Supplementary Information

Asymmetric addition of N-methyl C(sp³)–H bond to cyclic alkenes enabled by an iridium/phosphine-olefin catalyst

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1. **General information**

All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under pre-dried nitrogen. NMR spectra were recorded on either a JEOL JNM ECZ-400 spectrometer (400 MHz for 1H, 100 MHz for 13C) or a Bruker Avance III HD 400 spectrometer (400 MHz for 1H, 100 MHz for 13C). Chemical shifts are reported in \( \delta \) (ppm) referenced to the residual peaks of CDCl\(_3\) (\( \delta \) 7.26) for 1H NMR, and CDCl\(_3\) (\( \delta \) 77.00) for 13C NMR. The following abbreviations are used; s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet; br, broad. Optical rotations were measured on a JASCO P-2200 polarimeter. High-resolution mass spectra were obtained with JEOL AccuTOF LC-plus 4G spectrometer. Flash column chromatography was performed with Silica Gel 60 N (Wako). Preparative thin-layer chromatography was performed with Wakogel® B-5F (Wako).

2. **Materials**

Dehydrated solvents were purchased and used after being deoxygenated by bubbling N\(_2\). [IrCl(coe)\(_2\)]\(_2\) and NaBAr\(_4\) [Ar\(_4\) = 3,5-(CF\(_3\))\(_2\)C\(_6\)H\(_3\)]\(_2\) were prepared according to the reported procedures.

3. **Preparation of substrates 1 and 2**

Compounds 1a (CAS: 1036584-14-1), 1b (CAS: 468718-67-4), 1c (CAS: 103976-61-0), 1d (CAS: 1251349-49-1), 1e (CAS: 156267-13-9), 1g (937602-15-8), 1a-d, 2b (CAS: 78383-19-4), 2c (CAS: 2576641-39-7), 2d (CAS: 2576641-40-0), 2e (CAS: 2576641-41-1), 2f, 2g (CAS: 2576641-44-4), 2h, 2i, 2m (CAS: 4453-90-1), 2n (CAS: 75715-21-8), 2q (CAS: 19345-99-4), and 2r (CAS: 912329-24-9) were prepared according to the reported procedures. Compounds 2j, 2k, and 2o (CAS: 62791-44-0) were prepared as shown below. Other chemicals were purchased from commercial suppliers and used as received.

![Chemical structure](image)

To a solution of 4-bromoindanone (2.1 g, 10 mmol) in THF (20 mL) and MeOH (20 mL) was added NaBH\(_4\) (378 mg, 10 mmol, 1.0 equiv) at 0 °C and the mixture was stirred at the same temperature for 3 h. The reaction was quenched with NH\(_4\)Claq, and the resulting mixture was extracted with EtOAc (x3). The combined organic layer was dried over Na\(_2\)SO\(_4\), filtered, and concentrated on a rotary evaporator. The residue was passed through a short column of silica gel with EtOAc as an eluent, and the filtrate was concentrated on a rotary evaporator. The residue was subjected to the next reaction without further purifications. The residue and \(N,N\)-
diisopropylethylamine (DIPEA, 5.1 mL, 30 mmol, 2.0 equiv) were dissolved in CH$_2$Cl$_2$ (15 mL). Chloromethyl methyl ether (MOMCl, 1.8 mL, 24 mmol, 1.2 equiv) was added dropwise to the solution at 0 ºC under N$_2$, and the mixture was stirred at room temperature for 24 h. The reaction was quenched with H$_2$O, and the aqueous layer was extracted with CH$_2$Cl$_2$ (x3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (20:1) to give 4-bromo-2,3-dihydro-1-(methoxymethoxy)-1H-indene (2.52 g, 80% yield). To a suspension of Mg turnings (280 mg, 11.5 mmol, 1.2 equiv) in a small amount of THF was added 4-bromo-2,3-dihydro-1-(methoxymethoxy)-1H-indene (2.47 g, 9.6 mmol) in THF (10 mL) dropwise under N$_2$, and the resulting solution was stirred at room temperature for 2 h. BnBr (1.70 mL, 14.4 mmol, 1.5 equiv) and CuBr•SMe$_2$ (19.7 mg, 0.096 mmol, 1 mol%) were added to the mixture at 0 ºC, and the mixture was stirred at room temperature for 15 h. The reaction was quenched with NH$_4$Claq, and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (20:1) to give 4-benzyl-2,3-dihydro-1-(methoxymethoxy)-1H-indene (1.24 g, 4.6 mmol, 48% yield). A mixture of 4-benzyl-2,3-dihydro-1-(methoxymethoxy)-1H-indene (1.07 g, 4.0 mmol) and PPTS (2.01 g, 8.0 mmol, 2.0 equiv) in 1,2-dichloroethane (20 mL) was heated to 90 ºC and stirred overnight. The reaction was quenched with H$_2$O, and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane to give 7-benzylindene (2j) (685 mg, 3.3 mmol, 83% yield).

To a solution of 4-bromo-2,3-dihydro-1-(methoxymethoxy)-1H-indene (1.29 g, 5 mmol) in THF was added dropwise BuLi (15 w/w% hexane solution, 3.8 mL, 6 mmol, 1.2 equiv) at −78 ºC under N$_2$, and the resulting mixture was stirred at the same temperature for 1 h. Chlorotrimethylsilane (TMSCl, 0.79 mL, 7.0 mmol, 1.3 equiv) was added dropwise to the mixture at −78 ºC, and the mixture was stirred overnight. The reaction was quenched with H$_2$O, and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane/EtOAc (20:1) to give 2,3-dihydro-1-(methoxymethoxy)-4-trimethylsilyl-1H-indene (554 mg, 2.2 mmol, 55% yield). The mixture of 2,3-dihydro-1-(methoxymethoxy)-4-trimethylsilyl-1H-indene (554 mg, 2.2 mmol) and pyridinium p-toluene sulfonate (PPTS, 1.10 g, 4.4 mmol, 2.0 equiv) in 1,2-dichloroethane (10 mL) was heated to 90 ºC and stirred overnight. The reaction was quenched with H$_2$O, and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated on a
rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane to give 7-benzylindene (2j, 160 mg, 0.85 mmol, 39% yield).

Carbic anhydride was prepared according to the reported procedure. To a solution of LiAlH₄ (797 mg, 21 mmol, 2.1 equiv) in THF (20 mL) was added carbic anhydride (1.64 g, 10 mmol) in portions at 0 °C, and the resulting mixture was stirred at room temperature overnight. The reaction was quenched by adding H₂O (0.8 mL) slowly, 15% NaOH (0.8 mL), and then, H₂O (2.4 mL) at 0 °C. The mixture was stirred at room temperature for 2 h. The resulting precipitate was removed through a pad of celite eluted with Et₂O. The filtrate was concentrated on a rotary evaporator and the residue was used for the next reaction without further purification. To a solution of the residue, 4-dimethylaminopyridine (DMAP, 12.2 mg, 0.10 mmol, 10 mol%), and NEt₃ (4.2 mL, 30 mmol, 3.0 equiv) in CH₂Cl₂ (50 mL) was added Ac₂O (2.8 mL, 30 mmol, 3.0 equiv) dropwise at 0 °C. The resulting mixture was stirred overnight at room temperature. The reaction was quenched with H₂O, and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography on silica gel with hexane/EtOAc to give 2o (2.19 g, 9.2 mmol, 92% yield).

