Supporting Information

Lithium Amide-Assisted Asymmetric Mannich-Type Reactions of Menthyl Acetate with PMP-Aldimines

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Extracts were dried over sodium sulfate unless otherwise noted. Purification was carried out by silica gel column chromatography unless otherwise noted. All melting points are uncorrected. IR spectra were expressed in cm^{-1} . ^1H and ^{13}C NMR spectra were taken in CDCl_3 . Chemical shift values are expressed in ppm relative to internal tetramethylsilane. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

Acetic acid L-menthyl ester (**1**):

to a solution of L-menthol (25.0 g, 0.16 mol) and DMAP (1.9 g, 0.016 mmol) in pyridine (19 mL) was added acetic anhydride (32.6 g, 0.32 mol) dropwise over 3 min. After being stirred at room temperature for 1 h, the reaction mixture was quenched with ice water (80 mL) and extracted with Et_2O (200 mL, 100 mL x 2). The combined organic layers were washed with 0.5 M HCl (100 mL x 3), water (80 mL), sat. NaHCO_3 (80 mL), and brine (80 mL), and then dried. Concentration gave a colorless oil (33.2 g). Purification by fractional distillation (bp 119–120 °C/26 mmHg) gave **1** (23.3 g, 74%) as a colorless oil of $[\alpha]_D^{20} -82.2$ (c 8.10, C_6H_6). ^1H NMR: 0.76 (3H, d, $J = 7.0$ Hz), 0.88 (1H, m), 0.89 (3H, d, $J = 3.4$ Hz), 0.91 (3H, d, $J = 2.8$ Hz), 0.96 (1H, m), 1.06 (1H, m), 1.34 (1H, m), 1.48 (1H, m), 1.67 (2H, m), 1.87 (1H, m), 1.99 (1H, m), 2.05 (3H, s, Me), 4.67 (1H, ddd, $J = 11, 11, 4.3$ Hz). ^{13}C NMR: 16.3, 20.7, 21.2, 21.9, 23.4, 26.2, 31.3, 34.2, 40.9, 46.9,

74.0, 170.6. IR (neat): 1730. CIMS m/z : 198 (M^+). Anal. Calcd for $C_{14}H_{26}O_4$: C 72.68, H 11.18. Found: C 72.52, H 11.44.

Asymmetric Mannich-Type Reactions. (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-(4-methoxyphenylamino)-3-phenylpropanoate (4a):

a solution of L-menthyl acetate (794 mg, 4.0 mmol) in THF (6 mL) was added dropwise over 5 min to a solution of LDA (9.0 mmol) in THF (6 mL) at $-78\text{ }^{\circ}\text{C}$, and the resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 0.5 h. A solution of imine **3a** (423 mg, 2.0 mmol) in THF (6 mL) was added dropwise over 10 min to the mixture at $-78\text{ }^{\circ}\text{C}$, and the mixture was stirred at $-30\text{ }^{\circ}\text{C}$ for 4 h. The reaction was quenched with sat. NH_4Cl (20 mL) at $-78\text{ }^{\circ}\text{C}$ and extracted with AcOEt (30 mL x 3). The combined organic layers were washed with brine (20 mL), and dried. Concentration gave a pale yellow solid (1.30 g). Chromatography (toluene/AcOEt = 200/1) gave **4a** (622 mg, 76%, 92% de) as colorless needles. Recrystallization of the diastereomeric mixture from MeOH gave a pure major isomer (70%) as colorless needles of mp $149.5\text{--}150\text{ }^{\circ}\text{C}$ and $[\alpha]_D^{25} -38.4$ (c 0.58, CHCl_3). ^1H MR: 0.57 (3H, d, $J = 7.0$ Hz), 0.72 (3H, d, $J = 7.0$ Hz), 0.80–0.91 (5H, m), 0.95–1.02 (1H, m), 1.28–1.32 (1H, m), 1.41–1.44 (1H, m), 1.60–1.66 (3H, m), 1.87–1.89 (1H, m), 2.72 (1H, dd, $J = 8.2, 14.7$ Hz), 2.78 (1H, dd, $J = 5.8, 14.7$ Hz), 3.69 (3H, s), 4.24 (1H, br), 4.66 (1H, ddd, $J = 4.3, 10.4, 10.4$ Hz), 4.75 (1H, dd, $J = 5.8, 8.2$ Hz), 6.49 (2H, d, $J = 8.8$ Hz), 6.69 (2H, d, $J = 8.8$ Hz), 7.23 (1H, m), 7.29–7.32 (2H, m), 7.36–7.38 (2H, d, $J = 7.7$ Hz). ^{13}C NMR: 15.9, 20.7, 22.0, 23.2, 25.9, 31.4, 34.2, 40.9, 43.5, 47.0, 55.7, 55.9, 74.6, 114.7, 114.8, 126.3, 127.3, 128.7, 140.9, 142.4, 152.2, 170.7. IR (nujol): 3350, 1710. EIMS m/z : 409 (M^+), 212. Anal. Calcd for $\text{C}_{26}\text{H}_{35}\text{NO}_3$: C, 76.25; H, 8.61; N, 3.42. Found: C, 76.33; H, 8.48; N, 3.38.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-phenyl-3-(phenylamino)propanoate (4b):

