Supporting Information

Asymmetric Cyclization via Memory of Chirality: A Concise Access to Cyclic Amino Acids with a Quaternary Stereo-Center.

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(*S*)-*N*-(3-Bromopropyl)-*N*-(*tert*-butoxycarbonyl)phenylalanine ethyl ester (1)

A mixture of L-phenylalanine ethyl ester hydrochloride (1.00 g, 4.3 mmol), K_2CO_3 (1.32g, 9.6 mmol), NaI (65 mg, 0.43 mmol), 3-bromopropanol (0.91 g, 6.5 mmol) and DMF (5 mL) was heated at 70ºC with stirring for 2 h. The reaction mixture was poured into ice-water and extracted with ethyl acetate (3 x 25 mL). The combine organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give a syrupy oil. To a solution of the oil in dichloromethane were added di-*tert*-butyl dicarbonate (1.14 g, 5.2 mmol) and diisopropylethylamine (0.83 mL, 4.8 mmol), and the mixture was stirred at room temperature for 24 h. 20 mL of 0.5 M aq. HCl were added to the mixture and the resulting mixture was extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated in *vacuo* to give a residue, which was used directly to the next step without further purification. To a solution of the residue in dichloromethane (10 mL) were added carbon tetrabromide (1.88g, 5.7 mmol) at 0 ºC followed by triphenylphosphine (1.82 g, 6.9 mmol). After stirring for 30 min, the reaction mixture was poured into saturated aq. $NaHCO_3$ (10 mL) and extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated in *vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate:hexane=15:85) to give **1** (>99% ee, 1.10 g, 63% overall from L-phenylalanine ethyl ester hydrochloride).

Colorless crystals, m.p.54.0–54.5 ° C (hexane-AcOEt). Daicel Chialcel AD, hexane:2-propanol=99:1, flow: 1.0 mL/min, t_R = 19 (*R*), 22 (*S*) min. $[\alpha]_D^{21}$ = −118 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.14 (m, 5H), 4.30–4.10 (m, 2H), 4.10–3.90 (m, 1H), 3.45–3.10 (m, 5H), 2.78–2.54 (m, 1H), 1.95–1.75 (m, 2H), 1.46 (s, 9H), 1.32, 1.26 (two t, *J* = 6.5, 6.5 Hz, ratio = 1:1, 3H). IR (neat) 2978, 1741, 1696, 1366, 1267, 1168 cm^{-1}, MS *m/z* (rel intensity) 415 (M^+, 10), 413 (M^+, 10), 359 (10), 322 (15), 284 (20), 222 (100), 176 (50). Anal. Calcd for $C_{19}H_{28}BrNO_4$: C, 55.08; H, 6.81; N, 3.38 %. Found: C, 54.97; H, 6.82; N, 3.39 %.

(*S*)-*N*-(*tert*-Butoxycarbonyl)-α-benzylproline ethyl ester (2): A General Procedure for Intramolecular Alkylation

Potassium hexamethyldisilazide (KHMDS)* (0.50 M in THF, 0.60 mL, 0.30 mmol) was added to a solution of **2** (104 mg, 0.25 mmol) in dry DMF (2.4 mL) at −60 °C. After stirring for 30 min, the reaction mixture was poured into saturated aq NH_4Cl and extracted with ethyl acetate. The organic phase was washed with saturated aq $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC (SiO_2, ether:hexane=1:2) to give (*S*)-**3** (78 mg, 94% yield, 98% *ee*).

* Brown, C. A. *J. Org. Chem*. **1974**, *39*, 3913.

Colorless oil. HPLC conditions (*N*-benzoate derived from **2**): Daicel Chialcel OD, hexane:2-

