

Asymmetric Synthesis of Succinic Semialdehyde Derivatives

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SUPPORTING INFORMATION

Compounds **3b-d,f-i**, **7b-d,f-i**, **6c,e** and **9f,h,i** were synthesized according to the general procedures described in the Experimental Section. Eluants, yields and spectral and analytical data for these compounds are as follows:

3b. Flash chromatography (Et₂O-PE 1:7, 1% Et₃N) gave 443 mg (95%) of **3b** as a 84:16 mixture of diastereoisomers. (*S,R*)-**3b**: ¹H NMR (300 MHz, CDCl₃) δ 0.03-0.29 (m, 1H) 0.78 (t, 3H, *J* = 7.5 Hz), 1.26-1.50 (m, 3H), 1.85-2.00 (m, 2H), 2.48-2.59 (m, 1H), 2.79-2.85 (m, 1H), 2.90-3.00 (m, 1H), 3.02 (s, 3H), 3.60 (d, 1H, *J* = 9.8 Hz), 3.70 (s, 6H), 4.67 (dd, 1H, *J* = 8.9 Hz, *J* = 2.0 Hz), 6.36 (d, 1H, *J* = 4.9 Hz), 7.22-7.36 (m, 10H). ¹³C NMR (75 MHz, CDCl₃) δ 10.4, 22.0, 23.9, 25.8, 42.8, 50.3, 51.2, 52.0, 52.2, 54.6, 67.3, 85.6, 126.8, 126.9, 127.1, 129.5, 130.1, 132.3, 140.8, 141.7, 169.0, 169.3. (*S,S*)-**3b**: ¹H NMR (300 MHz, CDCl₃) δ 0.03-0.29 (m, 1H). 0.88 (t, 3H, *J* = 7.3 Hz), 1.26-1.50 (m, 2H), 1.85-2.00 (m, 2H), 2.48-2.59 (m, 1H), 2.79-2.85 (m, 1H), 2.90-3.00 (m, 1H), 3.02 (s, 3H), 3.58 (d, 1H, *J* = 8.6 Hz, H-1), 3.66 (s, 6H), 4.71 (dd, 1H, *J* = 9.3 Hz, *J* = 2.1 Hz), 6.39 (d, 1H, *J* = 5.9 Hz), 7.22-7.36 (m, 10H); ¹³C NMR (75 MHz, CDCl₃) δ 11.4, 22.0, 24.5, 26.0, 43.4, 50.4, 51.1, 52.0, 52.2, 55.2, 66.9, 85.6, 126.8, 127.7, 129.5, 130.1, 132.7, 141.1, 142.0, 168.8, 169.2; IR (film, cm⁻¹) 2959, 1738. MS (CI) *m/z*: 467 (20, M⁺+1), 435 (100). Anal. Calcd for C₂₇H₃₄O₅N₂: C, 69.50; H, 7.35; N, 6.00. Found: C, 69.73; H, 7.38; N, 6.06.

3c. Flash chromatography (Et₂O-PE 1:6) gave 273 mg (57%) of crystalline (*S,R*)-**3c** and 197 mg (41%) of (*S,S*)-**3c**. (*S,R*)-**3c**: mp 104-106 °C; $[\alpha]_D^{25}$ -60.4 (*c* 1.1, CH₂Cl₂); ¹H NMR (300 MHz, C₆D₆) δ 0.20-0.27 (m, 1H), 0.83 (d, 3H, *J* = 6.8 Hz), 0.96 (d, 3H, *J* = 6.8 Hz), 1.09-1.19 (m, 1H), 1.69-1.80 (m, 1H), 1.92-2.03 (m, 2H), 2.39-2.48 (m, 1H), 2.72-2.78 (m, 1H), 3.09 (s, 3H), 3.34-3.38 (m, 1H), 3.41 (s, 3H), 3.48 (s, 3H), 4.20 (d, 1H, *J* = 10.6 Hz), 4.85 (dd, 1H, *J* = 9.4 Hz, *J* = 1.5 Hz), 6.53 (d, 1H, *J* = 5.0 Hz), 7.14-7.45 (m, 10H); ¹³C NMR (125 MHz, C₆D₆) δ 13.1, 17.0, 17.9, 21.6, 24.9, 43.4, 46.0, 46.8, 47.2, 47.4, 49.3, 63.3, 81.5, 122.6, 122.8, 122.9, 125.4, 126.4, 126.3, 137.1, 137.8, 164.5, 165.1; IR (film, cm⁻¹) 2957, 1738, 1651; MS (CI) *m/z* 481 (26, M⁺+1), 449 (100). Anal. Calcd for C₂₈H₃₆O₅N₂: C, 69.97; H, 7.55; N, 5.83. Found: C, 69.71, H, 7.83, N, 5.77.