4. Characterization of substrates

\[ \text{2f} \]

\(^1\)H NMR (CDCl₃) \(\delta\) 7.43 (dd, \(J = 7.4, 1.0\) Hz, 1H), 7.43–7.32 (m, 2H), 7.25 (d, \(J = 7.6\) Hz, 1H), 7.15 (d, \(J = 8.0\) Hz, 1H), 7.11 (t, \(J = 2.0\) Hz, 1H), 6.95 (td, \(J = 5.6, 2.0\) Hz, 1H), 6.93 (dd, \(J = 8.0, 2.8\) Hz, 1H), 6.59 (td, \(J = 5.6, 2.0\) Hz, 1H), 3.86 (s, 3H), 3.50 (t, \(J = 2.0\) Hz, 2H); \(^{13}\)C NMR (CDCl₃) \(\delta\) 159.6, 145.4, 142.6, 141.2, 137.7, 134.4, 132.0, 129.4, 126.9, 120.9, 120.2, 114.1, 112.5, 55.2, 39.1. HRMS (DART) m/z: [M + H]^+ Calcd for C₁₆H₁₅O₂ 223.1123; Found 223.1117.

\[ \text{2h} \]

\(^1\)H NMR (CDCl₃) \(\delta\) 7.45 (d, \(J = 7.2\) Hz, 1H), 7.46–7.29 (m, 3H), 7.19 (d, \(J = 7.6\) Hz, 1H), 7.08 (d, \(J = 8.8\) Hz, 1H), 7.03 (d, \(J = 8.8\) Hz, 1H), 6.96 (d, \(J = 5.6\) Hz, 1H), 6.58 (d, \(J = 5.6\) Hz, 1H), 3.80
(s, 3H), 3.33 (s, 2H); $^{13}$C NMR (CDCl$_3$) δ 156.4, 144.6, 142.8, 134.6, 134.4, 131.9, 131.0, 129.9, 128.7, 126.3, 126.2, 120.4, 120.1, 110.8, 55.3, 38.8. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{15}$O$_2$ 223.1123; Found 223.1123.

![Structure 2i]

$^1$H NMR (CDCl$_3$) δ 7.72 (s, 1H), 7.62 (d, $J = 8.0$ Hz, 2H), 7.52 (dd, $J = 7.6$, 2.0 Hz, 1H), 7.49–7.40 (m, 3H), 7.33 (t, $J = 7.4$ Hz, 1H), 6.92 (dt, $J = 5.6$, 2.0 Hz, 1H), 6.60 (dt, $J = 5.6$, 2.0 Hz, 1H), 3.48 (s, 2H); $^{13}$C NMR (CDCl$_3$) δ 145.9, 143.4, 140.6, 140.3, 139.3, 134.4, 131.8, 127.1, 124.7, 124.2, 123.5, 122.0, 121.4, 121.1, 40.2. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{17}$H$_{13}$S$_1$ 249.0738; Found 249.0732.

![Structure 2j]

$^1$H NMR (CDCl$_3$) δ 7.33–7.21 (m, 4H), 7.24–7.15 (m, 3H), 7.01 (d, $J = 7.6$ Hz, 1H), 6.89 (dt, $J = 5.6$, 2.0 Hz, 1H), 6.53 (dt, $J = 5.6$, 2.0 Hz, 1H), 4.08 (s, 2H), 3.26 (t, $J = 2.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$) δ 144.9, 142.3, 140.2, 135.9, 133.8, 132.2, 128.8, 128.4, 126.8, 126.0, 125.7, 119.3, 39.5, 37.9. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{16}$H$_{15}$O$_2$ 207.1174; Found 207.1181.

![Structure 2k]

$^1$H NMR (CDCl$_3$) δ 7.42 (dd, $J = 7.2$, 1.2 Hz, 1H), 7.35 (dd, $J = 7.2$, 1.2 Hz, 1H), 7.27 (t, $J = 7.2$ Hz, 1H), 6.90 (dt, $J = 5.4$, 2.0 Hz, 1H), 6.58 (dt, $J = 5.4$, 2.0 Hz, 1H), 3.44 (t, $J = 2.0$ Hz, 2H), 0.35 (s, 9H); $^{13}$C NMR (CDCl$_3$) δ 144.9, 143.8, 134.0, 132.0, 130.1, 125.7, 121.9, 40.2, 18.4, −0.76. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{12}$H$_{17}$Si$_1$ 189.1099; Found 189.1094.

![Structure 1a-d]

$^1$H NMR (CDCl$_3$) δ 7.64 (d, $J = 8.0$ Hz, 1H), 6.60 (dd, $J = 8.0$, 4.8 Hz, 1H), 8.29 (d, $J = 4.8$ Hz, 1H), 4.90 (bs, 1H); $^{13}$C NMR (CDCl$_3$) δ 155.2, 151.6, 134.8 (q, $J_{F-C} = 5$ Hz), 124.5 (q, $J_{F-C} = 270$ Hz).
Hz), 111.0, 108.6 (q, $J_{F-C} = 31$ Hz), 27.8 (sept, $J_{D-C} = 21$ Hz). HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_7$H$_5$F$_3$N$_2$ 180.0824; Found 180.0828.

5. **General procedure for Table 1 and Scheme 2**

A mixture of [IrCl(coe)$_2$]$_2$ (2.2 mg, 0.0025 mmol, 5 mol% Ir), ligand (6 mol%), and NaBAr$_4$ (9.2 mg, 0.010 mmol, 10 mol%) in toluene (0.2 mL) in a Schlenk tube was stirred at room temperature for 10 min under N$_2$, and then, 2-(N-methylamino)pyridine 1 (0.10 mmol) and indene (2a, 34.8 mg, 0.30 mmol) were added to the mixture. The mixture was stirred at 100 ºC for 18 h. After the reaction mixture was concentrated on a rotary evaporator, the residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give the addition product including a small amount of impurities. The mixture was subjected again to preparative TLC on silica gel eluted with hexane/CH$_2$Cl$_2$ (2:1) to give the product 3aa.

6. **General procedure for Scheme 3**

A mixture of [IrCl(coe)$_2$]$_2$ (4.5 mg, 0.0050 mmol, 10 mol% Ir), L1 (8.3 mg, 0.012 mmol, 12 mol%), and NaBAr$_4$ (18.4 mg, 0.020 mmol, 20 mol%) in toluene (0.2 mL) in a Schlenk tube was stirred at room temperature for 10 min under N$_2$, and then, 2-(N-methylamino)pyridine (1a, 17.8 mg, 0.10 mmol) and cyclic alkenes 2 (0.12–0.30 mmol) were added to the mixture. The mixture was stirred at 100 ºC for 18 h. After the reaction mixture was concentrated on a rotary evaporator, the residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give the addition product including a small amount of impurities. The mixture was subjected again to preparative TLC on silica gel eluted with hexane/CH$_2$Cl$_2$ (2:1) to give the product 3.
7. Unsuccessful substrates for Scheme 3

The above alkenes gave no addition product except for \( S2e \) and \( S2q \). \( S2e \) underwent the addition to give two regioisomers. \( S2q \) gave the corresponding addition product, but we failed to determine the ee by chiral HPLC analysis.

8. Procedure for Scheme 4

A mixture of \( 3aa \) (87.7 mg, 0.30 mmol, 91% ee), CICF\(_2\)COONa\(^{10} \) (68.6 mg, 0.45 mmol, 1.5 equiv), and 18-crown-6 (15.8 mg, 0.060 mmol, 20 mol%) in CHCN\(_3\) (1.2 mL, 0.25 M) was stirred at 120 °C for 3 h. Then, CICF\(_2\)COONa (1.5 equiv) was added to the mixture every 3 h twice during the mixture was heated at 120 °C. After cooling to room temperature, 1% KHSO\(_4\) aq (0.7 mL, 30 mol%) was added to the mixture and the resulting mixture was stirred at 100 °C overnight. The reaction mixture was basified by the addition of 1N NaOH and the aqueous layer was extracted with EtOAc (x3). The combined organic layer was dried over Na\(_2\)SO\(_4\), filtered, and concentrated on a rotary evaporator. The residue containing amine 4 was used for the following reactions without further purification.

