was the desired solvent for the reaction. Having established the optimized conditions, we then explored the scope of the reaction by using a wide variety of aromatic and heteroaromatic aldehydes as shown in Table 1. In the case of the aromatic aldehydes, the substituent on the ring had a substantial effect on the yield of the reaction. Aromatic aldehydes with electron-withdrawing substituents on the ring gave good yields in comparison to the aromatic aldehydes with electron-donating groups on the ring. Among all of the aromatic aldehydes listed in Table 1, 2,6-dichlorobenzaldehyde was the best substrate for this reaction. On the other hand, aliphatic aldehydes such as butanal and cyclohexane carboxaldehyde failed to yield the desired tetrahydroquinolines. The reason for this is presumed to be the instability of *N*-arylaldimine **9** (see Scheme 5), which is formed during the course of reaction. Moreover, in all of the cases studied, 2,3-disubstituted tetrahydroquinolines **8a**–**8j** were obtained in high purity without any side product and with a high degree of diastereoselectivity, as determined from the ^{1}H and ^{13}C NMR spectra of the crude product. Substituted anilines (see Table 1, Entries d and e) were also studied. Although methyl-substituted aniline (see Table 1, Entry d) gave a good yield, fluoro-substituted aniline (see Table 1, Entry e) failed to give the desired product, and the starting materials were recovered from the reaction mixture. The stereochem-

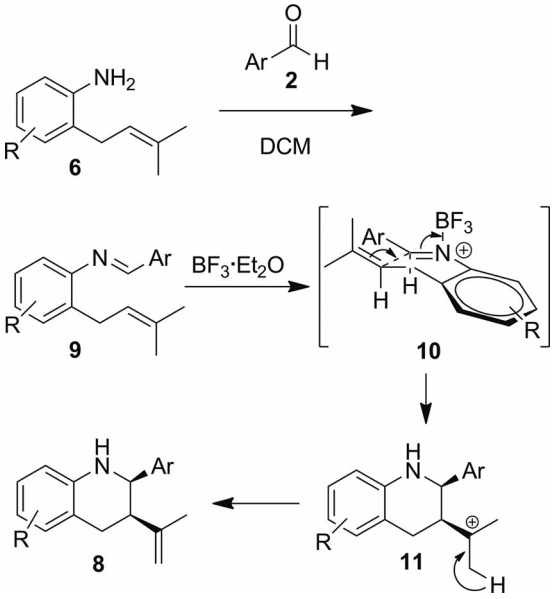
Table 1. Synthesis of 2,3-disubstituted tetrahydroquinolines.



Entry	Amine **6**	Aldehyde **2**	Product **8**	Yield (%)[a]
a				75
b				73
c				64
d				84
e				0
f				81
g				77
h				75
i				95
j				92
k				87
l				70

[a] Yields refer to isolated yield. The compounds are characterized by IR spectroscopy, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy, and mass spectrometry.

istry of the 2,3-disubstituted tetrahydroquinolines was established by COSY experiments and the values of the ^{1}H NMR coupling constants. The coupling constants of the H-2 and H-3 protons of major isomer are in the range of 2.8–4.0 Hz, which indicates a *cis* relationship of the substituents (see Figure 1). The *cis* geometry of the substituents was further confirmed unambiguously by the single-crystal X-ray structure analysis of compound **8d**.[15]



Scheme 5. Mechanism of the reaction.

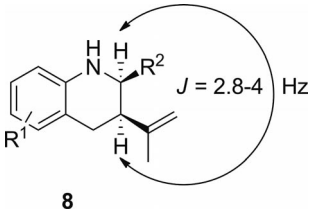


Figure 1. Confirmation of stereochemistry of 2,3-disubstituted tetrahydroquinoline **8**.