propanol=90:10, flow: 1.0 mL/min, t_R = 8.3 (*R*), 25 (*S*) min. $[\alpha]_D^{21}$ (98% ee) = −103 (*c* 0.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.20 (m, 3H), 7.16–7.13 (m, 2H), 4.32–4.09 (m, 2H), 3.77, 3.58 (two d, *J* = 13.6, 14.0 Hz, ratio = 3 : 5, 1H), 3.48, 3.38 (two dt, *J* = 10.7, 7.3 Hz, 10.4, 7.3 Hz, ratio = 5 : 3, 1H), 3.05, 3.04 (two d, *J* = 14.0, 13.6 Hz, ratio = 5 : 3, 1H), 3.01, 2.89 (two ddd, *J* = 10.4, 7.3, 4.1 Hz, 10.4, 7.3, 6.7 Hz, ratio = 5 : 3, 1H), 2.12–1.97 (m, 2H), 1.67–1.45 (m, 1H), 1.51, 1.50 (two s, ratio = 3 : 5, 9H), 1.30, 1.27 (two t, *J* = 7.2, 7.1 Hz, ratio = 5 : 3, 3H), 0.99–0.83 (m, 1H). IR (neat) 2977, 1738, 1696, 1391, 1171 cm^{-1}, MS *m/z* (rel intensity) 333 (M^+, 10), 260 (40), 242 (90), 204 (90), 142 (100), 114 (20). Anal. Calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20 %. Found: C, 68.29; H, 8.33; N, 4.17 %.

Determination of the Absolute Configuration of 2: A suspension of **2** (obtained by the reaction of **1**, 98% ee, 150 mg, 0.45 mmol) in 4 mL of 6 M aq. HCl was heated under reflux for 12 h. After evaporation of the solvent, the residue was purified by ion exchange resin (DOWEX 50W-X8 (H^+-form) to give α-benzylproline (85mg, 92% yield); $[\alpha]_D^{20}$ = 47 (*c* 1.0, 1 M aq HCl). On the other hand, (*R*)-α-benzylproline was prepared by the literature procedure**, which showed $[\alpha]_D^{20}$ = −47 (*c* 0.8, 1 M aq HCl).

Wang, H.; Germanas, J. P. *Synlett*, **1999, 33.

(*S*)-*N*-(3-Bromopropyl)-*N*-(*tert*-butoxycarbonyl)-*O*-ethyl-tyrosine ethyl ester (3)

62% overall yield from L-tyrosine. Colorless oil. $[\alpha]_D^{20}$ = −104 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.11 – 7.04 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 4.30 – 4.10 (m, 2H), 4.01 (q, *J* = 7.2 Hz, 2H), 4.04-3.96, 3.90 – 3.85 (two m, ratio=1:1, 1H), 3.45–3.05 (m, 5H), 2.79-2.70, 2.63–2.54 (two m, ratio=1:1, 1H), 1.92–1.73 (m, 2H), 1.45 (s, 9H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.34–1.21 (m, 3H). IR ($CHCl_3$) 2977, 1740, 1697, 1512, 1366, 1246, 1175, 1047cm^{-1}. Mass *m/z* (rel intensity) 459 (M^+, 5), 457 (M^+, 5), 386 (5), 384 (5), 340 (5), 312 (5), 284 (10), 220 (100), 135 (80), 107 (40); HRMS Calcd for $C_{21}H_{32}O_5NBr$ 459.1443, observed: 459.1449.

***N*-(*tert*-Butoxycarbonyl)-α-(4-ethoxyphenylmethyl)proline ethyl ester (4)**

Colorless oil. HPLC conditions (*N*-benzoate derived from **4**): Daicel Chialcel OD, hexane:2-propanol=95:5, flow: 1.0 mL/min, t_R = 15 (minor), 36 (major) min. $[\alpha]_D^{20}$ (97% ee) = −116 (*c* 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 7.06–7.00 (m, 2H), 6.83–6.78 (m, 2H), 4.31–4.21 (m, 1H), 4.18–4.08 (m, 1H), 4.05–3.98 (m, 2H), 3.69, 3.51 (two d, *J* = 15.6, 15.6 Hz, ratio=1:2, 1H), 3.52–3.435 (m, 1H), 3.05–2.86 (m, 1H), 2.98, 2.97 (two d, *J* = 15.6, 15.6 Hz, ratio=2:1, 1H), 2.10–1.94 (m, 2H), 1.61–1.53 (m, 1H), 1.51, 1.50 (two s, ratio=1:2, 9H), 1.40 (t, *J* = 7.2 Hz, 3H), 1.29, 1.27 (two d, *J* = 7.6, 7.2 Hz, ratio=2:1, 3H), 1.06-0.87 (m, 1H). IR ($CHCl_3$) 2977, 1737, 1696, 1511, 1391, 1246, 1173 cm^{-1}; Mass, *m/z* (rel intensity) 377 (M^+, 80), 304 (30), 276 (20), 242 (90), 204 (60), 174 (20), 142 (100), 135 (70), 107 (60), 57 (60). Anal. Calcd for $C_{21}H_{31}O_5N$: C 66.82, H 8.28, N 3.71. Found: C 66.58, H 8.23, N 3.72.