(*S,S*)-**3c**: $[\alpha]_D^{25}$ -117.6 (*c* 1.0, CH₂Cl₂); ¹H-NMR (300 MHz, CDCl₃) δ 0.17-0.26 (m, 1H), 0.84 (d, 3H, *J* = 6.8 Hz), 0.93 (d, 3H, *J* = 6.8 Hz), 1.35-1.39 (m, 1H), 1.75-1.84 (m, 1H), 1.80-2.01 (m, 2H), 2.48-2.57 (m, 1H), 2.80-2.85 (m, 1H), 2.86-2.90 (m, 1H), 3.01 (s, 3H), 3.64, (s, 3H), 3.73 (s, 3H), 3.75 (d, 1H, *J* = 10.0 Hz), 4.70 (dd, 1H, *J* = 9.3 Hz, *J* = 2.0 Hz), 6.43 (d, 1H, *J* = 6.5 Hz), 7.22-7.38 (m, 10H); ¹³C NMR (125 MHz, C₆D₆) δ 17.6, 21.5, 22.4, 26.1, 29.4, 47.9, 50.5, 51.3, 51.7, 51.9, 53.8, 67.9, 86.0, 127.1, 127.3, 127.3, 127.4, 129.9, 130.8, 130.9, 141.6, 142.3, 169.0, 169.6; MS (CI) *m/z* 481 (36, M⁺+1), 449 (98), 283 (100). Anal. Calcd for C₂₈H₃₆N₂O₅: C, 69.97; H, 7.55; N, 5.83. Found: C, 70.47; H, 7.74; N, 5.89.

3d. Flash chromatography (Et₂O-PE 1:7, 1% Et₃N) gave 379 mg (70%) of **3d** as a 85:15 mixture of diastereoisomers. (*S,R*)-**3d**: ¹H NMR (300 MHz, C₆D₆) δ 0.18-0.35 (m, 1H), 1.14-1.86 (m, 1H), 1.74-1.80 (m, 1H), 1.86-2.00 (m, 3H), 2.38-2.85 (m, 4H), 3.09 (s, 3H),

3.36-3.72 (m, 1H), 3.38 (s, 3H), 3.43 (s, 3H), 3.92 (d, 1H, $J = 9.2$ Hz), 4.82-4.86 (m, 1H), 6.51 (d, 1H, $J = 5.2$ Hz), 7.15-7.51 (m, 15H); ^{13}C NMR (75MHz, C_6D_6): δ 22.4, 26.2, 33.2, 33.6, 42.0, 50.4, 51.4, 51.7, 51.9, 55.7, 67.6, 86.0, 126.0, 127.2, 127.3, 127.4, 127.5, 128.6, 128.7, 128.8, 130.0, 130.8, 132.7, 141.7, 142.5, 142.6, 168.7, 169.2. (*S,S*)-**3d**: ^1H NMR (300 MHz, C_6D_6) δ 0.18-0.35 (m, 1H), 1.14-1.86 (m, 1H), 1.74-1.80 (m, 1H), 1.86-2.00 (m, 3H), 2.38-2.85 (m, 4H) 3.09 (s, 3H), 3.36-3.72 (m, 1H), 3.38 (s, 3H), 3.43 (s, 3H), 3.82 (d, 1H, $J = 8.1$ Hz), 4.82-4.86 (m, 1H), 6.60 (d, 1H, $J = 5.6$ Hz), 7.15-7.51 (m, 15H); ^{13}C NMR (75 MHz, C_6D_6): δ 22.4, 26.3, 33.8, 33.9, 42.1, 50.6, 51.3, 51.8, 51.9, 55.9, 67.4, 86.0, 126.0, 127.2, 127.3, 128.6, 128.8, 130.7, 133.0, 142.0, 142.6, 142.7, 168.8, 169.4. IR (film, cm^{-1}): 2949, 1736, 1599; MS (EI) m/z 542 (2, M^+), 511 (65), 389 (100). Anal. Calcd For $\text{C}_{33}\text{H}_{38}\text{N}_2\text{O}_5$: C, 73.04; H, 7.06; N, 5.16. Found: C, 73.28; H, 7.35; N, 5.19.

3f. Flash chromatography (Et_2O -PE 1:5) gave 493 mg (88%) of (*S,S*)-**3f** and 55 mg (10%) of (*S,R*)-**3f**. (*S,S*)-**3f**: $[\alpha]_{\text{D}}^{21} +11.2$ (c 0.7, CH_2Cl_2); ^1H NMR (300 MHz, C_6D_6) δ 0.01-0.18 (m, 1H), 0.94-1.18 (m, 1H), 1.63-1.83 (m, 1H), 1.98-2.05 (m, 1H), 2.28-2.37 (m, 1H), 2.61-2.67 (m, 1H), 3.01 (s, 3H), 3.08 (s, 3H), 3.47 (s, 3H), 4.42 (d, 1H, $J = 11.7$ Hz), 4.49 (dd, 1H, $J = 11.7$ Hz, $J = 3.5$ Hz), 4.84-4.87 (m, 1H), 6.21 (d, 1H, $J = 3.5$ Hz), 6.82-7.87 (m, 14H); ^{13}C NMR (125 MHz, C_6D_6) δ 22.2, 25.7, 47.9, 49.8, 51.6, 51.8, 52.0, 56.0, 69.1, 86.1, 123.6, 127.3, 127.4, 127.5, 128.2, 129.8, 129.9, 131.3, 139.8, 141.0, 147.0, 147.4, 168.2, 168.2. IR (film, cm^{-1}) 2951, 2828, 1753, 1601; MS (CI) m/z 560 (33, M^++1), 528 (100). Anal. Calcd for $\text{C}_{31}\text{H}_{33}\text{N}_3\text{O}_7$: C, 66.53; H, 5.94; N, 7.51. Found: C, 66.85; H, 6.21; N, 7.36. (*S,R*)-**3f**: $[\alpha]_{\text{D}}^{21} -177.4$ (c 0.7, CH_2Cl_2); ^1H NMR (300 MHz, C_6D_6): δ 0.20-0.37 (m, 1H), 0.99-1.12 (m, 1H), 1.67-1.94 (m, 2H), 2.29-2.38 (m, 1H), 2.62-2.67 (m, 1H), 3.06 (s, 3H),