To the mixture of amine 4, NEt\(_3\) (83 µL, 0.60 mmol, 2.0 equiv), and DMAP (3.6 mg, 0.0030 mmol, 10 mol%) in CH\(_2\)Cl\(_2\) (1.1 mL, 0.27 M) was added dropwise Ac\(_2\)O (28 µL, 0.30 mmol, 1.0 equiv) at 0 °C and the mixture was stirred at rt for 1 h. The reaction was quenched by adding H\(_2\)O, and the resulting mixture was extracted with CH\(_2\)Cl\(_2\) (x3). The combined organic layer was dried over Na\(_2\)SO\(_4\), filtered, and concentrated on a rotary evaporator. The residue was subjected to preparative TLC on silica gel eluted with hexane/Acetone (2:1) to give the acetyl amine 5 (colorless solid, 23.0 mg, 40% yield, 91% ee).
3aa (42.9 mg, 0.15 mmol) was transformed into 4 according to the same procedure as above. To the mixture of amine 4 and NEt₃ (26 µL, 0.18 mmol, 1.3 equiv) in CH₂Cl₂ was added dropwise Tf₂O (25 µL, 0.15 mmol, 1.0 equiv) at −78 °C and the mixture was stirred at −78 °C for 2 h. The reaction was quenched with H₂O, and the resulting mixture was extracted with CH₂Cl₂ (x3). The combined organic layer was dried over Na₂SO₄, filtered, and concentrated on a rotary evaporator. The residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give the trifluoromethyl sulfonyl amine 6 (colorless solid, 8.3 mg, 20% yield, 91% ee). The absolute configuration of trifluoromethylsulfonylamine 6 was determined to be S-(+) by the comparison of its specific rotation with that of the previously reported one.¹¹

9. Procedure for Scheme 5a

A mixture of [IrCl(coe)₂]: (4.5 mg, 0.0050 mmol, 10 mol% Ir), L₁ (8.3 mg, 0.012 mmol, 12 mol%), and NaBArF₄ (18.4 mg, 0.020 mmol, 20 mol%) in toluene (0.2 mL) in a Schlenk tube was stirred at room temperature for 10 min under N₂, and then, 1a-d₃ (17.9 mg, 0.10 mmol) and indene 2a (34.8 mg, 0.30 mmol) were added to the mixture. The reaction mixture was stirred at 100 °C for 18 h. After the reaction mixture was concentrated on a rotary evaporator, the residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give 3aa-d (25.8 mg, 87% yield). The deuterium content of 3aa-d was determined by ¹H NMR. ¹H NMR (CDCl₃) δ 8.28 (d, J = 5.0 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.38–7.10 (m, 4H), 6.62 (dd, J = 7.6, 5.0 Hz, 1H), 5.00 (bs, 1H), 3.90–3.76 (m, 0.88H), 3.75–3.60 (m, 0.92H), 3.60–3.48 (m, 0.87H), 3.10–2.80 (m, 1.84H), 2.41–2.25 (m, 1H), 1.95–1.83 (m, 0.78H).

10. Procedure for Scheme 5b

A mixture of [IrCl(coe)₂]: (4.5 mg, 0.0050 mmol, 10 mol% Ir), L₁ (8.3 mg, 0.012 mmol, 12 mol%), and NaBArF₄ (18.4 mg, 0.020 mmol, 20 mol%) in toluene (0.2 mL) in a Schlenk tube was stirred at room temperature for 10 min under N₂, and then, 2-(N-methylamino)pyridine (1a, 17.8 mg, 0.10 mmol) and 6-phenylindene (2r, 57.6 mg, 0.30 mmol) were added to the mixture. The mixture was stirred at 100 °C for 18 h. After the reaction mixture was concentrated on a rotary evaporator, the residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give the addition product including a small amount of impurities. The mixture was subjected again to preparative TLC on silica gel eluted with hexane/CH₂Cl₂ (2:1) to give a mixture of 3ar and 3ar¹. ¹H NMR (CDCl₃) δ 8.29 (d, J = 4.8 Hz, 1H, overlapped), 7.66 (d, J = 7.2 Hz, 1H, overlapped), 7.63–7.54 (m, 2H, overlapped), 7.53 (s, 0.41H, minor), 7.49 (s, 0.59H, major), 7.48–7.39 (m, 3H, overlapped), 7.39–7.29 (m, 2H, overlapped), 6.63 (dd, J = 7.2, 4.8 Hz, 1H, overlapped), 5.06 (bs, 1H, overlapped), 3.96–3.84 (m, 0.41H, minor), 3.78–3.86 (m, 0.59H, major), 3.78–3.64 (m, 1H, overlapped), 3.68–3.54 (m, 1H, overlapped), 3.12–2.86 (m, 2H, overlapped), 2.46–2.32 (m, 1H, S-8
overlapped), 2.02–1.88 (m, 1H, overlapped). HRMS (ESI) m/z: [M + Na]⁺ Calcd for C₂₂H₁₀F₃N₂Na₁ 391.1400; Found 391.1398.

11. Procedure for Scheme 5c and 5d

A mixture of [IrCl(coe)₂]₂ (2.2 mg, 0.0025 mmol, 5 mol% Ir), L₁ (4.5 mg, 0.0060 mmol, 6 mol%), and NaBAR₄ (9.2 mg, 0.010 mmol, 10 mol%) in toluene (0.2 mL) in a Schlenk tube was stirred at room temperature for 10 min under N₂, and then, indene 2 (0.10 mmol) were added to the mixture. The reaction mixture was stirred at 100 °C for 30 min. After the reaction mixture was concentrated on a rotary evaporator, the residue was subjected to preparative TLC on silica gel eluted with hexane/EtOAc (10:1) to give indene 2 and 2’. The ratio of 2 to 2’ was determined by ¹H NMR. Scheme 5c: ¹H NMR (CDCl₃) δ 7.72 (s, 0.67H, 2r), 7.65–7.59 (m, 2.33H, 2r+2r’), 7.56–7.49 (m, 1H, overlapped), 7.49–7.40 (m, 3H, overlapped), 6.96–6.89 (m, 1H, overlapped), 6.64–6.57 (m, 1H, overlapped), 3.47 (s, 1.33H, 2r), 3.45 (s, 0.67H, 2r’). Scheme 5d: ¹H NMR (CDCl₃) δ 7.50–7.19 (m, 7H, overlapped), 7.10–7.04 (m, 0.37H, 2c’), 6.98–6.89 (m, 0.63H, 2c), 6.62–6.55 (m, 1H, overlapped), 3.52–3.48 (m, 2H, overlapped), 2.42 (s, 3H, overlapped).
12. References
13. Characterization of the products

**Compound 3aa** (Scheme 2: colorless solid, 25.8 mg, 88% yield, 91% ee). The ee was measured by HPLC (Chiralcel OJ-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_1 = 16.6 min (minor), t_2 = 18.4 min (major)): [α]^{25}_D = -36 (c 0.95, CHCl_3) for 91% ee (S). ¹H NMR (CDCl_3) δ 8.27 (d, J = 5.0 Hz, 1H), 7.64 (d, J = 6.8 Hz, 1H), 7.31–7.23 (m, 2H), 7.23–7.14 (m, 2H), 6.61 (dd, J = 6.8, 5.2 Hz, 1H), 4.99 (bs, 1H), 3.85–3.73 (m, 1H), 3.66 (ddd, J = 12.6, 7.2, 4.8 Hz, 1H), 3.59–3.48 (m, 1H), 3.00 (ddd, J = 14.8, 8.0, 6.8 Hz, 1H), 2.89 (ddd, J = 14.8, 8.4, 6.4 Hz, 1H), 2.49–2.26 (m, 1H), 1.96–1.84 (m, 1H); ¹³C NMR (CDCl_3) δ 154.7, 151.7, 144.5, 144.3, 134.9 (q, J_F–C = 5 Hz), 126.9, 126.2, 124.7, 124.4 (q, J_F–C = 270 Hz), 124.1, 111.2, 108.5 (q, J_F–C = 32 Hz), 45.3, 44.3, 31.2, 29.9. HRMS (DART) m/z: [M + H]^+ Calcd for C_{16}H_{16}F_{3}N_{2} 293.1266; Found 293.1258.