(*S*)-*N*-(3-Bromopropyl)-*N*-(*tert*-butoxycarbonyl)methionine ethyl ester (5)

Colorless oil, $[\alpha]_D^{21}$ = −62 (*c* 1.8, $CHCl_3$), ^1H NMR (400 MHz, $CDCl_3$) δ 4.27–4.06 (m, 3H), 3.71–3.45 (m, 2H), 3.45, 3.42 (two t, *J* = 6.7, 6.7 Hz, ratio = 2 : 1, 1H), 3.22–3.14 (m, 1H), 2.65–2.49 (m, 2H), 2.41–2.32 (m, 1H), 2.25–2.05 (m, 3H), 2.11 (s, 3H), 1.47, 1.42 (two s, ratio = 1 : 2, 9H), 1.33–1.23 (two br t, 3H). IR (neat) 2923, 1740, 1697, 1160 cm^{-1}, MS *m/z* (rel intensity) 399 (M^+, 10), 397 (10), 267 (100), 224 (70), 176 (20), 57 (50). Anal Calcd for $C_{15}H_{28}BrNO_4S$: C, 45.23; H, 7.08; N, 3.52 %. Found: C, 44.96; H, 7.16; N, 3.58 %.

***N*-(*tert*-Butoxycarbonyl)-α-(2-methylthioethyl)proline ethyl ester (6)**

Colorless oil. HPLC conditions (*N*-benzoate derived from **6**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 10 (minor), 23 (major) min. $[\alpha]_D^{21}$ (97% ee) = −26 (*c* 0.9, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25–4.06 (m, 2H), 3.73, 3.59 (two ddd, J = 10.6, 8.1, 5.5 Hz, 10.6, 7.8, 6.0 Hz, ratio = 2 : 1, 1H), 3.46−3.37 (m, 1H), 2.61-2.37 (m, 3H), 2.20−1.99 (m, 6H), 1.98−1.76 (m, 2H), 1.45, 1.42 (two s, ratio = 1 : 2, 9H), 1.27, 1.24 (two t, *J* = 7.0, 7.0 Hz, ratio = 2 : 1, 3H). IR (neat) 2975, 1737, 1697, 1389, 1163 cm^{-1}, MS *m/z* (rel intensity) 317 (M^+, 10), 243 (30), 187 (100), 144 (90), 96 (30), 58 (90). HRMS Calcd for $C_{15}H_{27}NO_4S$; 317.1661, Found 317.1660.

(*S*)-*N*-(3-Bromopropyl)-*N*-(*tert*-butoxycarbonyl)valine ethyl ester (7)

Colorless oil, $[\alpha]_D^{20}$ = −53 (*c* 0.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23–4.11 (m, 3H), 3.70−3.30 (m, 4H), 2.38−2.05 (m, 3H), 1.46, 1.44 (two s, ratio = 1 : 1, 9H), 1.28 (br t, *J* = 7.7 Hz, 3H), 1.01 (brs, 3H), 0.90 (d, *J* = 6.7 Hz, 3H). IR (neat) 2972, 1738, 1697, 1457, 1367, 1153 cm^{-1} MS *m/z* (rel intensity) 367 (M^+, 3), 365 (3), 292 (20), 236 (50), 192 (50), 130 (50), 84 (90), 57 (100). Anal. Calcd for $C_{15}H_{28}BrNO_4$: C, 49.19; H, 7.70; N, 3.82 %. Found: C, 49.01; H, 7.77; N, 3.83 %.

