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Supporting Information

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Highly Regio-, Diastereo-, and Enantioselective [2 + 2 + 2] Cycloaddition of 1,6-Enynes with Electron-Deficient Ketones Catalyzed by a Cationic Rh(I)/H_8-binap Complex

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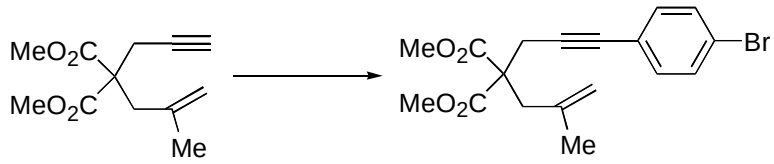
I. General

Anhydrous CH_2Cl_2 (No. 27099-7) and anhydrous $(CH_2Cl)_2$ (No. 28450-5) were obtained from Aldrich and used as received. H_8-binap, tol-binap, xyl-binap, and Segphos were obtained from Takasago International Corporation. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring. Enynes **1a**,[1] **1c**,[2] **1d**,[3] **1e**,[2] **1f**,[2] and ketone **2c**[4] were prepared according to the literatures.

II. Synthesis of 1,6-Enyne 1b

2-[3-(4-Bromophenyl)prop-2-ynyl]-2-(2-methylallyl)malonic acid dimethyl ester (1b)



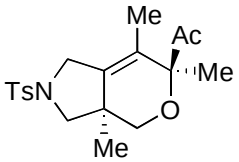
To a solution of 1-bromo-4-iodobenzene (605 mg, 2.14 mmol) and $PdCl_2(PPh_3)_2$ (25.0 mg, 0.0356 mmol) in *i*-Pr_2NH (25 mL) was added 2-(2-methylallyl)-2-prop-2-ynyl malonic acid dimethyl ester[5] (400 mg, 178 mmol), and the mixture was stirred at room temperature for 5 min. Then was added CuI (13.6 mg, 0.0713 mmol) and the resulting mixture was stirred at room temperature for 24 h. The reaction mixture was filtered and concentrated to give a residue (785 mg), a portion of which (421 mg) was purified by preparative TLC (hexane/ethyl acetate = 5:1) to furnish **1b** (324 mg, 0.854 mmol, 48% yield) as a pale yellow solid.

Mp 60.1–61.2 °C; IR (neat) 2952, 1733, 1208, 1071, 817 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) *d* 7.41 (dt, *J* = 8.7, 2.1 Hz, 2H), 7.22 (dt, *J* = 8.7, 2.1 Hz, 2H), 4.97–4.90 (m, 1H), 4.89–4.84 (m, 1H), 3.76 (s, 6H), 3.04 (s, 2H), 2.89 (s, 2H), 1.68 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 170.6, 139.8, 133.0, 131.4, 122.1, 116.3, 85.9, 82.8, 56.7, 52.7, 39.8, 23.6, 23.2; HRMS (FAB) calcd for $C_{18}H_{20}O_4Br$ $[M+H]^+$ 381.0527, found 381.0564.

III. Rh-Catalyzed Reactions of 1,6-Enynes with Electron-Deficient Ketones

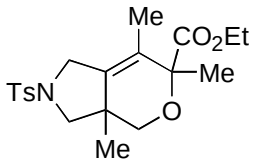
General Procedure (Table 2, entry 3). (*R*)-H_8-binap (18.9 mg, 0.030 mmol) and $[Rh(cod)_2]BF_4$ (12.2 mg, 0.030 mmol) were dissolved in CH_2Cl_2 (2.0 mL), and the mixture was stirred at room temperature for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 0.5 h, the resulting solution was concentrated to dryness and dissolved in $(CH_2Cl)_2$ (0.5 mL). To this solution was added a $(CH_2Cl)_2$ (1.0 mL) solution of **1a** (83.2 mg, 0.300 mmol) and **2b** (51.7 mg, 0.600 mmol) at room temperature. The mixture was stirred at 80 °C for 16 h. The resulting solution was concentrated and purified by preparative TLC (hexane/ethyl acetate = 5:1), which furnished **(–)-3ab** (79.6 mg, 0.219 mmol, 73% yield) as a pale yellow solid.

(3*R*,6*S*)-(–)-1-[3a,6,7-Trimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c] pyrrol-6-yl]ethanone [(3*R*,6*S*)-(–)-3ab, Table 2, entry 3, 73% yield, 98% ee]



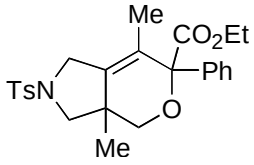
Pale yellow solid; Mp 98.5–99.4 °C; $[\alpha]^{25}_{D}$ –45.6° (*c* 2.34, acetone, 98% ee); IR (neat) 2926, 1713, 1344, 1163, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.71 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 4.00 (dd, *J* = 13.8, 1.5 Hz, 1H), 3.78 (d, *J* = 13.8 Hz, 1H), 3.71 (d, *J* = 10.2 Hz, 1H), 3.35 (d, *J* = 8.7 Hz, 1H), 3.18 (d, *J* = 10.2 Hz, 1H), 2.65 (d, *J* = 8.7 Hz, 1H), 2.45 (s, 3H), 2.16 (s, 3H), 1.55 (s, 3H), 1.40 (s, 3H), 1.13 (s, 3H);^{13}C NMR ($CDCl_3$, 75 MHz) *d* 208.8, 143.6, 134.9, 129.7, 127.4, 126.3, 81.5, 77.2, 69.9, 56.9, 48.5, 40.7, 24.8, 23.6, 22.6, 21.5, 15.3; HRMS (FAB) calcd for $C_{19}H_{26}O_4NS$ $[M+H]^+$ 364.1583, found 364.1562; CHIRALPAK AD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 22.7 min (major isomer) and 27.5 min (minor isomer).

(–)-3a,6,7-Trimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carboxylic acid ethyl ester [(–)-3aa, Table 2, entry 1, >99% yield, 95% ee]



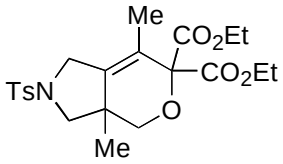
Pale yellow oil; $[\alpha]^{25}_{D}$ –57.4° (*c* 1.82, acetone, 95% ee); IR (neat) 2980, 1732, 1246, 1163, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.72 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.13 (q, *J* = 7.2 Hz, 2H), 4.00 (dd, *J* = 13.5, 1.5 Hz, 1H), 3.80 (d, *J* = 13.5 Hz, 1H), 3.68 (d, *J* = 10.5 Hz, 1H), 3.63 (d, *J* = 10.5 Hz, 1H), 3.34 (d, *J* = 9.0 Hz, 1H), 2.72 (d, *J* = 9.0 Hz, 1H), 2.43 (s, 3H), 1.70 (s, 3H), 1.54 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 172.0, 143.6, 135.4, 133.8, 129.7, 127.5, 125.6, 77.9, 70.0, 61.1, 57.1, 48.7, 40.6, 24.2, 22.7, 21.5, 14.6, 14.0; HRMS (FAB) calcd for $C_{20}H_{28}O_5NS$ $[M+H]^+$ 394.1688, found 394.1683; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 28.3 min (major isomer) and 22.9 min (minor isomer).

(+)-3a,7-Dimethyl-6-phenyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carboxylic acid ethyl ester [(+)-3ac, Table 2, entry 4, 24% yield, 97% ee]



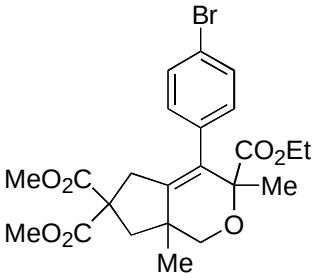
Pale yellow oil; $[\alpha]^{25}_{D}$ +10.9° (*c* 0.24, acetone, 97% ee); IR (neat) 2979, 1733, 1346, 1162, 666 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.74 (d, *J* = 8.1 Hz, 2H), 7.40–7.29 (m, 5H), 7.26–7.20 (m, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 4.09 (dd, *J* = 13.8, 1.5 Hz, 1H), 3.88 (d, *J* = 13.8 Hz, 1H), 3.87 (d, *J* = 10.5 Hz, 1H), 3.58 (d, *J* = 10.5, 1H), 3.41 (d, *J* = 9.0 Hz, 1H), 2.78 (d, *J* = 9.0 Hz, 1H), 2.46 (s, 3H), 1.57 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 171.2, 143.7, 139.3, 137.3, 133.9, 129.8, 128.4, 128.3, 127.5, 127.0, 125.2, 84.0, 71.0, 61.5, 57.2, 48.8, 40.7, 23.1, 21.5, 16.4, 14.1; HRMS (FAB) calcd for $C_{25}H_{30}O_5NS$ $[M+H]^+$ 456.1845, found 456.1803; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 18.7 min (major isomer) and 25.4 min (minor isomer).

(–)-3a,7-Dimethyl-2-(toluene-4-sulfonyl)-2,3,3a,4-tetrahydro-1H-pyrano[3,4-c]pyrrole-6,6-dicarboxylic acid diethyl ester [(–)-3ad, Table 2, entry 5, 89% yield, 97% ee]



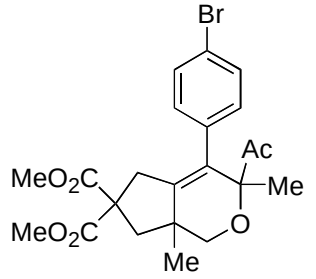
Pale yellow solid; Mp 77.0–77.5 °C; $[\alpha]^{25}_{D}$ –15.0° (*c* 2.84, acetone, 97% ee); IR (neat) 2980, 1738, 1347, 1162, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.71 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.30–4.13 (m, 4H), 4.07 (dd, *J* = 14.8, 1.2 Hz, 1H), 3.84 (d, *J* = 10.2 Hz, 1H), 3.80 (d, *J* = 14.8 Hz, 1H), 3.49 (d, *J* = 10.2 Hz, 1H), 3.37 (d, *J* = 9.3 Hz, 1H), 2.69 (d, *J* = 9.3 Hz, 1H), 2.44 (s, 3H), 1.69 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 167.8, 167.0, 143.8, 139.3, 133.5, 129.8, 127.5, 120.6, 82.1, 70.6, 62.2, 61.9, 56.9, 49.0, 40.6, 22.2, 21.5, 15.4, 13.91, 13.87; HRMS (FAB) calcd for $C_{22}H_{30}O_7NS$ $[M+H]^+$ 452.1743, found 452.1754; doubly connected CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 0.5 mL/min, retention times: 171.0 min (major isomer) and 166.7 min (minor isomer).

(+)-4-(4-Bromo-phenyl)-3,7a-dimethyl-3,5,7,7a-tetrahydro-1H-cyclopenta[c]pyran-3,6,6-tricarboxylic acid 3-ethyl ester 6,6-dimethyl ester [(+)-3ba, Table 2, entry 7, 49% yield, 98% ee]



Pale yellow oil; $[\alpha]^{25}_{D}$ +33.4° (*c* 2.87, acetone, 98% ee); IR (neat) 2953, 1736, 1262, 1063, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.47–7.40 (m, 2H), 6.92–6.87 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 4.01 (d, *J* = 10.5 Hz, 1H), 3.77 (d, *J* = 10.5 Hz, 1H), 3.72 (s, 3H), 3.67 (s, 3H), 3.02 (d, *J* = 16.5 Hz, 1H), 2.53 (d, *J* = 16.5 Hz, 1H), 2.29 (d, *J* = 13.5 Hz, 1H), 2.23 (d, *J* = 13.5 Hz, 1H), 1.42 (s, 3H), 1.23 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 172.3, 171.9, 171.7, 143.4, 136.2, 131.3, 131.2, 130.4, 121.6, 77.9, 72.2, 61.0, 57.7, 52.9, 52.8, 43.1, 40.3, 37.4, 24.5, 24.4, 14.0; HRMS (FAB) calcd for $C_{20}H_{22}O_5Br$ $[M–CO_2Et]^+$ 421.0651, found 421.0626; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 7.1 min (major isomer) and 8.2 min (minor isomer).

