**Regio- and Enantioselective *Intermolecular* Rhodium-Catalyzed [2+2+2]
Carbocyclization Reactions of 1,6-Enynes with Methyl Arylpropiolates**

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Supplemental Data

Methyl (7a*S*)-2-[(4-methylphenyl)sulfonyl]-6-phenyl-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carboxylate (*S*)-2a.

$[\alpha]_{\text{D}}^{25} -87.6$ ($c = 1.80$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 10:90 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 78.21 min, t_{R} (minor) 51.49 min, 97% *ee*; IR (film) 3057 (m), 2950 (m), 1715 (s), 1599 (m), 1435 (s), 1346 (s), 1263 (s), 1095 (s), 1029 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2 H), 7.33–7.24 (m, 5 H), 7.11–7.09 (m, 2 H), 6.16 (d, $J = 2.0$ Hz, 1 H), 4.20 (d, A of AB, $J_{\text{AB}} = 15.8$ Hz, 1 H), 3.92 (t, $J = 8.6$ Hz, 1 H), 3.85 (d, B of AB, $J_{\text{AB}} = 15.4$ Hz, 1 H), 3.44 (s, 3 H), 3.08–2.96 (m, 1 H), 2.73 (t, $J = 9.7$ Hz, 1 H), 2.63 (dd, $J = 17.2, 8.0$ Hz, 1 H), 2.41 (s, 3 H), 2.25 (t, $J = 17.8$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.00 (e), 143.78 (e), 143.15 (e), 140.82 (e), 137.97 (e), 132.77 (e), 129.74 (o), 128.01 (o), 127.80 (o), 127.64 (o), 127.18 (o), 126.09 (e), 116.00 (o), 54.38 (e), 51.44 (o), 50.38 (e), 37.76 (o), 34.70 (e), 21.47 (o); HRMS (CI, $\text{M}+\text{H}^+$) calcd for $\text{C}_{23}\text{H}_{24}\text{O}_4\text{N}_1\text{S}_1$ 410.1421, found 410.1418.

Methyl (7a*S*)-6-(4-methoxyphenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carboxylate (*S*)-2b.

$[\alpha]_{\text{D}}^{25} -77.7$ ($c = 0.84$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.6 mL/min flow rate, 240 nm detection light), t_{R} (major) 293.80 min, t_{R} (minor) 113.30 min, 97% *ee*; IR (film) 2950 (m), 2255 (w), 1709 (s), 1607 (s), 1510 (s), 1347 (s), 1252 (s), 1163 (s), 1030 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2 H), 7.31 (d, $J = 8.2$ Hz, 2 H), 7.06 (d, $J = 8.6$ Hz, 2 H), 6.81 (d, $J = 8.8$ Hz, 2 H), 6.14 (d, $J = 2.3$ Hz, 1 H), 4.19 (d, A of AB, $J_{\text{AB}} = 15.4$ Hz, 1 H), 3.92 (t, $J = 8.7$ Hz, 1 H), 3.84 (d, B of AB, $J_{\text{AB}} = 15.6$ Hz, 1 H), 3.77 (s, 3 H), 3.48 (s, 3 H), 3.04–2.93 (m, 1 H), 2.72 (t, $J = 9.7$ Hz, 1 H), 2.63 (dd, $J = 17.1, 7.9$ Hz, 1 H), 2.41 (s, 3 H), 2.20 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.39 (e), 159.36 (e), 143.74 (e), 142.65 (e), 137.40 (e), 132.81 (e), 132.77 (e), 129.72 (o), 128.74 (o), 127.63 (o), 125.40 (e),

116.19 (o), 113.42 (o), 55.13 (o), 54.40 (e), 51.46 (o), 50.37 (e), 37.77 (o), 34.69 (e), 21.45 (o); HRMS (CI, M^+) calcd for $C_{24}H_{25}O_5N_1S_1$ 439.1448, found 439.1451.

Methyl (7a*S*)-6-(4-methylphenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carboxylate (*S*)-2c.

