Supporting Information

A One-Pot Process for the Enantioselective Synthesis of Tetrahydroquinolines and Tetrahydroisoquinolines via Asymmetric Reductive Amination (ARA)

Tao Yang, Qin Yin, Guoxian Gu and Xumu Zhang*†

Department of Chemistry, Southern University of Science and Technology, Shenzhen, 518055, P. R. China.

† Shenzhen Grubbs Institute, Shenzhen, 518055, P. R. China.

zhangxm@sustc.edu.cn

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1. General information

Unless otherwise mentioned, all experiments were carried out under an atmosphere of argon in a glovebox or using standard Schlenk techniques. Solvents were dried with standard procedures and degassed with N\textsubscript{2}. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 300-400 mesh). NMR spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz for $^1$H NMR, 101 MHz for $^{13}$C NMR or a Bruker DPX 500 spectrometer at 500 MHz for $^1$H NMR, 126 MHz for $^{13}$C NMR. Chemical shifts (δ) are reported in ppm and respectively referenced to internal standard Me\textsubscript{4}Si and solvent signals (Me\textsubscript{4}Si, 0 ppm for $^1$H NMR in CDCl\textsubscript{3}; 77.0 ppm in CDCl\textsubscript{3} for $^{13}$C NMR). HPLC and UPLC analysis was carried out on Angilent 1200 Series instrument using chiral columns.

2. General procedure for the preparation of substrates

Step 1:
S\textsubscript{1} (10 mmol) and Et\textsubscript{3}N (11 mmol) were dissolved in dichloromethane (30 mL) at 0 °C, followed by addition of (Boc)$\textsubscript{2}$O (12 mmol) and DMAP (0.5 mmol). The resulting solution was warmed to rt and stirred for 6 h. The reaction was quenched with saturated NH\textsubscript{4}Cl aqueous solution (20 mL). The organic layer was extracted with dichloromethane (10 mL × 2), combined, dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, and then concentrate under reduced pressure. The crude product was further purified by column chromatography to quantitatively provide pure S\textsubscript{2}.

Step 2:
R\textsuperscript{3}MgBr (1.3 equiv) was added dropwise to a solution of S\textsubscript{2} (3 mmol) in dried THF (10 mL) at -65 °C. The resulting mixture was then stirred overnight. After warming up to rt, the reaction was quenched with saturated NH\textsubscript{4}Cl aqueous solution (15 mL) and extracted with EtOAc (10 mL × 2). The combined organic layers were dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and then concentrated under reduced pressure. The crude product was further purified by column chromatography to give 1.

\textit{tert-butyl (2-(3-oxobutyl)phenyl)carbamate (1a)}: an oil, 500 mg, 63% yield
$^1$H NMR (500 MHz, CDCl\textsubscript{3}) δ 7.72 (d, $J = 5.9$ Hz, 1H), 7.60 (s, 1H), 7.20 (m, 1H), 7.16-7.09 (m, 1H), 7.09-7.01 (m, 1H), 2.85 (m, 4H), 2.33-2.02 (m, 3H), 1.56 (s, 9H).

$^{13}$C\textsubscript{$^1$H} NMR (126 MHz, CDCl\textsubscript{3}) δ 209.2, 153.8, 136.0, 131.9, 129.4, 126.9, 124.2, 123.2, 80.0, 44.6, 29.9, 28.4, 24.0 ppm.

HRMS Calculated for C\textsubscript{16}H\textsubscript{24}NO\textsubscript{3} [M+H]\textsuperscript{+} 278.1751; found 278.1741.

\textit{tert-butyl (2-(3-oxopentyl)phenyl)carbamate (1b)}: an oil, 465 mg, 56% yield
$^1$H NMR (500 MHz, CDCl\textsubscript{3}) δ 7.71 (d, $J = 7.7$ Hz, 1H), 7.50 (s, 1H), 7.12 (dd, $J = 7.6$, 1.5 Hz, 1H), 7.04 (td, $J = 7.5$, 1.2 Hz, 1H), 2.84 (m, 4H), 2.42 (q, $J = 7.3$ Hz, 2H), 1.56 (s, 9H), 1.05 (t, $J = 7.3$ Hz, 3H).

$^{13}$C\textsubscript{$^1$H} NMR (126 MHz, CDCl\textsubscript{3}) δ 211.8, 153.8, 136.0, 132.0, 129.3, 126.9, 124.2, 123.3, 80.0, 43.1, 36.0, 28.4, 27.9, 24.1 ppm. HRMS Calculated for C\textsubscript{16}H\textsubscript{24}NO\textsubscript{3} [M+H]\textsuperscript{+} 278.1751; found 278.1741.

\textit{tert-butyl (2-(3-oxohexyl)phenyl)carbamate (1c)}: an oil, 611 mg, 70% yield
$^1$H NMR (500 MHz, CDCl\textsubscript{3}) δ 7.71 (d, $J = 7.7$ Hz, 1H), 7.49 (s, 1H), 7.12 (dd, $J = 7.6$, 1.5 Hz, 1H), 7.04 (td, $J = 7.5$, 1.2 Hz, 1H), 2.84 (m, 4H), 2.42 (q, $J = 7.3$ Hz, 2H), 1.56 (s, 9H), 1.05 (t, $J = 7.3$ Hz, 3H).
7.24-7.16 (m, 1H), 7.11 (dd, J = 7.6, 1.5 Hz, 1H), 7.04 (td, J = 7.5, 1.1 Hz, 1H), 2.91-2.72 (m, 4H), 2.37 (t, J = 7.4 Hz, 2H), 1.60 (dt, J = 7.4, 7.4 Hz, 2H). 1.56 (s, 9H), 0.88 (t, J = 7.4 Hz, 3H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 211.4, 153.8, 136.0, 131.9, 129.3, 126.9, 124.2, 123.7, 80.0, 44.8, 43.5, 28.4, 24.1, 17.3, 13.6 ppm. HRMS Calculated for C₁₉H₂₈NO₅ [M+H]$^+$ 292.1907; found 292.1896.

**tert-butyl (2-(3-oxoheptyl)phenyl)carbamate (1d):** an oil, 530 mg, 58% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.71 (d, J = 7.6 Hz, 1H), 7.50 (s, 1H), 7.25-7.17 (m, 1H), 7.11 (dd, J = 7.6, 1.6 Hz, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 2.83 (m, 4H), 2.38 (t, J = 7.6 Hz, 2H), 1.60-1.51 (m, 11H), 1.30 (m, 2H), 1.26-1.17 (m, 2H). 0.88 (t, J = 7.2 Hz, 3H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 211.6, 153.8, 136.0, 131.9, 129.3, 126.9, 124.2, 123.3, 80.0, 43.4, 42.7, 28.4, 25.9, 24.1, 22.2, 13.8 ppm. HRMS Calculated for C₁₉H₂₈NO₅ [M+H]$^+$ 306.2064; found 306.2053.

**tert-butyl (2-(3-oxooctyl)phenyl)carbamate (1e):** an oil, 440 mg, 46% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.71 (d, J = 7.7 Hz, 1H), 7.50 (s, 1H), 7.25-7.17 (m, 1H), 7.11 (dd, J = 7.6, 1.6 Hz, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 2.83 (m, 4H), 2.38 (t, J = 7.6 Hz, 2H), 1.60-1.51 (m, 11H), 1.30 (m, 2H), 1.26-1.17 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 211.6, 153.8, 136.0, 131.9, 129.3, 126.9, 124.2, 123.3, 80.0, 43.4, 42.7, 28.4, 25.9, 24.1, 22.1, 13.8 ppm. HRMS Calculated for C₂₀H₂₉NO₅ [M+H]$^+$ 320.2220; found 320.2210.

**tert-butyl (2-(3-oxononyl)phenyl)carbamate (1f):** an oil, 660 mg, 66% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.71 (d, J = 7.6 Hz, 1H), 7.51 (s, 1H), 7.23 - 7.15 (m, 1H), 7.11 (dd, J = 7.6, 1.5 Hz, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 2.83 (t, J = 3.7 Hz, 4H), 2.38 (t, J = 7.5 Hz, 2H), 1.56 (m, 11H), 1.35 - 1.11 (m, 6H), 0.88 (t, J = 7.0 Hz, 3H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 211.6, 153.8, 136.0, 132.0, 129.3, 126.9, 124.2, 123.3, 80.0, 43.4, 43.0, 31.5, 28.8, 28.4, 23.8, 22.4, 14.0 ppm. HRMS Calculated for C₂₀H₂₉NO₅ [M+H]$^+$ 334.2377; found 334.2365.

**tert-butyl (2-(3-oxodecyl)phenyl)carbamate (1g):** an oil, 560 mg, 54% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.71 (d, J = 7.8 Hz, 1H), 7.50 (s, 1H), 7.23-7.16 (m, 1H), 7.11 (dd, J = 7.7, 1.5 Hz, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 2.83 (m, 4H), 2.38 (t, J = 7.5 Hz, 2H), 1.56 (m, 11H), 1.33 - 1.16 (m, 8H), 0.89 (t, J = 7.0 Hz, 3H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 211.6, 153.8, 136.0, 131.9, 129.3, 126.9, 124.2, 123.3, 80.0, 43.4, 43.0, 31.6, 29.0, 29.0, 28.4, 24.1, 23.9, 22.5, 14.0 ppm. HRMS Calculated for C₂₁H₃₀O₅N [M+H]$^+$ 348.2533; found 348.2522.

**tert-butyl (2-(3-oxo-4-phenylbutyl)phenyl)carbamate (1h):** a white solid, 750 mg, 74% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.67 (d, J = 7.7 Hz, 1H), 7.38-7.22 (m, 4H), 7.22-7.15 (m, 1H), 7.15-7.10 (m, 2H), 7.06-6.96 (m, 2H), 3.65 (s, 2H), 2.83 (m, 2H), 2.79 (m, 2H), 1.52 (s, 9H). $^{13}$C ($^{1}$H) NMR (126 MHz, CDCl₃) δ 208.7, 153.8, 135.9, 133.8, 131.7, 130.6, 129.3, 128.4, 127.1, 126.9, 124.2, 123.3, 80.1, 50.2, 42.7, 28.4, 24.2 ppm. HRMS Calculated for C₂₂H₃₂O₅N [M+H]$^+$ 340.1907; found 340.1896.