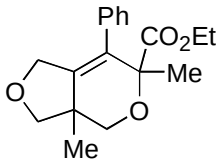
(+)-3-Acetyl-4-(4-bromophenyl)-3,7a-dimethyl-3,5,7,7a-tetrahydro-1H-cyclopenta[c]pyran-6,6-dicarboxylic acid dimethyl ester [(+)-3bb, Table 2, entry 8, 33% yield, 92% ee]



Pale yellow oil; $[\alpha]^{25}_{D}$ +36.4° (*c* 1.62, acetone, 92% ee); IR (neat) 2953, 1730, 1435, 1267, 734 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.47–7.40 (m, 2H), 6.92–6.90 (m, 2H), 3.79 (d, *J* = 10.5 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.60 (d, *J* = 10.5 Hz, 1H), 3.01 (d, *J* = 16.5 Hz, 1H), 2.54 (d, *J* = 16.5 Hz, 1H), 2.27 (d, *J* = 12.9 Hz, 1H), 2.20 (s, 3H), 2.19 (d, *J* = 12.9 Hz, 1H), 1.38 (s, 3H), 1.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 207.3, 172.2, 172.0, 143.4, 136.6, 131.6, 131.2, 130.7, 121.4, 81.4, 72.0, 57.9, 52.9, 42.9, 40.3, 37.5, 25.7, 24.8, 24.4; HRMS (FAB) calcd for $C_{20}H_{22}O_5Br$ $[M–Ac]^+$ 421.0651,

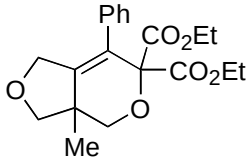
found 421.0643; CHIRALCEL OJ, hexane/*i*-PrOH = 90:10, 1.0 mL/min, retention times: 7.6 min (major isomer) and 11.9 min (minor isomer).

(+)-3a,6-Dimethyl-7-phenyl-1,3a,4,6-tetrahydro-3H-furo[3,4-c]pyran-6-carboxylic acid ethyl ester [(+)-3ca, Table 2, entry 10, 67% yield, >99% ee]



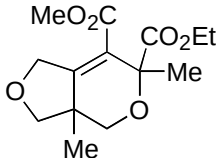
Pale yellow oil; $[\alpha]^{25}_{D}$ +19.6° (*c* 2.40, acetone, >99% ee); IR (neat) 2977, 1736, 1112, 1057, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.36–7.22 (m, 3H), 7.05–6.97 (m, 2H), 4.35 (d, *J* = 13.5 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.12 (d, *J* = 10.5 Hz, 1H), 3.96 (d, *J* = 13.5 Hz, 1H), 3.87 (d, *J* = 10.5 Hz, 1H), 3.81 (d, *J* = 7.8 Hz, 1H), 3.46 (d, *J* = 7.8 Hz, 1H), 1.47 (s, 3H), 1.37 (s, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 171.9, 142.2, 136.8, 130.7, 128.7, 128.3, 127.7, 77.7, 77.0, 70.0, 68.4, 61.1, 41.4, 24.4, 22.3, 14.0; HRMS (FAB) calcd for $C_{18}H_{21}O_4$ $[M–H]^+$ 301.1440, found 301.1397; CHIRALCEL OD-H, hexane/*i*-PrOH = 99:1, 1.0 mL/min, retention times: 9.5 min (major isomer) and 6.4 min (minor isomer).

(+)-3a-Methyl-7-phenyl-3a,4-dihydro-1H,3H-furo[3,4-c]pyran-6,6-dicarboxylic acid diethyl ester [(+)-3cd, Table 2, entry 11, 64% yield, 96% ee]



Colorless oil; $[\alpha]^{25}_{D}$ +13.8° (*c* 1.65, acetone, 96% ee); IR (neat) 2979, 1738, 1266, 1092, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.30–7.24 (m, 3H), 7.18–7.12 (m, 2H), 4.35 (d, *J* = 14.1 Hz, 1H), 4.40–4.20 (m, 5H), 3.99 (d, *J* = 14.1 Hz, 1H), 3.89 (d, *J* = 10.5 Hz, 1H), 3.84 (d, *J* = 8.1 Hz, 1H), 3.45 (d, *J* = 8.1 Hz, 1H), 1.39 (s, 3H), 1.12 (t, *J* = 6.9 Hz, 3H), 1.10 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 168.1, 167.0, 146.9, 136.6, 129.3, 128.0, 127.6, 125.1, 82.3, 76.8, 70.6, 68.9, 61.8, 61.6, 41.6, 21.6, 13.7; HRMS (FAB) calcd for $C_{20}H_{25}O_6$ $[M+H]^+$ 361.1651, found 361.1646; CHIRALPAK AD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, retention times: 7.2 min (major isomer) and 6.1 min (minor isomer).

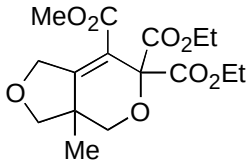
(–)-3a,6-Dimethyl-1,3a,4,6-tetrahydro-3H-furo[3,4-c]pyran-6,7-dicarboxylic acid 6-ethyl ester 7-methyl ester [(–)-3da, Table 2, entry 12, 17% yield, 98% ee]



Pale yellow oil; $[\alpha]^{25}_{D}$ –112.2° (*c* 0.55, acetone, 98% ee); IR (neat) 2941, 1747, 1715, 1062, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 4.88 (d, *J* = 17.1 Hz, 1H), 4.70 (d, *J* = 17.1 Hz, 1H), 4.29–4.10 (m, 2H), 3.82 (d, *J* = 8.4 Hz, 1H), 3.78–3.67 (m, 2H), 3.72 (s, 3H), 3.37 (d, *J* = 8.4 Hz, 1H), 1.62 (s, 3H), 1.31 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 170.5, 164.9, 160.1, 122.1, 75.6, 75.4, 71.0, 68.2, 61.2, 51.6, 43.6, 23.7, 22.1, 14.1; HRMS (EI) calcd for $C_{13}H_{17}O_5$ $[M–OMe]^+$ 253.1076, found 253.1057; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 7.7 min (major isomer) and 8.7 min (minor isomer).

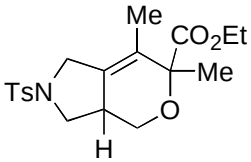
(–)-3a-Methyl-3a,4-dihydro-1H,3H-furo[3,4-c]pyran-6,6,7-tricarboxylic acid diethyl ester

methyl ester [(–)-3dd, Table 2, entry 13, 61% yield, 93% ee]



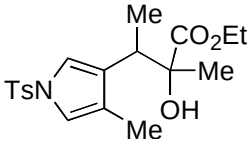
Pale yellow oil; $[\alpha]^{25}_{D}$ –20.2° (*c* 1.80, acetone, 93% ee); IR (neat) 2981, 1724, 1283, 1092, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 4.88 (d, *J* = 17.4 Hz, 1H), 4.69 (d, *J* = 17.4 Hz, 1H), 4.32–4.20 (m, 4H), 3.97 (d, *J* = 10.5 Hz, 1H), 3.83 (d, *J* = 8.1 Hz, 1H), 3.74 (s, 3H), 3.72 (d, *J* = 10.5 Hz, 1H), 3.37 (d, *J* = 8.1 Hz, 1H), 1.31 (s, 3H), 1.30 (t, *J* = 6.9 Hz, 3H), 1.29 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 167.8, 167.0, 164.9, 160.0, 117.8, 79.2, 75.6, 70.6, 69.7, 62.3, 62.2, 51.8, 43.0, 21.8, 13.90, 13.86; HRMS (FAB) calcd for $C_{16}H_{23}O_8$ $[M+H]^+$ 343.1393, found 343.1396; CHIRALPAK AD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, retention times: 10.5 min (major isomer) and 9.4 min (minor isomer).

(–)-6,7-Dimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carb oxylic acid ethyl ester [(–)-3ea, Table 2, entry 14, 25% yield, 94% ee]



Yellow oil; $[\alpha]^{25}_{D}$ –44.1° (*c* 0.93, acetone, 94% ee); IR (neat) 2981, 1732, 1346, 1165, 666 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.71 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 4.13 (dq, *J* = 7.2, 0.9 Hz, 2H), 4.03–3.94 (m, 2H), 3.77 (d, *J* = 14.1 Hz, 1H), 3.69 (dd, *J* = 9.0, 7.8 Hz, 1H), 3.50 (dd, *J* = 10.8, 5.4 Hz, 1H), 2.81–2.65 (m, 1H), 2.54 (dd, *J* = 10.8, 9.0 Hz, 1H), 2.44 (s, 3H), 1.62–1.56 (m, 3H), 1.43 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 172.2, 143.7, 133.5, 131.9, 129.8, 127.6, 126.5, 77.8, 64.3, 61.2, 50.2, 49.6, 37.5, 24.0, 21.5, 14.8, 14.1; HRMS (FAB) calcd for $C_{19}H_{26}O_5NS$ $[M+H]^+$ 380.1532, found 380.1562; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times: 25.4 min (major isomer) and 39.3 min (minor isomer).

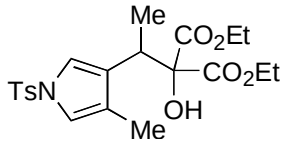
(–)-2-Hydroxy-2-methyl-3-[4-methyl-1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]butyric acid ethyl ester [(–)-5ea, Table 2, entry 14, 30% yield, dr = 2.8:1, >99% ee (major diastereomer) and 81% ee (minor diastereomer)]



Pale yellow oil; $[\alpha]^{25}_{D}$ –9.7° [*c* 1.54, acetone, mixture of diastereomer (dr = 2.8:1): >99% ee (major) and 81% ee (minor)]; IR (neat) 3516, 2979, 1728, 1368, 1171 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.66 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.12–7.05 (m, 1H), 6.76 (q, *J* = 1.2 Hz, 1H), 4.25, 3.93, 3.84 (q, *J* = 7.2 Hz, total 2H), 3.24 (s, 1H), 2.93 (q, *J* = 7.2 Hz, 1H), 2.39 (s, 3H), 1.92 (d, *J* = 1.2 Hz, 3H), 1.42 (s, 3H), 1.21 (d, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H); minor diastereomer: *d* 7.70 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.12–7.05 (m, 1H), 6.82 (q, *J* = 1.2 Hz, 1H), 4.25, 3.95, 3.81 (q, *J* = 7.2 Hz, total 2H), 3.17 (s, 1H), 2.93 (q, *J* = 7.2 Hz, 1H), 2.39 (s, 3H), 1.98 (d. *J* = 1.2 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.16 (s, 3H), 1.07 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 176.6, 144.4, 136.4, 130.5, 129.74, 129.70, 126.60, 126.55, 124.7, 123.9, 119.3, 118.6, 117.34, 117.30, 76.7, 76.4, 62.0, 61.5, 37.8, 37.2, 24.5, 24.4, 21.53, 21.51, 17.0, 15.7, 14.2, 13.7, 10.6, 10.2; HRMS (FAB) calcd for $C_{19}H_{26}O_5NS$ $[M+H]^+$ 380.1532, found 380.1664; CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 1.0 mL/min, retention times of major diastereomer: 8.7 min (major isomer) and 15.4 min (minor isomer); retention times of minor diastereomer: 9.9 min

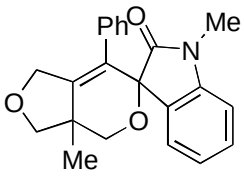
(major isomer) and 12.2 (minor isomer).

(–)-2-Hydroxy-2-{1-[4-methyl-1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]ethyl}malonic acid diethyl ester [(–)-5ed, Table 2, entry 15, 70% yield, 52% ee]



Pale yellow oil; $[\alpha]^{25}_{D}$ –4.6° (*c* 2.40, acetone, 52% ee); IR (neat) 3491, 2981, 1740, 1094, 676 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.66 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.19 (s, 1H), 6.77 (s, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.97–3.78 (m, 3H), 3.62 (q, *J* = 6.9 Hz, 1H), 2.39 (s, 3H), 1.98 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 169.8, 169.7, 144.3, 136.3, 129.7, 128.9, 126.6, 124.0, 119.1, 117.2, 82.0, 62.6, 62.3, 34.8, 21.5, 16.9, 14.0, 13.5, 10.2; HRMS (FAB) calcd for $C_{21}H_{28}O_7NS$ $[M+H]^+$ 438.1586, found 438.1608; doubly connected CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 0.5 mL/min, retention times: 46.3 min (major isomer) and 49.9 min (minor isomer).

(+)-Spiro[(3',8'-dioxabicyclo[4.3.0]-1-methyl-5-phenylnon-5-ene)-3,4'-(2,3-dihydro-1-methylidol-2-one)] [(+)-3cf, Scheme 3, 85% yield, 92% ee]

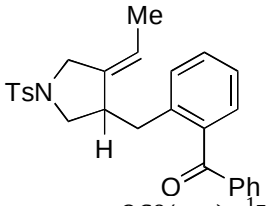


Pale yellow oil; $[\alpha]^{25}_{D}$ +52.8° (*c* 2.04, acetone, 92% ee); IR (neat) 2964, 1715, 1090, 1052, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.29 (d, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.15–6.99 (m, 4H), 6.87–6.75 (m, 2H), 6.57 (d, *J* = 7.5 Hz, 1H), 4.59 (d, *J* = 10.5 Hz, 1H), 4.45 (d, *J* = 13.8 Hz, 1H), 4.09 (d, *J* = 13.8 Hz, 1H), 3.93 (d, *J* = 10.5 Hz, 1H), 3.91 (d, *J* = 8.1 Hz, 1H), 3.62 (d, *J* = 8.1 Hz, 1H), 3.00 (s, 3H), 1.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 175.6, 144.3, 144.1, 135.3, 129.9, 128.7, 128.6, 128.0, 127.5, 127.2, 124.4, 122.9, 108.2, 79.1, 77.0, 69.7, 68.3, 41.4, 25.8, 23.0; HRMS (FAB) calcd for $C_{22}H_{22}O_3NS$ $[M+H]^+$ 348.1600, found 348.1601; CHIRALCEL OD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, retention times: 8.5 min (major isomer) and 12.9 min (minor isomer).