$[\alpha]_D^{25}$ -87.6 ($c = 1.85$, $CHCl_3$); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 10:90 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_R (major) 115.44 min, t_R (minor) 65.32 min, 97% *ee*; IR (film) 2949 (s), 2255 (m), 1713 (s), 1598 (s), 1347 (s), 1305 (s), 1164 (s) cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, $J = 8.0$ Hz, 2 H), 7.32 (d, $J = 8.0$ Hz, 2 H), 7.10 (d, $J = 7.8$ Hz, 2 H), 7.01 (d, $J = 8.0$ Hz, 2 H), 6.15 (s, 1 H), 4.20 (d, A of AB, $J_{AB} = 15.6$ Hz, 1 H), 3.93 (t, $J = 8.6$ Hz, 1 H), 3.85 (d, B of AB, $J_{AB} = 15.2$ Hz, 1 H), 3.48 (s, 3 H), 3.04–2.97 (m, 1 H), 2.73 (t, $J = 9.7$ Hz, 1 H), 2.63 (dd, $J = 17.1$, 7.9 Hz, 1 H), 2.42 (s, 3 H), 2.31 (s, 3 H), 2.22 (t, $J = 17.9$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.19 (e), 143.76 (e), 143.15 (e), 137.76 (e), 137.73 (e), 137.67 (e), 132.78 (e), 129.73 (o), 128.74 (o), 127.64 (o), 127.20 (o), 125.72 (e), 116.10 (o), 54.42 (e), 51.47 (o), 50.38 (e), 37.76 (o), 34.71 (e), 21.47 (o), 21.14 (o); HRMS (CI, $M+H^+$) calcd for $C_{24}H_{26}O_4N_1S_1$ 424.1577, found 424.1576.

Methyl (7a*S*)-6-(4-fluorophenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carboxylate (*S*)-2d.

$[\alpha]_D^{25}$ -27.8 ($c = 0.92$, $CHCl_3$); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 10:90 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_R (major) 100.24 min, t_R (minor) 66.16 min, 97% *ee*; IR (film) 2951 (m), 2256 (w), 1715 (s), 1600 (s), 1506 (s), 1347 (s), 1227 (s), 1163 (s), 1095 (s) cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.10–7.06 (m, 2 H), 6.99–6.94 (m, 2 H), 7.08 (dd, $J = 8.6$, 5.3 Hz, 2 H), 6.97 (t, $J = 8.6$ Hz, 2 H), 6.15 (d, $J = 2.1$ Hz, 1 H), 4.19 (d, A of AB, $J_{AB} = 15.6$ Hz, 1 H), 3.92 (t, $J = 8.7$ Hz, 1 H), 3.84 (d, B of AB, $J_{AB} = 15.4$ Hz, 1 H), 3.47 (s, 3 H), 3.04–2.97 (m, 1 H), 2.72 (t, $J = 9.7$ Hz, 1 H), 2.58 (dd, $J = 17.2$, 8.0 Hz, 1 H), 2.41 (s, 3 H), 2.24 (t, $J = 17.8$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.71 (e), 162.23 (e; d, $J_{C-F} = 247.2$ Hz), 143.80 (e), 142.16 (e), 138.14 (e), 136.78 (e; d, $J_{C-F} = 3.1$ Hz), 132.71 (e), 129.74 (o), 129.02 (o; d, $J_{C-F} = 7.7$ Hz), 127.63 (o), 126.27 (e), 115.93 (o), 115.03 (o; d, $J_{C-F} = 22.3$ Hz), 54.33 (e), 51.50 (o), 50.35 (e), 37.70 (o), 34.85 (e), 21.46 (o); HRMS (CI, $M+H^+$) calcd for $C_{23}H_{23}O_4N_1F_1S_1$ 428.1326, found 428.1326.

Methyl (7a*S*)-2-[(4-methylphenyl)sulfonyl]-6-[4-(trifluoromethyl)phenyl]-2,3,7,7a-tetrahydro-1*H*-isoindole-5-carboxylate (*S*)-2e.

