SUPPORTING INFORMATION: PART A

Enantioselective Direct Vinylogous Allylic Alkylation of 4-Methylquinolones Under Iridium-Catalysis

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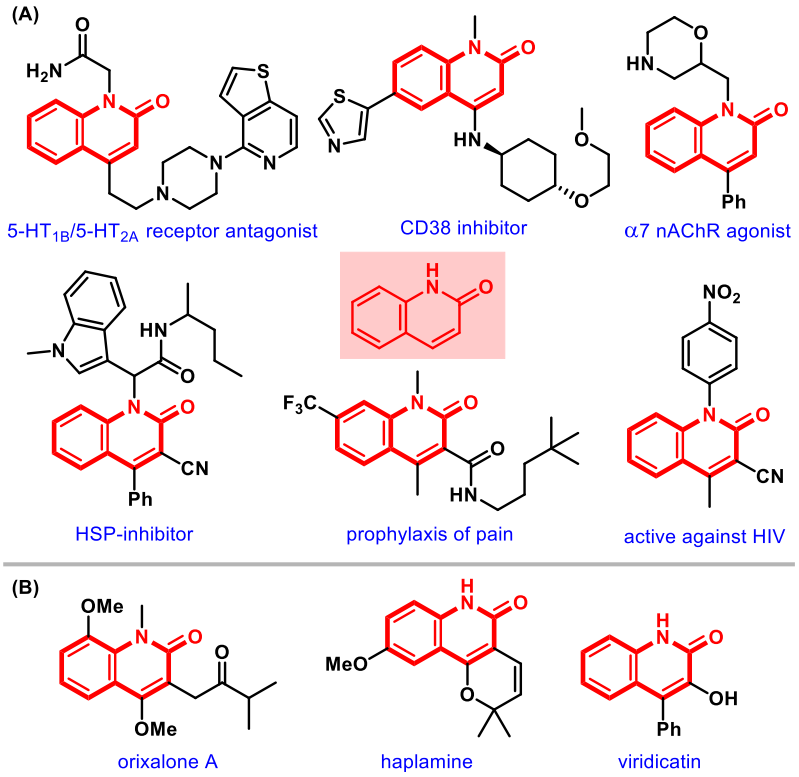
A. General information:

Infrared (FT-IR) spectra were recorded on a Bruker Alfa FT-IR, ν_{max} in cm^{-1} and the bands are characterized as broad (br), strong (s), medium (m), and weak (w). NMR spectra were recorded on Bruker Ultrashield spectrometer at 400 MHz (for ^{1}H-NMR) and 100 MHz (for ^{13}C-NMR). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as internal standard [$CDCl_3$: δ 7.26, CD_3OD: δ 3.31, $(CD_3)_2SO$: δ 2.50 for ^{1}H-NMR and $CDCl_3$: δ 77.16, CD_3OD: δ 49.00, $(CD_3)_2SO$: δ 39.52 for ^{13}C-NMR]. For ^{1}H-NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, ddd = doublet of doublet of doublets, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. High resolution mass spectrometry was performed on XEVO G2-XS QTof instrument. Optical rotations were measured on JASCO P-2000 polarimeter. Melting points were measured in open glass capillary using Buchi M-560 melting point apparatus and the values are uncorrected. Enantiomeric ratios were determined by Shimadzu LC-20AD HPLC instrument and SPD-20A Diode Array detector using stationary phase chiral columns (25 cm × 0.46 cm) in comparison with authentic racemic compounds.

Unless stated otherwise, all reactions were carried out with distilled and dried solvents under an atmosphere of nitrogen or argon in oven (120 °C) dried glassware with standard vacuum-line techniques. Organic solvents used for carrying out reactions were dried using standard methods. $[Ir(COD)Cl]_2$, (*S*)-BINOL and (*R*)-BINOL were purchased from Combi-Blocks, Inc.; (−)-bis[(*S*)-1-phenylethyl]amine was purchased from Alfa Aesar and used as received. All work up and purification were carried out with reagent grade solvents in air. Thin-layer chromatography was performed using Merck silica gel 60 F_{254} pre-coated plates (0.25 mm). Column chromatography was performed using silica gel (230-400 or 100-200 mesh). NMR yields were determined by using mesitylene as an internal standard. Unless otherwise noted, all reported yields of the Ir-catalyzed allylation reactions are isolated yields. Chiral ligands used in this work were prepared according to literature procedures.[1]

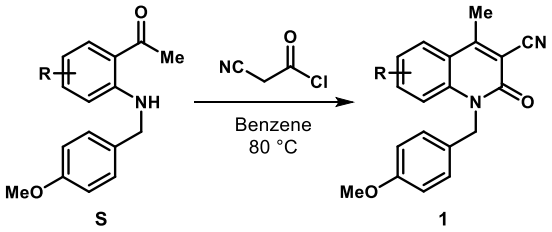
[1] a) Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. Enantioselective Catalytic Conjugate Addition of Dialkylzinc Reagents using Copper–Phosphoramidite Complexes; Ligand Variation and Non-linear Effects. *Tetrahedron* **2000**, *56*, 2865-2878; b) Polet, D.; Alexakis, A. Kinetic Study of Various Phosphoramidite Ligands in the Iridium-Catalyzed Allylic Substitution. *Org. Lett*. **2005**, *7*, 1621-1624; c) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. Iridium-Catalyzed Synthesis of Primary Allylic Amines from Allylic Alcohols: Sulfamic Acid as Ammonia Equivalent. *Angew. Chem. Int. Ed.* **2007**, *46*, 3139-3143.

B. Representative examples of (A) bioactive compounds and (B) bioactive natural products containing 2-quinolone core structures:



C. General procedure for the synthesis of 4-methylquinolones:

General procedure A: Starting material **S** and substituted 4-methylquinolones (**1a-1h**) were prepared according to the previously reported procedure.[2]

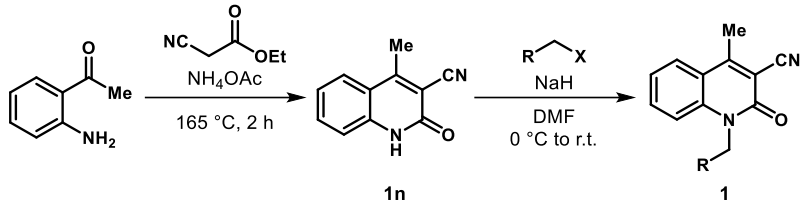


In an oven dried two neck round-bottom flask, equipped with reflux condenser, **S** (1.0 equiv.) was taken in absolute benzene (4.0 mL/mmol of **S**) under argon. To this, a solution of

[2] Ellis, D.; Kuhen, K. L.; Anaclerio, B.; Wu, B.; Wolff, K.; Yin, H.; Bursulaya, B.; Caldwell, J.; Karanewsky, D.; He, Y. Design, Synthesis, and Biological Evaluations of Novel Quinolones as HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4246-4251.

2-cyanoacetyl chloride (2.0 equiv.) in absolute benzene (1.0 mL/mmol of **S**) was added and the resulting solution was refluxed at 80 °C for 24 h. Solvent was removed under reduced pressure and the residue was purified by silica-gel flash column chromatography to obtain **1**.

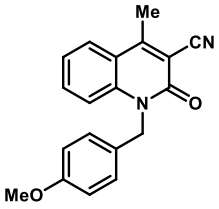
General procedure B: Substituted 4-methylquinolones (**1j-1m**) were prepared according to the modified literature procedure.[3]



In an oven dried round-bottom flask, equipped with reflux condenser, 2′-aminoacetophenone (1.0 equiv.) was taken along with NH_4OAc (2.5 equiv.) under air. To this, ethyl 2-cyanoacetate (1.5 equiv.) was added and the resulting solution was heated to 165 °C for 2 h. The mixture was then cooled to r.t., EtOH (0.8 mL/mmol of 2′-aminoacetophenone) was added and the mixture was triturated for 6 h. The precipitated solid is then filtered, washed with petroleum ether and dried under high vacuum to yield 2-quinolone **1n**.

4-Methylquinolones **1n** (1.0 equiv.) was taken along with NaH (55% assay, 1.1-1.3 equiv.) in an oven dried round-bottom flask under argon. To this, dry DMF (4.0 mL/mmol of **1n**) was added and the resulting solution was stirred at 0 °C for 30 min. A solution of alkyl halide (1.0-1.3 equiv.) in dry DMF (1.2 mL/mmol of **1n**) was then added dropwise to the reaction mixture at 0 °C, warmed to r.t. and stirred for 12-24 h. Reaction mixture was poured into ice-cold water, stirred for 15 min and extracted with EtOAc. Combined organic layer was washed with water, dried over anh. Na_2SO_4 and concentrated under reduced pressure to obtain a light-yellow oil. This residue was purified by silica-gel flash column chromatography to obtain **1**.

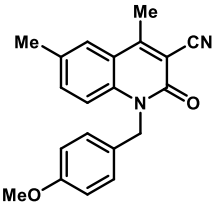
Compound 1a: Prepared according to the general procedure A, **Sa** (R = H, 2.14 g, 8.382 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); light yellow solid (1.89 g, 6.210 mmol, 74% yield); **m.p.** 157-159 °C; **FT-IR (Thin film):** 2226 (w), 1647 (s), 1610 (m), 1511 (m), 1249 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.83-7.81 (m, 1H), 7.60-7.56 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.31-7.27



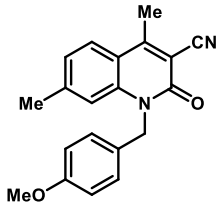
[3] Igoe, N.; Bayle, E. D.; Fedorov, O.; Tallant, C.; Savitsky, P.; Rogers, C.; Owen, D. R.; Deb, G.; Somervaille, T. C. P.; Andrews, D. M.; Jones, N.; Cheasty, A.; Ryder, H.; Brennan, P. E.; Müller, S.; Knapp, S.; Fish, P. V. Design of a Biased Potent Small Molecule Inhibitor of the Bromodomain and PHD Finger-Containing (BRPF) Proteins Suitable for Cellular and in Vivo Studies. *J. Med. Chem.* **2017**, *60*, 668-680.

(m, 1H), 7.18 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.48 (s, 2H), 3.75 (s, 3H), 2.81 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 159.0, 156.8, 139.7, 133.8, 128.3, 127.5, 126.8, 123.2, 119.9, 115.9, 115.2, 114.4, 107.2, 55.3, 46.0, 18.6; **HRMS (ESI+):** Calcd. for $C_{19}H_{16}N_2O_2Na$ ([M+Na]$^+$): 327.1109, Found: 327.1111.

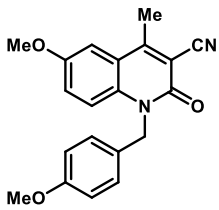
Compound 1b: Prepared according to the general procedure A, **Sb** (R = 3-Me, 497.0 mg, 1.845 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); light yellow solid (537.0 mg, 1.687 mmol, 91% yield); **m.p.** 216-217 °C; **FT-IR (Thin film):** 2923 (w), 2226 (m), 1646 (s), 1563 (m), 1510 (m), 1248 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.57 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 8.7 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.45 (s, 2H), 3.74 (s, 3H), 2.78 (s, 3H), 2.40 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 156.4, 137.8, 135.1, 132.9, 128.3, 127.7, 126.5, 119.9, 115.8, 115.4, 114.4, 107.2, 55.4, 46.0, 20.9, 18.6; **HRMS (ESI+):** Calcd. for $C_{20}H_{18}N_2O_2Na$ ([M+Na]$^+$): 341.1266, Found: 341.1268.



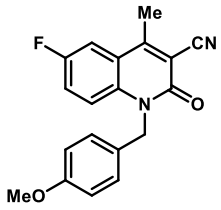
Compound 1c: Prepared according to the general procedure A, **Sc** (R = 4-Me, 130.0 mg, 0.483 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); light yellow sticky mass (136.0 mg, 0.427 mmol, 88% yield); **FT-IR (Thin film):** 2225 (w), 1650 (s), 1611 (s), 1512 (w), 1250 (m), 1029 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.68 (d, *J* = 8.3 Hz, 1H), 7.19-7.17 (m, 3H), 7.11 (d, *J* = 8.3 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.45 (s, 2H), 3.75 (s, 3H), 2.76 (s, 3H), 2.42 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 159.1, 156.5, 145.2, 139.9, 128.3, 127.7, 126.7, 124.7, 117.8, 116.0, 115.4, 114.4, 106.1, 55.4, 45.9, 22.5, 18.5; **HRMS (ESI+):** Calcd. for $C_{20}H_{18}N_2O_2Na$ ([M+Na]$^+$): 341.1266, Found: 341.1263.



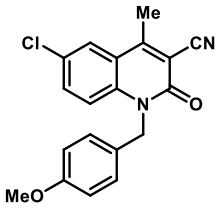
Compound 1d: Prepared according to the general procedure A, **Sd** (R = 3-OMe, 445.0 mg, 1.560 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (3% EtOAc in CH_2Cl_2); light yellow solid (510.0 mg, 1.525 mmol, 98% yield); **m.p.** 175-177 °C; **FT-IR (Thin film):** 2226 (w), 1644 (s), 1563 (m), 1508 (s), 1247 (m), 1034 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.30 (d, *J* = 8.9 Hz, 1H), 7.20-7.13 (m, 4H), 6.79 (d, *J* = 8.6 Hz, 2H), 5.43 (s, 2H), 3.84 (s, 3H), 3.72 (s, 3H), 2.75 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.0, 158.5, 155.9, 155.2, 134.2, 128.2, 127.6, 122.2, 120.6, 117.2, 115.3, 114.3, 108.6, 107.5, 55.8, 55.3, 46.0, 18.7; **HRMS (ESI+):** Calcd. for $C_{20}H_{18}N_2O_3Na$ ([M+Na]$^+$): 357.1215, Found: 357.1213.



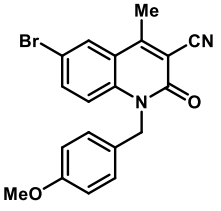
Compound 1e: Prepared according to the general procedure A, **Se** (R = 3-F, 355.0 mg, 1.299 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (3% EtOAc in CH_2Cl_2); light yellow solid (308.0 mg, 0.955 mmol, 74% yield); **m.p.** 203-205 °C; **FT-IR (Thin film):** 2228 (w), 1650 (s), 1566 (m), 1509 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.47 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.39-7.35 (m, 1H), 7.33-7.31 (m, 1H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.47 (s, 2H), 3.75 (s, 3H), 2.78 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.3, 158.6, 158.1 (d, *J* = 244.6 Hz), 155.6 (d, *J* = 3.2 Hz), 136.4, 128.2, 127.3, 121.7 (d, *J* = 23.8 Hz), 120.9 (d, *J* = 8.6 Hz), 117.8 (d, *J* = 8.3 Hz), 114.9, 114.5, 112.1 (d, *J* = 23.5 Hz), 108.6, 55.4, 46.4, 18.7; **HRMS (ESI+):** Calcd. for $C_{19}H_{15}FN_2O_2Na$ ($[M+Na]^+$): 345.1015, Found: 345.1014.



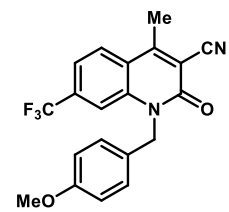
Compound 1f: Prepared according to the general procedure A, **Sf** (R = 3-Cl, 454.0 mg, 1.570 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1-2% EtOAc in CH_2Cl_2); light yellow solid (518.0 mg, 1.529 mmol, 97% yield); **m.p.** 226-228 °C; **FT-IR (Thin film):** 2228 (w), 1652 (s), 1513 (m), 1249 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 2.1 Hz, 1H), 7.51 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.33 (d, *J* = 9.0 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 5.46 (s, 2H), 3.76 (s, 3H), 2.79 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.3, 158.6, 155.5, 138.3, 133.7, 129.0, 128.2, 127.2, 126.2, 121.0, 117.5, 114.8, 114.6, 108.6, 55.4, 46.3, 18.6; **HRMS (ESI+):** Calcd. for $C_{19}H_{15}ClN_2O_2Na$ ($[M+Na]^+$): 361.0720, Found: 361.0719.



Compound 1g: Prepared according to the general procedure A, **Sg** (R = 3-Br, 350.0 mg, 1.047 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1-2% EtOAc in CH_2Cl_2); light yellow solid (393.0 mg, 1.025 mmol, 98% yield); **m.p.** 215-217 °C; **FT-IR (Thin film):** 2228 (w), 1651 (s), 1514 (m), 1249 (m), 1029 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.91 (s, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 5.44 (s, 2H), 3.74 (s, 3H), 2.78 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.5, 155.5, 138.6, 136.4, 129.2, 128.2, 127.1, 121.4, 117.7, 116.4, 114.8, 114.4, 108.3, 55.4, 46.2, 18.6; **HRMS (ESI+):** Calcd. for $C_{19}H_{15}BrN_2O_2Na$ ($[M+Na]^+$): 405.0215, Found: 405.0214.

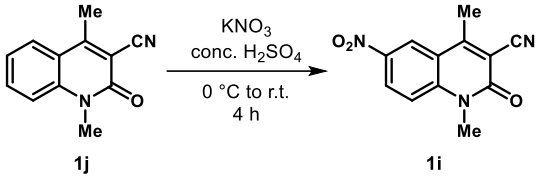


Compound 1h: Prepared according to the general procedure A, **Sh** (R = 4-CF_3, 317.0 mg, 0.980 mmol, 1.0 equiv.), reaction time 24 h, purified by silica-gel flash column chromatography (1-2% EtOAc in CH_2Cl_2); light yellow sticky mass (133.0 mg, 0.357 mmol, 36% yield); **FT-IR (Thin film):** 2229 (w), 1658 (s), 1513 (m), 1250 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.94 (d, *J* = 8.4



Hz, 1H), 7.70 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.49 (s, 2H), 3.76 (s, 3H), 2.84 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.4, 158.6, 155.9, 155.2, 139.6, 134.7 (q, *J* = 33.0 Hz), 128.5, 127.9, 126.9, 123.2 (q, *J* = 273 Hz), 122.0, 119.4 (q, *J* = 3.3 Hz), 114.5, 113.0 (q, *J* = 4.4 Hz), 109.5, 55.3, 46.3, 18.7; **HRMS (ESI+):** Calcd. for $C_{20}H_{15}F_3N_2O_2Na$ ($[M+Na]^+$): 395.0983, Found: 395.0981.