recrystallization of a diastereomeric mixture (92% de) from EtOH gave a pure major isomer as colorless needles of mp $137\text{--}137.5\text{ }^{\circ}\text{C}$ and $[\alpha]_D^{25} -41.9$ (c 0.99, CHCl_3). ^1H NMR: 0.56 (3H, d, $J = 7.0$ Hz), 0.71 (3H, d, $J = 7.0$ Hz), 0.83–0.93 (5H, m), 0.95–1.05 (1H, m), 1.27–1.33 (1H, m), 1.40–1.49 (1H, m), 1.57–1.68 (3H, m), 1.84–1.89 (1H, m), 2.75 (1H, dd, $J = 8.3, 14.4$ Hz), 2.81 (1H, dd, $J = 5.5, 14.4$ Hz), 4.50 (1H, br), 4.66 (1H, ddd, $J = 4.6, 10.7, 10.7$ Hz), 4.83 (1H, dd, $J = 5.5, 8.3$ Hz), 6.53 (2H, d, $J = 7.9$ Hz), 6.65 (1H, t, $J = 7.4$ Hz), 7.09 (2H, dd, $J = 7.4, 7.9$ Hz), 7.23 (1H, t, $J = 7.4$ Hz), 7.31 (2H, t, $J = 7.4$ Hz), 7.38 (2H, d, $J = 7.4$ Hz). ^{13}C NMR: 15.8, 20.6, 21.9, 23.1, 25.8, 31.3, 34.1, 40.8, 43.5, 46.9, 55.0, 74.6, 113.4, 117.6, 126.3, 127.4, 128.7, 129.1, 142.2, 146.7, 170.7. IR (neat): 3391, 1713. EIMS m/z : 379, 303, 182. Anal. Calcd for $\text{C}_{25}\text{H}_{33}\text{NO}_2$: C,

79.11; H, 8.76; N, 3.69. Found: C, 79.00; H, 8.74; N, 3.66.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-phenyl-3-[4-(trifluoromethyl)-phenylamino]propanoate (4c):

a diastereomeric mixture (60% de) as colorless needles of mp 142–153 °C

and $[\alpha]_D^{25} -37.9$ (c 1.02, CHCl_3). ^1H NMR: 0.56 (2.4H, d, $J = 7.0$ Hz, major), 0.60 (0.6H, d, $J = 7.0$ Hz, minor), 0.71 (2.4H, d, $J = 7.0$ Hz, major), 0.78 (0.6H, d, $J = 7.0$ Hz, minor), 0.78–0.91 (5H, m), 0.95–1.02 (1H, m), 1.28–1.33 (1H, m), 1.40–1.46 (1H, m), 1.58–1.67 (3H, m), 1.83–1.86 (1H, m), 2.72–2.89 (2H, m), 4.67 (1H, ddd, $J = 4.6, 11.0, 11.0$ Hz), 4.85 (1H, m), 4.91 (0.8H, m, major), 5.14 (0.2H, m, minor), 6.54 (2H, d, $J = 8.6$ Hz), 7.31–7.36 (7H, m). ^{13}C NMR: 15.7 (major), 16.0 (minor), 20.5 (major), 20.6 (minor), 21.9, 23.0 (major), 23.1 (minor), 25.8 (major), 25.9 (minor), 31.3 (major), 31.3 (minor), 34.0, 40.6 (minor), 40.8 (major), 42.7 (minor), 43.4 (major), 46.7 (minor), 46.9 (major), 54.5 (minor), 54.7 (major), 74.9, 112.6, 119.2 (q, $^2J_{\text{C-F}} = 31.9$ Hz), 124.9 (q, $^1J_{\text{C-F}} = 268.6$ Hz), 126.1, 126.5 (q, $^3J_{\text{C-F}} = 3.1$ Hz), 127.7 (minor), 127.8 (major), 128.9 (minor), 128.9 (major), 141.1 (minor), 141.2 (major), 149.2 (major), 149.3 (minor), 170.5 (major), 170.8 (minor). IR (nujol): 3350, 1705. EIMS m/z : 447 (M^+). Anal. Calcd for $\text{C}_{26}\text{H}_{32}\text{F}_3\text{NO}_2$: C, 69.78; H, 7.21; N, 3.13. Found: C, 69.68; H, 7.37; N, 3.21.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-[4-(isopropoxycarbonyl)phenyl-amino]-3-phenylpropanoate (4d):