3.08 (s, 3H), 3.44 (s, 3H), 4.29 (d, 1H, $J = 11.2$ Hz), 4.52 (dd, 1H, $J = 11.2$ Hz, $J = 4.8$ Hz), 4.77 (dd, 1H, $J = 9.0$ Hz, $J = 1.8$ Hz), 6.44 (d, 1H, $J = 4.8$ Hz), 7.13-7.92 (m, 14H); ^{13}C NMR (75 MHz, C_6D_6) δ 21.8, 26.4, 47.5, 49.8, 51.2, 51.8, 52.1, 56.0, 67.0, 86.1, 123.6, 127.4, 127.4, 127.5, 127.7, 127.8, 128.1, 129.7, 130.0, 130.2, 130.4, 141.1, 142.3, 147.3, 147.4, 168.1, 168.3; MS (CI) m/z 560(13, $\text{M}^+ + 1$), 528(72), 363(100). HRMS m/z calcd for $\text{C}_{31}\text{H}_{33}\text{N}_3\text{O}_7$ 560.2397; found 560.2387.

3g. Flash chromatography (Et_2O -PE 1:6) gave 525 mg (93%) of (*S,S*)-**3g** and 28 mg (5%) of (*S,R*)-**3g**. (*S,S*)-**3g**: $[\alpha]_{\text{D}}^{18} +5.9$ (c 0.7, CH_2Cl_2); ^1H NMR (300 MHz, C_6D_6) δ 0.06-0.19 (m, 1H), 0.66-1.13 (m, 1H), 1.54-1.76 (m, 1H), 1.93-2.00 (m, 1H), 2.28-2.39 (m, 1H), 2.57-2.63 (m, 1H), 2.95 (s, 3H), 3.06 (s, 3H), 3.48 (s, 3H), 4.63 (d, 1H, $J = 11.5$ Hz), 4.76 (dd, 1H, $J = 11.5$ Hz, $J = 3.7$ Hz), 4.88-4.91 (m, 1H), 6.42 (d, 1H, $J = 3.7$ Hz), 7.10-7.86 (m, 17H); ^{13}C NMR (125 MHz, C_6D_6) δ 22.3, 25.9, 48.8, 50.0, 51.5, 51.6, 51.9, 56.2, 68.6, 86.2, 125.9, 126.1, 127.1, 127.2, 127.4, 127.5, 128.3, 128.4, 130.0, 131.3, 132.0, 133.2, 134.0, 137.2, 140.6, 141.6 (Ph), 168.7, 168.8; IR (film, cm^{-1}) 3055, 2951, 1744, 1601; MS (CI) m/z 566 (7, $\text{M}^+ + 1$), 565 (37, M^+), 533 (100); HRMS m/z calcd for $\text{C}_{35}\text{H}_{36}\text{N}_2\text{O}_5$ 565.2702, found 565.2704.

(*S,R*)-**3g**: $[\alpha]_{\text{D}}^{21} -107.7$ (c 1.0, CH_2Cl_2); ^1H NMR (300 MHz, C_6D_6) δ 0.29-0.43 (m, 1H), 1.04-1.14 (m, 1H), 1.73-1.92 (m, 2H), 2.34-2.43 (m, 1H), 2.64-2.72 (m, 1H), 3.02 (s, 3H), 3.14 (s, 3H), 3.50 (s, 3H), 4.68 (d 1H, $J = 11.3$ Hz), 4.85 (m, 2H), 6.74 (d, 1H, $J = 4.7$ Hz), 7.15-7.84 (m, 17H); ^{13}C NMR (75 MHz, C_6D_6) δ 22.0, 26.6, 48.3, 50.3, 51.2, 51.6, 52.0, 56.0, 66.6, 86.1, 125.3, 126.0, 126.3, 126.8, 127.3, 127.3, 127.5, 128.1, 128.7, 129.0, 130.1,

130.4, 131.4, 132.9, 133.2, 134.0, 137.5, 141.9, 142.7, 142.9, 168.7, 168.9; MS (CI) m/z 566 (6, $M^+ + 1$), 565 (20, M^+); HRMS m/z calcd for $C_{35}H_{36}N_2O_5$ 565.2702, found 565.2708.

3h. Flash chromatography (Et₂O-PE 1:6) gave 536 mg (91%) of (*S,S*)-**3h** and 43 mg (7%) of (*S,R*)-**3h** as oils. (*S,S*)-**3h**: $[\alpha]_D^{26} +6.7$ (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz, C₆D₆) δ 0.07-0.24 (m, 1H), 1.06-1.16 (m, 1H), 1.64-1.82 (m, 1H), 1.98-2.05 (m, 1H), 2.33-2.42 (m, 1H), 2.65-2.71 (m, 1H), 3.11 (s, 3H), 3.15 (s, 3H), 3.53 (s, 3H), 4.61 (d, 1H, J = 11.6 Hz), 4.71 (dd, 1H, J = 11.6, J = 3.5 Hz), 4.93 (d, 1H, J = 8.8 Hz), 6.48 (d, 1H, J = 3.5 Hz), 7.16-7.89 (m, 19H); ¹³C NMR (125 MHz, C₆D₆): δ 22.4, 25.9, 48.4, 50.2, 51.6, 51.7, 51.9, 56.5, 68.8, 86.2, 127.2, 127.3, 127.3, 127.4, 127.4, 127.5, 127.7, 128.9, 129.8, 130.0, 131.3, 132.2, 138.9, 140.4, 140.7, 141.2, 141.7, 168.7, 168.8; IR (film, cm⁻¹) 3068, 1719; MS(CI) m/z 591 (12, $M^+ + 1$), 559 (100). Anal. Calcd for $C_{37}H_{38}N_2O_5$: C, 75.23; H, 6.48; N, 4.74. Found: C, 74.92; H, 6.70; N, 5.06.