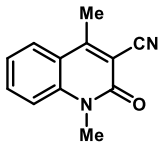
Compound 1i: Compound **1i** was prepared from compound **1j** (prepared following the general procedure B, see below) according to the following scheme:



1j **1i**

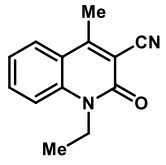
In an oven dried 25 mL round-bottom flask, **1j** (200.0 mg, 1.009 mmol, 1.0 equiv.) was taken in 1.3 mL concentrated H_2SO_4, cooled to 0 °C and stirred for 30 min. When all the **1j** was dissolved to give a pale-yellow solution, KNO_3 (107.0 mg, 1.059 mmol, 1.05 equiv.) was added and the resulting solution was stirred for 4 h. The reaction mixture was poured into ice-cold water to get a white precipitate, which was then filtered through sintered glass crucible and washed with water. The resulting solid was then kept in the crucible with hot EtOH for 10 min. After that, EtOH was removed and dried under high vacuum to yield 2-quinolone **1i** as a light yellow solid (163.0 mg, 0.670 mmol, 66% yield); **m.p.** 273-275 °C; **FT-IR (Thin film):** 2232 (w), 1654 (s), 1604 (s), 1332 (s), 1288 (s), 1084 (m); **^{1}H-NMR (400 MHz, DMSO-d_6):** δ 8.73 (s, 1H), 8.54 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 9.3 Hz, 1H), 3.69 (s, 3H), 2.83 (s, 3H); **^{13}C-NMR (100 MHz, DMSO-d_6):** δ 158.0, 157.3, 143.9, 142.1, 127.7, 123.1, 118.6, 117.3, 114.9, 107.6, 30.5, 18.4; **HRMS (ESI+):** Calcd. for $C_{12}H_9N_3O_3H$ ($[M+H]^+$): 244.0722, Found: 244.0720. The position of NO_2 group was determined by 1D NOE experiment (See Supporting Information: Part B).

Compound 1j: Prepared according to the general procedure B: 2-quinolone **1n** (500.0 mg, 2.714 mmol, 1.0 equiv.) was taken along with NaH (55% assay, 130.0 mg, 2.985 mmol, 1.1 equiv.) in an oven dried round-bottom flask under argon. To this, dry DMF (4.0 mL/mmol of **1n**) was added and the resulting solution was stirred at 0 °C for 30 min. A solution of methyl iodide (0.22 mL, 3.529 mmol, 1.3 equiv.) in dry DMF (1.2 mL/mmol of **1n**) was then added dropwise at 0 °C, warmed to r.t. and stirred for 12 h. The reaction mixture was poured into ice-cold water, stirred for 15 min. The precipitated solid was then filtered, washed with water and dried under high vacuum to yield 2-quinolone **1j** as an off-white solid (432.0 mg, 2.179 mmol, 80% yield); **m.p.** 244-246 °C; **FT-IR (Thin film):** 2225 (m), 1648 (s), 1557 (m), 1454 (m), 1090 (w); **^{1}H-NMR (400 MHz, DMSO-d_6):** δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.82-7.78 (m, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 3.63 (s, 3H),

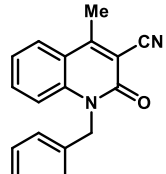


2.72 (s, 3H); **^{13}C-NMR (100 MHz, DMSO-d_6):** δ 157.9, 157.1, 139.8, 134.1, 127.2, 122.9, 118.8, 115.6, 105.5, 29.7, 18.1; **HRMS (ESI+):** Calcd. for $C_{12}H_{10}N_2OH$ ($[M+H]^+$): 199.0871, Found: 199.0873.

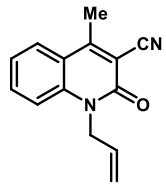
Compound 1k: Prepared according to the general procedure B, 2-quinolone **1n** (500.0 mg, 2.714 mmol, 1.0 equiv.), ethyl iodide (0.24 mL, 2.985 mmol, 1.1 equiv.), NaH (55% assay, 85.0 mg, 3.523 mmol, 1.3 equiv.), reaction time 12 h, purified by silica-gel flash column chromatography (5-6% EtOAc in CH_2Cl_2); yellow solid (117.0 mg, 0.551 mmol, 20% yield); **m.p.** 228-230 °C; **FT-IR (Thin film):** 2220 (m), 1644 (s), 1454 (m), 1199 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.73-7.69 (m, 1H), 7.42 (d, *J* = 8.6 Hz, 1H), 7.35-7.31 (m, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.76 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.2, 156.1, 139.3, 133.9, 127.0, 123.0, 119.8, 115.2, 114.9, 107.2, 38.0, 18.4, 12.7; **HRMS (ESI+):** Calcd. for $C_{13}H_{12}N_2OH$ ($[M+H]^+$): 213.1028, Found: 213.1029.



Compound 1l: Prepared according to the general procedure B, 2-quinolone **1n** (500.0 mg, 2.714 mmol, 1.0 equiv.), benzyl bromide (0.34 mL, 2.845 mmol, 1.05 equiv.), NaH (55% assay, 85.0 mg, 3.523 mmol, 1.3 equiv.), reaction time 12 h, purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); off-white solid (273.0 mg, 0.995 mmol, 37% yield); **m.p.** 198-200 °C; **FT-IR (Thin film):** 2226 (w), 1648 (s), 1559 (w), 1452 (m), 1316 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.57-7.53 (m, 1H), 7.34-7.26 (m, 4H), 7.23-7.20 (m, 3H), 5.53 (s, 2H), 2.79 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.9, 156.8, 139.6, 135.5, 133.9, 128.9, 127.6, 126.8, 126.7, 123.3, 119.8, 115.9, 115.1, 107.1, 46.5, 18.5; **HRMS (ESI+):** Calcd. for $C_{18}H_{14}N_2OH$ ($[M+H]^+$): 275.1184, Found: 275.1181.

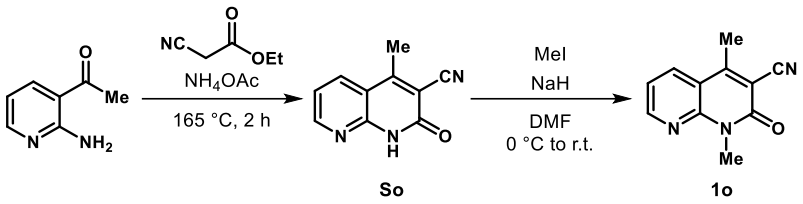


Compound 1m: Prepared according to the general procedure B, 2-quinolone **1n** (500.0 mg, 2.714 mmol, 1.0 equiv.), allyl bromide (0.25 mL, 2.845 mmol, 1.05 equiv.), NaH (55% assay, 85.0 mg, 3.523 mmol, 1.3 equiv.), reaction time 12 h, purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); off-white solid (129.0 mg, 0.575 mmol, 21% yield); **m.p.** 185-187 °C; **FT-IR (Thin film):** 2217 (m), 1641 (s), 1445 (m), 1187 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.83 (d, *J* = 8.1 Hz, 1H), 7.69-7.65 (m, 1H), 7.39-7.32 (m, 2H), 5.96-5.87 (m, 1H), 5.24 (d, *J* = 10.4 Hz, 1H), 5.12 (d, *J* = 17.3 Hz, 1H), 4.95-4.94 (m, 2H), 2.79 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.4, 156.6, 139.6, 133.8, 131.0, 126.8, 123.2, 119.7, 117.9, 115.7, 115.1, 107.2, 45.2, 18.5; **HRMS (ESI+):** Calcd. for $C_{14}H_{12}N_2OH$ ($[M+H]^+$): 225.1028, Found: 225.1027.



Compound 1n: Prepared according to the general procedure B, 2′-aminoacetophenone (4.0 mL, 32.907 mmol, 1.0 equiv.), NH_4OAc (6.34 g, 82.500 mmol, 2.5 equiv.), 2-cyanoacetate (5.3 mL, 49.400 mmol, 1.5 equiv.), reaction time 2 h, off-white solid (2.6 g, 14.115 mmol, 43% yield); **m.p.** 328-330 °C; **FT-IR (Thin film):** 2219 (m), 1591 (s), 1425 (m), 749 (s); **^{1}H-NMR (400 MHz, DMSO-d_6):** δ 10.91 (bs, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.35-7.27 (m, 2H), 2.70 (s, 3H); **^{13}C-NMR (100 MHz, DMSO-d_6):** δ 158.6, 158.5, 139.1, 133.7, 126.5, 122.8, 118.0, 116.1, 115.6, 105.9, 18.2; **HRMS (ESI+):** Calcd. for $C_{11}H_8N_2OH$ ($[M+H]^+$): 185.0715, Found: 185.0716.

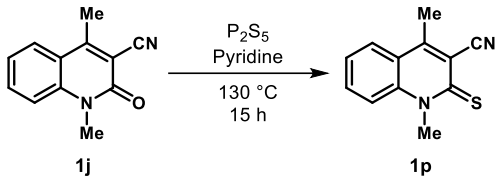
Compound 1o: Prepared according to the following scheme:



In an oven dried round-bottom flask, equipped with reflux condenser, 2-amino-3-acetylpyridine (500.0 mg, 3.670 mmol, 1.0 equiv.) was taken along with NH_4OAc (708.0 mg, 9.180 mmol, 2.5 equiv.) under air. To this, ethyl 2-cyanoacetate (0.59 mL, 5.510 mmol, 1.5 equiv.) was added and the resulting solution was heated to165 °C for 2 h. The mixture was then cooled to r.t., EtOH (0.8 mL/mmol of 2-amino-3-acetylpyridine) was added and the mixture was triturated for 6 h. The precipitated solid was then filtered, washed with petroleum ether and dried under high vacuum to yield **So** as an off-white solid (472.0 mg, 2.549 mmol, 69% yield), which was used for the next step without further purification.

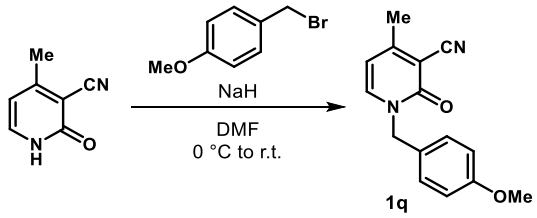
So (254.0 mg, 1.372 mmol, 1.0 equiv.) was taken along with NaH (55% assay, 66.0 mg, 1.510 mmol, 1.1 equiv.) in an oven dried round-bottom flask under argon. To this, dry DMF (4.0 mL/mmol of **So**) was added and the resulting solution was stirred at 0 °C for 30 min. A solution of methyl iodide (0.11 mL, 1.783 mmol, 1.3 equiv.) in dry DMF (1.2 mL/mmol of **So**) was the added dropwise at 0 °C, warmed to r.t. and stirred for 12-24 h. The reaction mixture was then poured into ice-cold water and stirred for 15 min. The precipitated solid was then filtered, washed with water and dried under high vacuum to yield **1o** as an off-white solid (185.0 mg, 0.929 mmol, 68% yield); **m.p.** 203-205 °C; **FT-IR (Thin film):** 2226 (w), 1648 (s), 1590 (m), 1450 (m), 1049 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.73 (d, *J* = 3.3 Hz, 1H), 8.12 (d, *J* = 6.8 Hz, 1H), 7.30 (dd, *J* = 4.6, 7.9 Hz, 1H), 3.85 (s, 3H), 2.78 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.4, 155.0, 153.0, 149.8, 135.1, 119.0, 114.9, 114.6, 108.3, 29.0, 17.7; **HRMS (ESI+):** Calcd. for $C_{11}H_9N_3OH$ ($[M+H]^+$): 200.0824, Found: 200.0824.

Compound 1p: Compound **1p** was prepared from compound **1j** according to the following scheme:



In an oven dried 25 mL round-bottom flask, **1j** (205.0 mg, 1.034 mmol, 1.0 equiv.) was taken along with P_2S_5 (690.0 mg, 3.102 mmol, 3.0 equiv.) under argon. To this, 5.0 mL pyridine was added and the resulting solution was refluxed at 130 °C for 15 h. The reaction mixture was then diluted with 5.0 mL water, quenched with 2.0 mL concentrated HCl and extracted with EtOAc. Combined organic layer was dried over anh. Na_2SO_4 and concentrated under reduced pressure to obtain a yellow oil. This residue was purified by silica-gel flash column chromatography (2% EtOAc in CH_2Cl_2) to obtain **1p** as a yellow solid (89.0 mg, 0.415 mmol, 40% yield); **m.p.** 275-277 °C; **FT-IR (Thin film):** 2223 (w), 1595 (s), 1547 (s), 1445 (m), 1218 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.90-7.88 (m, 1H), 7.80-7.76 (m, 1H), 7.61 (d, *J* = 8.7 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 4.30 (s, 3H), 2.81 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 180.8, 149.4, 140.9, 134.3, 126.9, 124.9, 122.9, 118.7, 116.4, 116.1, 38.7, 18.6; **HRMS (ESI+):** Calcd. for $C_{12}H_{10}N_2SH$ ($[M+H]^+$): 215.0643, Found: 215.0643.

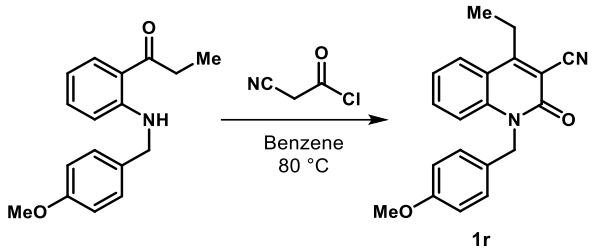
Compound 1q: Prepared according to the following scheme:



3-Cyano-4-methyl-2-pyridone (500.0 mg, 3.720 mmol, 1.0 equiv.) was taken along with NaH (55% assay, 211.0 mg, 4.840 mmol, 1.3 equiv.) in an oven dried round-bottom flask under argon. To this, dry DMF (4 mL/mmol of 3-cyano-4-methyl-2-pyridone) was added and the resulting solution was stirred at 0 °C for 30 min. A solution of 4-methoxybenzyl bromide (825.0 mg, 4.100 mmol, 1.1 equiv.) in dry DMF (1.2 mL/mmol of 3-cyano-4-methyl-2-pyridone) was then added dropwise at 0 °C, warmed to r.t. and stirred for 12 h. The reaction mixture was poured into ice-cold water, stirred for 15 min and extracted with EtOAc. Combined organic layer was washed with water, dried over anh. Na_2SO_4 and concentrated under reduced pressure to obtain a brown oil. This residue was purified by silica-gel flash column chromatography (2% EtOAc in CH_2Cl_2) yield **1q** as a peach colored solid (518.0 mg, 2.037 mmol, 55% yield); **m.p.** 133-135 °C; **FT-IR (Thin film):** 2223 (w), 1654 (s), 1514 (s), 1250 (m), 1031 (m); **^{1}H-NMR**

(400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 6.4 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 2H), 6.86 (d, *J* = 7.4 Hz, 2H), 6.15 (d, *J* = 6.8 Hz, 1H), 5.05 (s, 2H), 3.78 (s, 3H), 2.40 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 160.1, 159.7, 159.5, 140.5, 130.1, 127.2, 115.2, 114.4, 108.4, 104.5, 55.3, 52.0, 21.0; **HRMS (ESI+):** Calcd. for $C_{15}H_{14}N_2O_2Na$ ($[M+Na]^+$): 277.0953, Found: 277.0951.

Compound 1r (3-cyano-4-ethyl-2-quinolone): Prepared according to the general procedure A:



1r

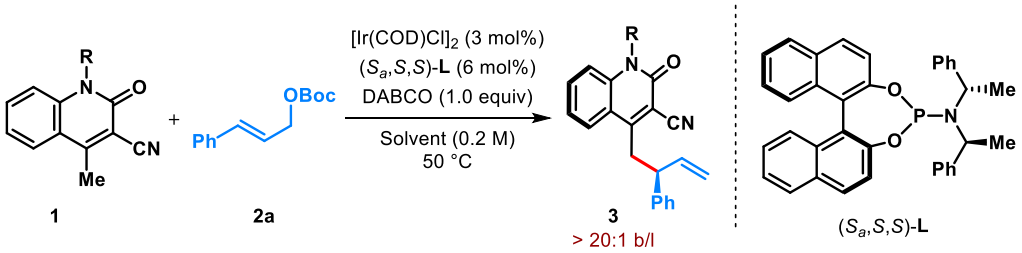
1-(2-((4-Methoxybenzyl)amino)phenyl)propan-1-one (350.0 mg, 1.299 mmol, 1.0 equiv.), reaction time 12 h, purified by silica-gel flash column chromatography (2-3% EtOAc in CH_2Cl_2); light yellow sticky solid (403.0 mg, 1.266 mmol, 97% yield); **m.p.** 159-161 °C; **FT-IR (Thin film):** 2926 (m), 2226 (m), 1648 (s), 1511 (m), 1249 (m), 1179 (m), 1034 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.84 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.60-7.56 (m, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.32-7.28 (m, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.48 (s, 2H), 3.75 (s, 3H), 3.19 (q, *J* = 7.6 Hz, 2H), 1.41 (t, *J* = 7.6 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 162.5, 159.2, 159.1, 140.3, 133.8, 128.3, 127.6, 126.7, 123.2, 118.7, 116.2, 114.9, 114.4, 106.2, 55.4, 46.1, 25.5, 14.5; **HRMS (ESI+):** Calcd. for $C_{20}H_{18}N_2O_2Na$ ($[M+Na]^+$): 341.1266, Found: 341.1266.

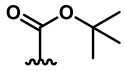
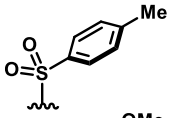
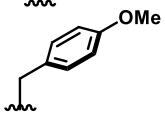
D. Procedure for the synthesis of allyl carbonates:

Allyl carbonates (**2a-t**) were prepared according to the previously reported procedure.[4]

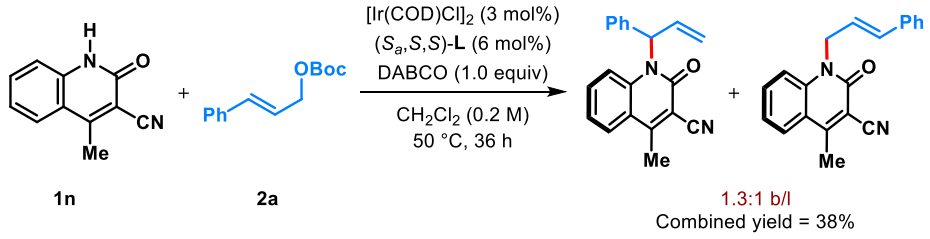
[4] a) Stanley, L. M.; Hartwig, J. F. Iridium-Catalyzed Regio- and Enantioselective N-Allylation of Indoles. *Angew. Chem. Int. Ed*. **2009**, *48*, 7841; b) Weix, D. J.; Marković, D.; Ueda, M.; Hartwig, J. F. Direct, Intermolecular, Enantioselective, Iridium-Catalyzed Allylation of Carbamates to Form Carbamate-Protected, Branched Allylic Amines. *Org. Lett.* **2009**, *11*, 2944-2947; c) Štambaský, J.; Malkov, A. V.; Kočovský, P. Synthesis of Enantiopure 1-Arylprop-2-en-1-ols and Their *tert*-Butyl Carbonates. *J. Org. Chem.* **2008**, *73*, 9148-9150.