IV. Rh-Catalyzed Reactions of 1,6-Enynes with Aryl Ketones

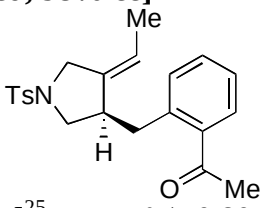
General Procedure (Table 3, entry 1). (*R*)-H_8-binap (9.5 mg, 0.015 mmol) and $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) were dissolved in CH_2Cl_2 (2.0 mL), and the mixture was stirred at room temperature for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at room temperature for 0.5 h, the resulting solution was concentrated to dryness and dissolved in CH_2Cl_2 (0.4 mL). To this solution was added a CH_2Cl_2 (0.6 mL) solution of **2g** (546.7 mg, 3.00 mmol). To this solution was added over 5 min a CH_2Cl_2 (0.5 mL) solution of **1e** (79.0 mg, 0.300 mmol) at room temperature. The mixture was stirred at 25 °C for 3 h. The resulting solution was concentrated and purified by silica gel column chromatography (CH_2Cl_2/hexane = 1:1), followed by preparative TLC (hexane/ethyl acetate = 5:1), which furnished (+)-**6eg** (79.4 mg, 0.178 mmol, 55% yield) as a colorless oil.

(+)-{2-[4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylmethyl]phenyl}phenyl methanone [(+)-6eg, Table 3, entry 1, 55% yield, 96% ee][6]



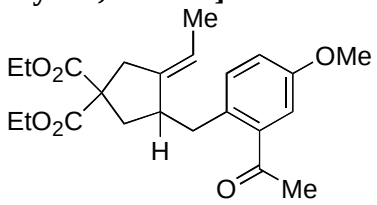
Colorless oil; $[\alpha]^{25}_{D}$ +44.5° (*c* 0.27, acetone, 96% ee); ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.82–7.73 (m, 2H), 7.66–7.57 (m, 3H), 7.53–7.40 (m, 3H), 7.35–7.20 (m, 5H), 5.20–5.07 (m, 1H), 3.70–3.65 (m, 2H), 3.13 (dd, *J* = 8.7, 6.3 Hz, 1H), 3.01 (dd, *J* = 13.2, 5.1 Hz, 1H), 2.95–2.80 (m, 2H), 2.60 (dd, *J* = 13.2, 9.3 Hz, 1H), 2.42 (s, 3H), 1.46 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 198.1, 143.5, 138.9, 138.3, 138.2, 137.7, 133.3, 132.4, 131.1, 130.5, 130.2, 129.6, 129.3, 128.5, 127.8, 125.8, 117.6, 52.9, 49.6, 44.4, 36.5, 21.5, 14.4; doubly connected CHIRALCEL OD-H, hexane/*i*-PrOH = 99:5, 0.5 mL/min, retention times: 95.1 min (major isomer) and 100.3 min (minor isomer).

(*R*)-(+)-1-{2-[4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylmethyl]phenyl}ethanone [(*R*)-(+)-6eh, Table 3, entry 4, 34% yied, 98% ee]



Colorless solid; Mp 94.2–94.8 °C; $[\alpha]^{25}_{D}$ +52.1° (*c* 0.80, acetone, 98% ee); IR (neat) 2922, 1683, 1345, 1161, 665 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.74 (d, *J* = 7.5, 2.5 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.42 (dt, *J* = 7.5, 2.5 Hz, 1H), 7.36–7.28 (m, 3H), 7.15 (dd, *J* = 7.5, 0.9 Hz, 1H), 5.37–5.25 (m, 1H), 3.88 (d, *J* = 10.8 Hz, 1H), 3.72 (d, *J* = 10.8 Hz, 1H), 3.25 (dd, *J* = 12.9, 5.1 Hz, 1H), 3.04 (d, *J* = 6.0 Hz, 2H), 2.98-2.91 (m, 1H), 2.65 (dd, *J* = 12.9, 9.6 Hz, 1H), 2.57 (s, 3H), 2.43 (s, 3H), 1.52 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 201.4, 143.5, 140.1, 138.7, 137.1, 132.7, 132.2, 131.7, 130.0, 129.6, 127.8, 126.5, 117.6, 52.7, 49.6, 44.2, 37.8, 29.6, 21.5, 14.4; HRMS (FAB) calcd for $C_{22}H_{26}O_3NS$ $[M+H]^+$ 384.1633, found 384.1648; CHIRALPAK AD-H, hexane/*i*-PrOH = 90:10, 1.0 mL/min, retention times: 22.0 min (major isomer) and 19.9 min (minor isomer).

(+)-3-(2-Acetyl-4-methoxybenzyl)-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester [(+)-6fi, Table 3, entry 5, 34% yield, 94% ee]

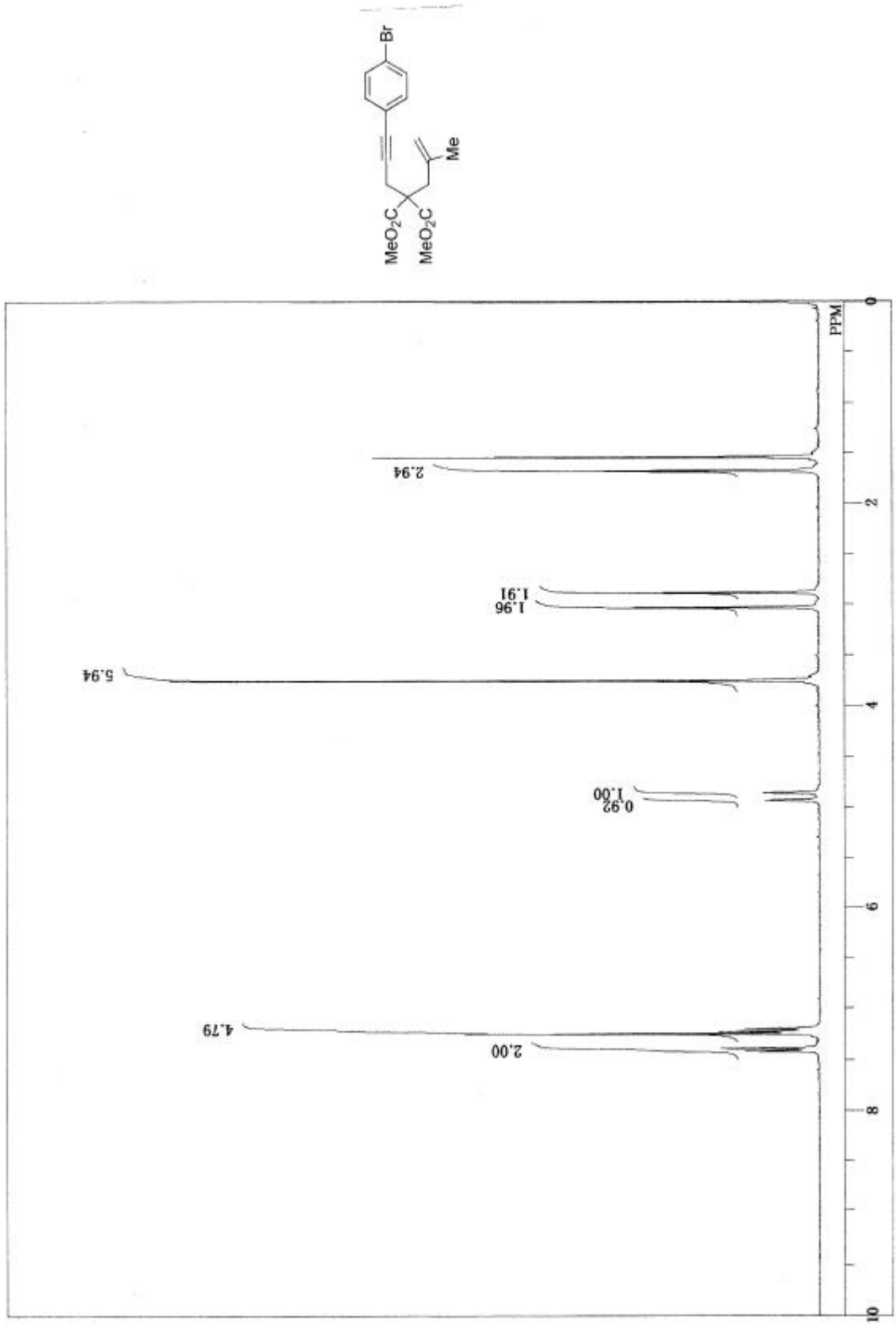


Colorless oil; $[\alpha]^{25}_{D}$ +58.3° (*c* 1.50, acetone, 94% ee); IR (neat) 2980, 1731, 1687, 1266, 1048 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) *d* 7.16 (d, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 2.4 Hz, 1H), 6.92 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.37–5.25 (m, 1H), 4.22–4.01 (m, 4H), 3.82 (s, 3H), 3.35 (dd, *J* = 13.2, 5.1 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 2.87 (d, *J* = 16.8 Hz, 1H), 2.79–2.64 (m, 1H), 2.54 (s, 3H), 2.47 (dd, *J* = 13.2, 9.9 Hz, 1H), 2.23 (dd, *J* = 12.9, 7.2 Hz, 1H), 1.78 (dd, *J* = 12.9, 9.9 Hz, 1H), 1.61 (dd, *J* = 6.6, 1.2 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *d* 201.9, 172.1, 171.8, 157.5, 142.3, 138.8, 132.7, 132.5, 116.2, 116.1, 115.1, 61.4, 61.3, 58.4, 55.4, 43.8, 39.7, 37.5, 37.1, 29.8, 14.5, 14.0, 13.9; HRMS (FAB) calcd for $C_{23}H_{31}O_6$ $[M+H]^+$ 403.2121, found 403.2084; doubly connected CHIRALCEL OD-H, hexane/*i*-PrOH = 95:5, 0.5 mL/min, retention times: 36.4 min (major isomer) and 34.9 min (minor isomer).