**Compound 3ba** (Scheme 2: colorless oil, 12.1 mg, 47% yield, 88% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_1 = 27.2 min (major), t_2 = 34.4 min (minor)): [α]^{25}_D = -21 (c 0.51, CHCl_3) for 88% ee (S). ¹H NMR (CDCl_3) δ 8.04 (dd, J = 5.2, 2.0 Hz, 1H), 7.44 (dd, J = 7.6, 2.0 Hz, 1H), 7.36–7.20 (m, 2H), 7.26–7.10 (m, 2H), 6.52 (dd, J = 7.6, 5.2 Hz, 1H), 5.10 (bs, 1H), 3.82–3.69 (m, 1H), 3.64 (ddd, J = 12.8, 6.8, 5.6 Hz, 1H), 3.59–3.47 (m, 1H), 3.08–2.94 (m, 1H), 2.89 (ddd, J = 15.4, 8.8, 6.4 Hz, 1H), 2.40–2.26 (m, 1H), 1.98–1.86 (m, 1H); ¹³C NMR (CDCl_3) δ 154.1, 146.0, 144.7, 144.4, 135.9, 126.9, 126.2, 124.5 (q, J_F–C = 270 Hz), 124.1, 115.4, 112.7, 45.3, 44.5, 31.2, 29.9. HRMS (DART) m/z: [M + H]^+ Calcd for C_{15}H_{16}Cl_{1}N_{2} 259.1002; Found 259.0990.

**Compound 3ca** (Scheme 2: colorless oil, 7.0 mg, 24% yield, 87% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_1 = 22.1 min (minor), t_2 = 23.9 min (major)): [α]^{25}_D = -37 (c 0.35, CHCl_3) for 87% ee (S). ¹H NMR (CDCl_3) δ 8.28
(dd, \( J = 5.2, 2.0 \text{ Hz}, 1H \)), 8.16 (bs, 1H), 8.13 (dd, \( J = 7.6, 2.0 \text{ Hz}, 1H \)), 7.38–7.30 (m, 1H), 7.24 (d, \( J = 4.0 \text{ Hz}, 1H \)), 7.22–7.13 (m, 2H), 6.52 (dd, \( J = 7.6, 5.2 \text{ Hz}, 1H \)), 4.32 (q, \( J = 7.2 \text{ Hz}, 2H \)), 3.95–3.83 (m, 1H), 3.60 (ddd, \( J = 12.6, 7.6, 5.2 \text{ Hz}, 1H \)), 3.59–3.47 (m, 1H), 3.01 (ddd, \( J = 16.2, 8.8, 6.0 \text{ Hz}, 1H \)), 2.95–2.81 (m, 1H), 2.42–2.28 (m, 1H), 1.98–1.85 (m, 1H), 1.37 (t, \( J = 7.2 \text{ Hz}, 3H \)); \(^{13}\text{C NMR (CDCl}_3 \)) \( \delta \) 167.5, 158.8, 153.5, 144.9, 144.3, 140.0, 126.8, 126.2, 124.6, 124.2, 110.8, 106.1, 60.7, 45.2, 44.7, 31.2, 30.3, 14.3. HRMS (DART) m/z: [M + H]^+ Calcd for C\(_{18}H_{27}N_2O_2\) 297.1603; Found 297.1590.

Compound 3ab (Scheme 3: colorless oil, 23.9 mg, 65% yield, 88% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, \( t_1 = 17.8 \text{ min (major)} \), \( t_2 = 20.5 \text{ min (minor)} \)): [\( \alpha \)]\(^{25}\text{D} \) = 77 (c 1.13, CHCl\(_3 \)) for 88% ee (S). \(^1\text{H NMR (CDCl}_3 \)) \( \delta \) 8.30 (d, \( J = 5.0 \text{ Hz}, 1H \)), 7.66 (d, \( J = 7.2 \text{ Hz}, 1H \)), 7.48–7.40 (m, 4H), 7.32–7.38 (m, 1H), 7.31–7.24 (m, 3H), 6.63 (dd, \( J = 7.2, 5.0 \text{ Hz}, 1H \)), 5.05 (bs, 1H), 3.92–3.81 (m, 1H), 3.71 (ddd, \( J = 12.6, 7.2, 5.2 \text{ Hz}, 1H \)), 3.66–3.54 (m, 1H), 3.07 (ddd, \( J = 16.0, 8.4, 6.4 \text{ Hz}, 1H \)), 2.93 (ddd, \( J = 16.0, 8.8, 6.0 \text{ Hz}, 1H \)), 2.38–2.23 (m, 1H), 1.96–1.82 (m, 1H); \(^{13}\text{C NMR (CDCl}_3 \)) \( \delta \) 154.7, 151.7, 145.3, 142.0, 141.2, 138.6, 134.9 (q, \( J_{F-C} = 5 \text{ Hz} \)), 128.5, 128.2, 127.5, 126.9, 124.5 (q, \( J_{F-C} = 270 \text{ Hz} \)), 123.1, 111.3, 108.5 (q, \( J_{F-C} = 32 \text{ Hz} \)), 45.3, 44.6, 31.1, 30.2. HRMS (DART) m/z: [M + H]^+ Calcd for C\(_{22}H_{20}F_3N_2\) O \( \delta \) 369.1579; Found 369.1592.

Compound 3ac (Scheme 3: colorless oil, 23.4 mg, 61% yield, 87% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, \( t_1 = 16.0 \text{ min (major)} \), \( t_2 = 19.8 \text{ min (minor)} \)): [\( \alpha \)]\(^{25}\text{D} \) = –77 (c 1.16, CHCl\(_3 \)) for 87% ee (S). \(^1\text{H NMR (CDCl}_3 \)) \( \delta \) 8.28 (d, \( J = 4.4 \text{ Hz}, 1H \)), 7.65 (dd, \( J = 7.6, 1.2 \text{ Hz}, 1H \)), 7.34 (d, \( J = 7.6 \text{ Hz}, 2H \)), 7.30–7.19 (m, 5H), 6.62 (dd, \( J = 7.6, 4.4 \text{ Hz}, 1H \)), 5.04 (bs, 1H), 3.92–3.78 (m, 1H), 3.70 (ddd, \( J = 12.6, 7.2, 5.2 \text{ Hz}, 1H \)), 3.64–3.51 (m, 1H), 3.06 (ddd, \( J = 16.0, 8.0, 6.6 \text{ Hz}, 1H \)), 2.92 (ddd, \( J = 16.0, 8.8, 6.0 \text{ Hz}, 1H \)), 2.40 (s, 3H), 2.36–2.22 (m, 1H), 1.94–1.82 (m, 1H); \(^{13}\text{C NMR (CDCl}_3 \)) \( \delta \) 154.7, 151.7, 145.3, 141.9, 138.6, 138.2, 136.6, 134.9 (q, \( J_{F-C} = 5 \text{ Hz} \)), 128.4, 127.5, 126.9, 125.8, 124.5 (q, \( J_{F-C} = 269 \text{ Hz} \)), 122.9,
111.2, 108.5 (q, J_F-C = 31 Hz), 45.3, 44.6, 31.1, 30.2, 21.2. HRMS (DART) m/z: [M + H]^+ Calcd for C_{23}H_{22}F_3N_2 383.1735; Found 383.1724.