E. Preliminary screening of *N*-protecting group of 4-methylquinolones:[a]

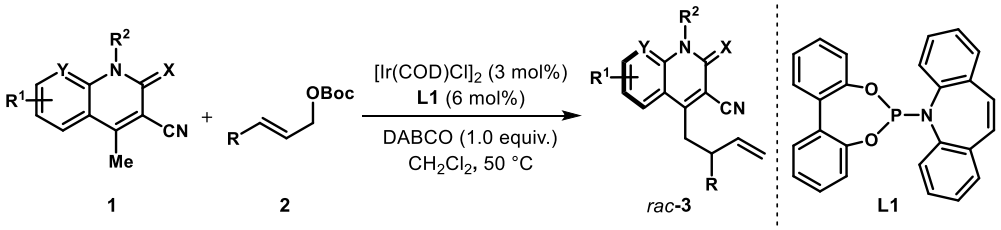


Entry	R	Solvent	*t* [h]	Yield [%]	er
1[b]	H	CH_2Cl_2	36	<5	n.d.
2		CH_2Cl_2	36	<5	n.d.
3		CH_2Cl_2	36	24	n.d.
4		$(CH_2Cl_2)_2$	72	35	98:2

[a] Reaction conditions: 3 mol% $[Ir(COD)Cl]_2$, 6 mol% **L**, 0.20 mmol of **1**, 0.24 mmol of **2a** and 0.2 mmol of DABCO in 1.0 mL solvent. The catalyst was prepared via *n*-$PrNH_2$ activation. Yields correspond to the isolated product after chromatographic purification. Er was determined by HPLC analysis on a chiral stationary phase. [b] For *N*-unprotected 2-quinolone (**1n**), *N*-allyl 2-quinolone was formed as 1.3:1 b/l and with 38% yield. n.d. = not determined.



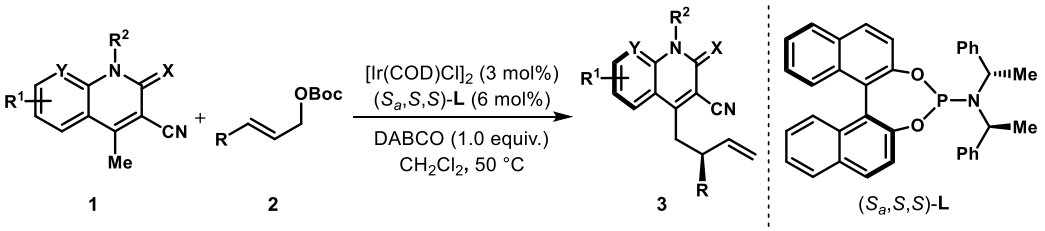
F. General procedure for the preparation of racemic products (*rac*-3):



In a glass-vial $[Ir(COD)Cl]_2$ (0.003 mmol, 3 mol%) and ligand **L1** (0.012 mmol, 12 mol%) were taken with 0.3 mL of CH_2Cl_2, and the resulting solution was stirred at r.t. for 15 min. To this, was added **1** (0.100 mmol, 1.0 equiv.) followed by addition of **2** (0.120 mmol, 1.2

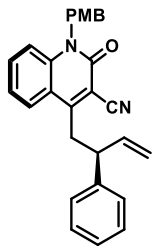
equiv.) in 0.2 mL CH_2Cl_2. The resulting suspension was stirred at 50 °C for 48 h. The crude mixture was purified by preparative TLC (Merck silica-gel 60 F_{254} pre-coated plates of 0.25 mm thickness) to obtain the racemic γ-allylated product (*rac*-**3**) samples for HPLC analysis.

G. Typical procedure for Ir-catalyzed enantioselective allylation of 4-methylquinolones with allyl carbonates:



In an oven and vacuum-dried reaction tube, $[Ir(COD)Cl]_2$ (0.006 mmol, 3 mol%) and ligand (*Sa*,*S*,*S*)-**L** (0.012 mmol, 6 mol%) were taken with 0.5 mL of absolute THF under positive argon pressure, followed by the addition of 0.3 mL dry *n*-$PrNH_2$. The solution was heated at 50 °C for 30 min, after which all volatiles were removed under vacuum to obtain a yellow solid. To this, 4-methylquinolones **1** (0.200 mmol, 1.0 equiv.) and DABCO (22.4 mg, 0.200 mmol, 1.0 equiv.) were introduced under positive argon pressure, followed by 0.8 mL of absolute CH_2Cl_2 and the suspension was stirred at 50 °C for 5 min. After 5 min, a solution of allyl carbonate **2** (0.240 mmol, 1.2 equiv.) in 0.2 mL absolute CH_2Cl_2 was added to it. The resulting mixture was purged with argon and the reaction tube was sealed with a glass stopper. The reaction mixture was stirred at 50 °C until TLC (30% EtOAc in petroleum ether) revealed complete consumption of **1**. The reaction mixture was then allowed to attain ambient temperature, diluted with 2.0 mL of CH_2Cl_2 and 5.0 mL of 1 N HCl solution. Organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 4.0 mL). Combined organic layer was washed with brine (10.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure to obtain a reddish-brown oil. This residue was purified by silica-gel flash column chromatography (13-15% EtOAc in petroleum ether) to obtain **3**.

Compound 3aa: Reaction performed on 0.1 mmol scale of **1a**; purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (38.0 mg, 0.090 mmol, 90% yield); **m.p.** 175-177 °C; **FT-IR (Thin film):** 3015 (w), 2227 (m), 1649 (s), 1607 (s), 1509 (s), 1452 (m), 1305 (m), 1249 (s); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.60-7.56 (m, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.34-7.29 (m, 3H), 7.29-7.26 (m, 3H), 7.14 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.22-6.14 (m, 1H), 5.53 (d, *J* = 12.9 Hz, 1H), 5.43 (d, *J* = 14.6 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 4.96 (d, *J* = 16.9 Hz, 1H), 3.77 (s, 3H), 3.77-3.73 (m, 1H), 3.62 (dd, *J* = 12.9, 8.3 Hz, 1H), 3.54 (dd, *J* = 12.9, 6.6 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ



159.1, 158.9, 158.2, 141.9, 140.0, 139.1, 133.7, 128.9, 128.1, 127.5, 127.3, 126.8, 123.2, 119.1, 116.4, 116.2, 115.3, 114.4, 107.9, 55.3, 50.8, 46.0, 38.4; **HRMS (ESI+):** Calcd. for $C_{28}H_{24}N_2O_2Na$ ($[M+Na]^+$): 443.1735, Found: 443.1736; **Optical rotation:** $[\alpha]_D^{23}$ –115.3 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{minor} = 17.4 min, τ_{major} = 22.6 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3aa** was assigned in analogy with **3af**.

Compound 3ab: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (71.0 mg, 0.163 mmol, 82% yield); **m.p.** 167-169 °C; **FT-IR (Thin film):** 2927 (w), 2226 (m), 1649 (s), 1608 (m), 1510 (m), 1451 (m), 1249 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.60-7.56 (m, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.31-7.27 (m, 1H), 7.13 (s, 6H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.20-6.11 (m, 1H), 5.53 (d, *J* = 13.7 Hz, 1H), 5.44 (d, *J* = 13.4 Hz, 1H), 5.05 (d, *J* = 10.0 Hz, 1H), 4.94 (d, *J* = 17.1 Hz, 1H), 3.76 (s, 3H), 3.74-3.70 (m, 1H), 3.63-3.57 (m, 1H), 3.54-3.50 (m, 1H), 2.33 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 158.3, 140.0, 139.4, 138.9, 136.9, 133.7, 129.6, 128.2, 127.5, 127.3, 126.8, 123.1, 119.1, 116.2, 116.1, 115.4, 114.4, 107.9, 55.4, 50.6, 46.0, 38.5, 21.1; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_2Na$ ($[M+Na]^+$): 457.1892, Found: 457.1896; **Optical rotation:** $[\alpha]_D^{23}$ –35.8 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 240 nm, τ_{minor} = 16.1 min, τ_{major} = 19.5 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ab** was assigned in analogy with **3af**.

Compound 3ac: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (84.0 mg, 0.182 mmol, 91% yield); **m.p.** 162-164 °C; **FT-IR (Thin film):** 2960 (m), 2227 (m), 1650 (s), 1511 (s), 1453 (s), 1378 (m), 1249 (s), 1180 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.59-7.55 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.29-7.25 (m, 1H), 7.19 (s, 4H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.21-6.13 (m, 1H), 5.54 (d, *J* = 14.0 Hz, 1H), 5.44 (d, *J* = 14.0 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.93 (d, *J* = 17.0 Hz, 1H), 3.76 (s, 3H), 3.76-3.71 (m, 1H), 3.63-3.57 (m, 1H), 3.55-3.50 (m, 1H), 2.92-2.85 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 6H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 158.4, 147.9, 139.9, 139.4, 139.2, 133.6, 128.1, 127.5, 127.3, 126.9, 126.8, 123.1, 119.1, 116.2, 115.4, 114.4, 107.8, 55.3, 50.6, 46.0, 38.5, 33.8, 24.1; **HRMS (ESI+):** Calcd. for $C_{31}H_{30}N_2O_2H$ ($[M+H]^+$): 463.2386, Found: 463.2386; **Optical rotation:** $[\alpha]_D^{22}$ –34.8 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC

analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/*i*-PrOH, 1.0 mL/min, 20 °C, 234 nm, τ_{major} = 18.1 min, τ_{minor} = 22.9 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ac** was assigned in analogy with **3af**.

Compound 3ad: Purified by silica-gel flash column chromatography (18% EtOAc in petroleum ether); Off-white solid (88.0 mg, 0.195 mmol, 98% yield); **m.p.** 156-158 °C; **FT-IR (Thin film):** 2837 (w), 2226 (m), 1649 (s), 1510 (s), 1453 (s), 1250 (s), 1179 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.59-7.55 (m, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.30-7.26 (m, 1H), 7.15-7.11 (m, 4H), 6.84-6.82 (m, 4H), 6.18-6.09 (m, 1H), 5.51 (d, *J* = 13.1 Hz, 1H), 5.42 (d, *J* = 14.4 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.94 (d, *J* = 16.9 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.71-3.66 (m, 1H), 3.60-3.55 (m, 1H), 3.52-3.47 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 158.7, 158.3, 139.9, 139.5, 133.8, 133.7, 128.5, 128.1, 127.5, 126.8, 123.1, 119.1, 116.2, 115.9, 115.4, 114.4, 114.2, 107.9, 55.3, 50.0, 46.0, 38.5; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_3Na$ ($[M+Na]^+$): 473.1841, Found: 473.1844; **Optical rotation:** $[\alpha]_D^{23}$ –46.3 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 350 nm, τ_{minor} = 23.7 min, τ_{major} = 32.4 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ad** was assigned in analogy with **3af**.

Compound 3ae: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (55.0 mg, 0.113 mmol, 56% yield); **m.p.** 186-188 °C; **FT-IR (Thin film):** 2227 (w), 1650 (s), 1610 (m), 1325 (s), 1121 (m), 1068 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.61-7.56 (m, 3H), 7.42-7.37 (m, 3H), 7.31-7.27 (m, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 6.15 (ddd, *J* = 17.2, 10.1, 8.1 Hz, 1H), 5.53 (d, *J* = 14.9 Hz, 1H), 5.43 (d, *J* = 15.3 Hz, 1H), 5.12 (d, *J* = 10.1 Hz, 1H), 4.99 (d, *J* = 16.9 Hz, 1H), 3.84 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.76 (m, 3H), 3.63 (dd, *J* = 13.2, 8.7 Hz, 1H), 3.54 (dd, *J* = 13.2, 6.8 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.8, 157.6, 145.9, 140.1, 138.2, 133.9, 129.6 (q, *J* = 32.0 Hz), 128.2, 128.0, 127.4, 126.6, 125.9 (q, *J* = 4.1 Hz), 124.1 (q, *J* = 272.2 Hz), 123.2, 118.9, 117.4, 116.4, 115.3, 114.4, 108.1, 55.4, 50.6, 46.1, 38.0; **HRMS (ESI+):** Calcd. for $C_{29}H_{23}F_3N_2O_2H$ ($[M+H]^+$): 489.1790, Found: 489.1797; **Optical rotation:** $[\alpha]_D^{22}$ –35.8 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IE column (85:15 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 305 nm, τ_{major} = 38.4 min, τ_{minor} = 41.2 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ae** was assigned in analogy with **3af**.

Compound 3af: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (98.0 mg, 0.196 mmol, 98% yield); **m.p.** 176-178 °C; **FT-IR (Thin film):** 2226 (w), 1647 (s), 1608 (m), 1554 (m), 1248 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.61-7.57 (m, 1H), 7.42-7.41 (m, 3H), 7.32-7.28 (m, 1H), 7.13-7.09 (m, 4H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.16-6.07 (m, 1H), 5.52 (d, *J* = 14.8 Hz, 1H), 5.41 (d, *J* = 13.4 Hz, 1H), 5.09 (d, *J* = 10.1 Hz, 1H), 4.97 (d, *J* = 17.1 Hz, 1H), 3.75 (s, 3H), 3.75-3.72 (m, 1H), 3.61-3.56 (m, 1H), 3.50 (dd, *J* = 13.1, 6.9 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.8, 157.8, 140.8, 140.0, 138.6, 133.8, 131.9, 129.3, 128.1, 127.4, 126.6, 123.2, 121.1, 118.9, 116.8, 116.3, 115.3, 114.4, 108.0, 55.3, 50.1, 46.0, 38.1; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}BrN_2O_2Na$ ([M+Na]$^+$): 521.0841, Found: 521.0844; **Optical rotation:** $[\alpha]_D^{21}$ –48.4 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 290 nm, τ_{minor} = 19.4 min, τ_{major} = 23.3 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3af** was determined by single crystal X-Ray diffraction analysis.

Compound 3ag: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (80.0 mg, 0.176 mmol, 88% yield); **m.p.** 170-171 °C; **FT-IR (Thin film):** 3010 (w), 2226 (m), 1649 (s), 1509 (m), 1452 (m), 1249 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 8.2 Hz, 1H), 7.60-7.56 (m, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.30-7.26 (m, 3H), 7.17-7.11 (m, 4H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.16-6.07 (m, 1H), 5.53 (d, *J* = 14.5 Hz, 1H), 5.42 (d, *J* = 14.5 Hz, 1H), 5.09 (d, *J* = 10.1 Hz, 1H), 4.97 (d, *J* = 17.0 Hz, 1H), 3.76 (s, 3H), 3.76-3.72 (m, 1H), 3.61-3.56 (m, 1H), 3.50 (dd, *J* = 13.0, 6.9 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.8, 157.8, 140.3, 140.0, 138.7, 133.8, 133.1, 129.1, 128.9, 128.2, 127.4, 126.7, 123.2, 119.0, 116.8, 116.3, 115.3, 114.4, 108.1, 55.4, 50.1, 46.1, 38.2; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}ClN_2O_2Na$ ([M+Na]$^+$): 477.1346, Found: 477.1342; **Optical rotation:** $[\alpha]_D^{22}$ –52.6 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 240 nm, τ_{minor} = 17.1 min, τ_{major} = 22.3 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ag** was assigned in analogy with **3af**.

Compound 3ah: Purified by silica-gel flash column chromatography (10% EtOAc in petroleum ether); Off-white solid (70.0 mg, 0.140 mmol, 70% yield); **m.p.** 155-157 °C; **FT-IR (Thin film):** 2226 (m), 1648 (s), 1609 (s), 1513 (s), 1452 (m), 1249 (m), 1070 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.60-7.56 (m, 1H), 7.40-7.35 (m, 3H), 7.31-7.27 (m, 1H), 7.21-7.17 (m, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.16-6.07 (m, 1H), 5.53 (d, *J* = 14.5 Hz, 1H), 5.44 (d, *J* = 14.7 Hz, 1H), 5.10 (d, *J* = 10.1 Hz, 1H), 4.97 (d, *J* = 16.8 Hz, 1H), 3.76 (m, 3H), 3.76-3.70 (m, 1H), 3.61-3.56 (m, 1H), 3.51 (dd, *J* = 13.0, 6.7 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.8, 157.7, 144.1, 140.1, 138.3, 133.8, 130.6, 130.5, 130.4, 128.1, 127.4, 126.6, 126.2, 123.2, 122.9, 118.9, 117.1, 116.3, 115.3, 114.4, 108.1, 55.4, 50.4, 46.1, 38.0; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}BrN_2O_2Na$ ($[M+Na]^+$): 521.0841, Found: 521.0839; **Optical rotation:** $[\alpha]_D^{23}$ –29.4 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{minor} = 17.7 min, τ_{major} = 20.7 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ah** was assigned in analogy with **3af**.

Compound 3ai: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (42.0 mg, 0.096 mmol, 48% yield); **m.p.** 157-159 °C; **FT-IR (Thin film):** 2839 (w), 2227 (m), 1649 (s), 1511 (s), 1249 (s), 1032 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.60-7.56 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.31-7.27 (m, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.95-6.91 (m, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.14 (ddd, *J* = 17.3, 10.0, 8.7 Hz, 1H), 5.53 (d, *J* = 15.0 Hz, 1H), 5.43 (d, *J* = 14.8 Hz, 1H), 5.11 (d, *J* = 10.2 Hz, 1H), 4.98 (d, *J* = 16.9 Hz, 1H), 3.76 (m, 3H), 3.76-3.73 (m, 1H), 3.59 (dd, *J* = 13.1, 8.5 Hz, 1H), 3.52 (dd, *J* = 13.1, 6.8 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 163.0 (d, *J* = 246.0 Hz), 159.2, 158.8, 157.8, 144.3 (d, *J* = 6.7 Hz), 140.1, 138.5, 133.8, 130.5 (d, *J* = 8.3 Hz), 128.1, 127.4, 126.6, 123.2, 123.1 (d, *J* = 2.8 Hz), 119.0, 117.0, 116.3, 115.3, 114.6 (d, *J* = 21.0 Hz), 114.5, 114.3 (d, *J* = 21.1 Hz), 108.1, 55.4, 50.4, 46.1, 38.1; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}FN_2O_2H$ ($[M+H]^+$): 439.1822, Found: 439.1826; **Optical rotation:** $[\alpha]_D^{23}$ –40.3 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 231 nm, τ_{minor} = 16.8 min, τ_{major} = 23.1 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ai** was assigned in analogy with **3af**.