**tert-butyl (5-methoxy-2-(3-oxobutyl)phenyl)carbamate (1i):** an oil, 550 mg, 63% yield

$^{1}$H NMR (500 MHz, CDCl₃) δ 7.64 (s, 1H), 7.42 (s, 1H), 6.99 (d, J = 8.5 Hz, 1H), 6.60 (dd, J = 8.5, 2.7 Hz, 1H), 3.80 (s, 3H), 2.83 (t, J = 6.4 Hz,
2H), 2.76 (t, J = 6.4 Hz, 2H), 2.15 (s, 3H), 1.56 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 209.4, 158.5, 153.5, 137.0, 130.0, 123.1, 110.5, 107.2, 80.1, 55.3, 44.8, 30.0, 28.4, 23.3 ppm. HRMS Calculated for C16H20O2N [M+H]+ 294.1700; found 294.1692.

tert-butyl (2-methoxy-6-(3-oxobutyl)phenyl)carbamate (1j): an oil, 410 mg, 47% yield

1H NMR (500 MHz, CDCl3) δ 7.49 (s, 1H), 7.25 (s, 1H), 6.75 (dd, J = 8.8, 3.0 Hz, 1H), 6.67 (d, J = 2.9 Hz, 1H), 3.78 (s, 3H), 2.85 (m, 2H), 2.83-2.78 (m, 2H), 2.15 (s, 3H), 1.54 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 208.9, 156.7, 154.4, 134.9, 128.9, 125.9, 114.8, 111.8, 79.8, 55.4, 44.5, 30.0, 28.4, 24.4 ppm. HRMS Calculated for C16H20O2N [M+H]+ 294.1700; found 294.1692.

tert-butyl (4-methyl-2-(3-oxobutyl)phenyl)carbamate (1k): an oil, 420 mg, 58% yield

1H NMR (500 MHz, CDCl3) δ 7.61-7.50 (m, 1H), 7.41 (s, 1H), 7.01 (dd, J = 8.2, 1.6 Hz, 1H), 6.92 (d, J = 1.5 Hz, 1H), 2.87-2.84 (m, 2H), 2.82-2.77 (m, 2H), 2.29 (s, 3H), 2.15 (s, 3H), 1.55 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 209.1, 154.0, 133.8, 133.3, 132.1, 130.0, 127.6, 123.6, 79.9, 44.6, 30.0, 28.4, 24.1, 20.8 ppm. HRMS Calculated for C19H24O2NBr [M+H]+ 278.1751; found 278.1741.

tert-butyl (5-(4-bromobutoxy)-2-(3-oxobutyl)phenyl)carbamate (II): an oil, 530 mg, 63% yield

1H NMR (500 MHz, CDCl3) δ 7.63 (s, 1H), 7.40 (s, 1H), 6.96 (d, J = 8.5 Hz, 1H), 6.56 (dd, J = 8.4, 2.6 Hz, 1H), 3.97 (t, J = 6.0 Hz, 2H), 3.47 (t, J = 6.7 Hz, 2H), 2.81 (t, J = 6.4 Hz, 2H), 2.74 (t, J = 6.5 Hz, 2H), 2.13 (s, 3H), 2.05 (dt, J = 14.5, 6.7 Hz, 2H), 1.97-1.85 (m, 2H), 1.54 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 209.4, 157.8, 153.5, 137.0, 130.1, 123.1, 110.6, 107.9, 80.1, 66.8, 44.8, 33.6, 30.0, 29.5, 28.4, 27.9, 23.3 ppm. HRMS Calculated for C19H29O2NBr [M+H]+ 414.1274; found 414.1260.

tert-butyl (2-fluoro-6-(3-oxobutyl)phenyl)carbamate (1m): an oil, 530 mg, 63% yield

1H NMR (500 MHz, CDCl3) δ 7.12 (m, 1H), 7.02-6.85 (m, 2H), 6.70 (s, 1H), 2.88 (dd, J = 10.5, 3.8 Hz, 2H), 2.81 (dd, J = 10.5, 3.8 Hz, 2H), 2.12 (s, 3H), 1.50 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 208.5, 158.24 (d, J = 248.4 Hz), 154.0, 140.0, 127.79 (d, J = 22.7 Hz), 127.47 (d, J = 8.7 Hz), 124.60 (d, J = 3.3 Hz), 113.86 (d, J = 20.9 Hz), 80.4, 44.3, 29.9, 28.2, 24.68 (d, J = 2.5 Hz) ppm. HRMS Calculated for C15H12F2O2NF [M+H]+ 282.1500; found 282.1491.

tert-butyl (4-bromo-2-(3-oxobutyl)phenyl)carbamate (1n): a white solid, 798 mg, 78% yield

1H NMR (500 MHz, CDCl3) δ 7.74 (s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.30 (dd, J = 8.7, 2.4 Hz, 1H), 7.23 (d, J = 2.3 Hz, 1H), 2.88 (t, J = 6.2 Hz, 2H), 2.79 (t, J = 6.2 Hz, 2H), 2.17 (s, 3H), 1.55 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 209.0, 153.6, 153.3, 133.8, 132.1, 129.9, 124.7, 116.6, 80.3, 44.4, 29.9, 28.3, 23.7 ppm. HRMS Calculated for C19H25O2NB [M+H]+ 342.0699; found 342.0688.

tert-butyl (2-(3-oxo-3-phenylpropyl)phenyl)carbamate (1o): an oil, 690 mg, 71% yield

1H NMR (500 MHz, CDCl3) δ 7.99 (dd, J = 8.2, 1.1 Hz, 2H), 7.75 (d, J = 7.3 Hz, 1H), 7.65-7.56 (m, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.25-7.16 (m, 2H), 7.07 (m, 1H), 3.41 (t, J = 6.7 Hz, 2H), 3.04 (t, J = 6.7 Hz, 2H), 1.56 (s, 9H). 13C{1H} NMR (126 MHz, CDCl3) δ 199.9, 153.8, 136.5, 136.1, 133.4, 132.0, 129.5, 128.6, 128.1, 127.0, 124.2, 123.3, 80.1, 39.6, 28.4, 24.4 ppm.

tert-butyl (2-(3-(4-fluorophenyl)-3-oxopropyl)phenyl)carbamate (1p): a white solid, 500 mg, 49% yield
$^{1}$H NMR (500 MHz, CDCl$_3$) δ 8.09-7.91 (m, 2H), 7.73 (d, J = 7.6 Hz, 1H), 7.57 (s, 1H), 7.21 (m, 2H), 7.14 (t, J = 8.6 Hz, 2H), 7.06 (td, J = 7.6, 1.2 Hz, 1H), 3.37 (t, J = 6.7 Hz, 2H), 3.03 (t, J = 6.7 Hz, 2H), 1.56 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 198.3, 165.9 (d, J = 255.3 Hz), 153.8, 136.0, 132.9 (d, J = 9.4 Hz), 129.5, 127.0, 124.3, 123.4, 115.7 (d, J = 21.9 Hz), 80.1, 39.5, 28.4, 24.9 ppm.

**tert-butyl (2-(3-(4-fluorophenyl)-3-oxopropyl)-6-methoxyphenyl)carbamate (1q):** a white solid, 650 mg, 58% yield

$^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.98 (dd, J = 8.8, 5.4 Hz, 2H), 7.47 (s, 1H), 7.18 (s, 1H), 7.11 (t, J = 8.6 Hz, 2H), 6.82 - 6.69 (m, 2H), 3.76 (s, 3H), 3.33 (t, J = 6.8 Hz, 2H), 2.98 (t, J = 6.8 Hz, 2H), 1.51 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 198.1, 165.8 (d, J = 255.2 Hz), 156.8, 154.4, 133.0 (d, J = 3.0 Hz), 130.7 (d, J = 9.3 Hz), 128.9, 127.7, 126.2, 115.7 (d, J = 21.9 Hz), 115.0, 111.8, 79.9, 55.4, 39.5, 28.4, 24.9 ppm. HRMS Calculated for C$_{21}$H$_{25}$O$_4$NF [M+H]$^+$ 374.1762; found 374.175.

**tert-butyl (4-bromo-2-(3-(4-fluorophenyl)-3-oxopropyl)phenyl)carbamate (1r):** a white solid, 860 mg, 68% yield

$^{1}$H NMR (500 MHz, CDCl$_3$) δ 8.07 - 7.95 (m, 2H), 7.73 (s, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.30 - 7.28 (m, 2H), 7.13 (t, J = 8.6 Hz, 2H), 3.36 (t, J = 6.5 Hz, 2H), 2.98 (t, J = 6.5 Hz, 2H), 1.54 (s, 9H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 198.0, 166.0 (d, J = 255.8 Hz), 153.6, 135.4, 134.0, 132.7 (d, J = 3.0 Hz), 132.2, 130.8 (d, J = 9.4 Hz), 129.9, 124.8, 116.8, 115.8 (d, J = 21.9 Hz), 80.4, 39.4, 28.4, 24.0 ppm. HRMS Calculated for C$_{20}$H$_{22}$BrFNO$_3$ [M+H]$^+$ 422.0761; found 422.0746.

S3 were synthesized according to a known procedure.$^3$

**Step 1:**

S3 (10 mmol) and Et$_3$N (11 mmol) were dissolved in dichloromethane (30 mL) at 0 °C, followed by addition of (Boc)$_2$O (12 mmol) and DMAP (0.5 mmol). The resulting solution was warmed to rt and stirred for 6 h. The reaction was quenched with saturated NH$_4$Cl aqueous solution (20 mL). The organic layer was extracted with dichloromethane (10 mL × 2), combined, dried over anhydrous Na$_2$SO$_4$, and then concentrated under reduced pressure. The crude product was further purified by column chromatography to quantitatively provide pure S4.

**Step 2:**

R$_2$MgBr (1.3 equiv) was added dropwise to a solution of S4 (3 mmol) in dried THF (10 mL) at 0 °C. The resulting mixture was then stirred overnight at rt. The reaction was quenched with saturated NH$_4$Cl aqueous solution (15 mL) and extracted with EtOAc (10 mL × 2). The combined organic layers were dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography to give 3.