The mechanism of the reaction can be explained. The aldehyde upon reaction with an amine forms imine **9**, which is activated by the Lewis acid and then undergoes nucleophilic attack by the alkene moiety to produce cationic intermediate **11** through the six-membered cyclic transition state **10**. In transition state structure **10**, the six-membered aromatic ring takes a position in such a way that the other aryl and isopropenyl groups are *trans* to it. In this configuration, the protons appear on the same side of the aromatic ring to make the system more stable. Finally, intermediate **11** eliminates a proton to furnish tetrahydroquinoline **8**.

Conclusions

In conclusion, we have developed a mild and efficient method for the synthesis of 2,3-disubstituted 1,2,3,4-tetrahydroquinolines from aldehydes and 2-allylic anilines. This method is highly diastereoselective. Furthermore, it can be used for the synthesis of functionalized quinolines.

Experimental Section

General Methods: All of the reagents were commercially obtained. $BF_3{\cdot}Et_2O$ was distilled from CaH_2 prior to use.^{1}H NMR spectroscopic data were recorded with a Varian AS 400 (400 MHz) spectrometer, and the samples were dissolved in $CDCl_3$ with TMS as the internal standard. The ^{13}C NMR spectroscopic data were obtained with a Varian AS 400, which operated at 100 MHz. IR spectra were recorded with a Nicolet Impact 410 FTIR spectrometer. HRMS spectra were recorded using the APCI mode. Elemental analyses were performed with a Perkin–Elmer 2400 series II CHNS analyzer. Melting points were measured in open capillary tubes.

General Procedure for the Synthesis Tetrahydroquinolines

(2*R,3*R**)-1,2,3,4-Tetrahydro-2-phenyl-3-(prop-1-en-2-yl)quinoline (8a):** An oven-dried round-bottomed flask was charged with the aldehyde (53 mg, 0.5 mmol, 1 equiv.) and dichloromethane (2 mL), and the resulting solution was cooled to –20 °C. To this solution was added aniline (80 mg, 0.5 mmol, 1 equiv.) in CH_2Cl_2 (2 mL) all at once. The mixture was stirred at the same temperature for 5 min. To this stirring solution was added boron trifluoride–diethyl ether (90 mg, 0.6 mmol, 1.2 equiv.). After stirring at room temperature for 1 h, the mixture was poured into a saturated solution of $NaHCO_3$ (5 mL). The reaction mixture was extracted with dichloromethane (2 × 10 mL) and then washed with brine and water. The organic layers were collected, dried with Na_2SO_4, filtered, and concentrated. The resultant crude residue was purified by column chromatography over silica gel (petroleum ether/EtOAc, 98:2) to afford **8a** as a colorless solid (93 mg, 75%); m.p. 58–60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (s, 3 H), 2.69 (dd, J = 16.0 and 5.2 Hz, 1 H), 2.76 (dd, J = 16.0 and 10.8 Hz, 1 H), 2.86 (ddd, J = 10.8, 5.2, and 4.0 Hz, 1 H), 4.42 (br. s, 2 H), 4.68 (br. s, 1 H), 4.77 (t, J = 1.2 Hz, 1 H), 6.58 (d, J = 8.0 Hz, 1 H), 6.67 (t, J = 7.6 Hz, 1 H), 7.00–7.10 (m, 2 H), 7.12–7.15 (m, 2 H), 7.21–7.25 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 28.3, 43.8, 57.9, 112.8, 113.4, 117.0, 120.7, 127.2, 127.3, 127.5, 127.9, 129.6, 142.7, 144.1, 144.8 ppm. IR: $\tilde{\nu}$ = 2917, 1607, 1492, 1451, 1265, 1156, 746, 700 cm^{-1}. HRMS [APCI (atmospheric pressure chemical ionization)]: calcd. for $C_{18}H_{19}N$ [M + H]$^+$ 250.1590; found 250.1586. $C_{18}H_{19}N$ (249.35): calcd. C 86.70, H 7.68, N 5.62; found C 86.64, H 7.72, N 5.59.