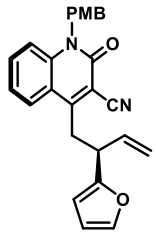
Compound 3aj: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (92.0 mg, 0.196 mmol, 98% yield); **m.p.** 164-166 °C; **FT-IR (Thin film):** 2927 (w), 2361 (s), 2225 (m), 1648 (s), 1607 (m), 1555 (m), 1248 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.87-7.81 (m, 3H), 7.79-7.77 (m, 1H), 7.66 (s, 1H), 7.59-7.55 (m, 1H), 7.47-7.44 (m, 3H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.29-6.20 (m, 1H), 5.52 (d, *J* = 15.1 Hz, 1H), 5.42 (d, *J* = 14.7 Hz, 1H), 5.11 (d, *J* = 10.1 Hz, 1H), 4.98 (d, *J* = 16.9 Hz, 1H), 3.97-3.91 (m, 1H), 3.77 (m, 3H), 3.74-3.71 (m, 1H), 3.68-3.64 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.0, 158.8, 158.2, 139.9, 139.3, 139.0, 133.7, 133.5, 132.6, 128.7, 128.1, 127.7, 127.4, 126.7, 126.3, 125.9, 125.7, 123.2, 119.0, 116.7, 116.2, 115.4, 114.3, 107.9, 55.3, 51.0, 46.0, 38.2; **HRMS (ESI+):** Calcd. for $C_{32}H_{26}N_2O_2Na$ ($[M+Na]^+$): 493.1892, Found: 493.1894; **Optical rotation:** $[\alpha]_D^{22}$ –25.8 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 231 nm, τ_{minor} = 22.3 min, τ_{major} = 26.7 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3aj** was assigned in analogy with **3af**.

Compound 3ak: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (77.0 mg, 0.157 mmol, 79% yield); **m.p.** 146-148 °C; **FT-IR (Thin film):** 2926 (w), 2360 (m), 2226 (m), 1649 (s), 1606 (m), 1555 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 8.2 Hz, 1H), 7.61-7.57 (m, 1H), 7.42-7.37 (m, 2H), 7.32-7.29 (m, 2H), 7.17-7.11 (m, 3H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.08 (ddd, *J* = 17.2, 10.0, 8.1 Hz, 1H), 5.52 (d, *J* = 14.8 Hz, 1H), 5.43 (d, *J* = 14.3 Hz, 1H), 5.12 (d, *J* = 10.2 Hz, 1H), 4.98 (d, *J* = 16.8 Hz, 1H), 3.75 (m, 3H), 3.75-3.70 (m, 1H), 3.57 (dd, *J* = 13.1, 8.7 Hz, 1H), 3.49 (dd, *J* = 13.1, 6.9 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.7, 157.4, 142.0, 140.1, 138.0, 133.9, 132.8, 131.4, 130.9, 129.6, 128.1, 127.3, 126.9, 126.5, 123.3, 118.9, 117.4, 116.4, 115.3, 114.4, 108.1, 55.4, 49.8, 46.1, 37.9; **HRMS (ESI+):** Calcd. for $C_{28}H_{22}Cl_2N_2O_2Na$ ($[M+Na]^+$): 511.0956, Found: 511.0959; **Optical rotation:** $[\alpha]_D^{23}$ –38.5 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{minor} = 17.4 min, τ_{major} = 22.1 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ak** was assigned in analogy with **3af**.

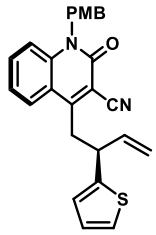
Compound 3al: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Light yellow solid (91.0 mg, 0.196 mmol, 98% yield); **m.p.** 133-135 °C; **FT-IR (Thin film):** 2226 (m), 1648 (s), 1508 (s), 1492 (s), 1247 (s), 1036 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.59-7.56 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.31-7.27 (m, 1H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 8.3 Hz, 2H), 6.73-6.69 (m, 2H), 6.64-6.63 (m, 1H), 6.16-6.07 (m, 1H), 5.90-5.89 (m, 2H), 5.50 (d, *J* = 11.8 Hz, 1H), 5.43 (d, *J* = 11.6 Hz, 1H), 5.06 (d, *J* = 10.1 Hz, 1H), 4.96 (d, *J* = 16.9 Hz, 1H), 3.74 (s, 3H), 3.71-3.65 (m, 1H), 3.58-3.53 (m, 1H), 3.47 (dd, *J* = 12.8, 6.9 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.0, 158.8, 158.1, 147.9, 146.6, 139.9, 139.2, 135.6, 133.7, 128.1, 127.4, 126.7, 123.1, 120.5, 118.9, 116.2, 116.1, 115.3, 114.3, 108.4, 107.8, 101.1, 55.3, 50.3, 45.9, 38.4; **HRMS (ESI+):** Calcd. for $C_{29}H_{24}N_2O_4Na$ ($[M+Na]^+$): 487.1634, Found: 487.1634; **Optical rotation:** $[\alpha]_D^{22}$ –60.5 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. To determine the enantiomeric ratio, compound **3al** was converted to the corresponding hydrogenated compound **3al´** by using catalytic Pd/C under H_2 balloon pressure. The enantiomeric ratio of compound **3al´** was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 380 nm, τ_{minor} = 28.5 min, τ_{major} = 31.0 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3al** was assigned in analogy with **3af**.

Compound 3am: Purified by silica-gel flash column chromatography (10% EtOAc in dichloromethane); Off-white solid (58.0 mg, 0.138 mmol, 69% yield); **m.p.** 176-178 °C; **FT-IR (Thin film):**, 2922 (w), 2226 (m), 1647 (s), 1510 (m), 1249 (w), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.48 (s, 1H), 8.37 (s, 1H), 7.77 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.59-7.55 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.31-7.26 (m, 2H), 7.11 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 6.13 (ddd, *J* = 17.3, 10.1, 7.9 Hz, 1H), 5.45 (s, 2H), 5.13 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 16.9 Hz, 1H), 3.83-3.78 (m, 1H), 3.72 (s, 3H), 3.61 (dd, *J* = 13.3, 8.5 Hz, 1H), 3.51 (dd, *J* = 13.3, 7.2 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.0, 158.7, 157.4, 149.0, 148.8, 140.0, 138.0, 137.1, 135.0, 133.9, 128.1, 127.2, 126.5, 123.9, 123.3, 118.7, 117.3, 116.3, 115.3, 114.3, 107.9, 55.3, 47.9, 46.1, 37.8; **HRMS (ESI+):** Calcd. for $C_{27}H_{23}N_3O_2H$ ($[M+H]^+$): 422.1869, Found: 422.1866; **Optical rotation:** $[\alpha]_D^{21}$ –13.9 (*c* 2.0, $CHCl_3$). The absolute stereochemistry of the product **3am** was assigned in analogy with **3af**.

Compound 3an: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (74.0 mg, 0.180 mmol, 90% yield); **m.p.** 147-148 °C; **FT-IR (Thin film):** 2227 (m), 1648 (s), 1606 (m), 1510 (m), 1249 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.82 (d, *J* = 8.1 Hz, 1H), 7.59-7.55 (m, 1H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.35 (s, 1H), 7.30-7.28 (m, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 6.28 (s, 1H), 6.13-6.04 (m, 2H), 5.51 (d, *J* = 14.7 Hz, 1H), 5.45 (d, *J* = 14.5 Hz, 1H), 5.14 (d, *J* = 9.9 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 3.88-3.82 (m, 1H), 3.75 (s, 3H), 3.71-3.68 (m, 1H), 3.46 (dd, *J* = 12.9, 8.6 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 157.6, 154.4, 141.9, 140.0, 136.1, 133.7, 128.2, 127.5, 126.7, 123.2, 119.0, 117.9, 116.2, 115.1, 114.4, 110.5, 108.1, 106.2, 55.3, 46.1, 44.5, 36.3; **HRMS (ESI+):** Calcd. for $C_{26}H_{22}N_2O_3Na$ ([M+Na]$^+$): 433.1528, Found: 433.1530; **Optical rotation:** $[\alpha]_D^{22}$ –20.4 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98.5:1.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{minor} = 36.2 min, τ_{major} = 38.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3an** was assigned in analogy with **3af**.



Compound 3ao: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Light yellow solid (67.0 mg, 0.157 mmol, 79% yield); **m.p.** 172-174 °C; **FT-IR (Thin film):** 2928 (w), 2226 (m), 1649 (s), 1608 (m), 1555 (m), 1249 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.58-7.56 (m, 1H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.30-7.28 (m, 1H), 7.21-7.19 (m, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.96 (s, 1H), 6.91 (s, 1H), 6.83 (d, *J* = 8.1 Hz, 2H), 6.17-6.08 (m, 1H), 5.51-5.48 (m, 2H), 5.10 (d, *J* = 9.9 Hz, 1H), 4.98 (d, *J* = 16.9 Hz, 1H), 4.07-4.01 (m, 1H), 3.76 (s, 3H), 3.66-3.56 (m, 2H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.9, 157.5, 145.2, 140.1, 138.5, 133.8, 129.9, 128.2, 127.5, 127.2, 126.6, 124.3, 123.3, 119.1, 117.1, 116.3, 115.2, 114.4, 108.2, 55.4, 46.2, 46.0, 39.0; **HRMS (ESI+):** Calcd. for $C_{26}H_{22}N_2O_2SNa$ ([M+Na]$^+$): 449.1300, Found: 449.1307; **Optical rotation:** $[\alpha]_D^{23}$ –15.5 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 99:1 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 363 nm, τ_{minor} = 21.8 min, τ_{major} = 25.3 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ao** was assigned in analogy with **3af**.



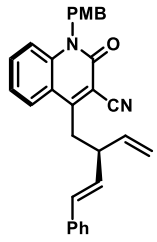
Compound 3ap: Purified by silica-gel flash column chromatography (12% EtOAc in petroleum ether); Off-white solid (62.0 mg, 0.166 mmol, 83% yield); **m.p.** 161-162 °C; **FT-IR (Thin film):** 2963 (m), 2228 (m), 1642 (s), 1510 (m), 1248 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.59-7.55 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 1H), 7.31-7.27 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 5.74-5.65 (m, 1H), 5.50-5.47 (m, 2H), 4.96 (d, *J* = 10.1 Hz, 1H), 4.78 (d, *J* = 16.9 Hz, 1H), 3.74 (s, 3H), 3.26 (dd, *J* = 13.3, 5.7 Hz, 1H), 3.12 (dd, *J* = 12.8, 9.0 Hz, 1H), 2.43-2.37 (m, 1H), 1.68-1.62 (m, 1H), 1.60-1.50 (m, 1H), 0.94 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 159.0, 158.9, 140.0, 139.9, 133.6, 128.2, 127.5, 126.9, 123.1, 119.3, 116.7, 116.1, 115.5, 114.3, 107.7, 55.3, 47.7, 46.1, 37.6, 28.1, 11.9; **HRMS (ESI+):** Calcd. for $C_{24}H_{24}N_2O_2Na$ ($[M+Na]^+$): 395.1735, Found: 395.1735; **Optical rotation:** $[\alpha]_D^{21}$ –1.2 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 97:3 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 229 nm, τ_{minor} = 25.8 min, τ_{major} = 27.3 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ap** was assigned in analogy with **3af**.

Compound 3aq: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); White solid (44.0 mg, 0.101 mmol, 50% yield); **m.p.** 149-151 °C; **FT-IR (Thin film):** 2224 (m), 1648 (s), 1510 (m), 1248 (m), 1032 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.53-7.49 (m, 1H), 7.35-7.31 (m, 4H), 7.27-7.23 (m, 3H), 7.18-7.11 (m, 3H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.89-5.80 (m, 1H), 5.46 (s, 2H), 4.96 (d, *J* = 10.3 Hz, 1H), 4.71 (d, *J* = 17.0 Hz, 1H), 3.75 (s, 3H), 3.28-3.24 (m, 1H), 3.12-3.07 (m, 1H), 3.00-2.95 (m, 1H), 2.85-2.79 (m, 1H), 2.77-2.75 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.9, 158.8, 140.1, 139.6, 139.3, 133.5, 129.5, 128.7, 128.2, 127.6, 126.7, 123.0, 119.1, 117.0, 116.1, 115.6, 114.4, 108.0, 55.4, 47.9, 46.2, 42.2, 36.7; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_2H$ ($[M+H]^+$): 435.2073, Found: 435.2072; **Optical rotation:** $[\alpha]_D^{22}$ –5.8 (*c* 1.0, $CHCl_3$). The absolute stereochemistry of the product **3aq** was assigned in analogy with **3af**.

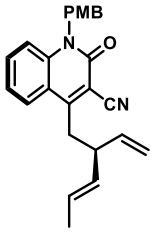
Compound 3ar: Purified by silica-gel flash column chromatography (10% EtOAc in petroleum ether); Off-white solid (42.0 mg, 0.098 mmol, 49% yield); **m.p.** 196-198 °C; **FT-IR (Thin film):** 2926 (s), 2851 (m), 2228 (m), 1648 (s), 1606 (s), 1511 (m), 1249 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.57-7.53 (m, 1H), 7.39-7.36 (m, 1H), 7.30-7.28 (m, 1H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.79-5.70 (m, 1H), 5.48-5.44 (m, 2H), 4.89 (d, *J* = 11.6 Hz, 1H), 4.57 (d, *J* = 15.7 Hz, 1H), 3.75 (s, 3H), 3.38 (dd, *J* = 13.1, 4.2 Hz, 1H), 3.09 (dd, *J* = 12.9, 10.8 Hz, 1H), 2.32-2.25 (m, 1H), 1.92-1.79 (m, 4H), 1.71-1.68 (m, 1H), 1.54-1.48 (m, 1H), 1.33-1.26 (m, 2H), 1.22-1.15 (m, 2H), 1.08-1.04 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.9,

159.2, 159.0, 140.0, 138.2, 133.5, 128.2, 127.6, 126.9, 123.0, 119.4, 117.3, 116.2, 115.6, 114.4, 107.9, 55.4, 52.2, 46.1, 42.5, 34.9, 33.0, 31.3, 30.1, 26.6, 26.5; **HRMS (ESI+):** Calcd. for $C_{28}H_{30}N_2O_2Na$ ([M+Na]$^+$): 449.2205, Found: 449.2203; **Optical rotation:** $[\alpha]_D^{21}$ –6.2 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 92.5:7.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 358 nm, τ_{minor} = 8.9 min, τ_{major} = 10.9 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ar** was assigned in analogy with **3af**.

Compound 3as: Regioselectivity (r.r.) > 20:1 was determined by ^{1}H NMR analysis of the crude reaction mixture. Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (88.0 mg, 0.197 mmol, 98% yield); **m.p.** 148-150 °C; **FT-IR (Thin film):** 3078 (w), 2226 (m), 1649 (s), 1608 (m), 1510 (m), 1249 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.85 (d, *J* = 8.1 Hz, 1H), 7.59-7.55 (m, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.33-7.25 (m, 5H), 7.21-7.20 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 6.30-6.21 (m, 2H), 6.03-5.95 (m, 1H), 5.47-5.44 (m, 2H), 5.10 (d, *J* = 10.2 Hz, 1H), 5.06 (d, *J* = 17.1 Hz, 1H), 3.72 (s, 3H), 3.48-3.38 (m, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 158.1, 140.1, 138.7, 136.7, 133.8, 131.4, 129.9, 128.6, 128.1, 127.6, 127.4, 126.8, 126.4, 123.2, 119.1, 116.3, 116.2, 115.5, 114.4, 107.9, 55.3, 48.6, 46.0, 37.3; **HRMS (ESI+):** Calcd. for $C_{30}H_{26}N_2O_2Na$ ([M+Na]$^+$): 469.1892, Found: 469.1895; **Optical rotation:** $[\alpha]_D^{22}$ –102.1 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 259 nm, τ_{minor} = 18.6 min, τ_{major} = 21.0 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3as** was assigned in analogy with **3af**.



Compound 3at: Regioselectivity (r.r.) > 20:1 was determined by ^{1}H NMR analysis of the crude reaction mixture. Purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether); Off-white solid (70.0 mg, 0.182 mmol, 91% yield); **m.p.** 165-167 °C; **FT-IR (Thin film):** 2226 (m), 1649 (s), 1607 (m), 1555 (m), 1451 (m), 1249 (m), 1033 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.59-7.55 (m, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.31-7.28 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 5.89 (ddd, *J* = 17.4, 10.2, 7.6 Hz, 1H), 5.55-5.51 (m, 1H), 5.49-5.42 (m, 2H), 5.40-5.33 (m, 1H), 5.02 (d, *J* = 10.2 Hz, 1H), 4.94 (d, *J* = 17.0 Hz, 1H), 3.74 (s, 3H), 3.30-3.21 (m, 2H), 3.17-3.10 (m, 1H), 1.63 (d, *J* = 6.2 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 158.5, 139.9, 139.3, 133.6, 131.3, 128.1, 127.5, 127.1, 126.8, 123.1, 119.2, 116.2, 115.6, 115.4, 114.3, 107.7, 55.3, 48.4, 46.0, 37.5, 17.9; **HRMS (ESI+):** Calcd. for $C_{25}H_{24}N_2O_2Na$ ([M+Na]$^+$): 407.1735, Found: 407.1732; **Optical rotation:**



$[\alpha]_D^{22}$ –17.6 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 96:4 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 231 nm, τ_{minor} = 14.2 min, τ_{major} = 16.4 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3at** was assigned in analogy with **3af**.