**tert-butyl (2-benzoylphenethyl)carbamate (3a):** a white solid, 575 mg, 59% yield

$^{1}$H NMR (400 MHz, CDCl$_3$) δ 7.82 (d, J = 7.4 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.12 (t, J = 7.4 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 3.98 (s, 2H), 2.93 (t, J = 6.7 Hz, 2H), 1.52 (s, 9H).
7.48 (t, J = 7.5 Hz, 3H), 7.41 (d, J = 7.5 Hz, 1H), 7.32 (dd, J = 10.8, 6.9 Hz, 2H), 5.03 (s, 1H), 3.40 (m, 2H), 2.88 (t, J = 6.8 Hz, 2H), 1.42 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 198.5, 155.9, 138.6, 138.5, 137.6, 133.3, 130.9, 130.6, 130.4, 129.0, 128.4, 125.7, 79.0, 42.1, 33.1, 28.4 ppm.

tert-butyl (2-(4-methylbenzoyl)phenethyl)carbamate (3b): an oil, 488 mg, 48% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.72 (d, J = 8.2 Hz, 2H), 7.51-7.43 (m, 1H), 7.40 (d, J = 7.6 Hz, 1H), 7.34-7.24 (m, 4H), 5.06 (s, 1H), 3.39 (m, 2H), 2.85 (t, J = 6.8 Hz, 2H), 2.44 (s, 3H), 1.41 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 198.2, 156.0, 144.3, 138.8, 138.3, 135.0, 130.8, 130.5, 129.2, 128.8, 125.6, 78.9, 42.1, 33.0, 28.4, 21.7 ppm.

tert-butyl (2-(3-methylbenzoyl)phenethyl)carbamate (3c): an oil, 478 mg, 47% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.66 (s, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.47 (td, J = 7.6, 1.8 Hz, 1H), 7.42 (m, 2H), 7.36 (d, J = 7.6 Hz, 1H), 7.32 (m, 2H), 5.05 (s, 1H), 3.48-3.31 (m, 2H), 2.87 (t, J = 6.8 Hz, 2H), 2.42 (s, 3H), 1.42 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 198.7, 156.0, 138.7, 138.5, 138.3, 137.6, 134.2, 130.8, 130.6, 130.5, 129.0, 128.3, 127.8, 125.6, 78.9, 42.1, 33.1, 28.4, 21.3 ppm.

tert-butyl (2-(4-fluorobenzoyl)phenethyl)carbamate (3d): an oil, 576 mg, 56% yield

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.90 - 7.81 (m, 2H), 7.53-7.45 (m, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.34-7.30 (m, 1H), 7.15 (t, J = 8.6 Hz, 2H), 5.00 (s, 1H), 3.40 (q, J = 6.6 Hz, 2H), 2.86 (t, J = 6.9 Hz, 2H), 1.42 (s, 9H). $^{13}$C $^{1}$H NMR (101 MHz, CDCl$_3$) δ 196.8, 165.9 (d, J = 255.8 Hz), 155.9, 138.5, 138.2, 134.0 (d, J = 2.9 Hz), 133.0 (d, J = 9.4 Hz), 130.9, 130.7, 128.8, 125.7, 115.6 (d, J = 22.0 Hz), 79.0, 42.1, 33.1, 28.4 ppm.

tert-butyl (2-(3-fluorobenzoyl)phenethyl)carbamate (3e): an oil, 545 mg, 53% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.55 (m, 2H), 7.51-7.39 (m, 3H), 7.31 (m, 3H), 4.99 (s, 1H), 3.40 (m, 2H), 2.88 (t, J = 6.8 Hz, 2H), 1.41 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 197.0, 162.6 (d, J = 248.4 Hz), 155.9, 139.8 (d, J = 6.2 Hz), 138.8, 137.8, 131.1, 131.0 (d, J = 11.5 Hz), 130.1 (d, J = 7.6 Hz), 129.1, 126.3 (d, J = 2.9 Hz), 125.8, 120.3 (d, J = 21.5 Hz), 116.8 (d, J = 22.3 Hz), 79.0, 42.1, 33.2, 28.3 ppm.

tert-butyl (2-(4-chlorobenzoyl)phenethyl)carbamate (3f): an oil, 594 mg, 55% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.76 (d, J = 8.5 Hz, 2H), 7.52-7.43 (m, 3H), 7.41 (d, J = 7.4 Hz, 1H), 7.30 (d, J = 4.0 Hz, 2H), 5.00 (s, 1H), 3.39 (m, 2H), 2.86 (t, J = 6.8 Hz, 2H), 1.41 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 197.1, 155.9, 139.9, 138.7, 138.0, 136.0, 131.7, 131.0, 130.9, 128.9, 128.8, 125.8, 79.0, 42.1, 33.2, 28.4 ppm.

tert-butyl (2-benzoyl-4-fluorophenethyl)carbamate (3g): an oil, 370 mg, 54% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.80 (d, J = 7.3 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 7.40-7.31 (m, 1H), 7.16 (td, J = 8.4, 2.7 Hz, 1H), 7.01 (dd, J = 8.7, 2.7 Hz, 1H), 4.93 (s, 1H), 3.35 (dd, J = 12.5, 6.3 Hz, 2H), 2.81 (t, J = 6.8 Hz, 2H), 1.40 (s, 9H). $^{13}$C $^{1}$H NMR (126 MHz, CDCl$_3$) δ 197.0, 160.4 (d, J = 247.4 Hz), 155.9, 140.0 (d, J = 5.9 Hz), 136.9, 134.1 (d, J = 2.6 Hz), 133.7, 132.6 (d, J = 7.6 Hz), 130.3, 128.6, 117.5 (d, J = 20.9 Hz), 115.6 (d, J = 22.6 Hz), 79.1, 42.0, 32.5, 28.3 ppm.

HRMS Calculated for C$_{20}$H$_{15}$O$_3$NF [M+H]$^+$ 344.1657; found 344.1646.

tert-butyl (2-benzoyl-6-chlorophenethyl)carbamate (3h): an oil, 396 mg, 55% yield

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.79 (d, J = 7.2 Hz, 2H), 7.65-7.56 (m, 1H), 7.53...
(dd, \( J = 7.8, 1.2 \) Hz, 1H), 7.47 (t, \( J = 7.8 \) Hz, 2H), 7.24 (t, \( J = 7.7 \) Hz, 1H), 7.19 (dd, \( J = 7.6, 1.3 \) Hz, 1H), 5.07 (s, 1H), 3.42 (d, \( J = 6.1 \) Hz, 2H), 2.98 (t, \( J = 6.7 \) Hz, 2H), 1.38 (s, 9H). \(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 197.4, 155.9, 140.9, 137.1, 136.1, 135.8, 133.7, 131.6, 130.4, 128.6, 127.0, 126.9, 78.9, 40.0, 30.8, 28.3 ppm. HRMS Calculated for C\(_{20}\)H\(_{29}\)O\(_5\)NCl [M+H]\(^{+}\) 360.1361; found 360.1348.

tert-butyl (2-benzoyl-4-bromophenethyl)carbamate (3i): an oil, 363 mg, 45% yield

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.82-7.77 (m, 2H), 7.66-7.61 (m, 1H), 7.58 (dd, \( J = 8.3, 2.1 \) Hz, 1H), 7.49 (t, \( J = 7.8 \) Hz, 2H), 7.43 (d, \( J = 2.1 \) Hz, 1H), 7.27 (d, \( J = 6.4 \) Hz, 1H), 4.90 (s, 1H), 3.35 (dd, \( J = 12.5, 6.2 \) Hz, 2H), 2.79 (t, \( J = 6.8 \) Hz, 2H), 1.40 (s, 9H). \(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 196.7, 155.9, 140.4, 137.3, 136.8, 133.7, 132.5, 132.5, 131.3, 130.3, 128.6, 119.5, 79.1, 41.8, 32.7, 28.3 ppm. HRMS Calculated for C\(_{20}\)H\(_{28}\)O\(_5\)NBr [M+H]\(^{+}\) 404.0856; found 404.0842.

tert-butyl (2-(4-chlorobenzoyl)-4-fluorophenethyl)carbamate (3j): an oil, 430 mg, 47% yield

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.77 (m, 2H), 7.58 (dd, \( J = 8.5 \) Hz, 2H), 7.48 (d, \( J = 8.5 \) Hz, 2H), 7.42-7.34 (m, 1H), 7.19 (td, \( J = 8.3, 2.7 \) Hz, 1H), 7.01 (dd, \( J = 8.6, 2.7 \) Hz, 1H), 4.89 (s, 1H), 3.35 (dd, \( J = 12.5, 6.3 \) Hz, 2H), 2.81 (t, \( J = 6.8 \) Hz, 2H), 1.41 (s, 9H). \(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 195.7, 160.4 (d, \( J = 247.6 \) Hz), 155.9, 140.4, 139.5 (d, \( J = 6.3 \) Hz), 135.2, 134.2 (d, \( J = 3.8 \) Hz), 132.7 (d, \( J = 7.6 \) Hz), 131.6, 129.0, 117.8 (d, \( J = 20.9 \) Hz), 115.5 (d, \( J = 22.6 \) Hz), 79.1, 42.0, 32.5, 28.3 ppm. HRMS Calculated for C\(_{20}\)H\(_{28}\)O\(_5\)NCl [M+H]\(^{+}\) 378.1267; found 378.1253.

tert-butyl (2-chloro-6-(4-chlorobenzoyl)phenethyl)carbamate (3k): an oil, 413 mg, 53% yield

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.76 (d, \( J = 8.5 \) Hz, 2H), 7.55 (dd, \( J = 8.0, 1.1 \) Hz, 1H), 7.46 (d, \( J = 8.6 \) Hz, 2H), 7.28 (d, \( J = 9.3 \) Hz, 1H), 7.19 (dd, \( J = 7.6, 1.2 \) Hz, 1H), 5.02 (s, 1H), 3.43 (dd, \( J = 12.1, 5.9 \) Hz, 2H), 2.99 (t, \( J = 6.7 \) Hz, 2H), 1.40 (s, 9H). \(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 196.1, 155.8, 140.4, 140.4, 136.3, 135.9, 135.4, 131.8, 131.8, 128.9, 127.0, 126.9, 78.9, 40.0, 30.8, 28.3 ppm. HRMS Calculated for C\(_{20}\)H\(_{28}\)O\(_5\)NCl [M+H]\(^{+}\) 394.0971; found 394.0957.

tert-butyl (4-bromo-2-(4-chlorobenzoyl)phenethyl)carbamate (3l): an oil, 360 mg, 41% yield

\(^{1}\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.74 (d, \( J = 8.5 \) Hz, 2H), 7.58 (dd, \( J = 8.3, 2.1 \) Hz, 1H), 7.46 (d, \( J = 8.5 \) Hz, 2H), 7.41 (d, \( J = 2.0 \) Hz, 1H), 7.27 (d, \( J = 8.0 \) Hz, 1H), 4.87 (s, 1H), 3.34 (dd, \( J = 12.4, 6.2 \) Hz, 2H), 2.78 (t, \( J = 6.8 \) Hz, 2H), 1.40 (s, 9H). \(^{13}\)C\(^{1}\)H NMR (126 MHz, CDCl\(_3\)) \( \delta \) 195.5, 155.9, 140.4, 139.9, 137.5, 135.2, 133.7, 132.7, 131.7, 131.2, 129.0, 119.6, 79.2, 41.8, 32.8, 28.3 ppm. HRMS Calculated for C\(_{20}\)H\(_{28}\)O\(_5\)NBrCl [M+H]\(^{+}\) 438.0466; found 438.0453.