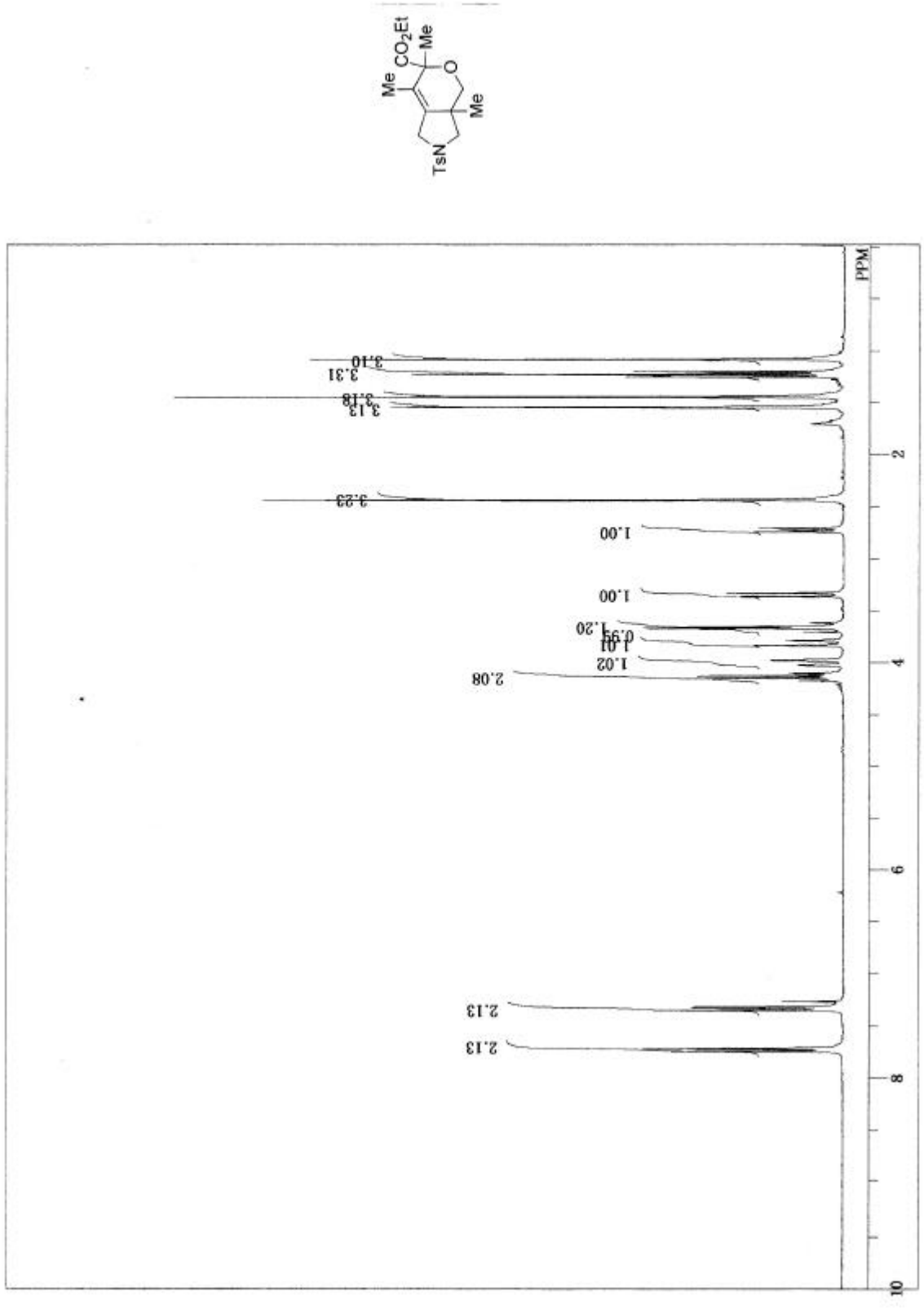
V. References

(1) T. Kitamura, Y. Sato, M. Mori, *Adv*. *Synth*. *Cat.* **2002**, *344*, 678.
(2) F. Y. Kwong, H. W. Lee, L. Qiu, W. H. Lam, Y.-M. Li, H. L. Kwong, A. S. C. Chan, *Adv*. *Synth*. *Cat*. **2005**, *347*, 1750.
(3) Y. Yamamoto, S. Kuwabara, Y. Ando, H. Nagata, H. Nishiyama, K. Itoh, *J. Org*. *Chem*. **2004**, *69*, 6697.
(4) X. Creary, *J. Org*. *Chem*. **1987**, *52*, 5026.
(5) J. W. Faller, P. P. Fontaine, *J. Organomet*. *Chem*. **2006**, *691*, 1912.
(6) K. Tsuchikama, Y. Kuwata, Y. Tahara, Y. Yoshinami, T. Shibata, *Org*. *Lett*. **2007**, *9*, 3097.

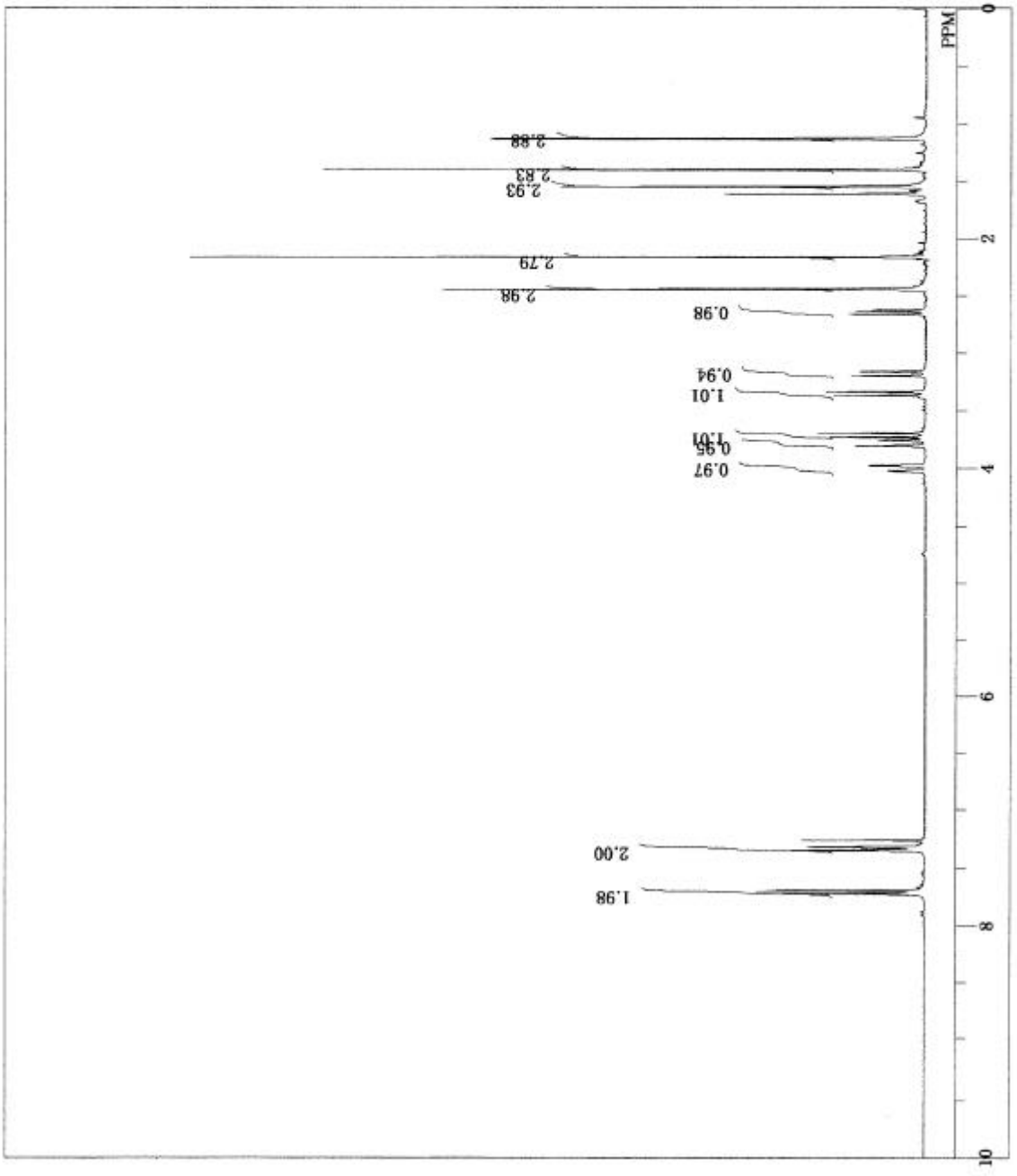
2-[3-(4-Bromophenyl)prop-2-ynyl]-2-(2-methylallyl)malonic acid dimethyl ester (1b)



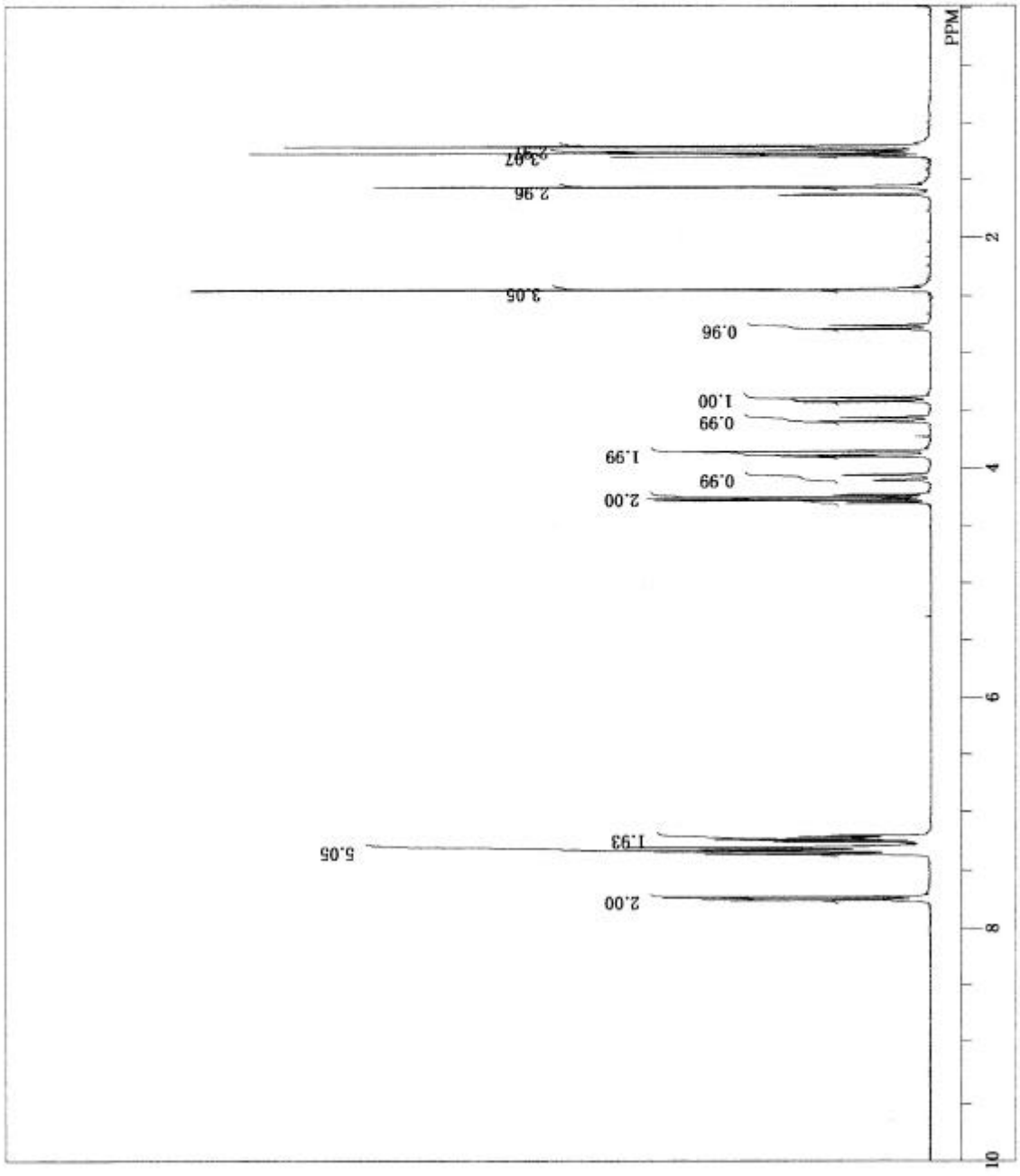
3a,6,7-Trimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carboxylic acid ethyl ester (3aa)



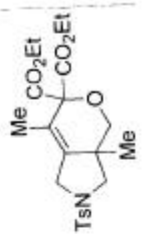
1-[3a,6,7-Trimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrol-6-yl]ethanone (3ab)

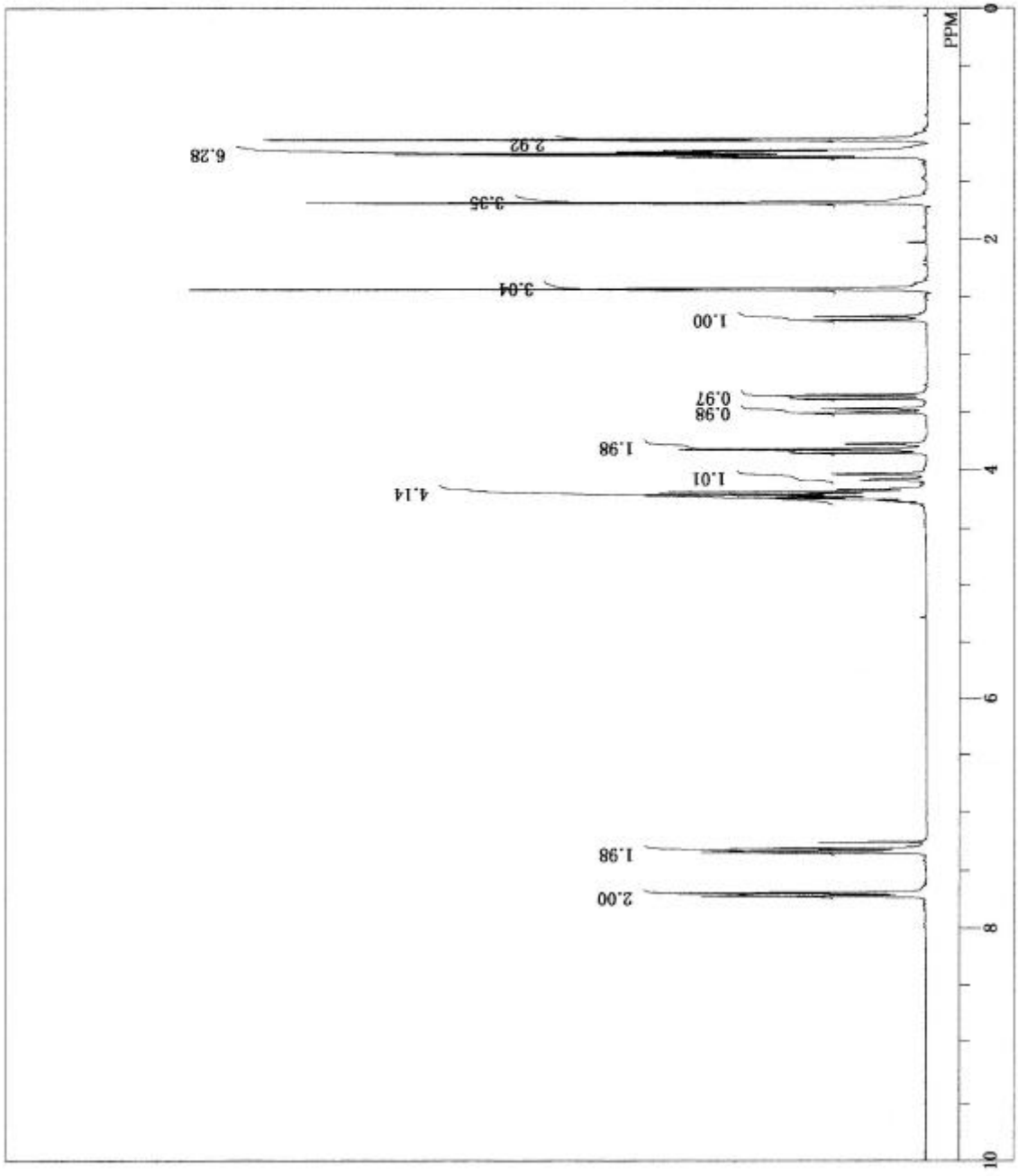


3a,7-Dimethyl-6-phenyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carboxylic acid ethyl ester (3ac)