Compound 3ba: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Light-yellow sticky liquid (69.0 mg, 0.159 mmol, 79% yield); **FT-IR (Thin film):** 3016 (m), 2227 (m), 1648 (s), 1560 (m), 1511 (s), 1250 (s), 1033 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.53 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 7.36-7.32 (m, 3H), 7.29-7.26 (m, 3H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.22 (ddd, *J* = 17.5, 10.0, 8.0 Hz, 1H), 5.54 (d, *J* = 15.2 Hz, 1H), 5.43 (d, *J* = 15.4 Hz, 1H), 5.11 (d, *J* = 10.1 Hz, 1H), 5.01 (d, *J* = 17.0 Hz, 1H), 3.81-3.76 (m, 4H), 3.62 (dd, *J* = 13.1, 8.5 Hz, 1H), 3.54 (dd, *J* = 13.1, 6.8 Hz, 1H), 2.42 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.8, 158.0, 142.0, 139.2, 138.0, 135.0, 132.8, 128.9, 128.1, 127.6, 127.5, 127.3, 126.4, 119.1, 116.3, 116.1, 115.5, 114.4, 107.8, 55.3, 50.8, 45.9, 38.3, 20.9; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_2H$ ($[M+H]^+$): 435.2073, Found: 435.2072; **Optical rotation:** $[\alpha]_D^{22}$ –29.6 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 97.5:2.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 229 nm, τ_{minor} = 18.6 min, τ_{major} = 22.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ba** was assigned in analogy with **3af**.

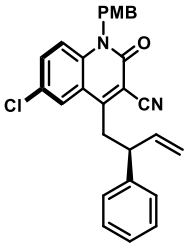
Compound 3ca: Reaction performed on 0.1 mmol scale of **1c**; purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (35.0 mg, 0.081 mmol, 81% yield); **m.p.** 127-129 °C; **FT-IR (Thin film):** 2224 (m), 1650 (s), 1511 (s), 1248 (m), 1032 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 8.4 Hz, 1H), 7.34-7.30 (m, 2H), 7.26-7.23 (m, 3H), 7.18 (s, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.16 (ddd, *J* = 17.9, 9.9, 8.0 Hz, 1H), 5.51 (d, *J* = 14.5 Hz, 1H), 5.41 (d, *J* = 15.5 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.94 (d, *J* = 17.0 Hz, 1H), 3.77 (s, 3H), 3.75-3.71 (m, 1H), 3.58 (dd, *J* = 13.1, 8.7 Hz, 1H), 3.50 (dd, *J* = 13.1, 6.7 Hz, 1H), 2.42 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 159.1, 158.1, 145.0, 142.0, 140.2, 139.2, 129.0, 128.2, 127.7, 127.5, 127.3, 126.6, 124.7, 117.0, 116.4, 116.3, 115.6, 114.4, 106.8, 55.4, 51.0, 46.0, 38.4, 22.5; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_2H$ ($[M+H]^+$): 435.2073, Found: 435.2073; **Optical rotation:** $[\alpha]_D^{22}$ –16.7 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 89.5:10.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 233 nm, τ_{minor} = 17.5 min, τ_{major} = 20.2 min). See

Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ca** was assigned in analogy with **3af**.

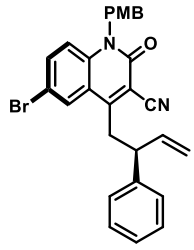
Compound 3da: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Yellow solid (76.0 mg, 0.169 mmol, 84% yield); **m.p.** 163-165 °C; **FT-IR (Thin film):** 2927 (w), 2226 (m), 1645 (s), 1558 (s), 1508 (s), 1244 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.35-7.32 (m, 3H), 7.28-7.26 (m, 3H), 7.23-7.20 (m, 1H), 7.17-7.13 (m, 3H), 6.85 (d, *J* = 6.9 Hz, 2H), 6.26-6.18 (m, 1H), 5.53 (d, *J* = 14.3 Hz, 1H), 5.43 (d, *J* = 15.1 Hz, 1H), 5.12 (d, *J* = 9.7 Hz, 1H), 5.00 (d, *J* = 16.7 Hz, 1H), 3.84 (s, 3H), 3.80-3.76 (m, 4H), 3.64-3.59 (m, 1H), 3.53-3.48 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.5, 157.4, 155.1, 142.0, 139.2, 134.5, 129.0, 128.1, 127.6, 127.4, 127.3, 122.1, 119.8, 117.5, 116.4, 115.4, 114.4, 108.7, 108.3, 55.8, 55.3, 50.7, 46.1, 38.7; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_3H$ ($[M+H]^+$): 451.2022, Found: 451.2023; **Optical rotation:** $[\alpha]_D^{22}$ –25.8 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 97:3 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 240 nm, τ_{minor} = 19.1 min, τ_{major} = 22.5 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3da** was assigned in analogy with **3af**.

Compound 3ea: Purified by silica-gel flash column chromatography (12% EtOAc in petroleum ether); Yellow sticky liquid (86.0 mg, 0.196 mmol, 98% yield); **FT-IR (Thin film):** 2927 (w), 2228 (m), 1650 (s), 1561 (m), 1508 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.35 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.31-7.28 (m, 1H), 7.26-7.22 (m, 3H), 7.19-7.15 (m, 3H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 6.10 (ddd, *J* = 17.2, 10.1, 8.0 Hz, 1H), 5.46-5.33 (m, 2H), 5.03 (d, *J* = 10.2 Hz, 1H), 4.93 (d, *J* = 16.9 Hz, 1H), 3.69-3.64 (m, 4H), 3.50 (dd, *J* = 13.3, 8.4 Hz, 1H), 3.38 (dd, *J* = 13.2, 6.7 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.5, 158.0 (d, *J* = 245.3 Hz), 157.3 (d, *J* = 3.4 Hz), 141.6, 138.9, 136.5, 129.0, 128.1, 127.5, 127.2, 121.6 (d, *J* = 24.0 Hz), 120.1 (d, *J* = 8.3 Hz), 118.1 (d, *J* = 7.9 Hz), 116.5, 115.0, 114.5, 111.9 (d, *J* = 23.7 Hz), 109.2, 55.4, 50.6, 46.3, 38.5; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}FN_2O_2Na$ ($[M+Na]^+$): 461.1641, Found: 461.1641; **Optical rotation:** $[\alpha]_D^{22}$ –39.9 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 96.5:3.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{minor} = 13.9 min, τ_{major} = 16.0 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ea** was assigned in analogy with **3af**.

Compound 3fa: Purified by silica-gel flash column chromatography (12% EtOAc in petroleum ether); Yellow sticky liquid (90.0 mg, 0.196 mmol, 99% yield); **FT-IR (Thin film):** 2838 (w), 2228 (w), 1651 (s), 1513 (m), 1248 (m), 1178 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.68 (s, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.33-7.30 (m, 3H), 7.26-7.23 (m, 3H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.23-6.15 (m, 1H), 5.50 (d, *J* = 12.5 Hz, 1H), 5.41 (d, *J* = 14.8 Hz, 1H), 5.13 (d, *J* = 9.8 Hz, 1H), 5.03 (d, *J* = 17.0 Hz, 1H), 3.77-3.71 (m, 4H), 3.61-3.56 (m, 1H), 3.50-3.45 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.4, 157.3, 141.5, 138.9, 138.4, 133.5, 129.0, 128.9, 128.1, 127.5, 127.0, 126.0, 120.2, 117.7, 116.6, 114.9, 114.5, 109.0, 55.4, 50.7, 46.2, 38.4; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}ClN_2O_2Na$ ($[M+Na]^+$): 477.1346, Found: 477.1349; **Optical rotation:** $[\alpha]_D^{22}$ –30.3 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 235 nm, τ_{minor} = 15.2 min, τ_{major} = 17.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3fa** was assigned in analogy with **3af**.



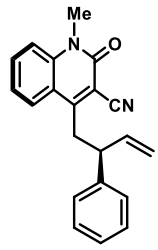
Compound 3ga: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Yellow sticky liquid (96.0 mg, 0.192 mmol, 96% yield); **FT-IR (Thin film):** 3016 (w), 2227 (m), 1651 (s), 1515 (m), 1249 (m), 1179 (m); **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 7.81 (s, 1H), 7.62-7.59 (m, 1H), 7.33-7.29 (m, 2H), 7.26-7.21 (m, 4H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.23-6.14 (m, 1H), 5.49 (d, *J* = 15.2 Hz, 1H), 5.39 (d, *J* = 15.9 Hz, 1H), 5.13 (d, *J* = 10.0 Hz, 1H), 5.03 (d, *J* = 16.9 Hz, 1H), 3.76-3.70 (m, 4H), 3.57 (dd, *J* = 13.0, 8.1 Hz, 1H), 3.46 (dd, *J* = 13.1, 7.1 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.4, 157.3, 141.5, 138.9, 138.8, 136.3, 129.1, 129.0, 128.1, 127.5, 127.0, 120.6, 117.9, 116.6, 116.2, 114.9, 114.5, 109.0, 55.4, 50.7, 46.1, 38.3; **HRMS (ESI+):** Calcd. for $C_{28}H_{23}BrN_2O_2Na$ ($[M+Na]^+$): 521.0841, Found: 521.0843; **Optical rotation:** $[\alpha]_D^{22}$ –21.6 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 251 nm, τ_{minor} = 16.4 min, τ_{major} = 19.5 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ga** was assigned in analogy with **3af**.



Compound 3ha: Purified by silica-gel flash column chromatography (10% EtOAc in petroleum ether); Light yellow sticky liquid (89.0 mg, 0.182 mmol, 91% yield); **FT-IR (Thin film):**, 2920 (m), 2229 (m), 1658 (s), 1554 (w), 1513 (m), 1132 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.93 (d, *J* = 8.5 Hz, 1H), 7.72 (s, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.36-7.32 (m, 2H), 7.29-7.24 (m, 3H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.20 (ddd, *J* = 17.6, 10.0, 7.9 Hz, 1H), 5.56 (d, *J* = 15.6 Hz, 1H), 5.46 (d, *J* = 15.5 Hz, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 5.01 (d, *J* = 16.9 Hz, 1H), 3.79 (s, 3H), 3.76-3.72 (m, 1H), 3.66 (dd, *J* = 13.1, 8.7 Hz, 1H), 3.56 (dd, *J* = 13.1, 6.8 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.4, 158.5, 157.5, 141.5, 139.8, 138.9, 134.5 (q, *J* = 33.4 Hz), 129.0, 128.4, 127.8, 127.5, 127.4, 126.8, 123.1 (q, *J* = 273.3 Hz), 121.2, 119.3 (q, *J* = 3.4 Hz), 116.6, 114.6, 113.4 (q, *J* = 4.2 Hz), 110.2, 55.3, 50.8, 46.3, 38.4; **HRMS (ESI+):** Calcd. for $C_{29}H_{23}F_3N_2O_2Na$ ($[M+Na]^+$): 511.1609, Found: 511.1607; **Optical rotation:** $[\alpha]_D^{22}$ – 23.9 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 88:12 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 234 nm, τ_{minor} = 8.8 min, τ_{major} = 9.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ha** was assigned in analogy with **3af**.

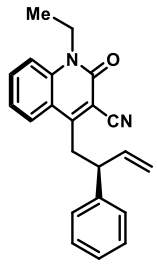
Compound 3ia: Purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2); Light-yellow solid (62.0 mg, 0.172 mmol, 86% yield); **m.p.** 227-229 °C; **FT-IR (Thin film):** 2920 (m), 2852 (w), 2229 (m), 1661 (s), 1610 (s), 1339 (s), 1084 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.57 (s, 1H), 8.47 (d, *J* = 9.3 Hz, 1H), 7.49 (d, *J* = 9.3 Hz, 1H), 7.30-7.17 (m, 5H), 6.24-6.15 (m, 1H), 5.13 (d, *J* = 10.1 Hz, 1H), 5.05 (d, *J* = 16.9 Hz, 1H), 3.78 (s, 3H), 3.75-3.70 (m, 1H), 3.62 (dd, *J* = 13.3, 8.1 Hz, 1H), 3.52 (dd, *J* = 13.2, 7.4 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.3, 158.1, 144.1, 142.6, 141.3, 138.6, 129.2, 127.7, 127.6, 127.5, 123.1, 118.6, 116.9, 116.1, 114.3, 109.9, 51.1, 38.7, 30.9; **HRMS (ESI+):** Calcd. for $C_{21}H_{17}N_3O_3H$ ($[M+H]^+$): 360.1348, Found: 360.1346; **Optical rotation:** $[\alpha]_D^{22}$ +16.4 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 275 nm, τ_{minor} = 15.4 min, τ_{major} = 16.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ia** was assigned in analogy with **3af**.

Compound 3ja: Purified by silica-gel flash column chromatography (1% EtOAc in CH_2Cl_2);



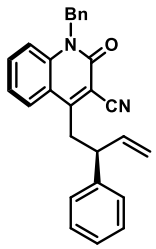
Off-white solid (58.0 mg, 0.184 mmol, 92% yield); **m.p.** 150-152 °C; **FT-IR (Thin film):** 2925 (m), 2226 (m), 1649 (s), 1607 (m), 1557 (m), 1088 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.73-7.69 (m, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.33-7.30 (m, 3H), 7.26-7.22 (m, 3H), 6.18-6.10 (m, 1H), 5.04 (d, *J* = 10.0 Hz, 1H), 4.92 (d, *J* = 17.0 Hz, 1H), 3.73 (s, 3H), 3.73-3.70 (m, 1H), 3.60-3.55 (m, 1H), 3.53-3.48 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.7, 157.8, 142.1, 140.7, 139.1, 133.8, 129.0, 127.5, 127.3, 126.8, 123.1, 118.9, 116.5, 115.4, 115.3, 108.1, 51.0, 38.4, 30.2; **HRMS (ESI+):** Calcd. for $C_{21}H_{18}N_2OH$ ($[M+H]^+$): 315.1497, Found: 315.1495; **Optical rotation:** $[\alpha]_D^{23}$ +8.7 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 231 nm, τ_{minor} = 16.9 min, τ_{major} = 20.4 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ja** was assigned in analogy with **3af**.

Compound 3ka: Purified by silica-gel flash column chromatography (14% EtOAc in petroleum



ether); Off-white solid (65.0 mg, 0.198 mmol, 99% yield); **m.p.** 115-117 °C; **FT-IR (Thin film):** 2978 (w), 2226 (m), 1647 (s), 1608 (m), 1555 (m), 1093 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.86 (d, *J* = 8.1 Hz, 1H), 7.78-7.42 (m, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.39-7.34 (m, 3H), 7.31-7.29 (m, 3H), 6.23-6.15 (m, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 4.96 (d, *J* = 17.0 Hz, 1H), 4.47-3.36 (m, 2H), 3.81-3.76 (m, 1H), 3.65-3.59 (m, 1H), 3.57-3.52 (m, 1H), 1.41 (t, *J* = 6.9 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.2, 157.6, 142.1, 139.6, 139.1, 133.7, 128.9, 127.4, 127.3, 126.9, 122.9, 119.1, 116.5, 115.3, 115.2, 108.0, 50.9, 38.4, 38.2, 12.6; **HRMS (ESI+):** Calcd. for $C_{22}H_{20}N_2OH$ ($[M+H]^+$): 329.1654, Found: 329.1655; **Optical rotation:** $[\alpha]_D^{21}$ +10.0 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 234 nm, τ_{minor} = 8.8 min, τ_{major} = 10.5 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ka** was assigned in analogy with **3af**.

Compound 3la: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum



ether); Off-white solid (72.0 mg, 0.184 mmol, 92% yield); **m.p.** 176-178 °C; **FT-IR (Thin film):** 3029 (w), 2226 (m), 1650 (s), 1605 (m), 1451 (m), 1028 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.60-7.56 (m, 1H), 7.37-7.31 (m, 6H), 7.29-7.27 (m, 3H), 7.26-7.24 (m, 1H), 7.18 (d, *J* = 7.2 Hz, 2H), 6.20 (ddd, *J* = 17.3, 10.1, 8.2 Hz, 1H), 5.62 (d, *J* = 15.6 Hz, 1H), 5.52 (d, *J* = 15.8 Hz, 1H), 5.10 (d, *J* = 10.1 Hz, 1H), 4.99 (d, *J* = 16.9 Hz, 1H), 3.79 (dd, *J* = 15.3, 7.8 Hz, 1H), 3.65 (dd, *J* = 12.9, 8.6 Hz, 1H), 3.56 (dd, *J* = 13.1, 6.9 Hz, 1H); **^{13}C-NMR (100 MHz,**

$CDCl_3$): δ 158.9, 158.3, 141.9, 140.0, 139.1, 135.5, 133.8, 129.0, 128.9, 127.7, 127.5, 127.4, 126.8, 126.7, 123.2, 119.1, 116.4, 116.3, 115.3, 108.0, 50.9, 46.5, 38.4; **HRMS (ESI+):** Calcd. for $C_{27}H_{22}N_2OH$ ($[M+H]^+$): 391.1810, Found: 391.1813; **Optical rotation:** $[\alpha]_D^{22}$ –34.1 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 303 nm, τ_{minor} = 12.4 min, τ_{major} = 15.8 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3la** was assigned in analogy with **3af**.

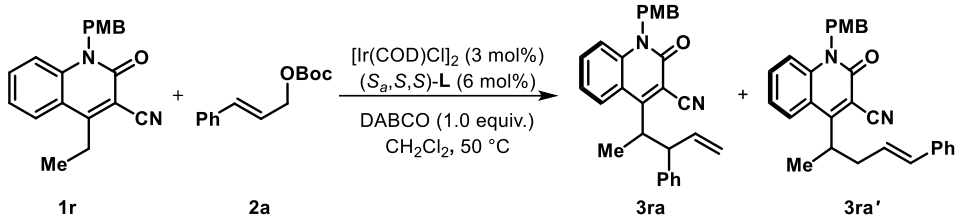
Compound 3ma: Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether); Off-white solid (67.0 mg, 0.197 mmol, 98% yield); **m.p.** 125-127 °C; **FT-IR (Thin film):** 3024 (w), 2226 (m), 1650 (s), 1605 (m), 1556 (m), 1190 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.81 (d, *J* = 8.1 Hz, 1H), 7.69-7.65 (m, 1H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.34-7.30 (m, 3H), 7.26-7.24 (m, 3H), 6.20-6.11 (m, 1H), 5.96-5.89 (m, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.08-5.04 (m, 2H), 4.96-4.91 (m, 3H), 3.78-3.72 (m, 1H), 3.62-3.57 (m, 1H), 3.52 (dd, *J* = 13.0, 6.5 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.3, 158.1, 142.0, 139.9, 139.1, 133.6, 130.9, 128.9, 127.5, 127.3, 126.8, 123.1, 119.0, 117.8, 116.4, 116.1, 115.2, 107.9, 50.9, 45.2, 38.4; **HRMS (ESI+):** Calcd. for $C_{23}H_{20}N_2ONa$ ($[M+Na]^+$): 363.1473, Found: 363.1476; **Optical rotation:** $[\alpha]_D^{22}$ +4.2 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 240 nm, τ_{minor} = 13.8 min, τ_{major} = 16.7 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3ma** was assigned in analogy with **3af**.