a diastereomeric mixture (44% de) as colorless needles of mp

153–155 °C and $[\alpha]_D^{25} -32.1$ (c 1.15, CHCl_3). ^1H NMR: 0.57 (2.16H, d, $J = 7.0$ Hz, major), 0.59 (0.84H, d, $J = 7.0$ Hz, minor), 0.72 (2.16H, d, $J = 7.0$ Hz, major), 0.77 (0.84H, d, $J = 7.0$ Hz, minor), 0.77–0.92 (5H, m), 0.97–1.00 (1H, m), 1.26–1.30 (7H, m), 1.40–1.44 (1H, m), 1.49–1.54 (1H, m), 1.60–1.66 (2H, m), 1.82–1.85 (1H, m), 2.76 (1H, dd, $J = 8.2, 14.4$ Hz), 2.85 (1H, dd, $J = 5.5, 14.4$ Hz), 4.67 (1H, ddd, $J = 4.3, 10.7, 10.7$ Hz), 4.88 (1H, m), 5.01 (0.72H, d, $J = 7.4$ Hz, major), 5.16 (1H, m), 5.23 (0.28H, d, $J = 7.0$ Hz, minor), 6.50 (2H, d, $J = 8.8$ Hz), 7.23–7.25 (1H, m), 7.32 (4H, m), 7.79 (2H, d, $J = 8.8$ Hz). ^{13}C NMR: 15.9 (major), 16.0 (minor), 20.6 (major), 20.7 (minor), 21.9 (minor), 22.0 (major), 23.1 (major), 23.2 (minor), 25.9 (major), 26.0 (minor), 31.3, 34.1, 40.7 (minor), 40.8 (major), 42.9 (minor), 43.2 (major), 46.8 (minor), 46.9 (major), 54.4 (minor), 54.6 (major), 67.2, 74.8, 112.2, 119.5 (minor), 119.6 (major), 126.1, 127.5, (major), 127.6 (major), 128.8, 131.3, 141.0 (minor), 141.1 (major), 150.2 (major), 150.4 (minor), 166.2, 170.3 (major), 170.7

(minor). IR (neat): 3350, 1700. EIMS m/z : 465 (M^+). Anal. Calcd for $C_{29}H_{39}NO_4$: C, 74.81; H, 8.44; N, 3.01. Found: C, 74.55; H, 8.51; N, 2.88.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-(4-cyanophenylamino)-3-phenylpropanoate (4e):