$[\alpha]_{\text{D}}^{25}$ -83.2 ($c = 0.97$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 10:90 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 124.32 min, t_{R} (minor) 61.79 min, 98% *ee*; IR (film) 2953 (w), 1713 (s), 1616 (m), 1325 (s), 1163 (s), 1124 (s), 1069 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, $J = 8.2$ Hz, 2 H), 7.55 (d, $J = 8.2$ Hz, 2 H), 7.33 (d, $J = 8.2$ Hz, 2 H), 7.22 (d, $J = 8.2$ Hz, 2 H), 6.20 (d, $J = 2.1$ Hz, 1 H), 4.22 (d, A of AB, $J_{\text{AB}} = 15.8$ Hz, 1 H), 3.93 (t, $J = 8.7$ Hz, 1 H), 3.86 (d, B of AB, $J_{\text{AB}} = 15.4$ Hz, 1 H), 3.47 (s, 3 H), 3.08–2.99 (m, 1 H), 2.73 (t, $J = 9.7$ Hz, 1 H), 2.58 (dd, $J = 17.0, 8.0$ Hz, 1 H), 2.42 (s, 3 H), 2.30 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.12 (e), 144.80 (e), 143.90 (e), 141.97 (e), 139.03 (e), 132.76 (e), 129.81 (o), 129.35 (e; q, $J_{\text{C-F}} = 33.0$ Hz), 127.70 (o), 127.56 (o), 126.97 (e), 125.05 (o; q, $J_{\text{C-F}} = 3.8$ Hz), 123.97 (e; q, $J_{\text{C-F}} = 272.0$ Hz), 115.80 (o), 54.31 (e), 51.64 (o), 50.41 (e), 37.69 (o), 34.76 (e), 21.508 (o); HRMS (CI, $\text{M}+\text{H}^+$) calcd for $\text{C}_{24}\text{H}_{23}\text{O}_4\text{N}_1\text{F}_3\text{S}_1$ 478.1294, found 478.1295.

Trimethyl (7a*R*)-6-phenyl-1,3,7,7a-tetrahydro-2*H*-indene-2,2,5-tricarboxylate (*R*)-2f.

$[\alpha]_{\text{D}}^{25}$ -23.6 ($c = 0.83$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.7 mL/min flow rate, 240 nm detection light), t_{R} (major) 124.87 min, t_{R} (minor) 134.75 min, $\geq 99\%$ *ee*; IR (neat) 2953 (m), 1733 (s), 1435 (s), 1251 (s), 1201 (s), 1169 (m), 1068 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.22 (m, 3 H), 7.16–7.14 (m, 2 H), 6.18 (d, $J = 2.3$ Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.46 (s, 3 H), 3.24 (d, A of AB, $J_{\text{AB}} = 18.6$ Hz, 1 H), 3.06 (d, B of AB, $J_{\text{AB}} = 18.6$ Hz, 1 H), 2.89–2.82 (m, 1 H), 2.71 (t, $J = 7.8$ Hz, 1 H), 2.68 (dd, $J = 11.7, 7.4$ Hz, 1 H), 2.33 (t, $J = 17.7$ Hz, 1 H), 1.89 (t, $J = 11.9$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.94 (e), 171.82 (e), 168.65 (e), 143.14 (e), 142.73 (e), 141.53 (e), 127.98 (o), 127.49 (o), 127.33 (o), 126.80 (e), 116.22 (o), 59.42 (e), 52.87 (o), 51.38 (o), 40.49 (e), 38.50 (o), 38.10 (e), 37.92 (o), 37.01 (e); HRMS (CI, M^+) calcd for $\text{C}_{21}\text{H}_{22}\text{O}_6$ 370.1411, found 370.1397.

Trimethyl (7a*R*)-6-(4-methoxyphenyl)-1,3,7,7a-tetrahydro-2*H*-indene-2,2,5-tricarboxylate (*R*)-2g.

$[\alpha]_{\text{D}}^{25}$ -21.4 ($c = 1.00$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 3:97 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 111.43 min, t_{R} (minor) 80.65 min, 98% *ee*; IR (neat) 2953 (m), 1733 (s), 1607 (m), 1510 (s), 1435 (s), 1250 (s), 1176 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.08 (d, $J = 8.6$ Hz, 2 H), 6.82 (d, $J = 8.6$ Hz, 2 H),