3. General procedure for one-pot N-Boc deprotection and asymmetric reductive amination

Part 1: Asymmetric reductive amination for synthesizing tetrahydroquinolines

\[
\text{R}^1\text{NHBOc} \xrightarrow{1} \text{HCl/\(\text{Et}_2\)O, DCM} \rightarrow \text{R}^1\text{NH} \xrightarrow{2}[\text{Ir(COD)Cl}_2/\text{ZhaoPhos (0.5 mol%)}, \text{DCM}, \text{H}_2 (30 \text{ atm}), 25 \text{ }^\circ\text{C}] \rightarrow \text{R}^1\text{NHR}^2
\]

To a 2.5 mL vial was added the catalyst precursor [Ir(COD)Cl]\(_2\) (3.4 mg, 0.005 mmol), ZhaoPhos (9.5 mg, 0.011 mmol) and anhydrous CH\(_2\)Cl\(_2\) (0.3 mL) under argon atmosphere. The
mixture was stirred for 0.5 h at room temperature to give a clear solution.

A mixture of substrate I (0.2 mmol) and HCl (2 M in Et2O) (4 equiv.) was dissolved in CH2Cl2 (1 mL) and then stirred at rt for 6 h. All volatiles were removed, and the crude intermediate was transferred to a nitrogen-filled glovebox. An aliquot of the above in situ prepared catalyst solution (60 μL, 0.001 mmol) was transferred to a vial containing crude intermediate via a syringe, followed by addition of 0.8 mL more DCM. The vial was placed in an autoclave which was then charged with 30 atm of H2. The reaction was stirred at 25 °C for 24 h. After carefully releasing the hydrogen, the solution was neutralized with aqueous sodium bicarbonate solution (5 mL), and then extracted with DCM (5 mL×2). The combined organic phases were concentrated and passed through a short column of silica gel with EtOAc/Petroleum ether (1/20) as eluents to give the chiral tetrahydroquinoline products. The obtained products were pure enough for NMR analysis and determination of the enantiomeric excess.

(S)-2-methyl-1,2,3,4-tetrahydroquinoline (2a)^2:

![Structure of 2a]

an oil, 28.5 mg, 97% yield, 97% ee; [α]20D = -76.5 (c 0.15, CHCl3); 1H NMR (500 MHz, CDCl3) δ 6.95 (t, J = 6.7 Hz, 2H), 6.60 (t, J = 7.3 Hz, 1H), 6.46 (d, J = 8.2 Hz, 1H), 3.58-3.24 (m, 2H), 2.86-2.80 (m, 1H), 2.75-2.61 (m, 1H), 1.94-1.89 (m, 1H), 1.65-1.47 (m, 1H), 1.20 (d, J = 6.3 Hz, 3H). 13C[1H] NMR (126 MHz, CDCl3) δ 144.8, 129.3, 126.7, 121.1, 117.0, 114.0, 47.2, 30.1, 26.6, 22.6 ppm. Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): t1 = 14.1 min (major), t2 = 15.6 min (minor).

(S)-2-ethyl-1,2,3,4-tetrahydroquinoline (2b)^2:

![Structure of 2b]

an oil, 30.6 mg, 95% yield; 97% ee; [α]20D = -68.9 (c 0.21, CHCl3); 1H NMR (500 MHz, CDCl3) δ 6.95 (t, J = 7.5 Hz, 2H), 6.59 (t, J = 7.6Hz, 1H), 6.47 (d, J = 7.7 Hz, 1H), 3.71 (brs, 1H), 3.23-3.11 (m, 1H), 2.84-2.77 (m, 1H), 2.72 (m, 1H), 2.01-1.92 (m, 1H), 1.64-1.55 (m, 1H), 1.55-1.48 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H). 13C[1H] NMR (126 MHz, CDCl3) δ 144.7, 129.2, 126.7, 121.4, 116.9, 114.0, 53.0, 29.4, 27.6, 26.4, 10.1 ppm. Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): t1 = 12.0 min (major), t2 = 13.1 min (minor).

(S)-2-propyl-1,2,3,4-tetrahydroquinoline (2c)^2:

![Structure of 2c]

an oil, 33.2 mg, 95% yield; 96% ee; [α]20D = -77.5 (c 0.18, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.01 (t, J = 7.4 Hz, 2H), 6.76-6.60 (m, 1H), 6.52 (d, J = 7.7 Hz, 1H), 3.78 (s, 1H), 3.30 (m, 1H), 2.86 (m 1H), 2.78 (dt, J = 16.3, 4.7 Hz, 1H), 2.11-1.92 (m, 1H), 1.65 (m 1H), 1.59-1.42 (m, 4H), 1.02 (t, J = 7.0 Hz, 3H). 13C[1H] NMR (126 MHz, CDCl3) δ 144.7, 129.3, 126.7, 121.4, 116.9, 114.0, 51.3, 38.9, 28.1, 26.4, 18.9, 14.2 ppm. Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): t1 = 10.8 min (major), t2 = 13.3 min (minor).

(S)-2-butyl-1,2,3,4-tetrahydroquinoline (2d)^2:

![Structure of 2d]

an oil, 36.6 mg, 97% yield; 97% ee; [α]20D = -70.4 (c 0.15, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.01 (t, J = 7.5 Hz, 2H), 6.65 (t, J = 7.4, 1H), 6.53 (d, J = 7.8 Hz, 1H), 3.81 (s, 1H), 3.37-3.23 (m, 1H), 2.87 (m 1H), 2.78 (m 1H), 2.11-1.95 (m, 1H), 1.65 (m 1H), 1.55 (m 2H), 1.50-1.35 (m, 4H), 1.00 (t, J = 7.6, 3H). 13C[1H] NMR (126 MHz, CDCl3) δ 144.7, 129.3, 126.7, 121.4, 116.9, 114.0, 51.6, 36.4, 28.1, 27.9, 26.4, 22.9, 14.1 ppm. Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): t1 = 9.3 min (major), t2 = 10.8 min (minor).
(S)-2-penty1-1,2,3,4-tetrahydroquinoline (2e):

\[
\begin{align*}
\text{an oil, 38.6 mg, 95% yield; [\alpha]_{D}^{20} & = -67.9 (c 0.12, \text{CHCl}_3); \ 1^H \text{NMR (500 MHz, CDCl}_3) \delta 7.01 (t, J = 7.5 Hz, 2H), 6.65 (td, J = 7.4, 0.9 Hz, 1H), 6.52 (d, J = 7.8 Hz, 1H), 3.80 (s, 1H), 3.36-3.23 (m, 1H), 2.86 (m, 1H), 2.78 (dt, J = 16.3, 4.7 Hz, 1H), 2.15-1.91 (m, 1H), 1.65 (m, 1H), 1.59-1.49 (m, 2H), 1.49-1.31 (m, 6H), 0.96 (t, J = 6.9 Hz, 3H).} \\
1^3C\{1^H\} \text{NMR (126 MHz, CDCl}_3) \delta 144.6, 129.2, 126.6, 121.3, 116.8, 113.9, 51.5, 36.6, 31.9, 28.0, 26.4, 25.3, 22.6, 14.0 ppm. \text{Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): } t_1 = 8.5 \text{ min (major), } t_2 = 9.2 \text{ min (minor).}
\end{align*}
\]

(S)-2-hexyl-1,2,3,4-tetrahydroquinoline (2f):

\[
\begin{align*}
\text{an oil, 41.6 mg, 96% yield; 94% ee; [\alpha]_{D}^{20} & = -78.3 (c 0.14, \text{CHCl}_3); \ 1^H \text{NMR (500 MHz, CDCl}_3) \delta 7.02 (t, J = 7.5 Hz, 2H), 6.66 (td, J = 7.4, 0.9 Hz, 1H), 6.53 (d, J = 7.8 Hz, 1H), 3.82 (s, 1H), 3.38-3.22 (m, 1H), 2.87 (m, 1H), 2.79 (dt, J = 16.3, 4.7 Hz, 1H), 2.12-1.95 (m, 1H), 1.66 (m, 1H), 1.60-1.49 (m, 2H), 1.49-1.27 (m, 8H), 0.97 (t, J = 6.8 Hz, 3H).} \\
1^3C\{1^H\} \text{NMR (126 MHz, CDCl}_3) \delta 144.7, 129.3, 126.7, 121.4, 116.9, 114.0, 51.6, 36.7, 31.9, 29.5, 28.1, 26.5, 25.7, 22.7, 14.1 ppm. \text{Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): } t_1 = 8.8 \text{ min (major), } t_2 = 9.5 \text{ min (minor).}
\end{align*}
\]

(S)-2-heptyl-1,2,3,4-tetrahydroquinoline (2g):

\[
\begin{align*}
\text{an oil, 43.9 mg, 95% yield; 92% ee; [\alpha]_{D}^{20} & = -68.2 (c 0.21, \text{CHCl}_3); \ 1^H \text{NMR (500 MHz, CDCl}_3) \delta 7.00 (t, J = 7.5 Hz, 2H), 6.64 (t, J = 7.1 Hz, 1H), 6.51 (d, J = 7.8 Hz, 1H), 3.80 (s, 1H), 3.37-3.20 (m, 1H), 2.85 (m, 1H), 2.77 (dt, J = 16.3, 4.7 Hz, 1H), 2.12-1.82 (m, 1H), 1.76-1.58 (m, 1H), 1.58-1.49 (m, 2H), 1.49-1.27 (m, 10H), 0.94 (t, J = 6.9 Hz, 3H).} \\
1^3C\{1^H\} \text{NMR (126 MHz, CDCl}_3) \delta 144.7, 129.2, 126.7, 121.4, 116.9, 114.0, 51.6, 36.7, 31.8, 29.7, 29.3, 28.1, 26.4, 25.7, 22.7, 14.1 ppm. \text{Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): } t_1 = 9.3 \text{ min (major), } t_2 = 9.9 \text{ min (minor).} \text{HRMS Calculated for C}_{18}H_{23}N \text{[M+H]}^+ \text{ 232.2060; found 232.0522.}
\end{align*}
\]