a diastereomeric mixture (20% de) as colorless needles of mp 119–127 °C

and $[\alpha]_D^{25} -38.7$ (c 0.99, $CHCl_3$). 1H NMR: 0.56 (1.8H, d, $J = 7.0$ Hz, major), 0.58 (1.2H, d, $J = 7.0$ Hz, minor), 0.72 (1.8H, d, $J = 7.0$ Hz, major), 0.77 (1.2H, d, $J = 7.0$ Hz, minor), 0.80–0.89 (5H, m), 0.95–1.02 (1H, m), 1.24–1.32 (1H, m), 1.43–1.47 (1H, m), 1.55–1.67 (3H, m), 1.80–1.86 (1H, m), 2.75 (0.6H, dd, $J = 8.6, 14.7$ Hz, major), 2.79 (0.4H, dd, $J = 7.3, 14.7$ Hz, minor), 2.86 (0.6H, dd, $J = 4.9, 14.7$ Hz, major), 2.88 (0.4H, dd, $J = 4.9, 14.7$ Hz, minor), 4.64 (0.4H, ddd, $J = 4.3, 11.1, 11.1$ Hz, minor), 4.66 (0.6H, ddd, $J = 4.3, 11.1, 11.1$ Hz, major), 4.84 (1H, m), 5.15 (1H, d, $J = 6.4$ Hz, major), 5.43 (1H, d, $J = 6.8$ Hz, minor), 6.51 (2H, d, $J = 8.8$ Hz), 7.33 (7H, m). ^{13}C NMR: 15.8 (major), 16.1 (minor), 20.6 (major), 20.7 (minor), 21.9, 23.1 (major), 23.2 (minor), 25.9, 31.3, 34.0, 40.7 (minor), 40.8 (major), 42.5 (minor), 43.2 (major), 46.7 (minor), 46.9 (major), 54.3 (minor), 54.6 (major), 75.0, 99.3, 113.0, 120.2, 126.0, 127.8, 128.9, 133.6, 140.4, 149.9 (major), 150.0 (minor), 170.6. IR (nujol): 3380, 2200, 1700. EIMS m/z : 404 (M^+). Anal. Calcd. for $C_{26}H_{32}N_2O_2$: C, 77.19; H, 7.97; N, 6.92. Found: C, 76.95; H, 8.00; N, 6.82.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-(4-nitrophenylamino)-3-phenylpropanoate (4f):

a diastereomeric mixture (14% de) as pale yellow needles of mp

100–114 °C and $[\alpha]_D^{25} -49.3$ (c 1.19, $CHCl_3$). 1H NMR: 0.57 (1.7H, d, $J = 7.0$ Hz, major), 0.58 (1.3H, d, $J = 7.0$ Hz, minor), 0.73 (1.7H, d, $J = 7.0$ Hz, major), 0.76 (1.3H, d, $J = 7.0$ Hz, minor), 0.79–0.91 (5H, m), 0.95–1.04 (1H, m), 1.23–1.32 (1H, m), 1.38–1.47 (1H, m), 1.57–1.67 (3H, m), 1.80–1.86 (1H, m), 2.76–2.94 (2H, m), 4.62–4.70 (1H, m), 4.88–4.94 (1H, m), 5.49 (1H, d, $J = 6.4$ Hz), 5.79 (1H, d, $J = 6.8$ Hz), 6.50 (2H, d, $J = 8.8$ Hz), 7.27–7.35 (5H, m), 8.02 (2H, d, $J = 8.8$ Hz). ^{13}C NMR 15.9 (minor), 16.0 (major), 20.6 (minor), 20.7 (major), 23.1 (minor), 23.2 (major), 26.0 (major), 26.0 (minor), 31.3, 34.0, 40.7 (major), 40.8 (minor), 42.2 (major), 42.9 (minor), 46.7 (major), 46.9 (minor), 54.4 (major), 54.7 (minor), 75.1, 111.9, 126.0 (major), 126.1 (minor), 126.2, 127.9, 128.9, 138.3 (major), 138.4 (minor), 140.1 (major), 140.2 (minor), 151.9 (minor), 152.0 (major), 170.2 (minor), 170.6 (major). IR (nujol): 3350, 1710, 1500, 1330. EIMS m/z : 425 (M^+). Anal. Calcd for $C_{25}H_{32}N_2O_4$: C, 70.73; H, 7.60; N, 6.60. Found: C, 71.00; H, 7.82; N, 6.68.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 3-(2-methoxyphenylamino)-3-phenylpropanoate

(4g):