6.15 (d, $J = 2.3$ Hz, 1 H), 3.77 (s, 3 H), 3.72 (s, 3 H), 3.71 (s, 3 H), 3.49 (s, 3 H), 3.22 (d, A of AB, $J_{AB} = 18.8$ Hz, 1 H), 3.04 (d, B of AB, $J_{AB} = 18.4$ Hz, 1 H), 2.85–2.77 (m, 1 H), 2.71 (t, $J = 6.6$ Hz, 1 H), 2.67 (dd, $J = 10.1, 7.1$ Hz, 1 H), 2.27 (t, $J = 17.6$ Hz, 1 H), 1.88 (dd, $J = 12.5, 11.1$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.89 (e), 171.78 (e), 168.96 (e), 159.10 (e), 142.60 (e), 142.15 (e), 133.54 (e), 128.78 (o), 126.11 (e), 116.34 (o), 113.36 (o), 59.40 (e), 55.12 (o), 52.79 (o), 51.34 (o), 40.44 (e), 38.45 (o), 38.03 (e), 37.89 (o), 36.96 (e); HRMS (CI, M^+) calcd for $\text{C}_{22}\text{H}_{24}\text{O}_7$ 400.1517, found 400.1514.

Trimethyl (7aR)-6-(4-methylphenyl)-1,3,7,7a-tetrahydro-2H-indene-2,2,5-tricarboxylate (R)-2h.

$[\alpha]_{\text{D}}^{25} -25.1$ ($c = 0.94$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.7 mL/min flow rate, 240 nm detection light), t_{R} (major) 210.47 min, t_{R} (minor) 187.88 min, 95% *ee*; IR (neat) 2952 (m), 1733 (s), 1435 (s), 1250 (s), 1200 (s), 1169 (s), 1067 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.24–7.03 (m, 4 H), 6.16 (s, 1 H), 3.72 (s, 3 H), 3.71 (s, 3 H), 3.49 (s, 3 H), 3.23 (d, A of AB, $J_{AB} = 18.8$ Hz, 1 H), 3.05 (d, B of AB, $J_{AB} = 18.6$ Hz, 1 H), 2.87–2.80 (m, 1 H), 2.71 (t, $J = 7.8$ Hz, 1 H), 2.67 (dd, $J = 12.1, 7.4$ Hz, 1 H), 2.31 (s, 3 H), 2.29 (t, $J = 18.0$ Hz, 1 H), 1.89 (t, $J = 11.8$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.91 (e), 171.80 (e), 168.78 (e), 143.12 (e), 142.41 (e), 138.41 (e), 137.31 (e), 128.68 (o), 127.30 (o), 126.41 (e), 116.28 (e), 59.41 (e), 52.82 (o), 51.36 (o), 40.48 (e), 38.47 (o), 38.06 (e), 37.89 (o), 37.00 (e), 21.16 (o); HRMS (CI, M^+) calcd for $\text{C}_{22}\text{H}_{25}\text{O}_6$ 384.1567, found 384.1579.

Trimethyl (7aR)-6-(4-fluorophenyl)-1,3,7,7a-tetrahydro-2H-indene-2,2,5-tricarboxylate (R)-2i.

$[\alpha]_{\text{D}}^{25} -30.1$ ($c = 0.88$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 3:97 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 46.38 min, t_{R} (minor) 40.95 min, 98% *ee*; IR (neat) 2954 (m), 1733 (s), 1602 (mw), 1507 (m), 1435 (m), 1250 (s), 1202 (m), 1161 (m), 1068 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.14–7.09 (m, 2 H), 7.00–6.96 (m, 2 H), 6.17 (d, $J = 2.1$ Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.49 (s, 3 H), 3.24 (d, A of AB, $J_{AB} = 18.6$ Hz, 1 H), 3.05 (d, B of AB, $J_{AB} = 18.6$ Hz, 1 H), 2.88–2.81 (m, 1 H), 2.70 (dd, $J = 12.7, 7.6$ Hz, 1 H), 2.63 (dd, $J = 16.8, 7.6$ Hz, 1 H), 2.31 (t, $J = 17.7$ Hz, 1 H), 1.89 (t, $J = 11.8$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.89 (e), 171.77 (e), 168.36 (e), 162.14 (e; d, $J_{\text{C-F}} = 247.2$ Hz), 142.91 (e), 142.12 (e), 137.47 (e; d, $J_{\text{C-F}} = 3.0$ Hz), 129.08 (o; d, $J_{\text{C-F}} = 8.4$ Hz), 126.97 (e), 116.15 (o), 114.96 (o; d, $J_{\text{C-F}} = 21.5$ Hz), 59.40 (e), 52.87 (o), 51.43 (o), 40.42 (e), 38.47 (o), 38.09 (e), 37.86 (o), 37.16 (e); HRMS (CI, M^+) calcd for $\text{C}_{21}\text{H}_{21}\text{O}_6\text{F}_1$ 388.1317, found 388.1312.