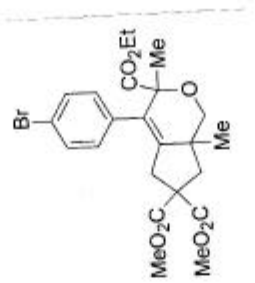


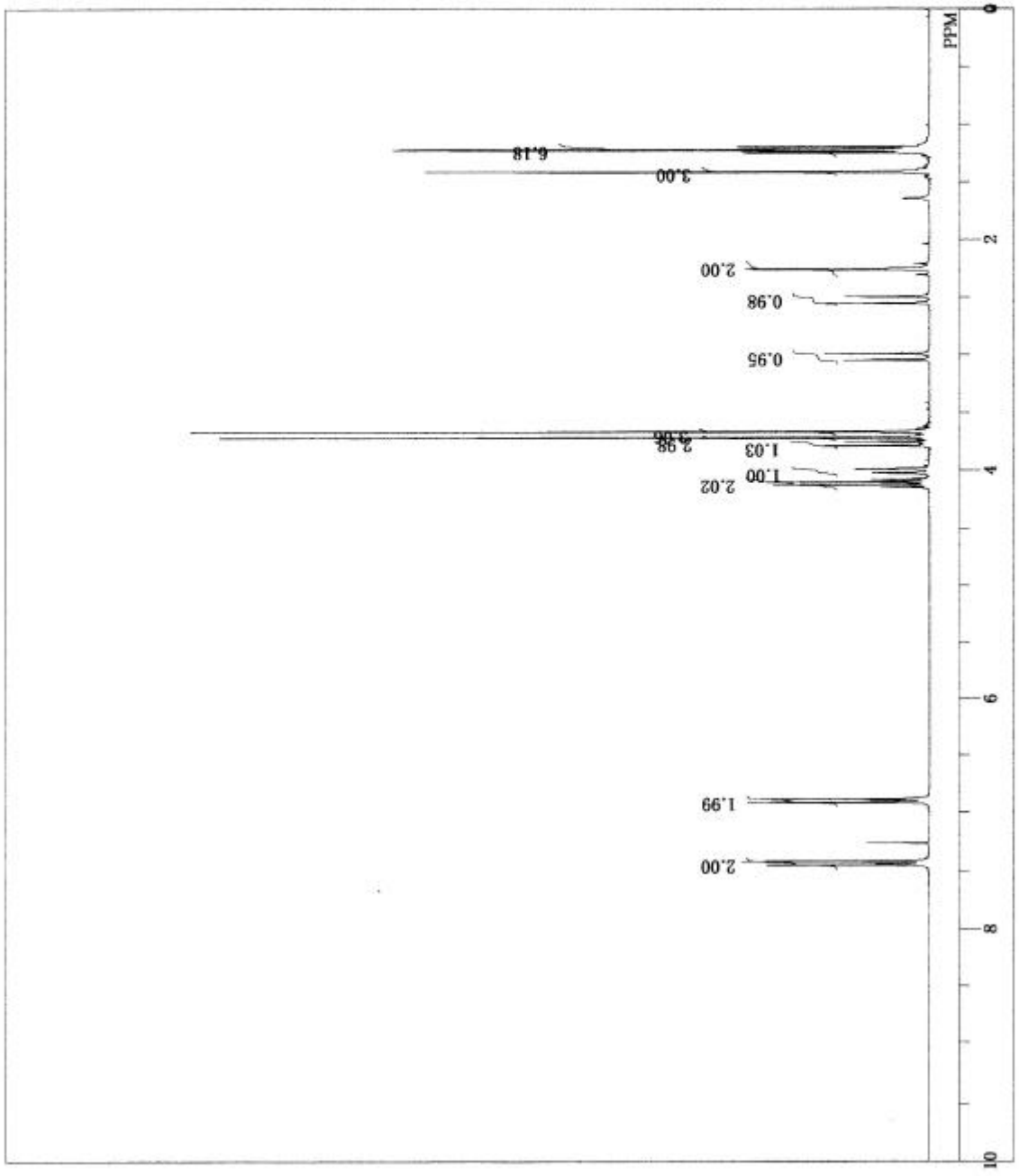
3a,7-Dimethyl-2-(toluene-4-sulfonyl)-2,3,3a,4-tetrahydro-1H-pyrano[3,4-c]pyrrole-6,6-dicarboxylic acid diethyl ester (3ad)



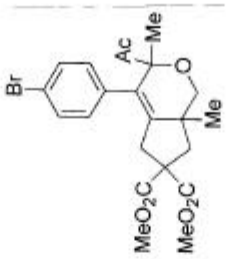


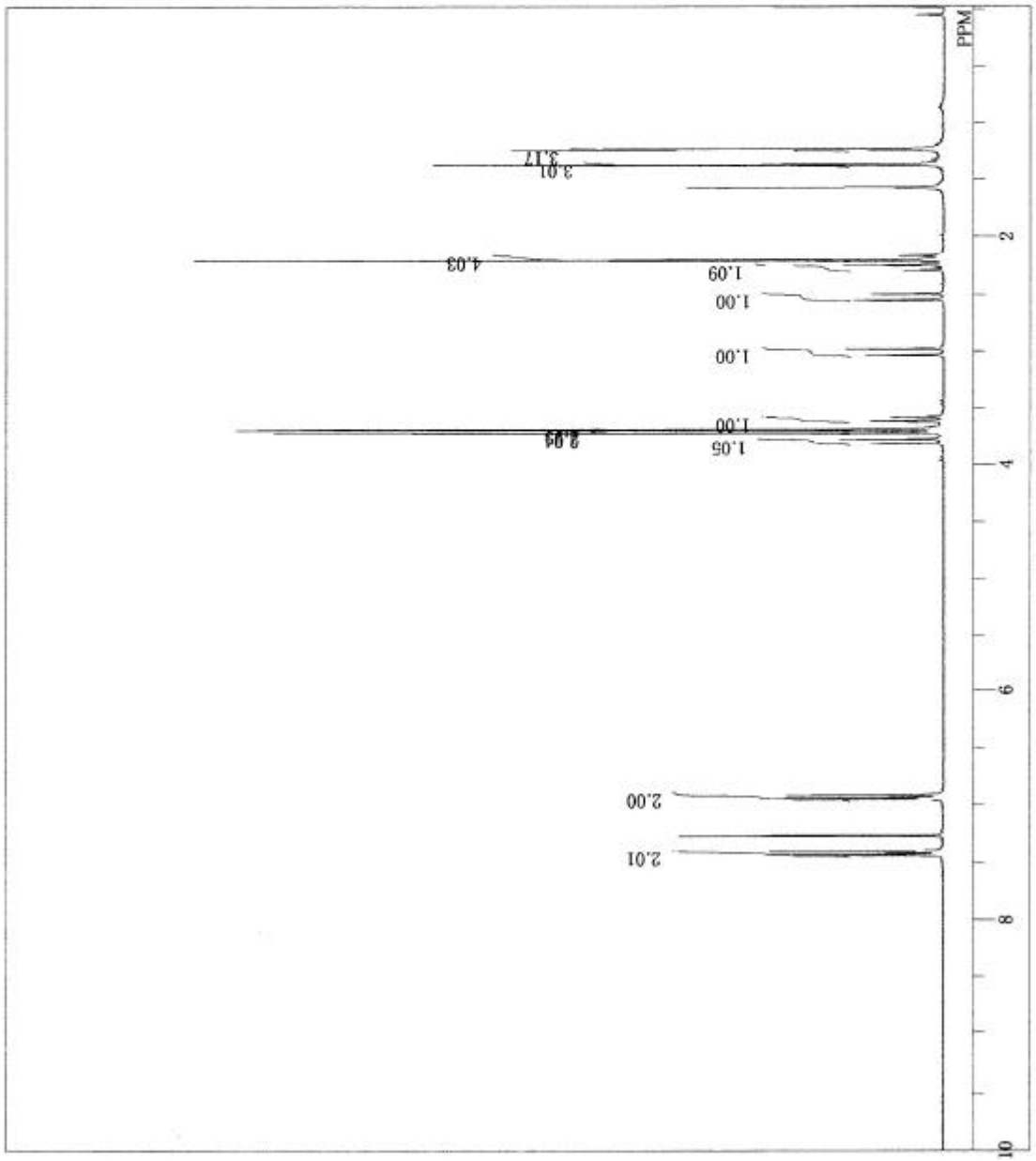
4-(4-Bromo-phenyl)-3,7a-dimethyl-3,5,7,7a-tetrahydro-1H-cyclopenta[c]pyran-3,6,6-tricarboxylic acid 3-ethyl ester 6,6-dimethyl ester (3ba)



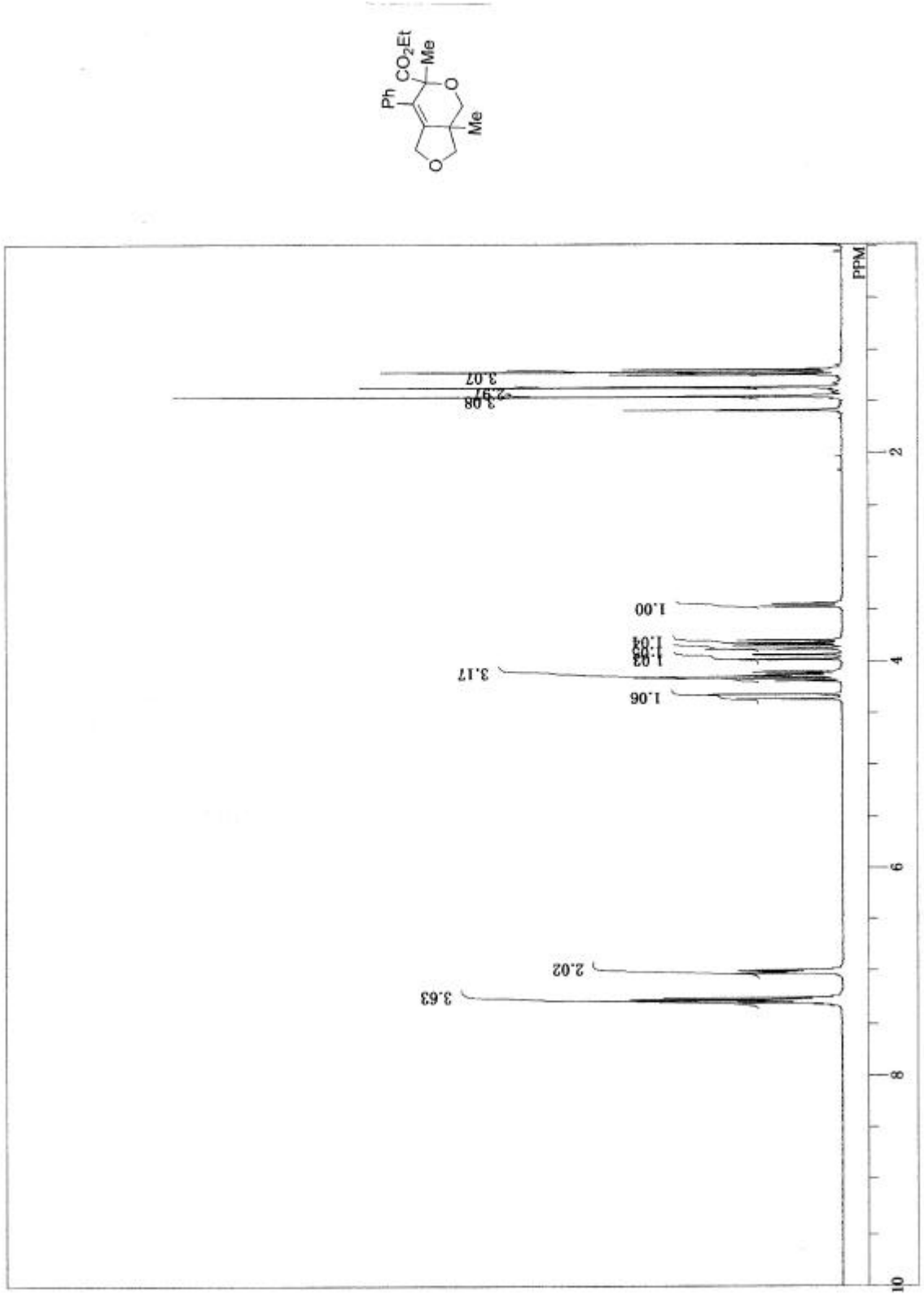


3-Acetyl-4-(4-bromophenyl)-3,7a-dimethyl-3,5,7,7a-tetrahydro-1H-cyclopenta[c]pyran-6,6-dic arboxylic acid dimethyl ester (3bb)