Compound 3oa: Purified by silica-gel flash column chromatography (12% EtOAc in petroleum ether); Off-white solid (48.0 mg, 0.152 mmol, 76% yield); **m.p.** 141-143 °C; **FT-IR (Thin film):** 2227 (w), 1655 (s), 1591 (m), 1451 (m), 1072 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.73 (dd, *J* = 4.5, 1.7 Hz, 1H), 8.05 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.34-7.24 (m, 6H), 6.16 (ddd, *J* = 17.1, 10.2, 8.1 Hz, 1H), 5.10 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 3.85 (s, 3H), 3.75-3.69 (m, 1H), 3.58 (dd, *J* = 13.1, 8.3 Hz, 1H), 3.49 (dd, *J* = 13.1, 6.8 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.4, 156.8, 152.9, 150.0, 141.6, 138.9, 135.0, 129.0, 127.4, 118.8, 116.7, 114.8, 114.2, 108.9, 50.8, 37.7, 29.2; **HRMS (ESI+):** Calcd. for $C_{20}H_{17}N_3OH$ ($[M+H]^+$): 316.1450, Found: 316.1453; **Optical rotation:** $[\alpha]_D^{22}$ –21.6 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 355 nm, τ_{minor} = 17.3 min, τ_{major} = 24.2 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3oa** was assigned in analogy with **3af**.

Compound 3pa: Purified by silica-gel flash column chromatography (15% EtOAc in petroleum ether); Yellow solid (58.0 mg, 0.176 mmol, 88% yield); **m.p.** 170-172 °C; **FT-IR (Thin film):** 2924 (w), 2222 (w), 1593 (m), 1545 (s), 1451 (m), 1104 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.81 (d, *J* = 8.2 Hz, 1H), 7.79-7.75 (m, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.42-7.38 (m, 1H), 7.33-7.21 (m, 5H), 6.16 (ddd, *J* = 17.4, 9.9, 8.4 Hz, 1H), 5.03 (d, *J* = 10.1 Hz, 1H), 4.91 (d, *J* = 16.9 Hz, 1H), 4.30 (s, 3H), 3.79-3.73 (m, 1H), 3.61 (dd, *J* = 13.1, 9.1 Hz, 1H), 3.51 (dd, *J* = 13.2, 6.3 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 180.6, 151.0, 142.1, 141.2, 138.9, 134.2, 129.0, 127.4, 127.3, 126.9, 124.8, 122.2, 119.2, 116.7, 116.6, 116.3, 51.1, 38.8, 38.3; **HRMS (ESI+):** Calcd. for $C_{21}H_{18}N_2SH$ ($[M+H]^+$): 331.1269, Found: 331.1266; **Optical rotation:** $[\alpha]_D^{22}$ +22.6 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 97:3 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 292 nm, τ_{minor} = 18.3 min, τ_{major} = 19.6 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3pa** was assigned in analogy with **3af**.

Compound 3qa: Reaction performed on 0.40 mmol scale of **1q**; purified by silica-gel flash column chromatography (20% EtOAc in petroleum ether); Yellow thick oil (44.0 mg, 0.119 mmol, 30% yield); **FT-IR (Thin film):** 2921 (w), 2221 (w), 1652 (s), 1516 (m), 1249 (s), 1032 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.29-7.26 (m, 3H), 7.22-7.17 (m, 5H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.01 (ddd, *J* = 17.4, 10.2, 7.6 Hz, 1H), 5.92 (d, *J* = 7.1 Hz, 1H), 5.07 (d, *J* = 10.3 Hz, 1H), 5.04-4.99 (m, 3H), 3.78 (s, 3H), 3.70-3.63 (m, 1H), 3.12 (dd, *J* = 13.3, 7.9 Hz, 1H), 3.04 (dd, *J* = 13.3, 7.8 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 161.3, 160.2, 159.9, 141.8, 139.9, 139.6, 130.2, 128.9, 127.6, 127.2, 127.0, 116.1, 115.1, 114.6, 107.9, 105.3, 55.5, 52.1, 49.7, 41.1; **HRMS (ESI+):** Calcd. for $C_{24}H_{22}N_2O_2Na$ ($[M+Na]^+$): 393.1579, Found: 393.1576; **Optical rotation:** $[\alpha]_D^{22}$ –18.1 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 339 nm, τ_{minor} = 16.9 min, τ_{major} = 18.9 min). See Supporting Information: Part B for HPLC chromatograms. The absolute stereochemistry of the product **3qa** was assigned in analogy with **3af**.

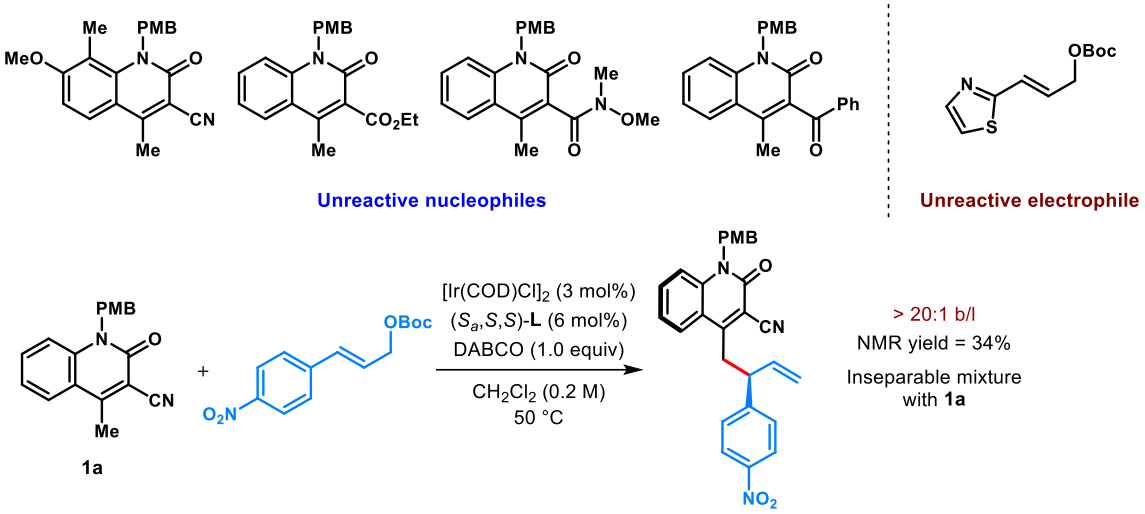
H. Attempted vinylogous allylic alkylation of 3-cyano-4-ethyl-2-quinolone 1r:



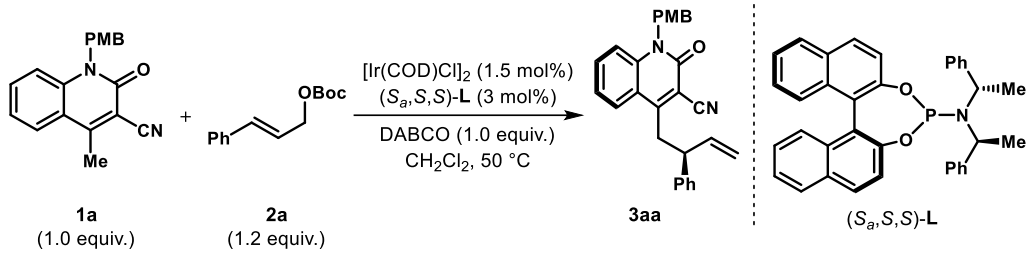
1r **2a** **3ra** **3ra′**

The same procedure as above was followed. Product was obtained as 1:1.1 mixture of branched/linear and 1.1:1 dr for the branched product (as determined from ^{1}H-NMR of the crude). Purified by silica-gel flash column chromatography (13% EtOAc in petroleum ether). After purification b/l = 1:1 and dr = 1:1 for the branched product; Off-white solid (76.0 mg, 0.174 mmol, 87% yield); **FT-IR (Thin film):** 2926 (m), 2224 (w), 1646 (s), 1550 (m), 1512 (m), 1248 (m), 1030 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** Signals corresponding to the linear allyl product and both diastereomers of the branched allyl product: δ 8.27-8.23 (m, 2H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 7.64-7.59 (m, 3H), 7.53-7.43 (m, 12H), 7.37-7.16 (m, 15H), 7.07-7.03 (m, 5H), 6.96-6.94 (m, 4H), 6.87-6.85 (m, 5H), 6.80-6.78 (m, 4H), 6.20-6.09 (m, 2H), 6.03-5.95 (m, 1H), 5.84-5.75 (m, 1H), 5.57 (br s, 2H), 5.49 (br s, 4H), 5.35 (d, *J* = 13.2 Hz, 2H), 5.28-5.23 (m, 3H), 5.08 (d, *J* = 16.9 Hz, 1H), 4.79 (d, *J* = 9.8 Hz, 1H), 4.73 (d, *J* = 9.8 Hz, 1H), 4.63 (d, *J* = 16.9 Hz, 1H), 4.46-4.41 (m, 2H), 4.14-3.98 (m, 6H), 3.77 (s, 12H), 1.73-1.71 (m, 6H), 1.40-1.39 (m, 6H); **^{13}C-NMR (100 MHz, $CDCl_3$):** Signals corresponding to the linear allyl product and both diastereomers of the branched allyl product: δ 164.3, 164.2, 163.1, 162.7, 159.7, 159.4, 159.1, 158.9, 142.1, 141.7, 141.2, 140.2, 140.0, 139.7, 139.6, 138.9, 138.7, 133.9, 133.6, 133.4, 133.2, 129.2, 129.0, 128.5, 128.4, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 127.3, 127.2, 127.1, 126.8, 126.5, 126.2, 125.6, 123.3, 122.9, 122.5, 122.3, 119.9, 119.5, 118.5, 117.5, 117.4, 116.6, 116.5, 116.4, 116.2, 116.1, 115.6, 115.4, 114.4, 114.2, 108.4, 108.3, 105.2, 56.5, 56.4, 55.3, 53.4, 46.9, 46.3, 46.2, 45.8, 45.6, 39.1, 38.3, 18.5, 18.2, 17.4, 16.9; **HRMS (ESI+):** Calcd. for $C_{29}H_{26}N_2O_2H$ ($[M+H]^+$): 435.2073, Found: 435.2074.

I. Unsuccessful substrates for enantioselective vinylogous allylic alkylation reaction:



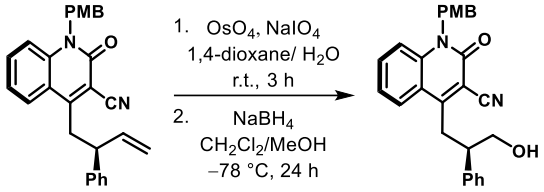
J. Large scale synthesis of 3aa:



In an oven dried 25 mL 2-necked round-bottom flask, equipped with a reflux condenser, $[Ir(COD)Cl]_2$ (40.0 mg, 0.060 mmol, 1.5 mol%) and ligand (*S*$_a$,*S*,*S*)-**L** (65.0 mg, 0.120 mmol, 3 mol%) were taken with 10.0 mL of absolute THF under a positive argon pressure followed by addition of 6.0 mL dry *n*-$PrNH_2$. The solution was heated at 50 °C for 30 min, after which all volatiles were removed under vacuum to obtain a yellow solid. To this, 2-quinolone **1a** (1.22 g, 4.00 mmol, 1.0 equiv.) and DABCO (449 mg, 4.00 mmol, 1.0 equiv.) were introduced under a positive argon pressure followed by 12.0 mL of absolute CH_2Cl_2 and the suspension was stirred at 50 °C for 5 min. After 5 min, a solution of allyl carbonate **2a** (1.125 g, 4.80 mmol, 1.2 equiv.) in 8.0 mL absolute CH_2Cl_2 was added. The resulting mixture was purged with argon and the reaction was refluxed at 50 °C until TLC (20% EtOAc in petroleum ether) revealed complete consumption of **1a**. After 18 h, the reaction mixture was allowed to attain ambient temperature, diluted with 10.0 mL of CH_2Cl_2 and 10.0 mL 1 N HCl solution. Organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10.0 mL). Combined organic layer was washed with brine (20.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure to obtain a reddish-brown oil. This oil was purified by silica-gel flash column chromatography

(12-13% EtOAc in petroleum ether) to obtain **3aa** as off-white solid (1.43 g, 3.400 mmol, 85% yield) with 97:3 er. Isolated **3aa** was further recrystallized form EtOH to obtain 1.06 g of **3aa** with 98:2 er.

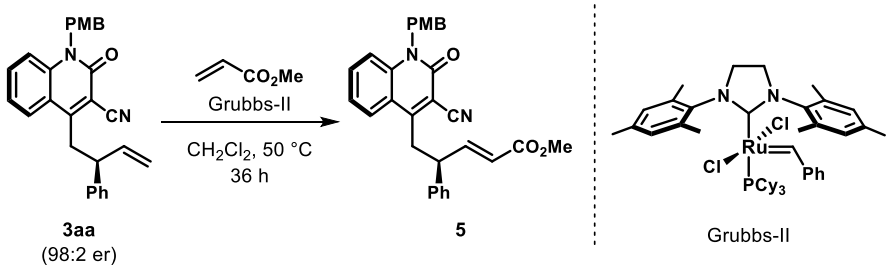
K. Procedure for the preparation of alcohol 4:



3aa (98:2 er) **4**

In a 5 mL round-bottom flask, **3aa** (42.0 mg, 0.100 mmol, 1.0 equiv.) and $NaIO_4$ (107.0 mg, 0.500 mmol, 5.0 equiv.) was taken in 5.0 mL of 1,4-dioxane/H_2O (3:1) mixture. To this solution, was added OsO_4 (5.1 mg, 0.020 mmol, 0.2 equiv.) and stirred at r.t. for 3 h. The reaction mixture was diluted with 2.0 mL of sat. $Na_2S_2O_3$ solution and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic layer was washed with sat. $NaHCO_3$ solution (5.0 mL) and brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was taken in (2:1) CH_2Cl_2/MeOH mixture, cooled to –78 °C. To this solution, was added $NaBH_4$ (15.0 mg, 0.400 mmol, 4.0 equiv.) and the resulting solution was stirred at –78 °C under argon. After 24 h, the reaction mixture was diluted with 2.0 mL of sat. NH_4Cl solution and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic layer was dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (35% EtOAc in petroleum ether) to obtain **4** as an off-white solid (20.0 mg, 0.047 mmol, 47% yield); **m.p.** 140-142 °C; **FT-IR (Thin film):** 2934 (w), 2229 (w), 1643 (s), 1510 (m), 1452 (m), 1249 (s); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.57-7.54 (m, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.32-7.24 (m, 4H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.45 (s, 2H), 4.02-3.94 (m, 2H), 3.79-3.74 (m, 1H), 3.76 (s, 3H), 3.41-3.36 (m, 1H), 3.33-3.28 (m, 1H), 1.94-1.87 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 158.9, 158.8, 140.1, 139.9, 133.8, 129.1, 128.2, 128.1, 127.9, 127.5, 127.2, 123.2, 119.2, 116.2, 115.3, 114.5, 107.8, 66.2, 55.4, 49.2, 46.1, 35.5; **HRMS (ESI+):** Calcd. for $C_{27}H_{24}N_2O_3H$ ($[M+H]^+$): 425.1865, Found: 425.1867; **Optical rotation:** $[\alpha]_D^{22}$ –73.1 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IE column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 237 nm, τ_{major} = 16.3 min, τ_{minor} = 19.0 min). See Supporting Information: Part B for HPLC chromatograms.

L. Procedure for the cross-metathesis reaction of 3aa:

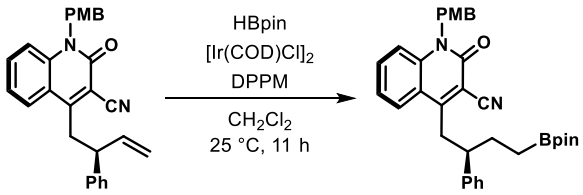


3aa
(98:2 er)

5

In an oven dried 10 mL 2-necked round-bottom flask, equipped with a reflux condenser, **3aa** (42.0 mg, 0.100 mmol, 1.0 equiv.) and Grubbs-II (4.3 mg, 0.005 mmol, 0.05 equiv.) were taken in 2.0 mL of absolute CH_2Cl_2 under argon and the resulting solution was heated to 50 °C. To this, was added methyl acrylate (53 µL, 0.500 mmol, 5.0 equiv.) at once and the resulting mixture was stirred at 50 °C for 36 h. Solvent was evaporated to obtain a yellow residue, which was purified by silica-gel flash column chromatography (17% EtOAc in petroleum ether) to obtain **5** as a thick red oil (34.0 mg, 0.071 mmol, 71% yield); **FT-IR (Thin film):** 2920 (w), 2226 (m), 1720 (m), 1649 (s), 1450 (m), 1033 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.62-7.59 (m, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.36-7.28 (m, 5H), 7.23 (d, *J* = 6.8 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.83 (d, *J* = 15.6 Hz, 1H), 5.56 (d, *J* = 15.7 Hz, 1H), 5.45 (d, *J* = 15.9 Hz, 1H), 3.99-3.93 (m, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.72-3.69 (m, 1H), 3.63 (dd, *J* = 13.3, 7.6 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 166.3, 159.2, 158.7, 157.2, 148.2, 140.1, 139.6, 133.9, 129.2, 128.1, 128.0, 127.8, 127.4, 126.6, 123.3, 122.3, 118.9, 116.4, 115.0, 114.6, 108.1, 55.4, 51.8, 49.0, 46.1, 37.8; **HRMS (ESI+):** Calcd. for $C_{30}H_{26}N_2O_4Na$ ($[M+Na]^+$): 501.1790, Found: 501.1792; **Optical rotation:** $[\alpha]_D^{21}$ –27.2 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 230 nm, τ_{minor} = 20.2 min, τ_{major} = 53.6 min). See Supporting Information: Part B for HPLC chromatograms.