Trimethyl (7aR)-6-[4-(trifluoromethyl)phenyl]-1,3,7,7a-tetrahydro-2H-indene-2,2,5-tricarboxylate (R)-2j.

$[\alpha]_D^{25} -39.8$ ($c = 1.45$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.7 mL/min flow rate, 240 nm detection light), t_R (major) 216.39 min, t_R (minor) 167.64 min, 98% *ee*; IR (neat) 2955 (m), 1733 (s), 1616 (m), 1436 (s), 1326 (s), 1252 (s), 1167 (s), 1125 (s), 1069 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 8.2$ Hz, 2 H), 7.27 (d, $J = 8.6$ Hz, 2 H), 6.22 (d, $J = 2.2$ Hz, 1 H), 3.75 (s, 3 H), 3.74 (s, 3 H), 3.50 (s, 3 H), 3.27 (d, A of AB, $J_{AB} = 18.6$ Hz, 1 H), 3.09 (d, B of AB, $J_{AB} = 18.8$ Hz, 1 H), 2.97–2.86 (m, 1 H), 2.73 (dd, $J = 12.6, 7.5$ Hz, 1 H), 2.64 (dd, $J = 16.8, 7.6$ Hz, 1 H), 2.38 (t, $J = 17.7$ Hz, 1 H), 1.92 (t, $J = 11.9$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.86 (e), 171.71 (e), 167.75 (e), 149.82 (e), 145.47 (e), 143.80 (e), 141.89 (e), 129.34 (e; q, $J_{\text{C-F}} = 33.0$ Hz), 127.64 (o), 124.97 (o; q, $J_{\text{C-F}} = 3.8$ Hz), 124.09 (e; q, $J_{\text{C-F}} = 271.8$ Hz), 115.99 (o), 59.35 (e), 52.92 (o), 51.52 (o), 40.37 (e), 38.48 (o), 38.13 (e), 37.79 (o), 37.01 (e); HRMS (CI, M^+) calcd for $\text{C}_{22}\text{H}_{21}\text{O}_6\text{F}_3$ 438.1285, found 438.1290.

Methyl (7aS)-6-phenyl-1,3,7,7a-tetrahydro-2-benzofuran-5-carboxylate (S)-2k.

$[\alpha]_D^{25} -13.9$ ($c = 2.39$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.6 mL/min flow rate, 240 nm detection light), t_R (major) 38.43 min, t_R (minor) 48.98 min, $\geq 99\%$ *ee*; IR (neat) 2949 (s), 2853 (s), 1714 (s), 1584 (m), 1435 (s), 1252 (s), 1161 (s), 1028 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.34–7.24 (m, 3 H), 7.19–7.17 (m, 2 H), 6.21 (d, $J = 2.1$ Hz, 1 H), 4.60 (d, A of AB, $J_{AB} = 14.7$ Hz, 1 H), 4.42 (d, B of AB, $J_{AB} = 14.7$ Hz, 1 H), 4.33 (t, $J = 8.0$ Hz, 1 H), 3.48 (s, 3 H), 3.43 (dd, $J = 9.8, 8.4$ Hz, 1 H), 3.12–3.01 (m, 1 H), 2.68 (dd, $J = 17.0, 7.8$ Hz, 1 H), 2.38 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.45 (e), 143.07 (e), 142.75 (e), 141.37 (e), 128.02 (o), 127.64 (o), 127.32 (o), 126.87 (e), 113.37 (o), 74.45 (e), 69.22 (e), 51.42 (o), 39.29 (o), 34.03 (e); HRMS (CI, M^+) calcd for $\text{C}_{16}\text{H}_{16}\text{O}_3$ 256.1094, found 256.1088.

Methyl (7aS)-6-(4-methoxyphenyl)-1,3,7,7a-tetrahydro-2-benzofuran-5-carboxylate (S)-2l.