(2*R,3*R**)-1,2,3,4-Tetrahydro-3-(prop-1-en-2-yl)-2-*p*-tolylquinoline (8b):** Colorless solid (96 mg, 73%); m.p. 65–67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 3 H), 2.30 (s, 3 H), 2.69 (dd, J = 15.6 and 4.8 Hz, 1 H), 2.75 (dd, J = 15.6 and 10.4 Hz, 1 H), 2.84 (ddd, J = 10.4, 4.8, and 3.6 Hz, 1 H), 4.37 (br. s, 1 H), 4.44 (br. s, 1 H), 4.63 (d, J = 3.6 Hz, 1 H), 4.77 (t, J = 1.2 Hz, 1 H), 6.56 (d, J = 8.0 Hz, 1 H), 6.66 (t, J = 7.2 Hz, 1 H), 7.00–7.10 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 23.0, 28.3, 43.9, 57.7, 112.7, 113.5, 117.0, 120.8, 127.3, 127.4, 128.6, 129.6, 136.8, 139.8, 144.2, 145.0 ppm. IR: $\tilde{\nu}$ = 2920, 2854, 1606, 1492, 1438, 1265, 1154, 744 cm^{-1}. HRMS (APCI): calcd. for $C_{19}H_{21}N$ [M + H]$^+$ 264.1747; found 264.1738. $C_{19}H_{21}N$ (263.38): calcd. C 86.65, H 8.04, N 5.32; found C 86.75, H 7.97, N 5.41.

(2*R,3*R**)-1,2,3,4-Tetrahydro-2-(4-methoxyphenyl)-3-(prop-1-en-2-yl)quinoline (8c):** Gum (89 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (s, 3 H), 2.68 (dd, J = 16.0 and 4.8 Hz, 1 H), 2.74 (dd, J = 16.0 and 10.4 Hz, 1 H), 2.82 (ddd, J = 10.4, 4.8, and 2.8 Hz, 1 H), 3.76 (s, 3 H), 4.36 (br. s, 1 H), 4.44 (br. s, 1 H), 4.62 (d, J =

2.8 Hz, 1 H), 4.78 (s, 1 H), 6.56 (d, J = 8.0 Hz, 1 H), 6.65 (t, J = 7.2 Hz, 1 H), 6.75–6.77 (m, 2 H), 7.00–7.10 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 28.3, 43.9, 55.3, 57.3, 112.8, 113.2, 113.4, 117.0, 120.7, 127.3, 128.5, 129.6, 134.9, 144.2, 145.0, 158.8 ppm. IR: $\tilde{\nu}$ = 2923, 2851, 1607, 1494, 1246, 1073, 1035, 830, 745 cm^{-1}. HRMS (APCI): calcd. for $C_{19}H_{21}NO$ [M + H]$^+$ 280.1696; found 280.1686. $C_{19}H_{21}NO$ (279.38): calcd. C 81.68, H 7.58, N 5.01; found C 81.57, H 7.62, N 4.95.

(2*R,3*R**)-1,2,3,4-Tetrahydro-6-methyl-2-(4-nitrophenyl)-3-(prop-1-en-2-yl)quinoline (8d):** Red solid (129 mg, 84%); m.p. 96–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76 (s, 3 H), 2.26 (s, 3 H), 2.62 (dd, J = 15.6 and 10.8 Hz, 1 H), 2.69 (dd, J = 15.6 and 4.8 Hz, 1 H), 2.86 (ddd, J = 10.8, 4.8, and 3.6 Hz, 1 H), 4.33 (br. s, 1 H), 4.38 (br. s, 1 H), 4.77 (d, J = 3.6 Hz, 1 H), 4.80 (s, 1 H), 6.54 (d, J = 8.0 Hz, 1 H), 6.85 (s, 1 H), 6.89 (d, J = 8.4 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 1 H), 6.08 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 23.1, 28.0, 43.8, 57.4, 113.5, 113.7, 123.0, 124.5, 126.9, 128.2, 128.3, 130.2, 140.9, 143.9, 147.2, 150.4 ppm. IR: $\tilde{\nu}$ = 2918, 1617, 1509, 1343, 1107, 804 750 cm^{-1}. HRMS (APCI): calcd. for $C_{19}H_{20}N_2O_2$ [M + H]$^+$ 309.1598; found 309.1660. $C_{19}H_{20}N_2O_2$ (308.38): calcd. C 74.00, H 6.54, N 9.08; found C 73.92, H 6.58, N 9.15.