(R)-2-benzyl-1,2,3,4-tetrahydroquinoline (2h):

\[
\begin{align*}
\text{an oil, 43.8 mg, 94% yield; [\alpha]_{D}^{20} & = -79.9 (c 0.21, \text{CHCl}_3); \ 1^H \text{NMR (500 MHz, CDCl}_3) \delta 7.33 (dd, J = 10.2, 4.5 Hz, 2H), 7.29-7.20 (m, 3H), 6.93 (dd, J = 13.3, 7.0 Hz, 2H), 6.59 (td, J = 7.4, 1.0 Hz, 1H), 6.38 (d, J = 4.5Hz, 1H), 3.73 (s, 1H), 3.67-3.42 (m, 1H), 2.89-2.72 (m, 2H), 2.69 (dd, J = 13.3, 8.7 Hz, 1H), 2.03-1.98 (m, 1H), 1.75-1.68 (m, 1H).} \\
1^3C\{1^H\} \text{NMR (126 MHz, CDCl}_3) \delta 144.4, 138.5, 129.3, 129.2 128.6, 126.7, 126.5, 121.3, 117.2, 114.2, 52.7, 43.0, 28.3, 26.2 ppm. \text{Enantiomeric excess was determined by HPLC (OD-H column, hexane/iPrOH 85/15, 0.80 mL/min, 254 nm): } t_1 = 6.4 \text{ min (minor), } t_2 = 7.1 \text{ min (major).}
\end{align*}
\]

(S)-7-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (2i):

\[
\begin{align*}
\text{an oil, 33.2 mg, 94% yield; 96% ee; [\alpha]_{D}^{20} & = -69.6 (c 0.17, \text{CHCl}_3); \ 1^H \text{NMR (500 MHz, CDCl}_3) \delta 6.89 (d, J = 8.2 Hz, 1H), 6.24 (dd, J = 8.2, 2.5 Hz, 1H), 6.08 (d, J = 2.5 Hz, 1H), 3.76 (s, 4 H), 3.41 (m, 1H), 2.92-2.76 (m, 1H), 2.76-2.67 (m, 1H), 1.95 (m, 1H), 1.60 (m, 1H), 1.24 (d, J = 6.3 Hz, 3H).} \\
1^3C\{1^H\} \text{NMR (126 MHz, CDCl}_3) \delta 158.8, 145.6, 129.9, 113.7, 102.9, 99.2, 55.1, 47.1, 30.4, 25.9, 22.6 ppm. \text{Enantiomeric excess was determined by HPLC (AD-3 column, hexane/iPrOH 95/5, 0.50 mL/min, 254 nm): } t_1 =
\end{align*}
\]
12.2 min (minor), \( t_2 = 13.5 \) min (major). HRMS Calculated for \( \text{C}_{11}\text{H}_{16}\text{O} \) [M+H]\(^+\) 178.1226; found 178.1221.

**(S)-8-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (2j):**

\[
\text{an oil, 33.9 mg, 96\% yield; 95\% ee; } [\alpha]^{20}_D = -63.5 \ (c \ 0.16, \text{CHCl}_3); \ \text{^1H NMR (500 MHz, CDCl}_3) \ \delta 6.62 \ (m, 2H), 6.48 \ (d, J = 8.4 \text{ Hz, 1H}), 3.75 \ (s, 3H), 3.43-3.30 \ (m, 1H), 2.91-2.84 \ (m, 1H), 2.76-2.71 \ (m, 1H), 1.97-1.91 \ (m, 1H), 1.73-1.53 \ (m, 1H), 1.23 \ (d, J = 6.3 \text{ Hz, 3H}). \ \text{^13C} \{^1H \} \ \text{NMR (126 MHz, CDCl}_3) \ \delta 151.8, 138.9, 122.5, 115.3, 114.6, 112.8, 55.8, 47.5, 30.3, 26.9, 22.5 \text{ ppm}. \]

Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): \( t_1 = 25.4 \) min (major), \( t_2 = 30.1 \) min (minor).

**(S)-2,6-dimethyl-1,2,3,4-tetrahydroquinoline (2k):**

\[
\text{an oil, 31.2 mg, 97\% yield; 95\% ee; } [\alpha]^{20}_D = -68.4 \ (c \ 0.15, \text{CHCl}_3); \ \text{^1H NMR (500 MHz, CDCl}_3) \ \delta 6.81 \ (m, 2H), 6.44 \ (d, J = 7.7 \text{ Hz, 1H}), 3.42-3.36 \ (m, 1H), 2.88-2.79 \ (m, 1H), 2.75-2.70 \ (m, 1H), 2.23 \ (s, 3H), 1.97-1.92 \ (m, 1H), 1.65-1.60 \ (m, 1H), 1.23 \ (d, J = 6.3 \text{ Hz, 3H}). \ \text{^13C} \{^1H \} \ \text{NMR (126 MHz, CDCl}_3) \ \delta 142.4, 129.8, 127.2, 126.3, 121.2, 114.3, 47.3, 30.3, 26.6, 22.4, 20.4 \text{ ppm}. \]

Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): \( t_1 = 19.8 \) min (major), \( t_2 = 24.4 \) min (minor).

**(S)-7-(4-bromobutoxy)-2-methyl-1,2,3,4-tetrahydroquinoline (2l):**

\[
\text{an oil, 51.2 mg, 86\% yield; 97\% ee; } [\alpha]^{20}_D = -79.3 \ (c \ 0.16, \text{CHCl}_3); \ \text{^1H NMR (400 MHz, CDCl}_3) \ \delta 6.87 \ (dd, J = 8.2, 0.9 \text{ Hz, 1H}), 6.21 \ (dd, J = 8.2, 2.5 \text{ Hz, 1H}), 6.05 \ (d, J = 2.5 \text{ Hz, 1H}), 3.94 \ (t, J = 6.1 \text{ Hz, 2H}), 3.50 \ (t, J = 6.7 \text{ Hz, 2H}), 3.45 - 3.32 \ (m, 1H), 2.78 \ (m, 1H), 2.69 \ (m, 1H), 2.07 \ (m, 2H), 1.98 - 1.84 \ (2m, 2H), 1.58 \ (m, 1H), 1.22 \ (d, J = 6.3 \text{ Hz, 3H}). \ \text{^13C} \{^1H \} \ \text{NMR (101 MHz, CDCl}_3) \ \delta 158.0, 145.5, 129.8, 113.8, 103.4, 99.8, 66.6, 47.1, 33.6, 30.3, 29.5, 27.9, 25.8, 22.5 \text{ ppm}. \]

Enantiomeric excess was determined by UPLC (OJ-3 column, hexane/iPrOH 65/35, 0.50 mL/min, 254 nm): \( t_1 = 7.1 \) min (major), \( t_2 = 8.8 \) min (minor). HRMS Calculated for \( \text{C}_{19}\text{H}_{23}\text{ONBr} \) [M+H]\(^+\) 298.0801; found 298.0793.

**(S)-8-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (2m):**

\[
\text{an oil, 31.0 mg, 94\% yield; 98\% ee; } [\alpha]^{20}_D = -67.9 \ (c \ 0.14, \text{CHCl}_3); \ \text{^1H NMR (500 MHz, CDCl}_3) \ \delta 6.87 - 6.70 \ (m, 2H), 6.53 \ (td, J = 7.8, 5.4 \text{ Hz, 1H}), 3.91 \ (s, 1H), 3.47-3.41 \ (m, 1H), 2.90-2.84 \ (m, 1H), 2.81-2.76 \ (m, 1H), 2.06 - 1.94 \ (m, 1H), 1.74-1.60 \ (m, 1H), 1.29 \ (dd, J = 10.9, 6.3 \text{ Hz, 3H}). \ \text{^13C} \{^1H \} \ \text{NMR (126 MHz, CDCl}_3) \ \delta 150.7 \ (d, J = 237.3 \text{ Hz), 133.2 (d, J = 12.2 Hz), 124.2 (d, J = 2.8 Hz), 123.3 (d, J = 3.8 Hz), 115.6 (d, J = 7.4 \text{ Hz, 1H}), 112.1 (d, J = 18.3 \text{ Hz), 46.6, 29.7, 26.2 (d, J = 2.9 \text{ Hz), 22.4 \text{ ppm. Enantiomeric excess was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): } t_1 = 6.2 \text{ min (major), } t_2 = 6.6 \text{ min (minor). HRMS Calculated for } \text{C}_{10}\text{H}_{13} \text{NF} \ [M+H]\(^+\) 166.1027; found 166.1021.}

**(S)-6-bromo-2-methyl-1,2,3,4-tetrahydroquinoline (2n):**

\[
\text{an oil, 43.3 mg, 96\% yield; 95\% ee; } [\alpha]^{20}_D = -78.1 \ (c \ 0.18, \text{CHCl}_3); \ \text{^1H NMR (500 MHz, CDCl}_3) \ \delta 7.07-7.04 \ (m, 1H), 7.01 \ (dd, J = 8.4, 2.3 \text{ Hz, 1H}), 6.32 \ (d, J = 8.4 \text{ Hz, 1H}), 3.67 \ (s, 1H), 3.42-3.29 \ (m, 1H), 2.81-2.75 \ (m, 1H), 2.71-2.61 \ (m, 1H), 1.92-1.87 \ (m, 1H), 1.59-1.46 \ (m, 1H), 1.19 \ (d, J = 6.3 \text{ Hz, 3H}). \ \text{^13C} \{^1H \} \ \text{NMR (126 MHz, CDCl}_3) \ \delta 143.8, 131.6, 129.3, 123.1, 115.4, 108.2, 47.1, 29.6, 26.4, 22.5 \text{ ppm. Enantiomeric excess}
\]
was determined by HPLC (OJ-H column, hexane/iPrOH 95/5, 0.80 mL/min, 254 nm): \( t_1 = 14.9 \) min (major), \( t_2 = 17.7 \) min (minor).

**(R)-2-phenyl-1,2,3,4-tetrahydroquinoline (2a):**

![Structure](image)

an oil, 35.5 mg, 85% yield; 80% ee; [%alpha]_D^20 = +23.8 (c 0.25, CHCl₃); ^1^H NMR (500 MHz, CDCl₃) \( \delta 7.44 \) (d, \( J = 7.2 \) Hz, 2H), 7.40 (t, \( J = 7.5 \) Hz, 2H), 7.34 (t, \( J = 7.1 \) Hz, 1H), 7.06 (t, \( J = 7.7 \) Hz, 2H), 6.71 (t, \( J = 7.3 \) Hz, 1H), 6.59 (d, \( J = 7.8 \) Hz, 1H), 4.49 (dd, \( J = 9.4, 3.2 \) Hz, 1H), 4.10 (s, 1H), 3.01-2.94 (m, 1H), 2.81-2.76 (m, 1H), 2.20-2.15 (m, 1H), 2.12-1.94 (m, 1H). ^1^C[^1^H] NMR (126 MHz, CDCl₃) \( \delta 144.8, 144.7, 129.3, 128.6, 127.4, 126.9, 126.5, 120.9, 117.2, 114.0, 56.2, 31.0, 26.4 \) ppm. Enantiomeric excess was determined by HPLC (OD-H column, hexane/iPrOH 85/15, 0.80 mL/min, 250 nm): \( t_1 = 8.9 \) min (minor), \( t_2 = 10.8 \) min (major).