$[\alpha]_D^{25} -15.4$ ($c = 4.00$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 1:99 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_R (major) 56.62 min, t_R (minor) 53.39 min, 98% *ee*; IR (neat) 2949 (m), 1710 (s), 1607 (s), 1510 (s), 1252 (s), 1179 (s), 1027 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.14–7.12 (m, 2 H), 6.85–6.83 (m, 2 H), 6.19 (d, $J = 2.3$ Hz, 1 H), 4.58 (d, A of AB, $J_{AB} = 14.5$ Hz, 1 H), 4.41

(d, B of AB, $J_{AB} = 14.5$ Hz, 1 H), 4.32 (t, $J = 8.0$ Hz, 1 H), 3.79 (s, 3 H), 3.52 (s, 3 H), 3.42 (dd, $J = 10.1, 8.9$ Hz, 1 H), 3.10–2.98 (m, 1 H), 2.68 (dd, $J = 16.9, 7.7$ Hz, 1 H), 2.33 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.82 (e), 159.25 (e), 142.59 (e), 142.20 (e), 133.39 (e), 128.83 (o), 126.20 (e), 113.54 (o), 113.43 (o), 74.46 (e), 69.21 (e), 55.15 (o), 51.44 (o), 39.32 (o), 34.02 (e); HRMS (CI, M^+) calcd for $\text{C}_{17}\text{H}_{18}\text{O}_4$ 286.1200, found 286.1188.

Methyl (7a*S*)-6-(4-methylphenyl)-1,3,7,7a-tetrahydro-2-benzofuran-5-carboxylate (*S*)-2m.

$[\alpha]_{\text{D}}^{25} - 28.2$ ($c = 1.91$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.8:99.2 2-propanol–hexane; 0.8 mL/min flow rate, 240 nm detection light), t_{R} (major) 39.72 min, t_{R} (minor) 41.75 min, 98% *ee*; IR (neat) 2948 (m), 1712 (s), 1511 (m), 1435 (m), 1249 (m), 1160 (m), 1029 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.14–7.08 (m, 4 H), 6.20 (d, $J = 2.3$ Hz, 1 H), 4.60 (d, A of AB, $J_{AB} = 14.7$ Hz, 1 H), 4.42 (d, B of AB, $J_{AB} = 14.7$ Hz, 1 H), 4.33 (t, $J = 8.0$ Hz, 1 H), 3.52 (s, 3 H), 3.43 (dd, $J = 9.8, 8.4$ Hz, 1 H), 3.12–3.00 (m, 1 H), 2.68 (dd, $J = 16.9, 7.7$ Hz, 1 H), 2.35 (t, $J = 17.7$ Hz, 1 H), 2.34 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.61 (e), 143.07 (e), 142.44 (e), 138.26 (e), 137.52 (e), 128.72 (o), 127.31 (o), 126.48 (e), 113.45 (o), 74.45 (e), 69.20 (e), 51.42 (o), 39.28 (o), 34.02 (e), 21.17 (o); HRMS (CI, M^+) calcd for $\text{C}_{17}\text{H}_{18}\text{O}_3$ 270.1250, found 270.1241.

Methyl (7a*S*)-6-(4-fluorophenyl)-1,3,7,7a-tetrahydro-2-benzofuran-5-carboxylate (*S*)-2n.

$[\alpha]_{\text{D}}^{25} - 29.2$ ($c = 2.63$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 0.7:99.3 2-propanol–hexane; 0.6 mL/min flow rate, 240 nm detection light), t_{R} (major) 66.28 min, t_{R} (minor) 96.85 min, $\geq 99\%$ *ee*; IR (neat) 2951 (m), 1715 (s), 1602 (m), 1507 (s), 1436 (m), 1227 (s), 1161 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.17–7.13 (m, 2 H), 7.02–6.98 (m, 2 H), 6.20 (d, $J = 2.3$ Hz, 1 H), 4.59 (d, A of AB, $J_{AB} = 14.3$ Hz, 1 H), 4.42 (d, B of AB, $J_{AB} = 14.7$ Hz, 1 H), 4.32 (t, $J = 8.0$ Hz, 1 H), 3.51 (s, 3 H), 3.42 (dd, $J = 9.8, 8.4$ Hz, 1 H), 3.11–3.00 (m, 1 H), 2.63 (dd, $J = 16.9, 7.7$ Hz, 1 H), 2.37 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.17 (e), 162.21 (e; d, $J_{\text{C-F}} = 247.2$ Hz), 142.92 (e), 142.07 (e), 137.31 (e; d, $J_{\text{C-F}} = 3.1$ Hz), 129.11 (o; d, $J_{\text{C-F}} = 8.4$ Hz), 127.05 (e), 115.02 (o; d, $J_{\text{C-F}} = 21.5$ Hz), 113.30 (o), 74.38 (e), 69.20 (e), 51.48 (o), 39.25 (o), 34.18 (e); HRMS (CI, M^+) calcd for $\text{C}_{16}\text{H}_{15}\text{O}_3\text{F}$ 274.1000, found 274.0991.