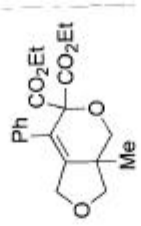


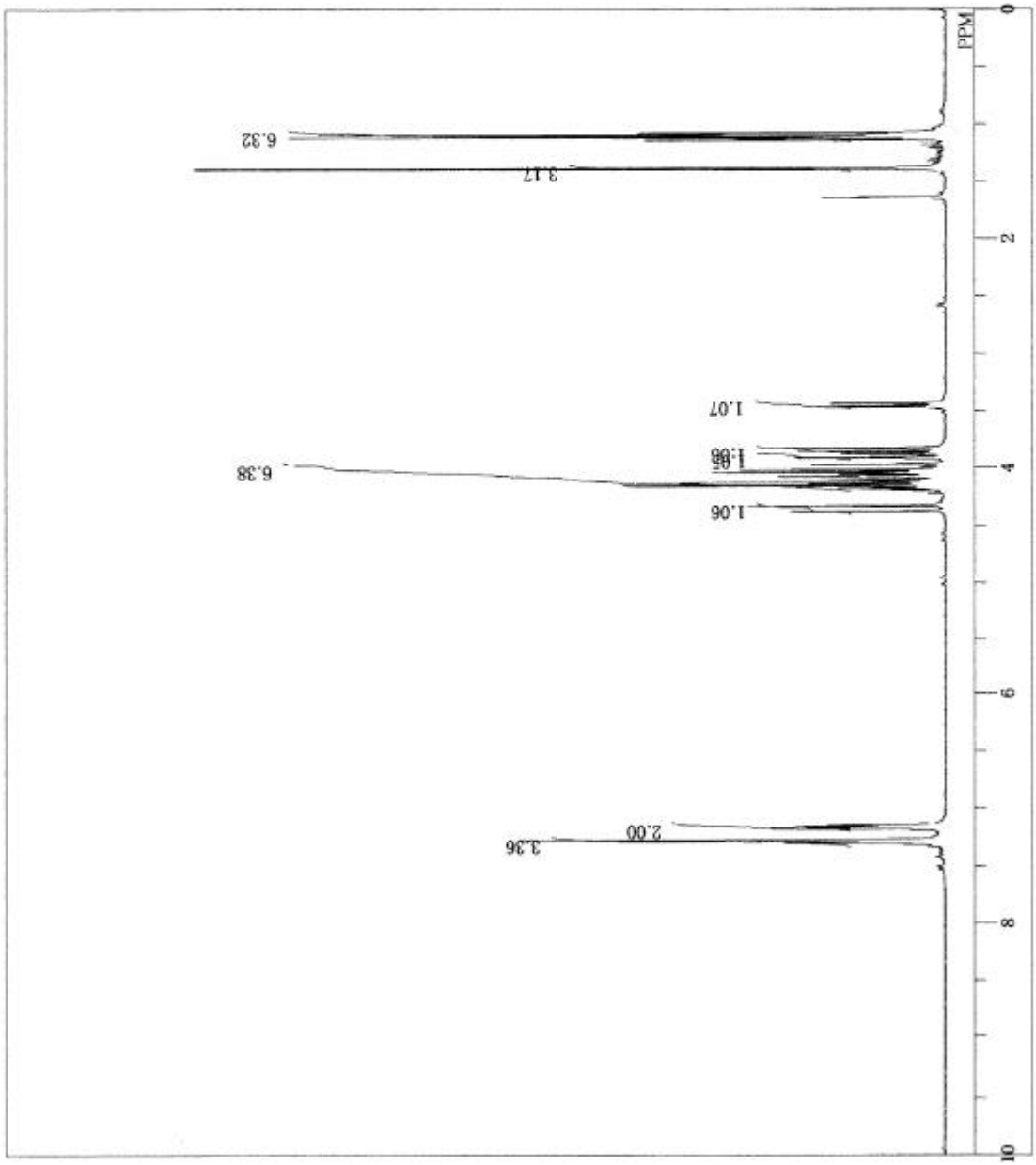


3a,6-Dimethyl-7-phenyl-1,3a,4,6-tetrahydro-3H-furo[3,4-c]pyran-6-carboxylic acid ethyl ester (3ca)

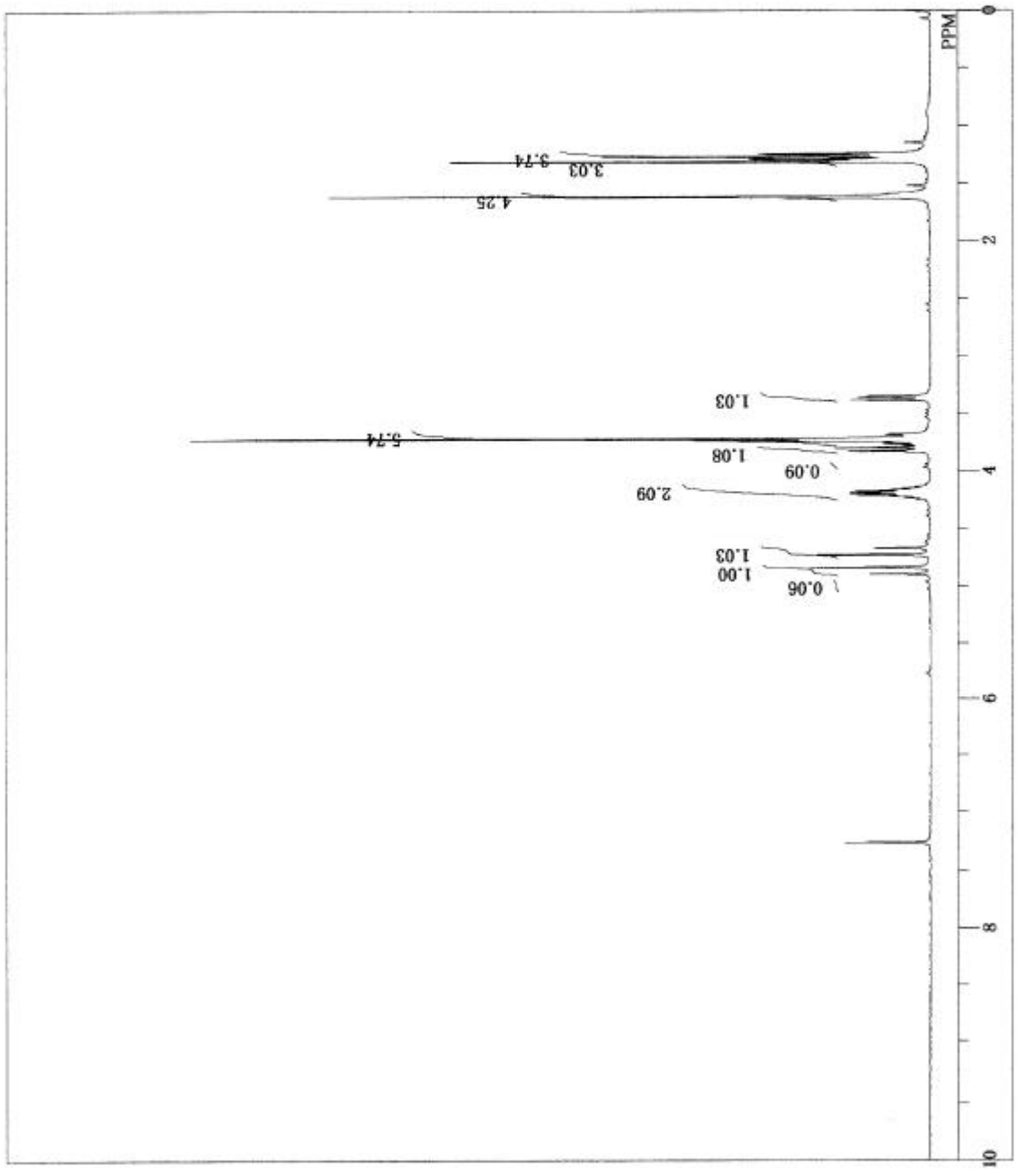


3a-Methyl-7-phenyl-3a,4-dihydro-1H,3H-furo[3,4-c]pyran-6,6-dicarboxylic acid diethyl ester (3cd)

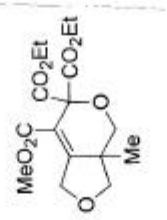


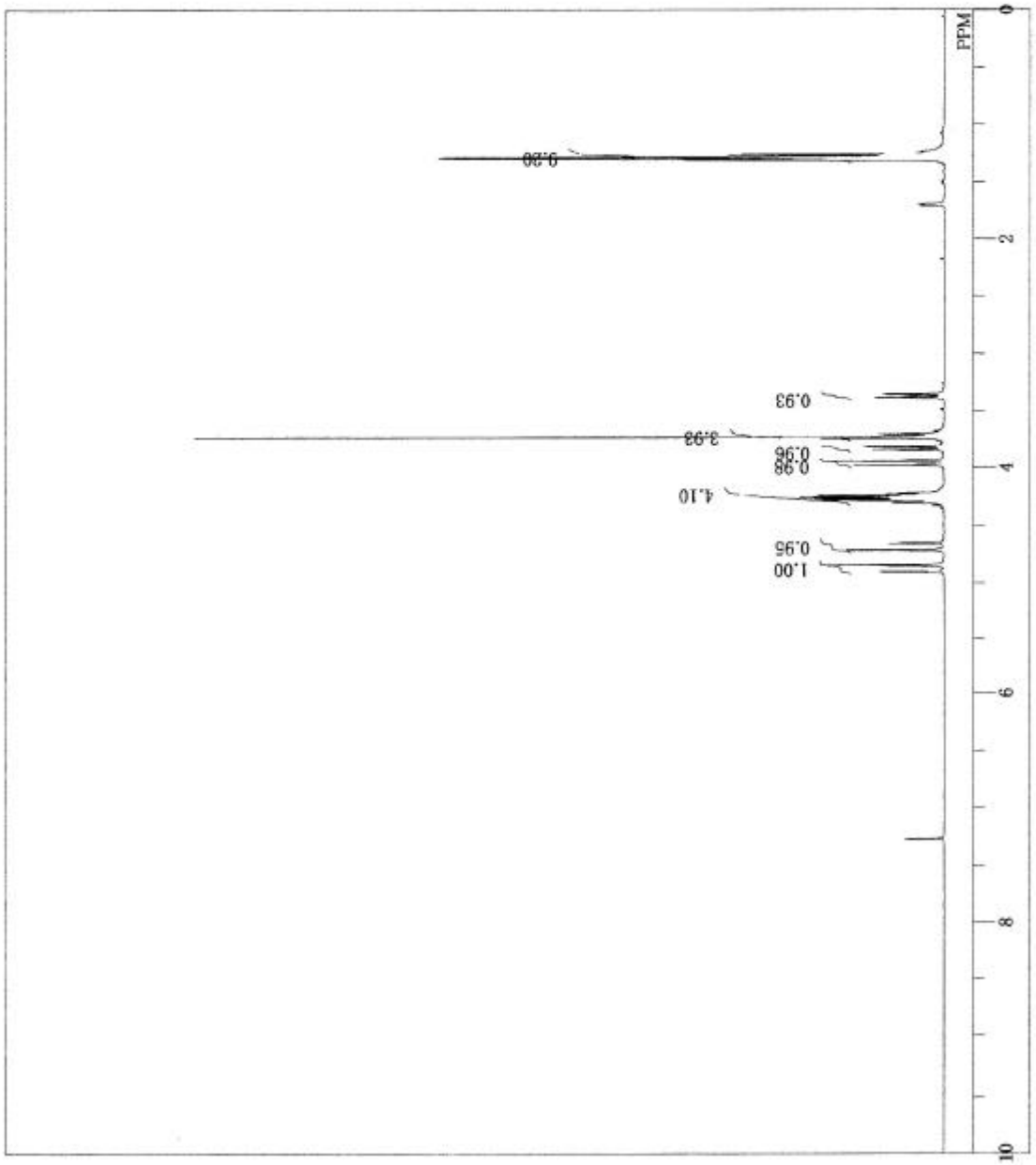


3a,6-Dimethyl-1,3a,4,6-tetrahydro-3H-furo[3,4-c]pyran-6,7-dicarboxylic acid 6-ethyl ester 7-methyl ester (3da)