**(R)-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinoline (2p):**

![Structure](image)

an oil, 39.0 mg, 86% yield; 84% ee; [%alpha]_D^20 = +25.2 (c 0.16, CHCl₃); ^1^H NMR (500 MHz, CDCl₃) \( \delta 7.34 \) (dd, \( J = 8.4, 5.6 \) Hz, 2H), 7.01 (dd, \( J = 16.9, 8.3 \) Hz, 4H), 6.65 (t, \( J = 7.4 \) Hz, 1H), 6.53 (d, \( J = 7.8 \) Hz, 1H), 4.41 (dd, \( J = 9.4, 3.1 \) Hz, 1H), 3.99 (s, 1H), 2.94-2.88 (m, 1H), 2.74-2.69 (m, 1H), 2.11-2.05 (m, 1H), 2.02 -1.77 (m, 1H). ^1^C[^1^H] NMR (126 MHz, CDCl₃) \( \delta 162.1 \) (d, \( J = 245.2 \) Hz), 144.5, 140.5 (d, \( J = 3.0 \) Hz), 129.3, 128.1 (d, \( J = 7.9 \) Hz), 126.9, 120.8, 117.3, 115.3 (d, \( J = 21.2 \) Hz), 114.0, 55.6, 31.1, 26.3 ppm. Enantiomeric excess was determined by HPLC (OD-H column, hexane/iPrOH 85/15, 0.80 mL/min, 250 nm): \( t_1 = 8.4 \) min (minor), \( t_2 = 12.2 \) min (major).

**(R)-2-(4-fluorophenyl)-8-methoxy-1,2,3,4-tetrahydroquinoline (2q):**

![Structure](image)

an oil, 45.2 mg, 88% yield; 85% ee; [%alpha]_D^20 = +21.6 (c 0.18, CHCl₃); ^1^H NMR (500 MHz, CDCl₃) \( \delta 7.41-7.30 \) (m, 2H), 7.02 (t, \( J =8.6 \) Hz, 2H), 6.68 - 6.55 (m, 1H), 6.50 (d, \( J = 8.5 \) Hz, 2H), 4.34 (dd, \( J = 9.7, 2.9 \) Hz, 1H), 3.74 (s, 4H), 2.96-2.89 (m, 1H), 2.71 (dt, \( J = 16.6, 4.6 \) Hz, 1H), 2.26-2.02 (m, 1H), 1.98-1.90 (m, 1H). ^1^C[^1^H] NMR (126 MHz, CDCl₃) \( \delta 162.1 \) (d, \( J = 245.0 \) Hz), 152.0, 140.6 (d, \( J = 3.0 \) Hz), 138.7, 128.1 (d, \( J = 7.9 \) Hz), 122.1, 115.4, 115.2, 114.6, 113.1, 55.9, 55.8, 31.3, 26.8 ppm. Enantiomeric excess was determined by HPLC (OD-H column, hexane/iPrOH 85/15, 0.80 mL/min, 250 nm): \( t_1 = 6.3 \) min (minor), \( t_2 = 8.5 \) min (major). HRMS Calculated for C_{18}H_{19}ONF\[M+H]^+ 258.1289; found 258.1280.

**(R)-6-bromo-2-(4-fluorophenyl)-1,2,3,4-tetrahydroquinoline (2r):**

![Structure](image)

an oil, 55 mg, 90% yield; 90% ee; [%alpha]_D^20 = +25.6 (c 0.24, CHCl₃); ^1^H NMR (500 MHz, CDCl₃) \( \delta 7.38-7.34 \) (m, 2H), 7.16-7.09 (m, 2H), 7.09-7.03 (m, 1H), 6.44 (d, \( J = 8.4 \) Hz, 1H), 4.43 (dd, \( J = 9.2, 3.2 \) Hz, 1H), 4.07 (s, 1H), 2.93-2.86 (m, 1H), 2.74-2.68 (m, 1H), 2.13-2.08 (m, 1H), 2.00 -1.85 (m, 1H). ^1^C[^1^H] NMR (126 MHz, CDCl₃) \( \delta 162.1 \) (d, \( J = 245.5 \) Hz), 143.5, 140.0 (d, \( J = 3.1 \) Hz), 131.7, 129.6, 128.0 (d, \( J = 8.0 \) Hz), 122.8, 115.5 (d, \( J = 8.0 \) Hz), 115.3, 108.7, 55.4, 30.5, 26.0 ppm. Enantiomeric excess was determined by HPLC (OD-H column, hexane/iPrOH 85/15, 0.80 mL/min, 254 nm): \( t_1 = 7.2 \) min (minor), \( t_2 = 13.6 \) min (major). HRMS Calculated for C_{18}H_{19}ONBrF\[M+H]^+ 306.0288; found 306.0278.

**Part 2:** Asymmetric reductive amination for synthesizing tetrahydroisoquinolines

**Table S1.** Optimization of reaction conditions for the synthesis of THIQs.
**Procedure for asymmetric reductive amination for the synthesis of tetrahydroisoquinolines**

To a 2.5 mL vial was added the catalyst precursor [Ir(COD)Cl]₂ (3.4 mg, 0.005 mmol), ZhaoPhos (9.5 mg, 0.011 mmol) and anhydrous CH₂Cl₂ (0.3 mL) under argon atmosphere. The mixture was stirred for 0.5 h at room temperature to give a clear solution.

A mixture of substrate 3 (0.2 mmol) and HCl (2 M in Et₂O) (4 equiv.) was dissolved in CH₂Cl₂ (1 mL) and then stirred at rt for 6 h. All volatiles were removed, and the resulting crude intermediate was transferred to a nitrogen-filled glovebox. An aliquot of the above in situ prepared catalyst solution (60 μL, 0.001 mmol) was transferred to a vial containing crude intermediate via a syringe, followed by addition of EtOAc (0.8 mL) and Ti(O'Pr)₄ (1.0 equiv). The vial was placed in an autoclave which was then charged with 30 atm of H₂. The reaction was stirred at 25 °C for 24 h. After carefully releasing the hydrogen, the solution was neutralized with aqueous sodium bicarbonate solution (5 mL), extracted with DCM (5 mL × 2). The combined organic phases were dried over anhydrous Na₂SO₄, concentrated and passed through a short column of silica gel with

---

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^a Reaction conditions: 2a (0.1 mmol), [Ir(cod)Cl]₂ (0.5 mol%), ligand (1.1 mol%), additive (1.0 equiv.), solvent (0.6 mL); ^b Determined by 'H NMR analysis; ^c Determined by HPLC analysis of the corresponding benzamides. ^d 15 atm H₂; ^e 0.1 mol% [Ir(cod)Cl]₂ was used; ^f [Rh(cod)Cl]₂ was used; ^g [Rh(NBD)(Cl)₂] was used.
petroleum/EtOAc (3:1) as eluents to give the chiral tetrahydroisoquinoline products. The obtained products were pure enough for NMR analysis. The enantiomeric excesses were determined by HPLC analysis of the corresponding benzamides.

(S)-1-phenyl-1,2,3,4-tetrahydroisoquinoline (4a)^3:

A white solid, 39.2 mg, 94% yield; 93% ee; [α]^20_D = +11.2 (c 0.61, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.35-7.30 (m, 2H), 7.29-7.23 (m, 3H), 7.14 (d, J = 4.2 Hz, 2H), 7.04 (dd, J = 8.1, 4.7 Hz, 1H), 6.75 (d, J = 7.7 Hz, 1H), 5.10 (s, 1H), 3.27 (dt, J = 8.7, 4.6 Hz, 1H), 3.20-2.97 (m, 1H), 2.83 (dt, J = 8.6, 3.8 Hz, 1H). 13C [1H] NMR (126 MHz, CDCl3) δ 144.8, 138.2, 135.4, 129.6, 129.0, 128.2, 128.2, 128.1, 126.2, 126.1, 125.6, 62.1, 42.2, 29.8 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 0.80 mL/min, 220 nm): t_1 = 11.2 min (major), t_2 = 13.6 min (minor).

(S)-1-(p-tolyl)-1,2,3,4-tetrahydroisoquinoline (4b)^4:

A white solid, 41.0 mg, 92% yield; 90% ee; [α]^20_D = +8.3 (c 0.41, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.18-7.10 (m, 2H), 7.03 (dt, J = 8.3, 4.2 Hz, 1H), 6.76 (d, J = 7.7 Hz, 1H), 5.07 (s, 1H), 3.27 (dt, J = 8.8, 4.6 Hz, 1H), 3.17-2.96 (m, 2H), 2.83 (dt, J = 8.4, 3.7 Hz, 1H), 2.34 (s, 3H). 13C [1H] NMR (126 MHz, CDCl3) δ 141.9, 138.4, 137.0, 135.4, 129.1, 129.0, 128.8, 128.1, 126.2, 125.6, 61.7, 42.2, 29.8, 21.1 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 0.80 mL/min, 220 nm): t_1 = 9.1 min (major), t_2 = 13.3 min (minor).

(S)-1-(m-tolyl)-1,2,3,4-tetrahydroisoquinoline (4c)^5:

A white solid, 41.4 mg, 93% yield; 90% ee; [α]^20_D = +7.6 (c 0.22, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.23 (t, J = 10.3 Hz, 1H), 7.17 (d, J = 4.2 Hz, 2H), 7.12 (d, J = 6.1 Hz, 2H), 7.09-7.04 (m, 2H), 6.79 (d, J = 7.7 Hz, 1H), 5.09 (s, 1H), 3.38-3.27 (m, 1H), 3.21-3.02 (m, 2H), 2.86 (dt, J = 8.1, 7.5 Hz, 1H), 2.35 (s, 3H). 13C [1H] NMR (126 MHz, CDCl3) δ 144.7, 138.3, 138.1, 135.4, 129.6, 129.0, 128.2, 128.1, 126.2, 126.1, 125.6, 62.1, 42.4, 29.8, 21.4 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 1.0 mL/min, 220 nm): t_1 = 8.1 min, t_2 = 8.6 min (major).