***N*-(*tert*-Butoxycarbonyl)-α-isopropylproline ethyl ester (8)**

Colorless oil. HPLC conditions (*N*-benzoate derived from **8**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 8.7 (minor), 16 (major) min. $[\alpha]_D^{20}$ (94% ee) = −33 (*c* 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.21–4.06 (m, 2H), 3.86−3.82, 3.73−3.68 (two m, ratio = 3 : 1, 1H), 3.26−3.19 (m, 1H), 2.94, 2.79 (two septet, *J* = 6.9, 6.9 Hz, ratio = 1 : 3, 1H), 2.04−1.92 (m, 3H), 1.82−1.74 (m, 1H), 1.44, 1.41 (two s, ratio = 1 : 3, 9H), 1.26, 1.23 (two t, *J* = 7.3, 7.3 Hz, ratio = 3 : 1, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.9 Hz, 3H). IR (neat) 2976, 1741, 1697, 1393, 1162 cm^{-1}, MS *m/z* (rel intensity) 285 (M^+, 1), 212 (70), 156 (70), 142 (50), 112 (100), 84 (40), 57 (50). HRMS Calcd for $C_{15}H_{27}NO_4$; 285.1941, Found, 285.1949.

(*S*)-*N*-(3-Bromopropyl)-*N*-(*tert*-butoxycarbonyl)alanine ethyl ester (9)

Colorless oil, $[\alpha]_D^{20}$ = −28 (*c* 1.2, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40−4.30 (m, 1/2H), 4.23−4.10 (m, 2H), 4.05−3.97 (m, 1/2H), 3.60−3.40 (m, 3H), 3.28−3.15 (m, 1H), 2.21−2.05 (m, 2H), 1.46, 1.42 (two br s, ratio = 1 : 1, 9H), 1.47 (d, *J* = 7.3 Hz, 3H), 1.31−1.23 (br, 3H). IR (neat) 2979, 1742, 1697, 1366, 1158 cm$^{-1,}$ MS *m/z* (rel intensity) 339 (M^+, 2), 337 (M^+, 2), 264 (10), 208 (20), 164 (20), 114 (20), 84 (100). Anal. Calcd for $C_{13}H_{24}BrNO_4$: C, 46.16; H, 7.15; N, 4.14 %. Found: C, 45.97; H, 7.06; N, 4.16 %.

(*R*)-*N*-(*tert*-Butoxycarbonyl)-α-methylproline ethyl ester (10)

Colorless oil. HPLC conditions (*N*-benzoate derived from **10**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 12 (*S*), 20 (*R*) min. $[\alpha]_D^{20}$ (95% ee) = 20 (*c* 0.6, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26−4.06 (m, 2H), 3.62-3.44 (m, 2H), 2.22−2.09 (m, 1H), 1.95−1.80 (m, 3H), 1.56, 1.51 (two s, ratio = 1 : 3, 3H), 1.45, 1.41 (two s, ratio = 1 : 3, 9H), 1.27, 1.25 (two t, *J* = 7.3, 6.9 Hz, ratio = 3 : 1, 3H), IR (neat) 2978, 1740, 1698, 1391, 1258 cm^{-1}, MS *m/z* (rel intensity) 257 (M^+, 1), 184 (30), 156 (20), 128 (100), 84 (60). Anal. Calcd for $C_{13}H_{23.}NO_4$: C, 60.68; H, 9.01; N, 5.44 %. Found: C, 60.66; H, 9.12; N, 5.43 %.

Determination of the Absolute Configuration of 10: A solution of **10** (obtained by the reaction of **9** at −78 °C ~ room temperature, 76% ee, 20 mg, 0.08 mmol) in 0.2 mL of methanol containing 0.5 mmol of sodium methoxide was stirred at room temperature for 19 h The mixture was diluted with ethyl acetate

and washed with saturated aq. $NaHCO_3$ and brine, dried over anhydrous Na_2CO_3, filtered, and concentrated *in vacuo*. The residue was dissoved in 2 mL of 4 M HCl in dioxane and the mixture was stirred at room temperature for 2 h. After evaporation of the solvent, the residue was recrystallized from MeOH-ethyl acetate to give α-methylproline methyl ester hydrochloride (4.1mg, 29% yield); $[\alpha]_D^{20} = 24$ (*c* 0.2, MeOH) [lit*: (*S*)-α-methylproline methyl ester hydrochloride $[\alpha]_D^{20} = -31.6$ (*c* 1.3, MeOH).
*Lewis, A.; Wilkie, J.; Rutherford, T. J.; Gani, D. *J. Chem. Soc Perkin I.* **1998**, 3777-3793.