M. Procedure for the Ir-catalyzed hydroboration of 3aa:



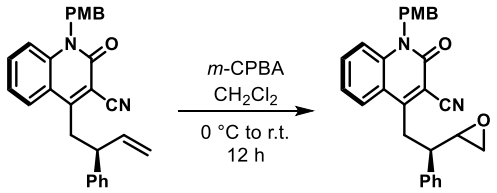
3aa
(98:2 er)

6

In an oven dried 10 mL round-bottom flask, **3aa** (42.0 mg, 0.100 mmol, 1.0 equiv.) was taken along with $[Ir(COD)Cl]_2$ (2.0 mg, 0.003 mmol, 0.03 equiv.) and

bis(diphenylphosphino)methane (DPPM; 2.3 mg, 0.006 mmol, 0.06 equiv.) under a positive argon pressure. Then 1.0 mL CH_2Cl_2 was added followed by the addition of HBpin (30 µL, 0.200 mmol, 2.0 equiv.) and the resulting solution was stirred at r.t. for 11 h under argon atmosphere. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica-gel flash column chromatography (16% EtOAc in petroleum ether) to obtain **6** as a thick colorless oil (44.0 mg, 0.080 mmol, 80% yield); **FT-IR (Thin film):** 2926 (w), 2226 (w), 1650 (s), 1452 (m), 1375 (m), 1248 (m), 1031 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.73 (d, *J* = 7.5 Hz, 1H), 7.48-7.44 (m, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.18-7.10 (m, 4H), 7.04-7.02 (m, 4H), 6.75 (d, *J* = 7.8 Hz, 2H), 5.46-5.28 (m, 2H), 3.68 (m, 3H), 3.48-3.43 (m, 1H), 3.31-3.26 (m, 1H), 2.98 (s, 1H), 1.90 (s, 2H), 1.09-1.08 (m, 12H), 0.66-0.53 (m, 2H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.1, 158.9, 142.4, 140.0, 133.5, 128.7, 128.3, 128.2, 127.9, 127.6, 127.1, 127.1, 122.9, 119.3, 116.1, 115.3, 114.4, 107.8, 83.1, 55.4, 49.1, 46.0, 39.8, 30.0, 24.9, 24.8; **HRMS (ESI+):** Calcd. for $C_{34}H_{37}N_2O_4BH$ ($[M+H]^+$): 548.2961, Found: 548.2963; **Optical rotation:** $[\alpha]_D^{22}$ –54.3 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IB column (90:10 *n*-Hexane/*i*-PrOH, 1.0 mL/min, 20 °C, 236 nm, τ_{minor} = 34.8 min, τ_{major} = 37.2 min). See Supporting Information: Part B for HPLC chromatograms.

N. Procedure for the epoxidation of 3aa:

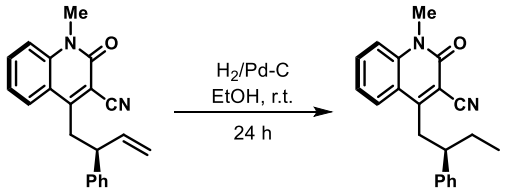


3aa (98:2 er) **7**

In an oven and vacuum-dried 5 mL round-bottom flask, **3aa** (46.0 mg, 0.109 mmol, 1.0 equiv.) was taken in 0.6 mL of abs. CH_2Cl_2 and cooled it to 0 °C. To this solution, was added *m*-CPBA (79.0 mg, 55% assay, 0.251 mmol, 2.3 equiv.) and the resulting suspension was stirred at r.t. under argon. After 48 h, the reaction mixture was diluted with 2.0 mL of sat. $Na_2S_2O_3$ solution and 5.0 mL of CH_2Cl_2. The organic phase was separated and aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic layer was washed with sat. $NaHCO_3$ solution (5.0 mL) and brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue (with 1.3:1 dr, as determined from ^{1}H-NMR) was purified by silica-gel flash column chromatography (2-3% EtOAc in CH_2Cl_2) to obtain **7** as white solid (28.0 mg, 0.064 mmol, 59% yield); **m.p.** 154-156 °C; **FT-IR (Thin film):** 3014 (w), 2926 (w), 2838 (w), 2227 (m), 1649 (s), 1510 (m), 1557 (m), 1452 (m), 1250 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** Signals corresponding to the major diastereomer: δ 7.86 (d, *J* = 7.9 Hz, 1H), 7.59-7.54

(m, 1H), 7.41-7.20 (m, 7H), 7.15-7.11 (m, 2H), 6.85-6.81 (m, 2H), 5.54-5.46 (m, 2H), 3.85 (dd, *J* = 13.4, 7.0 Hz, 1H), 3.76 (m, 3H), 3.62 (dd, *J* = 13.4, 8.1 Hz, 1H), 3.45-3.36 (m, 2H), 2.79-2.73 (m, 2H); Representative signals corresponding to the minor diastereomer: δ 7.79 (d, *J* = 7.8 Hz, 1H), 7.59-7.54 (m, 1H), 7.41-7.20 (m, 7H), 7.15-7.11 (m, 2H), 6.85-6.81 (m, 2H), 5.54-5.46 (m, 2H), 3.77 (m, 3H), 3.69-3.61 (m, 1H), 3.45-3.36 (m, 1H), 3.14-3.10 (m, 1H), 2.86-2.84 (m, 1H), 2.53-2.51 (m, 2H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 159.1, 158.8, 158.7, 158.0, 157.7, 140.1, 140.0, 139.1, 138.7, 133.9, 133.7, 129.1, 129.0, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.5, 127.4, 126.9, 126.7, 123.3, 123.2, 119.1, 118.9, 116.3, 115.3, 115.0, 114.5, 114.4, 108.0, 107.9, 55.6, 55.4, 54.5, 50.7, 48.2, 47.0, 46.4, 46.2, 46.1, 36.9, 34.8, 29.8; **HRMS (ESI+):** Calcd. for $C_{28}H_{24}N_2O_3Na$ ($[M+Na]^+$): 459.1685, Found: 459.1685; The enantiomeric ratio of compound **7** (dr = 1.3:1) is 98:2 er. for the major diasteromer and 99:1 er. for the minor diastereomer. The enantiomeric ratios were determined by HPLC analysis using Daicel Chiralpak IA column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 227 nm, for major diasteromer τ_{minor} = 11.1 min, τ_{major} = 12.1 min, and for minor diasteromer τ_{minor} = 15.2 min, τ_{major} = 18.4 min). See Supporting Information: Part B for HPLC chromatograms.

O. Procedure for the selective reduction of the allylic double bond of 3ja & 3aa:



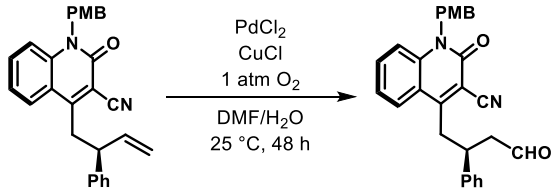
3ja (98:2 er) **8**

In an oven and vacuum-dried 10 mL two-necked round-bottom flask, a solution of **3ja** (80.0 mg, 0.254 mmol, 1.0 equiv.) in EtOH (2.5 mL), 10% Pd/C (13.0 mg, 0.013 mmol, 0.05 equiv.) was added. The resulting mixture was degassed and stirred under H_2 balloon pressure for 24 h at r.t. The reaction mixture was filtered over Celite® and washed with CH_2Cl_2. The filtrate was concentrated under reduced pressure and the residue was purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether) to obtain **8** as a white solid (73.0 mg, 0.231 mmol, 91% yield); **m.p.** 160-162 °C; **FT-IR (Thin film):** 2925 (w), 2225 (w), 1647 (s), 1455 (m), 1091 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.74 (d, *J* = 8.3 Hz, 1H), 7.71-7.67 (m, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.31-7.24 (m, 3H), 7.20-7.15 (m, 3H), 3.71 (s, 3H), 3.47 (dd, *J* = 13.3, 7.8 Hz, 1H), 3.34 (dd, *J* = 13.3, 7.1 Hz, 1H), 2.96-2.89 (m, 1H), 1.92-1.76 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 158.7, 158.6, 142.7, 140.5, 133.7, 128.7, 127.6, 127.0, 126.9, 123.0, 118.9, 115.3, 115.2, 107.5, 48.8, 39.7, 30.1, 28.3, 12.2; **HRMS (ESI+):** Calcd. for $C_{21}H_{20}N_2OH$ ($[M+H]^+$): 317.1654, Found: 317.1651; **Optical rotation:** $[\alpha]_D^{21}$ –46.3 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was

determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 234 nm, τ_{minor} = 9.8 min, τ_{major} = 10.5 min). See Supporting Information: Part B for HPLC chromatograms.

Compound 9: Reaction was performed on a 0.100 mmol scale of **3aa**; purified by silica-gel flash column chromatography (13-14% EtOAc in petroleum ether); White solid (41.0 mg, 0.097 mmol, 97% yield); **m.p.** 179-181 °C; **FT-IR (Thin film):** 2928 (w), 2226 (w), 1647 (s), 1511 (m), 1452 (m), 1249 (m), 1032 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.76 (d, *J* = 8.1 Hz, 1H), 7.57-7.53 (m, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 7.29-7.27 (m, 1H), 7.25-7.24 (m, 1H), 7.22-7.18 (m, 1H), 7.16-7.12 (m, 4H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.52 (d, *J* = 14.9 Hz, 1H), 5.40 (d, *J* = 15.2 Hz, 1H), 3.76 (s, 3H), 3.52 (dd, *J* = 13.2, 7.7 Hz, 1H), 3.37 (dd, *J* = 13.2, 7.3 Hz, 1H), 3.00-2.92 (m, 1H), 1.98-1.81 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.2, 159.1, 158.9, 142.7, 140.0, 133.6, 128.7, 128.2, 127.7, 127.5, 127.1, 127.0, 123.0, 119.2, 116.1, 115.4, 114.4, 107.7, 55.4, 48.9, 46.0, 39.8, 28.4, 12.3; **HRMS (ESI+):** Calcd. for $C_{28}H_{26}N_2O_2H$ ($[M+H]^+$): 423.2073, Found: 423.2070; **Optical rotation:** $[\alpha]_D^{22}$ –80.4 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 98.5:1.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 238 nm, τ_{minor} = 15.8 min, τ_{major} = 18.2 min). See Supporting Information: Part B for HPLC chromatograms.

P. Procedure for the Wacker oxidation of 3aa:

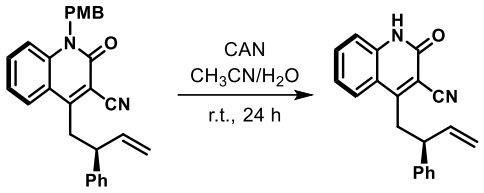


3aa (98:2 er) **10**

In an oven dried 10 mL round-bottom flask, **3aa** (42.0 mg, 0.100 mmol, 1.0 equiv.) was taken in 2.5 mL of (9:1) DMF/H_2O mixture. Then $PdCl_2$ (3.5 mg, 0.020 mmol, 0.20 equiv.) and CuCl (20.0 mg, 0.200 mmol, 2.0 equiv.) was added to the solution. The round-bottom flask was quickly evacuated and backfilled three times with a balloon of O_2, and then stirred at 25 °C under a balloon of O_2 for 48 h. Reaction mixture was diluted with 2.0 mL of H_2O and 5.0 mL of EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 5.0 mL). Combined organic layer was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (30% EtOAc in petroleum ether) to obtain **10** as white solid (30.0 mg, 0.069 mmol, 69% yield); **m.p.** 204-206 °C; **FT-IR (Thin film):** 2923 (m), 2227 (m), 1647 (s), 1511 (m), 1452 (m), 1249 (m), 1030 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 9.77 (s, 1H), 8.10 (d, *J* =

7.7 Hz, 1H), 7.60-7.57 (m, 1H), 7.38-7.33 (m, 2H), 7.26-7.25 (m, 3H), 7.12-7.08 (m, 4H), 6.83-6.82 (m, 2H), 5.53-5.35 (m, 2H), 3.76 (s, 3H), 3.76-3.72 (m, 1H), 3.66-3.61 (m, 1H), 3.38-3.33 (m, 1H), 3.10-3.08 (m, 2H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 200.6, 159.2, 158.7, 157.9, 140.9, 140.0, 133.9, 129.0, 128.1, 127.8, 127.5, 127.4, 127.3, 123.5, 119.1, 116.2, 115.2, 114.4, 107.9, 55.4, 49.6, 46.0, 40.3, 39.2; **HRMS (ESI+):** Calcd. for $C_{28}H_{24}N_2O_3H$ ($[M+H]^+$): 437.1865, Found: 437.1864; **Optical rotation:** $[\alpha]_D^{22}$ –95.7 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 99:1 er. To determine the enantiomeric ratio, compound **10** was converted to alcohol **10´** by $NaBH_4$ reduction. The enantiomeric ratio of compound **10´** was determined by HPLC analysis using Daicel Chiralpak IG column (60:40 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 229 nm, τ_{minor} = 19.5 min, τ_{major} = 36.6 min). See Supporting Information: Part B for HPLC chromatograms.

Q. Procedure for the deprotection of 4-methoxybenzyl group of 3aa:

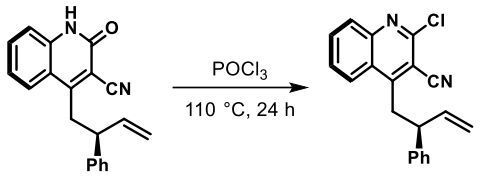


3aa (98:2 er) **3na**

In an oven dried 10 mL round-bottom flask, **3aa** (84.0 mg, 0.200 mmol, 1.0 equiv.) was taken in 2.0 mL of (9:1) CH_3CN/H_2O mixture. To this solution, ceric ammonium nitrate (CAN) (658.0 mg, 1.200 mmol, 6.0 equiv.) was added and the resulting solution stirred at 25 °C for 24 h. Reaction mixture was diluted with 2.0 mL of H_2O and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (1% MeOH in CH_2Cl_2) to obtain **3na** as a white solid (47.0 mg, 0.156 mmol, 78% yield) with 97:3 er. A single recrystallization from EtOH afforded **3na** with 99.5:0.5 er; **m.p.** 195-197 °C; **FT-IR (Thin film):** 2928 (w), 2227 (m), 1663 (s), 1601 (m), 1431 (m), 1036 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 12.76 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.70-7.66 (m, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.35-7.31 (m, 3H), 7.27-7.25 (m, 3H), 6.21-6.12 (m, 1H), 5.07 (d, *J* = 10.0 Hz, 1H), 4.96 (d, *J* = 17.1 Hz, 1H), 3.79 (dd, *J* = 14.9, 6.9 Hz, 1H), 3.66-3.60 (m, 1H), 3.55 (dd, *J* = 12.6, 6.7 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 160.9, 160.6, 141.9, 139.1, 139.0, 133.9, 129.1, 127.5, 127.4, 125.7, 123.9, 118.3, 117.9, 116.6, 115.2, 107.3, 51.0, 38.6; **HRMS (ESI+):** Calcd. for $C_{20}H_{16}N_2OH$ ($[M+H]^+$): 301.1341, Found: 301.1339; **Optical rotation:** $[\alpha]_D^{21}$ +20.2 (*c* 0.25, $CHCl_3$) for an enantiomerically enriched sample with 99.5:0.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (75:25 *n*-Hexane/EtOH, 1.0

mL/min, 20 °C, 231 nm, τ_{minor} = 9.3 min, τ_{major} = 10.3 min). See Supporting Information: Part B for HPLC chromatograms.

R. Procedure for the preparation of 2-chloroquinoline derivative 11:

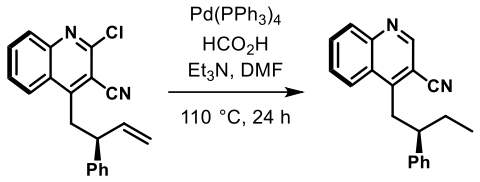


3na
(99.5:0.5 er)

11

In an oven dried 10 mL round-bottom flask, equipped with a reflux condenser, **3aa** (30.0 mg, 0.100 mmol, 1.0 equiv.) was taken in 0.8 mL of $POCl_3$ under argon. The resulting solution was refluxed at 110 °C for 24 h. The reaction mixture was evaporated to obtain a yellow residue which then diluted with 2.0 mL of H_2O and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). The combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (3% EtOAc in petroleum ether) to obtain **11** as a sticky white liquid (31.0 mg, 0.097 mmol, 97% yield); **FT-IR (Thin film):** 2924 (w), 2229 (m), 1564 (s), 1497 (m), 1315 (m), 1169 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.06 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.88-7.84 (m, 1H), 7.68-7.64 (m, 1H), 7.32-7.29 (m, 2H), 7.26-7.24 (m, 1H), 7.22-7.19 (m, 2H), 6.16 (ddd, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 4.88 (d, *J* = 17.0 Hz, 1H), 3.79-3.68 (m, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 156.8, 148.7, 148.0, 141.8, 138.9, 133.3, 129.9, 129.0, 128.4, 127.5, 127.4, 124.9, 124.7, 116.6, 115.1, 108.8, 51.5, 38.4; **HRMS (ESI+):** Calcd. for $C_{20}H_{15}ClN_2H$ ($[M+H]^+$): 319.1002, Found: 319.1003; **Optical rotation:** $[\alpha]_D^{21}$ –6.2 (*c* 2.0, $CHCl_3$) for an enantiomerically enriched sample with 99.5:0.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (99:1 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 245 nm, τ_{minor} = 12.7 min, τ_{major} = 13.9 min). See Supporting Information: Part B for HPLC chromatograms.

S. Procedure for the preparation of quinoline derivative 12:

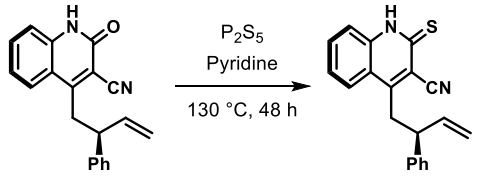


11
(99.5:0.5 er)

12

In an oven dried 10 mL round-bottom flask, **11** (25.0 mg, 0.078 mmol, 1.0 equiv.) was taken along with $Pd(PPh_3)_4$ (9.0 mg, 0.00784 mmol, 0.1) in 0.3 mL of dry DMF under argon. To this, HCO_2H (17 µL, 0.431 mmol, 5.5 equiv.) and Et_3N (175 µL, 1.254 mmol, 16.0 equiv.) were added and the resulting solution was refluxed at 110 °C for 24 h. The reaction mixture was diluted with 2.0 mL of H_2O and 5.0 mL of EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 5.0 mL). Combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (4-5% EtOAc in petroleum ether) to obtain **12** as a sticky white liquid (14.0 mg, 0.048 mmol, 62% yield); **FT-IR (Thin film):** 2924 (s), 2225 (m), 1572 (s), 1499 (s), 1455 (s), 1380 (m), 1029 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.87 (s, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.85-7.81 (m, 1H), 7.65-7.61 (m, 1H), 7.26-7.18 (m, 3H), 7.09-7.07 (m, 2H), 3.66 (dd, *J* = 13.3, 7.2 Hz, 1H), 3.50 (dd, *J* = 13.4, 7.7 Hz, 1H), 3.00-2.93 (m, 1H), 1.98-1.89 (m, 1H), 1.84-1.76 (m, 1H), 0.81 (t, *J* = 7.3 Hz, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 153.7, 150.0, 148.7, 142.7, 132.1, 130.7, 128.7, 128.1, 127.7, 127.0, 126.1, 124.7, 117.3, 107.6, 49.5, 39.3, 28.4, 12.4; **HRMS (ESI+):** Calcd. for $C_{20}H_{18}N_2H$ ($[M+H]^+$): 287.1548, Found: 287.1544; **Optical rotation:** $[\alpha]_D^{22}$ –29.2 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 99.5:0.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (99:1 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 233 nm, τ_{minor} = 21.1 min, τ_{major} = 25.9 min). See Supporting Information: Part B for HPLC chromatograms.