(S)-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (4d)^5:

A white solid, 43.1 mg, 95% yield; 94% ee; [α]^20_D = +9.6 (c 0.26, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.27-7.21 (m, 2H), 7.15 (d, J = 4.0 Hz, 2H), 7.08-6.97 (m, 3H), 6.72 (d, J = 7.7 Hz, 1H), 5.09 (s, 1H), 3.26 (dt, J = 8.8, 4.7 Hz, 1H), 3.07 (m, 2H), 2.82 (dt, J = 8.3, 3.9 Hz, 1H). 13C [1H] NMR (126 MHz, CDCl3) δ 162.1 (d, J = 245.5 Hz), 140.5, 138.0, 135.3, 130.5 (d, J = 8.0 Hz, 129.1, 128.0, 126.4, 125.7, 115.2 (d, J = 21.2 Hz), 61.3, 42.2, 29.6 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 0.80 mL/min, 220 nm): t_1 = 11.0 min (major), t_2 = 11.7 min (minor).

(S)-1-(3-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (4e)^5:

A white solid, 42.2 mg, 94% yield; 88% ee; [α]^20_D = +13.3 (c 0.22, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.31 (m, 1H), 7.23-7.16 (m, 2H), 7.13-7.05 (m, 2H), 7.00 m, 2H), 6.78 (d, J = 7.7 Hz, 1H), 5.13 (s, 1H), 3.28 (dt, J = 11.3, 4.9 Hz, 1H), 3.16-2.98 (m,
2.86 (dt, J = 16.1, 4.3 Hz, 1H). $^{13}$C $^{[1]}$H NMR (126 MHz, CDCl$_3$) δ 162.9 (d, J = 245.9 Hz), 147.4 (d, J = 6.6 Hz), 137.5, 135.4, 129.8 (d, J = 8.1 Hz), 129.1, 128.0, 126.5, 125.7, 124.6 (d, J = 2.8 Hz), 115.8 (d, J = 21.4 Hz), 114.3 (d, J = 21.2 Hz), 61.5 (d, J = 1.6 Hz), 42.0, 29.6 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 1.0 mL/min, 220 nm): t$_1$ = 10.4 min (major), t$_2$ = 11.3 min (major).

(S)-1-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline (4f):

a white solid, 45.2 mg, 93% yield; 93% ee; [α]$^{[20]}$$^b$ = +17.8 (c 0.21, CHCl$_3$); $^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.29 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 4.1 Hz, 2H), 7.04 (dt, J = 8.3, 4.2 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 5.08 (s, 1H), 3.25 (dt, J = 11.1, 4.8 Hz, 1H), 3.06 (m, 2H), 2.82 (dt, J = 8.5, 4.0 Hz, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 143.3, 137.7, 135.4, 133.1, 130.3, 129.1, 128.5, 127.9, 126.4, 125.7, 121.4, 42.2, 29.6 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 0.80 mL/min, 210 nm): t$_1$ = 10.3 min (major), t$_2$ = 12.9 min (minor).

(S)-7-flouro-1-phenyl-1,2,3,4-tetrahydroisoquinoline (4g):

a white solid, 43.1 mg, 95% yield; 94% ee; [α]$^{[20]}$$^b$ = +23.4 (c 0.63, CHCl$_3$); $^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.41-7.30 (m, 3H), 7.29 (dd, J = 5.9, 2.4 Hz, 2H), 7.12 (dd, J = 8.4, 5.8 Hz, 1H), 6.87 (td, J = 8.4, 2.6 Hz, 1H), 6.48 (dd, J = 9.9, 2.6 Hz, 1H), 5.08 (s, 1H), 3.37-3.19 (m, 1H), 3.10 (ddd, J = 11.8, 9.2, 4.3 Hz, 1H), 3.07-2.93 (m, 1H), 2.82 (dt, J = 16.0, 4.1 Hz, 1H). $^{13}$C $^{[1]}$H NMR (126 MHz, CDCl$_3$) δ 160.8 (d, J = 243.4 Hz), 144.0, 140.1 (d, J = 6.5 Hz), 130.9 (d, J = 3.0 Hz), 130.3 (d, J = 7.6 Hz), 128.9, 128.5, 127.6, 114.3 (d, J = 21.5 Hz), 113.5 (d, J = 21.4 Hz), 62.2 (d, J = 1.7 Hz), 42.3, 29.0 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 80/20, 1.0 mL/min, 210 nm): t$_1$ = 15.1 min (major), t$_2$ = 15.7 min (minor). HRMS Calculated for C$_{15}$H$_{13}$NF [M+H]$^+$ 228.1183; found 228.1176.

(S)-5-chloro-1-phenyl-1,2,3,4-tetrahydroisoquinoline (4h):

a white solid, 44.7 mg, 92% yield; 86% ee; [α]$^{[20]}$$^b$ = +72.9 (c 0.96, CHCl$_3$); $^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.40-7.30 (m, 3H), 7.28-7.20 (m, 2H), 7.01 (t, J = 7.8 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.11 (s, 1H), 3.33 (dt, J = 12.2, 5.3 Hz, 1H), 3.22-3.03 (m, 1H), 3.03-2.69 (m, 2H). $^{13}$C $^{[1]}$H NMR (126 MHz, CDCl$_3$) δ 144.2, 140.6, 134.4, 133.6, 128.9, 128.5, 127.6, 127.0, 126.6, 62.1, 41.7, 27.7 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 80/20, 1.0 mL/min, 210 nm): t$_1$ = 13.3 min (major), t$_2$ = 20.6 min (minor). HRMS Calculated for C$_{15}$H$_{13}$NCI [M+H]$^+$ 244.0888; found 244.0881.

(S)-7-bromo-1-phenyl-1,2,3,4-tetrahydroisoquinoline (4i):

a white solid, 52.4 mg, 91% yield; 94% ee; [α]$^{[20]}$$^b$ = -75.8 (c 0.76, CHCl$_3$); $^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.41-7.31 (m, 3H), 7.31 7.25 (m, 2H), 7.05 (d, J = 8.2 Hz, 1H), 6.92 (d, J = 1.7 Hz, 1H), 5.07 (s, 1H), 3.53-3.16 (m, 1H), 3.11-3.06 (m, 1H), 3.02-2.96 (m, 1H), 2.82-2.77 (m, 1H), 2.01-1.47 (m, 1H). $^{13}$C $^{[1]}$H NMR (126 MHz, CDCl$_3$) δ 143.9, 140.4, 134.4, 130.7, 130.7, 129.4, 128.9, 128.6, 127.7, 119.2, 61.8, 42.0, 29.3 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 70/30, 1.0 mL/min, 210 nm): t$_1$ = 8.1 min (major), t$_2$ = 8.6 min (minor). HRMS Calculated for C$_{15}$H$_{13}$NBr [M+H]$^+$ 288.0382; found 288.0374.

(S)-1-(4-chlorophenyl)-7-flouro-1,2,3,4-tetrahydroisoquinoline (4j):
a white solid, 49.0 mg, 94% yield; 93% ee; $[\alpha]_{D}^{20} = +43.3$ (c 0.69, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33 (d, $J = 8.5$ Hz, 2H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.12 (dd, $J = 8.5$, 5.8 Hz, 1H), 6.91-6.85 (m, 1H), 6.45-6.42 (m, 1H), 5.05 (s, 1H), 3.35-3.21 (m, 1H), 3.12-3.06 (m, 1H), 3.05-2.97 (m, 1H), 2.83-2.77 (m, 1H). $^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ 160.8 (d, $J = 243.7$ Hz), 142.5, 139.6 (d, $J = 6.4$ Hz), 133.4, 130.9 (d, $J = 3.0$ Hz), 130.5 (d, $J = 7.7$ Hz), 130.2, 128.7, 114.2 (d, $J = 21.6$ Hz), 113.7 (d, $J = 21.3$ Hz), 61.5 (d, $J = 1.8$ Hz), 42.3, 28.9 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 80/20, 0.5 mL/min, 210 nm): $t_1 = 24.8$ min (major), $t_2 = 28.8$ min (minor). HRMS Calculated for C$_{15}$H$_{12}$NCl [M+H]$^+$ 262.0793; found 262.0784.

(S)-5-chloro-1-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline (4k):

a white solid, 50.6 mg, 91% yield; 85% ee; $[\alpha]_{D}^{20} = +85.4$ (c 0.85, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32 (d, $J = 8.5$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 1H), 7.21 (d, $J = 8.5$ Hz, 2H), 7.02 (t, $J = 7.8$ Hz, 1H), 6.66 (d, $J = 7.7$ Hz, 1H), 5.08 (s, 1H), 3.33-3.27 (m, 1H), 3.15-3.08 (m, 1H), 2.94 (q, $J = 5.6$, 5.0 Hz, 2H). $^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ 142.71, 140.12, 134.56, 133.59, 133.38, 130.33, 128.65, 127.25, 126.45, 126.39, 61.42, 41.71, 27.67 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 80/20, 1.0 mL/min, 220 nm): $t_1 = 17.0$ min (major), $t_2 = 24.1$ min (minor). HRMS Calculated for C$_{15}$H$_{14}$NCl$_2$ [M+H]$^+$ 278.0498; found 278.0489.

(S)-7-bromo-1-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinoline (4l):

a white solid, 57.3 mg, 89% yield; 98% ee; $[\alpha]_{D}^{20} = -10.1$ (c 0.96, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.31 (d, $J = 8.4$ Hz, 2H), 7.29-7.24 (m, 1H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8.2$ Hz, 1H), 6.84 (d, $J = 2.1$ Hz, 1H), 5.02 (s, 1H), 3.43-3.16 (m, 1H), 3.09-3.02 (m, 1H), 3.01-2.89 (m, 1H), 2.76 (dt, $J = 16.2$, 4.4 Hz, 1H). $^{13}$C ($^1$H) NMR (101 MHz, CDCl$_3$) $\delta$ 142.4, 139.9, 134.3, 133.5, 130.8, 130.6, 130.2, 129.6, 128.7, 119.3, 61.2, 42.0, 29.2 ppm. Enantiomeric excess was determined by HPLC for the corresponding benzamide (AD-3 column, hexane/iPrOH 80/20, 0.5 mL/min, 210 nm): $t_1 = 28.9$ min (major), $t_2 = 34.6$ min (minor). HRMS Calculated for C$_{15}$H$_{14}$NCIBr [M+H]$^+$ 321.9993; found 321.9966.
4. References:
5. NMR Spectra

$^1$H NMR for 1a (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1a (126 MHz, CDCl$_3$)
$^1$H NMR for 1b (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1b (126 MHz, CDCl$_3$)
$^1$H NMR for 1c (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1c (126 MHz, CDCl$_3$)
$^1$H NMR for 1d (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1d (126 MHz, CDCl$_3$)
\(^1\)H NMR for 1e (500 MHz, CDCl\(_3\))

