

Supporting Information for the Letter Entitled

**“Self-Regeneration of Stereocenters: A Practical Enantiospecific Synthesis of
LFA-1 Antagonist BIRT-377”**

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5: mp 146 °C; $[\alpha]_D^{20} = +72.0$ (c = 1.07, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 8.81 (br. s, 1H), 7.46 (s, 2H), 7.06 (s, 1H), 4.93 (br. d, *J* = 6.6 Hz, 1H), 4.28 (br. dt, *J* = 7.0 Hz, 1H), 1.47 (s, 9H), 1.42 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 171.5, 156.5, 139.6, 134.9, 123.8, 117.6, 81.0, 50.9, 17.4; Anal. Calcd for C₁₄H₁₈Cl₂N₂O₃: C, 50.46; H, 5.44; N, 8.41. Found: C, 50.40; H, 5.42; N, 8.27.

6: oil; $[\alpha]_D^{20} = +0.364$ (c = 1.10, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 9.66 (br. s, 1H), 7.56 (s, 2H), 7.06 (s, 1H), 3.60 (q, *J* = 7.0 Hz, 1H), 1.62 (br. s, 2H), 1.41 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 174.0, 139.5, 135.1, 123.8, 117.4, 51.0, 21.4; Anal. Calcd for C₉H₁₀Cl₂N₂O: C, 46.37; H, 4.32; N, 12.02. Found: C, 46.14; H, 4.32; N, 11.89.

7: mp 126 °C; $[\alpha]_D^{20} = -12.1$ (c = 1.30, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.32 (s, 2H), 7.19 (s, 1H), 4.85 (s, 1H), 3.76 (q, *J* = 6.8 Hz, 1H), 2.05 (br. s, 1H), 1.36 (d, *J* = 6.8 Hz, 2H), 0.84 (s, 9H).; ¹³C NMR (CDCl₃, 100 MHz) δ 175.3, 140.5, 135.1, 126.0, 122.8, 82.0, 55.5, 39.5, 26.1, 18.2; Anal. Calcd for C₁₄H₁₈Cl₂N₂O: C, 55.82; H, 6.02; N, 9.30. Found: C, 55.80; H, 6.05; N, 9.15.

8: mp 131 °C; $[\alpha]_D^{20} = +119.1$ (c = 1.25, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.48 (s, 2H), 7.28 (s, 1H), 6.20 (br. s, 1H), 4.52 (q, J = 6.6 Hz, 1H), 1.68 (d, J = 6.3 Hz, 3H), 0.87 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ 169.5, 138.6, 135.6, 127.0, 122.2, 117.3, 114.5, 79.0, 57.8, 42.1, 26.3; Anal. Calcd for C₁₆H₁₇Cl₂F₃N₂O₂: C, 48.38; H, 4.31; N, 7.05. Found: C, 48.31; H, 4.36; N, 6.79.

9: mp 164 °C; $[\alpha]_D^{20} = +89.8$ (c = 1.01, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) two rotamers δ 7.23 – 7.29 (m, 3H), 6.93 (s, 1H), 6.76 – 6.79 (m, 3H), 5.66 (s, 0.4H), 5.40 (s, 0.6H), 3.72 (d, J = 14 Hz, 0.6H), 3.26 (d, J = 14 Hz, 0.4H), 3.08 (t, J = 15 Hz, 1H), 1.96 (s, 0.6H), 1.93 (s, 0.4H), 0.86 (s, 6.4H), 0.73 (s, 3.6H); Anal. Calcd for C₂₃H₂₂BrCl₂F₃N₂O₂: C, 48.79; H, 3.92; N, 4.95. Found: C, 49.02; H, 3.95; N, 4.88.

2: mp 81 °C; $[\alpha]_D^{20} = +176.6$ (c = 1.07, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 9.74 (br. s, 1H), 7.52 (d, J = 1.9 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.08 (t, J = 1.9 Hz, 1H), 7.05 (d, J = 8.3 Hz, 2H), 3.47 (d, J = 13 Hz, 1H), 2.61 (d, J = 13 Hz, 1H), 1.45 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 174.7, 139.4, 135.3, 135.1, 131.8, 131.6, 123.9, 121.2, 117.5, 58.8, 45.6, 28.0; Anal. Calcd for C₁₆H₁₅BrCl₂N₂O: C, 47.79; H, 3.76; N, 6.97. Found: C, 47.89; H, 3.81; N, 6.75.

10: foam; $[\alpha]_D^{20} = -120.0$ (c = 1.02, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 7.46 (d, J = 8.3 Hz, 2H), 7.34 (s, 1H), 7.06 (d, J = 8.3 Hz, 2H), 6.98 (s, 2H), 6.84 (br. s, 1H), 3.13 (d, J = 13 Hz, 1H), 2.91 (d, J = 13 Hz, 1H), 1.60 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ

174.1, 154.7, 135.2, 132.8, 132.7, 131.7, 128.5, 124.5, 122.0, 62.7, 43.5, 23.3; Anal.

Calcd for $C_{17}H_{13}BrCl_2N_2O_2$: C, 50.46; H, 5.44; N, 8.41. Found: C, 50.40; H, 5.42; N, 8.27.

1: mp 135-136 °C; $[\alpha]_D^{25} = +127.3$ (c = 0.78, EtOH); 1H NMR ($CDCl_3$, 400 MHz) δ 7.42 (br. d, $J = 8.3$ Hz, 2H), 7.28 (t, $J = 1.8$ Hz, 1H), 6.94 (br. d, $J = 8.3$ Hz, 2H), 6.84 (d, $J = 1.8$ Hz, 2H), 3.08 (d, $J = 14$ Hz, 1H), 3.06 (s, 3H), 2.96 (d, $J = 14$ Hz, 1H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.3, 153.4, 135.0, 132.9, 132.8, 131.8, 131.0, 128.3, 124.4, 121.9, 65.6, 40.6, 25.2, 21.0; Anal. Calcd for $C_{18}H_{15}BrCl_2N_2O_2$: C, 48.90; H, 3.42; N, 6.34; Br, 18.07; Cl, 16.04. Found: C, 48.98; H, 3.40; N, 6.38; Br, 18.33; Cl, 16.07.