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\text{Compound 3ad (Scheme 3: colorless oil, 23.1 mg, 60\% yield, 90\% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_l = 15.8 min (major), t_r = 24.3 min (minor)): } [\alpha]^{25}_D = -75 (c 1.13, CHCl}_3) \text{ for 90\% ee (S).} \]

\[^{1}H \text{ NMR (CDCl}_3) \delta 8.28 (d, J = 5.0 Hz, 1H), 7.65 (d, J = 7.8, 1H), 7.39 (d, J = 8.8 Hz, 1H), 7.38 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 2.4 Hz, 1H), 7.26 (d, J = 5.9 Hz, 1H), 7.20 (dd, J = 5.9, 2.4 Hz, 1H), 7.11 (d, J = 8.8 Hz, 1H), 7.09 (d, J = 8.8 Hz, 1H), 6.62 (dd, J = 7.8, 5.0 Hz, 1H), 5.02 (bs, 1H), 3.91–3.80 (m, 1H), 3.70 (ddd, J = 12.6, 7.4, 5.0 Hz, 1H), 3.63–3.53 (m, 1H), 3.01 (ddd, J = 16.0, 8.0, 6.8 Hz, 1H), 2.89 (ddd, J = 16.0, 8.8, 6.0 Hz, 1H), 2.37–2.22 (m, 1H), 1.95–1.81 (m, 1H); ^{13}C \text{ NMR (CDCl}_3) \delta 154.7, 151.7, 145.4, 141.9, 137.6, 137.1 (d, J_F-C = 3 Hz), 135.0 (q, J_F-C = 5 Hz), 130.0 (d, J_F-C = 8 Hz), 127.4, 127.0, 124.5 (q, J_F-C = 271 Hz), 123.2, 115.1 (d, J_F-C = 21 Hz), 111.3, 108.5 (q, J_F-C = 31 Hz), 45.3, 44.6, 31.1, 30.1. HRMS (DART) m/z: [M + H]^+ Calcd for C_{22}H_{19}F_4N_2 387.1484; Found 387.1496.

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\text{Compound 3ae (Scheme 3: colorless oil, 16.0 mg, 40\% yield, 88\% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_l = 14.7 min (major), t_r = 18.5 min (minor)): } [\alpha]^{25}_D = -69 (c 0.80, CHCl}_3) \text{ for 88\% ee (S).} \]

\[^{1}H \text{ NMR (CDCl}_3) \delta 8.29 (d, J = 5.0 Hz, 1H), 7.66 (dd, J = 5.0 Hz, 1H), 7.43–7.34 (m, 4H), 7.32–7.24 (m, 2H), 7.21 (dd, J = 6.8, 2.0 Hz, 1H), 6.63 (dd, J = 7.8, 5.0 Hz, 1H), 5.02 (bs, 1H), 3.91–3.80 (m, 1H), 3.70 (ddd, J = 12.8, 7.2, 5.6 Hz, 1H), 3.64–3.53 (m, 1H), 3.03 (ddd, J = 16.0, 8.4, 6.8 Hz, 1H), 2.89 (ddd, J = 16.0, 8.4, 5.8 Hz, 1H), 2.38–2.23 (m, 1H), 1.95–1.83 (m, 1H); ^{13}C \text{ NMR (CDCl}_3) \delta 154.7, 151.2, 145.5, 141.9, 139.6, 137.4, 135.0 (q, J_F-C = 5 Hz), 133.0, 129.8, 128.4, 127.3, 127.0, 124.5 (q, J_F-C = 270 Hz), 123.4, 111.3, 108.5 (q, J_F-C = 31 Hz), 45.3, 44.6, 31.1, 30.1. HRMS (DART) m/z: [M + H]^+ Calcd for C_{23}H_{19}ClF_3N_2 403.1189; Found 403.1170.

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Compound 3af (Scheme 3: colorless oil, 24.2 mg, 61% yield, 91% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t₁ = 45.0 min (major), t₂ = 56.6 min (minor)): [α]$_{D}^{25}$ = –32 (c 1.68, CHCl$_3$) for 91% ee (S). $^1$H NMR (CDCl$_3$) δ 8.30 (d, $J$ = 4.8 Hz, 1H), 7.66 (dd, $J$ = 7.6, 1.0 Hz, 1H), 7.35 (t, $J$ = 8.0 Hz, 1H), 7.32–7.24 (m, 3H), 7.04 (ddd, $J$ = 8.0, 1.4, 1.0 Hz, 1H), 6.99 (dd, $J$ = 2.6, 1.4 Hz, 1H), 6.90 (ddd, $J$ = 8.0, 2.6, 1.0 Hz, 1H), 6.63 (dd, $J$ = 7.6, 4.8 Hz, 1H), 5.05 (bs, 1H), 3.92–3.81 (m, 1H), 3.85 (s, 3H), 3.71 (ddd, $J$ = 12.6, 7.2, 5.4 Hz, 1H), 3.64–3.54 (m, 1H), 3.08 (ddd, $J$ = 16.0, 8.2, 6.6 Hz, 1H), 2.94 (ddd, $J$ = 16.0, 8.4, 5.6 Hz, 1H), 2.38–2.22 (m, 1H), 1.96–1.81 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 159.4, 154.7, 151.7, 145.3, 142.6, 142.0, 138.5, 134.9 (q, $J_{F-C}$ = 5 Hz), 129.2, 127.4, 126.9, 124.5 (q, $J_{F-C}$ = 270 Hz), 123.2, 121.0, 114.2, 112.5, 111.3, 108.5 (q, $J_{F-C}$ = 31 Hz), 55.2, 45.4, 44.6, 31.2, 30.2. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{23}$H$_{22}$F$_3$N$_2$O$_1$ 399.1684; Found 399.1677.

Compound 3ag (Scheme 3: colorless oil, 21.3 mg, 53% yield, 87% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t₁ = 45.0 min (major), t₂ = 17.5 min (minor)): [α]$_{D}^{25}$ = –74 (c 0.99, CHCl$_3$) for 87% ee (S). $^1$H NMR (CDCl$_3$) δ 8.28 (d, $J$ = 4.0 Hz, 1H), 7.64 (dd, $J$ = 7.8, 1.0 Hz, 1H), 7.49–7.42 (m, 1H), 7.35–7.21 (m, 5H), 7.10 (d, $J$ = 7.2 Hz, 1H), 6.61 (dd, $J$ = 8.0, 5.2 Hz, 1H), 5.02 (bs, 1H), 3.90–3.79 (m, 1H), 3.69 (ddd, $J$ = 12.4, 7.0, 5.4 Hz, 1H), 3.65–3.55 (m, 1H), 3.08–2.49 (m, 2H), 2.40–2.18 (m, 1H), 1.96–1.78 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 153.7, 151.7, 144.7, 143.2, 140.0, 136.4, 134.9 (q, $J_{F-C}$ = 5 Hz), 133.0, 130.9, 129.5, 128.6, 127.9, 126.5, 126.3, 124.5 (q, $J_{F-C}$ = 270 Hz), 123.1, 111.3, 108.5 (q, $J_{F-C}$ = 31 Hz), 45.4, 44.7, 30.4, 29.6. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{22}$H$_{19}$ClF$_3$N$_2$ 403.1189; Found 403.1182.
Compound 3ah (Scheme 3: colorless oil, 33.6 mg, 84% yield, 90% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t₁ = 19.1 min (major), t₂ = 22.0 min (minor)): [α]D²⁵ 32 (c 1.68, CHCl₃) for 90% ee (S). ¹H NMR (CDCl₃) δ 8.29 (d, J = 5.0 Hz, 1H), 7.66 (dd, J = 7.0, 1.2 Hz, 1H), 7.34 (td, J = 8.0, 1.6 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 7.2 Hz, 1H), 7.22 (d, J = 7.8, 1.8 Hz, 1H), 7.18 (dd, J = 7.4, 1.4 Hz, 1H), 7.02 (td, J = 7.6, 1.2 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.62 (dd, J = 7.0, 5.0 Hz, 1H), 5.06 (bs, 1H), 3.90–3.80 (m, 1H), 3.79 (s, 3H), 3.71 (ddd, J = 12.8, 7.2, 5.4 Hz, 1H), 3.64–3.54 (m, 1H), 2.85 (ddd, J = 16.0, 8.2, 6.6 Hz, 1H), 2.73 (ddd, J = 16.0, 8.0, 6.0 Hz, 1H), 2.35–2.21 (m, 1H), 1.91–1.78 (m, 1H); ¹³C NMR (CDCl₃) δ 156.4, 154.7, 151.7, 144.4, 143.6, 135.6, 134.9 (q, JF–C = 5 Hz), 131.0, 130.0, 128.6, 128.4, 126.2, 124.5 (q, JF–C = 270 Hz), 123.0, 120.4, 111.2, 110.7, 108.5 (q, JF–C = 32 Hz), 55.3, 45.4, 44.6, 30.6, 29.8. HRMS (DART) m/z: [M + H]⁺ Calcd for C₂₃H₂₂F₃N₂O₁ 399.1684; Found 399.1698.