(*S*)-*N*-(2-Bromoethyl)-*N*-(*tert*-butoxycarbonyl)phenylalanine ethyl ester (11)

Colorless oil, $[\alpha]_D^{20} = -99$ (*c* 1.1, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.15 (m, 5H), 4.33−4.05 (m, 3H), 3.54−3.30 (m, 2H), 3.26−2.97 (m, 3H), 1.44 (s, 9H), 1.30, 1.26 (two t, *J* = 7.2, 7.2 Hz, ratio = 1 : 1, 3H). IR (neat) 2977, 1741, 1699, 1158 cm^{-1}, MS *m/z* (rel intensity) 401 (M^+, 4), 399 (4), 326 (6), 270 (8), 208 (50), 176 (100). HRMS Calcd for $C_{18}H_{26}{}^{81}BrNO_4$; 401.1024, Found 401.1029, $C_{18}H_{26}{}^{79}BrNO_4$; 399.1045, Found 399.1047.

Ethyl *N*-(*tert*-butoxycarbonyl)-2-benzylazetidine-2-carboxylate (12)

Colorless oil. HPLC conditions (*N*-benzoate derived from **12**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 9.0 (minor), 12 (major) min. $[\alpha]_D^{20}$ (95% ee) = −103 (*c* 0.7, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.23 (m, 5H), 4.35-4.19 (m, 2H), 3.81, 3.75 (two q, *J* = 6.8, 6.8 Hz, ratio = 2 : 1, 1H), 3.50, 3.34 (two d, *J* = 14.3 Hz, ratio = 1 : 2, 1H), 3.14 (q, *J* = 6.8 Hz, 2/3H), 3.06 (d, *J* = 14.3 Hz, 1H), 3.10-3.02 (br, 1/3H), 2.15−2.05 (m, 2H), 1.48 (s, 9H), 1.34 (t, *J* = 7.2 Hz, 3H). IR (neat) 2976, 1738, 1705, 1391, 1151 cm^{-1}, MS *m/z* (rel intensity) 319 (M^+, 10), 246 (60), 190 (90), 146 (40), 128 (100), 57 (50). Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39 %. Found: C, 67.43; H, 7.96; N, 4.25 %.

(*S*)-*N*-(4-Bromobutyl)-*N*-(*tert*-butoxycarbonyl)phenylalanine ethyl ester (13)

A mixture of L-phenylalanine ethyl ester (1.00 g, 5.18 mmol), tetrahydrofuran-2-ol{prepared from γ-butyrolactone (1.34 g, 15 mmol) with DIBAL-H}, 4A powdered molecular sieves (5 g) and ether (20 mL) was stirred at room temperature for 12 h. The solid materials were filtered off and the residue was washed with ether. The filtrate was concentrated *in vacuo* to give a he syrupy oil. The oil was dissolved in methanol (5 mL) and cooled at 0 ºC. $NaBH_4$ (0.76 g, 20 mmol) was added to the solution in one portion. After stirring for 1h, the mixture was poured into saturated aq NH_4Cl and extracted with ethyl acetate (3x20 mL). The combined organic layer were washed with brine, dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was dissolved in dichloromethane and treated with di-*tert*-butyl dicarbonate (1.42 g, 6.5 mmol) at room temperature for 10 min. Diisopropylethylamine (1.05 mL, 6.1 mmol) was added and the mixture was stirred at room temperature for 24 h. The reaction mixture was poured into saturated aq. NH_4Cl (20 mL) and extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate:hexane=1:1) to give a colorless oil (1.60 g). This material was dissolved in dichloromethane (10 mL) and treated with carbon tetrabromide (1.89 g, 5.7 mmol) and triphenylphosphine (1.86 g, 7.0 mmol) at 0 ºC for 30min. The reaction mixture was poured into saturated aq. $NaHCO_3$ (10 mL) and extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated in *vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate:hexane=15:85) to give **13** (>99% ee, 1.67 g, 75% overall from L-phenylalanine ethyl ester).