\(^{13}\)C NMR for 1e (126 MHz, CDCl\(_3\))
$^1$H NMR for 1f (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1f (126 MHz, CDCl$_3$)
$^1$H NMR for 1g (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1g (126 MHz, CDCl$_3$)
$^1$H NMR for 1h (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1h (126 MHz, CDCl$_3$)
$^1$H NMR for 1i (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1i (126 MHz, CDCl$_3$)
$^1$H NMR for $1j$ (500 MHz, CDCl$_3$)

$^{13}$C NMR for $1j$ (126 MHz, CDCl$_3$)
$^1$H NMR for 1k (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1k (126 MHz, CDCl$_3$)
$^1\text{H NMR for 11 (500 MHz, CDCl}_3\text{)}$ 

$^{13}\text{C NMR for 11 (126 MHz, CDCl}_3\text{)}$
$^1$H NMR for 1m (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1m (126 MHz, CDCl$_3$)
$^1$H NMR for 1n (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1n (126 MHz, CDCl$_3$)
$^1$H NMR for $\mathbf{1o}$ (500 MHz, CDCl$_3$)

$^{13}$C NMR for $\mathbf{1o}$ (126 MHz, CDCl$_3$)
$^1$H NMR for 1p (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1p (126 MHz, CDCl$_3$)
$^1$H NMR for 1q (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1q (126 MHz, CDCl$_3$)
$^1$H NMR for 1r (500 MHz, CDCl$_3$)

$^{13}$C NMR for 1r (126 MHz, CDCl$_3$)
$^1$H NMR for 3a (400 MHz, CDCl$_3$)

$^{13}$C NMR for 3a (126 MHz, CDCl$_3$)
$^1$H NMR for 3b (500 MHz, CDCl$_3$)

$^{13}$C NMR for 3b (126 MHz, CDCl$_3$)
$^1$H NMR for 3c (500 MHz, CDCl$_3$)

$^{13}$C NMR for 3c (126 MHz, CDCl$_3$)
**1H NMR for 3d (500 MHz, CDCl₃)**

![1H NMR spectrum for 3d](image)

**13C NMR for 3d (126 MHz, CDCl₃)**

![13C NMR spectrum for 3d](image)
$^1$H NMR for 3e (500 MHz, CDCl$_3$)

$^{13}$C NMR for 3e (126 MHz, CDCl$_3$)
$^1$H NMR for 3f (500 MHz, CDCl$_3$)

$^{13}$C NMR for 3f (126 MHz, CDCl$_3$)
$^1$H NMR for 3g (500 MHz, CDCl$_3$)

$^{13}$C NMR for 3g (126 MHz, CDCl$_3$)
$^1$H NMR for 3h (500 MHz, CDCl$_3$) (A trace amount of EtOAc)

$^{13}$C NMR for 3h (126 MHz, CDCl$_3$)
$^1$H NMR for 3i (500 MHz, CDCl$_3$) (A trace amount of EtOAc)

$^{13}$C NMR for 3i (126 MHz, CDCl$_3$)
$^1$H NMR for 3j (500 MHz, CDCl$_3$) (A trace amount of EtOAc)

$^{13}$C NMR for 3j (126 MHz, CDCl$_3$)
$^1$H NMR for $3k$ (500 MHz, CDCl$_3$)

$^{13}$C NMR for $3k$ (126 MHz, CDCl$_3$)
$^1$H NMR for 3l (126 MHz, CDCl$_3$) (A trace amount of EtOAc)

$^{13}$C NMR for 3l

---

46
$^1$H NMR for 2a (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2a (126 MHz, CDCl$_3$)
$^1$H NMR for 2b (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2b (126 MHz, CDCl$_3$)
$^1$H NMR for 2c (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2c (126 MHz, CDCl$_3$)
$^1$H NMR for 2d (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2d (126 MHz, CDCl$_3$)
$^1$H NMR for 2e (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2e (126 MHz, CDCl$_3$)
$^1$H NMR for 2f (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2f (126 MHz, CDCl$_3$)
$^1$H NMR for 2g (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2g (126 MHz, CDCl$_3$)
$^1$H NMR for 2h (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2h (126 MHz, CDCl$_3$)
$^1$H NMR for 2i (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2i (126 MHz, CDCl$_3$)
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$^{13}$C NMR for $2j$ (126 MHz, CDCl$_3$)
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$^{13}$C NMR for 2k (126 MHz, CDCl$_3$)
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$^{13}$C NMR for 2n (126 MHz, CDCl$_3$)
$^1$H NMR for 2o (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2o (126 MHz, CDCl$_3$)
$^1$H NMR for 2p (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2p (126 MHz, CDCl$_3$)
$^1$H NMR for 2q (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2q (126 MHz, CDCl$_3$)
$^1$H NMR for 2r (500 MHz, CDCl$_3$)

$^{13}$C NMR for 2r (126 MHz, CDCl$_3$)
$^1$H NMR for 4a (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4a (126 MHz, CDCl$_3$)
$^1$H NMR for $4b$ (500 MHz, CDCl$_3$)

$^{13}$C NMR for $4b$ (126 MHz, CDCl$_3$)
$^1$H NMR for 4c (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4c (126 MHz, CDCl$_3$)
$^1$H NMR for 4d (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4d (126 MHz, CDCl$_3$)
$^1$H NMR for 4e (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4e (126 MHz, CDCl$_3$)
$^1$H NMR for 4f (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4f (126 MHz, CDCl$_3$)
$^1$H NMR for 4g (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4g (126 MHz, CDCl$_3$)
$^1$H NMR for 4h (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4h (126 MHz, CDCl$_3$)
$^1$H NMR for 4i (500 MHz, CDCl$_3$)

$^{13}$C NMR for 4i (126 MHz, CDCl$_3$)
$^1$H NMR for $4j$ (400 MHz, CDCl$_3$)

$^{13}$C NMR for $4j$ (101 MHz, CDCl$_3$)
$^1$H NMR for 4k (400 MHz, CDCl$_3$)

$^{13}$C NMR for 4k (101 MHz, CDCl$_3$)
$^1$H NMR for 4l (400 MHz, CDCl$_3$)

$^{13}$C NMR for 4l (101 MHz, CDCl$_3$)
6. HPLC spectra

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Additional Info: Peaks manually integrated

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Totals: 8738.00313 3290.829

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Multiplier: 1.0000
Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Area Percent Report

Signal 1: DADI A, Sig=254.4 Ref=360.100

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Sorted By: Signal
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Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DADI A, Sig=254.4 Ref=360.100
Peak RetTime Type Width Area Height Area
# [min] [min] [A.U.] [A.U] %
1 13.846 0.3893 3444.4016 142.8560 33.1550 2 15.462 0.2617 3291.3137 196.8097 68.8500

Totals: 8738.00313 3290.829

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Additional Info: Peaks manually integrated

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Sorted By: Signal
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Dilution: 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DADI A, Sig=254.4 Ref=360.100

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Peak RetTime Type Width Area Height Area
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1 14.067 0.2366 3294.30479 217.60071 98.8978 2 15.600 0.2529 42.45958 2.5408 1.2722

Totals: 3337.36437 220.25550
Acq. Operator: SYSTEM
Acq. Instrument: 1260-GAD
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Inj Volume: 1.000 µl
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Additional Info: Peaks manually integrated.

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Peak RetTime Type Width Area Height Area
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2 0.578 sum 0.1523 3464.4930 351.4585 51.4303
Totals: 6696.6131 718.3812

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Signal 1: DAD B, Sig=254.4 Ref=360.100
Peak RetTime Type Width Area Height Area
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2 9.874 M 0.1758 296.67639 28.1973 3.7212
Totals: 7970.50891 825.87407
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Last Changed: 3/27/2018 8:43:22 PM by SYSTEM
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Additional Info: Peaks manually integrated

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**Dilution:** 1.0000

Use Multiplier & Dilution Factor with ISTDs

**Sorted By:** Signal

**Peak Area Type:** Width | Area | Height

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**Totals:**

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Additional Info: Peaks manually integrated

Area Percent Report

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2 4.541 [RF] 0.1000 518.9700 85.6053 47.8995
Totals: 1165.3103 184.3383

Signal 2: DADI A, Sig=254.4 Ref=360,100
Peak RetTime Type Width Area Height Area
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1 6.160 RF 0.1054 1966.8439 321.2563 98.9761
2 6.856 RF 0.1006 20.3407 3.18360 1.0839
Totals: 1987.1906 324.44892

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Last changed: 9/13/2017 5:32:41 PM by SYSTEM
Additional Info: Peaks manually integrated

Area Percent Report

Signal 1: DADI A, Sig=254.4 Ref=360,100
Peak RetTime Type Width Area Height Area
# [min] [min] [µA] [µA] [%]
1 6.164 [RF] 0.102 697.3400 36.6779 32.1090
2 4.541 [RF] 0.1000 518.9700 85.6053 47.8995
Totals: 1165.3103 184.3383

Signal 2: DADI A, Sig=254.4 Ref=360,100
Peak RetTime Type Width Area Height Area
# [min] [min] [µA] [µA] [%]
1 6.160 RF 0.1054 1966.8439 321.2563 98.9761
2 6.856 RF 0.1006 20.3407 3.18360 1.0839
Totals: 1987.1906 324.44892

89
Acq. Operator : SYSTEM
Acq. Instrument : 1260-DAD
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Injection Volume : 1.000 μl
Coil Volume : 1.000 ml

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Last charged : 9/21/2017 7:19:50 PM by SYSTEM
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Last charged : 9/21/2017 7:31:50 PM by SYSTEM

Acq. Line : 2
Seq. Line : 3
Location : P2-C-02
Inj : 1

Signal 1: DAD A, Sig=250,4 Ref=360,100

Signal 2: DAD A, Sig=250,4 Ref=360,100

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000

Use Multiplier & Dilution Factors with ISTDs

Signal 1: DAD A, Sig=250,4 Ref=360,100

Signal 2: DAD A, Sig=250,4 Ref=360,100

Peak Width Type Width Area Height Area
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Totals : 2760.22632 215.67901
Area Percent Report

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Totals: 652.5295 88.86878

Injection Volume: 1.000 μl


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Last changed: 1/27/2018 12:18:05 by SYSTEM
(modified after loading)

Additional Info: Peaks manually integrated
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Last changed: 11/28/2017 09:10:06 by SYSTEM
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Additional Info: Peaks manually integrated

Area Percent Report

Sorted By: Signal
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Dilution: 1.0000
Use Multiplier & Dilution factors with ISTDs

Signal 1: DADI C, Sig=210.4 Ref=360.100

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