(*S,R*)-**3h**: $[\alpha]_D^{20} -178.9$ (c 1.2, CH₂Cl₂); ¹H NMR (300 MHz, C₆D₆) δ 0.27-0.41 (m, 1H), 1.05-1.14 (m, 1H), 1.66-1.95 (m, 2H), 2.34-2.43 (m, 1H), 2.66-2.72 (m, 1H), 3.15 (s, 3H), 3.17 (s, 3H), 3.49 (s, 3H), 4.61 (d, 1H, J = 11.3 Hz), 4.75 (dd, 1H, J = 11.3 Hz, J = 4.7 Hz), 4.81-4.84 (m, 1H), 6.71 (d, 1H, J = 4.7 Hz), 7.07-7.66 (m, 19H); ¹³C NMR (125 MHz, C₆D₆) δ 22.1, 26.6, 47.8, 50.4, 51.2, 51.7, 52.0, 56.2, 66.8, 86.1, 127.3, 127.4, 129.0, 129.8, 130.1, 130.5, 133.0, 139.2, 140.4, 141.2, 141.9, 142.9, 168.6, 168.9; MS (CI) m/z 591 (7, $M^+ + 1$), 560 (18), 183 (100); HRMS calcd for $C_{37}H_{38}N_2O_5$ 591.2859, found 591.2856.

3i. Flash chromatography (Et₂O-PE 1:6) gave 484 mg (77%) of (*S,S*)-**3i** as an oil: $[\alpha]_D^{26} +14.3$ (c 1.2, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 0.03-0.11 (m, 1H), 0.83-0.97 (m, 1H),

1.14-1.43 (m, 1H), 1.86-1.93 (m, 1H), 2.45-2.54 (m, 1H), 2.75-2.81 (m, 1H), 3.02 (s, 3H), 3.49 (s, 3H), 3.78 (s, 3H), 3.95 (d, 1H, $J = 11.7$ Hz), 4.11 (dd, 1H, $J = 11.7$ Hz, $J = 3.6$ Hz), 4.62-4.66 (m, 1H), 5.92 (s, 2H), 6.31-6.41 (m, 5H), 6.62-6.65 (m, 1H), 7.26-7.57 (m, 10H); ^{13}C NMR (125MHz, C_6D_6) δ 22.4, 25.8, 48.3, 50.2, 51.6, 51.8, 53.3, 56.5, 69.2, 86.2, 100.8, 108.3, 109.4, 122.6, 127.1, 127.3, 127.5, 127.7, 128.2, 130.0, 131.2, 132.3, 133.4, 140.3, 141.4, 147.2, 148.2, 168.6, 168.7; IR (film, cm^{-1}) 3084, 2951, 1757, 1736, 1601. MS (CI) m/z 560 (7, $\text{M}^+ + 1$), 559 (18, M^+), 527 (100); HRMS m/z calcd for $\text{C}_{32}\text{H}_{35}\text{N}_2\text{O}_7$ 559.2444, found 559.2445.

7b. Flash chromatography (Et_2O -PE 1:6) gave 195 mg (70%) of **7b** as an oil: 68% ee by ^1H NMR [45% $\text{Eu}(\text{hfc})_3$]; $[\alpha]_{\text{D}}^{26} +11.8$ (c 0.9, CH_2Cl_2); ^1H NMR (500 MHz, CDCl_3) δ 0.98 (t, 3H, $J = 7.4$ Hz), 1.64-1.69 (m, 2H), 2.51-2.53 (m, 1H), 3.15-3.25 (m, 4H), 3.73 (s, 3H), 3.74 (s, 3H), 3.86 (d, 1H, $J = 5.0$ Hz), 4.84 (d, 1H, $J = 6.2$ Hz); ^{13}C NMR (166 MHz, CDCl_3) δ 12.4, 24.2, 38.2, 38.7, 46.8, 52.2, 52.4, 53.1, 56.3, 169.2, 169.3; IR (film, cm^{-1}) 1736, 1633. MS (CI): m/z 279 (8, $\text{M}^+ + 1$), 247 (100). Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_4\text{S}_2$: C, 47.46; H, 6.52. Found: C, 47.83; H, 6.68.