a diastereomeric mixture (68% de) as colorless amorphous of mp 83–94 °C and

$[\alpha]_D^{25} -50.8$ (c 1.13, CHCl_3). ^1H NMR: 0.54 (2.5H, d, $J = 6.7$ Hz), 0.63 (0.5H, d, $J = 6.7$ Hz), 0.70 (2.5H, d, $J = 6.7$ Hz), 0.79 (0.5H, d, $J = 6.7$ Hz), 0.81 (1H, m), 0.88 (3H, d, $J = 7.0$ Hz), 0.93 (1H, m), 0.97 (1H, m), 1.26 (1H, m), 1.43 (1H, m), 1.59–1.66 (3H, m), 1.88–1.91 (1H, m), 2.81 (2H, d, $J = 7.4$ Hz), 3.86 (2.5H, s), 3.87 (0.5H, s), 4.66 (1H, ddd, $J = 4.3, 11, 11$ Hz), 4.83 (1H, dt, $J = 6.1, 7.4$ Hz), 5.00 (1H, d, $J = 6.1$ Hz), 6.38 (1H, m), 6.61 (1H, m), 6.69–6.75 (2H, m), 7.21–7.32 (3H, m), 7.38–7.39 (2H, m). ^{13}C NMR: 15.8, 20.7, 22.0, 23.1, 25.8, 31.3, 34.2, 40.8, 43.8, 47.0, 54.9, 55.4, 74.5, 109.2, 110.8, 116.6, 121.0, 126.3, 126.3, 127.3, 128.6, 128.6, 136.5, 142.3, 146.7, 170.5. IR (nujol): 1710, 3400. EIMS m/z : 409 (M^+). Anal. Calcd for $\text{C}_{26}\text{H}_{35}\text{NO}_3$: C, 76.25; H, 8.61; N, 3.42. Found: C, 76.51; H, 8.46; N, 3.43.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl

3-(4-methoxyphenylamino)-3-[4-(trifluoromethyl)phenyl]propanoate (4h):

recrystallization of a diastereomeric mixture (94% de) from MeOH gave a

pure major isomer as colorless needles of mp 141.0–142.0 °C and $[\alpha]_D^{25} -25.0$ (c 1.00, CHCl_3). ^1H NMR: 0.57 (3H, d, $J = 7.0$ Hz), 0.72 (3H, d, $J = 7.0$ Hz), 0.78–0.90 (5H, m), 0.94–1.03 (1H, m), 1.23–1.34 (1H, m), 1.37–1.50 (1H, m), 1.52–1.69 (3H, m), 1.77–1.88 (1H, m), 2.72–2.82 (2H, m), 3.67 (3H, s), 4.36 (1H, br), 4.65 (1H, ddd, $J = 4.3, 10.7, 10.7$ Hz), 4.81 (1H, m), 6.47 (2H, d, $J = 8.9$ Hz), 6.69 (2H, d, $J = 8.9$ Hz), 7.50 (2H, d, $J = 7.9$ Hz), 7.57 (2H, d, $J = 7.9$ Hz). ^{13}C NMR: 15.8, 20.5, 21.8, 23.1, 25.9, 31.3, 34.0, 40.8, 43.2, 46.9, 55.5, 55.6, 74.8, 114.8, 114.9, 124.1 (q, $^1J_{\text{C-F}} = 270.7$ Hz), 125.7, (q, $^3J_{\text{C-F}} = 4.1$ Hz), 126.8, 129.7 (q, $^2J_{\text{C-F}} = 31.9$ Hz), 140.4, 146.6, 152.5, 170.4. IR (neat): 3402, 1709. EIMS m/z : 477 (M^+), 339, 280. Anal. Calcd for $\text{C}_{27}\text{H}_{34}\text{F}_3\text{NO}_3$: C, 67.91; H, 7.18; N, 2.93. Found: C, 67.87; H, 7.07; N, 2.96.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl

3-(4-methoxyphenylamino)-3-(4-methoxyphenyl)propanoate (4i):

recrystallization of a diastereomeric mixture (92% de) from EtOH gave a

pure major isomer as colorless needles of mp 120.5–121 °C and $[\alpha]_D^{25} -28.7$ (c 1.00, CHCl_3). ^1H NMR: 0.57 (3H, d, $J = 7.0$ Hz), 0.73 (3H, d, $J = 7.0$ Hz), 0.78–1.02 (6H, m), 1.26–1.32 (1H, m),

1.40–1.46 (1H, m), 1.58–1.66 (3H, m), 1.86–1.88 (1H, m), 2.73–2.75 (2H, m), 3.69 (3H, s), 3.78 (3H, s), 4.18 (1H, br), 4.62–4.67 (1H, ddd, $J = 4.3, 10.7, 10.7$ Hz), 4.69–4.71 (1H, m), 6.50 (2H, d, $J = 8.9$ Hz), 6.69 (2H, d, $J = 8.9$ Hz), 6.84 (2H, d, $J = 8.6$ Hz), 7.28 (2H, d, $J = 8.6$ Hz). ^{13}C NMR: 15.8, 20.6, 21.9, 23.1, 25.8, 31.1, 34.1, 40.9, 43.6, 46.9, 55.2, 55.3, 55.7, 74.5, 114.1, 114.7, 114.9, 127.5, 134.4, 141.0, 152.2, 158.9, 170.9. IR (neat): 3387, 1717. EIMS m/z : 439 (M^+), 242, 123. Anal. Calcd for $\text{C}_{27}\text{H}_{37}\text{NO}_4$: C, 73.77; H, 8.48; N, 3.19. Found: C, 73.56; H, 8.51; N, 2.99.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl

3-(4-methoxyphenylamino)-3-(naphthalen-1-yl)propanoate (4j):

recrystallization of a diastereomeric mixture (64% de) from MeOH gave a diastereomeric mixture (1% de) as colorless needles of mp 122–123 °C and $[\alpha]_{\text{D}}^{25} -57.4$ (c 1.00, CHCl_3). ^1H NMR: 0.58 (3H, d, $J = 7.0$ Hz), 0.72 (3H, d, $J = 7.0$ Hz), 0.81–0.91 (5H, m), 0.98–1.03 (1H, m), 1.26–1.36 (1H, m), 1.42–1.46 (1H, m), 1.61–1.64 (2H, m), 1.69–1.73 (1H, m), 1.86–1.92 (1H, m), 2.72 (0.5H, dd, $J = 8.5, 14.7$ Hz, major), 2.82 (0.5H, dd, $J = 8.3, 14.7$ Hz, minor), 3.04 (1H, m), 3.67 (3H, s), 4.42 (1H, br), 4.70 (1H, ddd, $J = 4.3, 11, 11$ Hz), 5.55 (1H, m), 6.44 (1H, d, $J = 8.8$ Hz, major), 6.48 (1H, d, $J = 8.8$ Hz, minor), 6.64 (1H, d, $J = 8.8$ Hz, major), 6.67 (1H, d, $J = 8.8$ Hz, minor), 7.39 (1H, t, $J = 7.6$ Hz), 7.50–7.54 (1H, m), 7.57–7.63 (2H, m), 7.76 (1H, d, $J = 8.3$ Hz), 7.91 (1H, d, $J = 8.3$ Hz), 8.21 (1H, d, $J = 8.6$ Hz). ^{13}C NMR: 15.8 (major), 16.0 (minor), 20.6, 21.9, 23.1 (minor), 23.2 (major), 26.0, 31.3, 34.1, 40.7 (minor), 40.9 (major), 41.9 (minor), 42.5 (major), 46.8 (minor), 47.0 (major), 51.9, 52.1, 55.7, 74.8, 114.5 (minor), 114.6 (major), 114.8, 122.3 (major), 122.4 (minor), 123.2, 125.6, 125.8, 126.4, 128.0, 129.2 (minor), 129.3 (major), 130.6 (major), 130.7 (minor), 134.2, 137.1 (major), 137.2 (minor), 140.9 (major), 141.0 (minor), 152.2, 171.1 (minor), 171.2 (major). IR (neat): 1713, 3341. EIMS m/z : 459 (M^+). Anal. Calcd for $\text{C}_{30}\text{H}_{37}\text{NO}_3$: C, 78.40; H, 8.11; N, 3.05. Found: C, 78.25; H, 8.01; N, 3.03.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl

3-(4-methoxyphenylamino)-3-(naphthalen-2-yl)propanoate (4k):

recrystallization of a diastereomeric mixture (88% de) from MeOH gave a pure major isomer as colorless needles of mp 116.0–117.0 °C and $[\alpha]_{\text{D}}^{25} -18.1$ (c 1.00, CHCl_3). ^1H NMR: 0.50 (3H, d, $J = 7.0$ Hz), 0.64 (3H, d, $J = 7.0$ Hz), 0.76–0.86 (5H, m), 0.92–1.00 (1H, m), 1.24–1.29 (1H, m), 1.41–1.46 (1H, m), 1.50–1.54 (1H, m), 1.59–1.64 (2H, m), 1.82–1.84 (1H, m), 2.81–2.89 (2H, m), 3.67 (3H, s), 4.34 (1H, br), 4.64 (1H, ddd, $J = 4.3, 11, 11$ Hz), 4.91 (1H, m),

6.54 (2H, d, $J = 8.8$ Hz), 6.67 (2H, d, $J = 8.8$ Hz), 7.42–7.45 (2H, m), 7.50 (1H, d, $J = 8.6$ Hz), 7.77–7.83 (4H, m). ^{13}C NMR: 15.7, 20.5, 21.9, 23.0, 25.8, 31.3, 34.1, 40.8, 43.4, 46.9, 55.7, 56.2, 74.6, 114.8, 114.9, 124.4, 125.3, 125.8, 126.1, 127.7, 128.0, 128.6, 133.0, 133.5, 139.8, 140.9, 152.3, 170.8. IR (neat): 1717, 3387. EIMS m/z : 459 (M^+). Anal. Calcd for $\text{C}_{30}\text{H}_{37}\text{NO}_3$: C, 78.40; H, 8.11; N, 3.05. Found: C, 78.21; H, 8.35; N, 2.96.