(2*R,3*R**)-1,2,3,4-Tetrahydro-2-(3-nitrophenyl)-3-(prop-1-en-2-yl)-quinoline (8f):** Red solid (119 mg, 81%); m.p. 73–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.78 (s, 3 H), 2.64 (dd, J = 16.4 and 10.8 Hz, 1 H), 2.74 (dd, J = 16.4 and 4.0 Hz, 1 H), 2.88 (ddd, J = 10.8, 4.4, and 4.0 Hz, 1 H), 4.36 (br. s, 1 H), 4.44 (br. s, 1 H), 4.81 (br. s, 2 H), 6.62 (d, J = 8.0 Hz, 1 H), 6.70 (t, J = 6.8 Hz, 1 H), 7.02 (d, J = 7.2 Hz, 1 H), 7.08 (t, J = 7.6 Hz, 1 H), 7.40 (t, J = 8.0 Hz, 1 H), 7.50 (d, J = 7.6 Hz, 1 H), 7.96 (s, 1 H), 8.07 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1, 28.0, 43.6, 57.1, 113.6 (2 C), 117.7, 120.2, 122.3, 122.5, 127.6, 128.8, 129.7, 133.5, 143.3, 143.9, 144.7, 147.8 ppm. IR: $\tilde{\nu}$ = 2926, 2853, 1608, 1531, 1493, 1350, 1265, 740, 704 cm^{-1}. HRMS (APCI): calcd. for $C_{18}H_{18}N_2O_2$ [M + H]$^+$ 295.1441; found 295.1435. $C_{18}H_{18}N_2O_2$ (294.35): calcd. C 73.45, H 6.16, N 9.52; found C 73.56, H 6.22, N 9.47.

(2*R,3*R**)-2-(4-Bromophenyl)-1,2,3,4-tetrahydro-3-(prop-1-en-2-yl)quinoline (8g):** Brown gum (122 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 3 H), 2.67 (d, J = 7.6 Hz, 2 H), 2.82 (ddd, J = 7.6, 4.5, and 4.0 Hz, 1 H), 4.35 (br. s, 1 H), 4.41 (br. s, 1 H), 4.60 (d, J = 4.0 Hz, 1 H), 4.79 (t, J = 1.2 Hz, 1 H), 6.55 (d, J = 8.0 Hz, 1 H), 6.66 (t, J = 7.6 Hz, 1 H), 6.97–7.06 (m, 4 H), 7.30–7.34 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.0, 28.1, 43.7, 57.3, 113.2, 113.5, 117.3, 120.5, 121.1, 127.4, 129.2, 129.7, 131.0, 141.7, 143.8, 144.4 ppm. IR: $\tilde{\nu}$ = 2919, 1605, 1485, 1265, 896, 825, 746 cm^{-1}. HRMS (APCI): calcd. for $C_{18}H_{18}BrN$ [M + H]$^+$ 318.0811; found 318.0823. $C_{18}H_{18}BrN$ (328.25): calcd. C 65.86, H 5.53, N 4.27; found C 65.76, H 5.47, N 4.35.