7c. Flash chromatography (Et_2O -PE 1:5) gave 248 mg (85 %) of **7c** as an oil: >98% ee by ^1H NMR [50% $\text{Eu}(\text{hfc})_3$]; $[\alpha]_{\text{D}}^{24} +25.5$ (c 1.0, CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3) δ 0.87 (d, 3H, $J = 6.9$ Hz), 1.00 (d, 3H, $J = 6.9$ Hz), 2.12-2.25 (m, 1H), 2.54 (ddd, 1H, $J = 8.3$ Hz, $J = 3.2$ Hz, $J = 3.2$ Hz), 3.08-3.28 (m, 4H), 3.72 (s, 3H), 3.73 (s, 3H), 3.76 (d, 1H, $J = 3.2$ Hz), 4.98 (d, 1H, $J = 8.3$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 18.6, 21.3, 29.8, 37.7, 38.5,

49.9, 52.0, 52.3, 52.5, 54.6, 170.0, 175.6; IR (film, cm^{-1}) 3146, 1746; MS (CI) m/z 293 (10, $M^+ + 1$), 261 (100); HRMS m/z calcd for $\text{C}_{12}\text{H}_{21}\text{O}_4\text{S}_2$ 293.0881, found 293.0869.

7d. Flash chromatography (Et_2O -PE 1:6) gave 212 mg (60%) of **7d** as an oil: 70% ee by HPLC (Chiralpak AD, 2-propanol:hexane 5:95, 0.5 mL/min, 25 °C), *R* isomer 12.3 min, *S* isomer 13.1 min; $[\alpha]_D^{26} +0.8$ (c 1.0, CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3) δ 1.89-1.97 (m, 2H), 2.60-2.62 (m, 1H), 2.68-2.74 (m, 2H), 3.18-3.22 (m, 4H), 3.73 (s, 3H), 3.74 (s, 3H), 3.90 (d, 1H, $J = 4.8$ Hz), 4.86 (d, 1H, $J = 4.9$ Hz), 7.17-7.30 (m, 5H); ^{13}C NMR (75 MHz, CDCl_3) δ 33.1, 34.4, 38.4, 38.6, 44.8, 52.3, 52.5, 53.2, 56.5, 126.1, 128.4, 141.6, 168.9, 169.2; IR (film, cm^{-1}) 2855, 1734; MS (CI) m/z 355 (68, $M^+ + 1$), 323 (100). Anal. Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_4\text{S}_2$: C, 57.60; H, 6.26. Found: C, 57.38; H, 6.38.

7f. Flash chromatography (Et_2O -PE 1:6) gave 241 mg (65%) of (*S*)-**7f** as an oil: >98% ee by ^1H NMR [40% $\text{Eu}(\text{hfc})_3$]; $[\alpha]_D^{24} -2.1$ (c 1.0, CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3) δ 2.56-2.61 (m, 1H), 2.75-2.79 (m, 1H), 2.98-3.06 (m, 2H), 3.49 (s, 3H), 3.79 (s, 3H), 3.88 (dd, 1H, $J = 9.8$ Hz, $J = 6.1$ Hz), 4.10 (d, 1H, $J = 9.8$ Hz), 4.99 (d, 1H, $J = 6.1$ Hz), 7.55-7.59 (m, 2H), 8.11-8.16 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 38.0, 38.9, 51.5, 52.5, 53.0, 55.1, 55.9, 122.6, 130.8, 144.7, 147.2, 167.1, 167.8; IR (film, cm^{-1}) 2847, 1734, 1605; MS (CI) m/z 372 (13, $M^+ + 1$), 340 (46), 105 (100). Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_6\text{S}_2$: C, 48.50; H, 4.61; N, 3.77. Found: C, 48.37; H, 4.92; N, 3.64.

7g. Flash chromatography (Et_2O -PE 1:4) gave 237 mg (63%) of **7g** as an oil: >98% ee by HPLC (Chiralpak AD, 2-propanol:hexane 8:92, 0.5 mL/min, 40 °C), *S* isomer 15.5 min, *R*

isomer 16.9 min; $[\alpha]_D^{22} +10.2$ (c 1.2, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 2.52-2.62 (m, 1H), 2.77-2.84 (m, 1H), 2.95-3.04 (m, 2H), 3.39 (s, 3H), 3.79 (s, 3H), 3.96 (dd, 1H), 4.19 (d, 1H, *J* = 9.6 Hz), 5.09 (d, 1H, *J* = 6.5 Hz), 7.43-7.53 (m, 4H), 7.74-7.85 (m, 3H); ¹³C NMR (75MHz, CDCl₃) δ 37.9, 38.8, 52.0, 52.3, 52.7, 56.1, 56.5, 125.8, 127.1, 127.4, 127.6, 127.9, 128.7, 132.6, 132.7, 134.9, 167.6, 168.5; IR (film, cm⁻¹) 3059, 2844, 1746; MS (CI) *m/z* 377 (13, M⁺+1), 345 (41), 245 (100); HRMS *m/z* calcd for C₁₉H₂₀O₄S₂ 377.0881, found 377.0878.

7h. Flash chromatography (Et₂O-PE 1:5) gave 302 mg (75%) of **7h** as an oil: >98% ee by ¹H NMR [50% Eu(hfc)₃]; $[\alpha]_D^{22} -5.8$ (c 1.0, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 2.59-2.69 (m, 1H), 2.82-2.92 (m, 1H), 2.99-3.07 (m, 2H), 3.47 (s, 3H), 3.79 (s, 3H), 3.83 (dd, 1H, *J* = 9.7 Hz, *J* = 6.5 Hz), 4.11 (d, 1H, *J* = 9.7 Hz), 5.03 (d, 1H, *J* = 6.5 Hz) 7.26-7.69 (m, 9H); ¹³C NMR (75MHz, CDCl₃) δ 37.9, 38.8, 51.7, 52.3, 52.8, 56.0, 56.4, 126.2, 126.8, 126.9, 127.2, 128.6, 130.1, 136.3, 140.1, 140.4, 167.6, 168.5; IR (film, cm⁻¹) 3055, 2856, 1744; MS (CI) *m/z* 403 (32, M⁺+1), 371 (23), 133 (100). Anal Calcd for C₂₁H₂₂O₄S₂: C, 62.66; H, 5.51. Found: C, 62.58; H, 5.63.