Compound 3ai (Scheme 3: colorless solid, 14.0 mg, 33% yield, 86% ee). The ee was measured by HPLC (Chiralpak AD-H, hexane/2-propanol = 30:1, flow 0.5 mL/min, 254 nm, t₁ = 14.6 min (major), t₂ = 15.4 min (major)): [α]D²⁵ 32 (c 1.68, CHCl₃) for 86% ee (S). ¹H NMR (CDCl₃) δ 8.30 (d, J = 4.8 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.67 (d, J = 6.8 Hz, 1H), 7.52 (dd, J = 6.4, 2.4 Hz, 1H), 7.42 (s, 1H), 7.41–7.23 (m, 4H), 6.64 (dd, J = 6.8, 4.8 Hz, 1H), 5.04 (bs, 1H), 3.89–3.79 (m, 1H), 3.72 (ddd, J = 12.8, 7.4, 5.6 Hz, 1H), 3.67–3.56 (m, 1H), 3.29 (ddd, J = 15.6, 8.4, 6.8 Hz, 1H), 3.17 (ddd, J = 15.6, 8.8, 5.6 Hz, 1H), 3.09–2.99 (m, 1H), 2.03–1.91 (m, 1H); ¹³C NMR (CDCl₃) δ 156.6, 151.7, 146.0, 143.4, 141.9, 140.4, 139.6, 135.0 (q, JF–C = 5 Hz), 131.3, 127.4, 127.1, 124.5 (q, JF–C = 270 Hz), 124.4, 124.2, 124.0, 123.5, 122.0, 121.9, 111.4, 108.5 (q, JF–C = 31 Hz), 45.4, 44.5, 32.0, 29.9. HRMS (DART) m/z: [M + H]⁺ Calcd for C₂₄H₂₀F₃S₁ 425.1299; Found 425.1288.
Compound 3aj (Scheme 3: colorless oil, 18.7 mg, 49% yield, 87% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t₁ = 28.1 min (major), t₂ = 36.6 min (minor)): [α]$_{D}^{25}$ = –42 (c 0.78, CHCl$_3$) for 87% ee (S). $^1$H NMR (CDCl$_3$) δ 8.28 (dd, J = 5.2, 1.2 Hz, 1H), 7.65 (dd, J = 7.6, 1.2 Hz, 1H), 7.33–7.23 (m, 2H), 7.25–7.11 (m, 5H), 7.01 (dd, J = 6.8, 2.0 Hz, 1H), 6.62 (dd, J = 7.6, 5.2 Hz, 1H), 4.98 (bs, 1H), 3.97 (s, 2H), 3.84–3.73 (m, 1H), 3.65 (dd, J = 12.8, 6.8, 5.2 Hz, 1H), 3.60–3.49 (m, 1H), 2.89 (ddd, J = 15.6, 8.8, 6.8 Hz, 1H), 2.78 (ddd, J = 15.6, 8.8, 6.0 Hz, 1H), 2.38–2.22 (m, 1H), 1.95–1.81 (m, 1H); $^{13}$C NMR (CDCl$_3$) δ 154.7, 151.7, 149.6, 143.6, 135.8, 135.0 (q, J$_{F-C}$ = 5 Hz), 128.8, 128.4, 127.8, 126.7, 125.9, 124.4 (q, J$_{F-C}$ = 270 Hz), 122.1, 111.2, 108.5 (q, J$_{F-C}$ = 31 Hz), 45.4, 44.5, 39.6, 29.8, 29.4. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{23}$H$_{22}$F$_3$N$_2$Si 383.1735; Found 383.1736.

Compound 3ak (Scheme 3: colorless solid, 19.1 mg, 52% yield, 86% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane only, flow 0.5 mL/min, 254 nm, t₁ = 18.9 min (major), t₂ = 22.7 min (minor)): [α]$_{D}^{25}$ = –48 (c 0.97, CHCl$_3$) for 86% ee (S). $^1$H NMR (CDCl$_3$) δ 8.28 (d, J = 4.8 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.29 (d, J = 7.2 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 6.61 (dd, J = 7.6, 4.8 Hz, 1H), 4.99 (bs, 1H), 3.83–3.74 (m, 1H), 3.65 (ddd, J = 12.6, 7.2, 5.6 Hz, 1H), 3.55–3.45 (m, 1H), 3.12–3.00 (m, 1H), 3.01–2.90 (m, 1H), 2.30–2.25 (m, 1H), 2.00–1.82 (m, 1H), 0.31 (s, 9H); $^{13}$C NMR (CDCl$_3$) δ 154.7, 151.7, 149.6, 143.6, 135.8, 135.0 (q, J$_{F-C}$ = 5 Hz), 132.6, 125.7, 125.0, 124.5 (q, J$_{F-C}$ = 270 Hz), 111.2, 108.4 (q, J$_{F-C}$ = 31 Hz), 45.5, 43.8, 32.3, 29.7, –0.48. HRMS (DART) m/z: [M + H]$^+$ Calcd for C$_{19}$H$_{24}$F$_3$Si 365.1653; Found 365.1661.

Compound 3al (Scheme 3: colorless solid, 28.0 mg, 85% yield, 88% ee). The ee was measured by HPLC (Chiralcel OD-H, hexane/2-propanol = 19:1, flow 0.5 mL/min, 254 nm, t₁ = 10.2 min S-16
(minor), \( t_2 = 11.3 \text{ min (major)} \): \([\alpha]^{25}_D = -42 \) (c 0.74, CHCl\(_3\)) for 88\% ee (S). \( ^1H\) NMR (CDCl\(_3\)) \( \delta 8.30 \) (d, \( J = 4.8 \text{ Hz, 1H} \)), 7.66 (d, \( J = 8.4 \text{ Hz, 2H} \)), 7.63 (d, \( J = 8.0 \text{ Hz, 1H} \)), 7.52–7.42 (m, 2H), 7.36 (d, \( J = 7.2 \text{ Hz, 1H} \)), 7.29 (d, \( J = 6.8 \text{ Hz, 1H} \)), 6.64 (dd, \( J = 8.0, 4.8 \text{ Hz, 1H} \)), 5.15 (bs, 1H), 4.10 (qd, \( J = 7.2, 2.8 \text{ Hz, 1H} \)), 3.90 (ddd, \( J = 12.8, 7.2, 5.6 \text{ Hz, 1H} \)), 3.77 (ddd, \( J = 13.2, 7.2, 5.6 \text{ Hz, 1H} \)), 3.63 (dd, \( J = 17.6, 8.0 \text{ Hz, 1H} \)), 3.18 (dd, \( J = 17.6, 3.2 \text{ Hz, 1H} \); \( ^{13}C\) NMR (CDCl\(_3\)) \( \delta 154.5, 151.7, 146.5, 143.9, 138.8, 135.0 \) (q, \( J_{F-C} = 5 \text{ Hz} \)), 131.6, 128.0, 127.8, 124.5 (q, \( J_{F-C} = 270 \text{ Hz} \)), 123.3, 122.5, 119.5, 119.4, 111.4, 108.9 (q, \( J_{F-C} = 31 \text{ Hz} \)), 46.5, 42.8, 35.7. HRMS (DART) m/z: [M + H]\(^+\) Calcd for C\(_{19}\)H\(_{16}\)F\(_3\)N\(_2\) 329.1263; Found 329.126.