T. Procedure for the preparation of thiolactam 13:



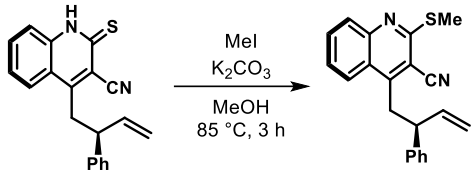
3na
(99.5:0.5 er)

13

In an oven dried 10 mL round-bottom flask, equipped with a reflux condenser, **3na** (29.0 mg, 0.098 mmol, 1.0 equiv.) was taken along with P_2S_5 (65.0 mg, 0.294 mmol, 3.0 equiv.) in 2.0

mL of pyridine under argon. The resulting solution was refluxed at 130 °C for 48 h. The reaction mixture was cooled to r.t., quenched with 2.0 mL of conc. HCl and diluted with 2.0 mL of H_2O and 5.0 mL of EtOAc. The organic phase was separated and the aqueous phase was extracted with EtOAc (2 × 5.0 mL). The combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (15% EtOAc in petroleum ether) to obtain **13** as a yellow sticky solid (22.0 mg, 0.070 mmol, 71% yield); **FT-IR (Thin film):** 2922 (m), 2225 (m), 1612 (s), 1568 (s), 1214 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 12.91 (s, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.73-7.69 (m, 1H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.43-7.39 (m, 1H), 7.34-7.30 (m, 2H), 7.26-7.24 (m, 3H), 6.21-6.12 (m, 1H), 5.07 (d, *J* = 10.1 Hz, 1H), 4.95 (d, *J* = 17.0 Hz, 1H), 3.80-3.74 (m, 1H), 3.65 (dd, *J* = 12.9, 8.7 Hz, 1H), 3.56 (dd, *J* = 12.9, 6.5 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 177.9, 155.7, 141.8, 139.2, 138.8, 134.5, 129.1, 127.5, 125.9, 125.8, 121.4, 117.2, 117.1, 116.8, 115.7, 51.2, 38.6; **HRMS (ESI+):** Calcd. for $C_{20}H_{16}N_2SH$ ($[M+H]^+$): 317.1112, Found: 317.1114; **Optical rotation:** $[\alpha]_D^{22}$ –17.3 (*c* 0.2, $CHCl_3$) for an enantiomerically enriched sample with 99.5:0.5 er. The enantiomeric ratio was determined by HPLC analysis using Phenomenex Cellulose-2 (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 303 nm, τ_{minor} = 18.8 min, τ_{major} = 23.1 min). See Supporting Information: Part B for HPLC chromatograms.

U. Procedure for the preparation of quinolone derivative 14:

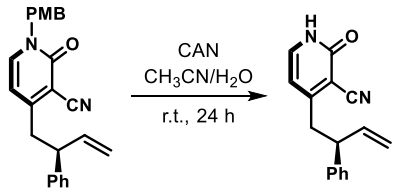


13 (99.5:0.5 er) **14**

In an oven dried 10 mL 2-necked round-bottom flask, equipped with a reflux condenser, **13** (21.0 mg, 0.065 mmol, 1.0 equiv.) was taken along with anh. K_2CO_3 (38.0 mg, 0.273 mmol, 4.2 equiv.) in 0.8 mL of dry MeOH under argon. To this solution, was added a solution of methyl iodide (17 µL, 0.273 mmol, 4.2 equiv.) in 0.2 mL of dry MeOH and the resulting solution was refluxed at 85 °C for 3 h. The reaction mixture was cooled to r.t. and concentrated under reduced pressure. The residue was dissolved in 5.0 mL of CH_2Cl_2 and washed with 5.0 mL of H_2O. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). The combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (10% EtOAc in petroleum ether) to obtain **14** as a yellow solid (20 mg, 0.061 mmol, 93% yield); **m.p.** 102-104 °C; **FT-IR (Thin film):** 2925 (m), 2221 (m), 1553 (s), 1301 (m), 1082 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.01-7.99 (m, 1H), 7.93 (d, *J* = 8.3 Hz, 1H),

7.80-7.76 (m, 1H), 7.55-7.51 (m, 1H), 7.35-7.32 (m, 2H), 7.28-7.24 (m, 3H), 6.21-6.13 (m, 1H), 5.03 (d, *J* = 10.2 Hz, 1H), 4.84 (d, *J* = 16.9 Hz, 1H), 3.81-3.74 (m, 1H), 3.69-3.60 (m, 2H), 2.74 (s, 3H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 159.3, 153.2, 148.5, 142.3, 139.2, 132.3, 129.3, 128.9, 127.5, 127.2, 126.4, 124.6, 123.5, 116.4, 115.8, 106.9, 51.3, 37.9, 13.4; **HRMS (ESI+):** Calcd. for $C_{21}H_{18}N_2SH$ ($[M+H]^+$): 331.1269, Found: 331.1265; **Optical rotation:** $[\alpha]_D^{22}$ +2.4 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 99.5:0.5 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IG column (95:5 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 267 nm, τ_{minor} = 6.5 min, τ_{major} = 6.9 min). See Supporting Information: Part B for HPLC chromatograms.

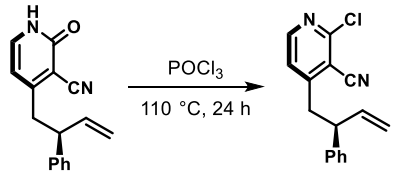
V. Procedure for the deprotection of 4-methoxybenzyl group of 3qa:



3qa **15**

In an oven dried 10 mL round-bottom flask, **3qa** (60.0 mg, 0.162 mmol, 1.0 equiv.) was taken in 2.0 mL of (9:1) CH_3CN/H_2O mixture. To this, ceric ammonium nitrate (CAN) (534.0 mg, 0.972 mmol, 6.0 equiv.) was added and the resulting solution stirred at 25 °C for 24 h. The reaction mixture was diluted with 2.0 mL of H_2O and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). The combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (32% EtOAc in petroleum ether) to obtain **15** as a yellow liquid (18 mg, 0.072 mmol, 44% yield); **FT-IR (Thin film):** 2922 (w), 2223 (m), 1648 (s), 1232 (m), 1163 (w); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 13.15 (s, 1H), 7.51 (d, *J* = 6.6 Hz, 1H), 7.32-7.29 (m, 2H), 7.24-7.19 (m, 3H), 6.13 (d, *J* = 6.6 Hz, 1H), 6.04 (ddd, *J* = 17.4, 10.1, 7.7 Hz, 1H), 5.11 (d, *J* = 10.2 Hz, 1H), 5.05 (d, *J* = 17.1 Hz, 1H), 3.71-3.65 (m, 1H), 3.22-3.17 (m, 1H), 3.11 (dd, *J* = 13.2, 7.9 Hz, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 163.6, 163.3, 141.6, 139.4, 138.3, 128.9, 127.6, 127.3, 116.2, 114.9, 109.3, 104.7, 49.9, 41.5; **HRMS (ESI+):** Calcd. for $C_{16}H_{14}N_2OH$ ($[M+H]^+$): 251.1184, Found: 251.1183; **Optical rotation:** $[\alpha]_D^{21}$ +18.9 (*c* 0.3, $CHCl_3$).

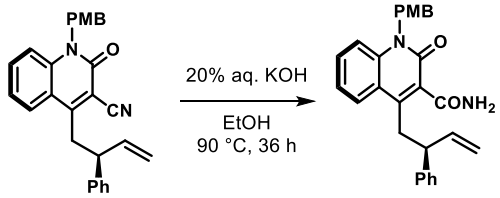
W. Procedure for the preparation of γ-allyl-2-chloropyridine 16:



15 **16**

In an oven dried 10 mL round-bottom flask, equipped with a reflux condenser, **15** (16.0 mg, 0.062 mmol, 1.0 equiv.) was taken in 2.0 mL of $POCl_3$ under argon. The resulting solution was refluxed at 110 °C for 24 h. The reaction mixture was concentrated under reduced pressure to obtain a yellow residue which diluted with 2.0 mL of H_2O and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (10% EtOAc in petroleum ether) to obtain **16** as a white sticky liquid (12.0 mg, 0.045 mmol, 72% yield); **FT-IR (Thin film):** 2924 (m), 2230 (m), 1580 (s), 1544 (s), 1378 (s), 922 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 8.36 (d, *J* = 4.5 Hz, 1H), 7.35-7.32 (m, 2H), 7.28-7.24 (m, 1H), 7.20-7.19 (m, 2H), 7.00 (d, *J* = 4.4 Hz, 1H), 6.11-6.02 (m, 1H), 5.14 (d, *J* = 10.2 Hz, 1H), 5.04 (d, *J* = 17.1 Hz, 1H), 3.72-3.66 (m, 1H), 3.35-3.29 (m, 1H), 3.27-3.21 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 156.8, 153.4, 151.5, 141.4, 139.2, 129.0, 127.6, 127.3, 123.6, 116.5, 114.1, 111.5, 50.4, 40.9; **HRMS (ESI+):** Calcd. for $C_{16}H_{13}ClN_2H$ ($[M+H]^+$): 269.0846, Found: 269.0844; **Optical rotation:** $[\alpha]_D^{22}$ –34.6 (*c* 1.0, $CHCl_3$).

X. Procedure for the preparation of amide 17:

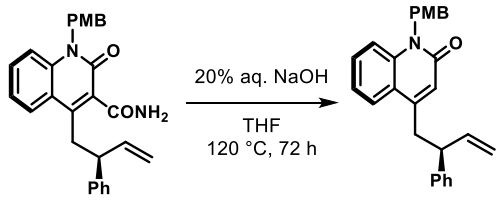


3aa (98:2 er) **17**

In an oven dried 10 mL round-bottom flask, equipped with a reflux condenser, **3aa** (114.0 mg, 0.271 mmol, 1.0 equiv.) was taken in 2.7 mL of EtOH. To this, 1.36 mL of 20% aqueous KOH solution was added and the resulting solution was refluxed at 90 °C for 36 h. The reaction mixture was concentrated under reduced pressure to obtain a yellow residue which diluted with 2.0 mL of H_2O and 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The

residue was purified by silica-gel flash column chromatography (20% EtOAc in dichloromethane) to obtain **17** as a yellow sticky liquid (81.0 mg, 0.185 mmol, 68% yield); **FT-IR (Thin film):** 3464 (w), 3309 (w), 2926 (m), 1676 (s), 1633 (s), 1583(s), 1249 (s), 919 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.87 (d, *J* = 7.9 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.36-7.34 (m, 1H), 7.30-7.24 (m, 3H), 7.23-7.21 (m, 1H), 7.17-7.11 (m, 4H), 6.84 (d, *J* = 8.2 Hz, 2H), 6.60 (s, 1H), 6.22-6.13 (m, 1H), 5.81 (s, 1H), 5.50 (s, 2H), 5.07 (d, *J* = 10.3 Hz, 1H), 5.03 (d, *J* = 17.4 Hz, 1H), 3.91-3.86 (m, 1H), 3.77 (s, 3H), 3.77-3.73 (m, 1H), 3.63-3.58 (m, 1H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 168.2, 160.3, 158.9, 149.9, 142.9, 140.3, 139.0, 131.6, 128.7, 128.0, 127.9, 127.9, 126.9, 126.7, 122.7, 120.4, 115.8, 115.3, 114.3, 55.4, 50.4, 45.8, 35.4; **HRMS (ESI+):** Calcd. for $C_{28}H_{26}N_2O_3H$ ($[M+H]^+$): 439.2022, Found: 439.2023; **Optical rotation:** $[\alpha]_D^{21}$ –56.9 (*c* 1.0, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (75:25 *n*-Hexane/ *i*-PrOH, 1.0 mL/min, 20 °C, 293 nm, τ_{major} = 28.5 min, τ_{minor} = 31.0 min). See Supporting Information: Part B for HPLC chromatograms.

Y. Procedure for the preparation of 18:



17 (98:2 er) **18**

In an oven dried 10 mL round-bottom flask, equipped with a reflux condenser, **17** (40.0 mg, 0.102 mmol, 1.0 equiv.) was taken in 2.0 mL of THF. To this, 2.0 mL of 20% aqueous NaOH solution was added and the resulting solution was refluxed at 120 °C for 72 h. The reaction mixture was acidified with 5.0 mL of 1 M HCl and diluted with 5.0 mL of CH_2Cl_2. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5.0 mL). Combined organic phase was washed with brine (5.0 mL), dried over anh. Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica-gel flash column chromatography (14% EtOAc in petroleum ether) to obtain **18** as a white sticky liquid (16.0 mg, 0.041 mmol, 40% yield); **FT-IR (Thin film):** 2924 (m), 2365 (w), 1655 (s), 1590 (m), 1511 (m), 1248 (m), 1031 (m); **^{1}H-NMR (400 MHz, $CDCl_3$):** δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.44-7.40 (m, 1H), 7.35-7.30 (m, 3H), 7.25-7.23 (m, 1H), 7.21-7.18 (m, 3H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 6.51 (s, 1H), 6.08 (ddd, *J* = 17.3, 10.2, 7.3 Hz, 1H), 5.52-5.42 (m, 2H), 5.09 (d, *J* = 10.2 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 3.77-3.72 (m, 1H), 3.76 (s, 3H), 3.29-3.19 (m, 2H); **^{13}C-NMR (100 MHz, $CDCl_3$):** δ 162.1, 158.8, 148.2, 142.9, 140.5, 139.5, 130.4, 128.9, 128.6, 127.9, 127.6, 127.0, 125.0, 122.1, 121.9, 120.9, 115.8, 115.7, 114.3, 55.4, 48.9, 45.3, 38.5;

HRMS (ESI+): Calcd. for $C_{27}H_{25}NO_2H$ ($[M+H]^+$): 396.1964, Found: 396.1961; **Optical rotation:** $[\alpha]_D^{21}$ –29.1 (*c* 0.5, $CHCl_3$) for an enantiomerically enriched sample with 98:2 er. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak IA column (75:25 *n*-Hexane/EtOH, 1.0 mL/min, 20 °C, 234 nm, τ_{minor} = 8.4 min, τ_{major} = 9.5 min). See Supporting Information: Part B for HPLC chromatograms.

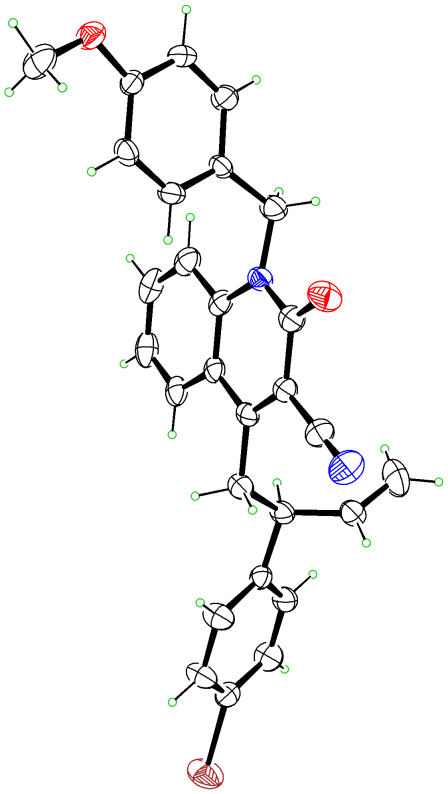
Z. Single crystal X-ray diffraction analysis of 3af:

A single crystal of **3af** (recrystallized from 5:1 *n*-Hexane/$CHCl_3$ at 0 °C) was mounted and the diffraction data were collected at 296 K on a Bruker SMART APEX CCD diffractometer using SMART/SAINT software. Intensity data were collected using graphite-monochromatized Mo-Kα radiation (0.71073 Å). The structures were solved by direct methods using the SHELX-97 and refined by full-matrix least-squares on F^2. Empirical absorption corrections were applied with SADABS. All Non-hydrogen atoms were refined anisotropically and hydrogen atoms were included in geometric positions. Structure was drawn using Olex-2 and ORTEP-3. The crystallographic refinement parameters are given below:

Table 1. Crystal data and structure refinement for **3af**

Identification code	**3af**
CCDC	1895445
Empirical formula	$C_{28}H_{23}BrN_2O_2$
Formula weight	499.39
Temperature/K	296(2)
Crystal system	monoclinic
Space group	$P2_1$
a	5.6996(4) Å
b	7.7973(5) Å
c	26.3857(17) Å
α	90°.
β	90.373(2)°.
γ	90°.
Volume	1172.59(13) $Å^3$
Z	2
Density (calculated)	1.414 Mg/m^3
Absorption coefficient	1.781 mm^{-1}
F(000)	512.0
Crystal size	0.25 × 0.15 × 0.12 mm^3

Radiation	MoKα (λ = 0.71073)
Theta range for data collection	6.07 to 55.112°.
Index ranges	$-7 \leq h \leq 7$, $-10 \leq k \leq 10$, $-34 \leq l \leq 34$
Reflections collected	37814
Independent reflections	5415 [R(int) = 0.0931]
Data/restraints/parameters	5415/1/299
Goodness-of-fit on F^2	1.001
Final R indexes [I>=2σ (I)]	R_1 = 0.0522, wR_2 = 0.0824
Final R indexes [all data]	R_1 = 0.1302, wR_2 = 0.1010
Largest diff. peak and hole	0.23 and -0.24 e.Å^{-3}
Flack parameter	0.044(7)



ORTEP representation of the X-ray structure of enantiopure **3af** (thermal ellipsoids at 30% probability)