(2*R,3*R**)-2-(4-Fluorophenyl)-1,2,3,4-tetrahydro-3-(prop-1-en-2-yl)quinoline (8h):** Colorless liquid (100 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.63 (s, 3 H), 2.63 (d, J = 8.0 Hz, 1 H), 2.76 (ddd, J = 8.0, 4.0, and 3.6 Hz, 1 H), 4.31 (br. s, 1 H), 4.34 (br. s, 1 H), 4.59 (s, 1 H), 4.72 (s, 1 H), 6.50 (d, J = 7.6 Hz, 1 H), 6.60 (t, J = 7.6 Hz, 1 H), 6.82–6.86 (m, 2 H), 6.93–6.98 (m, 2 H), 7.00–7.04 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 28.1, 43.8, 57.2, 113.0, 113.5, 114.7 (d, J = 21.3 Hz), 117.2, 120.5, 127.4, 128.9 (d, J = 7.5 Hz), 129.6, 138.4, 143.9, 144.6, 162.1 (d, J = 244.3 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3/C_6F_6$): δ = 45.82–45.90 (m, F) ppm. IR: $\tilde{\nu}$ = 2922, 2853, 1605, 1223, 1157, 839, 746 cm^{-1}. HRMS (APCI): calcd. for $C_{18}H_{18}FN$ [M + H]$^+$ 268.1496; found 268.1501. $C_{18}H_{18}FN$ (267.34): calcd. C 80.87, H 6.79, N 5.24; found C 80.93, H 6.82, N 6.88.

(2*R,3*R**)-2-(2,6-Dichlorophenyl)-1,2,3,4-tetrahydro-3-(prop-1-en-2-yl)quinoline (8i):** Colorless gum (155 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3 H), 2.92–3.07 (m, 3 H), 4.33 (br. s, 1 H), 4.35 (br. s, 1 H), 4.70 (s, 1 H), 5.55 (t, J = 3.6 Hz, 1 H), 6.50 (d, J = 8.0 Hz, 1 H), 6.67 (t, J = 7.2 Hz, 1 H), 7.00–7.05 (m, 2 H), 7.10 (t, J = 8.0 Hz, 1 H), 7.29 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.0, 32.3, 43.4, 57.2, 114.0, 114.4, 117.4, 121.4, 127.0, 128.5, 129.3, 130.0, 136.1, 136.3, 144.4, 145.5 ppm. IR: $\tilde{\nu}$ = 2920, 1608, 1588, 1483, 1266, 888, 780, 745 cm^{-1}. HRMS (APCI): calcd. for $C_{18}H_{17}Cl_2N$ [M + H]$^+$ 318.0811; found 318.0823. $C_{18}H_{17}Cl_2N$ (318.25): calcd. C 67.93, H 5.38, N 4.40; found C 67.87, H 5.35, N 4.48.

(2*R,3*R**)-1,2,3,4-Tetrahydro-2-(2,4-dinitrophenyl)-3-(prop-1-en-2-yl)quinoline (8j):** Red solid (156 mg, 92%); m.p. 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69 (s, 3 H), 2.61 (dd, J = 16.4 and 10.8 Hz, 1 H), 2.76 (dd, J = 16.4 and 4.0 Hz, 1 H), 2.88 (dt, J = 10.8, 4.0, and 3.6 Hz, 1 H), 4.15 (br. s, 1 H), 4.47 (d, J = 3.6 Hz, 1 H), 4.77 (t, J = 1.2 Hz, 1 H), 5.75 (t, J = 4.0 Hz, 1 H), 6.63 (d, J = 8.0 Hz, 1 H), 6.74 (d, J = 7.6 Hz, 1 H), 7.03 (d, J = 7.2 Hz, 1 H), 7.10 (t, J = 7.6 Hz, 1 H), 7.79 (d, J = 8.8 Hz, 1 H), 8.30 (d, J = 8.8 Hz, 1 H), 8.61 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.6, 28.6, 42.9, 52.6, 113.9, 114.8, 118.2, 119.4, 120.0, 126.3, 127.8, 129.8, 131.7, 142.8, 143.8, 144.6, 146.8, 149.3 ppm. IR: $\tilde{\nu}$ = 2922, 2850, 1606, 1588, 1530, 1494, 1349, 1265, 747 cm^{-1}. HRMS (APCI): calcd. for $C_{18}H_{17}N_3O_4$ [M + H]$^+$ 340.1292; found 340.1287. $C_{18}H_{17}N_3O_4$ (339.35): calcd. C 63.71, H 5.05, N 12.38; found C 63.65, H 5.14, N 12.50.