Colorless oil HPLC conditions: Daicel Chialcel AD, hexane:2-propanol=99:1, flow: 0.4

mL/min, t_R = 28 (*R*), 32 (*S*) min. $[\alpha]_D^{20}$ = −71 (*c* 1.0, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.16 (m, 5H), 4.30–4.10 (m, 2H), 4.04, 3.89 (two dd, *J* = 8.8, 5.2 Hz, 10.1, 4.9 Hz, ratio = 2 : 3, 1H), 3.35–3.09 (m, 5H), 2.70-2.58, 2.55-2.45 (two m, ratio = 2 : 3, 1H), 1.80–1.64 (m, 2H), 1.46 (s, 9H), 1.50–1.30 (m, 2H), 1.29, 1.25 (two br t, *J* = 7.5, 7.8 Hz, ratio = 3 : 2, 3H). IR (neat) 2977, 1740, 1696, 1366, 1252, 1169 cm^{-1}, MS *m/z* (rel intensity) 429 (M^+, 3), 427 (3), 354 (10), 336 (10), 298 (20), 254 (20), 236 (100), 176 (40). Anal. Calcd for $C_{20}H_{30}BrNO_4$: C, 56.08; H, 7.06; N, 3.27 %. Found: C, 55.92; H, 7.11; N, 3.24 %.

Ethyl *N*-(*tert*-butoxycarbonyl)-2-benzylpiperidine -2-carboxylate (14)

Colorless oil. HPLC conditions (*N*-benzoate derived from **14**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 7.7 (minor), 24 (major) min. $[\alpha]_D^{20}$ (97% ee) = −126 (*c* 1.1, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.15 (m, 5H), 4.35–4.08 (m, 2H), 3.90–3.60 (m, 2H), 2.98 (d, *J* = 13.7 Hz, 1H), 2.36–2.15 (br, 1H), 1.97–1.87 (m, 1H), 1.78–1.52 (m, 3H), 1.47 (s, 9H), 1.50–1.25 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), ^{1}H NMR (400 MHz, d_8-tolunene, 90 °C) δ 7.25-7.00 (m, 5H), 4.16-4.00 (m, 2H), 3.95 (d, *J* = 14.0 Hz, 1H), 3.84-3.73 (m, 1H), 3.08 (d, *J* = 14.0 Hz, 1H), 2.45 (br t, *J* = 8.0 Hz, 1H), 1.87-1.77 (m, 1H), 1.63-1.38 (m, 3H), 1.45(s, 9H), 1.27-1.01 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H). IR (neat) 2976, 1737, 1694, 1397, 1160 cm^{-1}, MS *m/z* (rel intensity) 347 (M^+, 1), 274 (30), 256 (100), 218 (90), 174 (90), 156 (95), 128 (30), 91 (50). Anal. Calcd for $C_{20}H_{29}NO_4$: C, 69.14; H, 8.41; N, 4.03 %. Found: C, 69.04; H, 8.68; N, 3.76 %.

(*S*)-*N*-(5-Bromopentyl)-*N*-(*tert*-butoxycarbonyl)phenylalanine ethyl ester (15)

A mixture of L-phenylalanine ethyl ester (1.00 g, 5.18 mmol), 2-hydroxy tetrahydropyran {prepared from 3,4-dyhydro-2*H*-pyran (1.41 mL, 15 mmol) and aq. HCl }, 4A powdered molecular sieves (5 g) and ether (20 mL) was stirred at room temperature for 12 h. The solid materials were filtered off and residue was washed with ether. Concentration of the filtrate gave a syrupy oil. The oil was dissolved in methanol (5 mL) and cooled at 0 ºC. $NaBH_4$ (0.76 g, 20 mmol) was added to the solution in one portion, and the mixture was stirred for 1 h. The reaction mixture was poured into saturated aq NH_4Cl and extracted with ethyl acetate (3x20 mL). The combined organic layer were washed with brine, dried over Na_2SO_4, filtered, and evaporated under reduced pressure to give an oily residue (1.05 g). The residue was dissolved in dichloromethane and treated with di-*tert*-butyl dicarbonate (0.99 g, 4.5 mmol) at room temperature for 10 min Diisopropylethylamine ((0.73 mL, 4.3 mmol) was added and the mixture was stirred at room temperature for 24 h. The reaction mixture was poured into saturated aq. NH_4Cl (20 mL) and extracted with dichloromethane. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was purified by column chromatography (SiO_2, ethyl acetate:hexane=1:1) to give a colorless oil (1.28 g). The residue was dissolved in dichloromethane (10 mL) and treated with tetrabromomethane (1.49g, 4.5 mmol) and triphenylphosphine (1.44 g, 5.4 mmol) at room temperaturet for 30 min. The reaction mixture was evaporated under vacuum and the residue was purified by flash column chromatography (hexane:AcOEt = 7:1) to give **15** as a colorless oil (1.37 g, 60% overall yield from phenylalanine ethyl ester, 99% ee).