3am

Compound 3am (Scheme 3: colorless oil, 23.8 mg, 75\% yield, 42\% ee). The ee was measured by HPLC (Chiralcel OJ-H-OJ-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, \( t_1 = 40.4 \) min (major), \( t_2 = 42.6 \) min (minor)): \([\alpha]^{25}_D +28 \) (c 1.12, CHCl\(_3\)) for 42\% ee. \( ^1H\) NMR (CDCl\(_3\)) \( \delta 8.26 \) (d, \( J = 4.8 \text{ Hz, 1H} \)), 7.65 (d, \( J = 7.4, 1.0 \text{ Hz, 1H} \)), 7.16 (d, \( J = 5.2 \text{ Hz, 1H} \)), 7.14 (d, \( J = 5.2 \text{ Hz, 1H} \)), 7.07 (d, \( J = 5.2 \text{ Hz, 1H} \)), 7.05 (d, \( J = 5.2 \text{ Hz, 1H} \)), 6.61 (dd, \( J = 7.4, 4.8 \text{ Hz, 1H} \)), 4.97 (bs, 1H), 3.71–3.54 (m, 2H), 3.36 (s, 1H), 3.21 (s, 1H), 1.92–1.74 (m, 3H), 1.58–1.50 (m, 2H); \( ^{13}C\) NMR (CDCl\(_3\)) \( \delta 154.7, 151.7, 148.2, 148.2, 135.0 \) (q, \( J_{F-C} = 5 \text{ Hz} \)), 125.6, 125.6, 124.5 (q, \( J_{F-C} = 270 \text{ Hz} \)), 120.7, 120.4, 111.2, 108.5 (q, \( J_{F-C} = 31 \text{ Hz} \)), 46.5, 46.4, 46.0, 43.8, 40.8, 33.1. HRMS (DART) m/z: [M + H]\(^+\) Calcd for C\(_{18}\)H\(_{18}\)F\(_3\)N\(_2\) 319.1422; Found 319.1409.

3an

Compound 3an (Scheme 3: colorless oil, 31.8 mg, 74\% yield, 89\% ee). Hexane was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak AD-H, hexane/2-propanol = 9:1, flow 0.5 mL/min, 254 nm, \( t_1 = 28.4 \) min (minor), \( t_2 = 31.2 \) min (major)): \([\alpha]^{25}_D +37 \) (c 1.54, CHCl\(_3\)) for 89\% ee. \( ^1H\) NMR (CDCl\(_3\)) \( \delta 8.20 \) (d, \( J = 4.8 \text{ Hz, 1H} \)), 7.62 (d, \( J = 7.4 \text{ Hz, 1H} \)), 7.45–7.36 (m, 2H), 7.29–7.20 (m, 3H), 6.60 (dd, \( J = 7.4, 4.8 \text{ Hz, 1H} \)), 4.61 (s, 2H), 4.53 (bs, 1H), 3.31 (ddd, \( J = 12.8, 6.8, 5.2 \text{ Hz, 1H} \)), 3.16 (ddd, \( J = 12.8, 8.0, 5.2 \text{ Hz, 1H} \)), 3.13–3.01 (m, 2H), 2.74 (d, \( J = 4.2 \text{ Hz, 1H} \)), 2.60 (d, \( J = 4.2 \text{ Hz, 1H} \)), 1.82–1.69 (m, 1H), 1.57–1.39 (m, 2H), 1.27–1.04 (m, 2H); \( ^{13}C\) NMR (CDCl\(_3\)) \( \delta 177.6, 177.5, 154.4, 151.5, 136.1, 134.9 \) (q, \( J_{F-C} = 5 \text{ Hz} \)), 129.0, 128.4, 128.1, 124.3 (q, \( J_{F-C} = 271 \text{ Hz} \)), 111.4, 108.5 (q, \( J_{F-C} = 31 \text{ Hz} \)), 48.3, 47.9, 45.8, 42.4, 42.1, 39.6,
39.4, 36.6, 30.1. HRMS (DART) m/z: [M + H]^+ Calcd for C_{23}H_{23}F_{3}N_{3}O_{2} 430.1742; Found 430.1736.

**3ao**

**Compound 3ao** (Scheme 3: colorless oil, 34.9 mg, 84% yield, 81% ee). Hexane was used as an eluent for preparative TLC. The ee was measured by HPLC (Chiralpak AD-H, hexane/2-propanol = 9:1, flow 0.5 mL/min, 254 nm, t_1 = 13.1 min (minor), t_2 = 14.0 min (major)): [α]^{25}D = −5 (c 1.75, CHCl_3) for 81% ee. 1H NMR (CDCl_3) δ 8.24 (d, J = 5.2 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 6.59 (dd, J = 7.6, 5.2 Hz, 1H), 4.90 (bs, 1H), 4.18 (dd, J = 10.6, 5.8 Hz, 1H), 4.10 (t, J = 10.6 Hz, 1H), 4.06 (s, 1H), 4.04 (s, 1H), 3.39–3.20 (m, 2H), 2.38–2.28 (m, 3H), 2.25–2.20 (m, 1H), 2.12–2.05 (m, 1H), 2.03 (s, 3H), 1.98 (s, 3H), 1.73 (ddd, J = 13.2, 8.8, 2.4 Hz, 1H), 1.58 (d, J = 10.4 Hz, 1H), 1.34 (d, J = 10.4 Hz, 1H), 1.03 (dt, J = 13.2, 4.4 Hz, 1H); 13C NMR (CDCl_3) δ 171.0, 170.9, 154.5, 151.7, 134.8 (q, J_{F-C} = 5 Hz), 124.5 (q, J_{F-C} = 273 Hz), 111.1, 108.2 (q, J_{F-C} = 32 Hz), 62.5, 61.4, 45.9, 41.9, 39.7, 39.6, 38.3, 36.3, 33.3, 28.7, 21.0, 20.6. HRMS (DART) m/z: [M + H]^+ Calcd for C_{20}H_{26}F_{3}N_{2}O_{4} 415.1845; Found 415.1835.

**3ap**

**Compound 3ap** (Scheme 5: colorless oil, 21.2 mg, 70% yield, 81% ee). The ee was measured by HPLC (Chiralcel OJ-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t_1 = 12.4 min (minor), t_2 = 13.2 min (major)): [α]^{25}D = −42 (c 0.13, CHCl_3) for 81% ee. 1H NMR (CDCl_3) δ 8.28 (d, J = 4.4 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.30–7.12 (m, 4H), 6.61 (dd, J = 7.8, 4.4 Hz, 1H), 4.95 (bs, 1H), 3.84–3.70 (m, 2H), 3.15 (dd, J = 15.6, 8.0 Hz, 1H), 3.08 (q, J = 6.0 Hz, 1H), 2.54 (dd, J = 15.6, 6.2 Hz, 1H), 2.34 (sept, J = 6.8 Hz, 1H), 1.78 (d, J = 6.8 Hz, 3H); 13C NMR (CDCl_3) δ 154.7, 151.7, 143.9, 143.4, 134.9 (q, J_{F-C} = 5 Hz), 127.0, 126.3, 124.8, 124.4 (q, J_{F-C} = 270 Hz), 124.1, 111.2, 108.5 (q, J_{F-C} = 34 Hz), 52.1, 44.2, 39.9, 38.2, 20.3. HRMS (DART) m/z: [M + H]^+ Calcd for C_{17}H_{18}F_{3}N_{2} 307.1422; Found 307.1414.
Compound 3aq (Scheme 5: colorless oil, 21.2 mg, 62% yield, 84% ee). The ee was measured by HPLC (Chiralcel OJ-H, hexane/2-propanol = 200:1, flow 0.5 mL/min, 254 nm, t₁ = 21.9 min (minor), t₂ = 27.1 min (major)): [α]D –49 (c 0.84, CHCl₃) for 84% ee. ¹H NMR (CDCl₃) δ 8.30 (d, J = 4.8 Hz, 1H), 7.72–7.61 (m, 3H), 7.54–7.45 (m, 2H), 7.36 (d, J = 6.8 Hz, 1H), 7.27 (d, J = 6.8 Hz, 1H), 6.64 (dd, J = 7.2, 4.8 Hz, 1H), 5.15 (bs, 1H), 3.91 (t, J = 6.4 Hz, 2H), 3.63 (td, J = 6.4, 3.2 Hz, 1H), 3.51 (qd, J = 7.2, 3.2 Hz, 1H), 1.48 (d, J = 7.4 Hz, 3H). 