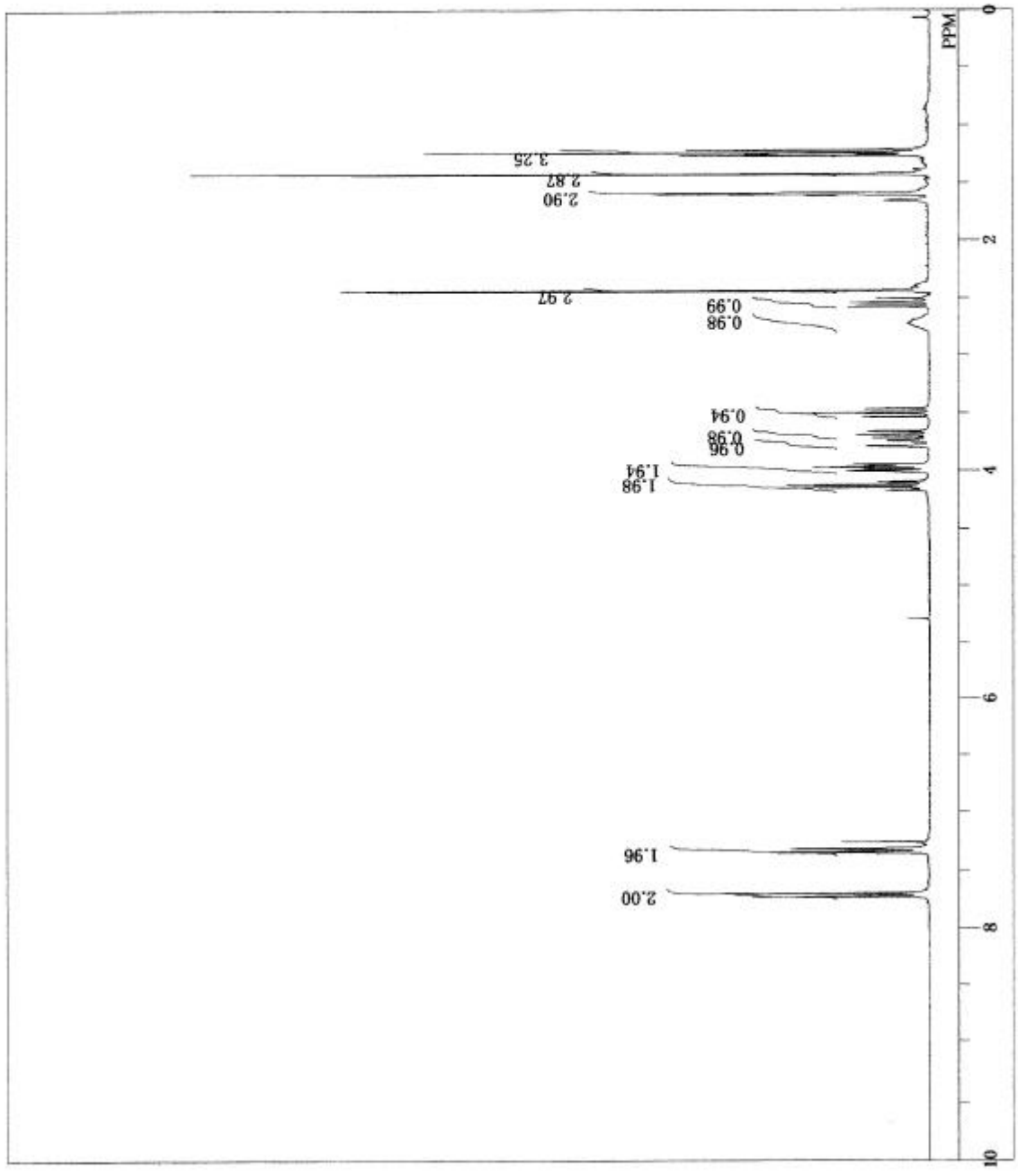


3a-Methyl-3a,4-dihydro-1H,3H-furo[3,4-c]pyran-6,6,7-tricarboxylic acid diethyl ester methyl ester (3dd)

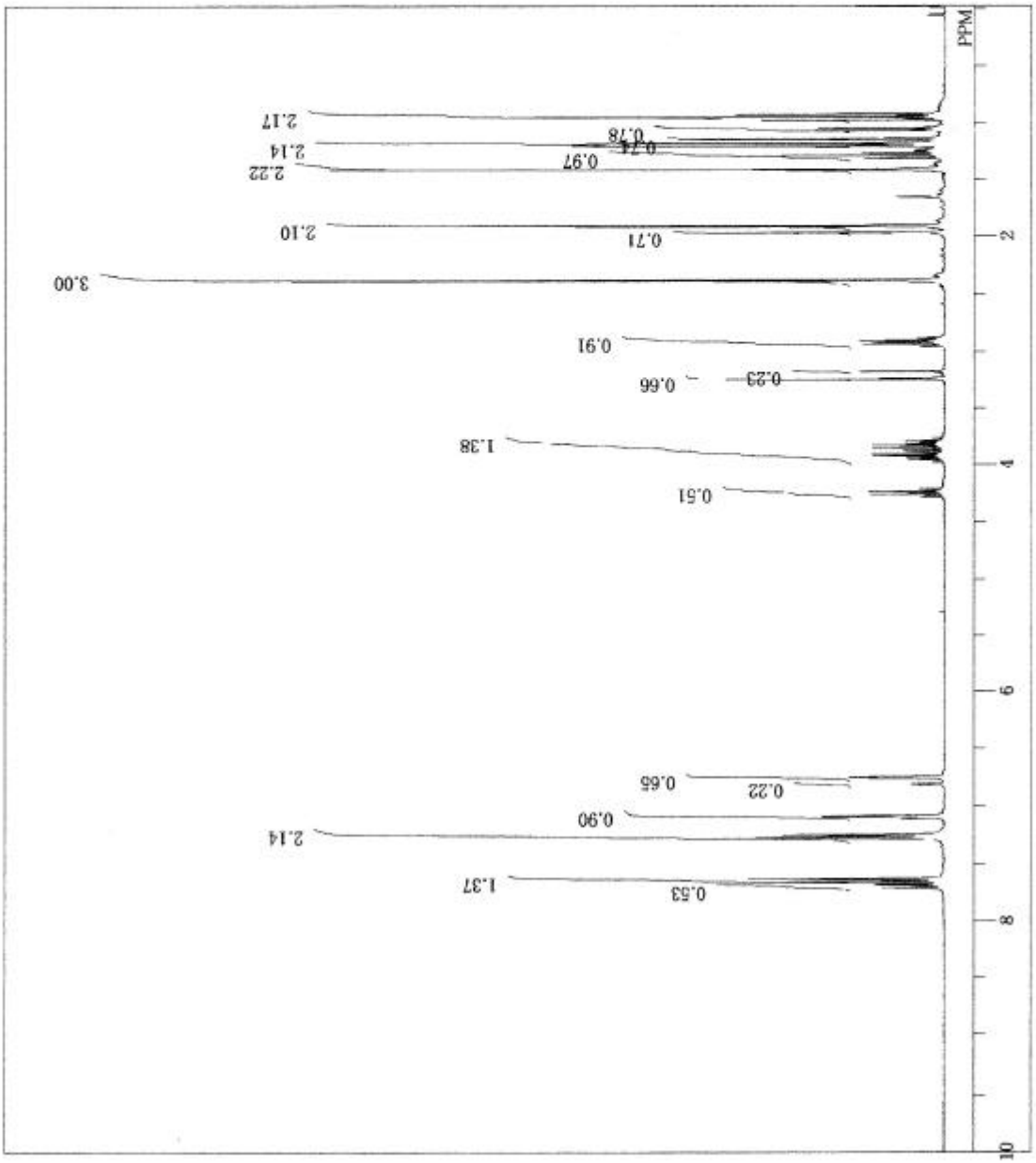




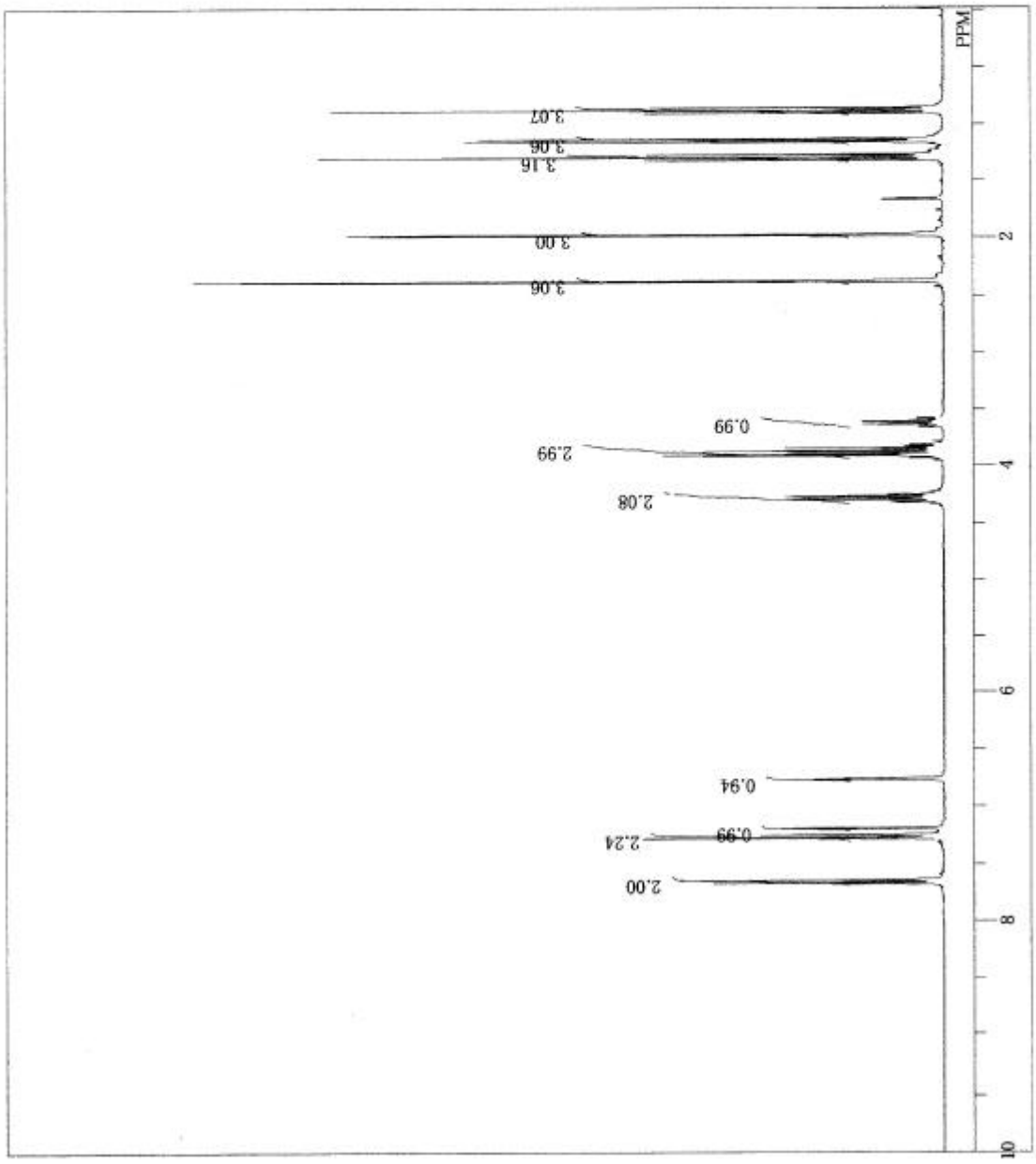
6,7-Dimethyl-2-(toluene-4-sulfonyl)-1,2,3,3a,4,6-hexahydropyrano[3,4-c]pyrrole-6-carboxylic acid ethyl ester (3ea)