7i. Flash chromatography (AcOEt -PE 1:10) gave 250 mg (70%) of **7i** as an oil: >98% ee by HPLC (Chiralpak AD, 2-propanol:hexane 8:92, 0.5 mL/min, 40 °C), *S* isomer 15.6 min, *R* isomer 16.6 min; $[\alpha]_D^{24} +28.1$ (c 1.3, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ 2.65-2.75 (m, 1H), 2.86-2.96 (m, 1H), 3.00-3.09 (m, 2H), 3.51 (s, 3H), 3.68 (dd, 1H, *J* = 9.5 Hz, *J* = 6.6 Hz), 3.76 (s, 3H), 4.00 (d, 1H, *J* = 9.5 Hz), 4.95 (d, 1H, *J* = 6.6 Hz), 5.94 (s, 2H), 6.70-6.88 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 37.9, 38.8, 51.7, 52.3, 52.7, 56.1, 56.5, 100.8,

107.5, 110.0, 122.9, 131.0, 146.8, 146.9, 167.5, 168.4; IR (film, cm^{-1}) 2955, 2853, 1730; MS (CI) m/z 371 (14, $\text{M}^+ + 1$), 339 (20), 239 (100). Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{O}_6\text{S}_2$: C, 51.88; H, 4.90. Found: C, 52.17; H, 5.21.

6c. Flash chromatography (Et_2O -PE 1:4) gave 160 mg (74 %) of **6c** as an oil: ^1H NMR (300 MHz, CDCl_3): δ 0.93 (d, 3H, $J = 6.9$ Hz), 1.16 (d, 3H, $J = 7.1$ Hz), 1.96-2.04 (m, 1H), 3.21 (ddd, 1H, $J = 10.0$ Hz, $J = 4.6$ Hz, $J = 1.3$ Hz), 3.72 (s, 3H), 3.75 (s, 3H), 3.85 (d, 1H, $J = 10.0$ Hz), 9.85 (d, 1H, $J = 1.3$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ 18.3, 20.7, 27.5, 50.2, 52.7, 55.8, 168.4, 168.6, 201.9. IR: (film, cm^{-1}): 2957, 2851, 1730, 1397. MS (CI): 217 (17%, $\text{M}^+ + 1$), 197 (13), 185 (100), 183 (38). HRMS m/z calcd. for $\text{C}_{10}\text{H}_{17}\text{O}_5$ 217.1075, found 217.1076.

6e. Flash chromatography (Et_2O -PE 1:3) gave 150 mg (60 %) of **6e** as an oil: ^1H NMR (300 MHz, CDCl_3): δ 3.48 (s, 3H), 3.78 (s, 3H), 4.15 (d, 1H, $J = 11.2$ Hz), 4.50 (d, 1H, $J = 11.2$ Hz), 7.17-7.40 (m, 5H), 9.67 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3): δ 52.5, 52.6, 53.0, 57.7, 128.6, 129.2, 129.6, 131.1, 167.7, 168.0, 196.5. IR: (film, cm^{-1}): 2957, 2851, 1740, 1437, 1092. MS (CI): 251 (27%, $\text{M}^+ + 1$), 219 (100), HRMS m/z calcd for $\text{C}_{13}\text{H}_{14}\text{O}_5$ 251.0919, found 251.0927.

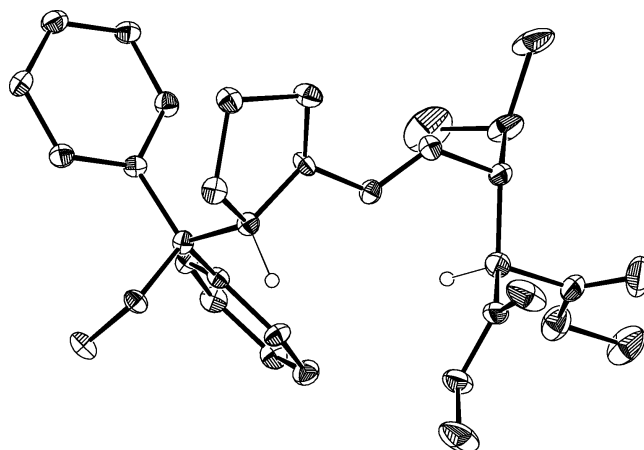
9f. 203 mg (65 %, oil): $[\alpha]_D^{26} +4.8$ (c 0.9, CH_2Cl_2). ^1H NMR (500 MHz, CDCl_3): δ 2.83 (dd, 1H, $J = 16.0$ Hz, $J = 9.9$ Hz), 3.03-3.19 (m, 5H), 3.54-3.56 (m, 1H), 3.56 (s, 3H), 4.80 (d, 1H, $J = 7.4$ Hz), 7.48 (d, 2H, $J = 8.7$ Hz), 8.17 (d, 2H, $J = 8.6$ Hz). ^{13}C NMR (125 MHz, CDCl_3): δ 34.3, 34.4, 34.8, 44.9, 47.6, 53.6, 119.1, 125.2, 142.9, 144.1, 167.2. IR: (film,