Methyl (7a*S*)-6-[4-(trifluoromethyl)phenyl]-1,3,7a-tetrahydro-2-benzofuran-5-carboxylate (*S*)-2o.

$[\alpha]_{\text{D}}^{25}$ -39.0 ($c = 1.65$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel OD-H column, 0.5:99.5 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 41.57 min, t_{R} (minor) 44.67 min, 97% *ee*; IR (neat) 2952 (w), 1724 (m), 1616 (w), 1326 (s), 1164 (s), 1124 (s), 1069 (s) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 8.2$ Hz, 2 H), 7.29 (d, $J = 8.2$ Hz, 2 H), 6.24 (d, $J = 2.3$ Hz, 1 H), 4.61 (d, A of AB, $J_{\text{AB}} = 14.8$ Hz, 1 H), 4.43 (d, B of AB, $J_{\text{AB}} = 14.8$ Hz, 1 H), 4.34 (t, $J = 8.0$ Hz, 1 H), 3.51 (s, 3 H), 3.44 (dd, $J = 9.7, 8.5$ Hz, 1 H), 3.14–3.03 (m, 1 H), 2.62 (dd, $J = 17.0, 7.8$ Hz, 1 H), 2.42 (t, $J = 17.7$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 167.59 (e), 145.34 (e), 143.79 (e), 141.88 (e), 129.54 (e; q, $J_{\text{C-F}} = 32.5$ Hz), 127.75 (e), 127.67 (o), 125.04 (o; q, $J_{\text{C-F}} = 3.8$ Hz), 124.06 (e; q, $J_{\text{C-F}} = 272.0$ Hz), 113.18 (o), 74.37 (e), 69.24 (e), 51.61 (o), 39.20 (o), 34.07 (e); HRMS (CI, M^+) calcd for $\text{C}_{17}\text{H}_{15}\text{O}_3\text{F}_3$ 324.0968, found 324.0965.

1-[(7a*S*)-2-[(4-Methylphenyl)sulfonyl]-6-phenyl-2,3,7a-tetrahydro-1*H*-isoindol-5-yl]ethanone (*S*)-4a.

$[\alpha]_{\text{D}}^{25}$ -56.8 ($c = 1.70$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 4:96 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 190.62 min, t_{R} (minor) 112.24 min, 95% *ee*; IR (film) 2862 (m), 2254 (w), 1668 (s), 1347 (s), 1166 (s), 1095 (s); ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J = 8.0$ Hz, 2 H), 7.32–7.31 (m, 5 H), 7.14–7.13 (m, 2 H), 6.13 (s, 1 H), 4.18 (d, A of AB, $J_{\text{AB}} = 15.4$ Hz, 1 H), 3.94 (t, $J = 8.6$ Hz, 1 H), 3.82 (d, B of AB, $J_{\text{AB}} = 15.4$ Hz, 1 H), 3.07–2.98 (m, 1 H), 2.71 (t, $J = 9.7$ Hz, 1 H), 2.66 (dd, $J = 17.3, 7.9$ Hz, 1 H), 2.41 (s, 3 H), 2.22 (t, $J = 17.8$ Hz, 1 H), 1.69 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 203.28 (e), 143.76 (e), 141.15 (e), 140.35 (e), 137.77 (e), 135.77 (e), 132.70 (e), 129.73 (o), 128.68 (o), 128.62 (o), 128.10 (o), 127.66 (o), 116.13 (o), 54.42 (e), 50.38 (e), 37.88 (o), 34.51 (e), 30.13 (o), 21.47 (o); HRMS (CI, $\text{M}+\text{H}^+$) calcd for $\text{C}_{23}\text{H}_{24}\text{O}_3\text{N}_1\text{S}_1$ 394.1471, found 394.1470.