Colorless oil. HPLC conditions (*N*-benzoate derived from **15**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow: 1.0 mL/min, t_R = 10 (*R*), 17 (*S*) min. $[\alpha]_D^{20}$ = −102 (*c* 0.7, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.15 (m, 5H), 4.28–4.14 (br m, 2H), 4.14–3.87 (m, 1H), 3.35–3.08 (m, 5H), 2.70–2.50 (m, 1H), 1.80–1.68 (br, 2H), 1.45 (s, 9H), 1.35–1.20 (br m, 7H). IR (neat) 2977, 1740, 1696, 1169 cm^{-1}, MS *m/z* (rel intensity) 443 (M^+, 5), 441 (5), 350

(15), 312 (20), 268 (30), 250 (100), 176 (30). HRMS Calcd for $C_{21}H_{32}{}^{79}BrNO_4$; 441.1514, Found 441.1501, Calcd for $C_{21}H_{32}{}^{81}BrNO_4$; 443.1494, Found 443.1494.

(*S*)-Ethyl *N*-(*tert*-butoxycarbonyl)-2-benzylazepane-2-carboxylate (16)

Colorless oil. HPLC conditions (*N*-benzoate derived from **16**): Daicel Chialcel OD, hexane:2-propanol=90:10, flow:1.0 mL/min, t_R = 7.9 (*R*), 13 (*S*) min. $[\alpha]_D^{20}$ (83% ee) = −157 (*c* 0.6, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.20 (m, 3H), 7.12−7.09 (m, 2H), 4.35−4.08 (m, 2H), 3.84, 3.53 (two dd, *J* = 14.5, 6.7 Hz, 14.5, 6.7 Hz, ratio = 1 : 1, 1H), 3.77, 3.55 (two d, *J* = 13.4, 13.4 Hz, ratio = 1 : 1, 1H), 2.97, 2.94 (two d, *J* = 13.4, 13.4 Hz, ratio = 1 : 1, 1H), 2.0−1.55 (m, 7H), 1.51 (s, 9H), 1.53−1.37 (m, 2H), 1.34, 1.29 (two t, *J* = 7.2, 7.2 Hz, ratio = 1 : 1, 3H), 0.98−0.84 (m, 1H). IR (neat) 2928, 1734, 1692, 1365, 1286, 1154 cm^{-1}, MS *m/z* (rel intensity) 361 (M^+, 1), 270 (60), 260 (20), 232 (20), 170 (100), 142 (10), 96 (60). HRMS Calcd for $C_{21}H_{31}NO_4$: 361.2253, Found, 361.2242.

Determination of the Absolute Configuration of 16: A solution of **16** (obtained by the reaction of **15**, 72% ee, 134 mg, 0.37 mmol) in 5 mL of 4 M HCl in dioxane was stirred at room temperature for 6 h The mixture was diluted with ethyl acetate and washed with saturated aq. K_2CO_3 and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC (SiO_2, ethyl acetate:hexane=1:3) to give (*S*)-Ethyl 2-benzylazepane-2-carboxylate (80mg, 83% yield); $[\alpha]_D^{20}$ = 5.3 (*c* 1.0, $CHCl_3$) [lit*: (*R*)-ethyl 2-benzylazepane-2-carboxylate. $[\alpha]_D^{20}$ = −7.6 (*c* 1.0, $CHCl_3$).

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