¹³C NMR (CDCl₃) δ 154.6, 151.7, 149.0, 145.1, 137.7, 135.0 (q, JF–C = 5 Hz), 131.5, 128.1, 127.9, 124.4 (q, JF–C = 270 Hz), 123.4, 122.8, 119.4, 118.7, 111.4, 108.5 (q, JF–C = 31 Hz), 52.2, 45.7, 43.7, 21.4. HRMS (DART) m/z: [M + H]+ Calcd for C₂₀H₁₈F₃N₂ 343.1422; Found 343.1409.

Compound 5 (Scheme 4: colorless solid, 23.0 mg, 40% yield, 91% ee). The ee was measured by HPLC (Chiralpak IB, hexane/CHCl₃/EtOH = 8:2:1, flow 0.5 mL/min, 254 nm, t₁ = 9.6 min (major), t₂ = 10.0 min (minor)): [α]D +14 (c 0.67, CHCl₃) for 91% ee (S). ¹H NMR (CDCl₃) δ 7.28–7.12 (m, 4H), 6.25 (s, 1H), 3.72–3.62 (m, 1H), 3.60–3.49 (m, 1H), 3.53–3.39 (m, 1H), 3.09–2.80 (m, 2H), 2.39–2.23 (m, 1H), 1.90–1.78 (m, 1H).

Compound 6 (Scheme 4: colorless solid, 8.3 mg, 20% yield, 91% ee, CAS: 2088274-15-9 for (R)-6). The ee was measured by HPLC (Chiralcel OJ-H, hexane/2-propanol = 18:1, flow 0.5 mL/min, 254 nm, t₁ = 35.2 min (minor), t₂ = 44.5 min (major)): [α]D +5 (c 0.26, CHCl₃) for 91% ee (S). ¹H NMR (CDCl₃) δ 7.28–7.12 (m, 4H), 6.25 (s, 1H), 3.72–3.62 (m, 1H), 3.60–3.49 (m, 1H), 3.53–3.39 (m, 1H), 3.09–2.80 (m, 2H), 2.39–2.23 (m, 1H), 1.90–1.78 (m, 1H).
14. $^1$H, $^{13}$C NMR spectra and chiral HPLC charts
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### Proton Spectroscopy

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eluent Hex/IPA=19:1
flow speed 0.5 mL/min
wavelength 254 nm

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**Flow Speed:** 0.6 mL/min

**Wavelength:** 254 nm

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![Diagram 1](image1.png)

![Diagram 2](image2.png)
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flow speed 0.5 mL/min
wavelength 254nm

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flow speed 0.5 mL/min
wavelength 254 nm

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Column: AD-Hx3 (LJ097, LJ096, BL040)

Eluent: Hex/IPA = 200/1

Flow speed: 0.5 mL/min

Wavelength: 254 nm

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Sample: ACV200-1-254-2

LC: LC-2

Column: AD-Hx3 (LJ097, LJ096, BL040)

Eluent: Hex/IPA = 200/1

Flow speed: 0.5 mL/min

Wavelength: 254 nm

<table>
<thead>
<tr>
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<th>Area Percent</th>
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sample yd11080-rac-AD-Hx3-200-1-254-2
LC LC-2
column AD-Hx3 (LJ097, LJ096, BL040)
eluent Hex/IPA= 200/1
flow speed 0.5 mL/min
wavelength 254nm

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LC LC-2 column OD-H EA038
eluent Hex/IPA=200:1
flow speed 0.5 mL/min
wavelength 254 nm

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### Table 2

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LC LC-2 column AS-H
eluent Hex/IPA=30:1
flow speed 0.5 mL/min
wavelength 254 nm

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<th>Area</th>
<th>Area Percent</th>
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<th>Area</th>
<th>Area Percent</th>
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LC LC2
column IA
eluent Hex/IPA=30/1
flow speed 0.5 mL/min
wavelength 254 nm

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<th>Area</th>
<th>Area Percent</th>
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<tbody>
<tr>
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<td>2</td>
<td>11.252</td>
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Sample yd11080-rac-AD-Hx3-200-1-254-2

LC LC-2

Column AD-Hx3 (LJ097, LJ096, BL040)

Eluent Hex/IPA = 200/1

Flow speed 0.5 mL/min

Wavelength 254 nm

<table>
<thead>
<tr>
<th>Pk #</th>
<th>Retention Time</th>
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<table>
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**Sample yd11080-rac-AD-Hx3-200-1-254-2**

**Column AD-Hx3 (LJ097, LJ096, BL040)**

- Eluent: Hex/IPA = 200/1
- Flow speed: 0.5 mL/min
- Wavelength: 254 nm

---

### Retention Time and Area Analysis

<table>
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<th>Retention Time</th>
<th>Area</th>
<th>Area Percent</th>
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<tr>
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**2**

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### Retention Time and Area Analysis

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</table>
LC LC-2 column OD-H EA038
eluent Hex/IPA=200:1
flow speed 0.5 mL/min
wavelength 254 nm

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<tr>
<th>Pk #</th>
<th>Retention Time</th>
<th>Area</th>
<th>Area Percent</th>
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<tbody>
<tr>
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<td>14.018</td>
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<td>90.468</td>
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<table>
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<th>Area Percent</th>
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<tr>
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<td>2</td>
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</table>
The document contains chemical structures, a table of retention times, areas, and area percentages, and two chromatograms. Here is the extracted data:

**Chemical Structure**: 
\[
\text{CF}_3 \quad \text{H} \quad \text{N} \quad \text{H} \quad \text{C} \quad \text{H} 
\]

**Table**: 

<table>
<thead>
<tr>
<th>Pk #</th>
<th>Retention Time</th>
<th>Area</th>
<th>Area Percent</th>
</tr>
</thead>
<tbody>
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<td>9.579</td>
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<td>2</td>
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<td>90.421</td>
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</table>

**Chromatogram 1**: Retention Time:
- Peak 1: 12.427 min
- Peak 2: 13.232 min

**Chromatogram 2**: Retention Time:
- Peak 1: 12.522 min
- Peak 2: 13.368 min
LC LC-7 column IA eluent Hex/CHCl3/EtOH = 90/30/1
flow speed 0.5 mL/min
wavelength 254nm

<table>
<thead>
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<th>Pk #</th>
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<th>Area Percent</th>
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**Sample yd11080-rac-AD-Hx3-200-1-254-2**

**Column**: AD-Hx3 (LJ097, LJ096, BL040)

**Eluent**: Hex/IPA = 200/1

**Flow Speed**: 0.5 mL/min

**Wavelength**: 254 nm

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<thead>
<tr>
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<th>Area Percent</th>
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