Methyl (*R*)-(+)-3-(4-methoxyphenylamino)-3-phenylpropanoate (Scheme 3):

to a solution of enantiomerically and diastereomerically pure **4a** (615 mg, 1.5 mmol; recrystallized **4a** with 96:4 dr in 70% recovery from methanol) in dry THF (3.0 mL) was added dropwise a THF (3.0 mL) solution of anhydrous *n*-Bu₄NOH, prepared from a 40 wt % aqueous solution (1.95 g, 3.0 mmol) by azeotropic removal of water with DME (7.5 mL) and toluene (7.5 mL) twice. After stirred at 0 °C for 1 h, the mixture was quenched with 3N HCl (10 mL) and extracted with EtOAc (100 + 50 + 25 mL). The combined organic layers were dried and concentrated. The resulting crude mixture was dissolved in MeOH (5 mL), and a 1M hexane solution of Me₃SiCHN₂ was added to the solution at room temperature. The mixture was stirred until gas evolution ceased, and subsequently quenched with HCO₂H until no more N₂ evolution was observed. The mixture was diluted with EtOAc (125 mL), washed with water (50 mL), sat. NaHCO₃ (50 mL x 2), and brine (50 mL), and then dried. Concentration gave a brown oil (630 mg). Chromatography (hexane/EtOAc = 9/1) gave the titled methyl ester (320 mg, 75%) as colorless needles of mp 69.0–70.5 °C and $[\alpha]_{\text{D}}^{25} +8.1$ (c 1.03, CHCl₃). ^1H NMR: 2.78 (1H, dd, $J = 6.7, 15.3$ Hz), 2.82 (1H, dd, $J = 6.7, 15.3$ Hz), 3.65 (3H, s), 3.69 (3H, s), 4.27 (1H, bs), 4.75 (1H, dd, $J = 6.7, 6.7$ Hz), 6.51–6.54 (2H, m), 6.65–6.71 (2H, m), 7.24 (1H, m), 7.30–7.37 (4H, m). ^{13}C NMR: 42.7, 51.8, 55.6, 55.8, 114.7, 115.2, 126.2, 127.4, 128.7, 140.9, 142.4, 152.3, 171.6. IR (nujol): 1712, 3368. EIMS m/z : 285 (M^+). Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.44; H, 6.60; N, 4.87.

Methyl (*R*)-(+)-3-amino-3-phenylpropanoate (**7**):

to a solution of CAN (526 mg, 0.96 mmol) in water (3.3 mL) was added the above methyl ester (68 mg, 0.24 mmol) in MeCN (2.5 mL) at 0 °C over 10 min. The mixture was stirred for 1 h, and water (5 mL) was added. The mixture was washed with Et₂O (25 + 15 mL), and Na₂CO₃ was added to the aqueous layer until its pH became 7. The mixture was filtrated through a pad of celite, and the filtrate was extracted with EtOAc (20 mL x 3). The combined organic layers were dried, concentrated, and purified by chromatography (EtOAc) to give **7** (21 mg, 49%) as a brown oil of $[\alpha]_{\text{D}}^{26} +20.9$ (c 1.05, CHCl₃): ^1H NMR: 1.90 (2H, bs), 2.67 (2H, d, $J = 7.0$ Hz), 3.68 (3H, s), 4.42 (1H, t, $J = 7.0$ Hz), 7.25–7.27 (1H, m), 7.32–7.36 (4H, m). ^{13}C NMR: 43.9, 51.6, 52.6, 126.1, 127.4, 128.6, 144.5, 172.4. IR (nujol): 1740, 3350. EIMS m/z : 179 (M^+).

4a

4c

4e

4f (benzene-d6)

4g

4h

De was determined by crude ^{13}C -NMR.

4i

De was determined by crude ^1H -NMR.

4k (DMSO-d6)