Methyl 4-[(2*R,3*R**)-3-(Prop-1-en-2-yl)-1,2,3,4-tetrahydroquinolin-2-yl]benzoate (8k):** Colorless solid (133 mg, 87%); m.p. 106–108 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70 (s, 3 H), 2.70 (d, J = 7.6 Hz, 2 H), 2.87 (ddd, J = 7.6, 4.0, and 3.6 Hz, 1 H), 3.89 (s, 3 H), 4.39 (br. s, 1 H), 4.42 (br. s, 1 H), 4.73 (d, J = 3.6 Hz, 1 H), 4.77 (t, J = 1.2 Hz, 1 H), 6.59 (d, J = 7.6 Hz, 1 H), 6.68 (t, J = 7.6 Hz, 1 H), 7.01 (d, J = 7.6 Hz, 1 H), 7.06 (t, J = 7.2 Hz, 1 H), 7.20 (d, J = 8.4 Hz, 2 H), 7.89 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.9, 28.1, 43.6, 52.1, 57.6, 113.1, 113.4, 117.2, 120.4, 127.3, 127.4, 128.9, 129.1, 129.5, 143.7, 144.2, 147.9, 167.1 ppm. IR: $\tilde{\nu}$ = 2918, 2854, 1717, 1602, 1494, 1276, 1109, 748 cm^{-1}. HRMS (APCI): calcd. for $C_{20}H_{21}NO_2$ [M + H]$^+$ 308.1645; found 308.1652. $C_{20}H_{21}NO_2$ (307.39): calcd. C 78.15, H 6.89, N 4.56; found C 78.23, H 6.78, N 4.62.

(2*R,3*R**)-2-(Furyl-2-yl)-1,2,3,4-tetrahydro-3-(prop-1-en-2-yl)-quinoline (8l):** Colorless solid (84 mg, 70%); m.p. 63–65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.76 (s, 3 H), 2.76 (dd, J = 15.2 and 4.0 Hz, 1 H), 2.85 (ddd, J = 11.2, 4.0, and 3.6 Hz, 1 H), 2.88 (dd, J = 15.2 and 11.2 Hz, 1 H), 4.31 (br. s, 1 H), 4.64 (br. s, 1 H), 4.74 (d, J = 3.6 Hz, 1 H), 3.82 (br. s, 1 H), 6.04 (d, J = 2.8 Hz, 1 H), 6.25 (dd, J = 3.2 and 1.6 Hz, 1 H), 6.54 (d, J = 7.2 Hz, 1 H), 6.67 (t, J = 7.2 Hz, 1 H), 6.98–7.00 (m, 2 H), 7.27 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3, 28.3, 42.6, 52.2, 106.6, 110.3, 111.9, 114.7, 120.9, 127.2, 129.5, 141.4, 143.1, 145.0, 156.0 ppm. IR: $\tilde{\nu}$ = 2966, 2919, 1607, 1493, 1263, 1144, 1011, 894, 743 cm^{-1}. HRMS (APCI): calcd. for $C_{16}H_{17}NO$ [M + H]$^+$ 240.1383; found 240.1387. $C_{16}H_{17}NO$ (239.32): calcd. C 80.30, H 7.16, N 5.85; found C 80.36, H 7.21, N 8.79.

Supporting Information (see footnote on the first page of this article): ^{1}H, ^{13}C, and ^{19}F NMR spectra of all compounds and X-ray structure and crystal parameters of compound **8d**.

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[15] CCDC-873455 (for **8d**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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