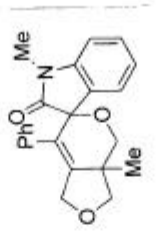
2-Hydroxy-2-methyl-3-[4-methyl-1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]butyric acid ethyl ester (5ea)

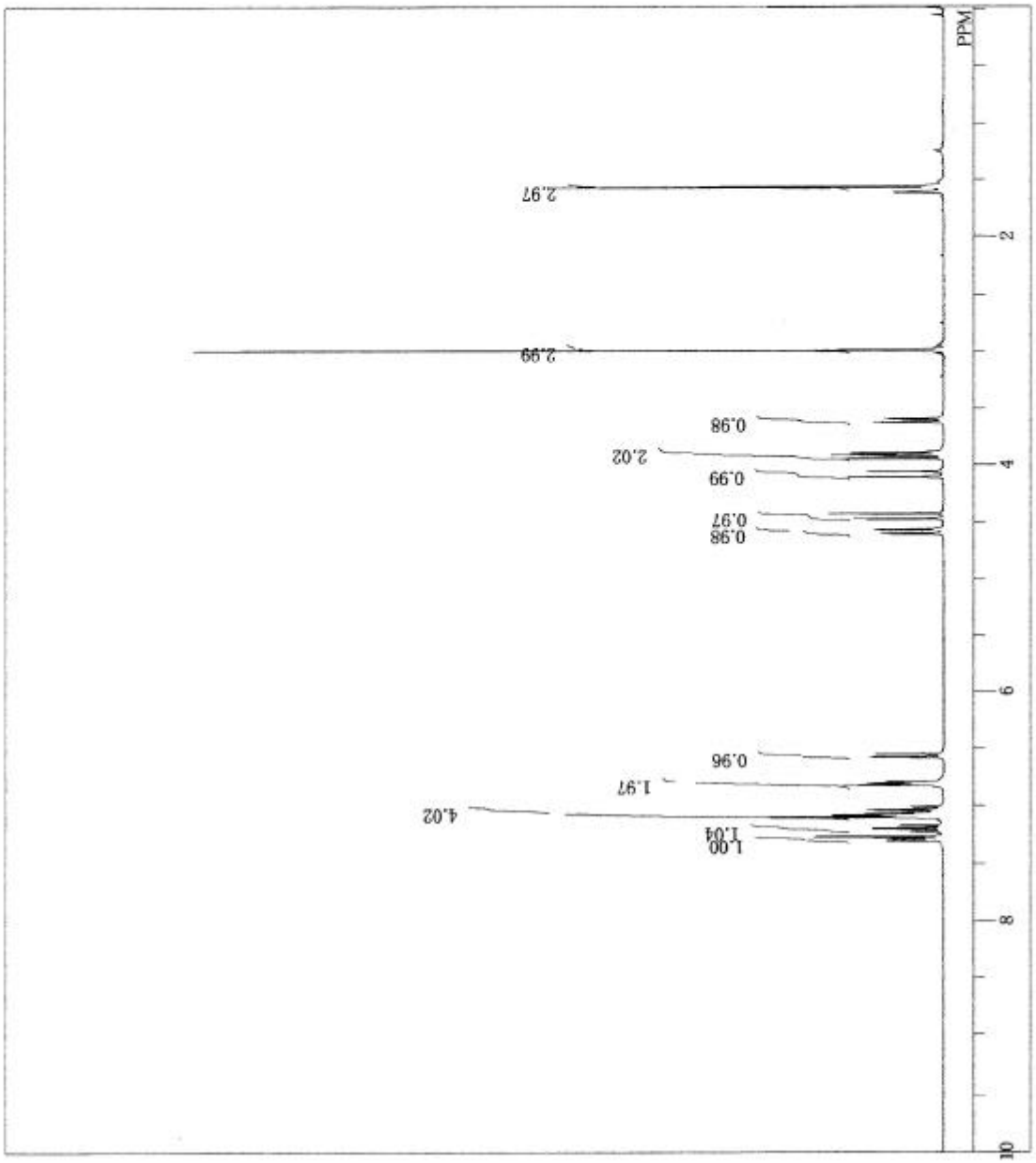


2-Hydroxy-2-{1-[4-methyl-1-(toluene-4-sulfonyl)-1H-pyrrol-3-yl]ethyl}malonic acid diethyl ester (5ed)

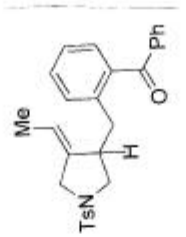


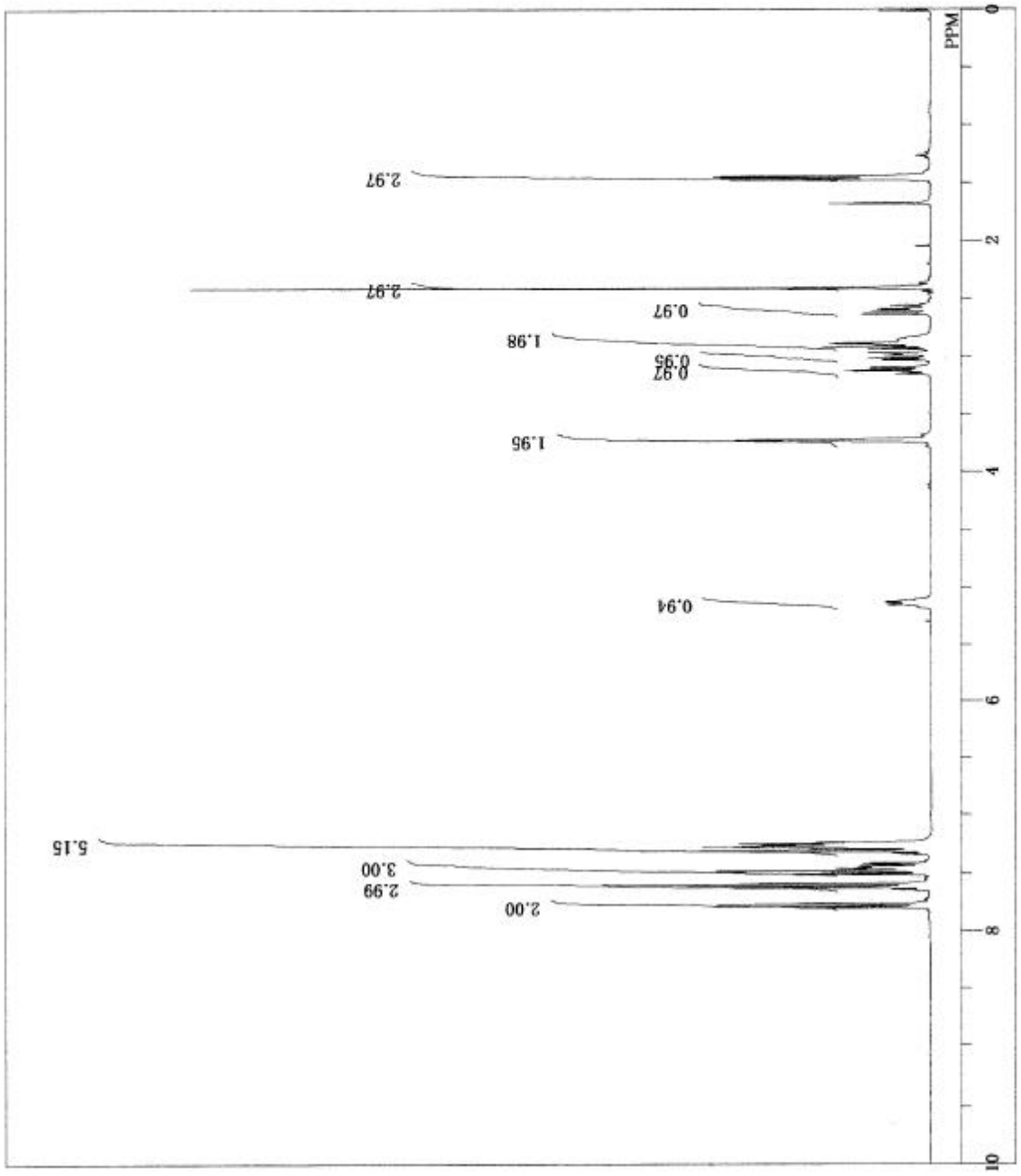
Spiro[(3’,8’-dioxabicyclo[4.3.0]-1-methyl-5-phenylnon-5-ene)-3,4’-(2,3-dihydro-1-methylidol-2-one)] (3cf)



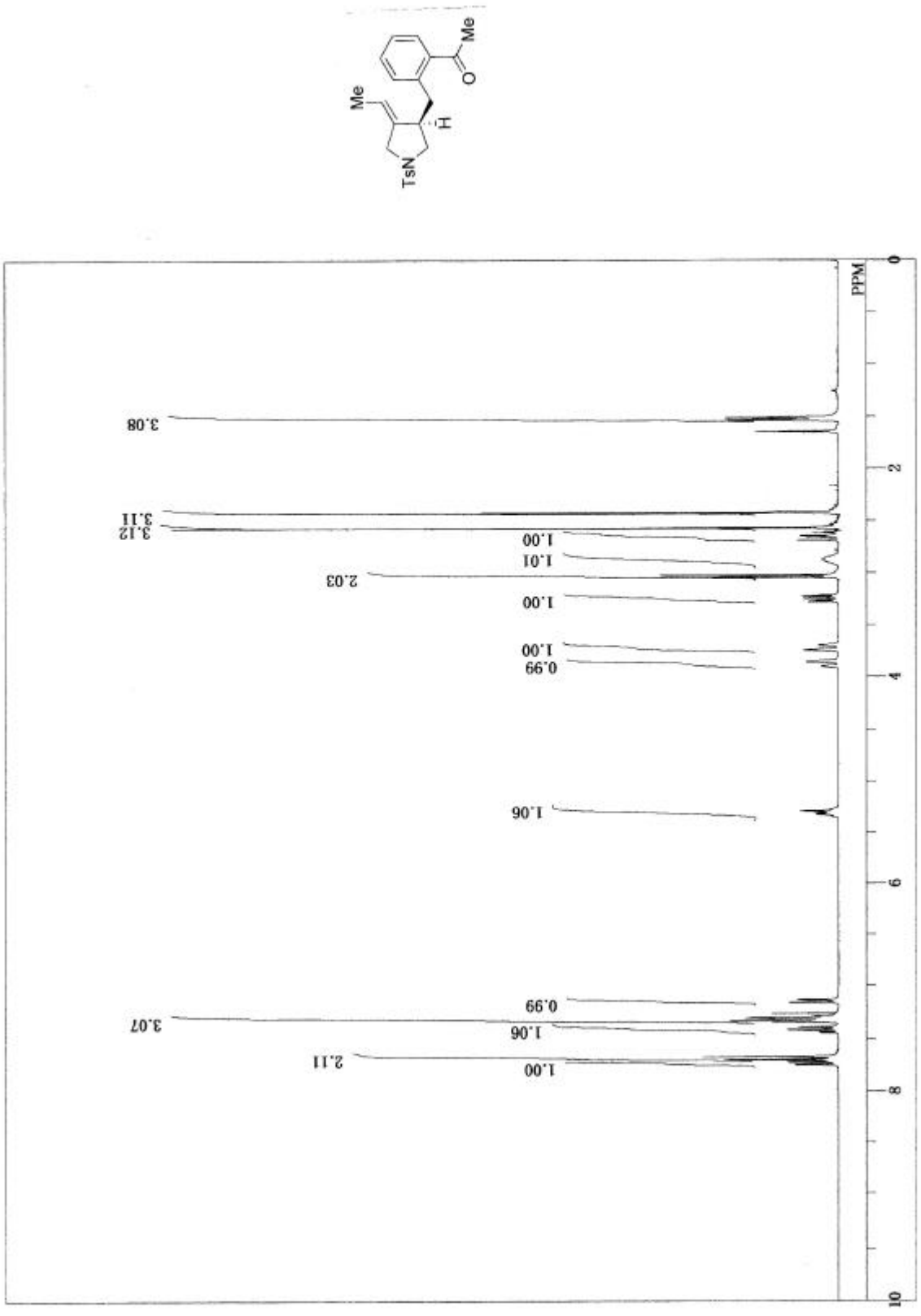


{2-[4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylmethyl]phenyl}phenyl methanone (6eg)





1-{2-[4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylmethyl]phenyl}ethanone (6eh)



3-(2-Acetyl-4-methoxybenzyl)-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester (6fi)