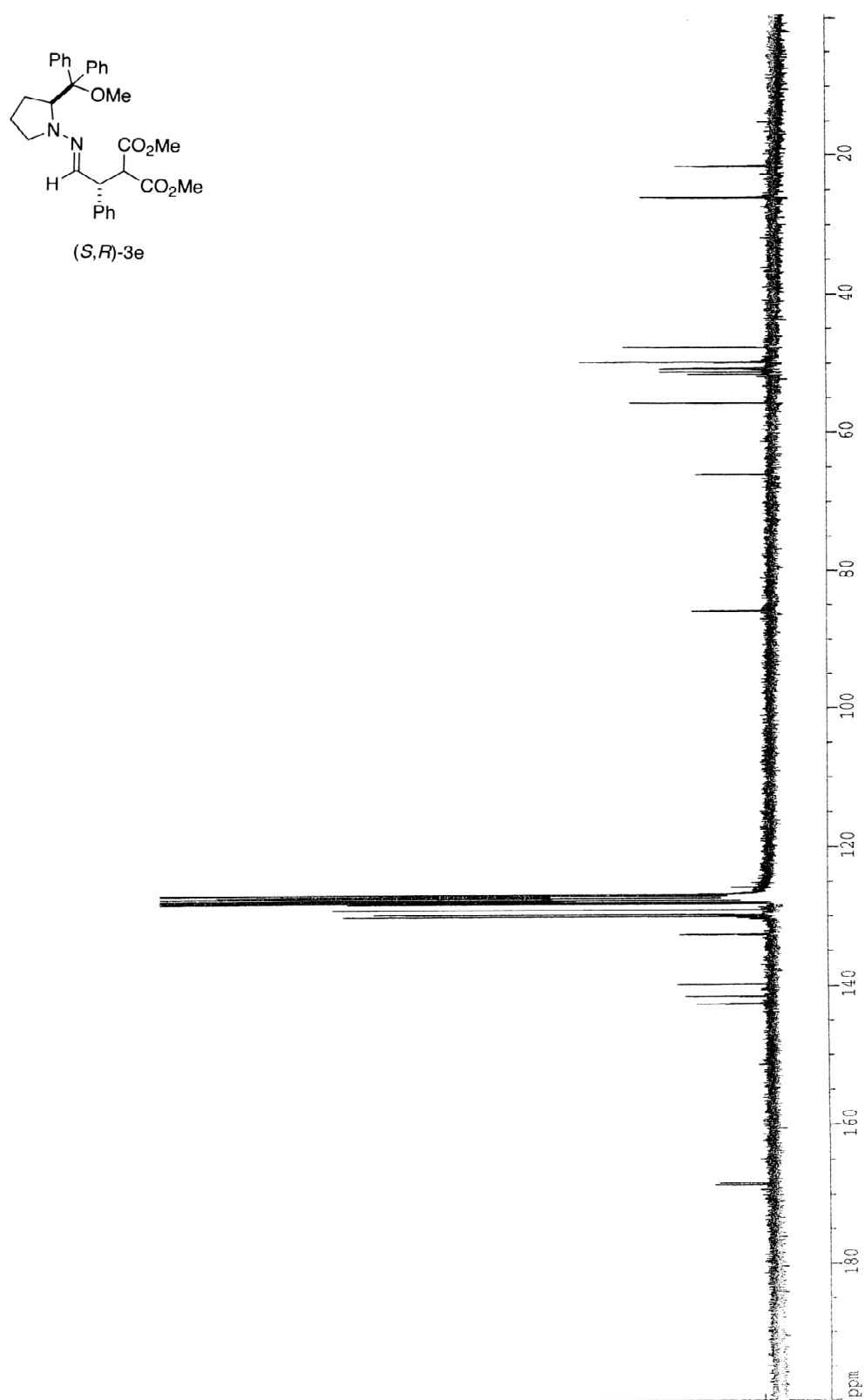
cm⁻¹): 2924, 2853, 1736, 1601, 1518, 1435m MS (EI): 313 (1%, M⁺), 282 (4), 239 (5), 105 (100). HRMS *m/z* calcd. for C₁₃H₁₅NO₄S 314.0521, found 314.0517.