1-[(7a*S*)-7a-Methyl-2-[(4-methylphenyl)sulfonyl]-6-phenyl-2,3,7a-tetrahydro-1*H*-isoindol-5-yl]ethanone (*S*)-4a'.

$[\alpha]_{\text{D}}^{25}$ $+75.4$ ($c = 0.68$, CHCl_3); Chiral HPLC analysis (25 cm x 4.6 mm Daicel AD-H column, 10:90 2-propanol–hexane; 1.0 mL/min flow rate, 240 nm detection light), t_{R} (major) 42.05 min, t_{R} (minor) 27.03 min, $\geq 99\%$ *ee*; IR (film) 2925 (m), 1672 (s), 1347 (s), 1160 (s), 1093 (s); ^1H NMR (400 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2 H), 7.34–7.31 (m, 5 H), 7.13–7.11 (m, 2 H), 6.06 (s, 1 H), 4.24 (d, A of AB, $J_{\text{AB}} = 15.3$ Hz, 1 H), 3.82 (d, B of AB, J_{AB}

= 15.4 Hz, 1 H), 3.58 (d, A of AB, J_{AB} = 9.0 Hz, 1 H), 2.81 (d, B of AB, J_{AB} = 9.2 Hz, 1 H), 2.50 (s, 2 H), 2.42 (s, 3 H), 1.69 (s, 3 H), 1.16 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 203.19 (e), 143.76 (e), 142.04 (e), 140.77 (e), 140.24 (e), 134.55 (e), 132.94 (e), 129.75 (o), 128.74 (o), 127.91 (o), 127.69 (o), 115.04 (o), 61.56 (e), 49.86 (e), 42.44 (e), 41.27 (e), 30.17 (o), 21.54 (o), 21.34 (o); HRMS (CI, $\text{M}+\text{H}^+$) calcd for $\text{C}_{24}\text{H}_{26}\text{O}_3\text{N}_1\text{S}_1$ 408.1628, found 408.1632.

Indiana University Molecular Structure Center

Report 05149: $C_{23}H_{23}NO_4S$

Compound (S)-2a

by John C. Huffman

May 10, 2005

Empirical Formula:	C ₂₃ H ₂₃ NO ₄ S
Color of Crystal:	colorless
Crystal System:	Monoclinic
Space Group:	P2(1)
Cell Dimensions (at 120(2) K; 1883 data)	
a =	10.9212(10)
b =	5.3916(5)
c =	17.0437(16)
alpha =	90
beta =	90.270(3)
gamma =	90
Z (Molecules/cell):	2
Volume:	1003.57(16)
Calculated Density:	1.355
Molecular Weight:	409.48
Linear Absorption Coefficient:	0.191
Final residuals are:	
R(F) (observed data) =	0.0425
Rw(F2) (refinement data) =	0.0733

The sample was submitted by James Sawyer from the research group of Prof. P.A. Evans, Department of Chemistry, Indiana University. The crystals occur as transparent colorless rectangular plates that tend to grow in clumps. A typical crystal of approximate dimensions $0.40 \times 0.18 \times 0.15$ mm onto the tip of a 0.1 mm diameter glass fiber which was subsequently mounted on a SMART6000 (Bruker) and cooled to 120(2) K.

Data collection

A preliminary set of cell constants was calculated from reflections obtained from three nearly orthogonal sets of 20 frames. The data collection was carried out using graphite monochromated Mo K α radiation with a frame time of 30 seconds and a detector distance of 5.0 cm. A randomly oriented region of a sphere in reciprocal space was surveyed. Three sections of 606 frames were collected with 0.30° steps in ω at different ϕ settings with the detector set at -43° in 2θ . Final cell constants were calculated from the xyz centroids of 1883 strong reflections from the actual data collection after integration (SAINT).

Structure solution and refinement

Intensity statistics and systematic absences suggested the non-centrosymmetric space group P2₁ and subsequent solution and refinement confirmed this choice. The structure was solved using SHELXS-97 and refined with SHELXL-97. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located in subsequent Fourier maps and included as isotropic contributors in the final cycles of refinement.

Complete data are available at

<http://bl-chem-iumsc110.chem.indiana.edu/recipnet/showsample.jsp?sampleId=64531609&sampleHistoryId=-1>