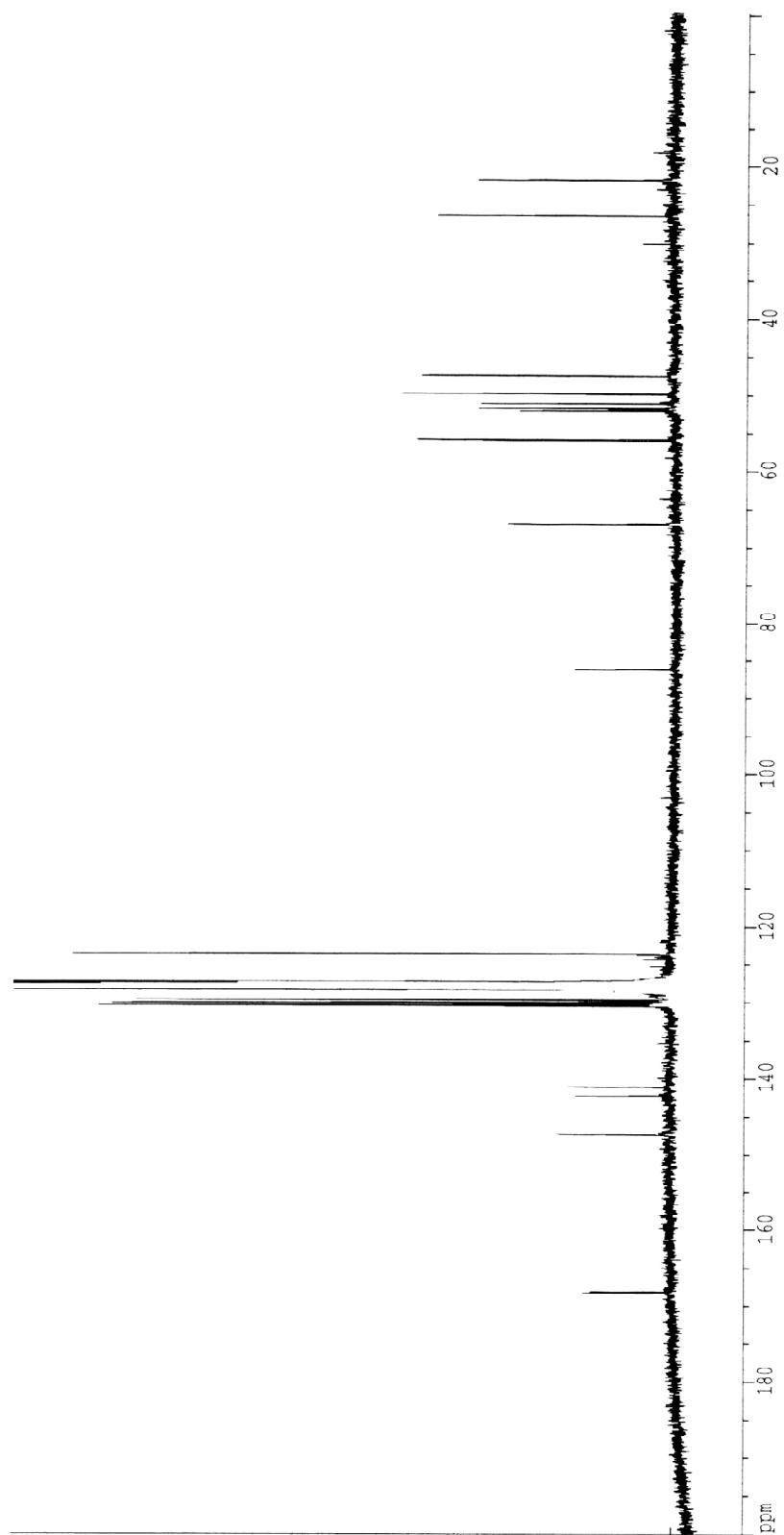
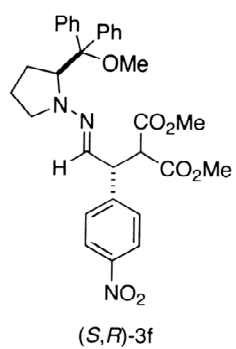
9h. 217 mg (63 %, oil): [α]_D²⁶ +14.1 (c 1.3, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ 2.82 (dd, 1H, *J* = 15.6 Hz, *J* = 9.6 Hz), 3.03-3.19 (m, 5H), 3.44-3.51 (m, 1H), 3.55 (s, 3H), 4.84 (d, 1H, *J* = 7.6 Hz), 7.24-7.59 (m, 9H). ¹³C NMR (75MHz, CDCl₃): δ 38.5, 38.7, 38.8, 48.8, 51.5, 58.7, 126.8, 127.1, 128.5, 128.6, 139.9, 140.0, 140.5, 172.0. IR: (film, cm⁻¹): 3028, 2924, 1738, 1443. MS (CI): 345 (35%, M⁺+1), 313 (100), 105 (76). HRMS *m/z* calcd. for C₁₉H₂₀O₂S₂ 345.0983, found 345.0982. Anal. Calcd for C₁₉H₂₀O₂S₂: C, 66.24; H, 5.85. Found: C, 66.24; H, 6.09.

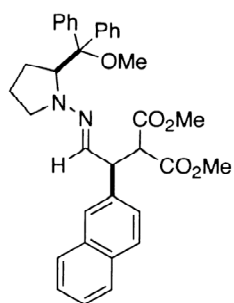
9i. 218 mg (70 %, oil): [α]_D²⁶ +15.0 (c 1.4, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ 2.70 (dd, 1H, *J* = 15.6 Hz, *J* = 9.9 Hz), 2.99 (dd, 1H, *J* = 15.6 Hz, *J* = 4.9 Hz), 3.04-3.15 (m, 4H), 3.29-3.36 (m, 1H), 3.55 (s, 3H), 4.73 (d, 1H, *J* = 7.7 Hz), 5.91 (s, 2H), 6.68-6.75 (m, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 38.5, 38.8, 39.0, 48.9, 51.5, 58.9, 100.8, 107.9, 108.4, 121.4, 134.8, 146.6, 147.4, 172.0. IR: (film, cm⁻¹): 2957, 2851, 1738, 1499, 1437, 1258, 1094. MS (FAB): *m/z* 335 (100%, M⁺+23), 312 (35, M⁺). Anal. Calcd for C₁₄H₁₆O₄S₂: C, 53.82; H, 5.16. Found: C, 53.86; H, 5.32.

Figure 1. ORTEP drawing of (*S,R*)-**3c**.









(S,S)-3g

